‘ACTING WITHOUT ASKING’[1]: AN ETHICO-LEGAL ANALYSIS OF THE PROBLEM OF EMERGENCY CARE RESEARCH WITH INCAPACITATED ADULTS

Christopher Owen Alexander Stein

(324567)

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DECLARATION

I Christopher Owen Alexander Stein declare that this Thesis is my own, unaided work. It is being submitted for the Degree of Doctor of Philosophy in Bioethics and Health Law at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.

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7th October 2025, Johannesburg

1 '*Acting without asking*' is adapted from: Adams JG, Wegener J. Acting without asking: an ethical analysis of the Food and Drug Administration waiver of informed consent for emergency research. Ann Emerg Med. 1999 Feb;33(2):218-23.

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ABSTRACT

Emergency care research, both internationally and in South Africa, holds great prospect for advances in clinical care that could significantly address mortality and morbidity across a wide range of conditions including severe injury, stroke and ischaemic heart disease. However, many of these conditions are associated with physiological derangements and other factors that render potential research participants incapable of providing informed consent. Moreover, in some cases, very narrow therapeutic windows make the use of proxy decision-makers impossible. The Constitution of South Africa along with the National Health Act mandate that research without informed consent is unlawful. The statutory research ethics regulator has attempted to remedy this constraint, however its guidance for research with incapacitated adults in not coherent and in certain instances contradictory. Waivers of informed consent for research in emergencies, which are in place in North America, the United Kingdom, European Union and Australia have not been implemented in South African research ethics guidelines. Thus, considering the imperative to engage in emergency care research with incapacitated adults, South African statute and research ethics guidelines are not ethically justifiable. This thesis critically analyses the ethical principle of respect for autonomy and the process of informed consent, the consideration and roles of dignity and vulnerability in research with the incapacitated and the complex interactions of ethical decision-making and risk analysis in the emergency care research context. This is followed by a detailed ethico-legal analysis of both local and international regulations and research ethics guidelines as these apply to emergency care research with incapacitated adults, especially the application of waivers of informed consent. Finally, by drawing on the preceding analysis, a novel categorisation of capacity with mappings to time-sensitive levels of informed consent modalities is presented. This is followed by a proposed ethical framework arguing for a different approach to informed consent for those in emergency situations typified by factors such as acute severe pain or anxiety which affect capacity. For emergency situations with incapacitation, and especially those where proxy consent is not viable, a proposed approach to risk analysis is given and it is argued that waivers of informed consent are ethically defensible in such situations and preferable to the current South African research ethics guidelines. A set of conditions and a framework for a waiver of informed consent is proposed.

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1.1. Introduction

1.1.1. Background

Many disease processes, if left untreated or inappropriately treated, will eventually result in derangements of physiology dangerous enough that affected patients *in extremis* are considered to constitute emergency cases. The term emergency, '*…a sudden catastrophe, which calls for immediate medical attention*…' was defined in South African law in 1997 ('Soobramoney v Minister of Health (Kwazulu-Natal) (CCT32/97) [1997] ZACC 17; 1998 (1) SA 765 (CC); 1997 (12) BCLR 1696 (27 November 1997)', no date). There can be no doubt that research into care of the critically ill and injured holds the prospect of decreased mortality, improved quality of life and the alleviation of suffering for many. However, the very nature of emergencies, involving patients who frequently experience altered levels of consciousness or emotional states that render rational decision-making extremely difficult or impossible, gives rise to the problem of obtaining informed consent from such incapacitated patients. Informed consent for health research is required in terms of s71(1)(b) of the National Health Act (No 61 of 2003).(South Africa, 2003) South African national research ethics guidelines also stress the importance of informed consent for health research participation.(Department of Health, 2024:10)

The centrality of informed consent for research participation has a long history in research ethics, dating back mainly to the Nuremberg Code of 1946 where it is cited as an absolute requirement.(Annas and Grodin, 2008:139) The Nuremberg Code did not justify this absolute requirement in terms of any broader moral principles. Rather, it was seen simply as a protective measure to prevent the abuses that had taken place with experimentation on prisoners during World War II. Later, after several other ethical scandals in health research that occurred up until the 1970s in the USA, the Belmont Report proposed the principle of respect for persons as fundamental to ethical conduct in research and saw the process of obtaining informed consent from capable participants as a practical implementation of this principle.(National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979) At around the same time, Beauchamp and Childress (1979)

published the first edition of *The Principles of Biomedical Ethics* which was to become extremely influential. In it, they recast the principle of respect for persons as respect for autonomy and intensified the already established focus on informed consent as a way of honouring this principle. This emphasis on the importance of informed consent for research participation has since been codified into international research ethics guidelines and local statute and guidelines as mentioned above.

Decision-making capacity is a pivotal concept related to informed consent and for the underlying broader conception of autonomy which can be understood for now as one of individual self-determination. Generally, this capacity refers to the ability of an individual who may be a prospective research participant to understand information relevant to the proposed research and its consequences – what Beauchamp and Childress (2013:114-120) call '*the capacity for autonomous choice*'. Capacity has a legal definition – in part, determined by age – but in the practical context of research it is also typically defined or judged empirically. That is, by the judgement of the researcher or clinician tasked with enrolling participants. This judgement tends to be focused on the empirical threshold of competence or rather, as it is probably more commonly applied, incompetence. Whether tested formally through the use of an instrument designed for this purpose or whether assessed by means of an impression, incompetence at the most basic level is associated with the demonstrated inability of a prospective participant to comprehend information about the research or its consequences. Thus, decision-making capacity, as a whole, is also determined significantly by this ability.

Patients and prospective research participants in the emergency care environment, whether outside of the hospital or in the emergency department, present with a broad spectrum of acuities. Higher acuity cases can be thought of as the seriously or critically ill or injured which aligns closely with the public perception of emergency care popularised by television series such as ER and Rescue 911. However, a significant case load in emergency care is of lower acuity covering a wide range of less serious conditions. Moreover, researchers in the field of emergency care may be interested in research questions related to many different facets of this field. These may be of a clinical nature in many cases, or they may be of a non-clinical nature and directed towards human factors in emergency care or emergency care

systems. This spectrum of emergency care research is extremely broad and not all of it presents potential problems with decision-making capacity and informed consent. However, for emergency care research of a clinical nature, particularly interventional research, several factors may affect the viability of informed consent for emergency care research participation to varying degrees. These are described below.

1.1.1.1. Level of Consciousness and Decision-making Capacity

In an emergency setting, a patient's level of consciousness may be negatively influenced by a wide range of pathophysiological derangements more common in higher acuity conditions such as the direct effects of injury (e.g. traumatic brain injury), hypoxia, acidosis, hypoglycaemia, the effects of drugs given for sedation and analgesia or other substances such as alcohol which may be ingested prior to acute injury or illness. In lower acuity cases these effects may be minimal and decision-making capacity may not be an obstacle for the purposes of gaining informed consent. Alternatively, in higher acuity cases decision-making capacity may be negatively affected to the point where a patient may be considered incapacitated. The most extreme form of this is the patient who is completely unconscious and unresponsive.

1.1.1.2. Distractors

Several distractors may be present in the emergency care environment, and these may also negatively affect a patient's decision-making capacity. These factors also tend to vary according to patient acuity, although in some cases they may be more consistently present. Such factors include anxiety brought about by being exposed to a sudden emergency situation and the acute onset of serious symptoms along with the context of some (especially higher acuity) emergencies with many clinicians present and a sense of urgency that patients may find overwhelming. Symptoms such as acute severe pain or severe dyspnoea are also potent distractors. Pain in particular is a common presenting symptom in emergencies, particular higher acuity ones as described in further detail in Chapter 3. While these distractors are not known to exert an effect on level of consciousness in the same way as the pathophysiological factors in 1.2.1 above, they could be expected to make the comprehension of detailed information, such as that typically presented to prospective participants in clinical research, difficult.

1.1.1.3. Time

Decision-making takes time – time to take in, process and understand information and time to weigh up alternatives and reach a decision. In situations where prospective research participants are not able to make decisions (for reasons related to level of consciousness) having adequate time to do so is irrelevant. However, for those judged to have decision-making capacity clinical emergency care research can sometimes be of such a nature that it involves an intervention intended for a time-sensitive condition with a narrow therapeutic window. A good example of this is research investigating fibrinolytic drugs for myocardial infarction or stroke, but many other examples exist. In such situations, time constraints in obtaining informed consent - which is often dependent on the understanding of a large volume of complex information – can negatively affect comprehension possibly pressurising prospective participants and making them more likely to consent without adequate time for decision-making.

1.1.1.4. Availability of Proxy Decision-Makers

While the Nuremberg Code was silent regarding research with those lacking capacity for informed consent, the Belmont report suggested that the protection from harm that is embodied in the principle of respect for persons extends to allowing '*other parties*' to make decisions about research participation on their behalf.(National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979) This approach has subsequently become commonplace in research ethics guidelines, both local and international. Although questions have been asked about the validity of proxy decision-making and its associated potential burden for proxies, it does arguably offer a way forward for research with the incapacitated. In the emergency setting, this can be limited by the availability of proxy decision-makers who may not be readily available at all places and times when emergencies occur particularly outside the emergency department.

1.1.1.5. Combinations of Factors

Each of the factors discussed above can pose an independent problem for the viability of informed consent in emergency care research or, in the case of proxy decision-makers, the viability of an alternative. But in some cases, there may be interactions between them

making the situation more complex. For example, a decreased level of consciousness caused by physiological derangement or primary injury can be worsened by the concomitant administration of an opioid analgesic for acute severe pain. While this may make the severe pain more manageable thus reducing its effect as a distractor, this gain may be offset by the significant sedating effect of such drugs on decision-making capacity. Using the example given above of research involving fibrinolytic agents for the treatment of myocardial infarction, the time-sensitive nature of these interventions and the need for their rapid administration would aggravate the impact of severe pain (almost uniformly present in the acute phase of myocardial infarction) as a distractor and its negative effect on decision-making capacity. In situations where patients are incapacitated from the outset, a narrow therapeutic window may preclude the availability of a proxy decision-maker where this may have otherwise been a viable alternative.

1.1.1.6. Informed Consent in Emergency Care Research: Factors and Zones

Taking the above discussion regarding informed consent, decision-making capacity and the factors presented in 1.2.1 – 1.2.4 in combination, Figure 1 is a matrix-like arrangement identifying several zones into which combinations of these factors fall. Each zone is associated with a graded problem level for considerations of autonomy and informed consent as discussed below.

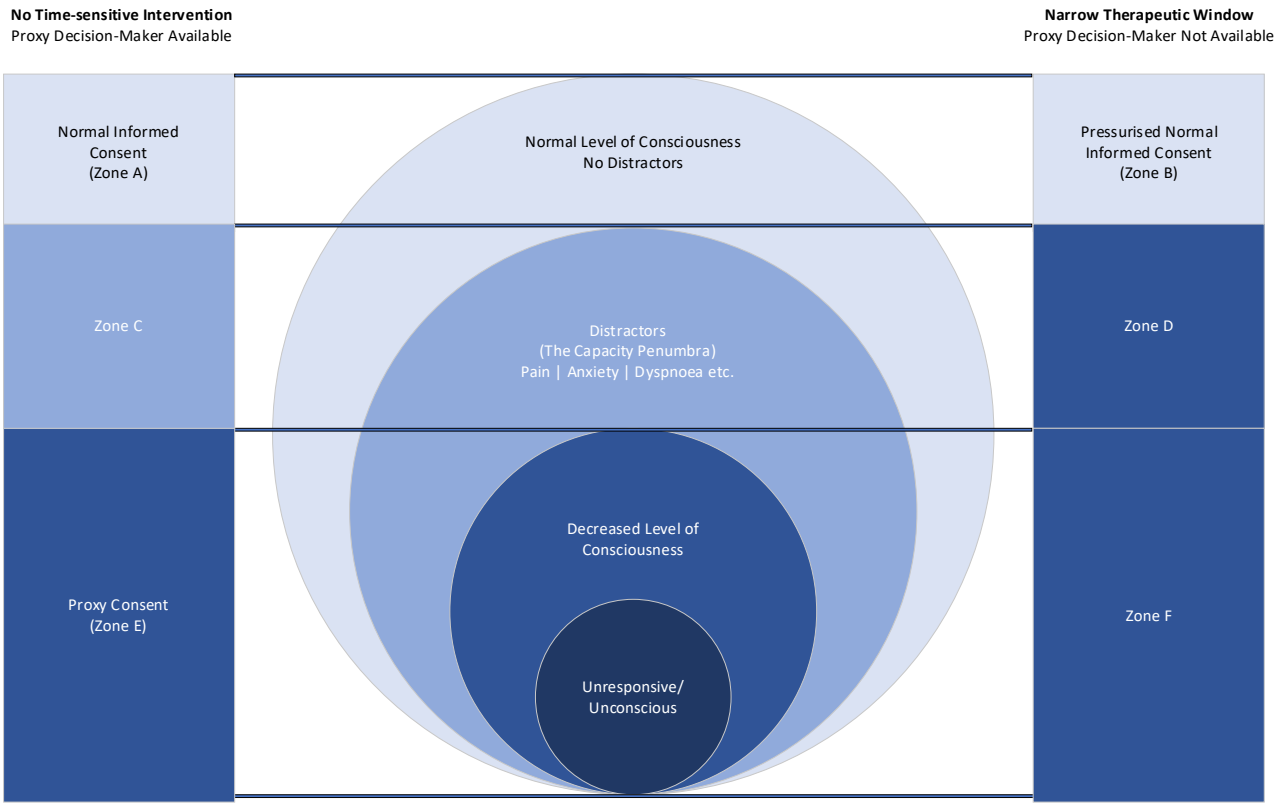

Figure 1: Factors and Zones: Informed Consent in Emergency Care Research

Zone A

Zone A is the zone in which no factors specific to emergency care research as described above require consideration. Primarily because research in Zone A is mostly of a non-clinical nature, prospective participants have full decision-making capacity and there are no distractors or time constraints for decision-making. A mapping of the different zones (including Zone A) to typical research designs is given in Table 1.1 below.

Zone B

Zone B adds the problem of a narrow therapeutic window in a clinical interventional research context. However, decision-making capacity is normal and there are no distractors. The main problem in Zone B is the negative effect of time pressure on decision-making when prospective participants are presented with large volumes of complex information.

Zone C

Zone C includes what I have referred to as the capacity penumbra. Choice of the word penumbra is intended to convey the uncertainty inherent in this zone regarding the effects of distractors such as anxiety, pain, severe dyspnoea or the influence of drugs with psychoactive effects (such as analgesic or sedative agents) on decision-making capacity. Prospective participants in this zone are often considered, from the perspective of their level of consciousness, to have full decision-making capacity. Yet it is highly likely that these distractors negatively affect decision-making capacity despite a lack of empirical evidence clearly describing this effect.

Zone D

Zone D effectively adds the complicating effect of a narrow therapeutic window to the problems inherent in Zone C. This places the prospective participant already in the capacity penumbra under greater pressure due to the difficulty of understanding large volumes of complex information in a short space of time due to the time sensitive nature of their condition vis-a-vis the intervention under consideration.

Zone E

Zone E is mainly characterised by a drop below the level of consciousness threshold for decision-making capacity which may take the form of reduced consciousness or a state of unresponsiveness (the latter would include scenarios in resuscitation research where prospective participants have no spontaneous circulation of breathing). In such cases, no informed consent from prospective participants themselves is possible and reliance is made on a proxy decision-maker which this zone assumes is available.

Zone F

Zone F adds the additional difficulty to Zone E of a proxy decision-maker not being available. This may be circumstantial - for example, in a pre-hospital setting where an emergency occurs at a location or time when a proxy is not present. However, in Figure 1, the more significant cause of a narrow therapeutic window is depicted. If an experimental intervention is of such a nature that it can be delayed, it may be possible for a proxy

decision-maker to be found in many cases. However, if the intervention is time-sensitive this will often preclude the availability of a proxy.

1.1.1.7. Emergency Care Research Design and Informed Consent

Finally, in addition to the interactions described in Figure 1, it is worth considering how these different zones map to research design choices which were briefly mentioned above. Table 1.1 shows how broad categories of research design that might be used in emergency care research relate to the more detailed purpose of informed consent (i.e. other than as a normative and legal requirement in all cases) and to each of the zones presented in Figure 1.

Table 1.1: Emergency Care Research Designs and Informed Consent Implications

Research Design	Example Procedures	Informed Consent	Zone (Fig 1)
Qualitative E.g. Qualitative descriptive or phenomenology	Individual or focus group interviews.	Informed consent is for participation in activities such as interviews or completing surveys and associated privacy-related factors.	Zone A Participants typically have full capacity and with no distractors or influence of other factors
Quantitative Non-clinical e.g. Surveys	Completing questionnaires.		
Quantitative Clinical Observational e.g. (record reviews, case-control or cohort studies)	Accessing of health records, routine clinical procedures.	Informed consent is primarily for the purposes of access to clinical records and privacy-related factors. With retrospective designs informed consent may be waived after review by a Research Ethics Committee.	Zones A, B Possible effects of level of consciousness and distractors
Quantitative Clinical Interventional e.g. quasi-experimental, pragmatic, individual or cluster randomised trials	Experimental (i.e. new) procedures, standard of care procedures (if this is the comparator) and other procedures carried out only for the research.	Informed consent is for experimental intervention(s), other research-related procedures and privacy-related factors.	Zones B - F Many different permutations with possible effects of level of consciousness, distractors, time and availability of proxies and synergistic effects of these

This table clearly shows that the research designs associated with the greatest variety and potential complexity of factors negatively affecting decision-making capacity are quantitative clinical and interventional designs.

1.1.2. The Main Problem Areas in Emergency Care Research with Incapacitated Adults

Emergencies and emergency care are not centred only on the critically ill and injured. Consequently, emergency care research is broad in its scope and encompasses both clinical and non-clinical research utilising a range of different research designs. Research across this broad spectrum has one thing in common and that is the legal requirement for informed consent which is also aligned with the bioethical principle of respect for persons in research ethics guidelines. For research of a qualitative or quantitative but observational nature, there are usually no serious impediments to obtaining informed consent as depicted in the first three rows of Table 1.1. Consequently, research of this nature will not be considered further in this thesis.

This thesis concerns itself with clinical interventional emergency care research mainly where prospective participants do not have decision-making capacity. This encompasses Zones E and F in Figure 1. While research with those not able to make decisions for themselves under these conditions is difficult from an ethical perspective, it is not the only difficulty facing researchers and participants. The capacity penumbra falling into Zones C and D in Figure 1, mainly under the influence of distractors commonly encountered in clinical emergency care, burdens prospective participants by expecting them to process large volumes of complex information at a time when they are preoccupied with very difficult life circumstances. Additionally, it creates uncertainty for researchers about the validity of informed consent obtained under these conditions. Thus, the focus of this thesis will encompass both of these important problems, but with primary emphasis on the incapacitated.

1.1.3. The Status Quo: South African Health Research Legislation and Research Ethics Guidelines

In the following subsections I will briefly set out the status quo regarding research with incapacitated adults and the ethico-legal framework.

1.1.3.1. The Legal Position

Currently in South Africa, all research participants are required to give informed consent in terms of both s12 of Chapter 2 of the Constitution (South Africa, 1996) and s71(1)(b) of the

National Health Act (South Africa, 2003). Neither of these make provision for informed consent by any other means in the case of incapacitated patients for the purposes of research participation. Regulations published in 2014 refer to research with adults having decision-making incapacity, however these regulations refer only to the risk level considered acceptable.(Department of Health, 2014) They make no reference to proxy consent or any other conditions and apply broadly to those lacking capacity rather than the context of emergency care research.

1.1.3.2. Research Ethics Guidelines

The National Health Research Ethics Council (NHREC), a statutory body provided for by the National Health Act, publishes national research ethics guidelines in South Africa. These NHREC guidelines, the most recent of which was revised in 2024, provide some suggestions about the approach to informed consent in emergency care research involving incapacitated patients centred around two main strategies – proxy consent and deferred consent. (Department of Health, 2024)

Proxy consent, consent given on behalf of a research participant by a proxy decision-maker, is not provided for in the National Health Act for research, however in s7(1)(b) the Act does provide for this in relation to treatment decisions affecting incapacitated patients (South Africa, 2003). Section 3.1.10.2 b) of the NHREC guidelines puts forward the argument that it would be reasonable to apply the notion of proxy consent in the research setting. (Department of Health, 2024:26-27) The rationale for this is based not on an argument that proxy consent is directly applicable in research, but rather that it would be ethically unjustifiable to exclude incapacitated patients from emergency care research if proxy consent were not acceptable. The NHREC suggests the use of proxy decision-makers in situations where research participants lack capacity. In the 2024 guidelines, they classify proxy consent as one of several alternative '*formats*' of consent (along with electronic and deferred consent).

In the case of deferred consent (also referred to as delayed consent), the NHREC's guidelines list a number of other criteria to be considered by research ethics committees during the review process including the prospect of direct benefit for the participant

(compared to standard care), the existence of a temporary loss of capacity and participation that is not contrary to the medical interests of the patient. The 2024 revision of the NHREC guidelines do not set any conditions for risk and deferred consent. This is a departure from the previous (2015) version which stated in section 3.2.4.4 that for deferred consent to be considered acceptable, research risks must be minimal or '…*greater than minimal risk*…', where greater than minimal risk '…*represents no more than a minor increase above minimal risk*' (Department of Health, 2015). While the same section did define minimal risk (as an '*everyday risk standard*' in line with '*routine medical examinations*'), it did not give any guidance as to what might be considered a '*minor increase*'. Furthermore, it was not clear whether '*routine*' referred to elective or emergency care - from a treatment perspective these might be quite different, with the emergent nature of clinical care expected to be inherently riskier and requiring possibly riskier interventions.

Notably, the NHREC 2024 guidelines do not explicitly permit waivers of or exceptions from informed consent for research with incapacitated adults. The only informed consent waivers condoned by the guidelines have as conditions, in Section 3.1.10.1, no infringements of the rights of individuals or a minimal rights infringement counterbalanced by research capable of generating knowledge with social value and where informed consent is impracticable. This type of waiver is clearly intended to apply only to research such as retrospective record reviews (if data are anonymised), observational studies and the use of archived human biological material. (Department of Health, 2024:24)

1.1.3.3. The Problem of Emergency Care Research with Incapacitated Adults in South Africa

As described above, researchers in the field of emergency care face uncertainty when contemplating research with incapacitated adults who are, by definition, unable to consent. Taken literally, such research is unlawful – forbidden by both the National Health Act and the Bill of Rights. The NHREC argues in its guidelines that disallowing research with the incapacitated (broadly, not just in emergency settings) would be unconstitutional because it would exclude this category of individuals from research participation without a valid reason, amounting to unfair discrimination. Inclusion of the incapacitated in research, they argue, is an application of the constitutional principle of equality and is thus legally and morally justifiable. Although the NHREC focus their argument on constitutionality, it could

also be argued that exclusion of this nature is ethically unjust in the sense that it would deprive the incapacitated of possible benefits related to participation in research. Because of the vulnerability of incapacitated individuals, special protections must be put in place to protect them. Provided this can be done, there seems to be no convincing reason why an inability to consent should exclude those who cannot do so from research participation.

Unfortunately, having made this important point, the NHREC does not provide a coherent framework to facilitate emergency care research with incapacitated adults and to offer the protections referred to above. A detailed critique of the 2024 NHREC guidelines (and the previous version from 2015) is given in Chapter 6. For now, their main deficiencies are summarised below:

a) In condoning deferred consent, the NHREC guidelines seem to be *de facto* supporting the idea of waiving the informed consent requirement for incapacitated patients - yet this is explicitly stated to not be the case. The guidelines state that '*deferred consent is personal consent, with an alteration of the requirement for prospective consent*' and '*deferred consent is not an example of fully waived consent*'.(Department of Health, 2024:27) The first statement seems to fundamentally misinterpret the single most important feature of consent – that it must be prospective. No participant can possibly consent to actions or interventions in the past that they were unaware of when subject to. The second statement seems equally mistaken – if a requirement for prospective consent is '*altered*' and no consent is required at the time of participant enrolment or application of an intervention then the requirement to obtain consent has self-evidently been waived. The NHREC seem to suggest that obtaining consent after this somehow negates the fact that it has been waived or as the guidelines state (without explanation), '*<u>fully</u> waived*'. This is contradictory, confusing and a source of concern for researchers contemplating this kind of research.

b) The situation regarding deferred consent is further obscured by the fact that there is no clear set of conditions for allowing the enrolment of incapacitated patients in research other than that the loss of capacity should be temporary. If this is not the case, or impossible to interpret, researchers are left with no alternative strategies – seemingly if

deferred consent cannot be justified because it does not meet this one condition this rules out any research.

c) The level of acceptable research risk for consideration of deferred consent is left unstated. While this could be interpreted as allowing any level of risk, it is unlikely that this is the intention. Researchers and research ethics committees are thus faced with uncertainty when planning and reviewing research where deferred consent is envisaged as a strategy.

d) Ethical considerations relevant to research with incapacitated adults are divided amongst three parts of NHREC's 2024 guidelines. Two of these, covering proxy and deferred consent, are included under Section 3.1.10.2 ('*formats*' of consent).(Department of Health, 2024:26-28) Guidance on incapacitated research participants as a broader category is included under Section 3.2.5.3 on minimum conditions for research with involving adults with incapacity.(Department of Health, 2024:39-40) This approach leads to a disjointed presentation of different facets relevant to research with the incapacitated. For example, neither proxy consent nor deferred consent are mentioned under minimum standards making it unclear whether proxy consent should always be sought or whether, under some circumstances, deferred consent is preferable or whether the intention is that both should be used where both are possible. As another example, acceptable levels of research risk are described under minimum standards, but (as mentioned above) not in the sections on proxy or deferred consent. Because neither proxy nor deferred consent are referred to under minimum standards, it is unclear whether these statements of risk apply to proxy and deferred consent and in what ways.

e) Section 3.2.5.3 on minimum standards for research with the incapacitated contains several statements about the interests of research participants and research risk that seem to convey a fundamental misconception on the part of the NHREC. Points a), b) and d) of this section include observational research in the scope of these statements – for example, in a); '*the research, including observational research, is not contrary to the best interest of the individual*' and in b): '*the risk of harm assessment shows that the*

research, including observational research, places the incapacitated adult at no more than minimal risk'.(Department of Health, 2024:39-40) Because observational research by definition only involves interventions considered to be standard of care, these interventions must be in the relevant patient's interests and of acceptable risk given the clinical context. It is a *non sequitur* to place restrictions on interventional risks in observational research as the interventions are not new or experimental (the only exception may be non-interventional procedures conducted as part of the research, but this should be clearly explained if intended). This misconception has significant implications for emergency care research which, because of the context in which it takes place, is often considered to be inherently risky.

The deficiencies described above support what I believe is a *prima facie* claim that the NHREC 2024 research ethics guidelines do not uphold or enable emergency care research with incapacitated adults in South Africa and do not offer researchers a clear understanding of the protections required. This is an inherently risky area of research, fraught with ethical complexity. While the potential gains from new knowledge for a large population of sick and injured patients are significant, researchers will only be attracted to do this kind of research if the ethical and compliance framework that they are required to work within is clear, coherent and practically implementable. Likewise, public trust in research with the incapacitated – likely already viewed with a degree of scepticism – is not strengthened by uncertainty amongst researchers due to the deficiencies pointed out above. The very unique context of emergency care research – spanning Zones C to F in Figure 1 – requires clear guidelines accounting for, among others, situations where proxy decision-makers are unavailable and interventional research with narrow therapeutic windows.

Despite the NHREC emphatically denying that waivers of informed consent for research with incapacitated adults should be allowed, many other international regulations and research ethics guidelines explicitly define and allow these for emergency care research under clearly set out conditions (also sometimes referred to as exceptions from the requirement of informed consent).(McRae and Weijer, 2008; European Parliament and of the Council, 2014; Canadian Institutes of Health Research; Natural Sciences and Engineering Research Council of Canada and Social Sciences and Humanities Research Council of Canada, 2022; National

Health and Medical Research Council; Australian Research Council and Universities Australia, 2023) Contrary to what appears to be the NHREC's view that waiving the requirement of informed consent under such conditions may be morally questionable, the opposite might be true. Such a waiver, with clear scope and conditions, could offer greater protection to incapacitated research participants and create greater confidence in researchers thus facilitating emergency care research of this nature with its potential benefits. On the contrary, the current lack of coherence in NHREC's guidelines as described above does neither of these.

1.1.4. Research Question

What would a comprehensive normative framework for emergency care research with incapacitated adults look like?

1.1.5. Rationale for the Study

There is tremendous potential for emergency care research to benefit many in South Africa across a diverse range of socio-economic strata. However, legal barriers to the realisation of these benefits exist due to statute that imposes an absolute requirement of informed consent for any health research participation. South African research ethics guidelines promulgated by the NHREC correctly respond to this situation by attempting to provide an ethical framework that facilitates this research. However, these guidelines lack coherence, are at times contradictory and seem to misinterpret certain core elements of research ethics such as consent and research risk. Thus, a comprehensive normative ethical framework for approaching this problem in South Africa is needed.

1.1.6. Thesis Statement

I will argue that waivers of informed consent for incapacitated adults in emergency care research should be allowed under certain well-defined conditions as a way of providing greater certainty for researchers engaging in this research but also as a way of offering greater protection to this vulnerable population. I will further argue that South African law related to informed consent for research is deficient in this area, not morally justifiable and requires amendment to facilitate waivers of informed consent.

1.1.7. Research Aim

To critically analyse the foundational ethical, clinical, legal and regulatory factors relevant to emergency care research with incapacitated adults in South Africa and to develop a normative framework to guide research in this area.

1.1.8. Research Objectives

The research objectives are:

a) To discuss and critically analyse the concepts of autonomy and informed consent within the context of emergency care research along with dignity, vulnerability and risk in research ethics and with specific reference to emergency care research with incapacitated adults.

b) To discuss and critically analyse the current South African legal framework and ethics guidelines on informed consent for emergency care research involving incapacitated adults.

c) To conduct a comparative analysis of international research ethics guidelines and regulations on informed consent for emergency care involving incapacitated adults.

d) To develop a normative framework offering guidance for researchers in emergency care based on a) – c).

1.2. Research Design

This research utilised a purely normative research design drawing from ethico-legal principles. Normative ethics sets out to give answers to questions regarding what ought to be done in a particular ethically challenging situation. (Sulmasy and Sugarman, 2001) In this thesis, the question asked was: when faced with an incapacitated adult patient who may benefit from emergency care research participation how ought we to proceed, and specifically, is it morally justifiable to waive the requirement of prospective informed consent under any circumstances? This question was answered in a systematic, critical fashion.

1.3. Research Methods

Being normative in nature, this research was purely literature-based and did not involve the collection or analysis of empirical data from human participants. Typical research methods and standards applicable to philosophical research were used, based upon the

interpretation and critical analysis of the most important statutory and other legal literature, bioethics literature and guidelines to answer the research question. Analysis included the definition and clarification of concepts, the identification and criticism of assumptions, the analysis and evaluation of theoretical frameworks, and the articulation of the most reasonable interpretation of significant concepts found in the above sources.

Sources of literature and other texts included*, inter alia*, journal articles, books, monographs, government legislation, case law, guidelines and other relevant material gathered through search interfaces, databases and online resources such as Pubmed (Medline), Embase, Google Scholar, Jutastat, LexisNexis and various government and Non-governmental Organisation internet sites.

1.3.1. Argumentative Strategy

The main argument made in this thesis is ultimately in favour of waivers of informed consent for emergency care research with incapacitated adults in South Africa as a way of realising the potential direct benefits of research for participants and the social value of new knowledge in this field. This argument is grounded in large part on the acceptance of decisional autonomy as an appropriate conception of autonomy in bioethics along with the principle of respect for autonomy. However, I argue that the rationale for making informed consent indispensable primarily because it respects the autonomy of research participants is far from well established. Even if this was the case, this argument would only be logically consistent when applied to those capable of autonomous actions. Thus, research with the incapacitated does not seem to be constrained on the basis of appeals to respect for autonomy.

Because the incapacitated have moral status, there is a duty for researchers to protect them, but I argue that approaching this duty by prohibiting research with the incapacitated would be over-protective and unjust. Rather, I put forward two main arguments that I believe both play a role in balancing the benefits of including the incapacitated in research with their protection. The first is a re-assessment of risk in emergency care research where I argue for a specific method of risk analysis and a more contextual consideration of the concept of minimal risk in emergency care research. The second is an argument for the

foundational role of human dignity as a constraint on researcher behaviour capable of balancing the benefits of including the incapacitated in research with adequate protection.

While the main argumentative thrust described above is related to research with those considered to be incapacitated, I believe that an important argument is also to be made regarding prospective research participants in emergency care research who find themselves in the capacity penumbra of Figure 1. Informed consent is certainly required in such cases, but I argue that the normal approach to this – characterised by large volumes of complex information – does not result in valid informed consent. I propose that consideration should be given to alternative approaches to informed consent that have the potential to be less of a burden to prospective participants yet still achieve the basic function of protecting them from deception and coercion.

1.4. Waiver for Ethics Review

This research did not involve the collection of any new data or human participation. A waiver of ethics review was granted by the Human Research Ethics Committee (Medical). (Appendix A).

1.5. Overview of Chapters

Chapter 2 is a detailed critical analysis of various conceptions of autonomy and the bioethical principle of respect for autonomy, how this differs from respect for persons, what I consider to be the foundational origins of respect for autonomy and how it came to be the most important principle in bioethics.

Chapter 3 provides more detail about emergency care as a discipline and emergency care research, highlighting some of the challenges with informed consent. This is followed by a description of the standard view of informed consent, a critical analysis of the rationale for informed consent as being grounded in respect for autonomy and the presentation of several alternative views on informed consent.

Chapter 4 deals with human dignity and its role as a factor influencing researcher behaviour with the incapacitated. A detailed discussion on various conceptions of human dignity is followed by a critical analysis of human dignity and autonomy in the setting of emergency care research. This is followed by a discussion of the concept of vulnerability in research

ethics, how this has been variously conceived and how it offers protection to the incapacitated in emergency care research.

Chapter 5 is a detailed analysis of research risk and specifically a critical appraisal of different approaches to the assessment of risk. This is followed by a discussion of research risk and its analysis in emergency care settings with specific emphasis on interpretation of the minimal risk standard.

Chapter 6 is a detailed and critical analysis of South African law and research ethics guidelines with specific emphasis on research with the incapacitated and research in emergency settings.

Chapter 7 adopts a similar approach to that in the previous chapter but focuses on international research regulations and research ethics guidelines.

Chapter 8 is the final thesis chapter and sets out a proposed normative framework for emergency care research with the incapacitated drawing on the argumentative strategy described above. This framework addresses waivers of informed consent as offering a justifiable and structured approach to emergency care research with the incapacitated making use of a set of clearly articulated conditions. It also addresses the approach to informed consent with prospective participants in the capacity penumbra of Figure 1 and an approach to research risk analysis specific to the emergency care context.

CHAPTER 2: AUTONOMY IN HEALTH RESEARCH

2.1. Introduction

The problem of research with those lacking the capacity to give informed consent can be thought of as a problem centred on autonomy. This is because of the view, entrenched in bioethics, that informed consent is closely related to autonomy. This view sees obtaining informed consent as showing respect for the autonomy of research participants which is foundational to the way such participants are treated from a moral perspective. While widely accepted, adopted and taught – particularly in research ethics – this view does not rest on a firm foundation. In part, because the concept of autonomy is such a complex and unsettled one and in part, because of a desperate desire for research ethics to emerge from its tainted past, the superficially strong allegiance of informed consent and autonomy does not hold up well to critical analysis.

In this chapter, I present a discussion of autonomy. In the first section, this discussion places some emphasis on Kantian and Millian conceptions of autonomy because of the foundational prominence that these have enjoyed in research ethics. After this, I include other more modern conceptions of autonomy in particular that of decisional autonomy which is widely employed in bioethics. Decisional autonomy constitutes a broader platform for discussion of principlism's incorporation of autonomy as respect for autonomy. At this point I direct some attention to discussing the transition from respect for persons to respect for autonomy starting in the late 1970s onwards and how this relates to autonomy's Kantian and Millian roots. I end this chapter by critiquing the conventional view that respect for autonomy is derived from Kant's conception of autonomy and examine the influence of liberal democratic frameworks on the ascent of the dominant individualist conception of autonomy in bioethics more broadly and research ethics specifically.

2.2. Autonomy Defined?

The word autonomy is composed of two Greek root words *autos* (meaning '*self*') and *nomos* (a reference to '*rule*' or '*governance*') and was originally intended as a way of referring to self-governance in a political sense.(Beauchamp and Childress, 2013b; Mackenzie, 2014) Similarly, autonomy can be understood in its linkage to another Greek word – '*autarkeia*' – which refers to an ideal of what May (2005:304-306) explains as self-sufficiency or purity of

purpose. Autarkeia was deliberated upon by Aristotle, also predominantly within the context of the city-state. More recently, in the context of bioethics, use of the word autonomy has been transferred to the context of individuals and is broadly understood as a description of their personal authority to make their own life decisions, considered here more narrowly in a health and bioethics context (this very simple explanation is given for now but will be expanded on – and its validity probed – later in this chapter).

As might be expected with any complex idea, there seems to be very little agreement on a definition for the word autonomy. Dworkin (1988:5-6) sums this up well in giving an overview of how the word has been used with different meanings in a range of different contexts:

> '*It is used sometimes as an equivalent of liberty (…), sometimes as identical to self-rule or sovereignty, sometimes as identical with freedom of the will. It is equated with dignity, integrity, individuality, independence, responsibility, and self-knowledge. It is identified with qualities of self-assertion, with critical reflection, with freedom from obligation, with absence of external causation, with knowledge of one's own interests. It is related to actions, to beliefs, to reasons for acting, to rules, to the will of other persons, to thoughts and to persons. About the only features held constant from one author to another are that autonomy is a feature of persons and that it is a desirable quality to have*.'

The present bioethical understanding of autonomy as an individual's authority to make their own life decisions, to be self-sufficient or simply to be free from external interference, owes much to a similar concept – respect for autonomy – made popular as one of four fundamental principles of bioethics by Beauchamp and Childress in their seminal *Principles of Biomedical Ethics*.(Beauchamp and Childress, 2013a) However, autonomy as a concept in moral and political philosophy has much deeper roots than this. In fact, whether there is any direct or traceable lineage between these deeper roots and the more modern bioethical conception of autonomy is far from certain.

It seems obvious, given the research question presented in Chapter 1, that autonomy is a key concept needing to be critically discussed in this thesis. I will approach this discussion by turning first to autonomy as conceived in moral theory, specifically that of Immanual Kant and John Stuart Mill. Following this, I will provide some more contemporary conceptions of autonomy grounded in both socio-political theory and other perspectives such as feminism and communitarianism. Lastly, I will discuss two concepts related to autonomy that have played central roles in research ethics in the last few decades – respect for persons and respect for autonomy. My aim in examining these latter two concepts is to highlight the tenuous link between autonomy as currently understood in a research ethics context and moral theory, particularly Kantian moral theory. I will suggest that approaching autonomy as a function of the liberal political framework may explain more of its modern allure and application in research ethics.

2.2.1. Kantian Autonomy - Reason, Freedom and Morality

Kant's moral philosophy was centred on the notion of freedom of choice and action. This freedom was not only from the influence of external effects, but also (and perhaps more importantly) from the effects of our own inclinations. Kant saw free actions, which are the only actions with moral weight, as those arising from an individual's will.(Brassington, 2012:167) According to Guyer (2011:85), Kant conceived of a free will as '*our ultimate metaphysical property*' and the intrinsic value of freedom so expressed was the normative foundation for Kant's moral philosophy. By a will, Kant – according to Hill (2014:97) – means the ability to act in line with an individual's idea of laws or principles. That is, according to practical reason. A free will and everything that flows from it is the domain of the rational being.

It is quite probable that most modern views on freedom, broadly speaking, would see this in a relational sense. In other words, freedom would most likely be conceived as applying to individuals and meaning that such individuals are free from something. However, this is not what Kant meant by freedom or autonomy. As Brassington (2012:168) puts it, Kant's autonomy implies a freedom to be bound by law, as contradictory as that might sound. Rather than freedom from something, such as an externally imposed regime, Kant means that autonomy involves the freedom to be bound by a law that is '*self-given*'. This insight

follows from the will being seen as a '*law unto itself*' and implies that the freedom so valued as a grounding for morality is a freedom of the will and not a literal, relational idea of freedom. Furthermore, the reason that undergirds the will is considered by Kant to be universal.(Brassington, 2012:168) He saw the subjection of individual inclinations to the rule of reason, the '*property of the will by which it is a law unto itself*', as the most important characteristic of individuals in realisation of the moral law.(Guyer, 2011:85)

According to Schaab (2022:45), Kant sees a good will as the will of an agent who performs their duty '*from duty*' alone and not for any other reasons including any characteristics of a particular action or consideration of the purpose or outcome of an action. Actions following duties are guided by the agent's maxim with the moral worth of a maxim determined by its characteristics, namely that it is lawful. Because moral actions arise from duties and duties assume a law, the maxim in question must be lawful and an action arising from duty has respect for this law. The law Kant refers to is not a real, existing law but rather a law that possesses the form of laws (i.e. it could function as a law). The lawful form of a maxim is such that it could be willed to become a universal law – this he sees as the principle of morality. He further classifies this, for rational beings, as an imperative and categorical which leads to the basic formulation of his categorical imperative; to '*act only according to that maxim through which you can at the same time will that it become a universal law*'.(Schaab, 2022:46)

Schaab's (2022:47) interpretation of Kantian autonomy of the will asks whether it should be understood as a metaphysical property, a normative principle or a psychological capacity. He concludes that it is all three. Its metaphysical nature rests on independence of the will – not only independence in an 'external' or negative sense (from factors external to the individual) but also in an 'internal' sense (from factors specific to the individual identity). Its normative nature can be seen from the perspective of what Schaab (2022:47) calls '*positive freedom*' – the complement of negative freedom which is the absence of external constraints. Positive freedom arises from autonomous agents being bound by the self-given moral law – as mentioned above. This translates into a normative principle determining what the individual ought to do – to not choose in any way other than that mandated by the categorical imperative. Finally, positive freedom implies a psychological capacity for

autonomy because rational agents must be capable of '*recognising and being motivated by*' the self-given moral law.(Schaab, 2022:47) This implies, as part of such a capacity, that rational agents have an incentive to comply with the law, but this incentive must be derived from personal feelings in order to overcome inclination and desire, which are also personal feelings. Kant sees this incentive as being derived from pure reason and this is what he construes as respect for the moral law.

The bioethical principle of respect for autonomy, discussed in greater detail in Section 2.3.4 below, assumes a conception of autonomy quite different from that described above; one based on valuing the self-determination and choice of individuals. Kant does not seem to be suggesting that autonomy is a property of individuals but rather a property, a freedom, of the will in a way that is generalised rather than individualised. In grounding respect for autonomy in Kantian terms, an alternative formulation of the categorical imperative is sometimes used. This is the well-known Humanity Formulation, to '*act in such a way that you treat humanity, whether in your own person or in the person of any other, never merely as a means to an end, but always at the same time as an end*'.(Reath, 2003:352) While it may seem that this formulation intuitively supports the modern principle of respect for autonomy and that the latter could be derived from it due to a suggestion of the special moral standing of persons, it is doubtful that Kant meant this so literally. It seems Kant did not value autonomy independently, in a way that the bioethics principle does. Persons have a special value to Kant, but this is because their dignity is derived from their autonomy which in turn makes each individual part of a larger group over whom maxims are universalizable. Or, as Schaab puts it more directly: '*in order to avoid using someone as a mere means, we have to act on a maxim that they could also rationally will*', that is a maxim that is consistent with the categorical imperative.(Schaab, 2022:51)

While Kantian moral theory occupies a particularly important and influential place in ethics, the status of autonomy as conceived by Kant as grounding for a similar concept in bioethics, and more specifically in research ethics, is not as certain. This theme will be expanded upon and discussed in more detail below, within the context of the bioethical principles of respect for persons and respect for autonomy. The concept of autonomy in bioethics has also been significantly influenced by the work of John Stuart Mill. As O'Neill (2002:30) states:

'*contemporary admiration for individual or personal autonomy still owes, I believe, far more to Mill than to Kant*'. Mill's conception of autonomy will be discussed below.

2.2.2. Millian Autonomy - Liberty

As mentioned above, the word autonomy was originally used in a political sense to refer to the self-governing status of cities. Then, following Kant's account of autonomy, the focus shifted to morality and rational beings. Importantly though, this was not autonomy of the individual as we would think of such a notion today but rather autonomy of the will expressed in a universalizable way. The origins of individual autonomy lie with John Stuart Mill and in particular his 1859 treatise *On Liberty*.(Smith, 2003) Unlike Kant, Mill attempted to give a naturalistic account of autonomy (he did not actually use the word autonomy, but his usage of the word liberty is taken to embody a like concept).(Macleod, 2022:75) That is, an account based on the view that human action is brought about by natural occurrences and acts, such as aspirations and convictions.

Mill saw a state of societal liberty – freedom – as the singular way to bring about autonomy, which is the development of an authentic individuality or character. Importantly, Mill does not see autonomy as the mere freedom to make choices according to fleeting desires. Rather, autonomy is encapsulated by the freedom to make choices in a particular way that involves the moderation of such desire by '*taking charge of those desires, as reflecting on and selecting among them in distinctive ways*'.(O'Neill, 2002a:31) Or has Skorupski (1989:354-355) puts it, Mill's view of the capacity of autonomy as moral freedom means that it is does not equate to the individual ability to do whatever one wants to but rather it is the capacity to refrain from that, recognising good reasons for doing so. In a description of Mill's liberal egalitarian worldview, Donner (2009:138) refers to his recognition of a virtue-ethical grounding for the development of worthy traits such as individuality and autonomy. Accordingly, Mill's liberal autonomy is characterised by the individual capacity for '*self-determination, critical reflection and authenticity*' or a form of self-governance.(Skorupski, 1989:348) Provided an individual lives according to their own nature, rather than another regime externally imposed, they live by a self-determined law. Mill believes that such an individual has character which is '*the rule of conduct*'. (Macleod, 2022:75)

While individuality is clearly an important part of autonomy, Smith (2003:396-397) interprets Mill as not suggesting that individuality is the only determinant of a good life (or a good society) but rather only one of the elements associated with prosperity. The '*developed character*' referred to above is seen by Mill as resulting from the effects of multiple desirable traits, not just individuality. Smith emphasises the historical context at the time Mill wrote *On Liberty* as being important in understanding the '*accentuated individualism*' which is not consistent with some of his other writings on economics and culture. In his third chapter of *On Liberty*, Mill had in mind a counterpoint to what he saw at the time as a threatening uniformity inherent in commerce, education and Victorian society in general.(Smith, 2003:396) Acting in opposition to the development of the virtue of autonomy, as characterised above, is the spectre of conformity which Mill sees as an abandonment of autonomy and a fundamental threat to individual welfare.(Donner, 2009:139) This threat is pervasive because the need to belong is such a basic human one but, at the same time, potentially the seed for a human submission to the '*tyranny of the magistrate*' and perhaps more importantly the tyranny of society and the majority.(O'Neill, 2002a:31) In arguing against the potential damage done by conformity, Mill highlights the virtue of autonomy and spontaneity in securing individual prosperity.(Skorupski, 1989:348) But ultimately, he makes a much more important point about autonomy and society. Mill sees individuals of character as contributing to the well-being of society, the utilitarian project and thus morality as a whole.(O'Neill, 2002a:32)

Mill's appeals to individualism expressed as a desire for each individual to live according to their nature raise a contradiction if we pause to consider the characteristics of that nature. Mill realised that human nature is variant, subject to socialisation and not always desirable (in fact, his view was that the default state of human nature without socialisation is undesirable).(Macleod, 2022:78) Thus, living according to a nature expressing undesirable traits would be incompatible with autonomy and its role in shaping a good life. Consequently, Mill emphasises that it is enriched nature that should be pursued – what he refers to as *second* nature which is, seemingly in the form of a contradiction, both part natural and part acquired. Macleod (2022:78) explains this as being facilitated by an associationist account of mind, which accomplishes a development and elevation of elements already inherent in the individual nature to be integrated into the second nature.

While this account might explain the transformational property of socialisation and development of the second nature, it also presents a difficulty for Mill's original assertion that autonomy is expressed primarily through individual behaviour.

It seems difficult to retain a coherent vision of non-interference but accept that there may be exceptions to this and to identify a line beyond which development of the second nature becomes interference in autonomy to the point of heteronomy. Mill seems to entertain the idea that autonomy, as individualistic as it is, inherently admits to some degree of acceptable external influence by the state (he refers to this as non-authoritative state action) and also in the provision of education, but without eroding self-identity and the freedom to determine individual goals and actions.(Macleod, 2022:81) A more troubling form of interference is the phenomenon of false consciousness, that is the situation where an individual acquires a second nature but one which they are unaware does not align with their original nature or interests. Mill sees this as remediable by deep analysis of the individual's own character and associations thus identifying elements at odds with the former but perhaps more importantly, exposure to others in '*different experiments of living*'.(Macleod, 2022:82) In other words, through being exposed to other cultures and social values Mill believes that we are likely to become aware of alternative ways of living or thinking and that these might highlight our own deficiencies or offer alternatives which can be adopted. As Macleod, 2022:82) points out though, according to Mill, these judgements can only be made relative to the happiness that other ways of living result in and false consciousness may convince the observing individual of their own ways akin to a form of confirmation bias. But this is inescapable in the utilitarian scheme of things.

Another contradictory aspect of Mill's conception of autonomy goes to the heart of both autonomy as an idea and its utilitarian expression. Skorupski's (1989:356) interpretation of Mill is that he only casts autonomy as capacity in chapter three of *On Liberty*, and not as freedom. He does not differentiate between autonomy and happiness as distinct categorical ends but rather sees autonomy as capacity having value in producing happiness. Skorupski asserts that the value of autonomy does indeed lie in its association with happiness but as an end in its own right, because the consciousness of being autonomous makes the individual happy.(Skorupski, 1989:357) He supports this view by pointing out a contradiction

that arises from thinking of autonomy as a good only insofar as it affects happiness in a utilitarian sense as Mill does. He argues that if an infringement of autonomy only causes harm indirectly, by diminishing happiness, then disallowing such an infringement is itself prohibited according to the Liberty Principle (that power can only be brought to bear over an individual to prevent harm).(Skorupski, 1989:358) This argument holds because there may be situations, for example where an individual is unaware of an infringement of their autonomy, where such an infringement does not negatively influence happiness thus making the wrong of infringing autonomy conditional and not an absolute wrong. Thus, according to Skorupski, although autonomy as an end in itself is not compatible with the Liberty Principle it can be seen as such by promoting it as a primary utility in which case Mill's theory of justice protects autonomy for those having capacity as '*a just claim to carry on their own lives in their own way*'.(Skorupski, 1989:358-359)

2.2.3. Post-Kantian and -Millian Thoughts on Autonomy

In her discussion of Mill's conception of autonomy, O'Neill (2002a:34) refers to more recent work on other naturalistic accounts of autonomy which she collectively refers to as '*neo-Millian*'. These are assembled in a review by Christman (1988:109-124). While this review is rather dated, it does touch on a number of important perspectives of autonomy, some of which have direct relevance to the context of this thesis and for this reason I will briefly discuss a few of them here. After this, four bioethical conceptions of autonomy will be discussed, namely libertarian, conscientious, relational and decisional autonomy.

Christman (1988:109-124) attempts to provide some clarity on basic ideas about autonomy based on the work of other authors in the first part of his review. The following discussion touches on some of the concepts and questions that he elaborates on.

The psychological condition of autonomy (PC autonomy): Citing the work of Feinberg, Christman (1988:109-110) identifies four basic meanings of autonomy; a capacity for self-government, actual self-government, an '*ideal of virtue*' (inferred from the conception of self-government) and a '*sovereign authority*' for self-governance. Feinberg also identifies a set of virtues illuminating autonomy which include moral authenticity, self-legislation, self-identity or individuality and self-control. From these, and broadly speaking from Feinberg's

meanings, the Millian influence seems fairly clear. Expanding on this, Christman (1988:110) further cites Hill who notes that, in a similar vein to Feinberg, autonomy is what he refers to as a psychological condition (PC) of governing oneself.

Autonomy as a right: Hill also extends this idea to a different meaning, that of a right to autonomy, that is the right to not be interfered with or treated in a way that counteracts the PC of autonomy. Manipulation or coercion would be examples of infringements of autonomy as a right although Christman also points out some vagueness in this area as PC autonomy does not necessarily always have to be disturbed but rather in some cases the right to autonomy may be infringed when an individual is treated as if they do not '*have*' PC autonomy. Nevertheless, the distinction of a right to autonomy from other meanings is an important one and features prominently in discussions about autonomy as applied to research ethics. Christman (1988:111) incorporates another conception of autonomy as a right which Meyer describes as '*rights-sensitive*' autonomy – a normative property entailing the protection of individual liberties.

'Stoic' autonomy: Meyer further proposes a somewhat more unique idea about autonomy which he refers to as the '*Stoic*' position on autonomy. This refers to a situation where individuals exercise '*active control*' over their desires. As Christman (1988:111) points out, this idea sounds Kantian in nature but there is a subtle difference in the sense that autonomy in the face of desires can be maintained in two possible ways. The first is for the individual to simply exercise control over the desires while the second is for the individual to revise their inclinations to more favourably align to the attainable choices. By doing this, a best possible scale of achievable desires can be realised. However, this alone does not support the conclusion that an autonomous choice has been made because the choice made may simply be a case of '*sour grapes*' – the recalibration of a desire simply because it is not achievable. The autonomous recalibration is different, being motivated by a revision of character and associated actions in the face of limitations. Thus, although potentially offering an interesting perspective on autonomy the Stoic position seems to be too obscure to be useful.

The Dworkin/Frankfurt (DF) model of autonomy: This model is based on work by Frankfurt and Dworkin and is described in Dworkin (1988:3-20). The DF model, sometimes referred to as a split-level model of autonomy, differentiates between first-order and second-order desires. The former are desires leading to actual actions of some sort while second-order desires are those directed towards other first-order desires (what Christman (1988:112) describes as '*a desire to desire to do X*'). An individual will identify with some first-order desires, meaning that the individual reflects critically on these desires and approves of having them. According to Christman (1988:112), the DF model holds that an individual is autonomous if they identify with their first-order desires and do so in a way that does not make this process '*alien*' to the individual. However, in a later version of the DF model Dworkin revises his views on this condition of identification stating that the presence or absence of identification is not the factor determining autonomy but rather whether an individual has the capacity to '*raise the question of whether [they] will identify with or reject the reasons for which [they] now act*'.(Dworkin, 1988:15) This distinction is evident in the revised definition of autonomy as '*a second-order capacity of persons to reflect critically upon their first-order preferences, desires, … and the capacity to accept or attempt to change these in light of higher-order preferences and values*'.(Dworkin, 1988:20)

Several criticisms have been levelled at the DF model (summarised by Christman (1988:113-114)), including by Beauchamp and Childress (2013b:102-104) who claim that the DF model is not suitable as a theoretical basis for autonomy. They argue that it is possible for a causal relationship to exist such that a second-order desire is caused by a strong first order desire and in this case, identification will not always be helpful in distinguishing autonomy from non-autonomy. Perhaps more interestingly though, Beauchamp and Childress object to the DF model because to them the requirement of reflective identification renders the model unusable in a practical sense. They state for example that '*it [DF] needs a way for ordinary persons to qualify as deserving respect for their autonomy even when they have not reflected on their preferences at a higher level*' and that '*it [DF] presents an ideal beyond the reach of normal choosers*'.(Beauchamp and Childress, 2013b:103) While they clearly seem to see the kind of reasoning inherent in the DF model as too onerous and not suited to a health care environment (i.e. clinical or research), they unfortunately do not clearly articulate who the '*ordinary persons*' or '*normal choosers*' are.

The scope of autonomy: Beauchamp and Childress' rejection of the DF model as a suitable framework for considering autonomy of the '*normal chooser*' highlights an unsettled question regarding the scope of autonomy. That is, whether autonomy should be considered to operate at the scope of what Christman (1988:111) calls a '*property of preferences*' or within a short-term or immediate decisional scope or at the scope of a whole individual over extended periods or even the lifetime of an individual. This seems to be an important question that has a significant influence on not only how autonomy is conceived but also on how useful it is considered to be in application. Beauchamp and Childress (2013b:103-104) clearly see autonomy in bioethics as decisional in scope, as applying to decisions made by individuals at a particular moment – perhaps under quite significant constraints – without the ability to engage in long-term reflection and adoption of attitudes towards their first-order desires. This is not the same view expressed in the DF model. Dworkin (1988:15-16) sees autonomy as a '*global rather than local concept*' that can only be evaluated over long periods of the life of an individual. However, he differentiates between autonomy and identification (as described above) with identification occurring over shorter time-frames.

Autonomy and rationality: A feature of both the Kantian and Millian conceptions of autonomy and of the PC of autonomy along with the DF model is that the individual, the autonomous agent, must be capable of rational thought. Christman (1988:115-116) sets out the views of different authors on the finer details of what sort of rationality underpins autonomy conceived in specific ways. However, the distinctions between these views of rationality are operative at a high level and tend to reflect '*global*' functioning (as referred to above by Dworkin) rather than a minimal threshold of rationality related to a decisional level of functioning.

Christman (1988:116) identifies two questions concerning rationality and autonomy with implications for this latter scope. In the first of these questions he asks whether making the characteristic of autonomy contingent upon rationality renders it inconclusive because individuals with varying degrees of '*decision-making competence*' will possess this characteristic of autonomy to equally varying degrees. Christman then states '*While this does not seem problematic in itself, it seems to conflict with the intuition that autonomy is a*

property that can be valued equally in one's treatment of individual persons'.(Christman, 1988:116) This view seems to be based upon conceiving autonomy as a right implying that all individuals are equally owed respect as autonomous agents. It highlights the conceptual rift between such a rights-based conception and others (such as the DF model) and Christman later seems to doubt the veracity of any claim to autonomy as a right when he refers to it as '*a notion too weak to support the further normative requirement that autonomy must be respected equally in all persons*'.(Christman, 1988:116) Yet this is, broadly speaking, the bioethical conception of autonomy according to the principle of respect for autonomy which will be discussed in greater detail in Section 2.3.4 below.

2.3. Four Bioethical Conceptions of Autonomy

The discussion of autonomy above has dealt with the concept in a general sense, attempting to present a description of its main philosophical roots, development through to more recent views and some remaining questions. In the following subsections I present a descriptive account of four conceptions of autonomy relevant to bioethics, as highlighted by Mackenzie (2014:277-290). Each of these have relevance to subsets of bioethical areas of inquiry in some cases with a clinical or broader health care focus and in other cases with a research focus. The last of these, decisional autonomy, deals with the principle of respect for autonomy from Beauchamp and Childress' (2013a) canonical *Principles of Biomedical Ethics*.

2.3.1. Libertarian Autonomy

The basis of libertarian autonomy can be equated to the existence of negative liberty – in other words, the absence of external influence and interference in personal decision-making. Individual freedom, and the right of each individual to choose how to live their life, is the single central determinant of autonomy. Libertarians, ever conscious of the threat to autonomy constituted by societal opinion and the state, see the subjective opinions of individuals as the standard of free choice and the marker of autonomy regardless of how such opinions (and choices) may be perceived by others. The only restriction on this freedom of choice is the constraint put forward by Mill, that the exercising of a choice should not harm others. Because the libertarian ideal sees promotion of autonomy as the creation of conditions that broaden choice, autonomy is represented by a state of minimal

interference by others.(Mackenzie, 2014:282-285) Bioethical debates drawing on libertarian autonomy as an argumentative strategy include those on controversial reproductive, surgical or genetic technologies such as sex selection or enhancement of offspring, cloning and sale of organs.(Mackenzie, 2014:282).

Critics of libertarian autonomy point out that negative liberty alone provides an imbalanced framework for a socially acceptable conception of autonomy. This criticism comes mainly from those adopting a relational approach to autonomy (described below), who emphasise that freedom of choice and lack of interference are not enough for autonomy. Autonomy can only be expressed, according to this argument, when there is also opportunity and access to opportunity, which may take several forms but includes social goods such as education, security and housing. Furthermore, the same argument is extended to encompass distribution of such goods as a requirement for autonomy, suggesting that opportunities for self-expression based upon socially provided goods are as important as the freedom to choose them. A harder form of this argument goes a little further to suggest that the libertarian conception of autonomy can, under circumstances of socially constrained choice, exacerbate social injustice or allow exploitation which are both in direct conflict to the notion of autonomy.(Mackenzie, 2014:282-285)

2.3.2. Conscientious Autonomy

Conscientious autonomy, as put forward by Kukla (2005:34-44) questions the expression of autonomy clustering around discrete events of decision-making – '*punctate decisions*' as Kukla refers to them. Rather, the contention is that autonomy in bioethics is a feature of a patient's more consistent and longer-term functioning in a dynamic, collaborative relationship with health care authority, typically represented by doctors (but theoretically any health care professional). The emphasis in this conception of autonomy is on the independent decision-making and functioning of patients which is an expression of their autonomy outside of decision-making in a more formal health care context.

Kukla (2005:38-41) claims that conscientiousness (on the part of patients) is a form of autonomy, and that conscientious actions are autonomous actions. However, this is not suggested as a form of autonomy in the strict ethical theoretical sense but rather a

'*concrete, limited*' form of autonomy well suited to consideration in the context of health care. The idea of conscientiousness is central to the idea of a conscientious autonomy, and this is described broadly as responsible and committed action. More specifically, conscientiousness is seen as a willingness and responsibility to stand by whatever actions have been committed to, and to understand and evaluate their rightness or wrongness – and even before this, to have the capacity to interrogate and evaluate these actions as right or wrong. Trust in, and respect for, health care experts and authorities is seen as an inherent part of this process although these are still open to question and critical appraisal.(Kukla, 2005:38-41)

While the claim is made above that conscientious autonomy is well-suited in application to health care in general, it is perhaps best suited to situations that decisional autonomy is not. Kukla (2005:36-38) uses the example of antenatal care to illustrate the key ideas of conscientious autonomy, and this turns out to be a good vehicle for conveying this information. However, not all types of clinical patient care or health research follow a similar pattern of prolonged engagement between patient and health care professional. In situations where contact and engagement between patient and professional are of a shorter duration and the exercising of autonomy does tend to be expressed more in terms of decision-making, decisional autonomy (discussed below) may be a more helpful conception.

2.3.3. Relational Autonomy

According to Mackenzie (2014:285-289), relational autonomy contains elements of decisional, conscientious and libertarian autonomy but moderates or perfects these by the consideration of social factors and relationships in determining what is referred to as '*autonomy competence*'. Relational autonomy is concerned with competences required for the exercising of autonomy (like decisional autonomy), values the role of freedom of choice (like libertarian autonomy) and emphasises the role of critical reflection, judgement and accountability. Relational autonomy competence is dependent on a set of skills developed over time and exercised to varying degrees – these include skills related to self-discovery, self-definition and self-direction. In an important departure from other conceptions of autonomy, relational autonomy is content neutral. That is, the extent to which an individual's decisions are autonomous are dependent not on their content, but rather on

the extent to which their reflective skills have been utilised to make a decision that is an expression of that individuals self-conception.(Mackenzie, 2014:285-289)

There is a very conspicuous social constructivist and social justice thread running through much of the relational conception of autonomy. This is suggested as a strength, and something that makes relational autonomy applicable to assessment of autonomy in health care.(Mackenzie, 2014:285-289) However, it does produce some stark differences in fundamental thinking about autonomy when compared to other conceptions. For example, in the relational view of autonomy there is an acceptance of (in fact a reliance on) autonomy being embedded in social relationships. This stems from the assumption of autonomy being shaped by inter-personal relationship and the vulnerabilities inherent in these relationships. However, it is fundamentally different to the usual bioethical meaning of autonomy which emphasises personal independence. Similarly, the relational view rejects the idea of individual authenticity in autonomous decision-making in favour of highlighting the role of socially acquired reflective skills in revealing life preferences. Relational autonomy also tries to account for injustice and exploitation by emphasising that opportunity, and equality of opportunity, amongst individuals and social groups is as important in the expression of autonomy as freedom of choice. Taking this into account, respect for autonomy in the relational form means going beyond honouring choices and extends to the ambitious project of upholding social relationships and societal characteristics that allow individuals to lead '*self-governing*' lives.(Mackenzie, 2014:285-289)

2.3.4. Decisional Autonomy and the Principle of Respect for Autonomy

The three conceptions of autonomy discussed above (in Sections 2.3.1 – 2.3.3) offer counterarguments to the most influential and widely adopted bioethical conception of autonomy. Decisional autonomy, as the name implies, refers to a focus on autonomy as part of a moral framework for decision-making, in both clinical patient care and health research contexts.(Mackenzie, 2014:278-282) The best-known proponents of this conception of autonomy are Beauchamp and Childress, as expressed in their seminal work on bioethics.(Beauchamp and Childress, 2013a) The autonomy referred to here is indirectly invoked as *respect for* autonomy, one of Beauchamp and Childress' four principles the other

three being the principles of beneficence, non-maleficence and justice. Ethical principlism is an approach to biomedical ethics that proposes a framework of ethical principles which are, in essence, what W. D. Ross identified as *prima facie* obligations.(Beauchamp and Rauprich, 2016:2286) In any given scenario, all obligations are *prima facie* obligations but a decision regarding actual obligations (those that must be finally acted upon) is made by weighing the relative importance of opposing *prima facie* obligations of which no single obligation takes absolute precedence in all situations. Ethical principles are viewed in much the same way and take their '*universal validity*' from the larger constellation of moral requirements constituting the common morality.(Beauchamp and Rauprich, 2016:2822-2293) While principlism, in the incarnation of the *Principles of Biomedical Ethics*, has been very widely adopted and applied in bioethics it is not without criticism.(Clouser and Gert, 1990; Davis, 1995) However, in this section I focus only on one principle and not principlism as a whole and thus will not engage further in these critiques of the approach.

Decisional autonomy is centred on a local understanding of autonomy, that is, autonomy '*located*' to a particular point in time when a clinical or research-related decision needs to be made by a patient or research participant. This is different to a more global view of autonomy, which extends beyond an immediate decision-point in time and is rather seen in relation to an autonomous person (as a whole) or the global conduct of an individual in living an autonomous life (Cf. Dworkin (1988:15-16)). Beauchamp and Childress believe that their view of autonomy as local and decision-based offers a more pragmatic and clinically useable conception.(Beauchamp and Childress, 2013b) Clearly, their intention is to closely couple this conception to informed consent so that decisional autonomy is more or less equivalent to the latter. In doing this, they reduce the requirements necessary to make clinical or research decisions autonomous and thus make it as inclusive as possible in what is a complicated and diverse environment. Specifically, Beauchamp and Childress ignore the more complex requirements of critical reflection and authenticity (Beauchamp and Childress, 2013b) that differentiate what Mackenzie refers to as the difference between informed choice and autonomy.(Mackenzie, 2014:280-282)

While the emphasis on autonomous actions, rather than autonomous persons, that Beauchamp and Childress put forward is intended to map directly to the informed consent

process in a practical way it has also been a source of criticism of their position. As Mackenzie (2014:280-281) outlines, several arguments can be put forward to reject notions of autonomy as decisional and based only on actions. All these arguments in some way have to do with the way decisional autonomy ignores the importance of social oppression and its effects on global autonomy, as well as its narrow focus which excludes consideration of the individual's self-conception and values. Beauchamp and Childress in turn argue that such preconditions for autonomy are an '*aspirational ideal*' but are not helpful in allowing for judgements about the likelihood of an action or choice being autonomous and representing adequate capacity (on behalf of the chooser) for informed consent in a biomedical context.

Beauchamp and Childress' specify three conditions for autonomous action that are derived from an analysis of autonomy that is pragmatic and can be usefully understood under real, that is non-ideal, conditions. Without engaging further in any of the more complex social and personal conditions associated with conscientious or relational autonomy, they suggest that choices about clinical care or health research participation are autonomous if made by competent patient-participants.(Beauchamp and Childress, 2013b:104-105) As already highlighted above, this creates a direct logical connection between autonomy and informed consent – with competence as the common denominator. The three conditions for this conception of autonomy are described below.

Intentionality

To be intentional an act must correspond to the patient-participant's preconceived ideas and conception of the action and events that are believed to constitute the execution of the action. Two further important characteristics of intentional acts apply; that an intentional act does not necessarily need to unfold in the same way that it was conceived to by the patient-participant and that an intentional act does not necessarily need to be one desired by the patient-participant. In short, fate may intervene despite our intentions and sometimes we are called upon to do unpleasant, but necessary, things.(Beauchamp and Childress, 2013b:104)

Understanding

An autonomous action must be understood by the patient-participant, but this understanding does not need to be complete or completely free of constraints such as factors that may affect the cognitive ability to understand or to communicate. Beauchamp and Childress emphasise the practical application of autonomy in relation to this condition, highlighting that the standard set for understanding cannot be unrealistic.(Beauchamp and Childress, 2013b:104)

Noncontrol

In order to act autonomously, a patient-participant should be free of both internal and external influences. Internal influences may be related to mental state, although this has some overlap with the previous characteristic of understanding. External influences, where Beauchamp and Childress (2013b:104) place most of their emphasis, typically arise from other people as some form of coercion or manipulation.

Beauchamp and Childress (2013b:107) suggest that autonomy, as characterised by these three conditions, exists in any individual and circumstance as a point along a continuum. This is so because, while intentionality is considered to be more of a binary type of characteristic, understanding and freedom from control (noncontrol) exist in degrees depending on a specific context, situation and circumstance. While they acknowledge that it may be difficult to describe an objectively valid and absolute threshold at and beyond which '*substantial*' autonomy exists, they claim that such a threshold is not relevant and that what is '*substantial*' autonomy can be decided in relation to a specific objective and context.(Beauchamp and Childress, 2013b:105) In health research ethics the principle of respect for autonomy has its main practical expression in the process of informed consent which will be discussed later in this chapter.

In their final summing up, Beauchamp and Childress (2013b:106-108) portray the principle of respect for autonomy as an acknowledgement of the right of others. The right in question is described by them as the right '*to hold views, to make choices and to take actions based on their values and beliefs*'. They further emphasise that this respect is of necessity embodied in action and is not merely a sentiment, with actions shaped by both negative and positive obligations. The former translate into actions that facilitate and support

autonomous decision making, and the latter translate into the actions limiting constraints that interfere with autonomous decision making. They emphasise that as a principle, respect for autonomy has only *prima facie* standing and may be abrogated by other principles depending on the context.

Beauchamp and Childress (2013b:108) interpret the principle of respect for autonomy as it applies to those who cannot '*act in a sufficiently autonomous manner*' by stating that such individuals are not owed this respect or to put it another way, others are not obliged to respect their autonomy. Several examples of classes of individuals who may not be able to act autonomously are given, but within the context of this thesis, the most important category applies to those lacking decision-making capacity regarding research participation due to acute injury or illness in an emergency care research context. Intuitively this seems logical, as such individuals are unable to formulate or express their views and choices about participating in research. However, when considering that the principle of respect for autonomy is framed by Beauchamp and Childress as an obligation on the part of researchers towards a right of participants (see previous paragraph) it is not immediately clear why this obligation falls away for incapacitated participants. Two possibilities are (i) that the participant's right (to hold views, make choices etc.) falls away when incapacitated thus removing the associated obligation or (ii) that the right remains but the associated researcher obligation falls away. Beauchamp and Childress (2013:370) themselves state that the retention of a right is not contingent on an individual being able to exercise it thus suggesting the latter but the reason for this is not made explicit. Presumably, the researcher's obligation falls away for practical reasons because the incapacitated participant cannot meet the three conditions for autonomy described above.

Although Beauchamp and Childress claim that there is no obligation on the part of a researcher to respect the autonomy of an incapacitated participant, they do emphatically state that such participants are still owed '*moral respect*' by researchers on the basis of their moral status.(Beauchamp and Childress, 2013b:108) This creates an obligation on the part of researchers to protect them, based on the principle of non-maleficence and also due to their vulnerability. This protection may take several forms including the setting of restrictions on allowable research risk that incapacitated participants are exposed to and

requiring a proxy decision-maker's involvement. Despite the insistence of Beachamp and Childress that not having to respect the autonomy of the incapacitated is not tantamount to an abandonment of the broader notion of respecting these individuals, this position has been criticised. This criticism has been centred on the contrast between the principle of respect for persons, as articulated in the Belmont Report(National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979) and its '*transformation*' by Beauchamp and Childress into respect for autonomy with the associated loss of what some feel is an essential moral element. These critiques will be discussed in the next section.

2.3.4.1. Respect for Persons vs. Respect for Autonomy

The Belmont Report, published in 1979, centres respect for persons as its prime basic ethical principle. According to the Report, respect for persons entails two things. Firstly, that '*individuals should be treated as autonomous agents*' and secondly, that '*persons with diminished autonomy are entitled to protection*'.(National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979) The Report goes on to specify under its Applications section that capable research participants must be afforded the opportunity to choose '*what shall or shall not happen to them*' and that this opportunity is satisfied by '*adequate standards for informed consent*'. With respect to the latter statement about those with diminished autonomy, the Report states that respect for the incapacitated '*may require protecting them…while they are incapacitated*' and to utilise the '*permission of other parties*' in order to offer protection. The notion of respect for persons did not come into being with the Belmont Report, however. Lysaught (2004:665-680) provides a background for the development of respect for persons in bioethics from the early 1970s until publication of the Report almost a decade later.

Also in 1979, the first edition of the *Principles of Biomedical Ethics* by Beauchamp and Childress was published.(Beauchamp and Childress, 1979) Four eponymous principles were proposed, closely aligning with those of the Belmont Report with two major exceptions – respect for persons became respect for autonomy and non-maleficence was presented as a principle on its own having been teased out from the principle of beneficence. While these two principles sound similar, they differ in important ways most notably that respect for

autonomy no longer encompasses the non-autonomous in the realm of respect as the Report's principle of respect for persons does. As discussed above, Beauchamp and Childress (2013b:108) clearly state that those not capable of acting autonomously are not owed respect. Rather, there is a responsibility to protect such individuals because of their moral status.

Some see the change from respect for persons to respect for autonomy as problematic. For example, by drawing on the work of Paul Ramsey, published in 1970, Lysaught (2004:665-680) interprets '*respect*' as providing substantial protection for individuals because they are treated with care, not just as individuals, but in a relational sense. She sees the narrowing of Beauchamp and Childress' conception of autonomy to a concern with the details of informed consent limiting and criticises the lack of protection associated with respect for autonomy. Although she does acknowledge that protection is entailed under the principles of beneficence and non-maleficence, she claims that these do not '*carry the moral security of respect*' because they are described in utilitarian terms.

In a similar vein, Lebacqz (2005:99-110) refers to the transition from the Report's principle of respect for persons to Beauchamp and Childress' principle of respect for autonomy as a '*truncation*' of the original. She calls the change, which she interprets as meaning that those who lack autonomy are not due respect, '*a crucial and unfortunate move*'. In addition to the respect that should be due to those lacking autonomy being '*lost*', Lebacqz also objects to the singular focus on autonomy. She interprets this in the principle of respect for autonomy as mere self-determination or individual choice and disagrees with this limited conception of autonomy as having a role in defining persons rather than what she refers to (but does not explain) as '*true Kantian "autonomy"*'. She sees respect for autonomy having a direct but simplistic mapping onto '*the rule of "informed consent"*' and cites a feminist emphasis on relationality, connection and obligation as being of greater value than the singular focus on autonomy. By referring to the '*stultifying effects of contemporary liberal society*', Lebacqz (2005:103) clearly sees the prevailing liberal political framework with its emphasis on freedom of choice as a major causative factor in the '*lost*' respect for persons.
Taking a slightly different point of departure, Behrens (2018:126-134) at the outset of his article argues that the principles of respect for persons and respect for autonomy are in fact

one and the same. Despite not focusing initially on the transition the same way that Lysaught and Lebacqz do, he also takes issue with the strong individualism inherent in the principle of respect for autonomy and focuses his critique on what he sees as the inappropriateness of this principle in an African and broader communitarian context. Rejecting the adoption of moral relativism as a solution to this problem, Behrens suggests in a somewhat contradictory move that the principle of respect for persons is the better principle after framing it by reference to '*the Kantian tradition*' as partially interpretable in a communitarian sense and arguing for its compatibility in African society.(Behrens, 2018:131)

Responding to the problem of the person lacking capacity for rational thought, Behrens goes on to construct an account of personhood grounded in contemporary '*sub-Saharan moral notions*'.(Behrens, 2018:132-133) He draws on Metz' modal-relational approach to moral status which is based on the idea that moral status is derived from a communally situated relational capacity and is thus a spectral conception of moral status rather than a binary one. The degree of moral status thus entailed depends on whether an individual is capable of being both a subject and an object of a communal relationship or only an object. A normal adult would be the former but an individual with diminished capacity, such as a reduced level of consciousness, would be the latter. Behrens extends this conception of moral status to argue that those with full moral status also have agency – this is determined not by autonomy (self-determination) but by the ability to engage in communal relationships. Those unable to do so lack agency (but still retain a degree of moral status) and Behrens suggests that they should be protected in the same way that the Belmont Report characterises in its description of the principle of respect for persons.

For their part, Beauchamp and Childress state that Lysaught's criticism (and by extension that of Lebacqz) is '*mistaken*' because their position still implies moral respect due to the moral status of the individual who lacks capacity.(Beauchamp and Childress, 2013b:108) Whether this moral respect would be seen as equivalent to the respect due to personhood, as expressed by Lysaught and Lebacqz, is not clear. A weakness in the arguments made by Lysaught and Lebacqz about the turn away from respect for persons is that they never clearly explain how this position translates into the '*moral security*' deficit for those lacking autonomy that they claim it does or why the protection suggested by Beauchamp and

Childress is of lesser valence than that assumed by them to materialise from the notion of respect for persons. The charge made by Lysaught (2004:676) that the principles of beneficence and non-maleficence offer lesser protection because they are formulated by Beauchamp and Childress in utilitarian terms requires a stronger argument. It is hard to understand how the articulation of a duty of non-harm, even in rule utilitarian terms, would produce the effect claimed. Behrens' account of moral status and agency goes further than the communitarian arguments posed by Lysaught and Lebacqz, albeit with a completely different grounding, but in the end for those without capacity (or agency) Behrens falls back on the Belmont Report stating that respect translates into '*protecting them from exploitation and harm*' – something very close to what the principle of respect for autonomy requires.

Although the arguments are related, both Lysaught (2004:675-676) and Lebacqz (2005:101-103) both seem to take issue with the nature of autonomy proposed by Beauchamp and Childress rather than the shift of focus in respect from persons to autonomy. Behrens (2018:126-134) certainly does. They couch their aversion to autonomy as self-determination in the adoption of feminist, relational, communitarian and religious views of autonomy along with references to a Kantian grounding of respect for persons. Perhaps more importantly, both suggest a repudiation of a Millian conception of autonomy and the liberal political framework from which the principle of respect for autonomy draws its breath. These two examples are part of a broader pattern identified by May (2005:299-309) that he refers to as autonomy's '*fall from grace*', meaning that according to some communitarian and feminist critics autonomy (as expressed in the principle of respect for autonomy) is too individualist and lacking in its moral commitment to social roles, communal practices and relationships. May believes that these critiques are mistaken by conflating moral arguments and political obligations and also by adopting an incomplete perspective on autonomy. The impact of liberal political frameworks on autonomy in bioethics generally, and in research ethics specifically, will be discussed in the next section.

2.4. Respect for Autonomy and the Liberal Political Framework

In the critiques of Beauchamp and Childress' principle of respect for autonomy, limitations of the individualist idea of self-determination feature prominently. In pointing out these

limitations, critics typically lament a perceived break with Kantian tradition – which they see as the philosophical root of respect for persons – in favour of a Millian interpretation which is subsumed in the liberal political framework. Although Beauchamp and Childress have removed any foundational references to Kant from their explanation of the principle of respect for autonomy in the seventh edition of *Principles of Biomedical Ethics*,(Beauchamp and Childress, 2013b:101-140) the first edition did attempt to ground this principle in Kantian theory.(Beauchamp and Childress, 1979:56-60) Others have also invoked Kant when discussing the same principle, or just autonomy in a broader bioethical context (Dean, 2006:197-198) and Behrens (2018:128) sees the principles of respect for persons and respect for autonomy as roughly equivalent. But is this attribution of the principle of respect for persons or respect for autonomy to Kant's moral philosophy correct? Answering this question will help to illuminate the origins of individualism and self-determination in contemporary liberal politics which, I believe, is important in understanding the primacy of autonomy as a principle in modern bioethics discourse and in research ethics.

The contention that respect for persons derives from Kant's moral philosophy is usually based on interpretation of the second formulation of the categorical imperative, generally referred to as the Formula of Humanity: '*Act so that you treat humanity, whether in your own person or in that of another, always as an end and never as a means only*'.(Reath, 2003:352) For example, in criticising the turn from respect for persons as described above, Lysaught (2004:677) states: '*Kant has been turned on his head. Under the rhetoric of the principle of respect for persons—wherein persons ought to be seen as ends only and never solely as a means to others' ends—we find instead the principle of utility*'. However, this literal interpretation of person, humanity and ends, understood as describing individuals and social relations is in some real-world bioethical context, is unlikely to be what Kant was referring to. Neumann (2000:285-299) offers an interpretation of the formula of humanity that strongly suggests respect for persons, in the bioethical sense, was not what Kant had in mind.

Neumann (2000:285-299) thinks that this misinterpretation mainly centres on conflation of real empirical individuals (homo phaenomenon) with rational beings (homo noumenon) in Kant's writing. He clearly shows that, in the formula of humanity, Kant is referring to rational

beings and not flesh-and-blood empirical persons. Similarly, with this conception of a person in mind, personality refers to a very general, rational nature that is devoid of empirical and individual character traits, '*abstracts from everything that distinguishes me from other persons*' and is derived from what is shared with other rational beings, that is '*subjection to the non-natural, supersensible laws of morality*'.(Neumann, 2000:289) Furthermore, the basis for treating people as ends in themselves is their self-legislating, rational nature that exists as an end in itself. To treat another person as an end in themselves means to adopt the universal principles of practical reason – the same principles that they adopt for themselves as rational beings. Importantly, decisions about actions in the treatment of others are thus based only on universalizable principles of reason and not on the individual desires, inclinations or goals of others. Finally, contrary to the prevailing bioethical view that it is the individuality of persons that must be respected (and by extension, their choices), Neumann interprets Kant as holding that it is only the rational, self-legislating noumenal self, that deserves respect '*precisely for [its] capacity to transcend the confines of human individual natures, and therefore of nature itself*'.(Neumann, 2000:293-295)

Similar questions of interpretation as those posed by Neumann have been asked by Dean (2006:197-225) with regard to the principle of respect for autonomy, specifically whether it is reasonably possible to attribute the bioethical principle to Kantian moral theory and again specifically the Formula of Humanity. He notes the seemingly intuitive alure of what respect for autonomy stands for, namely self-determination and making one's own choices, and what the Formula of Humanity at face value seems to be saying about respecting the plans and values of individuals. However, Dean thinks it important not to rest on such an intuitive interpretation because mistaken attribution of the principle of respect for autonomy to Kant lends '*a false historical lustre*' to the bioethical principle and, perhaps more importantly, it prevents important conceptual analysis of the principle which might not only clearly differentiate it from Kant's conception of autonomy but also provide a '*clearer view*' of respect for autonomy as used today.(Dean, 2006:198)

Mirroring the case made above, Dean (2006:204-214) extracts they key features of Kant's writings about freedom and autonomy in order to provide a counterargument. He emphasises the importance of rationality and self-legislated moral principles in determining

actions rather than simply freedom of choice by stating that '*what makes a rational being free is not merely that she can choose, but that she can act on reasons, in the form of moral principles, that are produced by her own will*'.(Dean, 2006:207) Similarly, he clarifies that autonomy derives its importance in Kant's theory as the source of moral principles rather than the '*object of special moral treatment*'.(Dean, 2006:210) In agreement with Neumann's interpretation, he sees autonomy as a property of all rational agents because it is the source of moral obligations that are universally applicable. Finally, Dean dismisses the argument that '*humanity*' or the '*end in itself*' in the Formula of Humanity can be interpreted as freedom of choice, as proposed by some other interpretations. If it could, this might align the formula with the principle of respect for autonomy. However, he sees this as very unlikely given Kant's generally dismissive attitude towards the stature of freedom of choice alone as a defining characteristic of rational beings, making it an implausible instrument of unconditional worth for Kant.(Dean, 2006:212-214)

While the interpretations described above are certainly not the only ones, they do raise valid questions about the substance of claims that both the bioethical principles of respect for persons and respect for autonomy can be derived from Kantian moral theory. In addition to Neumann and Dean, others also share this position.(O'Neill, 2002; Kristinsson, 2007; Brassington, 2012) It is then difficult to see how the leitmotif of autonomy in bioethics, and particularly in research ethics, that of individualism, self-determination and freedom of choice as embodied in Beauchamp and Childress' respect for autonomy can be traced back to Kantian roots. If this is true, then what are the antecedents of this very dominant theme – where does it come from?

One obvious source is Mill. As described above, Mill's writings in *On Liberty* focus on his '*one very simple principle*' of liberty and his promotion of individuality and the development of individual character allowing growth according to internal principles and the following of individual nature.(Smith, 2003:395) This is for the betterment of the individual, who develops in an active and creative way and is pivotal to human happiness but also to the betterment of society. In arguing that there is no morally defensible reason for interfering with individuals in a free society, other than the promotion of safety to others, Mill also gives credence to the notion of respect for autonomy (i.e. to respect the autonomy of

others). This appears very close to Beauchamp and Childress' definition of autonomy, stated as a right '*to hold views, to make choices and to take actions based on their values and beliefs'* and the related duty to respect this right. That there is a strong flavour of Mill's philosophy on autonomy in the modern bioethical conception of autonomy and respect for autonomy seems undeniable.

But does reference to a particular moral theory such as Mill's alone explain the nature of autonomy as it is conceived in bioethics? May (2002, 2005) sees an important role for the prevailing political framework in determining how autonomy is conceived in society, and particularly how this applies in bioethics. While moral theory does certainly play an important role in shaping views on autonomy, May argues that regardless of the particular theoretical lens through which autonomy is viewed, '*political boundaries place fundamental limits on the social application of moral beliefs*'.(May, 2005:300) This view is based on accepting the social nature of decision-making in health care – related to both clinical patient care and research. Inasmuch as May is recognising the importance of the political framework in shaping how autonomy is conceived, he does this with reference to a particular political framework – that of liberal democracy. By this, he means a democratic system of government characterised by individual rights and freedoms and in which the deployment of political power is constrained by the rule of law (May writes with particular reference to the US).(May, 2005:301-302) He recognises that not all societies share such a framework and that this undoubtedly shapes how autonomy in health care is viewed and applied in those societies, but his main aim is to attempt to explain the nature of autonomy in modern bioethics discourse with the acknowledgement that this has been heavily influenced by liberal democratic socio-political values.

Liberal societies are characterised by tolerance of a plurality of values and the recognition of a diversity of views, in this case on morality but in a broader sense on a range of other things. Accepting this avoidance of a privileged position for any one moral theory or system, liberalism holds that the individual retains the right to decide on their own moral judgements rather than be subject to the imposition of a particular perspective.(May, 2002:2-3) This position is reminiscent of Mill's anti-conformist views and his determination to promote freedom of the individual in order to protect against '*tyranny*' of both the state

and the majority and maximise happiness in society. The liberal view on neutrality with regard to morality, and more broadly conceptions of the good, also draws on Rawls' theory of justice, itself premised upon an avoidance of particular philosophical or religious doctrines and promoting the judgement of individuals in determining the good.(May, 2002:2) This basic foundation of the liberal ideal is summed up succinctly by Taylor, cited in Neumann (2000:294) when he states that '*a liberal society must remain neutral on the good life, and restrict itself to ensuring that however they see things, citizens deal fairly with each other and the state deals equally with all*'.

In constructing an argument for the importance of the political framework as limiting the social application of moral theory, and hence a liberal conception of autonomy, May (1994:135-142) draws on two different perspectives of autonomy. The first is autonomy as '*autarkeia*', derived from Aristotle's use of the word for self-sufficiency primarily to describe a good and a primary aim of the early city-state in its independence from external influences (although it was also used to describe self-sufficiency in the context of friendship and character by Aristotle). May also sees in Kant's moral philosophy a likeness to autarkeia in the sense that the rational being and practical reason bring about self-legislated moral principles which are independent of principles that take into account the conditions of circumstance. The moral decisions autonomously made under the precept of universalizability are self-sufficient. While these features of moral reasoning may seem to be removed from a connection to political frameworks, May posits that over time there has been a transition and that Kant's moral conception of autonomy has '*influenced modern accounts of the autonomous determination of practical action, which have taken the Kantian idea of moral autonomy and developed notions of autonomous practical reasoning in Kantian terms*'.(May, 1994:136) He cites, among others, Rawls as having been influenced by Kant with the '*veil of ignorance*' representing a separation from extraneous contingencies in the interests of a pure formulation of justice.(May, 1994:138)

Having defined autonomy as autarkeia, May then points out that this conception is too burdensome for practical use associating its application to an '*austere*' existence.(May, 2005:305) This is because the very strict exclusion of personal interest in determining legitimate courses of action is at odds with the way individuals typically derive fulfilment

from life. In addition, autonomy as autarkeia does not permit appeals to authority of a legitimate form, such as drawing on the advice or expertise of a professional or abiding by regulations in everyday life. As an alternative conception, May proposes autonomy as self-rule. Although this might appear to be the same concept as that described by Beauchamp and Childress (2013b:106-108), for example, it is formulated in a way that emphasises not only self-determination of the individual but also, importantly, the social context, political framework and limitations within which individuals make their own decisions. Once again, May draws on Aristotle and his analogy of individuals in society being like sailors on a ship, focusing on the role of the helmsman who embodies the same characteristics as a ruler in a city-state. The role of ruler in this context is characterised as self-rule of the individual.(May, 2005:307)

The helmsman analogy in self-rule draws attention to the moderating effect of context, as a real helmsman on a ship would make their own decisions about steering the ship but within the constraints of prevailing weather conditions and other empirical factors. According to May (1994:139), Aristotle attributes the helmsman's abilities to '*practical wisdom*', an applied wisdom taking the individual's capabilities and contextual factors into account to determine a final course of action. On this account, external factors are not seen as impeding an individual's execution of self-rule if this is done through the application of practical wisdom. On the other hand, the abandonment of practical wisdom and reliance on purely external and unreconciled factors in determining action would not meet this definition of self-rule. May sees self-rule of this kind as typifying autonomous actions in a liberal democratic political framework.

Considering May's view, one possible argument weakening it might be that the system of rules inherent in a liberal democratic framework constitutes a source of interference with autonomous action as an external constraint. However, May contends that this conception of autonomy within such a framework serves as a footing for the attribution of responsibility for the actions of individuals. This is so because the framework itself does not take a position on the values that should guide individual decisions, leaving this to the individual as an expression of their autonomy. Consequently, conformity (or the opposite) to rules is brought about by autonomous decisions of individuals because the framework grants them

this power.(May, 2005:307-308) This idea is key in making the argument that autonomy is a coherent idea in a liberal political framework and this idea aligns with concept of self-rule following Aristotle's analogy. In May's words: '*this very role of autonomy within the liberal framework requires that external considerations such as rules, laws, social norms and other external influences be able to be taken into consideration consistent with an ascription of responsibility based on autonomy*'.(May, 2005:308) May also notes that this understanding constitutes an argument against communitarian critiques of autonomy as being too individualistic and isolationist. He sees the incorporation of external influences referred to above as including the important role of social relationships.

I have attempted to show in the above discussion that the modern bioethical principle of respect for autonomy, as defined by Beauchamp and Childress (2013b), does not have unequivocally valid grounding in Kantian moral theory despite the popularity of this view. Neither does the related principle of respect for persons. I have suggested that there is a fairly obvious and easily identifiable imprint of Mill's ideas about liberty in the principle of respect for autonomy, but this is less in the form of a distinct moral theory than it is in the form of Mill's political philosophy and his influence on liberal thought. As a modern bioethical concept, autonomy seems to owe most of its influence to the pervasiveness of the liberal democratic political frameworks in which it has evolved and within which its meaning and circumstances seem to be inextricably intertwined.

2.5. The Primacy of Autonomy in Bioethics

Beauchamp (2019:6-7) maintains that it was never the intention that principlism should prioritise the principle of respect for autonomy over other principles, or more broadly to prioritise any one principle over any other. While acknowledging that this was indeed the intention, Callahan (1996:41) argues that this is not how principlism has been applied in practice when he states: '*nothing has so exasperated me over the years as the deference given in bioethics to the principle of autonomy*'. Callahan (2003:505) sees principlism as a whole being simply an embodiment of liberal individualism and believes that the three principles (other than autonomy or respect for autonomy) are ultimately just autonomy in disguise: non-maleficence is really negative liberty, the autonomous '*right of bodily noninterference*', beneficence is a form of empowerment for individuals to '*live their*

autonomous lives' and justice enables individuals to make '*autonomous judgements in living their lives, unhampered by social inequities*'. Similarly, Wolpe (1998:43) argues, after also acknowledging the intentions of principlism as described above, that all four principles '*can never be given equal weight in American biomedical culture*', that autonomy has become '*the "default" principle of applied principlism, the principle to be appealed to when principles conflict*' and that this has produced a regrettable situation where this reliance '*asks autonomy to do the work of other principles*'.

Callahan (2003:497-498) attributes this primacy of autonomy to two factors – firstly, the decline in importance of what he refers to as '*foundational matters*' (broadly understood as moral theory) and secondly, '*the almost complete triumph of liberal individualism in bioethics*'. Wolpe (1998:43-53) provides an overview of factors that he considers having been responsible for the deep embedding of autonomy as a favoured principle in bioethics against the background of liberal individualism. He divides these into four broad clusters namely intrinsic factors, regulation and policy, the secularisation of bioethics and the role of medical authority. Intrinsic factors are those inherent in the four principles that prevent them being applied in an equally weighted fashion. Here Wolpe (1998:44-46) sees evolving and broader notions of harm in medicine (i.e. harm seen more as applying to ends than means), concerns about promotion of beneficence being construed as paternalism and a socio-political and health care system placing more emphasis on individual choice than justice as reasons all contributing to the diminution of these other three principles in favour of autonomy. Another important reason for this is the enabling of autonomy in practice because its application, relative to the other principles, is seen as well-established, easy to follow procedurally (through the process of informed consent) and uncontentious.

Within the domain of regulation and policy the principle of autonomy tends to also be easier to codify than the other principles, and this has certainly been the case in the USA.(Wolpe, 1998:46-48) Consequently, the principle of autonomy has been woven into the framework of rights and personal liberties, finding expression in rules, regulations and medical jurisprudence more generally. The secularisation of bioethics, which began in the 1970s, enhanced the prominence of rights, self-determination and principlism with the latter referred to as eventually becoming '*the secular equivalent of the Calvinist's*

decalogue'.(Wolpe, 1998:49) Medical authority, initially opposed to the intrusiveness of regulations in decision-making, soon accepted a growing influence of the principle of autonomy partly to shed the legacy of paternalism but also for other reasons. All of these factors, including the rise of institutional review boards in the case of research, and through legal processes in clinical medicine, has led to ethical problems being addressed by what Wolpe (1998:53) calls '*autonomy enhancers*' – longer, more technical and more complex informed consent documentation. Unfortunately, this has also led to a regulatory focus on the '*ritual*' of informed consent and less attention to the ethical nature of research and clinical care.

The views expressed above by Callahan and Wolpe relate to the early development of bioethics and how the US liberal political environment has influenced the approach to autonomy as a principle, an approach persisting to this day. However, Jennings (1998:258-261) traces even earlier roots of autonomy's development as a bioethical principle to the immediate post-war period and the ideological supremacy of the cold war Western alliance. As he puts it so clearly: '*Bioethics has grown out of and is unimaginable without the moral triumph and vindication of an open society: that is, a society respectful of individual rights and interests; dedicated to a moral style of reasonable moderation, compromise and mutual accommodation; and optimistic about the possibility of creating and sustaining a system of individual privacy, freedom of choice, equality of opportunity, and ordered liberty under law* '.(Jennings, 1998:259) This '*moral sensibility*' Jennings sees as meshing perfectly with the socio-political, anti-paternalistic liberalism of the 1960s and 1970s which '*rescued autonomy from the libertarian radicals of both the right and the left and turned it into the linchpin of mainstream ideological accommodation*'.(Jennings, 1998:259)

In summary then, the ascendence of respect for autonomy as a bioethical principle in research ethics seems to have fairly shallow roots in moral theory. As argued above, the Kantian notion of autonomy seems to bear little resemblance to the modern bioethical principle which is far more firmly grounded in Mill's ideas about individualism and liberty, ideas which have in turn been ingrained in the liberal political framework and its emphasis on individualism as described by May (2002, 2005). Acting in concert with the rise of the open society after World War II, and a product of the immediate aftermath of the war, the

importance of individual interests in research ethics was cemented by the Nuremberg Code and its insistence on voluntary research participation and informed consent. While informed consent is not necessarily a means of respecting autonomy (as I argue below), the Code's rigid urging of self-determination above all else did scaffold the broader rise of autonomy, often conceived of as meaning the same thing, during the later development of research ethics.

Much is made in the above discussion about the liberal democratic dispensation in the US. For example, this is the frame of reference for May (2002) and Wolpe's (1998) views on the political embedding of the principle of autonomy and also, but by contradistinction, Behrens' (2018) critique of individualism as a foundation of respect for autonomy. Considering the development of bioethics as a discipline, it is perhaps not surprising that research ethics inherits so much from Western liberal democratic political principles, regardless of whether one thinks this is a good or a bad thing. A natural question that arises is whether this influence, and particularly the influence of principlism and its foregrounding of the principle of respect for autonomy, transfers to non-Western settings, and particularly South Africa. Put another way, is the above discussion grounded as it is in Western liberal ideology, helpful in interpreting the role and influence of principlism and respect for autonomy in South African research ethics?

I believe that the answer to this question is that, regardless of any other characteristics of the South Africa's political milieu which may be interpreted as not classically liberal, it has since 1994 adopted fundamentally liberal values as a constitutional democracy. South Africa's Bill of Rights clearly prioritizes self-determination and freedom of choice – even with specific reference to research participation (as described in Chapter 1, Section 1.1.3.1). The health research legal framework, in the form of the National Health Act, is the same. Moreover, the research ethics regulatory framework as promulgated by the National Health Research Ethics Council's guidelines, espouses principlism as its foundational guide and highlights, in keeping with international research ethics guidelines(Council for International Organizations of Medical Sciences and World Health Organization, 2016; World Medical Association, 2024) the principle of respect for autonomy. Consequently, for better or worse, the interpretations and discussion above of influences exerted by moral theory and liberal

political principles on current conceptions of respect for autonomy in South African research ethics is transferable to this local context and explains, in foundational terms, these conceptions in more or less the same way it explains them in Western settings. In the next section I will discuss the relationship between the principle of respect for autonomy and informed consent.

2.6. Conclusion

In this chapter I have discussed a range of different conceptions of and ideas about autonomy, both those more conventionally associated with research ethics and others that have more recently attracted attention in bioethics more broadly. I have focused on the contemporary understanding of autonomy in research ethics – the principle of respect for autonomy – and I submit that its formulation in terms of individualism and self-determination is more a product of the liberal political framework in which it has evolved than any strong association with moral theory. This is an important point with reference to the moral weight assigned to autonomy's expression in research ethics in the form of informed consent – an argument that I take further in the following chapter. Respect for autonomy's grounding in the liberal political framework also explains why the principle of respect for autonomy – despite its originator's intentions – has come to dominate other principles so popular in research ethics today. This prominence of the principle of respect for autonomy has undoubtedly made consideration of how to approach research with those lacking the capacity for autonomous action challenging.

In the next chapter I provide greater detail about emergency care as a clinical discipline and about emergency care research after which I discuss in greater detail the problem of capacity and factors prevalent in emergency care research which interfere with capacity. This is followed by an in-depth discussion of informed consent building on the critical analysis of autonomy and the principle of respect for autonomy presented in this chapter.

CHAPTER 3: EMERGENCY CARE RESEARCH AND INFORMED CONSENT

3.1. Introduction

As described briefly in Chapter 1, emergency care research covers an extremely broad spectrum but for the purposes of this thesis the primary focus is on clinical interventional research. Even in this narrower band, a tremendous variation of clinical conditions and patient acuities exist because of the nature of emergency care itself and the settings that it is practiced in. This chapter begins by describing in greater detail the nature and heterogeneity of clinical emergency care and the scope of clinical interventional emergency care research. In a subset of research participants, capacity for informed consent can be a problem – ranging from those who are unconscious or unresponsive to those who are conscious and capable of decision-making but may be affected by factors in the capacity penumbra such as pain and anxiety. The interplay between such factors and capacity for informed consent is discussed in greater detail below with emphasis on a number of clinical emergency conditions for which empirical data exists. Finally, informed consent in health research is critically discussed in detail – its characteristics and constituents according to the most widely accepted view, its relationship with respect for autonomy and several alternative views of informed consent that claim to address what is perceived as the biggest limitation to valid informed consent – the understanding by research participants of large volumes of complex information.

3.2. Emergency Care: Anyone, Anything, Anytime

The right of all people in South Africa to not be refused emergency medical treatment is upheld in s7(3) of the Constitution and s5 of the National Health Act (No 61 of 2003). However, the word '*emergency*' is not defined in the Constitution, nor is it defined in the National Health Act. Legal definitions of the word emergency in South Africa come from two sources:

a) Regulation 7 of the Medical Schemes Act (No 131 of 1998), which defines an 'emergency medical condition' as: '*the sudden and, at the time, unexpected onset of a health condition that requires immediate medical or surgical treatment, where failure to provide medical or surgical treatment would result in serious impairment to bodily*

functions or serious dysfunction of a bodily organ or part, or would place the person's life in serious jeopardy'.(South Africa, no date)

b) The Soobramoney v Minister of Health High Court judgement, which defines an 'emergency' as: '*a dramatic, sudden situation or event which is of a passing nature in terms of time. There is some suddenness and at times even an element of unexpectedness in the concept "emergency medical treatment"*'.('Soobramoney v Minister of Health (Kwazulu-Natal) (CCT32/97) [1997] ZACC 17; 1998 (1) SA 765 (CC); 1997 (12) BCLR 1696 (27 November 1997)', no date)

As Kramer has pointed out,(Kramer, 2008:53-54) both of these definitions have deficiencies, although the Regulation 7 definition is more comprehensive. The above definitions are deficient mainly in relation to the use of words such as '*sudden*', '*unexpected*' and '*dramatic*' which should not be seen as prerequisites for the definition of all emergencies because many emergencies arise from the existence of chronic underlying disease making their occurrence, as an extension of those diseases, not necessarily '*sudden*' or '*unexpected*'. In criticising the above definitions, Kramer (2008:54) suggests a different definition of emergency medical treatment – however this is extremely long and complex and focuses on treatment rather than a description of what an emergency is.

In its definition of Emergency Medicine, the Emergency Medicine Society of South Africa refers to an emergency as '*acute and urgent aspects of illness and injury affecting patients of all age groups with a full spectrum of undifferentiated physical and behavioural disorders*.'(Emergency Medicine Society of South Africa, 2008) This reference to an emergency as something '*urgent*' or '*acute*' draws attention to the time sensitivity of emergencies, but avoids describing them as something unexpected or '*dramatic*'.

In terms of definitions used in other countries, the US Emergency Medical Treatment and Active Labor Act (EMTALA) provides perhaps the most comprehensive definition of an '*emergency condition*': (*U.S. Code § 1395dd - Examination and treatment for emergency medical conditions and women in labor*, no date)

'(A) a medical condition manifesting itself by acute symptoms of sufficient severity (including severe pain) such that the absence of immediate medical attention could reasonably be expected to result in-

(i) placing the health of the individual (or, with respect to a pregnant woman, the health of the woman or her unborn child) in serious jeopardy,

(ii) serious impairment to bodily functions, or

(iii) serious dysfunction of any bodily organ or part; or

(B) with respect to a pregnant woman who is having contractions—

(i) that there is inadequate time to effect a safe transfer to another hospital before delivery, or

(ii) that transfer may pose a threat to the health or safety of the woman or the unborn child.'

Once again, the acute nature of an emergency is highlighted together with the acuity of the condition and its potential to bring about serious impairment if not attended to '*immediately*'. Importantly, the EMTALA definition explicitly cites severe pain as an acute symptom worthy of classification as an emergency – something too frequently not done in emergency care.(Turturro, 2002)

It is clear from the above definitions that there is no all-encompassing, perfect definition of an emergency. However, a reasonable combination of the key, common features of these definitions emphasises that an emergency is:

A medical condition, including injury, that presents with acute symptoms, and that will likely cause significant dysfunction and impairment in a short period of time if not treated immediately.

Emergencies can occur at any time or place and spare nobody, encompassing an extremely diverse range of disorders and injury patterns. Hence the expression '*anyone, anything, anytime*' that has been used in the title of a popular account of the history of emergency medicine in the US.(Zinik, 2006)

The term '*emergency care*' refers simply to the professional care provided to anyone experiencing an emergency condition as defined above. Historically, the term '*emergency medicine*' has been used to describe the medical specialty concerned with the management of emergencies, while '*emergency care*' has been used to describe the broader discipline including that engaged in by non-medical professionals such as paramedics and nurses (this is the meaning used throughout this thesis).

The practice of emergency care is centred in health care facilities, with the point of entry being the Emergency Department (ED), and in the pre-hospital (also sometimes referred to as the out-of-hospital) environment. Emergency Departments may exist in a range of different health care facilities, from those in small towns servicing mainly rural areas to those in large urban centres. Likewise, the range of supporting services and specialties available to a given ED varies, with rural EDs having to transfer patients in need of more specialised investigations or referrals while those in urban centres typically have access to such support within the same facility or close by. Patients requiring emergency care in the ED are typically transported there by pre-hospital emergency care services – referred to collectively as Emergency Medical Services (EMS).

While hospital-based emergency care covers a diverse range of EDs in different geographic locations and populations and with a wide array of resources, emergency care in a hospital occurs in a relatively controlled environment. Emergency care delivered in the pre-hospital environment, on the other hand, occurs wherever and whenever the emergency occurs – encompassing a tremendous array of possibilities all of which necessitate adaptation to an uncontrolled and sometimes dangerous setting. Pre-hospital emergency care can take place in the privacy and intimacy of patient's homes, but also in full view of the public. It may involve a 20-minute trip to hospital in a city, or a five-hour flight in an aircraft from a remote location.

Emergency medicine as a specialty in South Africa is young, having been established only 20 years ago.(Balfour, 2006) While the opening of a specialist register in 2005 marked this point, EDs in South Africa have always offered emergency care in both private and public hospitals, albeit without the uniform academic structure that now exists. Pre-hospital

emergency care came into existence in a formalised way in the mid-1970s and progressed rapidly with parallel development of emergency vehicles and equipment, dispatch processes and training. The mid-1980s saw the introduction of pre-hospital emergency care education in the Higher Education band, a change from the short course training that had existed up until that point.(MacFarlane, van Loggerenberg and Kloeck, 2005) Several levels of pre-hospital emergency care qualifications and personnel currently exist from basic through to advanced life support level, all of which require registration with the Health Professions Council of South Africa.

Emergency care personnel in South Africa, at all levels and of all qualifications, are well known to face a challenging work environment characterised by the prevalence of major injury, much of it caused by inter-personal violence and road traffic accidents. Injury is one component of South Africa's quadruple burden of disease, with the other components being accounted for by maternal, newborn and child health, HIV/AIDS and tuberculosis and a growing prevalence of non-communicable diseases.(Norman *et al.*, 2007; Pillay-van Wyk *et al.*, 2016) While the structure of South Africa's health care system is designed in such a way that non-urgent cases are seen at primary health care facilities, in reality many of these patients find their way to EDs at district, regional or tertiary hospitals. For many years, the '*casualty department*' used to be the entry point to the hospital for many sick (but non-urgent) patients and this has not changed a great deal, placing a significant burden on ED staff due to overcrowding.(Ruit and Wallis, 2020)

A similar situation is found in the pre-hospital environment with a significant demand placed on the EMS. This is partly due to the large number of emergency calls – many of which are injury-related - but also due to usage of the EMS for transport of non-urgent cases – a situation analogous to the crowding of EDs with non-urgent patients. A further layer of demand is placed on EMS due to the servicing of inter-hospital transfers which draws resources away from primary response. Pre-hospital emergency care personnel find themselves not only having to cope with the challenges of clinical care in this environment, but also increasingly to deal with violent attacks perpetrated against them in the course of carrying out their duties.(Fambisa, 2019)

Because an emergency often involves an acute occurrence of discomfort or pain and may equally acutely bring a patient's awareness of their own mortality to the foreground, it is almost always associated with a degree of anxiety and fear. While this is true of emergency care in the ED, the effect is heightened in the pre-hospital environment due to the uncontrolled and sometimes hostile environment which can be characterised by adverse environmental conditions, poor lighting, noise and the presence of strangers. These factors all contribute to the difficulty with which patients in this kind of environment, even if they are fully conscious, are able to comprehend clinical or other information and make informed choices.

3.3. Emergency Care Research

In its earliest, formative stages – during the 1970s and early 1980s – the practice of emergency care relied on clinical management strategies and procedures that were mainly borrowed from other disciplines such as surgery and anaesthesia and translated for application in emergencies. This was true of emergency care practiced in the ED, but also of pre-hospital emergency care where little to no clinical evidence to support management approaches in this environment existed at the time. Since then, the accumulation of clinical evidence in emergency care has gained momentum through the steady increase in emergency care research conducted throughout the world over the last three decades.

3.3.1. The Growth of Emergency Care Research

In a retrospective review spanning the decade between 1996 and 2005, Wilson and Itagaki identified 14 708 published articles indexed in Medline having at least one author affiliation to an ED.(Wilson and Itagaki, 2007) This comprised 0.28% of all the indexed citations during this period. They also identified an annual increase in publication rate of 0.8% (117 articles per year) overall, and for all clinical trials as well as randomised clinical trials (five articles per year each). Countries with the greatest share of indexed emergency care literature output were the USA (59%), UK (8%) and Japan (5%). Analysis of clinical trial publications over a four year period, between 2008 and 2011, found that 163 emergency care-related clinical trials had been published (indexed in Medline) and that these trials covered a broad range of clinical topics including analgesia (most common), injury, cardiovascular emergencies and pre-hospital emergencies.(Jones *et al.*, 2013) Wilson *et al*. found a strong

positive correlation between emergency conditions treated in EDs and emergency conditions researched and published between 1996 and 2006, suggesting that emergency care research in this series was focused predominantly on conditions commonly encountered in EDs.(Wilson *et al.*, 2012)

Emergency care research in Africa has also undergone significant growth since the establishment of emergency medicine as a specialty in South Africa, and subsequently in other African countries. In a 15-year review of African emergency care literature Mould-Millman *et al.* (2019) describe a 10-fold increase in published research output per year when comparing the first half of the 1999 – 2014 review period to the last half. Most of the research in this review (75%) was observational in nature, focused on epidemiology or emergency care systems and involved undifferentiated emergencies. Only roughly a quarter (28%) of the reviewed literature was interventional, with six clinical trials. South African emergency care research comprised the greatest proportion of literature in this review (27%), with the most clinical care and interventional articles. The preponderance of observational research in this review of African review of emergency care research output underscores the early development phase of African emergency care research in general.

3.3.2. Examples of Emergency Care Research

Broadly speaking, emergency care research that involves considerations of informed consent falls into three main categories: (i) retrospective record reviews, (ii) observational research and (iii) clinical trials. A few examples of such research from the emergency care literature are summarised in Table 3.1 below.

Table 3.1: Emergency Care Research Examples

Research Category	Aim	Informed Consent Implications
Retrospective	To describe out-of-hospital cardiac arrest survival over a period of four years in 10 North American sites.(Zive *et al.*, 2018)	Patients were in cardiac arrest at the time of data collection and would not have been able to give informed consent. Data were collected as part of an ongoing epidemiological registry on resuscitation outcomes.
Observational: Cohort	To determine predictors of adverse outcomes in a cohort of older (age > 65	Only those patients having the capacity to give informed consent were included.

Research Category	Aim	Informed Consent Implications
	years) ED patients.(Zelis *et al.*, 2019)	
Observational: Case-Control	To describe associations between ED diagnoses and suicide among youth (10-25 years of age).(Rhodes *et al.*, 2019)	Cases would not have been able to give informed consent.
Observational: Case-Control	To determine whether helicopter transfer improved 30-day mortality over ground transfer in major trauma.(Stassen, Alkzair and Kurland, 2020)	Neither cases not controls would have been able to give informed consent.
Clinical Trial	To determine the effect of corticosteroids on death and disability after traumatic brain injury (MRC CRASH Trial).(Edwards *et al.*, 2005)	Patients would have had varying degrees of decreased levels of consciousness at the time of enrolment and would not have been able to give informed consent.
Clinical Trial	To determine whether primary percutaneous intervention or pre-hospital fibrinolysis is associated with better outcomes after S-T elevation myocardial infarction.(Roule *et al.*, 2016)*	Only those patients having the capacity to give informed consent were included. Patients would all have been experiencing a myocardial infarction at the time of enrolment in each of the trials.
Clinical Trial	To determine effect of tranexamic acid on death, disability, vascular occlusive events and other morbidities in patients with moderate to severe acute traumatic brain injury (CRASH-3 Trial).(CRASH-3 Trial Collaborators, 2019)	Patients would had decreased levels of consciousness at the time of enrolment and would not have been able to give informed consent.
Clinical Trial	To determine the effect of adrenaline on survival from out-of-hospital cardiac arrest (PARAMEDIC-2 trial).(Perkins *et al.*, 2018)	Patients would have been in cardiac arrest at the time of enrolment and would not have been able to give informed consent.
Clinical Trial	To determine if a supraglottic airway device was superior to tracheal intubation in the initial airway management of out-	Same as above.

Research Category	Aim	Informed Consent Implications
	of-hospital cardiac arrest patients (AIRWAYS-2 Trial).(Benger *et al.*, 2018)	

* Reference is a systematic review and meta-analysis of 10 similar clinical trials.

While there are also examples of emergency care research involving participants that are capable of giving informed consent, the above examples highlight some of the problems with lack of capacity in clinical research and particularly in clinical trials. In particular, excluding patients that do not have capacity for informed consent will typically either make the above studies unfeasible as they are the population of interest. Or it may significantly limit and possibly bias samples. Capacity for informed consent will be explored in greater depth below.

3.4. The Problem of Capacity in Emergency Care Research

Competence as a threshold requirement for informed consent has been described in the previous chapter. Many informed consent texts and guidelines, including the South African National Health Research Ethics Council's guidelines,(Department of Health, 2024) use the term capacity with reference to decision-making capability. Individuals lacking in this capability are considered to be incapacitated, although it is not clear at what point exactly this occurs. Because the terms capacity and incapacitated are used in the South African research ethics guidelines, they will be used here as of interchangeable meaning with the term competence (and incompetence) as proposed by Beauchamp and Childress. (Beauchamp and Childress, 2013c:114)

The most easily understood problem of informed consent in emergency care research is that of the incapacitated patient, most often imagined as the unconscious or unresponsive patient. In this case, the lack of decision-making capacity is obvious and the details of informational complexity, disclosure, voluntariness or anything else are irrelevant. All that is left in such cases, is to consider how the ethical principles of autonomy, beneficence and non-maleficence may be balanced through the possible adoption of strategies such as proxy consent or deferred consent that are suggested in various forms in a number of different research ethics guidelines.

The reality of emergency care and the effect of emergency conditions (as defined above) on decision-making capacity is more complex than the hypothetical dichotomous example of the unconscious (incapacitated) and conscious (capacitated) patients. Many patient-related factors associated with emergencies such as more subtle alterations in consciousness, pain, anxiety and the effect of drugs may interfere with capacity. Naturally, these factors exist in varying degrees in any given emergency or patient and may not always erode capacity to the extent that informed consent is not possible. However, given the complex nature of information that needs to typically be communicated in interventional clinical research, even relatively minor impairments of capacity may prove problematic.

Bester, Cole and Kodish (2016) have suggested that, in addition to patient-related factors such as those mentioned above, two other sets of factors – and interactions between them – may impede capacity to give meaningful informed consent. The set of information-related factors refers principally to the complexity of information disclosed to patients, which they are supposed to understand and on which they are required to base their decision-making. Bester, Cole and Kodish (2016) argue that this complexity can be considered to exist on a sliding scale, similar conceptually to the notion of capacity itself existing on a sliding scale. The context of their discussion of these factors is informed consent for clinical care, and in this case the sliding scale may range from information about a very simple and minor clinical procedure through to a major and very complex one. Information-related factors must also impact on the capacity for informed consent for research but would very likely constitute a more significant factor given that research information often tends to be of a more complex nature, as argued above. The complex nature of research information may thus interact with patient-related factors, for example pain, to make what may otherwise have been comprehensible information less so, thereby impeding capacity.

The second set of factors identified by Bester *et al*. as potentially having a negative effect on capacity is communication-related factors.(Bester, Cole and Kodish, 2016) This is taken to mean the factors influenced by a clinician's skill in communication and to what extent communication aids might be used if necessary. Once again, the context of Bester *et al*. is the clinical environment, but communication-related factors must play a role in research particularly considering that the clinical research environment in emergency care research is

effectively identical to the clinical environment. Bester *et al*. do not venture beyond the communication skill of the clinician when describing communication-related factors, perhaps because they imagine clinical encounters to take place in a relatively controlled and orderly environment. However, the environment in which research is taking place – particularly clinical research – must also have the potential to influence communication of information in a way that might negatively influence capacity. Noise, interruptions caused by fast-paced and urgent procedures together with the presence and interaction of a team of clinicians (rather than a one-on-one interaction) may well interfere with the smooth transmission of information and may interact with patient- and information-related factors to reduce capacity for meaningful informed consent.

While the three factors described above – patient-related, information-related and communication-related – offer a useful way of thinking about possible negative influences on capacity for informed consent in emergency care research, very little empirical evidence exists to support or add detail to them and gauge the magnitude of their effects on capacity. Of the patient-related factors mentioned above such as more subtle alterations of consciousness, pain and anxiety, only pain has been subjected to empirical research in relation to informed consent. Similarly, of the vast range of possible emergency conditions that may be encountered in the ED or prehospital environment, only the effects of two – acute myocardial infarction (AMI) and stroke – have been empirically studied in relation to capacity for informed consent. These studies will be summarised and discussed below.

3.4.1. Acute Pain

Acute pain is a presenting symptom in as many as 78% of ED visits.(Cordell *et al.*, 2003) Even in situations where acute pain is not necessarily the presenting symptom, it is commonly related to pathologies that are associated with emergency care. Logically, it would seem reasonable to assume that acute pain, especially severe pain, might adversely affect cognitive function of an individual experiencing it to the point that this may negatively influence capacity to give informed consent for research. However, there is a lack of empirical research investigating the effects of acute pain on cognition and capacity. The effects of chronic pain on cognitive dimensions such as attention, memory, information processing and executive function – all of which may be important in the determination of

capacity – have been collated in a systematic review by Moriarty *et al*.(Moriarty, McGuire and Finn, 2011) While some of these effects are quite significant, there are two limitations with regard to capacity as this relates to acute pain in an emergency setting. Firstly, the effects of chronic pain cannot be generalised to acute pain because of several factors which frequently accompany chronic pain and that may also affect cognition. These include anxiety, fatigue and depression – factors that are far less likely to be co-morbid with acute pain (although anxiety may be an exception). Secondly, even if the effects of chronic pain were transferable to acute pain, the effects that have been identified remain of a theoretical nature as they are based on standardised tests of various cognitive functions.

Only a single study, a pilot study, has directly investigated the effect of acute pain on capacity for informed consent. Cowan, Klerman and Ma (2015) quantified capacity for informed consent using the MacArthur Competence Assessment Tool for Clinical Research (MacCAT-CR) in a convenience sample of 34 18 - 60 year-old ED patients with acute pain of varying aetiologies. The mean pain score (measured on a visual scale) was 7/10 and pain score did not significantly correlate with any of the MacCAT-CR subscales of understanding, appreciation, reasoning and expressing a choice. The majority of patients did achieve a predefined score cut-off for the MacCAT-CR understanding subscale suggesting adequate understanding of the research information provided. An obvious limitation of this study is its small sample, drawn from a single ED. Nevertheless, this evidence suggests that the single symptom of pain at a moderate level does not significantly reduce capacity for informed consent measured with the MacCAT-CR. Other empirical research on capacity in emergencies has focused on specific conditions rather than discrete symptoms, with most of the available data derived from studies on AMI.

3.4.2. Acute Myocardial Infarction

Acute myocardial infarction involves a sudden interruption of oxygenated blood supply to a part of the heart. In most victims it is associated with acute, severe chest pain and what medical texts typically refer to as a '*sense of impending doom*'.(Zipes *et al.*, 2008) Aside from these two symptoms, there may be others such as nausea, or light-headedness and disorientation due to a sudden inability of the heart to adequately supply the brain with oxygenated blood. In a minority of cases, usually due to arrhythmias, patients may

experience a more severe cardiovascular collapse rendering them unresponsive or they may even experience cardiac arrest – a cessation of normal cardiac contraction which is equivalent to clinical death. For those in whom these acutely lethal complications do not occur, the most urgent goal of emergency care is to restore blood flow to the injured heart as quickly as possible either through percutaneous coronary intervention or the administration of a fibrinolytic drug. Because of the high prevalence of ischaemic heart disease and AMI in many populations, clinical trials of these interventions (and combinations of interventions) have been carried out since the 1970s.

Capacity for informed consent has been studied in the acute phase of AMI, either during real clinical trials or by using hypothetical information considered typical of the type presented to AMI patients during a clinical trial. Smithline, Mader and Crenshaw (1999) assessed the capacity of patients with AMI who had been enrolled into a fibrinolytic drug trial using the Wechsler Adult Intelligence Scale-Revised (WAIS-R). This scale, consisting of three subtests assessing digit span, comprehension and similarities was considered by the authors to quantify many of the cognitive functions underpinning capacity for informed consent. The WAIS-R was administered in approximately 10-15 minutes, within 15 minutes of trial enrolment and the authors considered a scaled score of less than five points on any subtest as suggesting inadequate capacity. Amongst 25 AMI patients, eight (32%) scored below five points on at least one subtest and were considered '*impaired*' in relation to capacity for informed consent. This was in contrast to only two patients (8%) who were judged by their treating emergency physicians to be impaired.

In a qualitative study by Ågård, Hermerén and Herlitz (2001) 31 patients who had been enrolled in two AMI-related clinical trials were interviewed after their initial treatment. The interviews were semi-structured and patients were asked about their knowledge of the research, their feelings about being included and their attitudes towards the informed consent process. After analysis and review of the data these authors concluded that very few patients interviewed believed they were competent at the time of giving informed consent. Most cited altered levels of consciousness or pain as reasons for this. Similar results were observed by Gammelgaard, Mortensen and Rossel (2004) in a survey conducted after a Danish trial comparing the effectiveness of percutaneous coronary

intervention and fibrinolysis in AMI. Participants included both those who had given consent and those who had not. In both groups, around a quarter of patients indicated that they did not feel capable of deciding whether or not to participate in the trial at the time that informed consent was sought.

3.4.3. Stroke

The pathology of most strokes somewhat resembles that of AMI, with a sudden interruption of blood flow to a part of the brain. Consequently, the fibrinolytic drugs used in treating AMI are sometimes used in the treatment of stroke and these have been the focus of clinical trials, along with other forms of treatment. Stroke research also shares the reliance on short intervention time frames with AMI research, with diagnostic screening and informed consent processes having to be completed in a very short space of time in order to maximise the benefit of trial interventions. However, because of its interference with blood flow to the brain, the potential of stroke to negatively affect capacity for informed consent appears to be significantly greater than that of AMI.

Few empirical studies have objectively assessed capacity for informed consent in patients with stroke. Janssen *et al.* (2019) used their own assessment rules, based on subsets of the National Institutes of Health Stroke Scale (NIHSS) scores derived from a sample of 1,526 stroke patients whose data were entered into an ischaemic stroke registry. Two assessment rules were applied, one '*strict*' and one '*mild*', based on selected elements and scores of the NIHSS elements related to decision-making capacity. When the strict assessment rule was applied on admission, only 57 (4%) of patients would have been considered to have adequate capacity for informed consent. When the mild rule was applied, this increased to 306 (20%). These percentages increased somewhat after 24-48 hours.

Other studies, while not objectively measuring informed consent capacity, have documented the number of patients in various stroke trials that have been clinically judged to have adequate capacity for informed consent. For example, Demarquay *et al.* (2005) found that 13 out of 56 stroke trial patients (23%) were considered able to give written informed consent. Aphasia was cited as the main factor for inadequate capacity in 29 patients (68%). Kane *et al.* (2006) in a similar type of study involving a population of stroke

trial patients found a very similar percentage (24%) that were considered to have adequate capacity for informed consent. In both of these studies, increasing age and stroke severity were predictors of inadequate capacity for informed consent. In a study that assessed the relationship between brain lesion volume and capacity for informed consent amongst 56 stroke trial participants, 18 (32%) had been judged to be capable of written informed consent and the remainder had been enrolled with proxy consent.(Dani, McCormick and Muir, 2008) Lesion volume and NIHSS score were found to be related to capacity for informed consent, with those patients having small lesions and lesser neurological deficits making up the majority of the informed consent group.

3.4.4. The Uncertain Penumbra of Capacity in Emergency Care Research

The empirical research described above, related to acute pain, AMI and stroke, sketches an incomplete but worrying picture of capacity for informed consent in emergency care research. All of these studies describe very questionable capacity in at least a subset of patients – patients that would most likely not be placed in the obviously incapacitated category by those screening them for enrolment in research.

In many instances, where research involved interviews with patients, specific reference was made to the difficulty of grappling with written informed consent during the early stages of an emergency (such as AMI for example).(Ågård, Hermerén and Herlitz, 2001; Gammelgaard, Mortensen and Rossel, 2004) Patients who self-assessed after the acute emergency said that they did not believe they had adequate capacity for informed consent the way this was done, which required them to read lengthy and complicated information letters in addition to any verbal explanations given to them. For example, one patient in the study by Agard *et al*. said:(Ågård, Hermerén and Herlitz, 2001)

> *'They asked me if I wanted to take part and I wrote down my name. I did not read what I signed. I didn't care because of my pain. I tried to read the information but I didn't get it.'*

Many patients, and researchers who have described their experiences and opinions of the consent process, have suggested that such '*standard*' approaches to informed consent are

not viable under emergency conditions and have recommended a variety of alternatives including the use of simpler, verbally-delivered information.(Ågård, Hermerén and Herlitz, 2001; Williams, French and White, 2003; Gammelgaard, Mortensen and Rossel, 2004; Dickert, Llanos and Samady, 2012)

The realisation that informed consent procedures in clinical trials involving emergency research may be too complex is at odds with the traditional view of informed consent and capacity under such circumstances. It is widely acknowledged that greater research risk requires a higher standard of evidence of competence. This approach does not seem to acknowledge what research participants have said – that the complexity of information is a factor on which competence depends. Paradoxically, lower risk research for which weaker evidence of competence is required may more often be associated with simpler information – a factor that appears to enhance competence. Higher risk research, for which stronger evidence of competence is required, may more often be associated with much more complex information – a factor that appears to reduce competence. Unfortunately, legal and other requirements that result in long and technically complex information letters in an attempt to make consent informed may have the opposite effect. As some of the above studies suggest, and the views of clinicians corroborate,(Iwanowski *et al.*, 2008) patients simply do not read them and make their decisions based on verbal information from researchers or clinicians.

In conclusion, there is some evidence to suggest that the line between sufficient and insufficient capacity for informed consent in emergency care research is difficult to establish. While this is a well acknowledged problem with the determination of capacity in general, the existence of pain, anxiety, altered consciousness and other factors may give rise to a '*penumbra*' of questionable capacity that is not well recognised and that may significantly increase the number of patients not capable of informed consent in such circumstances. It seems clear that the dichotomy of capacitated and incapacitated patients in emergency care research, with the latter comprised only of those who lack full consciousness, is false.

3.5. Informed Consent in Health Research

Conventionally, informed consent in health research is thought of as application of the principle of respect for persons (National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979) or, as Beauchamp and Childress conceive it respect for autonomy. (Beauchamp and Childress, 2013b:121) On this view, a researcher shows respect for the autonomy of research participants by engaging in the process of informed consent which, very simply, offers them a choice regarding their participation thus affirming their individuality and self-determination. Although this idea of a tight bond between respect for autonomy and informed consent is widely accepted in research ethics, it has been questioned by some.(O'Neill, 2002; Taylor, 2004; Kristinsson, 2007; Manson and O'Neill, 2007; Wilson, 2007) In the following section I will first describe in more detail the '*standard view*' as put forward by Beauchamp and Childress (2013b:121-141) and discuss the elements of informed consent referred to by the Belmont Report and other authors. After this, I will engage with the dissenting views that claim informed consent to be more of a legalistic ritual and that refute its role in respecting autonomy. Finally, I will discuss alternative approaches to informed consent that may have application in some emergency care research settings where prospective participants would be expected to struggle with the large volumes of information typically required to be understood in the standard approach to informed consent.

3.5.1. Beauchamp and Childress' Conception of Informed Consent

Beauchamp and Childress interpret informed consent in two ways – what they refer to as the two '*meanings*' of informed consent.(Beauchamp and Childress, 2013b:122) The first meaning is closely aligned to the principle of respect for autonomy as representing an authorisation of research participation that is arrived at by an individual without external control, with understanding and that represents an intentional action. The second meaning is not directly concerned with the principle of autonomy, but rather with social, institutional or legal norms or requirements. This meaning is concerned simply with a '*checkbox*' of having complied with, for example, an institutional (and most likely a legal) requirement to complete an informed consent process (for example a consent form) with a research participant. Clearly, this latter meaning is not one that should be taken, on its own, to have any kind of validity or substance as a research participant may well have met this

requirement without really having given informed consent if they do not adequately understand what their participation entails.

3.5.1.1. Elements of Informed Consent

In practice, informed consent is often broken down broadly into two elements; information and consent. The former is what is provided to a research participant, that they are required to understand, and the latter is a record of the fact that they have made a decision to participate (on the basis of the understood information) and have authorised this. These two elements characterise informed consent as it might be meant according to Beauchamp and Childress' (2013b:124) second meaning from the previous section.

The Belmont Report describes three elements of informed consent; information, comprehension and voluntariness. (National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979) Information is described as being, in its scope, what a '*reasonable volunteer*' would expect to be informed of emphasising the fact that research participation is different to receiving clinical (proven) care and that it is not known to be effective. The context and conditions under which informed consent is obtained are emphasised in relation to comprehension, as is the principle that those with impaired capacity should be given an opportunity to make choices regarding their participation to the extent that this is possible. Comprehension is also described as encompassing the choices of a proxy in cases where an individual is incapacitated. Voluntariness emphasises that research participants must make their choice to participate freely and not when influenced by coercion or undue influences such as inducements. The role of hierarchical power relationships in affecting voluntariness of participation is also described. Thus, these three elements bear relationship to both the first and second meanings of Beauchamp and Childress above. In them we see very basic '*check box*' elements, but also – especially by reference to voluntariness – purported linkage to the principle of autonomy.

Subsequent texts describing elements of informed consent, of which there are many, typically expand on the three elements of the Belmont Report. For example in work published shortly after the Belmont Report Faden, Beauchamp and King (1986:274) refer to

five elements; disclosure, comprehension, voluntariness, competence and consent. This is expanded even further by Beauchamp and Childress into seven elements, each placed into one of three broader grouping categories.(Beauchamp and Childress, 2013b:124) These seven elements will be discussed further below.

Threshold Elements

Competence

Competence, what Beauchamp and Childress (2013b:115-120) define as the ability to understand and decide, is considered a threshold element meaning that it is a foundational requirement for the other elements, rather than an element itself. While the definition of competence may be relatively simple, reaching a decision about whether a research participant may or may not be competent is notoriously difficult. This is particularly so in emergency care research where a range of factors such as alterations in consciousness, anxiety, pain and effects of treatment (for example sedation or analgesia) frequently interfere with cognitive ability and judgement. In some cases, such as unconsciousness, capacity (or the lack thereof) can be easy to judge, just as in cases where individuals have low acuity conditions. However, there are many possible grades of competence between these two that are subject to the effects of the factors mentioned above.

Determination of competence according to some standard cuts across a combination of ethical, legal and medical criteria and judgements. Rather than adopt an approach where the application of a standard is aimed at determining competence, Beauchamp and Childress (2013b:117-120) advocate a standard of incompetence. That is, working forward from an assumption of competence which holds unless a determination of incompetence can and should be made. A cluster of standards are proposed by Beauchamp and Childress that may be used alone, or in combination, as a way of determining competence. Broadly speaking, these cover the areas of ability to formulate a preference, ability to understand information and an ability to reason in relation to an important decision with consequences. It is a well-acknowledged principle that standards of evidence for determining competence are dependent on the level of research risk – the greater the risk, the higher the standard of evidence for competence should be.(Beauchamp and Childress, 2013b:119-120)

While the choice of one or more standards by which to judge competence is a key step in reaching such a determination, it is not a step that has practical application yielding an empirical answer to a question of competence (or incompetence). For such a practical application, one or more assessments of competence are required. Of these there are many, yet no single assessment or combination of them is reliable enough to be considered an adequate assessment of capacity to give informed consent. As Beauchamp and Childress (2013b:119-120) point out, this judgement – while it may be assisted by empirical assessments – is still very dependent upon the judgement of the researcher, or individual responsible for enrolling research participants.

Voluntariness

Voluntariness, or the ability of research participants to make decisions without internal or external constraints, is most closely aligned to the principle of autonomy and is also clearly linked to the third condition for autonomy, namely non-control. Voluntariness speaks to the themes of freedom and self-determination as expressions of autonomy and is arguably the most prominent aspect of informed consent arising from events immediately after World War II. Beauchamp and Childress (2013b:137-140) define voluntariness simply as an individual's ability to act without being under the control of other persons or conditions.

Three main threats to voluntariness of research participation are identified. The first is coercion, which is control of an individual by another through a believable threat of force or harm. Persuasion, on the other hand, is the creation of belief in one individual through and as a result of reasoning of another individual. A very fine line exists between acceptable reasoning, to bring about a reasonable action, and undue persuasion that deviates a course of action in such a way that a research participant's autonomy is undermined. Lastly, manipulation is a form of influence that does not fit the description of either coercion or persuasion. This kind of influence may find its expression in the way that information is communicated to a research participant which creates an impression designed to induce a particular type or direction of action. Manipulation may also be by omission of information, with similar effect. Because manipulation frequently plays out in the exchange of communication between researcher and research participant, it is of significance in the informed consent process.(Beauchamp and Childress, 2013b:137-140)

Information Elements

Disclosure

Disclosure is about the responsibility of researchers to provide adequate and accurate information about research to participants. While disclosure itself does not relate directly to any particular moral obligation it is essential for the purposes of facilitating the expression of autonomy, or self-determination as the local, decisional form of autonomy is sometimes referred to as. Without appropriate information research participants are not able to make informed decisions about choices that have a direct bearing on them. Many detailed guidelines exist that list the specific items of information required, but broadly speaking they are summarised by Beauchamp and Childress (2013b:125-131) as information pertaining to '*the aims and methods of the research, anticipated benefits and risks, any anticipated inconvenience or discomfort*' and the right to withdraw from the research without consequences.

In some cases, researchers may wish to deviate from the obligation to disclose required information to research participants. For example, the use of secondary data (i.e. data that already exists in clinical records or other sources) from patients without their informed consent, which may be very difficult or impossible to obtain because patients are not traceable or because they are not able to give consent (i.e. they are incapacitated). Alternatively, researchers may believe that participant knowledge of all information about research may compromise validity of the research and thus may want to introduce an element of deception into the research process and disclose all information. In some of these cases, the approach is relatively simple (e.g. with secondary data use) while in others it is a lot more complex. The typical approach taken in justifying non-disclosure is relative to participant and risk and typically involves disclosure at some point even if this is after data has been collected.(Beauchamp and Childress, 2013b:125-131)

Recommendation

Although Beauchamp and Childress (2013b:124) include the making of a recommendation as part of the informed consent process for clinical patient care, this does not apply to informed consent for research and will not be considered further here.

Understanding

Understanding of the information provided about research, and about the broader context and implication of participation, is arguably the most important element of the informed consent process. Without it, the information provided has no purpose and the voluntariness of participation cannot be evaluated directly, undermining one of the key components of autonomy. Despite the importance of understanding of information in the informed consent process, it is impossible to describe or even determine a level or '*standard*' of understanding – a minimum threshold – necessary for informed consent.(Beauchamp and Childress, 2013b:131-137)

While it is not possible to give an objective description of a level of understanding that is appropriate for informed consent to participate in research, reference is made to a '*reasonable participant*' standard of understanding – a standard reliant on the interpretation of the researcher and the context and risks of the research. However, even this benchmark is subject to the influence of several important factors which may negatively impact understanding:

i) Technical complexity of research designs and methods. For example, the use of placebo (or other) controls and the concept of randomisation as well as complex intervention protocols may be very difficult for most, if not all, '*reasonable*' participants to adequately understand even in a simplified form.(Beauchamp and Childress, 2013b:131-134)

ii) The difference between effective treatment and experimental intervention. Despite what researchers believe is adequate information and explanation, empirical data suggests that the therapeutic misconception is probably not an infrequent occurrence. Research participant's prior experiences of medical care, which is focused on individual interests and the application of proven treatments, appears to be a powerful determinant of understanding, even when clear information is given that their participation in research is not for this purpose.(Beauchamp and Childress, 2013b:133-134) There may also be a relationship between dependence on medical care (i.e. very sick patients) and a patient-participant's inability to distinguish

between treatment and research.(Berg *et al.*, 2001) In some cases, research participants over-estimate the probability of personal benefit in clinical research while still understanding that they are engaging in research rather than treatment. This is referred to by Beauchamp and Childress as therapeutic optimism, rather than therapeutic misconception, and is considered to not invalidate understanding and informed consent, Rather, it is seen as an expression of hope in a therapeutic effect based on an adequate understanding of the research.(Beauchamp and Childress, 2013b:133-134)

iii) The effects of clinical condition-related factors and contextual factors. Clinical condition-related factors include altered levels of consciousness attributable to various causes (such as brain injury, cerebral ischaemia, the effects of drugs or metabolic abnormalities), pain and discomfort and anxiety as described in Section 3.4 above. Contextual factors, which mainly contribute to anxiety, include conditions in hospitals or wherever care takes place which may also be outside of hospitals. These conditions include noise, poor or variable lighting and other distractions. Depending on the circumstances, these factors may vary in their effect on understanding of information. Typically, when emergency care is concerned, many of these would be expected to have an effect.

Consent Elements

Decision and Authorisation

The final steps in in an informed consent process for research participation involve a decision in favour of participation or not, and if in favour, authorisation of participation as it has been disclosed and understood by the participant. This is typically recorded with the signing of an informed consent form. (Beauchamp and Childress, 2013b:124)

3.5.2. Alternative Views on Informed Consent

As discussed above, the prevailing view in research ethics is that the process of informed consent is an application of the principle of respect for autonomy, and that the understanding of information by research participants, rather than the mere conveyance of information, is key to the validity of informed consent. However, not all agree with these

views. This is an important point because the principle of respect for autonomy is invoked as justification for informed consent. Without this justification, one might question the rationale for informed consent other than as a form of legal or other regulatory compliance. Likewise, if participants do not really need to comprehend the information presented to them during this process, then why engage in the process? The following sections discuss these challenges to the orthodoxy of respect for person and informed consent and their implications.

3.5.2.1. Does Informed Consent Respect Research Participant Autonomy?

O'Neill (2002:28) sets her critique of the idea that any choices made by individuals are inherently worthy of respect in very plain language when she says that some independent actions are: '*self-centred, pig-headed, impulsive, random, ignorant, out of control and regrettable or unacceptable*' and thus, plainly, not worthy of respect. The foundation of her argument has to do with what she calls individual autonomy – autonomy conceived as a capacity to act independently and make individual choices which is, she argues, a common bioethical interpretation. Accordingly, autonomous choices – choices made independently – are seen as intrinsically worthy of respect simply by virtue of being autonomous. Respect, in turn, is important because it suggests certain constraints on how those owed respect may be treated. (Wilson, 2007:353) Indirectly, it is the autonomous person who is respected by virtue of their capacity for individual autonomy and there are thus limits, generally defined by the perimeter of the individuals' choices, in how they may be treated.

O'Neill (2002:37-39) points out that the process of informed consent may enable autonomous choice. But importantly, informed consent does not require such choices or in any way ensure that they are made. Framing the problem slightly differently, but using O'Neill's arguments as a departure point, Wilson (2007:354) proposes two constraints that would have to be met in order to claim that autonomous choice is intrinsically worthy of respect. The first constraint is that there must be a feature of autonomous choice that clearly makes it worthy of respect and differentiates it from features of non-autonomous choice that are not worthy of respect. Echoing O'Neill's sentiments above it seems obvious that morally unjustifiable choices - unworthy of respect - could be made in ways that are, in all other respects, identical to morally justifiable choices such as being fully informed and

voluntary. The second constraint is that autonomous choice must be within the reach of all '*normal*' adults in order to render it of value in a bioethical context.

Wilson (2007:354) then claims that both constraints cannot be simultaneously met – the first because applying a factor which could differentiate autonomous choices worthy of respect from those not worthy of respect would be demanding enough to exclude many '*normal*' adults in a clinical or health research setting. If, in response to this problem, the first constraint was made less demanding in order to not be exclusionary it would lose its ability to discriminate autonomous choices worthy of respect from others. The main point of Wilson's argument is that if autonomous choice is seen simply as equating to informed consent, then the preceding sentence would apply. Thus, informed consent is not a differentiator of autonomous choices worthy of respect. As Wilson (2007:354) puts it: '*it seems at best somewhat misleading to claim that in seeking informed consent we are acting out of the intrinsic respect-worthiness of autonomous choices*'.

If O'Neill's line of reasoning above is sound the principled grounding of informed consent on respect for autonomy is in question, leading us to wonder what the purpose of informed consent might actually be if not as a way of respecting autonomy. Before exploring her answer to this question, it is illuminating to consider an objection similar to O'Neill's but approached from a somewhat different angle. Kristinsson (2007:253-264) also critiques grounding the process of informed consent on a principle of respect for persons by questioning the intrinsic value of self-determination in creating a moral obligation to respect autonomy. He also questions the value of self-determination in requiring a right to informed consent. In so doing, he poses two fundamental questions: (i) whether informed consent respects autonomy and (ii) whether autonomy – understood in the bioethical respect for autonomy sense – has the gravity to imbue informed consent with the moral status that it enjoys.(Kristinsson, 2007:254)

In tackling an answer to the first question, Kristinsson – who equates the Belmont Report principle of respect for persons with respect for autonomy – first highlights the commonly held view that the Report's individualist and self-determinist conception of autonomy has Kantian roots insofar as it is an expression similar to the that of Kant's Formula of Humanity.

He argues that this is a misconception, following reasoning similar to that in Section 2.4 of Chapter 2, that Kant's autonomy is not simply about a '*psychological capacity for personal deliberation*'.(Kristinsson, 2007:255) He proposes that it might be possible to '*hook up*' the Formula of Humanity to the Report's individual autonomy but that doing so would come at the price of individual autonomy's commitment to informed consent in the way that the latter is currently conceived (with its information-laden requirements).(Kristinsson, 2007:256) He believes that the only way to reconcile the Formula of Humanity with informed consent is to reduce informed consent to a narrower focus of avoiding deception and coercion as these undermine rational agency and respect for the rational agent. He concludes that, in the absence of a viable argument that informed consent respects individual autonomy we should rather pursue a respect based on the Formula of Humanity which dispenses with emphasis on personal deliberation and reflection and instead favours an interpretation of '*adequate informed consent*' as simply non-deception and non-coercion.(Kristinsson, 2007:256)

In relation to the second question, Kristinsson asks how – other than on Kantian terms – individual autonomy might still be of value and might by some other means pull informed consent into its slipstream of moral justification. He focuses on the potential value of individualism and personal deliberation and, unsurprisingly, draws on Mill's writings about liberty, individualism and individual value.(Kristinsson, 2007:258-259) However, Kristinsson's question about the value of autonomy is a very broad one and he considers whether there might be any societal conceptions of the good other than the Millian one. He concludes that there may be – in the form of a non-reflective allegiance to '*custom, faith or tradition*' – and asks how such a conception of the good and an individualist conception might co-exist in a liberal political framework. From a public policy perspective, such a framework requires neutrality of conceptions of the good that must be acceptable to all. Consequently, the Millian individualist conception of autonomy – and informed consent as a related form of public policy – would be subject to '*reasonable disagreement*' in such a framework from which Kristinsson concludes that it cannot explain autonomy's value.(Kristinsson, 2007:258-259)

Having argued the point that informed consent and the Belmont Report-styled respect for autonomy are not compatible, that a Formula of Humanity respect is compatible with informed consent albeit of a narrower scope and that an individualist Millian conception of autonomy is not compatible with a liberal political framework, Kristinsson (2007:259) invokes a sort of self-referential turn in stating that political liberalism is, in fact itself, committed to respect for persons. By reference to Rawls' liberal principle of legitimacy and arguing that a moral imperative is required to support a neutralist political stance, he maintains that individual autonomy cannot justify informed consent regulations without violating this neutrality and such a violation would run contrary to respect for persons. In contrast to the Belmont Report's insistence that respect for autonomy is achieved through the instrument of individual autonomy, Kristinsson maintains that quite the opposite is true – that such respect '*prohibits the promotion of individual autonomy from being a legitimate goal for public policy*'.(Kristinsson, 2007:259) In a more practical sense, he suggests that for most people the thought of being subject to research without consent, when one considers the very limited scope of research participation in life, would probably be a relatively small hindrance insofar as it would be contrary to the type of control that comes with individual autonomy (i.e. self-determination). That the typical reaction to such a turn of events is much more serious – '*a major offence against our dignity*' – is evidence to Kristinsson that the real concern is one of not being treated with respect. (Kristinsson, 2007:261) And the respect in question is not derived from any sense of individual autonomy but rather one compatible with the Formula of Humanity and informed consent based on non-deception and non-coercion.

This brings us back to O'Neill's point about the purpose of informed consent which, as described above, she argues – like Kristinsson - is not to respect individual autonomy. Kristinsson in fact draws on O'Neill's arguments and it is from these that he advocates O'Neill's approach of a simpler purpose for informed consent limited to preventing deception and coercion.(Kristinsson, 2007:256-257) To the earlier argument above regarding autonomous choices not necessarily being morally good choices, O'Neill (2002:42-44) further criticises the purported relationship between autonomy and informed consent by observing that the choices made in the process of informed consent tend to be unreflective and deferential. Such choices, she argues, are not what one would associate

with those of an autonomous agent. She sees choices associated with informed consent this way because informed consent has what she refers to as a '*propositional attitude*', meaning that the choices are based on proposals. In the context of informed consent for research, a researcher would typically propose participation with certain characteristics (including risks and benefits) to a prospective participant who would simply choose whether to accept the proposal or not. This O'Neill associates with consent being '*opaque*'.(O'Neill, 2002:42-44)

The opaqueness of informed consent constrains what research participants typically might associate with the literal description of what their participation involves. This can be expressed in several ways according to O'Neill (2002:43-44). For example, different ways of wording the information conveyed to participants may conceal an understanding of what is to be expected – a participant may consent to research worded '*euphemistically*' but deny that they would consent to the same thing described more candidly. Alternatively, the propositional nature of consent may limit participants' ability to truly grasp what is entailed or consequential to that which they consent, even if the consequences are explained to them. Thus, like a narrow beam, informed consent tends to cast light on the proposition offered and makes this visible to participants, but it leaves much that is equally important in the shadows. Add to this the practical constraints of the complexity of information (especially in a clinical context), the limited time available for the process and language barriers and O'Neill (2002:44) concludes that it is simply implausible that informed consent constitutes respect for autonomy: '*informed consent demands a lot both of patients and of professionals, although it does not demand any striking form of individual autonomy from either*'.

The discussion above has centred mainly on O'Neil's critique of informed consent as respect for autonomy with the additional arguments put forward by Wilson and Kristinsson (who both cite O'Neill regarding principled autonomy and the importance of informed consent in preventing deception and coercion respectively). However, other authors writing after O'Neill have made the same point and offered either similar or other supporting arguments. In the remainder of this paragraph and the next two, I give a brief summary of these before moving on to discuss principled autonomy in greater detail. The foundation of Taylor's (2004:383-391) argument denying respect for autonomy as the ethical basis of informed

consent is that an individual's autonomy is only curtailed if information about their research participation is wilfully withheld, in other words that they are deceived. The opposite state of affairs, where information is not available to an individual possibly impeding their understanding but where there is no intent on the part of the person providing the information to manipulate that individual's choices, cannot be argued to impede their autonomy. This is because the relationship between autonomy is not reversible – non-autonomous consent would clearly be deficient but consent not obtained from an individual whose autonomy is otherwise not compromised cannot be said to adversely affect their autonomy. Even if it can be argued that a detailed understanding might better reinforce autonomy by making it more likely that the person receiving it can make decisions more aligned with their desires, this also fails. Taylor (2004:388) argues that autonomy is not a success concept, meaning that it is not contingent on the meeting of an individual's desires but rather simply that it requires that they were not subject to deception. Finally, it might be argued that respect for autonomy is the concern not just that an individual acts autonomously or is constrained from doing so. Here Taylor (2004:388-391) interprets respect for autonomy as simply allowing an individual to make their own decisions and concludes that if this is not undermined (by deception for example), autonomy is respected. He concludes that informed consent should be ethically grounded in participant well-being and not autonomy or respect for autonomy.

Sreenivasan (2003:2016-2018) argues that comprehension is not required for informed consent and his argument is centred on the observation that the therapeutic misconception is often present in consenting clinical trial participants, but these participants are nevertheless considered to have given valid consent. In taking the position that this state of affairs is defensible (rather than simply ignoring it), he focuses his argument mainly on consent as a mistaken way of offering research participants protection. But he also argues that there is a poorly conceived association between consent and the individual's '*privileged authority*' to decide, which approximates to respecting autonomy as a form of sovereignty.(Sreenivasan, 2003:2017) He provides two counterarguments. Firstly, if privileged authority is based on the premise that an individual's own views of their interests are infallible then this is incorrect – individuals can be mistaken about what is in their interests (among other arguments, the therapeutic misconception is evidence of this).

Secondly, if privileged authority is based on the premise that an individual's views of their interests are superior to those of a research ethics committee all individuals already enjoy this authority by being able to refuse participation – it is not solely contingent on informed consent. He thus argues for an alternative, simplified minimum standard approach to informed consent rather than the current '*ethical aspiration*' that so often puts '*pressure on researchers to lapse into hypocrisy*'.(Sreenivasan, 2003:2017-2018)

Taking a step back from the argument above, Walker (2013:388-394) claims that aside from comprehension, disclosure of information as part of informed consent is not necessary to respect autonomy. His argument is structured according to the three interpretations of respect for autonomy relevant to informed consent put forward by Wilson (2007:353): autonomy as autonomous choices, autonomy as capacity and autonomy as personal sovereignty. Regardless of which one of these is chosen, Walker (2013:388-394) argues that not one of them supports the idea of informed consent being required to respect autonomy. With respect to autonomous choices, a dependency between consent and respect for autonomy could only exist if it could be argued that every individual not giving consent had made an autonomous choice. However, the individual with a lack of comprehension who refuses participation, and a participant included in research without their knowledge are both counter examples. With regard to autonomy as capacity, Walker (2013:390-392) poses a very similar argument to Taylor (2004:384-387) – that not all instances of not providing information (for example about the consequences of participation) are intentional or misleading and thus do not fail to respect autonomy. He agrees that respecting autonomy does mean that information must be given, but this can be limited to basic information that the participant wants. The requirement to not manipulate participants is not equivalent to a requirement to disclose detailed information, only to not withhold basic information. Finally, in terms of autonomy as sovereignty Walker (2013:392-394) claims again that there is a requirement to provide basic information facilitating decision-making, but that this is not the same as a requirement to disclose more detailed information. He reasons that not providing this information would not interfere with a participant's ability to choose and exercise their self-determination and would also not constitute deception or manipulation.

3.5.2.2. Can Informed Consent be Dispensed With?

The discussion above might seem to be leading in a direction that fundamentally questions the value of informed consent in research ethics. However, questioning the moral rationale for informed consent – that is, the premise that informed consent is a way of respecting participant autonomy – is not the same as questioning whether informed consent has any value or benefit. While Beauchamp and Childress (2013b:106-108) insist that this relationship between respect for autonomy and informed consent is valid, the arguments above at minimum create serious doubts that this position can be sustained. In particular, these arguments not only question informed consent as a moral prerequisite, but they question its present information-laden complexity which empirical evidence points to as often placing researchers under pressure to '*lapse into hypocrisy*' as Sreenivasan (2003:2017) puts it above.

It seems untenable that the burden of protection from harm should be placed mainly on participants through a process that is so ill-suited to this purpose. Shortcomings in the informed consent process seem to be addressed by adding more and more information that most likely just exacerbates the problem. Most research participants would probably like the ability to choose for themselves whether to participate in research and they would probably also agree that they would see these choices as protecting their interests. But, as suggested in the following sections, it may be that protection can be accomplished by means other than the standard approach of presenting participants, especially those in situations where time-sensitive interventions are involved or other contextual factors might negatively affect decision-making, with large volumes of complex information.

3.5.2.3. Principled Autonomy and Informed Consent

In order to offer an alternative to the information-laden, opaque consent that she claims to be at odds with individual autonomy, O'Neill (2002:83-89) turns to Kant. Drawing on Kant's conception of autonomy, not as self-determination or individual choice, but in line with what has been described above in Section 3.5.2.1 above and Section 2.4 of Chapter 2. That is, autonomy as freedom of the will to be bound by the self-given moral law that is of a particular form meaning that it can be willed to become a universal law. Duty arises from the constraints imposed by the principle of autonomy and O'Neill (2002:85) refers to this as

'*principled autonomy*'. She emphasises that, although there is some degree of commonality between individual and principled autonomy, they are not completely dependent on each other and may actually diverge when individual autonomy becomes the stronger influence. The key feature of principled autonomy, and its Kantian grounding, is that it is expressed through '*action whose principle could be adopted by all others*'.(O'Neill, 2002:85) The contrast between individual and principled autonomy is captured succinctly by O'Neill when she emphasises that: '*The stress [Kant] places on the term self-legislation is on the notion of legislation: the advocates of individual autonomy by contrast stress the notion of self and have little to say about any conception of (moral) legislation*'.(O'Neill, 2002:85-86)

O'Neill (2002:86-89) applies principled autonomy to argue that it can be used to identify fundamental ethical obligations. This is so because many basic principles of action cannot be willed as a universal law according to Kant's autonomy and it is precisely these principles that autonomous agents have an obligation to reject. A principle of action that cannot be willed as a universal law is one that if hypothetically willed would lead to internal contradiction, taking into account that willing entails taking any necessary steps and considering reasonably foreseeable consequences of the action. O'Neill demonstrates this using the example of coercion which, if willed as a universal principle of action, would be incoherent because a universal commitment to coerce would result in universally unavailable means to coerce. This is not to say that coercion may never be justified, but rather that its justification (for example in law enforcement) constitutes an exception to the otherwise broad commitment to reject it and that it aligns with other obligations. Having used the example of coercion, O'Neill then cites principles of action such as deception, violence and torture among others to which principled autonomy would equally apply. More generally she states this as: '*any principle of action whose universal adoption would destroy, damage or undermine capacities for action for some or for many cannot be willed as a universal law*'.(O'Neill, 2002:88)

Principled autonomy has been criticised by Wilson (2007:355) who holds that O'Neill's reasoning about the disjunction between informed consent and respecting autonomy is valid but disagrees that principled autonomy makes a strong case for duties of non-deception and non-coercion. He bases this disagreement on two criticisms: (i) that O'Neill's

argument regarding coercion is ambiguous and it is not clear whether she bases the wrongness of coercion on its effects on others or on the premise that it cannot be universalised and (ii) that, assuming the latter argument is the one she makes, this is false – in other words it could be universalised. Close attention to O'Neill's argument, however, makes it clear that the sole basis of her argument is universalizability. There appears to be nothing ambiguous about this.(O'Neill, 2002:86-87) Wilson's argument about universalizability rests on his assertion that O'Neill assumes a transitive nature to the coercive relationships between individuals.(Wilson, 2007:355) However, it is unclear why O'Neill's description would assume transitivity – she simply says that in a world where coercion is universalised, there would be at least some coercive action which would prevent some others from coercing as their capacity to do so would be undermined.(O'Neill, 2002:87) Wilson's claim that a world where '*everyone is able to coerce someone else*' is not contradictory seems, if anything, to strengthen O'Neill's example.(Wilson, 2007:355)

What does principled autonomy mean for informed consent and for the very prominent place that it occupies in research ethics and what implications might this have for emergency care research? In arguing for a fundamental shift in how the purpose of informed consent is conceived, O'Neill creates space for the possibility of addressing arguably the greatest problem with informed consent and that is its failure to facilitate understanding amongst those to whom it pitches its propositions. This problem has been studied and well documented in a range of different research settings but is heightened by many factors inherent in the emergency research setting such as time pressure, anxiety and pain amongst those who could be considered to have capacity, as discussed in greater depth in the following chapter. O'Neill's proposed move away from individual autonomy and the traditional approach to informed consent is not the only alternative viewpoint. In the next section, I will briefly discuss the fair transaction model of informed consent which similarly draws on the fundamental failings of the '*autonomous authorisation*' model of informed consent.

3.5.2.4. The Fair Transaction Model of Informed Consent

The fair transaction (FT) model of informed consent (Miller and Wertheimer, 2011:201-218) takes as its problem statement empirical evidence accumulated by Appelbaum, Lidz and

Grisso (2004:1-8) that in the majority of cases (of those studied) clinical trial research participants seem to not have a good understanding of what they have consented to. This particular study focused on the therapeutic misconception – that participants mistook standardised treatments allocated randomly within the framework of a clinical trial with proven treatment allocated on the basis of individualised need or that they misunderstood the probability of benefit due to a misconception of the purpose of their participation.(Appelbaum, Lidz and Grisso, 2004:2) However, other evidence cited by Miller and Wertheimer (2011:206) underscores the problem of broader misunderstanding of research participation. This is attributed by them to shortcomings of the autonomous authorisation model of informed consent, a term that they derive literally from a definition of consent by Beauchamp and Childress in the 6th edition of the *Principles of Biomedical Ethics* and which can be traced back to Faden, Beauchamp and King (1986:277-280). The main feature of the autonomous authorisation model is that it places all emphasis in determining the validity of consent on the participant's comprehension of research-related information.

The singular concern with what Miller and Wertheimer (2011:207) refer to as the '*quality*' of consent that is inherent in the autonomous authorisation model brings about four fundamental weaknesses of this model. It fails to factor risk-benefit considerations into the validity of consent, it fails to permit participation in situations where participants do not have the required understanding but where participation might otherwise be considered in their interests or at least not harmful to them, it does not offer any assistance to researchers in determining what valid consent is and it places unrealistic demands on researchers to meet the model's exacting levels of understanding. Consequently, they do not see validity of consent as being understood through analysis of any fundamental characteristic of consent itself, but rather through moral theory which they delimit as being concerned with personal sovereignty and well-being. The former they define as a '*zone of protection from intrusive intervention and freedom of action without interference*' with both negative and positive connotations. The latter they define as simply the state in which individuals are able to avoid their dislikes and pursue their interests. Miller and Wertheimer (2011:204-205) think that the autonomous authorisation model of informed consent, while offering protection in a negative sense, contradicts the pursuit of well-being because it does

not allow individuals to engage in arrangements with others without rigorous understanding of their terms if they wish to.

The criticism above, that individuals should be able to engage in activities that they do not fully understand if they wish to, seems to go against the grain of informed consent as commonly understood (i.e. the autonomous authorisation model) and the principle of respect for autonomy. However, Miller and Wertheimer (2011:209) argue that this observation is counterintuitive. They claim that there is more to respect than respecting the autonomy of individuals and suggest that, if the tenets of autonomous authorisation would render those with the therapeutic misconception incompetent, this would constitute a form of disrespect. This is premised on two main conditions. Firstly, that those with inadequate comprehension still can give valid, albeit less than autonomous, consent because they have been given '*adequate information*' about participation and can make a choice. Secondly, and related to the first condition, there is a favourable risk-benefit ratio meaning that harm is unlikely. Thus, Miller and Wertheimer (2011:209-210) under such conditions see it as quite unfair to deprive an individual of the opportunity to participate in potentially beneficial research that they have chosen to participate in because they lack some degree of detailed comprehension that the autonomous authorisation model insists on, and only for this reason.

To address these problems associated with the autonomous authorisation model of informed consent, Miller and Wertheimer (2011:211-214) propose the fair transaction model. Fairness as applied in the fair transaction model refers to '*fair terms of cooperation for the respective parties that reflect the context of the activity for which consent is given*' and is bounded by values of personal sovereignty and well-being (as described above).(Miller and Wertheimer, 2011:211) Thus, fairness is contextual and the most important component of that context is the relative degree of risk and benefit in a particular instance of research participation. The fair transaction model does '*not impose unreasonable costs of securing informed consent on subjects that do not advance their interests and that they would reject as unnecessary or disrespectful*'.(Miller and Wertheimer, 2011:212) However, it does not depart from basic responsibilities of researchers such as the provision of adequate information and the assessment of comprehension. Assessment of

comprehension in the fair transaction model is done in an '*informal way*' and palpable errors of understanding are corrected where necessary.

Another key component in the fair transaction model of informed consent is the role of institutional oversight and safeguarding (as implemented by research ethics committees). Rather than the autonomous authorisation model's focus being on institutional evaluation of the informational adequacy of consent instruments, the fair transaction model shifts this focus to safeguarding of research participants in a more holistic sense, through ethical review and approval but also post-approval monitoring. Miller and Wertheimer (2011:213-214) liken this to the role and importance of regulation in everyday activities requiring consent which reduce the burden on individuals engaging in those activities to understand all relevant details, some of which they may not understand. Sound regulatory frameworks protect consenting individuals who may give '*uncomprehending consent*'. As a specific example, they cite the subprime mortgage crisis of 2007 – 2008 which, in their view, would not have been avoided by adding more and more detailed information to mortgage agreement terms but rather to have had stronger and more effective regulatory checks in place. Analogously, they argue that inadequate research oversight cannot be compensated for by an ever-increasing complexity of informed consent processes which shifts the protective burden onto researchers and participants. This is particularly so when empirical evidence clearly points to the seemingly intractable problem of incomplete participant comprehension. Unlike the position of institutional oversight in the autonomous authorisation model, Miller and Wertheimer (2011:213-214) emphasise that institutional oversight is an inherent part of the '*fair conditions*' of informed consent which promote the interests of research participants even if they lack comprehension in consent.

3.6. Autonomy, Informed Consent and the Incapacitated

Regardless of how it is defined, and which conception is favoured of the many put forward, one feature of autonomy is central to all of them – rationality. In explaining their different ideas about autonomy, Kant referred to this directly (Section 2.2.1 of Chapter 2) while Mill referred to individuals with '*maturity of their faculties*'.(O'Neill, 2002:40) Beauchamp and Childress speak of capacity(Beauchamp and Childress, 2013b:114-120) and the liberal individualist form of autonomy equally requires this. Regardless of the terminology, to be

autonomous is to be capable of rational thought; to be able to think, reflect, choose and make decisions whether these decisions are in-the-moment or over longer time frames or even lifetimes. By extension, respect for autonomy must then be translated as respect for a feature of rational beings only – those capable of autonomous actions.

As discussed above in Section 2.3.4.1 of Chapter 2, the idea that non-rational individuals are not owed respect (for their autonomy) does not sit well with some who see the predominance of Beauchamp and Childress' turn away from the Belmont principle of respect for persons as eroding protection for a vulnerable population by equating autonomy to choice and, by extension, informed consent. The rights-based view of autonomy (Section 2.2.3 of Chapter 2) similarly would disagree with a position that differentiates those capable of autonomous actions and those not capable. Although the proponents of respect for persons as a more protective principle in bioethics invoke a Kantian conception of autonomy in their arguments based on the Formula of Humanity, I have argued above that this is unlikely to be a valid interpretation. The Belmont Report itself seems to draw a direct line between the principle of respect for persons and its application as informed consent – an approach similar to that of Beauchamp and Childress and one that suggests, as Behrens (2018:128) notes, that there is not much fundamental difference between the two principles. Moreover, when it comes to those lacking capacity, the principle of respect for autonomy seems rather irrelevant. If we accept that the requirement of informed consent is morally grounded in respect for autonomy we have to conclude, as mentioned above, that this does not apply to the incapacitated. If, as I suggest in Section 3.2.1, the relationship between respect for autonomy and informed consent is questionable or even non-existent we arrive at the same conclusion. Either way, the incapacitated have moral status, as argued by Beauchamp and Childress (2013c:108), and researchers have a duty to protect them from harm.

One way of approaching research with the incapacitated is to argue that due to their vulnerability the only appropriate level of protection is to prohibit research with their participation. However, as argued in Chapter 1, adopting this approach in emergency care research is not ethically justifiable because (i) it denies individuals with serious conditions the possibility of benefiting from new interventions through research participation and (ii) it

denies society the broader benefits of new knowledge that could reduce morbidity, mortality and suffering. Thus, the problem becomes how it may be possible to allow this research but also offer adequate protection to incapacitated participants. This problem is addressed in Chapter 8, after relevant factors such as analysis of risk in emergency care research and approaches to emergency care research with the incapacitated in local and international regulations and research ethics guidelines are discussed in greater detail in Chapters 5, 6 and 7.

Finally, the word '*incapacitated*' is used in a way that suggests a clear practical application. However, in reality this is often not true, particularly in situations where prospective research participants might seem to have decision-making capacity (from a mental status perspective) but are affected by factors relevant to the emergency care context such as acute pain, anxiety and the effects of treatment given early in the management of a condition (such as analgesia for example). Even the pressure experienced by prospective participants to make a decision due to time-sensitive interventions may adversely affect what may otherwise seem to be adequate decision-making capacity. Many of these factors lie in the capacity penumbra identified in Figure 1 in Chapter 1 whose characteristics remain indistinct – these factors have not been subject to much empirical investigation and they are largely ignored by regulations and research ethics guidelines. It is in this setting, however, that the greatest scope exists to rethink informed consent in emergency care research and how it is done with the conventional information-laden and opaque approaches clearly being inappropriate. While the main focus of this thesis is the incapacitated research participant, it would be wrong to ignore the challenge of those in the penumbra where a different approach to informed consent may be possible. This problem is also taken up in Chapter 8.

3.7. Conclusion

In this chapter, I have given a more detailed exposition of the nature of clinical emergency care aptly summarised by the expression '*anyone, anything, anytime*'. This has highlighted the clinically diverse nature of emergency care and the multitude of settings, from sophisticated to austere, in which it is practiced. Following this I provided an overview of the nature and growth of emergency car research along with several relevant examples of

clinical interventional research exemplifying the problems posed with regard to capacity and informed consent. This was followed by a more in-depth discussion of capacity and the factors that may negatively affect it in emergency settings, not only in more obvious ways such as unconsciousness but also in more subtle ways as embodied in the capacity penumbra.

In the latter part of this chapter, after describing what could be termed the standard view of informed consent, I have probed the conventional association of respect for autonomy with informed consent and critically discussed the notion that autonomous choices are intrinsically worthy of respect. I have concluded that there are several compelling arguments to the contrary and that the role and importance of informed consent is not convincingly demonstrated by appeals to the principle of respect for autonomy. The role played by informed consent in emergency care research could probably be summed up well by O'Neill's comment that '*where options are few, where cognitive and decision-making capacities are limited, procedures of informed consent may become a burden or a ritual, and ideas of "patient autonomy" may seem more inflationary than liberating*'.(O'Neill, 2002:27)

I have ended this chapter by discussing some alternative ideas about autonomy and informed consent. While the main challenge with emergency care research involving the incapacitated is to justify their inclusion and determine what constitutes adequate protection, rethinking informed consent and how it is operationalised is relevant to research participants in the capacity penumbra influenced by contextual factors often encountered in emergency care research. In particular, I believe that the ambitious goal of fully informed consent is not achievable, and especially not in emergency care research of this nature. While it may still be somewhat lacking in practical implementation, the narrower goal of principled autonomy in preventing coercion and manipulation seems more realistic. I also see the fair transaction model of informed consent as having some features that could be useful in the emergency care context, although its dependence between information detail and risk may be limiting. In the next chapter, I discuss human dignity and vulnerability of the incapacitated patient as potential constraints on researcher behaviour in emergency care research.

CHAPTER 4: DIGNITY AND VULNERABILITY IN EMERGENCY CARE RESEARCH

4.1. Introduction

In Chapter 2 of this thesis, the principle of respect for autonomy as set out by Beauchamp and Childress was described. In dealing with the problem of individuals who cannot act in an autonomous manner, these authors claim that no obligation exists to extend such respect.(Beauchamp and Childress, 2013b:108) They do emphasise, however, that moral respect is still owed under these conditions because incapacitated adults retain their moral status which creates an obligation for researchers to protect them.

Inherent in any consideration of moral respect is the notion of human dignity. While often cited in moral argument, particularly since the post-war period, the idea and meaning of human dignity itself remains contested. It is seen by some as a '*useless concept*'(Macklin, 2003b) and by others as the most fundamental grounding of all human rights. The history and varied interpretations of human dignity are explored in this chapter, following a framework that presents dignity as equality, status, virtue and collective virtue. This is followed by a contextual consideration of human dignity as an important consideration in emergency care research, particularly research involving incapacitated adults.

Flowing from the discussion of human dignity, which accentuates the Kantian expression that humans should never be seen as a means to an end,(Rosen, 2012:81) arises the concept of vulnerability and exploitation in research. Although, compared to human dignity, the idea of vulnerability is a much more recent one it too has come in for similar criticism for being ill-defined and of questionable value and application in research ethics. In this chapter, three different approaches to vulnerability are presented in an attempt clarify both its meaning and application. This is followed by a brief discussion of exploitation and harm arising from vulnerability, along with a discussion of two responses to the problem of vulnerability (and research risk in general); paternalism and protectionism. Finally, the vulnerability of incapacitated adults in emergency care research is re-emphasised together with the important role of protectionism and paternalism in ethical oversight of this research.

4.2. Human Dignity in Emergency Care Research

The word *dignitas*, from which dignity is derived, refers to '*social honour, position or rank*', things that themselves are dependent on the recognition of achievement.(Calhoun, 2013) Dignity, in its general usage, is a term of degree and contains within it the possibility of change, gain and loss. Similarly, in this usage conduct can be considered to display or not display dignity. *Human* dignity, the subject of this section, is a very different idea. In many ways, it is the complement of dignity meaning that it recognises that which is common to all humans, and not that which elevates one above another on the basis of acts or achievements. It is not an exceptional, transient high-water mark but rather a fundamental minimum possession of all humans, equally, as a result of their '*humanness*'. It is not , conceptually at least, gained or lost.(Byleveld and Brownsword, 1993)

Human dignity has played an increasingly important role in bioethics over the last several decades, rising to prominence most noticeably in response to the experiences of World War II. While appeals to human dignity as the basis of bioethical arguments have gained most traction even more recently – within the last five decades or so – the post-war socio-political landscape has been characterised by human dignity as a key feature of human rights in the United Nations' Universal Declaration of Human Rights.(Byleveld and Brownsword, 1993:12)

Despite this more recent emphasis on human dignity in both human rights and bioethics, it is certainly not a concept that bioethicists seem to agree on in terms of its role, importance or even its definition. The point is frequently made that human rights literature, while frequently invoking human dignity as a premise for universal rights, does not define it. Moreover, perhaps because of the religious roots of human dignity, there seems to be a degree of cynicism about its place in secular bioethics as Kass (quoted by Byleveld and Brownsword) comments:(Byleveld and Brownsword, 1993)

> *"the very idea of 'dignity' smacks too much of aristocracy for egalitarians and too much of religion for secularists and libertarians."*

While some question the place of human dignity in bioethical discourse, others claim that it simply has no utility because it is equivalent to other better defined ethical principles, most notably respect for autonomy.(Macklin, 2003b) The origins of the unease that many have about a place for human dignity in bioethics can be contextualised by a brief consideration of its origins and history, particularly the '*anthropocentric shift'* that marked a move in human dignity away from the *imago Dei* – the image of God (Calhoun, 2013) - and towards the principle of autonomy.

4.2.1. A Brief Historical Overview of Human Dignity

Human dignity is described by Calhoun as a tradition originating approximately 2000 years ago and based on the foundational idea of human distinctiveness. Human distinctiveness, in turn, is seen as arising from the human ability to reason and the *imago Dei* – the belief that humans represent a unique reflection of the divine image.(Calhoun, 2013) In identifying a precursor to dignity from Aristotle's Nicomachean Ethics, Calhoun predates the rational component of dignity as compared to the earliest divine notion. Aristotle's virtue of magnanimity – '*greatness of soul*' – is portrayed as the '*person of moral gravity and seriousness, excellence of action and character, and sufficient self-awareness to know what is due him and what is beneath him*.'(Calhoun, 2013) Magnanimity involves the optimised exercise of self-knowledge and self-governance, both distinctly human abilities and both achievable to some degree by all individuals. However, the magnanimous person rises – through the application of reason – above the ordinary mass of individuals to achieve something very similar to dignity.

The illumination of human dignity – *hominis dignitas* – is attributed to Cicero, through a historical philosophical development from Aristotle and including the Stoic philosophers. The main features of this development are the role of rationality in understanding the nature of being, and importantly, even divine being. The Aristotelian idea that reason allows humans to contemplate and understand divine things, and also contribute to a divine life, lead to the Stoic notion of a universal human brotherhood. It is this idea, that all humans are 'fellow-citizens', that Cicero builds on in his articulation of *hominis dignitas*, the most important aspect of which is not mere human exceptionalism because of the shared ability to reason, but also that this quality is shared equally by all humans.(Griffin, 2017) While

Cicero makes no explicit reference to the divine in his conception of human dignity, Calhoun points out that the connection between rationality and the divine is never far away in the writings of a Aristotle, Plato, the Stoics and Cicero. (Sulmasy, 2009; Calhoun, 2013)

In terms of its religious origins, it is perhaps surprising to learn that the term '*human dignity*' does not occur in the Bible in its Hebrew or Greek forms. Rather, the concept of dignity in its social honour or rank form appears to be represented by the word '*glory*' in Hebrew.(Calhoun, 2013) This is an important meaning, as the Jewish scriptures describe how the *glory* of God is embodied in humans. Thus, the dignity of humans has as its source this reflecting or '*imaging*' of God – the *imago Dei*. This dignity is present in all humans as beings created by God. If there is a hierarchical, rank-related meaning to dignity it is not in the differentiation of one from another, but rather in the prime position that humans occupy in relation to the rest of creation. In this view, to be human is to enjoy a type of honour, but not the honour of social recognition.

Western religious conceptions of dignity up until the renaissance contained a subtle hint of pagan philosophical thought, although this was considered highly controversial at the time. This did not represent any significant departure from the centrality of the *imago Dei*, but to some extent refined its meaning and de-emphasised the literal interpretation of an image. Saint Augustine attributed human exceptionalism, and the '*image and likeness*' of God in humans, solely to the human ability to know, understand and reason.(Calhoun, 2013) The notion of dignity linked to personhood is introduced by Saint Thomas Aquinas, who emphasised that humans are not just able to reason, but that they are free agents in doing so.(Calhoun, 2013) This Aquinas links to the way in which sin offends the sense of human dignity – that sin, committed by free agents with the capacity for reason, diminishes the rationality conferred upon humans by existing in God's image. Humanist philosopher Pico della Mirandola extended the idea of dignity still further beyond the *imago Dei.* He argued that – notwithstanding the conventional religious view of exceptional humans created in the image of God – the defining element of human dignity is free will and choice that facilitates self-definition.(Calhoun, 2013) This notion of human potential and transformation is a central one to many of the more modern, secular interpretations of human dignity as discussed later in this chapter.

Towards the end of the early Modern period, when natural philosophy and theology began emerging into the early Enlightenment a number of very significant changes in thought began to take root, changes that would alter forever the role of human exceptionalism based on the *imago Dei*, and its foundational role in the dominant conception of human dignity. A new mechanistic, atomistic and deterministic view of nature started to take shape around the ideas of Galileo and Descartes. Nature so envisaged did not require a place for God, either in a role as creator or as a means of accounting for observed phenomena. Another consequence of the deterministic natural world was to reduce human exceptionalism to mechanistic functioning not dissimilar to that of other animals. While some philosophers were willing to follow this line of reasoning to its conclusion, many (like Descartes for example) were not and promoted a kind of dualistic view of nature with humans considered to be different to, and above, other animals mainly by virtue of the human ability to reason. But the reliance on God and the *imago Dei* as the foundation for human exceptionalism, and human dignity, became progressively weaker as Enlightenment thinking grew more influential.(Calhoun, 2013)

The Enlightenment was also associated more generally with a subtle but progressive deterioration in the influence of religious authority. This was partly due to the evolving view of natural philosophy as outlined above but was also due to the secularisation of society based on a changing focus away from the guidance of God's will and towards more prominent consideration of the societal structure best suited to serve human interests, based on the application of reason. This '*anthropocentric shift*' placed greater emphasis on human responsibility and chipped away slowly at the influence of religion in many aspects of life, including conceptions of human dignity. While this shift towards human self-rule appeared that it may fortify the importance of human dignity, it led only to the strengthening of autonomy and the simultaneous demise of the religious understanding of human dignity based on the *imago Dei*. This is made clear by Kant, for example, in describing '*the power to set an end*' as '*the characteristic of humanity*'. As .Calhoun (2013) suggests, this power was seen as analogous to divine creative power and formed the basis of suggesting that humans should be autonomous (together with the ability to reason)

Towards the end of the Enlightenment, the development of socio-political theory produced a swing away from religious grounds as a justification for human rights, although the fundamental argument for these rights was still grounded in the idea of human exceptionalism, and this was still based on the unique human ability for rational thought. Greater emphasis on human rights brought about new ideas centred on democratic forms of social structure and these in turn initiated many important societal discussions concerning authority (including religious authority) and class. While the end of the early Modern period saw the above disruptive changes taking place, human dignity positively fragmented into a number of different variants by late Modernity. These variants were characterised broadly as either modification, refutation or stasis by what .Calhoun (2013) refers to as '*caretakers*' Modification involved adaptation of the hitherto more or less traditional meaning of human dignity into a form with a more individual meaning and more useful for the purpose of moral argument. Refutation involved both outright rejection of human dignity as a quaint, and ultimately useless idea and erosion of the ground supporting human dignity through advances in natural science that effectively neutralised the idea of human exceptionalism. Stasis involved the recession of human dignity from the mid-19th to 20th centuries and its preservation until it enjoyed somewhat of a resurgence later in the 20th century.

The devaluing of human life and welfare arising from the two World Wars lead to a post-war emphasis on universal human rights and the foregrounding of human dignity as a key foundation for these rights, as alluded to briefly above. Similar appeals to human dignity were seen in the 1960s and 1970s in bioethical debates about euthanasia. There has thus been a significant revival of human dignity in both law and bioethics, but the late Modern fragmentation of human dignity has resulted in the revival of a contested and, according to some, useless idea. The many different perspectives on human dignity will be discussed below.

4.2.2. Many Perspectives: Little Consensus

Contemporary literature provides a wide array of ideas and views on human dignity. Many authors have attempted to grapple with this difficult concept, particularly in its secular interpretation. Schopenhauer dismissed dignity as a '*shibboleth of all the perplexed and*

empty-headed moralists' and claimed that it was simply put forward to boost the '*moralist's*' self-esteem.(Rosen, 2012:1) Perhaps the most well-known piece in the recent literature was written by Ruth Macklin, questioning human dignity and labelling it a '*useless concept*', with no more real meaning than the principle of respect for persons.(Macklin, 2003b) Ashcroft, in a partitioning of authors into groups with differing views on human dignity, places the whole of mainstream English bioethics into a category of those deeming human dignity to be unhelpful as a concept or perhaps even misleading. To this category he adds three others; those seeing some value in human dignity, but equating it strictly to autonomy (Macklin belongs to this group, but overlaps into the first somewhat by branding human dignity as '*useless*'); those seeing dignity as just another concept amongst many in bioethics; and those considering human dignity to be a metaphysical property possessed only by humans.(Ashcroft, 2005)

A review of literature across, and even within, the above groups yields many divergent perspectives on the definition of human dignity. This is not surprising, as there is not even agreement about whether it is useful to consider human dignity from the perspective of moral theory (Ashcroft refers to it as quixotic to attempt to do so) and whether it might be more appropriate to simply study its linguistic usages in an attempt at conceptual clarity.(Ashcroft, 2005) Nevertheless, several broad themes can be identified amongst the authors representing the four groups which can to some extent illuminate the concept of human dignity. Most of these themes can be arranged under a taxonomy such as that suggested by Henry, consisting of four meanings of human dignity.(Henry, 2010) While acknowledging that the meanings of human dignity must be complex enough to go beyond the confines of this relatively simple suggested taxonomy, it provides a useful start.

4.2.2.1. Equality as Human Dignity

The first of these broad themes is about the concept of human dignity as it relates to humanness - a '*basic*' human dignity said to be irreducible and enjoyed equally by all humans regardless of their circumstances or actions. This conception of human dignity is at once the easiest to grasp intuitively, perhaps because of its alignment with human rights, but also the most difficult to define as an attribute of being human. As Foster argues, the conviction that all humans should be treated equally is undoubtedly right but is it equivalent to human dignity, and if so on what basis?(Foster, 2011) Stating that all humans should

enjoy equal dignity does not illuminate the nature or substance of this threshold concept of basic dignity. What is it about being human that we believe entitles us exclusively to an irrevocable, basic dignity?

To begin with, the question above does not seem to always be considered necessary in defining and acknowledging a basic dignity. Sulmasy describes what he sees as an intrinsic dignity – a value inherent in humans simply '*because they are human*'.(Sulmasy, 2009) This is contrasted with two other conceptions of dignity, namely attributed and inflorescent dignity. These latter two conceptions extend the notion of intrinsic dignity by attributing value to human characteristics that enhance human value and by describing the value of a course of action associated with human excellence. Sulmasy explains intrinsic dignity by referring to axiology and its theory of value, both intrinsic and attributed. Axiologically, intrinsic value is a self-evident value that something has and which is considered to be so independent of a valuer's convictions or aspirations. However, such recognition of value requires attribution by a valuer – something that contradicts the assertion that intrinsic value is objective or self-evident. Sulmasy (2009) argues that intrinsic value arises from an '*intelligent*' valuer conducting a '*correct*' evaluation. Unfortunately, such arguments appear to be circular and do not succeed in illuminating what it is about humanness that gives rise to the idea of a basic dignity, beyond faith or belief that this is so.

Most accounts of a basic dignity do present some kind of argument for the uniqueness of humans compared to other animals. This uniqueness has been identified and attributed to a range of different human capabilities since the writings of the ancient Greek philosophers. As alluded to above, often this difference is collectively attributed to the rationality of humans – our ability to reason. However, there are many distinctive human capabilities that have been put forward as evidence of this uniqueness. Rolston (2009) presents a detailed discussion of these, prefaced by the suggestion that dignity is a gestalt more than a quantitative concept. Evidence of the uniqueness of humans is linked to culture (the capacity to grow into and assimilate a '*cumulative transmissible culture*'); the ability to process thoughts, ideas and symbols through which the world is understood; idiographic uniqueness based on individuality; existential uniqueness related to subjectivity and

personal identity and ethical uniqueness, based on the assertion that only humans have the capacity to reason morally.

In mapping out the above framework for human uniqueness, Rolston (2009) believes that a case can be made for the existence of dignity. For example, he argues that the discontinuity between animals and humans establishes human dignity. Other examples include that the human ability to '*form a symbolic sense of self*' is associated with dignity, that the '*massive singularity*' of human evolutionary change resulting in our cognitive and linguistic abilities introduces '*massive dignity*', that the '*potential to forge endless thoughts and imaginations, and to incorporate these into our unique biographies*' is evidence of dignity. Lastly, in summary, Rolston suggests that:(Rolston, 2009)

> '*The is-ought divide continues, past, present, and future. Humans crossed it during their evolutionary history and now live in moral territory. That is dignity by heritage and endowment*.'

Continuing in a similar vein, Lee and George (2009) appeal to the notion of dignity as the elicitation of respect from others on the basis of the ability to excel in some way. However, they argue that this is what differentiates humans from other animals, rather than humans from humans – that humans excel other animals and thus deserve respect from other humans. The basis of the human ability to do this, and something that they argue is intrinsic to humanness, is the capacity for rational thought (which they argue is the foundation of moral worth) and free choice. Importantly, dignity is seen as purely contingent on existence as a human – as based on the type of being one is – and is thus not affected by any other factor most notably whether it is possible to exercise the capacity for rationality or not. Capacity for rationality and free choice alone are enough to warrant the expectation of a basic form of dignity for all who have it and thereupon rests the claim to equality on the basis of dignity.

Despite the more recent interest in human dignity in bioethics it has not enjoyed a great deal of philosophical analysis.(Byleveld and Brownsword, 1993:51) The most influential philosophical thinker in the area of human dignity remains Immanuel Kant, even though a

relatively small volume of his writings were devoted to it. Kant is known for articulating a similar view about human dignity to that described above – one that held dignity to be centred on the unique value of humans. However, Kant's reasoning about why all dignity is *human* dignity is not premised solely on the human ability to reason, but rather on the ability of all humans to follow their own laws of moral reason.(Killmister, 2010; Rosen, 2012:22-25) Only morality has dignity and it is only humans that have the ability to reason in this particular way and thus only humans have dignity.(Rosen, 2012:24) Going further, Kant recognises that dignity brings about a duty of respect on the part of others. While this may sound at first as if the bearer of dignity in some unequal way has a degree of status – deserving respect – this is incorrect. What Kant means is that dignity is seated in the law-giving function of morality which is common to all humans and for this reason there is an equality amongst all who have this dignity.(Rosen, 2012:26) Kant's end-in-itself formulation of the categorical imperative further cements the idea of dignity as equality on the basis of respect by equating the duty that each person has to not treat themselves as a means to an end only (the duty of self-esteem), with the obligation to acknowledge the self-esteem of others and hence their dignity.(Byleveld and Brownsword, 1993:52-53)

Any discussion of human dignity as equality would be incomplete without considering the relationship between human dignity and human rights. As mentioned briefly in the opening paragraphs of this chapter, human rights rose to prominence after World War II and were expressed in a variety of instruments, the most foundationally important of which were the Universal Declaration of Human Rights, the International Covenant on Economic, Social and Cultural Rights and the International Covenant on Civil and Political Rights spanning the period 1948 – 1966. As Byleveld and Brownsword (1993:12) point out, these grounding instruments recognised the relationship between human dignity as a basis for human rights - as "*the rock on which the superstructure of human rights is built*". According to this regime every person has inherent dignity, this grounds their human rights, such rights are therefore inalienable and because of all the aforementioned, all persons hold these rights equally. Following this chain backwards, basic human dignity is thus seen as the basis for human rights and equality.(Byleveld and Brownsword, 1993:13)

Byleveldt & Brownsword see human dignity that is a grounding of human rights as being a conception based on empowerment – dignity as empowerment.(Byleveld and Brownsword, 1993:9-28) While accepting that this conception seems to be intuitively sound on the basis again that all humans have some kind of inherent worth, it seems difficult to explain why this is so. The appeal to human dignity as a foundation for human rights seems to be more of an appeal to a standpoint that values the idea of rights than to a clear justification of human value as a starting point. An alternative position on human dignity as empowerment attempts to explain human worth – as the foundation for human dignity – on some kind of characteristic or capacity. The capacity that is most frequently invoked in this position is the capacity for autonomous action.(Byleveld and Brownsword, 1993:23)

The desire to associate human worth, and hence dignity, with capacity for autonomous action probably has something to do with the earlier association of human dignity with free will (in addition to rationality).(Byleveld and Brownsword, 1993:24) Once again, this seems to have intuitive appeal as a reason for valuing humans and thus arguing that they are unique and equal. But it falls away if that assumption is not made and cannot be argued for convincingly. Of greater significance, when attributing human value to the capacity for autonomous choice, is the contingency that this creates because not all humans have this capacity. Examples of limitations to capacity include age (cognitive maturity) and altered mental status. Naturally, this creates a problem for the idea that human rights lie on the foundation of human dignity, if not all humans '*have*' dignity due to their lack of capacity for autonomous action. This problem is not limited to the dignity as empowerment viewpoint but applies equally to dignity founded on the arguments of rationality and moral reasoning. Is it enough to accept that only the potential for this capacity is needed to establish human uniqueness and hence dignity? Or must individuals literally be capable of exercising this capacity otherwise they lack dignity or are not owed respect as individuals? These questions are of great importance for the normative coherence of both dignity and human rights but equally so in the context of research carried out in an environment where research participants lack such capacity. They will be addressed in detail in Section 4.2.3 below.

Byleveldt & Brownsword's view that dignity, as a grounding of human rights, can be conceived as being established in empowerment is a view that centres the value of

autonomy as discussed above. However, there is an opposing view of dignity that takes a different position – that of dignity as constraint. The conception of dignity as constraint can be attributed to Kant's Formula of Humanity expressed in the Metaphysics of Morals, where he writes that humanity (both in the form of the individual themselves and in the form of others) should be treated '*always at the same time as an end, never merely as a means*.(Rosen, 2012:81) Kant writes further, in the Groundwork of the Metaphysics of Morals, with regard to ends; '*In the kingdom of ends everything has either a price or a dignity. What has a price can be replaced by something else as its equivalent; what on the other hand is raised above all price and therefore admits of no equivalent has a dignity'*.(Rosen, 2012:20)

In terms of duties, one way of interpreting the Formula of Humanity as it applies to dignity is in relation to the duties that individuals have to themselves. A duty of self-esteem, as described above, means that individuals should uphold their own dignity and self-esteem and not merely become means to some other end or sell themselves to some end for a price. Perhaps more importantly though, a duty of self-esteem can be interpreted outwardly – as a duty to respect the self-esteem and dignity of others and to respect others.(Byleveld and Brownsword, 1993:52-53) This is the duty referred to above, that is owed on the basis of human equality. More recently however, as exemplified by what Byleveldt & Brownsword refer to as the '*new bioethics*', this duty to respect the dignity of others has taken on a communitarian form emphasising the setting of limits to the choices of individuals as an expression of a societal interpretation of dignity.(Byleveld and Brownsword, 1993:29) Under such a view, dignity can be considered to take on an objective value and if behaviour of an individual is considered to be at odds with this, it is considered to be weakened regardless of the choices of the individual.

In summary, human dignity that is considered to be basic and thus irreducible is shared equally by all humans on the basis that only humans are capable of rational thought and, perhaps more importantly, only humans are capable of following their own laws of moral reason. From a human rights perspective, dignity can be thought of as a form of empowerment and this is most often attributed to the capacity to act autonomously. This is an important aspect of human dignity when considering emergency care research with

incapacitated patients because in many instances, whether due to altered states of consciousness or other factors such as anxiety or pain, these patients will lack such capacity and the question then arises of whether the same duty of respect still applies. A different, and more recent, rights-based perspective on dignity is to see it as a constraint particularly one that limits certain acts on the basis that they are contrary to a shared, communitarian conception of dignity regardless of the choices made by individuals. Such a view of dignity as a constraint is also important in the context of emergency care research because it is likely to be expressed in legislated or community-based views on what constitutes dignified treatment of incapacitated patients under such circumstances. The tension between these two ways of thinking about dignity and how they might be interpreted and balanced in relation to autonomy, incapacity and community views on dignified treatment of research participants will be explored in greater detail in Section 4.2.3 below.

4.2.2.2. Status as Human Dignity

The basic dignity referred to in the previous section is considered to be a fundamental feature of being human (the specific attributes of humanness that warrant consideration of this form of dignity are discussed in more detail above). This is what Sulmasy (2013) in his description of three categories of dignity, calls '*intrinsic*' dignity. It is irrevocable and non-contingent. Dignity that is contingent on status conferred upon an individual by society does not share this property of being a basic or intrinsic consequence of humanness. Status-based dignity is a conception with a very long history, dating back to pre-modern times but stands in stark contrast to dignity as equality highlighted in modern human rights instruments and more recent bioethics literature.

The term status-based dignity would appear to very simply place all dignity that is not of a basic or intrinsic nature into a single category. However, several authors have approached this broad grouping of status-based dignity differently and interpreted it in slightly different ways. For example, Schroeder identifies what she calls aristocratic dignity as part of this grouping. She sees this as dignity attached by society to rank or social position, often in historical terms religious rank, and which is outwardly displayed.(Schroeder, 2008) A similar meaning is conveyed by the same author in identifying comportment dignity – dignity that is also founded upon social rank or position and outwardly displayed, but in this case what is

displayed is the human quality expected of an individual with this type of societal standing, what Schroeder refers to as '*well-mannered demeanour and bearing*'.(Schroeder, 2008) Lastly, Schroeder describes meritorious dignity as a type of dignity related to status, but conveying the essence that status (or honour) is deserved or earned rather than just displayed. In citing Aristotle, Schroeder links the conception of dignity as honour to the notion of dignity as virtue.(Schroeder, 2008)

A similar type of duality, with dignity seen as bestowed in some cases and displayed (as a virtue) in others (and perhaps both in some cases), is described by Sulmasy (2013) who refers to attributed and inflorescent dignity as set apart from the basic dignity considered above. Described in this way, attributed dignity is similar to Schroeder's aristocratic dignity because it is value-based and attributed to others on the basis of social standing, rank or achievement. Inflorescent dignity, described as the *'value of a process*' or '*state of affairs*' (Sulmasy, 2013) that displays human excellence, is similar to Schroeder's comportment dignity and also sounds similar to her description of meritorious dignity. While both Sulmasy and Schroeder differentiate between their two different types of non-basic dignity, Killmister (2010) proposes that these are actually different representations of what really amounts to the same thing (she offers this suggestion specifically with regard to Schroeder's description, but it could also apply to Sulmasy's if we accept the similarities between them). By proposing that Schroeder's comportment dignity can be rethought to refer to personal values and norms, rather than those of society, Killmister (2010) brings comportment dignity close enough to meritorious dignity for them to be merged into what she refers to as aspirational dignity – dignity as a function of being in alignment with one's own values and principles.

In putting forward the idea of aspirational dignity Killmister (2010) seems to be suggesting that this new conception is not a member of the set of status-based dignity, as are its predecessors, but rather that this transformation has yielded something more akin to a form of basic dignity, but one that is not grounded solely in the foundational human elements of reason and moral reason discussed above. While this seems to be true, it is equally apparent that aspirational dignity could not be equivalent to basic dignity (as described above) in its human universality because it would seemingly not apply to any

person unable to formulate their own principles – for example the very young or those with impaired consciousness. However, the proposal of aspirational dignity is not the final destination in Killmister's argument. She extends this even further in an effort to reconcile the basic, Kantian dignity described above, with her own aspirational dignity by arguing that neither of these alone are adequate as a pragmatic basis for the application of dignity in bioethics. The result is a unified conception of dignity that is based upon the capacity for the upholding of an individual's values and principles. Using this basis, Killmister (2010) proposes that evaluation of the wrongness of an act – in relation to dignity – can be assessed by consideration of the extent to which it creates a '*fracture between the capacity and the ability for principled action*'.

Killmister's attempt to unify the Kantian and aspirational strands of human dignity into a concept that brings capacity to the fore is novel, but beyond this it brings into focus one of the key problems when considering dignity in the context of emergency care research. There are distinct similarities between this idea and dignity conceived as empowerment which is most often premised on the capacity to act autonomously. However, Killmister recognises the weakness that this creates because dignity defined in this way could not be applied to those lacking the capacity to uphold their values. In an attempt to overcome this problem, she differentiates between capacity and ability – the former being a '*latent potential*' while the latter is an '*immediate possibility of action*'.(Killmister, 2010) From this differentiation flows the idea that capacity as latent potential must be present in all persons even if ability is either temporarily or permanently absent. Hence a solution to the problem of incapacity, although rarer instances where individuals have never and may never have capacity lingers as a challenge. The problem of dignity and incapacity, both temporary and permanent, will be revisited in greater detail in Section 4.2.3 below.

In sum, this section has dealt with dignity of a different sort compared to the basic, intrinsic and inhalable dignity discussed in Section 4.2.2.1. Dignity as status is typically thought of as a selective and discriminatory elevation, bestowing dignity only on those with a particular societal standing, authority or merit (however conceived) or those whose actions we feel portray the behaviour of one who is dignified, either by their office or because of fortitude displayed under trying circumstances. Yet this view of dignity as status may be simplistic as

the above discussion suggests. Consequently, and surprisingly perhaps, a path that starts with dignity as status and reworks this into the concept of aspirational dignity, eventually ends with dignity defined by the capacity to live life according to individual values and hence somewhat resembling a notion of intrinsic dignity. Dignity as displayed through behaviour has been mentioned in the discussion above but not in great detail. As Byleveldt and Brownsword point out, thinking about dignity as conduct can lead to a superficial emphasis on the social order associated with specific types of conduct.(Byleveld and Brownsword, 1993:58) Rather, they suggest, we should look to the contextual character of those whose conduct we consider to be virtuous. Dignity as virtue is explored in greater detail in the following section.

4.2.2.3. Virtue as Human Dignity

In contrast to other moral theories which emphasise the role of obligations, rules or consequences of actions virtue ethics emphasises the social and moral value of an individual's character – their virtues.(Beauchamp, 2001:184) Virtue ethics has a scope far wider than deontological or utilitarian moral theory. The latter tend to focus exclusively on what ought to be done with regard to a particular moral problem. Virtue ethics, on the other hand, concerns itself with a broad array of character traits considered to be virtuous – for example honesty, courage, generosity, politeness and many others.(Van Hooft, 2014:9) Not all of these are necessarily moral virtues, while others obviously are. But virtue ethics considers all virtues – both the moral and those that are just admirable – in the role that they play towards the flourishing of the individual. Virtue ethics is thus not about a duty to others or about the consequences to others of this or that action, but about the virtuous individual living up to the standards of excellence that they set for themselves.(Van Hooft, 2014:10)

Given that deontological and utilitarian moral theories seek normative answers to moral questions based either on universally applicable duties or the naturalistic weighing up of outcomes, it is not immediately clear on what normative basis virtue ethics operates, if any. It may be a natural inclination to try and understand virtues as personal characteristics grounded in a propensity to act according to moral duty or to act in a way that maximises good outcomes. However, although supported by some,(Beauchamp, 2001:184) such an

understanding would merely identify virtue ethics as a layer dependent on duty or consequentialist moral theory rather than a different way of thinking about morality. Rather, virtue ethics establishes itself upon the moral intuitions and sentiments of individuals considered to be of virtuous character. These intuitions and sentiments are shaped by the communities in which individuals live and reflect their traditions and the way in which honourable figures have contributed over time to a common understanding of virtue.(Van Hooft, 2014:30-31) Moreover, these intuitions and sentiments are considered to be foundational to ordered society and purposeful personal existence and development. In contrast to foundationalist, duty-based moral theory virtue ethics is described as being hermeneutic in nature. This points to virtue-based moral judgement as being interpretive and based on pre-existing attitudes.(Van Hooft, 2014:32-48)

Dignity can be conceptualised from a virtue ethics viewpoint in two ways. The first is derived from Sulmasy's notion of inflorescent dignity and related concepts such as meritorious or comportment dignity described above. In this sense, dignity is associated with those displaying virtues such as excellence, superior achievement or high social status. Virtues that are associated with dignity of this nature are not moral virtues and so, like the exclusive nature of this type of dignity, the associated virtues do not really contribute to the moral discourse. The second way of relating virtue to dignity is to consider the complimentary relationship. In other words, to see that there is virtue in respecting the dignity of others.(Jones, 2015) Unlike the first conception above, this one assumes our acceptance of a basic or intrinsic dignity.

Jones (2015) draws on the virtue of *observantia*, the acknowledgement of another's dignity articulated by Thomas Aquinas, in setting out this virtue-dignity relationship. Observantia in turn is comprised of two components: *dulia* – respect for an individual premised upon their status – and *obedientia* – obedience shown with respect to those in authority (i.e. with elevated status). In the original Aquinian description, the kind of dignity referred to was most certainly the status-based type. However, Jones argues that this original meaning can equally be applied to basic or intrinsic dignity on the basis that both *dulia* and *obedientia* (and thus *observantia* too) are general virtues applicable to all persons. In short:(Jones, 2015)

> *'Observantia is the virtue that inclines us to acknowledge the particular status or dignity of a person, and within this, the virtue of respect (dulia) specifically inclines us to show by signs and tokens the esteem and honour that is someone's due. As everyone possesses a certain dignity in virtue of their humanity, then everyone is due a certain level of respect.'*

While it may seem intuitive that *dulia* can be conceived as a general virtue, it is less obvious that *obedientia* – obedience towards those in authority – could be. After all, the notion of obedience seems to be steeped in an authoritarian, status-laden social framework rather than one stressing the egalitarian foundation mirroring the whole idea of a basic or intrinsic dignity. Jones tackles this problem by explaining *obedientia* in terms of obedience to the moral law (or, ultimately, human rights) rather than human authority and also by stressing that *obedientia* as a special virtue implies '*obedience*' of the individual to their own authority. Thus *observantia* framed by *obedientia* also involves respect for persons through a respect for their autonomy.(Jones, 2015)

Much of what is contained in our understanding of dignity, whether it is the status-based type or the basic, intrinsic type, emphasises the normality of the human condition. That is, when we think about human dignity, we tend to imagine the autonomous, rational and perhaps even flourishing individual acting in accordance with their values and principles. Yet the health care environment often involves individuals in very different circumstances. Taking this into account, Jones (2015) proposes a further virtue of *misericordia* that he argues could apply more generally, but that has special relevance in the dignity-virtue ethics relationship in health care. *Misericordia* is the virtue of fitting empathy for the adversity of others. This is not the same as pity which is an affirmation of elevated status of one over another. As a virtue it stresses the normality of dependence of humans on each other, rather than obscuring this fact by foregrounding independence as a key feature of dignity. Drawing on Thomas Aquinas again, Jones suggests that *observantia* and *misericordia* are complementary virtues.(Jones, 2015) *Observantia* unbalanced by *misericordia* might suggest an uncaring overemphasis on autonomy while the opposite might verge on paternalism – together they produce the balance and unity required to respect the dignity of those in need.

This section has explored two views of dignity from a virtue ethics perspective. The first attributes dignity to those with virtue of a status-based type which is exclusive and does not acknowledge dignity of a basic or intrinsic type. On the other hand, a starting assumption of basic dignity leads to a relationship with virtue that is precisely the other way around; that there is virtue is respecting the dignity of others. Of particular importance is the related virtue, in a health care context, of *misericordia* as described above. Having empathy as a counterbalance to the acknowledgement of dignity allows the dependence that is so often a feature of health care to be seen as a normal part of dignity. This theme will be revisited in the context of emergency care research in Section 4.2.3 below.

4.2.2.4. Collective Virtue as Human Dignity

If a relationship can be expressed between individual virtue and dignity, as argued by Jones and described above, can a claim be made that there is such a thing as collective virtue and if so, can this be related to dignity? Henry (2010) in the article from which the taxonomy used in this section (dignity as equality, status, virtue and collective virtue) appears, suggests that collective virtue equates simply to an iconographic view of dignity. By this she means that conceptions of dignity on an individual level can be translated by society to (presumably the same) conceptions of dignity at group level. As a result, an affront to individual dignity (or undignified behaviour) can be seen as diminishing not only the individual's dignity but also the collective societal notion of dignity. From this point, Henry carries the argument one step further by claiming that this '*diminishes*' both individual and collective virtue.

By way of example to illustrate the above point about collective virtue and dignity, Henry (2010) mentions prohibitions on acts such as baby-selling or cannibalism that, even if there was consent underpinning them, would be seen as violating the communal notion of dignified behaviour. What Henry is describing here is identical to the notion of dignity as constraint, as elucidated by Byleveld and Brownsword (1993:29-47) and described in Section 4.2.2.1 above. The link between dignity and virtue in this situation is unclear, as is the idea that virtue can be '*diminished*'. To make the point about societal norms related to dignity, as expressed frequently by what Bylefeldt and Brownsword refer to as the '*European bioethics*'

viewpoint, it is not necessary to make any reference to virtue ethics. Indeed, whether collective virtue is a sustainable idea at all, or one on which to base such arguments is doubtful, although views on this differ.(Byerly and Byerly, 2016; Cordell, 2017) It is not necessary to unpack the debate about collective virtue here as the point about dignity as constraint, which will be returned to in the context of emergency care research below, has already been made.

4.2.3. Human Dignity, Autonomy and the Incapacitated Adult in Emergency Care Research

The importance of human dignity in emergency care research, in particular research involving incapacitated adults, lies with understanding how consideration of dignity informs researcher conduct. The claim that all research participants have basic intrinsic dignity and are therefore owed respect, which in turn translates into a number of different responsibilities on the part of researchers, is well-accepted. However, as described above, this claim is premised upon two main ideas. Firstly, that this dignity is justified because of the human capability for rational thought. Secondly, as an expression of Kantian moral theory, that this dignity is justified not only by the ability for rational thought but by the human ability for moral reasoning and its associated law-giving role. In fact, as Rosen emphasises, Kant went further than this and made it clear that dignity is a feature of those who go beyond merely having the capacity for moral reasoning and who '*follow the moral law's commands*'.(Rosen, 2012:29)

With human dignity seemingly tightly bound to rationality, whether in the simpler form or Kant's abiding by the moral law, it is important to consider what the position might be in the case of individuals who lose this ability for rational thought. This has obvious application to research in an emergency care context where patients may have reduced levels of consciousness varying from disorientation to complete unresponsiveness due to a range of conditions or injuries such as stroke, various metabolic derangements, hypoxaemia (itself caused by a wide variety of disorders) or traumatic brain injury, among many others. Disorders or injuries directly affecting the central nervous system, and therefore consciousness, are the most obvious things to consider here. However, it is important to also recognise that other factors such as acute severe pain, severe dyspnoea and anxiety, while possibly not directly affecting consciousness (depending on the circumstances), may

render individuals unable to focus and comprehend important information required in order to participate meaningfully in the informed consent process (as described in Section 3.4 of Chapter 3). Thus, for whatever reason, an anxious patient or one with impaired consciousness lacks the fundamental cognitive substrate upon which dignity rests as part of the human condition. What does this mean for researchers?

Two interpretations of the above problem are possible. Firstly, that the loss of ability to think rationally on the part of such patients means that they do not meet the threshold condition for basic '*intrinsic*' dignity and therefore there is no duty for others to respect that which is not present. Secondly, that dignity is not actually contingent upon the demonstrable ability for rational thought (or following the moral law) but rather that it is contingent upon capacity for this, which is more like latent ability of the kind that could be argued to exist in any human who had such ability before an acute compromise.(Killmister, 2010) Simply put, the first argument is that dignity wanes together with cognition and is not a permanent feature of being human. The second argument is that dignity lives on with the individual regardless of cognition, even (as many argue) after death.

If the first interpretation above is true, that dignity can be '*lost*' by individuals who lose the ability to think rationally, what are the implications for the conduct of researchers wishing to include such individuals in research? Does it literally follow that in this case no respect for dignity is owed by researchers who can and will more or less do as they please in research with incapacitated patients, treating them as a means to an end rather than an end in themselves as prohibited by Kant on the basis of dignity? A counterargument to this position can be based on the following:

a) In Section 4.2.2.1 above, Byleveldt and Brownsword's notion of dignity as constraint is described.(Byleveld and Brownsword, 1993:29-47) That is, a societal interpretation of dignity that constrains the actions of individuals because these actions are considered to be in conflict with this interpretation. In essence, dignity as constraint is founded upon the idea of respect for the dignity of others but in a general, normative sense rather than on a case-by-case basis. Consequently, even if a logical argument could be made in an individual case that a lack of capacity results in a '*loss*' of dignity such a

societal norm would likely prevent the undignified treatment of the individual concerned. This may be a more significant factor when the norm for dignified conduct applies to a researcher who may also be a member of a profession and bound by a code of conduct or an oath.

b) As Killmister points out in her article on dignity, respect for the dignity of another is not the only (or necessarily the most important) consideration in the ethical conduct of research.(Killmister, 2010) Dignity of the researcher also determines what conduct would be considered acceptable under such circumstances. This sounds similar to the point above, however the locus is different. In this case, rather than being constrained by a societal norm for dignified conduct, in treating an incapacitated patient with respect the researcher is acting in a way that also respects their own dignity and standing as a professional.

c) Incapacitated patients, particularly those *in extremis*, are particularly vulnerable. A discussion about vulnerability in emergency care research follows below, but for now vulnerability can be considered to mean a lack of capacity for autonomous action and an inability (to at least some degree) to protect one's own interests. Identifying research participants as vulnerable means that there is a responsibility on the part of researchers, but also on the part of those providing ethical approval for research, to ensure that additional measures are in place to protect and safeguard the interests of such participants.

The arguments above, especially the second one, sound very familiar – they are closely associated with the virtue ethics notion of *observantia* (the acknowledgement of another's dignity) described above in Section 4.2.2.3 above. However, a component of *observantia* acknowledges the autonomy of others which in the case of an incapacitated patient, would not be applicable. What is more applicable and speaks to the idea of dignified conduct by a researcher when dealing with an incapacitated patient, is the virtue of *misericordia* – fitting empathy that reminds a researcher of the dignity of others, especially those who cannot protect their own interests.

The arguments above (a-c), about what might prevent undignified treatment of incapacitated patients by researchers, are important if the position is adopted that it is possible for an incapacitated patient to '*lose*' their dignity and therefore, theoretically at least, not be seen as owed a duty of respect. The alternative position, that dignity is contingent upon latent capacity for rational thought and self-legislation rather than immediate ability,(Killmister, 2010) bypasses the need for such considerations because according to this position an incapacitated patient would not '*lose*' their dignity and would be seen – even if completely unresponsive – as still being owed full respect.

At this point, when considering what dignity means for researcher conduct in emergency care research and for the treatment of incapacitated patients, it is relevant to ask whether it matters which position is taken. The important end-point is that considerations of dignity guide researchers in their conduct, whether this assumes either position above, and offers protection to those who cannot protect their own interests. There is doubtlessly a lingering unease, in fact as Killmister points out a sense of irrationality,(Killmister, 2010) in accepting that the most vulnerable patients may also not '*have*' dignity that needs to be respected. While this may be an important deeper, philosophical problem (for example how '*intrinsic*' or '*inalienable*' dignity can be '*lost*' in the first place) at a pragmatic level consideration of dignity in emergency care research, whichever way it is viewed, offers a useful framework to guide researcher conduct.

4.3. Vulnerability in Emergency Care Research

In the discussion of human dignity above, and its relevance to research ethics, the notion of a basic, intrinsic or inalienable dignity common to all humans was described. In a related way, a '*universal*' vulnerability of the human condition has been described by a range of authors, summarised well by Kottow (2003). This vulnerability is the main argument for political justice and rights in order to extend a basic form of protection to all in society. Yet at the same time it is recognised that some individuals, or groups of individuals, are at risk of greater vulnerability than broader society. This susceptibility may be brought about by destitution, or the failure of political justice and rights and it is well recognised that special protection should be afforded to those affected. This short summary describes vulnerability in society but not as it applies to research involving humans.

In principle, a similar picture emerges with human participant research although one might argue that the level and potential consequences of vulnerability are magnified. There exists a risk of harm to some degree for any human health research participant, but some situations – whether personal or contextual – heighten this risk and place some research participants in a more vulnerable position. In the discussion above of dignity as empowerment, dignity and respect for dignity is contingent upon autonomy – or at least the capacity for autonomous action. Under the same circumstances – a lack of capacity for autonomous actions – lies the greatest vulnerability for research participants. However, vulnerability as a concept in research ethics is much more complex than simply a reduction of autonomy. In this section approaches to vulnerability in health research will be discussed first in relation to definition and application more broadly and then with a specific focus on emergency care research towards the end.

4.3.1. A Brief Historical Overview of Vulnerability

As a concept in health research ethics, vulnerability has a relatively short history. It was first mentioned as such in the Belmont Report, published in 1979.(Beauchamp, 2008) The report was published by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, itself established by the US Congress in 1974. The Commission was tasked with identifying ethical principles and creating guidelines for conduct in research involving humans. This need was identified after a string of scandals in research ethics, perhaps the most notorious of which was the Tuskegee syphilis study. Given the context in which all of these scandals occurred, and the common denominator in all of them of marginalised and disadvantaged individuals who had to a greater or lesser degree been exploited, it is hardly surprising that the vulnerability of research participants was an important theme. This is summed up succinctly by Levine (quoted by Beauchamp):(Beauchamp, 2008)

> *'The Belmont Report…reflected the history of the 30 years immediately preceding it…. Our basic approach to the ethical conduct of research and approval of investigational drugs was born in scandal and reared in protectionism. Perceived as vulnerable, either because of their membership in groups lacking social power or because of personal*

characteristics suggesting a lack of autonomy, individuals were the primary focus of this concern.'

The Belmont Report is best known for its three guiding principles of research ethics – respect for persons, beneficence and justice. It is in the principle of justice that vulnerability of research participants is mainly expressed, with the principle stressing the need for fair distribution of both benefits and burdens of research. This was borne of the observation (based on some published data, testimony and press reports) that too often marginalised and disadvantaged populations were repeatedly targeted for research participation mainly for reasons of convenience.(National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979) The principle of justice requires that, because the goods arising from research are public goods and benefit society in general, the burdens or research participation should not be placed frequently on the vulnerable which the Report identified as racial minorities, the economically disadvantaged, the very sick and the institutionalised.(Beauchamp, 2008) The Report based the vulnerability of these groups on two factors: (i) their dependent status and (ii) their capacity for voluntary consent which was considered to be compromised.

Since publication of the Belmont Report, vulnerability in research ethics gained prominence in scholarly literature and eventually as a bioethical principle in its own right. In an analysis of vulnerability in scholarly literature, ten Have(ten Have, 2015) found that the word vulnerability was first used in the context of social or economic susceptibility in literature from the mid-1970s. This included ageing, crime, disasters, homelessness, economic stress, poverty and HIV/AIDS. From the mid-1990s, vulnerability was associated predominantly with literature related to climate change and globalisation and, more recently, bioterrorism and human security. Scholarly outputs referring to vulnerability in an ethics or research ethics context first appeared also in the late 1970s, but the vast majority have appeared much more recently – since 2000. The increasing focus on vulnerability from an academic perspective has been mirrored by the appearance and prominence of vulnerability in international declarations and guidelines. Reference to vulnerability first appeared in the Council for International Organizations of Medical Sciences (CIOMS) guidelines in 1991, as a lower-tier research ethics principle subsumed under the established principle of respect for

persons. Both the 2013 revision of the Declaration of Helsinki(World Medical Association, 2013b) and the United Nations Educational, Scientific and Cultural Organization (UNESCO) Universal Declaration on Bioethics and Human Rights(United Nations Educational Scientific and Cultural Organization Division of Ethics of Science and Technology Social and Human Science Sector, 2006) elevated vulnerability to the level of a specific bioethical principle in its own right.

Despite the relatively rapid uptake of vulnerability as a consideration in research ethics, it has been subject to the same definitional uncertainty as many other concepts. From the outset, as evidenced by the wording used in Section 3 of the Belmont Report, there was an emphasis on group identity as a way of defining and operationalising vulnerability.(Beauchamp, 2008) Even the bioethics lexicon reflects this, with only the term '*vulnerable population*' listed in the Bioethics Thesaurus and appearing as a Medical Subject Heading in the US National Library of Medicine's Medline database.(ten Have, 2015) While thinking about vulnerability in terms of affected groups may be intuitive and operationally convenient, the number of groups suggested to be vulnerable in guidelines and regulations increased significantly after the first four that were identified in the Belmont Report.(Hurst, 2008) This has attracted the criticism that, with the large and apparently ever-expanding number of vulnerable groups, it appears that almost all research populations are to some extent vulnerable. Other criticisms include a lack of coherence in assignment of groups and the fact that simply identifying vulnerable groups does not enhance understanding of vulnerability itself.(Kipnis, 2001; Levine *et al.*, 2004; Lange, Rogers and Dodds, 2013) More recently, different approaches to defining, understanding and operationalising vulnerability in research ethics have been suggested. These will be discussed below.

4.3.2. Vulnerability: Labels and Layers, Individuals and Groups

Kipnis suggests what he refers to as a bioethical taxonomy of vulnerability in research.(Kipnis, 2001) In doing so he argues that his analysis of vulnerability in the context of research provides a '*checklist*' of circumstances and related factors that questions the acceptability of research, provides a reasoned explanation of the source of vulnerability in each case and clearly demonstrates why vulnerability so identified is unjust (i.e. that it lends itself to exploitation). As a starting point, Kipnis asks six contextual questions about

hypothetical research participants (he uses the term '*candidate-subject*') and the research environment in order to identify six categories of vulnerability. These are, very briefly:

- *Cognitive vulnerability* (later called incapacitational vulnerability): due to impaired capacity from a range of sources.
- *Juridic vulnerability*: due to dependence involving overt or objective hierarchical structures.
- *Deferential vulnerability*: due to less obvious societal patterns of deferential behaviour.
- *Medical vulnerability*: due to illness and a reliance of care and those who deliver care (includes therapeutic misconception).
- *Allocational vulnerability*: due to lack of social goods that will be provided through research participation.
- *Infrastructural vulnerability*: due to deficient resources or integrity normally required to manage the research process and protect participants.

What stands out from Kipnis' taxonomy is an attempt to move away from the group identity approach to vulnerability that started with the identification of four '*vulnerable groups*' in the Belmont report. While this is generally successful, in some instances such as under the category of juridic vulnerability, there is still an emphasis on groups – for example those in the military or prisoners. In a later paper, published some two years after the first and with a focus on vulnerability of paediatric research participants, Kipnis makes some minor revisions to the above six categories, removes one (infrastructural vulnerability) and adds two more – social and situational vulnerability.

Social vulnerability is attributed to research participants belonging to a group whose '*rights and interests have been socially disvalued*'.(Kipnis, 2003) Within the context of the paper where this category of vulnerability is introduced, Kipnis argues that the values and views of young people historically have often been dismissed and it is from this that their vulnerability arises. Logically, this category could be extended to any other socially marginalised groups. Unfortunately, the addition of this seventh category somewhat weakens Kipnis' original goal of presenting a taxonomy that offers an alternative to thinking about vulnerability only from the perspective of group identity. Not only is this addition a

deviation from the first approach, but it seems to create a confusing series of intersections with existing categories where a type of vulnerability might also identify those from a socially marginalised or minority group.

Situational vulnerability is explained by Kipnis as being due to circumstantial factors presented by what he refers to as '*medical exigency*' and the negative effects that such factors might have on full understanding of the research by participants.(Kipnis, 2003) While this seems similar to cognitive vulnerability, it is different in the sense that it may occur even in the absence of cognitive or factual incapacity. Most often, situational vulnerability is related to time pressure where an intervention may need to be administered in a short time frame which does not allow for adequate explanation and deliberation by participants. Kipnis also includes in this category temporary psychological states that interfere with understanding and decision-making. Once again, as indicated above with social vulnerability, Kipnis has included this explanation in a paper on vulnerability in paediatric research participants, but the situational vulnerability could equally apply to research with adults. This category of vulnerability is of obvious importance when considering the context within which emergency care research often takes place.

Thus far, two approaches to vulnerability have been discussed. The first, set in place by the Belmont Report which centred vulnerability amongst research participants for the first time, is based on identity groups. The second, which Kipnis has proposed, is based on a taxonomy of circumstances and related factors which may contribute to vulnerability. In some cases, particularly in his later paper, Kipnis tends to drift towards the original approach of associating vulnerability with labels or group membership. As suggested above, a singular focus on group identity as a way of trying to identify vulnerability in research and as a way of understanding it is limited(Levine *et al.*, 2004; Resnik, 2004; Hurst, 2008; Lange, Rogers and Dodds, 2013) Not only is such an approach too expansive to be meaningful, but by relying on the broad brush strokes of group labels it invariably stereotypes research participants and may also make paternalistic treatment of some more likely. In response to this problem Luna (2019) has suggested an alternative way of thinking about vulnerability, namely that research vulnerability can be thought of as occurring in layers.

The layer metaphor is an attempt to break away from the limitations of conceptualising vulnerability primarily in terms of groups or labels, as described above, while still remaining flexible enough that existing definitions of vulnerability can still apply, at least to a certain degree.(Luna, 2019) The concept of layers involves taking into consideration a range of contextual factors that, to a greater or lesser extent, may reduce or amplify vulnerability. These could be a mix of personal characteristics, social circumstances or rights affecting informed consent or other potential risks of harm related to the research process. Layers can have an intersectional, additive effect but can also be removed meaning that in some cases research participants falling into groups typically identified as vulnerable may not be so due to consideration of these contextual factors.

While Luna's conception of layered vulnerability may offer useful insights compared to the standard approach of identifying vulnerable groups, it is not clear from the description how this could translate into practical application. Lange, Rogers and Dodds (2013) propose that although the concept is useful, application still requires a related taxonomy of vulnerability, incorporating categories of sources and states of vulnerability. Luna, in response to the suggested approach by Lange, Rogers and Dodds (2013) counters that taxonomies of any description are undesirable as they return to the same rigid, simplistic and stereotyped view of vulnerability. She then offers her own suggestion of a way to apply the layered conception of vulnerability. This involves two main steps – (i) the identification of layers and (ii) the evaluation of identified layers and associated obligations. In (i), layers are identified mainly from existing sources such as those mentioned in various guidelines or from Kipnis' taxonomy then conditions that may act as stimuli for these layers are identified, followed by further identification of what Luna refers to as '*cascade vulnerabilities*' – vulnerabilities that can induce further but different vulnerabilities in the same individuals. In (ii), the identified vulnerabilities (including cascade vulnerabilities) and stimulus conditions are ranked and prioritised and then obligations are determined in response to this information. Obligations generally are aimed at firstly, not worsening any existing vulnerabilities and then secondly and thirdly removing or minimising layers of vulnerability according to priority. Lastly, identified obligations are transformed into practical strategies that can be applied by the researchers.(Luna, 2019)

4.3.3. Exploitation and Harm of the Vulnerable

Exploitation is defined by Kottow as '*taking undue advantage of the needy*'.(Kottow, 2003) Macklin defines exploitation in research as '*when wealthy or powerful individuals or agencies take advantage of the poverty, powerlessness, or dependency of others by using the latter to serve their own ends without adequate compensating benefits*'.(Macklin, 2003a) With emphasis in both of the definitions on dependence, it is easy to appreciate how exploitative situations can quickly manifest in a research context of vulnerability, however it is thought of. Exploitation is always morally wrong because it involves utilisation of others without consideration of their interests or worth. Or to use the terminology encountered above in relation to dignity, to consider another as a means to an end. It is this wrongfulness, which is rooted in vulnerability, that distinguishes exploitation from non-exploitative utilisation.(Kottow, 2003)

The possibility of harm is an inherent part of vulnerability. Schroeder and Gefenas (2009) refer to the possibility of harm as the external element of vulnerability. They point out that, in the context of research, this potential for harm must go beyond the general potential for harm that everyone is susceptible to and must be a context-specific and significant risk for harm arising from exploitation. The internal element is a vulnerable individual's inability to protect their own interests. Not being able to protect one's own interests is further described as intrinsic – that is, fundamentally lacking competence as would be the case in a patient who is in a coma after experiencing a traumatic brain injury. In contrast to this type of inability is a situation where an individual is actually competent to protect their own interests but may not have the means to do so effectively. Examples of what Schroder and Gefenas (2009) refer to as contingent reasons for lacking the means to protect one's own interests include poverty, poor education or literacy and a high dependence on health care (either of a specific type, or generally due to lack of basic health care services) among others.

4.3.4. Paternalism and Protectionism

Paternalism is the father-like authoritative position taken by someone (in a health care context, often a doctor) to determine what is in the best interests of another under their care.(Beauchamp and Childress, 2013:215-217) Paternalistic decisions are assumed to be

made to the benefit of the other or to prevent harm. Miller and Wertheimer (2007) differentiate between soft and hard (sometimes referred to as weak and strong) paternalism. Soft paternalism applies when a decision restricting the freedom of another is taken in the context of impaired capacity. An example might be a decision of a doctor to intervene medically in a situation where a patient lacks the capacity to make an informed decision themselves because this is judged to be to their benefit or to avoid harm. Hard paternalism applies when a decision restricting the freedom of another is taken in the context of substantial capacity. In this case, a patient is fully able to make their own decision, but this is overruled against their will by someone who believes that the decision is to their benefit or that it will avoid harm.

Protectionism is the idea that humans should be protected from the risks associated with research participation.(Moreno, 2001) Inherent in this idea are the interests of research participants and the interests of science and the tension that exists between them with protectionism attempting to reach a dynamic balance. Moreno (2001) identifies three versions of protectionism that combine the above interests in different ratios. Weak protectionism places greatest responsibility for protection on the researcher with the modest limitation of guidelines. Moderate protectionism involves stricter constraints, more like rules than guidelines, but still allows some discretion for the researcher. Strong protectionism reduces the role of researcher discretion to an absolute minimum within a framework of direct third-party monitoring.

Emanuel and Grady (2007) have identified a general trend in research oversight that highlights the waning influence of both paternalism and protectionism. According to this analysis, researcher paternalism saw a high-water mark between the 1940s and early 1970s and was then replaced largely by a regime of protectionism following several scandals, most notably the Tuskegee Syphilis study, and the publication of Henry Beecher's exposé in 1966.(Beecher, 1966) This in turn gave way, with the influence of the AIDS epidemic, to a more participatory regime in the mid-1980s followed in the mid-1990s by one based increasingly on community partnership.

While it may be true that the transition in regulatory regimes above has been observed across the broader landscape of research ethics, and particularly in the USA, the authors admit that the current trend of collaborative partnerships in research as a regulatory regime is gaining traction, but far from widely established. In fact, if the views of radical research regulation critics are anything to go by, paternalism and protectionism are still the dominant, and in the view of some destructive, forces.(London, 2012) Miller and Wertheimer (2007) take the more considered view that research ethics is in fact inherently paternalistic, however they argue that what they identify as group soft paternalism in this case serves a necessary purpose under some circumstances, but raises some serious questions about the upper limit of risk that should be contemplated in research. Nevertheless, it seems that paternalism and protectionism – especially in relation to those with impaired capacity for decision-making – are not a passing trend.

4.3.5. Vulnerability and the Incapacitated Adult in Emergency Care Research

That incapacitated adults in the context of clinical interventional emergency care research are vulnerable is self-evident. Luna's approach described above involving the consideration of layers of vulnerability arising from personal characteristics, social circumstances or rights, could be applied to the emergency setting and might be particularly useful in capturing factors that differ between settings such as emergency care in high- versus low-to-middle income countries. However, as discussed above in Section 4.3.2, a combination of Kipnis' descriptions of cognitive and situational vulnerabilities probably best describe the spectrum ranging from unconsciousness, to the effects of severe pain and other distractors and even the contextual factor of simply having very little time (in some cases) to make an informed decision even if no or few other factors are present.(Kipnis, 2003)

The broad spectrum of emergency care research and associated vulnerabilities is mirrored in a wide range of possible harm, both of an intrinsic (inability) and contingent (able, but with inadequate means) nature. Risk of harm in emergency care may be minimal – as in the case of observational research – or significant – as in the case of a clinical trial involving a time-sensitive resuscitation treatment. Complicating this, at the higher-risk end of the spectrum, is the associated possible additional risk of exploitation due to both patient factors (such as reduced capacity, pain or anxiety) and situational factors such as the time-

sensitive and sometimes chaotic nature of emergencies. Thus, while it is true that not every instance of emergency care research involves a significant risk of harm and associated vulnerability, those situations involving higher acuity emergencies tend to be complex and encompass intersecting (to use Luna's expression) and additive factors heightening vulnerability and risk. Unfortunately, conditions associated with this type of situation are precisely those which are associated with the greatest benefits if effective treatments can be found.

While recognition of vulnerability of any form is an important first step in the protection of those unable to protect their own interests and who may thus otherwise be susceptible to exploitation, it is recognised that in the past this approach has sometimes been overly paternalistic. For example, women and children have in the past been over-protected and unjustly excluded requiring specific legal and policy measures to bring about their inclusion in clinical research .(Meslin and McCarthy, 2018:26-28) It would be a mistake to adopt a similar approach with the vulnerable in emergency care research. The difficult, but important, balance to achieve is to foster the protections that consideration of vulnerability offers through the ethical review and approval process but to do so in a way that still facilitates important research – important because of the potential for direct participant benefit but also because of the potential for new knowledge with social value. This theme of balancing protection of the vulnerable with the benefits of emergency care research necessitates consideration of research risk which is taken up in the next chapter.

4.4. Conclusion

In this chapter I have discussed human dignity and vulnerability as important considerations in research ethics that come into play when the research involves those lacking capacity for informed consent. These are important considerations because they guide and influence researcher behaviour in pursuit of the normative requirement to protect the incapacitated. After having discussed human dignity conceived as equality, status, virtue and collective virtue I have emphasised dignity as constraint and dignity as empowerment – of the researcher as well as the research participant. I highlight an association between dignity as researcher empowerment and the virtues of *observantia* and *misericordia* both of which may constitute the groundwork to guide researcher conduct in emergency care research.

Finally, I submit that this is not dependent on whether human dignity is interpreted as requiring the ability for rational thought on the part of research participants or not.

Following on from the discussion of human dignity, I have discussed vulnerability by first highlighting the link between a '*universal*' human vulnerability and the notion of an intrinsic or inalienable conception of dignity. Following this, after a brief historical overview of vulnerability in research, I have critically discussed three approaches to vulnerability highlighting the strengths and weaknesses of each followed by a brief discussion about vulnerability, exploitation and harm. This is followed, in closing off the latter part of the chapter, by discussion of the problem of protectionism and over-protection that may be associated with vulnerability and the need for a balance to be struck by RECs in emergency care research, between adequate protection of the incapacitated as a vulnerable group and the facilitation of potentially beneficial research. In weighing up these competing interests and attempting reach a compromise it is important to consider the role played by research risk which is discussed in detail in the next chapter.

CHAPTER 5: RISK IN EMERGENCY CARE RESEARCH WITH INCAPACITATED ADULTS

5.1. Introduction

This chapter is about research risk and specifically research risk in emergency care research with incapacitated adults. Risk is always a vital consideration in research with humans; assessing research risks and benefits and their relative equilibrium is one of the most frequent and arguably most important deliberations that Research Ethics Committees (RECs) engage in. The first section of this chapter begins with a definition and basic characteristics of research risk, followed by a description of risk types and a suggested mapping of research risk to different research designs showing that some research designs are inherently more risk-prone than others. Finally, a summary of the normative groundwork embodied in research ethics codes, declarations, guidelines and regulations is given.

As alluded to above, assessing research risk is an important function of REC work. Typically, research ethics guidelines and regulation refer to the '*balancing*' or '*weighing*' of research risks and benefits as part of this process yet offer no detailed way of doing this. Five different systematic methods for assessing research risk have been described in the literature since 2000. These five are described in the second section of this chapter along with a critique of each. Research ethics guidelines typically only allow the inclusion of incapacitated participants in emergency care research where the research risk is evaluated to be minimal – a risk standard most often interpreted absolutely and without consideration of context, anchored to the '*risks of everyday life*'. I end off this chapter by arguing that this interpretation, and the standard itself, does not lead to a useful application in risk analysis for emergency care research and that a relative interpretation can be defended.

5.2. Risk and Benefit in Health Research

5.2.1. The Definition of Risk

Risk may be defined as the chance or possibility of being harmed.(Rid, Emanuel and Wendler, 2010:1473; Coleman, 2021:130) Naturally, this would depend on a likelihood of harm occurring. But in estimating the harm, or more precisely the impact of the harm that may occur a second factor is important – the magnitude or severity of the possible harm. Thus, risk as a whole is the product of (i) the likelihood of harm occurring and (ii) the

severity of the possible harm.(Rid, Emanuel and Wendler, 2010:1473; Coleman, 2021:130) According to this definition, a lesser magnitude but frequently occurring potential harm and a greater magnitude but unlikely potential harm would be evaluated as having the same or similar risk.

Estimation of risk is a central part of two processes in research ethics. The first is the review or evaluation of research by a research ethics committee (REC) in order to determine whether the proposed research is ethically justifiable. The question asked during this process is whether the risk to which research participants will be exposed is reasonable, considering the potential benefits also associated with the research (benefits are considered in more detail below). This REC evaluation of research constitutes a gatekeeping function aimed at protection of participants from potentially harmful research procedures. Participation in research deemed by an REC to be too risky will not be offered to prospective participants.

The second process in which risk estimation plays an important part is the evaluation of risk by research participants themselves as part of the informed consent process. Even research considered to have a reasonable risk profile by an REC may be rejected by prospective participants as being too risky. However, it is only from these studies that prospective participants can make an informed choice about risks that they are willing to expose themselves to.

Risk posed by research procedures never exists in complete isolation from broader compound risks that all individuals face as a part of life. Thus, when considering the risks associated with research, it is necessary to separate these from other risks that research participants are likely to face as a result of their situation and the activities they are engaged in as part of the context in which research is conducted. In a clinical context, this means that risks associated with procedures that research participants would have been exposed to regardless of their participation are not considered to be research risks and would not be included in any risk-benefit evaluation.(Coleman, 2021:130) While this may sound simple enough, it is an idea that finds more complex expression in various approaches to the

analysis of research risk that are discussed below. It is also an idea that has much relevance to analysis of risk in the emergency care research context.

An additional factor complicating the analysis of research risk is the clinical context in which the research takes place and the way this influences risk. This is particularly relevant to some clinical emergency care research which takes place in a context characterised by sick and physiologically unstable patients, pressure on clinicians due to time constraints in carrying out clinical assessment and procedures, diagnostic uncertainty and austere or often suboptimal operating conditions. Any or all of these may increase either the likelihood or magnitude of harm thus increasing risk. However, it is important to note that this is the normal clinical context of emergency care and research procedures under investigation would be, if associated with evidence of benefit and promoted as standards of care, used in this context with all its attendant risk. This creates conceptual difficulty when combined with the fact that many patients in this same context will be incapacitated because under such circumstances the imperative to protect the incapacitated suggests that they should be exposed to no more than minimal research risk. But what is minimal research risk in such a context, and should it be correctly thought of as a relative risk standard or one anchored in an absolute, but perhaps contextually misaligned, level of risk? This question, one of the most important in relation to emergency care research with the incapacitated, will be addressed in the final section of this chapter.

5.2.2. Types of Research Risk and Types of Research

Health research may expose participants to risk of physical injury. An example of this might be a clinical trial of a new drug which brings about a severe adverse reaction in a participant leading to physical injury. However, harms that may occur as a result of research participation are not limited to physical injury. Depending on the type of research being done, harm may come in other forms. Qualitative research that involves interviewing of participants about previous experiences associated with psychological distress may trigger similar responses and bring about harm of this form. Many different types of research, both quantitative and qualitative, may document sensitive personal information for which there is a risk of unauthorised disclosure with the potential for social or other harm. Finally, there is even a possibility of harm being done to third parties in some types of research. Examples

include some forms of genetic research where results may have negative implications for those related to the research participants or research conducted in communities where results may give rise to possibly stigmatising information with a potential negative impact on a social or cultural group.(Coleman, 2021:131)

Based on the observation above that research risk does not include risk posed to patients from non-research related procedures, it follows that different types of research and different research designs will be inherently associated with differing potential for research risk. The spectrum of potential research risk across different research designs is summarised in Table 5.1 below.

Table 5.1: Research Types/Designs and Risk

Research Type/Design	Example Procedures	Potential Research Risk
Qualitative E.g. Qualitative descriptive or phenomenology	Individual or focus group interviews.	Procedures are only for the purposes of research and risks associated with them are research risks. For example, the risk of psychological distress (depending on the aims of the research) or the risk of a confidentiality breach.
Quantitative Non-clinical E.g. Surveys	Completing questionnaires.	
Quantitative Clinical E.g. Observational (record reviews, case-control or cohort studies)	Access of health records, routine clinical procedures	In the case of record reviews (and access to similar data for case-control or retrospective cohort studies) risks are only for the purposes of research and include the possibility of a confidentiality breach. For prospective cohort studies procedures would be those patients are exposed to in routine care and would carry no specific research risk. There may be other diagnostic procedures or access to clinical records which would carry research-only risk.
Quantitative Clinical Interventional E.g. RCT	Experimental (i.e. new) procedures, standard of care procedures (if this is the comparator) and other	There is a mix of research-only and non-research risk. Risks associated with the comparator if it is a standard of care would not be considered research risks as patients would typically receive this care outside of the research.

Research Type/Design	Example Procedures	Potential Research Risk
	procedures carried out only for the research.	Experimental research procedures and others (e.g. diagnostic procedures) carried out purely for purposes of the research would be considered research risks.

While any of the above research types and designs could be (and have been) utilised in the broader scope of emergency care research, quantitative and qualitative non-clinical research will not be discussed further in this chapter because a lack of capacity typically does not feature as a limitation of this kind of research. Rather, the remainder of this chapter will focus on risk (and benefit) in clinical research – particularly interventional research – where research risks, a potentially precarious clinical context and incapacitated patients converge to present serious ethical challenges.

5.2.3. Risk and Benefit: Normative Underpinnings

Questions related to research risk often constitute some of the most frequently asked during research ethics review by RECs. In response to numerous ethical scandals in research, first and foremost the atrocities committed during World War II, attempts have been made to establish ethical norms that protect human participants from risk while also facilitating valuable research with the propensity for health care improvement. Over time, these norms which have been established mainly through research ethics codes, declarations, guidelines and regulations have evolved along with conceptions of risk, benefit and the relationship between these within the context of clinical research. A detailed analysis of selected research ethics guidelines and regulations is the subject of Chapters 6 and 7. However, the main normative underpinnings of risk and benefit in research ethics are discussed below.

Assuming that no health research involving human participants is possible without at least some risk, the normative question is, what research risk is it acceptable to expose participants to? While informed consent may be thought of as moderating risk in the sense that research participants can choose whether to expose themselves or not, this question is of relevance mainly before the informed consent phase of research when RECs deliberate

about research risk and are expected to differentiate between risk that may be acceptable to offer participants and risk that may be unacceptable.

Stated as an inductive argument, the normative approach to research risk is fairly straightforward and embodied in the guidelines and regulations discussed in greater detail in Chapters 6 and 7. The argument is:

1. Human participation in research always exposes participants to at least some risk.
2. Researchers have an ethical duty, grounded in the principles of non-maleficence and respect for persons, to protect research participants from harm.
3. Therefore, research participation is only ethically justifiable if researchers minimise risks to participants.

While the conclusion reached above seems persuasive, its practical application is complex. It is not immediately clear what it means to '*minimise*' risks and against what standard risks could be considered to have been '*minimised*' and therefore ethically justifiable. Possible strategies for risk minimisation include:

a) To require research involving human participants to be critically reviewed and approved by a research ethics oversight body before the research may begin. This body in turn applies in its review processes certain broad risk minimisation or mitigation measures such as:
    (i) Ensuring that research procedures are consistent with sound research design and utilising procedures already carried out for clinical purposes for research data.
    (ii) Controlling or limiting risk in some way by imposing a criterion-referenced risk standard considered to be acceptable (e.g. minimal risk).
    (iii) Adopting the approach that risks can be balanced or justified by benefits (direct or indirect) to make them acceptable.
    (iv) In addition to (iii), setting an upper limit on research risk to avoid (iii) from being applied in a way that exposes participants to unacceptable risks on the basis of counterbalancing benefits.

b) To require participants to consent to research in order to protect their own interests and ensure that the degree of risk to which they are exposed is acceptable to them.

The normative argument and strategies above have all been implemented to various degrees and in various combinations in codes, decelerations, guidelines and regulations spanning the last seven decades (a detailed analysis of these is the subject of Chapter 6 and Chapter 7). The normative approach to research risk where b) above does not apply is more complex. The historical record has shown a progression of norms originating with a strict requirement for informed consent (as contained in, for example, the Nuremberg Code) which follows the argument below.

1. Emergency care research with the incapacitated is necessary to generate new knowledge in this field in order to improve emergency interventions and reduce morbidity and mortality but involves risk.
2. Incapacitated patients cannot consent.
3. Because of the ethical duty of researchers grounded in the principle of respect for persons, research with human participants may only be performed with their informed consent.
4. Therefore, emergency care research with the incapacitated cannot be conducted.

Over time and through revision of various research ethics guidelines, a gradually more permissive stance to research with the incapacitated has evolved. The normative argument (as contained in, for example, the 2016 CIOMS guidelines(Council for International Organizations of Medical Sciences, 2016)) has changed to become:

1. Emergency care research with the incapacitated is necessary to generate new knowledge in this field in order to improve emergency interventions and reduce morbidity and mortality but involves risk.
2. Incapacitated patients lack autonomy.
3. Researchers do not need to respect the autonomy of those who cannot act autonomously.

4. However, researchers have an ethical duty, grounded in the principle of non-maleficence, to protect research participants from harm. This duty is greater with regard to incapacitated patients because they are vulnerable and cannot protect their own interests.
5. Therefore, emergency care research with the incapacitated is only ethically justifiable if the research carries a reasonable prospect of direct benefit justifying research risks or exposes participants to no more than minimal risk (or a minor increase above minimal risk, the latter generally being accepted as the risks associated with '*daily life*').

Other than the nature of the argument above and how it differs from the first one, two other normative features are noteworthy. Firstly, this argument references the principle of respect for autonomy, rather than respect for persons. The Belmont report highlighted the principle of respect for persons as a way of conferring protection on those with and without capacity. Both are considered '*persons*' and worthy of respect. This conception takes a sharp turn, however, with the publication of the first edition of the *Principles of Biomedical Ethics* where respect for persons is transformed into respect for autonomy.(Beauchamp and Childress, 2013c) With this transformation, the non-autonomous are no longer bound by the principle of respect for autonomy because they cannot act autonomously in the first place. Instead, they are to be protected by application of the principles of beneficence and non-maleficence. Because both of these principles are grounded in utilitarian terms, the protection offered by their application has been argued by some to not have the same moral weight as that associated with respect for persons.(Lysaught, 2004)

Secondly, the argument above emphasises the normative concept of direct participant benefit as a way of balancing, offsetting or justifying risk. This is based on the idea that in clinical research there is a duty of care and conduct of researchers is determined by what Litton and Miller (2005) refer to as the ethics of care rather than the ethics of research, which foregrounds the production of new knowledge. This concept of the justification of risk – which does not reduce risk *per se* – is based on the principle of beneficence which was articulated in the Belmont Report with the dual meaning of (i) not harming research participants but also (ii) maximising benefits and minimising harms (risk). (Levine, 2005:128-130) The intertwining of duties to both protect research participants but also secure their

wellbeing originates in the ancient ethical institution of medicine but since the Belmont Report finds expression as a guiding principle of research.

Adopting a normative position of risk justification through application of the principle of beneficence since the Belmont Report has created difficulty in the assessment of research risk. While the principle may sound conceptually simple, its application is anything but. Several approaches to risk assessment are discussed below, some embracing the ethics of care and using constructs such as clinical equipoise and the differentiation of therapeutic and non-therapeutic research procedures. Others have outright rejected the idea of a researcher's primary duty to care for research participants and have adopted risk assessment methods more in line with an ethics of research combined with measures to curb exploitation. Normative questions regarding research risk in the emergency care context with the incapacitated will be returned to in the last section of this chapter, after discussion of the five approaches to risk assessment in clinical research.

5.3. The Assessment of Risk in Clinical Research

In the discussion below, five different approaches to clinical research risk assessment are described and critiqued. The last of these, the Systematic Evaluation of Research Risks, is a detailed method for evaluating specific research risks against comparator risk levels or benchmarks and could itself be used together with some of the other approaches discussed.

5.3.1. Component Analysis

Component analysis (CA), as described by Weijer (2000), has a long history drawing its conceptual roots from work published in several reports of the US National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. One of these reports, '*Research on the Fetus*' published in 1975, contained references to two conceptually different types of research. The first of these, termed therapeutic research, was considered to be research intended to improve the health of the research participant in the sense that it was associated with a '*reasonable expectation of success*'. The other type of research, non-therapeutic research, was simply the opposite – research designed and conducted with no expectation of improving participant health. This separation was seen as allowing a clean conceptual division of recommendations for the two types of research, one

of which concerned risk. Only minimal or no risk was allowed in the case of non-therapeutic research.

From this point, in the late 1970s, through a series of refinements in subsequent National Commission reports, therapeutic and non-therapeutic research as a whole was transformed into the finer-grained idea of therapeutic and non-therapeutic *components* of research, that is research procedures. While acknowledging that research very often includes both of these, by the early 1990s CA had begun to crystallise into its currently recognisable form with the proposition that ethical analysis should be separated along the lines of clinical intent with different requirements for risk depending on whether procedures were therapeutic or non-therapeutic. While this approach was already manifest in the Common Rule at the time, it was adopted by the US National Bioethics Advisory Commission on the basis of a commissioned paper by Weijer (2001).

In its current form, CA proposes a form of risk analysis that begins by dividing any clinical research protocol into separate components based on identifying each research procedure (sometimes referred to as interventions) as either therapeutic or non-therapeutic. Therapeutic procedures are those carried out with '*therapeutic intent*' or what is also sometimes referred to as a '*therapeutic warrant*', meaning that they are carried out as a function of the clinician's duty to provide the best possible care to a patient (whether the recipient is a patient or a research participant is debatable and speaks to one of the problems with CA as discussed further below – some resort to the all-encompassing term of patient-participant). One example is a new drug that shows promise in animal and preliminary human testing and is reasonably thought to offer advantages compared to one or more others that are standard care. On the other hand, non-therapeutic procedures are those devoid of therapeutic intent and are comprised of procedures typically conducted for scientific purposes or for answering the scientific question driving the research. Examples include diagnostic procedures or access to clinical or other data related to the research question. Both types of procedures may carry risk, but CA proposes two separate analyses of this and two separate risk standards.

The separation of risk analysis proposed by CA derives from the view that the procedural divide described above has moral significance.(Weijer, 2000:352) For therapeutic procedures, the moral justification rests on risks being balanced by the reasonable prospect of potential direct benefits to individual participants. This balancing is wrapped in the construct of clinical equipoise which is used to evaluate the risk-benefit profile of a new or experimental research procedure against a standard of care. Morally, both the experimental procedure and the standard of care must be considered aligned with a norm of competent care. When this is true, clinical equipoise may be defined as '*honest professional disagreement among expert clinicians about the preferred treatment*'.(Freedman, 1987:144) According to CA, this is the only requirement to be satisfied in order to justify the risks of a therapeutic procedure. Weijer (2000) explains that by using clinical equipoise in this way a numerical analysis of risk equivalence can be avoided. Instead, he invokes the concept of a '*therapeutic index*' that is used as an approximation, describing this as '*a compendious measure of potential benefits, risks and uncertainty*'.(Weijer, 2000:354)

In the case of non-therapeutic research procedures, no such claim to direct benefit and a consequent balancing of risk can be made. Rather, the balance to be considered is between risk and new scientific knowledge for future application. CA thus approaches these procedures differently requiring that risks are '*minimised*' in that (i) they are in line with appropriate research design and do not expose research participants to unnecessary risk and (ii) are likely to result in useful new knowledge (relative to the risk involved). For situations where research involves vulnerable participants, a third condition applies to non-therapeutic procedures – they must also constitute no more than a minor increase above minimal risk. Minimal risk is defined as:(Weijer, 2000:359)

> '*the probability and magnitude of harm…no greater than that encountered in the daily lives of all (or the great majority) of persons in the population from which research subjects are to be recruited*'.

Weijer (2000:356) attempts to explain a minor increase above minimal risk by drawing a comparison to research involving children. He sees the minor increase as being similar to the judgement of parents discharging their protective duties in allowing their children new

experiences which might involve greater risk than those of daily life. At the same time, he suggests that research ethics committees function – following this analogy – *in loco parentis* in evaluating the risks of non-therapeutic research procedures against this standard.

In summary then, for non-therapeutic research procedures two different sets of conditions for risk have been described above. The first, for research participants that are not vulnerable or otherwise compromised, only makes reference to points (i) and (ii) above without mention of any other specific risk level. The second, for vulnerable research participants, refers to points (i) and (ii) but adds the further condition that risk may not exceed a minor increase above minimal risk. A third set of conditions has been suggested by McRae and Weijer (2002) with specific application to the emergency care setting and research with incapacitated patients. This time, the risk threshold for non-therapeutic research procedures is set to minimal risk which is simply described as the risks of '*daily life*'. Regardless of these three differing sets of conditions for non-therapeutic research procedures, the same approach to risk for therapeutic procedures applies across all the scenarios above, that of the clinical equipoise-guided analysis.

5.3.2. Critique of Component Analysis

One of the main objections to CA is its foundational reliance on the distinction between therapeutic and non-therapeutic research procedures. Rid and Wendler (2010) claim that CA does not offer any convincing basis for this difference. On the one hand, they argue that researchers (who are also usually clinicians) do not typically have the singular intention of providing clinical benefit for research participants but also, simultaneously, wish to generate new knowledge for future application and the benefit of others. Thus, by such reasoning, they argue that most research procedures are both therapeutic and non-therapeutic based on these inextricably mixed intentions. On the other hand, assuming that non-therapeutic research procedures can be isolated the way that CA attempts to do, they argue that such a definition is simplistic referring to the possibility that many diagnostic or screening tests may also detect undiagnosed abnormalities and thus benefit participants albeit in an unanticipated way. The point they make is that such a counterexample undermines the definition of non-therapeutic procedures and therefore casts doubt on the validity of the absolute therapeutic-non-therapeutic divide upon which CA rests.

The above critique of definitions may appear to be a semantic debate; however it cuts to the heart of CA's thesis – that the different intents associated with therapeutic and non-therapeutic research procedures represent a morally significant difference that, in turn, justifies different ways of analysing risk in the two '*components*'. Precisely because of the intent driving therapeutic research procedures, Weijer (2000) argues that clinical equipoise – which may condone research procedures with heightened risk – is an appropriate construct to apply. Likewise, precisely because benefit is absent in non-therapeutic research procedures only a risk threshold slightly above minimal risk (for the non-vulnerable) is tolerable. If, in reality as Rid and Wendler (2010) argue, we cannot distinguish between these two types of research procedures clearly and reliably the rationale for CA's differential moral analysis of risk falls away.

A second, but related, criticism of CA focuses more closely on the validity of clinical equipoise as a means of assessing risk (this assumes that we may not be convinced of the argument above, otherwise this critique is moot). CA employs clinical equipoise as a justification for random allocation of research procedures that is, at the same time, claimed to also fully align with the clinician's duty to act in their patient's interests and provide care that benefits them. Quoting Charles Fried's view that '*good medicine*' arises from the consensus of professionals, Freedman (1987:145) affirms the intersection between patient care and clinical research when he states that '*in a state of clinical equipoise, "good medicine" finds the choice between [two randomised procedures] indifferent*'.

There has been a long-standing contention that this position is mistaken because research and clinical care are two divergent activities with fundamentally different ethical justifications and conflating them in this way is incorrect. Litton and Miller (2005) refer to these different justifications as the '*ethics of care*' and the '*ethics of research*', arguing that the important role of research in improving the human condition through medical care that has been proven sets research apart from medical care in a normative way and gives rise to the ethics of research which is fundamentally different to the ethics of care. This difference rests upon the disparate goals of the two activities, primarily typified by the emphasis on

individual care and benefit in medical care and the emphasis on protocolised care in pursuit of generalised knowledge in research.

A natural concern with Litton and Miller's position above is that it may commodify research with humans and lead to the exploitation of research participants. This concern is countered with two arguments. Firstly, that the clinician's duty to benefit patients is not completely dispensed with, but rather plays a secondary role to and is limited by the scientific objective of societal benefit through the generation of new knowledge.(Miller and Brody, 2007:162) Secondly, that it is possible to approach the analysis of risk in clinical research through a framework that does not involve clinical equipoise but does protect research participants from exploitation. This is proposed by Miller and Brody (2003:26-27) who modify the seven ethical requirements for clinical research originally proposed by Emanuel, Wendler and Grady (2000).

Critique of CA's therapeutic-non-therapeutic dichotomy and its reliance on clinical equipoise for the risk assessment of therapeutic research procedures account for much of its opposition. However, there are a few other criticisms of CA worth noting. Highlighting a point not far removed from these latter two, Rid and Wendler (2010) note that CA's use of different ethical requirements for risk analysis between therapeutic and non-therapeutic research procedures is not justified. One of the main concerns with analysing the risk of whole protocols (rather than individual research procedures) was that risky non-therapeutic research procedures might be allowed under the guise of therapeutic procedures with significant benefits which would '*mask*' the non-therapeutic risk.(Weijer, 2000:347) To overcome this, the recommendation was made that research procedures should be risk-assessed individually, which does solve this problem and is an improvement over whole protocol risk assessment. However, the reason for adopting what Weijer (2000:352) refers to as a '*rigorous separation of the moral calculi*' for the two types of procedure lacks a normative justification.

Another unconvincing aspect of CA is the justification for and explanation of different risk thresholds for non-therapeutic research procedures involving vulnerable and incapacitated participants. These thresholds, described above in more detail, are minimal risk where

participants are incapacitated(McRae and Weijer, 2002) and a slight increase above minimal risk where participants are considered to be vulnerable.(Weijer, 2000) In the latter description although the term '*vulnerable*' is used, in the same article at different points Weijer also ostensibly uses the term '*incapable adults*' and '*adults who are incapable of providing informed consent*' in referring to the same population to which a minor increase above minimal risk for non-therapeutic research procedures applies.(Weijer, 2000:359-360) Two years later, in a different article advocating the use of CA for risk analysis in emergency care research specifically, the same mix of terminology is used ('*vulnerable*' and '*incapable participants*' at different points) but this time the risk threshold is reduced to minimal risk.(McRae and Weijer, 2002:1148) While the context of the latter article is emergency care, muddled use of terminology seemingly applicable to a very broad population makes it difficult to understand whether a new risk threshold for CA is being proposed and what CA suggests regarding risk for vulnerable research populations.

Notwithstanding the above, the definition of a minor increase above minimal risk proposed by Weijer (2000:358) as applicable to vulnerable research participants also has two main problems. Firstly, equating vulnerable adults to children and then arguing that the same standard for risk analysis should apply to both seems incoherent. Vulnerable adults as a group are heterogeneous and include a spectrum of capacities for decision-making ranging from none (e.g. an unconscious adult) to relatively impaired (e.g. a prisoner). In the latter case, the problem is not necessarily an impairment of inherent decision-making ability but rather an impairment of the individual's ability to protect their infests because of a potential threat to voluntariness of decision-making. The line of reasoning followed by Weijer (2000:356) is that children have an absolute lack of capacity due to their age. Thus, it is clear that there is not a one-to-one relationship between vulnerable adults and children in terms of capacity. Moreover, it seems that Weijer's position regarding children and capacity is a strictly dichotomous one that does not take into consideration the by-now accepted view that older children who are capable can and should assent to research participation even though their age may classify them as not having full capacity for independent decision-making.(Rossi, Reynolds and Nelson, 2003; Oulton *et al.*, 2016)

Secondly, even if we set the above objection aside, casting RECs as acting *in loco parentis* regarding risk analysis and vulnerable participants might serve as an analogy, but it does not translate into practical application in trying to understand what exactly the '*minor increase*' above minimal risk might be or what kinds of incremental risks beyond minimal may or may not be acceptable. Weijer (2000:356) invokes expressions such as the '*new experiences*' of children to try and typify increased risk but why would a new experience necessarily by risky? Perhaps the idea is that there is an element of risk in the unknown and this somehow informs our understanding of a '*minor increase*', although this is an unlikely interpretation considering that RECs would not be weighing up vague '*new experiences*' when analysing non-therapeutic risks for vulnerable participants. Clearly, asking RECs to evaluate risk '*as a responsible parent would*' is unlikely to be reliably applied as a test.

5.3.3. The Agreement Principle

The agreement principle is an approach to risk analysis for clinical research that is offered primarily as an answer to shortcomings of approaches that rely on what Rajczi (2004:338) refers to as the improvement principle. That is, the principle based on assessments, however articulated – whether as '*risk benefit ratio*', '*weighing of risks and benefits*' and others – that have as their benchmark for acceptability a final judgement of greater good than harm. Rajczi cites the Common Rule's description of risk and benefit assessment as an example of the agreement principle and highlights two main problems with this approach. Firstly, that it is effectively impossible to use because to use it would require a form of expected value calculation and this is not possible due to the difficulties with judging the likelihood of harm and benefit and the impossibility of actually doing such a calculation. Secondly, Rajczi thinks that the improvement principle is at odds with other principles governing liberal political societies.

The key feature of liberal political societies that explains the above position and justifies the agreement principle is limited voluntarism. That is, the idea that an appropriate test of whether it is acceptable for one individual to offer another an opportunity involving risk is whether a '*competent and informed decision-maker*' would accept such an offer. If this decision-maker accepts the offer it is taken as meaning that the risks and benefits involved are acceptable. In reality, liberal political societies do not always follow such an approach

rather opting for more paternalistic interventions to protect individuals. According to Rajczi, this is because in most situations it is not possible to provide decision-makers with enough detailed information to facilitate a competent and informed decision. However, if the provision of such information is possible – as in the case of research information - then such paternalistic protections are not necessary.

Formally stated, the agreement principle is:(Rajczi, 2004:342)

> '*A protocol has an acceptable combination of risks and benefits if it would be entered into by competent and informed decision-makers – that is, people who (i) have a set of values that is at least minimally consistent, (ii) are informed about the nature of the protocol in question and (iii) reason clearly about whether to enter the protocol using those values. Otherwise, it does not*.'

The agreement principle views risk assessment from the perspective of the informed decision-maker who would be the hypothetical participant. However, RECs are tasked with the initial decision about risk and benefit before the possibility of participation can be offered to prospective participants. In order to accomplish this, RECs are required to assess research protocols from the perspective of the informed and competent decision-maker having the above three characteristics. If the REC, placing itself in the position of the informed decision-maker, would agree to participate in research described by a protocol then the research is considered to be acceptable.

5.3.4. Critique of the Agreement Principle

One of the proposed advantages of the agreement principle is that it offers a valid way of avoiding the difficulties associated with the normal approach to risk-benefit analysis regularly engaged in by RECs and which follows the improvement principle. Despite this claim, when considering how application of the agreement principle might work it seems unavoidable that part – likely the most significant part – of the determination of protocol acceptability would be the '*weighing*' of benefits and risks. After all, the agreement principle only refers to the competent and informed decision-maker finding a protocol acceptable, but it does not specify how this is done. This observation may simply be a function of how

entrenched the '*weighing*' of benefits and risks is in RECs, having been a part of the wording of most, if not all, influential research ethics guidelines and regulations. Nevertheless, the agreement principle does not specify an alternative form of risk analysis that could not end up drifting back towards the improvement principle if force of habit or dogma pushed it that way.

The agreement principle is unique in the sense that it is consistent with some situations that application of the improvement principle would not be. For example, a consequence of the agreement principle is that monetary compensation can be considered a benefit – contrary to the conventional view – simply because some informed and competent decision-makers might see monetary compensation that way.(Rajczi, 2004:344) This in turn permits a situation where research participants, at least some of them, may be willing to trade risk for monetary compensation – a possibility that Rajczi acknowledges as being embedded in the limited voluntarism worldview.(Rajczi, 2004:344-345) Another consequential example of the agreement principle is self-sacrifice. In other words, research participation where there are either (i) no benefits for the participant but there are benefits for society in the form of new knowledge or (ii) there are no benefits for the participant or society. Because the agreement principle places no constraints on how the informed and competent decision-maker decides it cannot be ruled out that some may go this way and decide that a research protocol with the implications of (i) or (ii) is acceptable.(Rajczi, 2004:345-346)

While the above implications of the agreement principle clearly highlight how different it is from risk analysis based on the improvement principle, they also raise questions about its practical application. As Rid and Wendler (2010:163) ask, of what practical relevance is the insight that some – and probably a very small minority of – informed and competent individuals might make decisions that deviate from the majority as exemplified above? The normative meaning of this is quite uncertain and if, as the agreement principle requires, REC members situate themselves as the informed and competent decision-makers, how would they decide? It is at this point that the uniqueness of the agreement principle fails to really distinguish it as a worthier alternative to the improvement principle.

Finally, one characteristic of the agreement principle is important to consider in the context of research involving those lacking capacity for informed consent. Formulation of the agreement principle refers explicitly to the *competent* and informed decision-maker. Rid and Wendler (2010:163-164), in their critique of the agreement principle, take this as meaning that it cannot be used for analysis of risk in research with those lacking capacity who would be, by implication, uninformed. However, this position seems to be incorrect. Rajczi (2004:342) explains that the agreement principle does not rule out the possibility that incompetent individuals would accept a given research protocol. While the literal interpretation of this seems absurd it is not, because the requirement of being competent and informed is a condition for the '*approvability*' of the research protocol rather than a concrete condition that each real participant must have capacity and be informed. Competence and being informed are proposed as a '*should*' for the purposes of decision-making rather than a '*must*' in application.

5.3.5. The Integrative Approach

The Integrative Approach (IA), first described by London in 2006, is suggested as an alternative approach to risk assessment that avoids the pitfalls of what London calls the '*two central dogmas*' of research ethics.(London, 2006, 2007) The central dogmas that London refers to, that clinical research is a fundamentally utilitarian activity and that the set of constraints put in place to curb this are based on clinician obligations, both feed into the argument that equipoise is a core component of risk assessment. The latter dogma is also referred to as an approach to risk analysis based on the (professional) duty of personal care owed by any clinician to any patient under their care, sometimes also referred to as therapeutic obligation.(London, 2007:101-104) London sees this as the fundamental premise upon which the principle of equipoise is based and devotes much of his first article to the nuances of equipoise and clinical equipoise.(London, 2006:2872-2875) However, he rejects the concept of equipoise grounded in a therapeutic obligation because it is '*overly paternalistic*' and thus does not see it as a valuable framework for the assessment of risk as applied, for example, in CA.(London, 2007:105) Hence, the need for an alternative framework – the IA.

The IA is based on a liberal democratic framework of shared basic interests in a community. Basic interests are those interests individuals have in developing capacities to live their lives according to a '*conception of the good*' and interact with others in accordance with '*principles of right*'.(London, 2007:109) The set of basic interests defines what London refers to as the '*space of equality*' in which all members of a community may lay claim to being treated equally. Arising from the space of equality is a common good aligned with the interests of individuals in seeking personal ends and social relations. The IA also draws on an egalitarian political model that sees clinical research as an activity that must be acceptable to individuals in a community whose interests will be protected and promoted by this activity. Within this model, social problems (such as those related to health) are approached by integrative solutions. That is, solutions that promote the basic interests of each individual through pairing duties with those individuals disposed to ensuring the basic interests of others in the community.(London, 2007:110) Thus, disease or injury which restrict the interests of some in a community can be addressed through clinical research enabled by the participation of others as a way of respecting the moral equality of all in the community – within the space of equality.

From the above framework, London proposes the following statement of reasonable research risks:(London, 2007:111)

> '*Risks to individual research participants are reasonable just in case they*
>
> 1. *require the least amount of intrusion into the interests of participants that is necessary in order to facilitate sound scientific inquiry and*
> 2. *are consistent with an equal regard for the basic interests of study participants and the members of the larger community whose interests that research is intended to serve.*'

The two parts of the above definition map onto personal and basic interests (personal interests are those related to personal formulations of the good and goals set to enact this). Part one addresses both personal and basic interests while part two addresses only basic interests. London explains this formulation as supporting a normative claim justifying a request for individuals to negate some of their personal interests in favour of promoting the

basic interests of others. There is, however, an important constraint on such requests namely that they should not negate the basic interests of research participants to a degree greater than would be considered acceptable for the basic interests of any other individual to be negated.(London, 2007:111) Importantly, the reasonable risk definition above represents a level risk that it is acceptable to offer research participants but there must also be unrestricted and informed consent on the part of the individual participant.

London posits two operational criteria for the condition of equal regard put forward in part two of the reasonable risk definition above. These criteria address the question of what conditions must be met for equal regard to be shown toward the basic interest of those participating in research and others (non-participants) in the community as a function of reasonable risk. The first of these is:(London, 2007:111-112)

> '*Equal regard for the basic interests of research participants and non-participants requires that when the basic interests of an individual participant are threatened or compromised by sickness, injury or disease, the basic interests of that individual must be protected and advanced in a way that does not fall below the threshold of competent medical care*.'

'*Competent medical care*' is described by London as '*the socially enforceable standard of professional knowledge, skill and ability that community members have a legitimate right to receive when they access the medical system*'.(London, 2006:2879) While the above definition appears to be very close to the application of clinical equipoise, London is quick to point out that the origin of this criterion, and specifically the requirement of maintaining the threshold of competent medical care, is not derived from the researcher's professional duty of care. Rather, this criterion originates from the constraint described above – that the negation of the basic interests of research participants must always be equivalent to that considered acceptable for any other individual in the community and that a threshold below competent medical care for research participants would alter this.(London, 2006:2878)

The second operational criterion for the condition of equal regard in part two of the reasonable risk definition is:(London, 2007:114)

'*In all cases, the cumulative incremental risks to the basic interests of individuals that derive from research activities that are not offset by the prospect of direct benefit to the individual must not be greater than the risks to the basic interests of individuals that are permitted in the context of other socially sanctioned activities that are similar in structure to the research enterprise*.'

This criterion embodies the idea that individuals in society ordinarily do take risks that impede their basic interests and thus setting a zero-risk threshold for the activities described above does not make sense. Rather, risk is unavoidable, but the challenge lies in determining an appropriate (reasonable) risk level. London uses a unique risk comparator by identifying the idea of '*socially sanctioned activities…similar in structure to…research*". He then suggests four features of research that could be used to guide the selection of a comparator activity. These are (i) that the activity must be associated with risks that do not add to its social value (i.e. they are '*necessary evils*'), (ii) that the activity must be the subject of public oversight making its risks socially acceptable, (iii) that the activity is associated with risks that benefit others and (iv) that the activity should involve a principal-agent relationship, meaning a relationship where another party (the researcher) has important responsibilities in protecting the participant's interests. While not committing to an example that satisfies all of these features, London suggests that the volunteer public service professions (such as emergency medical services) come close to the type of activities he has in mind.(London, 2007:114-115)

5.3.6. Critique of the Integrative Approach

London's main point of departure with the IA is that it avoids the two central dogmas of research ethics described above. In other words, IA is proposed as a fundamentally different normative approach to risk analysis in clinical research. To the extent that the IA is grounded in a less common (although not completely unique) normative justification, this proposal succeeds. However, despite this, the IA seems to arrive at a very similar destination to component analysis and ends up with one of its criteria for equal regard being what sounds identical to clinical equipoise. Even though it is clear that this is not based on the duty of

care, it seems to amount to a similar application as far as protection of research participants is concerned.

In a critical review of the IA, Rid and Wendler (2010:160-162) conclude that it differs from CA in only two respects. Firstly, that all research procedure risks are minimised and secondly that the conceptual basis and criterion for establishing a reasonable risk level for non-therapeutic research procedures is different to that used in CA. While the latter point is clear, the way that IA is described makes it quite difficult to evaluate the former point. This is because in describing two conditions for reasonable research risk, London does not clearly distinguish between research procedures that have a direct benefit to research participants and those that do not. Yet, when describing the two criteria for equal regard to research participants vs. non-participants a distinct therapeutic vs. non-therapeutic divide emerges. This can only be reconciled with the statement on reasonable research risk by assuming that the competent care referred to in the first criterion for equal regard is therapeutic in nature. It seems as though there was a desire to break away from CA (and a duty of care-derived reliance on clinical equipoise more generally) with the IA, but this has led to a rather blurred view of risk analysis which ends up closely resembling CA but without its clearer dichotomy of therapeutic vs. non-therapeutic research procedures.

In attempting to consider how the IA might be deployed in the analysis of risk for emergency care research involving incapacitated adults, two further limitations are evident. Firstly, it is not clear how a lack of capacity is explicitly dealt with in the IA. The description of reasonable risk could be applied to such a scenario broadly, as an analysis balancing personal and basic interests. However, London makes it clear that the reasonable risk he describes is a level of risk to be offered to research participants, but subject to their acceptance through the process of informed consent. How the analysis of risk should proceed in the absence of informed consent is not evident making the IA difficult to apply.

Secondly, assuming a solution can be found to the above limitation, the second criterion for equal regard that requires a socially acceptable comparator activity against which to judge the risk of non-therapeutic procedures lacks a valid normative basis.(Rid and Wendler, 2010:161-162) Even if this could be remedied, the criterion seems to be very difficult to

apply practically – it is very difficult to imagine a suitable comparator that meets all four of London's required features (the author himself seems to be at a loss to find one).(London, 2007:115)

5.3.7. The Net Risks Test

The net risks test, devised by Wendler and Miller (2007) in opposition to CA, also analyses risk by considering each individual research procedure. However, the approach used for this is fundamentally different compared to the therapeutic vs. non-therapeutic dichotomy used by CA. Wendler and Miller (2007:484) explain the concept of net risk by giving two scenarios with which it is associated. The first scenario, simply enough, is when procedural risks exceed benefits – with the example given of drawing a blood sample for research purposes which is associated with risks but no benefits for participants. The second scenario is a situation where an individual research procedure is associated with greater benefits than risks, but this positive '*risk-benefit profile*' is not as beneficial as another associated with an available alternative procedure.

The first step of the net risks test is to identify all research interventions or procedures and assess the risk-benefit profile of each. This is done in each case by comparing the procedure's risks with its potential clinical benefits and by comparing the risk-benefit ratio of each research procedure so obtained with the risk benefit ratio of available alternatives, including the application of no procedure if applicable. For those research procedures with net risks, the degree of net risk for each is proportional to the increased risk or reduced potential benefits when compared to available alternatives.(Wendler and Miller, 2007:484)

Following the above steps, each research procedure with net risks is assessed to establish that the risks are not excessive and are warranted in relation to new knowledge with social value generated by the research. No particular methodology is suggested for this evaluation. Finally, cumulative net risk is assessed. That is, the total of all net risks. This step avoids the problem of having a series of small individual net risks that appear reasonable on their own but are excessive when considered together.(Wendler and Miller, 2007:484-485) The net risks test only specifies one risk threshold for excessive risk – at most a minor increase over minimal risk where research participants are children or incapacitated adults. With regard to

a maximum risk limit in all other cases, Wendler and Miller (2007:484) simply state that there is a lack of consensus on this question.

5.3.8. Critique of the Net Risks Test

The most detailed critique of the net risks test has, unsurprisingly, been offered by Weijer and Miller (2007). Their first and most serious accusation is that the net risks test does not protect research participants adequately. This is because the net risks test's concept of '*excessive risk*' which it claims to protect participants from is never adequately defined. While this particular term is singled out, there is also broader critique of other imprecise concepts such as '*favourable risk-benefit ratio*' and practicalities such as how risks and benefits are compared and how conclusions are reached about their equilibrium. In addition, and specifically with regard to the third step described above (that assesses whether the risks of each research procedure are justified in relation to the new knowledge produced), Weijer and Miller(2007:488) further highlight the lack of protection potentially arising from what they refer to as a '*frankly utilitarian calculus*'. This is because, in the absence of a clear definition for excessive risk, they interpret this part of the net risks test as allowing any level of risk relative to the importance or social value of new knowledge generated by research, even that caused by research procedures with no benefits or '*substandard medical treatments*'.

A second critique of the net risks test is that it deviates from the ethics of care imperative and does not align with the duty of care owed by clinicians to their patients. This is intentional on the part of Wendler and Miller (2007), whose main rationale for proposing the net risks test is to offer an alternative to CA which centres its approach on the duty of care, justified by the use of clinical equipoise to analyse risk for therapeutic research procedures. The argument about whether research should be governed by the ethics of care or by the ethics of research is an ongoing and unresolved one typified in many ways by the adversarial nature of arguments for and against CA and the net risks test.(Lemmens and Miller, 2002; Steinberg, 2002; Miller, 2004; Litton and Miller, 2005)

Finally, in defending the net risks test from the criticism that it permits any level of risk as justification for the generation of new knowledge with social value, Rid and Wendler

(2010:165) refer to the limit of excessive risk but also to the net risk test's '*underlying principle of non-exploitation*'. However, the original description of the net risks test does not clearly explain any principle of non-exploitation and it is equally uncertain how this underlies the test.(Wendler and Miller, 2007) Although other work by Miller and Brody (2003) does articulate such a principle it is unclear what the relationship is between this and the net risks test.

5.3.9. The Systematic Evaluation of Research Risks

Most of the approaches to risk analysis described above suffer from the same basic weakness. They put forward different conceptual frameworks but they all, with the exception of the integrative approach, require at some point that there is a balancing or weighing of research risks and benefits in order to reach a conclusion about which outweighs the other and whether risks associated with proposed research procedures are reasonable. This may be explicit, such as with the net risks test, or implicit as with CA (i.e. part of the consideration of clinical equipoise) but regardless of which applies, these evaluations tend to be vaguely described.

In answer to this problem Rid, Emanuel and Wendler (2010) have proposed a systematic framework for exactly this type of risk-benefit analysis called the systematic evaluation of research risks (SERR). The SERR facilitates evaluation of the risk associated with research interventions by contrasting each with comparator activities considered to be of an acceptable risk level taken within a specific research context. The comparator activities can be aligned with a risk threshold – such as minimal risk – or they can represent standard care against which an experimental intervention is being tested. The SERR methodology follows four steps: (i) identifying the potential harms of each intervention, (ii) categorising the magnitude of each harm using a seven-point harm scale, (iii) estimating the likelihood of each harm and (iv) for each harm, comparing its likelihood with the likelihood of harms of the same magnitude in an appropriate comparator activity.(Rid, Emanuel and Wendler, 2010:1474) Once these steps have been followed a decision can be made about harm of the intervention relative to harm of the comparator activity.

Following a description of the SERR methodology, two examples are given: epicutaneous allergy skin testing and liver biopsy. Both are compared to the risks of daily life threshold. In each case the process followed to identify potential harms, harm magnitudes and likelihoods involved a team comprised of an expert in the field, physicians, a nurse and a philosopher and made several assumptions about participants (e.g. their response to treatment if harmed), likelihoods of harm and strength of evidence for empirical data for each harm. The end result for each intervention is a chart plotting estimated likelihood of harm against magnitude of harm and showing, for each of the seven categories of harm prevalence, differences between the intervention and the risk of daily life threshold. Strength of evidence for the intervention is also graphically displayed on the chart for each risk data point. Differences in risk between the two chosen interventions, with reference to the risk threshold, are easy to appreciate once plotted graphically.

5.3.10. Critique of the Systematic Evaluation of Research Risks

The SERR addresses a critical weakness in all forms of research risk analysis where decisions must be made about the relative weight of research risks and benefits. The SERR does not compete with any of the high-level approaches to risk analysis, such as for example CA or the net risks test, but it could be used with most of these as a more objective and systematic way of evaluating risk against a specific comparator or threshold. In this sense, the SERR represents an advance in risk analysis by suggesting a less error- and bias-prone way of evaluating research risk. However, despite this more rigorous approach the SERR makes many assumptions about factors linked to prevalence of harms, their magnitude and likelihood which themselves may be prone to bias. This comes a no surprise though, considering the well-known complexity of risk evaluation.

The problem of trying to quantify risk, through the product of its two constituents, likelihood and magnitude of harm, is a vexing one and this is exemplified by the SERR methodology and how it is explained by Rid, Emanuel and Wendler (2010). Some important and complex limitations of the SERR are listed below:

- The choice of two activities – driving and sport participation – as exemplars of the risk of daily life by Rid, Emanuel and Wendler (2010) seems reasonable. These are most

certainly two activities that most people, at some point in their lives, engage in that contain an element of risk but where that risk is also considered to be generally acceptable. However, once this decision has been made, the problem is then (i) to obtain suitable harm, magnitude and likelihood estimates and (ii) to decide whether these exemplify very broad categories - in this case '*sport*' is a good example. There are most certainly some sports associated with low risk (e.g. lawn bowls or chess) and some with high risk (e.g. boxing or rugby). One does not even have to exclude '*extreme*' sports (such as sky diving or rock climbing) to still face the problem of a very wide spectrum of risk across different sports. References cited by Rid, Emanuel and Wendler (2010:1475) in support of their analysis of sport as an exemplar of the risks of daily life include competitive surfing, athletics and alpine skiing.

- The availability of published data related to both the research interventions under consideration and the comparator activity is likely to be a significant limitation in the application of the SERR. Publication bias may contribute to this, with certain interventions or activities being well-represented in the literature but others not. The example above underscores this problem – it is not clear why these three sports were selected as being representative of sports engaged in by a particular population (this is not explained in the article) but at least two of the three seem to be unusual choices unless they were the only published data available.
- Related to the point above, published data used for the purposes of estimating harm likelihood and magnitude will invariably be limited to specific populations and contexts. For example, empirical data related to a particular intervention or activity may be derived from young generally healthy adults, but research with the same or similar intervention or activity amongst a different population of older adults or those with more comorbidities may be likely to produce a different magnitude of harm, or potential for recovery post-treatment if an acute harm does occur. The SERR tends to make assumptions about underlying health or other factors like comorbidities and participant outcomes which may not necessarily align with clinical reality.
- The context in which interventions are deployed is important, not just the interventions. This is particularly true of emergency care interventions many of which may also be used in non-emergent settings. For example, techniques such as endotracheal intubation or placement of a supraglottic device for airway management are frequently used in

anaesthesia under controlled conditions (an elective case with time to ensure an empty stomach and pre-anaesthetic examination which may detect warning signs of a difficult airway along with good lighting, more extensive backup equipment etc.). The same interventions may be used in emergencies but in a less controlled and comparatively austere environment with physiologically unstable patients. Despite the interventions being the same, this context can significantly alter both the likelihood and magnitude of harm. While this factor is accounted for to some degree by considering the '*study environment*' for empirical data, the two examples presented by Rid, Emanuel and Wendler (2010:1476) do not highlight it or show how such a consideration is practically applied to adjust the risk level.

- The evaluation of empirical data as part of the SERR methodology is complex. Not only does this require extraction of relevant estimates from identified sources, but it also requires qualitative judgements based on strength of the study methodology, generalisability of the population, relevance of the environment and timeliness of the intervention (clinical or diagnostic).(Rid, Emanuel and Wendler, 2010:1476) Considering that assessment of risk is the REC's responsibility it is uncertain whether the time or expertise would be available for the implementation of such a complex methodology. Although risk thresholds such as the risks of daily life would not need to be methodologically revised with every application once in place, research involving different thresholds would and every new set of research interventions would need to be engaged with methodologically *ab initio*.

In summary, although the SERR represents an important step towards identifying a more objective and reliable way of evaluating research risks, it is associated with some limitations as described above. Perhaps the greatest question, considering that the SERR is intended to be used by RECs that typically deal with large volumes of applications and are constrained for time and resources, is regarding its practical implementation. It is very doubtful that the SERR in its current form would be implementable for its intended purpose in the research ethics review process at present.

5.3.11. Is There an Ideal Risk Assessment Method?

As described in some detail above, each of the risk assessment methods have limitations and shortcomings (because it is not a high-level method but rather one that could be applied as a component of others, the SERR will not be included in this discussion). There is certainly no ideal method. The authors of each risk assessment method above typically begin their methodological description by identifying a problem that their approach is aimed at solving. For example, Rajczi (2004) claims as a problem statement that there is no rational way of '*weighing*' risks and benefits as the Common Rule requires. Wendler and Miller (2007) identify what they believe to be flawed premises in the idea of clinical equipoise as their problem statement, and so on for each of the methods. All the authors above make valid points in their problem statements and their rationale for wanting to propose a better solution.

The agreement principle and the integrative approach both suffer from a lack of practical applicability. While their theoretical rationales and normative arguments are quite convincing, they both invoke somewhat abstract yardsticks for determining the justifiability of risk – the '*competent and informed decision-maker*' and '*socially sanctioned activities*' respectively. Above all, a method that is proposed for the assessment of research risk must be capable of deployment in a setting where it will be used most often, that is during the deliberations of an REC. Unfortunately, neither of these approaches could reasonably be used in such a context at present.

That leaves CA and the Net Risks Test. Both of these are more amenable to practical application as they are both comprised of relatively straightforward systematically applied steps. Yet, from a normative perspective, CA is the antipode of the Net Risks Test and comparing them at this level tends to result in a zero sum, ethics of care vs. ethics of research type of evaluation overlooking the fact that both rely on indirect, even rather vague, methods of assessing risk. One could not say that either method encompasses an externally valid or reliable '*measure*' of research risk. Despite this, the Net Risks Test seems to suffer more from the affliction of vagueness in its methods than CA with concepts such as '*excessive risk*', '*favourable risk-benefit ratio*' and even '*non-exploitation*' which are pivotal to coherence of the test left undefined and of uncertain operability.

CA relies on the dichotomy of therapeutic and non-therapeutic research procedures and, in the case of the former, clinical equipoise to assess research risk. The assumption of CA is simply that if clinical equipoise exists, the risk profiles of both procedures under consideration must be (i) similar and (ii) acceptable when considered together with potential benefits. This approach does not offer any more detailed systematic analysis of risk but relies on a tacit analysis that is assumed to be carried out by the clinician-researcher in the process of reaching a conclusion that clinical equipoise does exist. Thus, it offers no real improvement in clarity over the vagueness of the Net Risks Test but relies on implicit acceptance of the validity and reliability of the broader clinician-researcher population's clinical reasoning abilities with regard to equipoise. For this reason, it is likely that CA's method of risk assessment for therapeutic research procedures is widely supported by clinician-researchers. The remaining risk assessment procedure for CA, that applicable to non-therapeutic procedures, is relatively non-controversial in requiring minimal risk (while there is some debate about exactly what minimal risk is, the '*risks of daily life*' standard seems to be widely accepted).

Therefore, notwithstanding ideological differences about the ethics of care vs. the ethics of research, if *prima facie* plausibility of method is the measure of conviction in a research risk assessment method, then CA appears to surpass the other methods discussed above. Both CA and the Net Risks Test also have important implications for research risk with the incapacitated which will be discussed in greater detail in the following section, against the backdrop of the emergency care research context and research risk.

5.4. Contextual Risk Assessment in Emergency Care Research with Incapacitated Adults

Section 3 above dealt with the assessment of research risk, but did not consider any emergency care-specific clinical or research characteristics as part of this process. The various methods described above do consider, in various ways, those who do not have capacity for consent this is done generally and is not specific to a particular research context while the clinical context of emergency care research differs from many others in a number of ways. It is characterised by patients who are in many cases suffering from acute severe illness or injury and are often physiologically unstable. Added to this is the effect that this context has on clinicians – in many cases an austere environment characterised by time

pressure to assess and carry out procedures, relatively low levels of control, incomplete diagnostic information and, to some degree, stress and anxiety. For these reasons, it seems credible to assume that research risk assessment in this context deserves special consideration.

A normative theme present in a number of research ethics guidelines (as discussed in greater detail in Chapters 6 and 7) is that of a moral compromise with regard to participant capacity and acceptable risk. This compromise holds that research with incapacitated adults, particularly that involving one or more clinical interventions, can only be justified if there is a reasonable prospect of direct benefit *and if research risk is kept to a minimum* – an expression of the principle that those lacking autonomy must be adequately protected. While this compromise seems morally sound in principle, its application – and specifically what constitutes minimising risk – is key to determining whether the compromise is reasonable or over-protective. Inherent in this notion of minimising risk is the meaning of minimal risk, a standard that has come to be associated widely with the justification of research including the incapacitated.

The minimal risk standard has been a feature of research ethics guidelines and regulations for several decades and serves as a conceptual risk filter applied by RECs primarily for the purposes of categorizing research. For example, research that is considered minimal risk is typically eligible for expedited review.(Department of Health, 2024:50) The minimal risk standard is also sometimes used as one component of the moral compromise referred to above, as a condition for the inclusion of incapacitated adults in research in some guidelines. For example, this is the case in the South African National Health Research Ethics Council guidelines,(Department of Health, 2024) the Declaration of Helsinki(World Medical Association, 2024) and the Council for International Organizations of Medical Sciences guidelines.(Council for International Organizations of Medical Sciences (CIOMS), 2016) Some national research ethics regulations, on the other hand, have taken a different approach and refer to risk standards for research with incapacitated adults using an array of terminology that is not the same as minimal risk. Examples include those of the USA,(McRae and Weijer, 2008) Canada(Canadian Institutes of Health Research; Natural Sciences and Engineering Research Council of Canada and Social Sciences and Humanities Research Council of Canada,

2022) and the European Union.(European Parliament and of the Council, 2014) Indeed, these descriptions tend to adopt a more contextual or relative interpretation of risk than an absolute minimal risk standard. Conceptually, there is an important difference here because, on the face of it, an absolute minimal risk standard does not take contextual factors into consideration while relative interpretations do, and this may have important implications for risk assessment. Below, a more detailed definition of minimal risk is given after which implications of the clinical emergency care context and absolute vs. relative interpretations will be discussed.

5.3.11. The Minimal Risk Standard

Minimal risk is defined most often in two ways, with many research ethics guidelines and regulations that employ this term using one, but sometimes both, definitions. The first definition is often referred to as the '*everyday risk*' standard. This definition anchors minimal risk to risks associated with activities of '*daily life*'.(Kopelman, 2004:360-361) The second definition is often referred to as the '*routine examination*' standard. This definition anchors minimal risk to risks associated with '*routine physical and psychological examinations or tests*'.(Kopelman, 2004:365) Wording of these two definitions varies across different guidelines and regulations but is broadly similar to that given above.

In an extensive, although rather dated, review of minimal risk definitions in research ethics guidelines and regulations, Kopelman (2004:360-372) identifies several broad interpretations of both definitions above. The first is the absolute interpretation, which uses as a benchmark the risks of daily life and risks of routine tests that all individuals could encounter – an '*average*' standard across the many differing real-world experiences of varying groups with divergent living conditions, health conditions and access to health care. The second interpretation is a relative one, which benchmarks the two minimal risk standards against experiences of particular groups defined possibly by social context or clinical health condition. Notwithstanding the conceptual and normative complexity of all these permutations, Kopelman (2004:372-374) argues that an absolute interpretation of the routine tests definition is the clearest and most defensible. This would seem to preclude emergency care research with incapacitated adults where minimal risk is a threshold

because an emergency could not be equated with such an absolute interpretation with routine tests as a risk comparator.

5.3.12. Can a Relative Interpretation of Minimal Risk in Emergency Care Research be Justified?

Kopelman (2004) argues that an absolute interpretation of minimal risk is just, because it does not allow risk to be determined in such a way that those living inherently riskier lives (for a range of reasons) are allowed to be exposed to greater research risk. She sees a relative interpretation as being unacceptable because it '*permit[s] high risks to count as "minimal*"'. However, Kopelman refers repeatedly in a general way to '*research*' or '*study*' risk in this article without it being clear where exactly the risk originates from. That is, whether the risk is research risk – risk associated with research procedures – or risk arising from the clinical context that patients would be exposed to regardless of research participation. In the case of emergency care, there may be substantial contextual risk due to acute illness or injury. If this is interpreted in a general way, no emergency care research would meet the absolute minimal risk interpretation standard and thus, according to at least some research ethics guidelines, it would not be permissible to include the incapacitated in this kind of research. Paradoxically, this could itself be seen as exclusionary and unjust.

It would seem that it is important to consider the clinical context in which emergency care takes place when evaluating risk – whether minimal risk or some other risk standard - and to carefully assess what risks arise from research participation and what risks are context specific. As Lantos *et al.* (2015) point out in relation to pragmatic clinical trials, the risks associated with a patient's condition and the risks associated with any routine clinical care procedures that are carried out should not be considered research risks. This is because any patient (who may subsequently become a research participant) would have ordinarily been exposed to these risks if they had not become a research participant. Only risks associated with interventions or procedures that are being performed specifically for the purposes of research should be considered when assessing the research risks posed to participants. These may be clinical procedures that could be associated with benefits or procedures

carried out purely to obtain data related to the research question with no prospect of benefit.

Perhaps because of the nature of the clinical emergency care context, with potentially very sick or severely injured patients highly dependent on care, there seems to be a perception that in such a context of heightened risk clinicians are likely to engage in riskier procedures, and in an open-ended fashion. For example, McRae and Weijer (2002:1147) believe that the relativistic description of '*reasonable risk*' in the Final Rule will lead to a situation where '*the more dire a patient's illness or injury, the riskier the … procedures that may be performed on the patient*'. Kopelman (2004:362-363) also claims that a relativistic interpretation of minimal risk '*permits high-risk studies just because potential subjects have high risks in their daily lives*'. These statements seem to assume a relationship between contextual risk and research risk, that these are somehow proportionally bound to each other in such a way that, almost inevitably, a precarious clinical state invites greater risk-taking on the part of researchers.

The above reasoning, stated as an inductive argument, might look like:

1. Patient P, who is incapacitated, is in a clinical context of heightened risk due to an emergency condition.
2. When incapacitated patients are in a clinical condition of heightened risk, researchers may apply interventions of equally proportional heightened risk for the purposes of research.
3. It is acceptable to expose patient P to a research intervention of equally proportional (increased) risk.

The question to be asked with respect to premise 2 above is why researchers may reasonably contemplate doing this? Researchers may conclude that to generalise premise 2 is reasonable only on condition that (i) the clinical context is inescapable and the patient's condition is an indication for the procedure in question, (ii) the procedure in question may reasonably offer a benefit over routine clinical care and (iii) there is new knowledge with social value to be gained from research application of the procedure in question. Any other

motivation for generalising premise 2 would be unreasonable. This is not to say that a situation meeting conditions (i)-(iii) would be routine in emergency care research or even common, only that it could occur and that it could only reasonably occur if conditions (i)-(iii) hold. Therefore, the argument above, without conditions (i) – (iii) applied to premise 2, is not ethically justifiable. It follows that arguments binding risk inherent in the clinical emergency care context and procedural research risk together without consideration of the factors listed as conditions (i) – (iii), and only these, are not justifiable.

Ultimately, objections to a relativist interpretation of risk in emergency care research – whether using the label of minimal risk or another one such as reasonable or incremental risk – are based on an incorrect reading that a context of heightened risk is simply used by researchers to *justify* further proportionally risky research procedures *without any other pretext*. Rather, the contextual risks associated with emergency care are an ineluctable feature of this clinical environment. Research risks must be assessed within and taking account of this environment rather than in ignorance of it, with due consideration of existing clinical conditions in the determination of possible harms.

5.3.13. How Could a Relative Interpretation of Research Risk in Emergency Care Research be Applied?

It is difficult to describe in practical terms what a relative interpretation of risk in emergency care research translates into, even if this interpretation gains acceptance. In other words, we might accept that there is a certain degree of clinical contextual risk in a particular emergency care setting, and we might further agree that, in anticipation of research with incapacitated adults in this setting, we would like to ensure that a research procedure constitutes only a reasonable increase in risk (i.e. research risk) above this. How would we (i) accurately describe what a reasonable increase in risk is and (ii) apply this consistently in an REC setting for the assessment of risk? This descriptor of a reasonable increase in risk sounds very much like a similar one – the '*minor increase beyond minimal risk*' used in several research ethics guidelines – that is equally difficult to interpret and apply.

One of the criticisms of research ethics guidelines and regulations is that they recommend abstract processes such as '*weighing*' or '*balancing*' research risks and benefits and specify

absolute and equally abstract standards such as minimal risk. With the exception of the US National Bioethics Advisory Commission which endorsed CA, no body that publishes research ethics guidelines has formally recommended a particular risk assessment method. However, if research risk is approached by applying one of these methods, along with relevant definitions wherever this is practically meaningful, a more contextually sensitive way of determining a relativistic and reasonable level of risk in emergency care research with incapacitated adults may be possible.

As argued above in Section 5.3.11, CA seems to be the most practical for this purpose. In an emergency care research context, if CA is applied as a risk assessment method, the use of clinical equipoise to evaluate therapeutic research procedures naturally factors in the clinical contextual risks when deciding whether the risk of an alternative procedure constitutes a '*reasonable*' risk. The fact that CA takes account of the clinical context in this process through the vehicle of clinical equipoise is one of its advantages. The Net Risks test, on the other hand, still applies the standard of minimal risk – and presumably in its absolute interpretation – if incapacitated adults are to be considered as participants, leading to the contradictory state of affairs alluded to above. CA does factor minimal risk into to the risk assessment process, but only for non-therapeutic procedures which are likely to be a natural fit (i.e. the '*routine tests*' definition would account for many non-therapeutic research procedures). Thus, in answer to the question posed in the subtitle above, the answer could be by relegating abstract terms like minimal risk to play a role only in the consideration of non-therapeutic research procedures and bringing clinical equipoise to the foreground to do the heavy lifting of contextually relevant research risk assessment in emergency care research with incapacitated adults.

5.4. Conclusion

In this chapter I have engaged in a critical discussion of research risk and its analysis, with specific focus on emergency care research with the incapacitated. After discussing the conceptual groundwork of research risk in general I have compared and contrasted the relative advantages and disadvantages of five different risk assessment methods. Based on this I am of the reasoned opinion that CA seems to be the most practically applicable and useful in general and also in the context of emergency care research with the incapacitated

because by its methodological approach it avoids the application of the absolute minimal risk standard to therapeutic research procedures. I believe that the role of minimal risk is part of a widespread moral compromise in research with the incapacitated – that if such research is allowed to proceed it may only be on the condition that risks are minimal. Independent of any particular risk analysis method, I submit that a widespread absolute interpretation of the minimal risk standard for therapeutic research procedures is not suited to research in the emergency care context and may, through its ignorance of contextual risk, result in application that disallows some valuable research.

CHAPTER 6: EMERGENCY CARE RESEARCH AND INCAPACITATED ADULTS: AN ETHICO-LEGAL ANALYSIS OF SOUTH AFRICAN STATUTE AND GUIDELINES

6.1. Introduction

This chapter is an in-depth analysis and critique of South African research ethics guidelines and statute as these apply to research with the incapacitated and the associated requirements for informed consent. The purpose of this analysis, and that of the next chapter which shifts focus to international guidelines and regulations, is to highlight the strengths and limitations of local guidelines and statute and to compare them to those available in the international arena. After giving an overview of the broader South African ethico-legal framework as this applies to research, I offer a critical analysis of the NHREC guidelines. These guidelines were updated in 2024, and I cover both the most recent version and the previous version (from 2015) and focus on changes relevant to research with the incapacitated between the two versions. I also critically discuss the South African Good Clinical Practice guidelines and the Health Professions Council of South Africa guidelines as these apply to research. This is followed by a critical analysis of law relevant to research ethics including the South African Constitution, the National Health Act (61 of 2003) and several other relevant acts and regulations. In this chapter and in the following chapter detailed reference is frequently made to sections, subsections of pages of various documents. Consequently, in-text citations are not given each time a reference to a document is made.

6.2. The Current Ethico-legal Framework in South Africa

The current research ethico-legal framework in South Africa has a relatively short history. The Bill of Rights of the Constitution of South Africa (1996), with a section referring specifically to research-related rights was established 29 years ago. The research ethics regulator – the National Heath Research Ethics Council (NHREC) – was only provided for in the National Health Act (61 of 2003) following which the Council was formally constituted in 2006.(Department of Health, 2008) Prior to this, health law had been silent regarding research and the only research ethics guidelines in place were those published by the Medical Research Council.

Since the mid-1990s, much has changed. South Africa has a research ethics regulator and a set of national research ethics guidelines, in addition to good clinical practice guidelines published by the National Department of Health. A raft of legislation now emphasises the primacy of autonomy and informed consent in the health research process. All of these will be discussed in greater detail below as they relate to health research in general, but more specifically, to emergency care research. While there are many positive factors associated with these advances, there simultaneously exists a tension between the now more clearly defined legal position regarding informed consent in health research and the ability to take emergency care research with incapacitated adults forward in such a way that its potential for benefit is realised.

6.2.1. Research Ethics Guidelines

6.2.1.1. National Health Research Ethics Council

According to s 72(6)(a) of the National Health Act 61 of 2003, the NHREC is responsible for determining guidelines for the functioning of research ethics committees.(South Africa, 2003) The first edition of these guidelines was published in 2004, followed by a second (and current) edition published in 2015 with the title '*Ethics in Health Research: Principles, Processes and Structures*' (referred to here as NHREC 2015).(Department of Health, 2015) While both the act and the foreword to this document written by the Minister of Health refer to it as a guideline, the foreword also refers to it as a '*minimum national benchmark of norms and standards*'. This is clarified somewhat in s 72(6)(a) and s 72(6)(b) of the act where guidelines apply to functioning of Research Ethics Committees (RECs) and norms and standards apply to the conduct of research.

A revised version of the NHREC guidelines was published in 2024. However, I begin this section with an analysis of the previous version of the guidelines (from 2015) because (i) they contain important information that has been removed from the 2024 version or altered but is still important and (ii) the 2015 version serves as an important point of comparison with several sections staying relatively unchanged in the 2024 revision. A comparative analysis of the 2024 version is provided in Section 6.2.1.3 below.

The NHREC 2015 guidelines contain a section specific to '*adults incapable of giving adequate informed consent*' (section 3.2.4.3). The section opens with a statement clarifying the legal position with regard to incapacitated adults and research in terms of both the National Health Act 61 of 2003 and the Mental Healthcare Act 17 of 2002 – namely that both acts are silent about proxy decision-makers for health research. Both acts do allow proxies for treatment decisions. Thus, the guidelines argue, it would be unethical to follow the acts and disallow research with incapacitated adults without further justification. Flowing from this argument, which although seemingly sound is not articulated in any further detail, the guidelines suggest that:

a) Statutory proxy decision-makers, as set out in the National Health Act 61 of 2003and the Mental Healthcare Act 17 of 2002, may be considered for the purposes of proxy consent for health research.
b) Delayed consent (which is not defined further) is permissible.

Delayed consent specifically (and not proxy consent) has the following conditions in this section (phrased as being for the purposes of '*emergency care research'*, although the section starts out with a much broader scope of research involving incapacitated adults):

- "*the research is based on valid scientific hypotheses that support a reasonable possibility of more benefit than that offered by standard care; and*
- *participation is not contrary to the medical interests of the patient;*
- *the research interventions pose no more risk of harm than that inherent in the patient's condition or alternative methods of treatment;*
- *the participant and her relatives or legal representatives will be informed of the participant's inclusion in the research as soon as reasonably possible, and advised of her right to withdraw from the research without any reduction in quality of care*."

Following the above list of conditions, the next section of the NHREC guidelines (3.2.4.4) describes a set of '*Minimum conditions for research involving incapacitated adults'*. This set repeats some of the conditions for delayed consent listed above, but it also adds others and in some cases contradicts these conditions. With '*emergency care research*' having been

mentioned in the previous section to which some of these conditions applied, it is not clear whether this is still the case. The minimum conditions referred to are:

i. *'The research, including observational research, is not contrary to the best interest of the individual;*
ii. *The research, including observational research, places the incapacitated adult at no more than minimal risk (i.e. the 'everyday risk standard' which means the risk is commensurate with 'daily life or routine medical, dental or psychological examinations and in social or education settings activities' – referred to as 'negligible risk' in some guidelines); or*
iii. *The research involves greater than minimal risk but provides the prospect of direct benefit for the incapacitated adult. The degree of risk must be justified by the potential benefit; or*
iv. *The research, including observational research, involves greater than minimal risk, with no prospect of direct benefit to the incapacitated adult, but has a high probability of providing generalizable knowledge; i.e. the risk should be justified by the risk-knowledge ratio;*
v. *Greater than minimal risk must represent no more than a minor increase over minimal risk;*
vi. *The legally appropriate person (treatment proxies as stipulated in NHA s 7 or s 27(1)(a) of the Mental Health Care Act 17 of 2002) gives permission for the person to participate; and*
vii. *Where appropriate, the person will assent to participation. Note that the incapacitated person's refusal or resistance to participate, as indicated by words or behaviour, takes precedence over permission by a proxy*.'

The conditions listed above include observational research in some of the statements but not all of them, most noticeably in condition ii compared to conditions iii-v, which all deal with risk. Observational research, as a specific type of research in addition to any other, is not mentioned in the previous section (3.2.4.3) dealing with proxy and delayed consent. It is thus unclear if the inclusion of observational research in the specific conditions listed above is intentional or whether it is meant to apply more broadly to others but was omitted.

Four of the seven minimum conditions listed above deal with permissible risk for research involving incapacitated adults. The first condition refers to minimal risk as being permissible, however the next two conditions each escalate the level of permissible risk by justification through either possible benefit to participants or the creation of generalizable knowledge (it is assumed that this would not change if the to justifications existed together). The last risk-related condition reiterates that, although the preceding two conditions permit research that is greater than minimal risk, this greater level of risk may only be what the guidelines refer to as a '*minor increase over minimal risk*', which is not explained in any greater detail. Importantly, the risk descriptors used in this section on minimum requirements for research with incapacitated adults are different compared to the way risk is described in the preceding section on '*emergency care'* research that deals with proxy and delayed consent. In the latter (the third bullet point), the permissible risk level is described as being no greater than that inherent in the patient's [*participant's*] condition or '*alternative methods of treatment*'.

In March 2022, the NHREC published an additional set of supplementary guidelines on '*major incidents and research, including public health emergencies*'.(Department of Health, 2022) The supplement is intended to add detail to section 3.4.1 of the NHREC 2015 guidelines and contains several subsections, one of which (3.4.1.6) deals with informed consent. This section starts with a general overview of the requirements for including incapacitated adults in research which touches on the minimum requirements for research involving incapacitated adults from the NHREC 2015 guidelines (points i – vii as set out above). It then continues to restate the sections from NHREC 2015 on proxy and delayed consent. In both cases, some new guidance is added.

In the supplementary guidelines allowance is made for situations, brought about by lockdown conditions during a pandemic, where neither a proxy decision-maker nor a surrogate decision-maker is available or where a treatment under investigation is time-sensitive (and access to a proxy or surrogate decision-maker is unlikely). In such situations, the guidelines suggest that a REC could allow delayed consent alone without the requirement for prospective proxy or surrogate consent.

The supplementary guidelines also add new guidance for delayed consent. This relates to situations where an incapacitated patient may be enrolled in research under proxy consent but does not recover sufficiently to provide delayed consent at a later stage, due to death (this subsection does not deal with a lack of sufficient capacity due to a permanent condition rather than death). In such situations, the supplementary guidelines recommend that existing data use should depend on the wishes of the patient's proxy decision-maker '*or surrogate*'. In situations where a proxy decision-maker does not agree to use of existing data, this may still be justified if the data can be anonymised and if use of the data may lead to benefit – phrased as '*promoting the public interest and common good*'. The final decision in this regard should lie with an REC that reviews and approves the research.

6.2.1.2. Critique of the NHREC 2015 Guidelines

The NHREC 2015 guidelines contain, for the first time in a set of local research ethics guidelines, guidance related specifically to emergency care research, and within this context, guidance on research with incapacitated adults. Prior to the first edition of NHREC guidelines in 2004, the Medical Research Council published and updated their own set of research ethics guidelines.(South African Medical Research Council, 2004) While these guidelines did contain sections on informed consent and research with incapacitated patients, this was rudimentary in nature and amounted to obtaining the consent of a '*competent relative*'. Thus, seen against the development of research ethics guidelines in South Africa, from an emergency care research perspective the NHREC 2015 guidelines represent a significant advance. Despite such progress, there are many inconsistencies and contradictions in the NHREC 2015 guidelines regarding the definition of emergency care research, the minimum requirements for inclusion of incapacitated adults and – perhaps most importantly – the evaluation of risk in the latter.

6.2.1.3. Definitions

The term '*emergency care research*' is used on p37 of the NHREC 2015 guidelines in the context of delayed consent. The word '*emergency*' is used again on p46, this time under the subheading of '*Major incidents and research*', where there is a reference to the importance of this context (major incidents – described earlier as including disasters such as floods,

earthquakes or disease outbreaks) in advancing '*emergency health care*' treatments and developing new drugs and treatments to treat '*emergency patients*'. In the 2022 guideline supplement referred to above, the main focus is on public health emergencies and what is referred to as '*emergency infectious disease outbreaks*'. In the preamble to this document, a very similar statement is made to that appearing on p46 of the NHREC 2015 guidelines – that '*major incident research*' is important for developing emergency care treatments.

The word '*emergency*' is never defined in the NHREC 2015 guidelines (or the 2022 supplement). Consequently, the only clue to its definition must be taken from the context in which it is used. For the most part, with the exception of p37, this is used in the context of major incidents. While it is true that disasters, and the illness or injury caused by them, most certainly do constitute an emergency as defined in Chapter 3 of this thesis it is not true that emergencies occur only in the setting of disasters or major incidents – they occur every day. Associating emergencies with major incidents – unusual or rare events – is unfortunate because it is unclear whether principles such as delayed consent, that might be applicable to patient care in emergencies, apply only in major incidents or all emergencies. Likewise, the additions contained in the supplementary guidelines of 2022 (as discussed above) appear to be limited to public health emergencies and major incidents, and not other ('*everyday*') emergencies.

6.2.1.4. Scope: Lack of Capacity in General or in Emergencies?

The scope and application of the NHREC guidelines on proxy and delayed consent is not clearly delineated. As already discussed above, it is not clear what the word '*emergency*' refers to when it is used – this has obvious implications for understanding the scope of guidelines described in terms of the word. The structure of subsection 3.2.4.3 does not assist in clarifying whether the guidelines on proxy and delayed consent apply to adults with a lack of capacity in general, or to a lack of capacity experienced during an emergency, or both. Other examples of a lack of capacity for informed consent include degenerative diseases affecting cognition (e.g. Alzheimer's disease) or psychiatric conditions.

Subsection 3.2.4.3 begins with a general argument about the legal and ethical justifications of proxy decision-makers in clinical care and research which could apply to any

incapacitated individuals. However, this is followed by mention of delayed consent that can be approved in '*particular circumstances*', followed by a reference to '*emergency care research*'. It seems that the intention is to describe proxy consent for all incapacitated adults (including in emergencies) and delayed consent for only that subset involved in emergency care research, however this is not made explicit on p37 of the guidelines. The situation with overlapping categories, for example an adult with a degenerative condition who then has a stroke (an emergency), is also not covered in this subsection.

6.2.1.5. Risk

The NHREC 2015 guidelines do not give clear guidance on the consideration of risk as this applies to incapacitated adults. As outlined above (2.1.2.2), the guidelines seem to be intended to apply to both non-emergency incapacitation (e.g. degenerative diseases such as Alzheimer's disease) and emergencies. On p37 of the guidelines there is a part of subsection 3.2.4.3 dealing with proxy consent and a separate part, immediately below this, dealing with delayed consent. These two parts are followed by a numbered list of minimum conditions for research involving incapacitated adults for RECs to consider (set out under 2.1.1 above). The level of risk to be considered in research with the incapacitated is mentioned five times in total – once in the description of circumstances justifying delayed consent and four times in the minimum conditions.

For the purposes of considering delayed consent, the NHREC 2015 guidelines state in subsection 3.2.4.3 that research interventions must constitute no more risk than that inherent in the patient's condition or '*alternative methods of treatment*'. This formulation of risk seemingly takes into account the context of an emergency, which may pose risks of harm greater than the risks of '*daily life*'. It also seems to acknowledge that emergency treatment, in general, may hold greater risks than treatment administered under more controlled, elective conditions. While this seems to be what the wording in this section implies, there is no further explanation.

In contrast, under the numbered list of minimum conditions for research with incapacitated adults, two different risk thresholds are described as:

- Minimal risk (the risk associated with '*daily life*').
- Greater than minimal risk, with the degree above minimal risk determined by the potential benefit. This applies if there is a prospect of direct benefit for incapacitated participants or, in the absence of such benefit, a high probability of producing generalizable knowledge.

In addition, it is emphasised that greater than minimal risk must involve no more than a '*minor increase*' above minimal risk.

Considering the above, it seems that the NHREC 2015 guidelines propose two different – possibly very different – risk thresholds for considering delayed consent in particular and the much more general question of research with incapacitated adults. This seems contradictory in emergency care research because delayed consent would typically apply to a subset of the larger population applying to research with incapacitated adults. It would therefore not make sense to have one risk standard for consideration of research with incapacitated adults as a whole and another (seemingly tolerating greater risk) for the subset of delayed consent.

In addition to this problem of apparently differing risk levels that would apply to the same population, the definition of risk levels applying under the minimum conditions for research with incapacitated adults is very difficult to interpret. For research with no direct participant benefits and a low probability of producing generalisable knowledge the appropriate risk level is described as '*minimal risk*' which is elaborated on immediately after this description. This is a fairly standard description of minimal risk, however (as already mentioned) it is contradicted by the risk level for the same population described under the subsection on delayed consent. For research with participant benefits or a high probability of generalisable knowledge, a greater than minimal level of risk is permitted but this must be '*no more than a minor increase over minimal risk*'. Without further guidance, it is impossible to know – particularly in an inherently uncontrolled or unpredictable emergency context – what this means.

6.2.1.6. Waivers

There is no explicit mention of waivers of the requirement for informed consent with incapacitated adults in emergency care research in the NHREC 2015 guidelines or the 2022 guidelines supplement. There is an explicit statement in both guidelines that delayed consent should not be considered to be a waiver of informed consent (in sections 3.2.4.3 and 3.4.1.6. a) respectively). Hence, unlike in countries such as the USA, Australia and others whose regulations are described in Section 7.2.2 of Chapter 7, an exception or waiver of this type is not possible.

While this sounds quite consistent, it is somewhat contradictory given the allowance of delayed consent which implies a waiver of the (normal) requirement of prospective informed consent *at the time of participant enrolment* - at this point informed consent has, in fact, been waived. The 2022 guideline supplement confirms this anomalous situation with the wording '*Delayed informed consent is informed consent volunteered by the participant but is obtained after the research has begun*'. Both guidelines should more fully explain what is meant by the short statement about informed consent not being waived.

6.2.1.3. National Health Research Ethics Council: Third Edition 2024

In early May 2024, the NHREC published an updated version of the above guidelines (NHREC 2024).(Department of Health, 2024) This revision contains many changes, however attention will only be given to those relevant to research involving incapacitated adults or research in emergency situations here.

6.2.1.4. Waivers of Consent

Waivers of consent for access to personal health information or biological material are supported providing a set of conditions are met. Section 3.1.10.1 on NHREC 2024 deals with such waivers and is an elaboration on what was a short section of a similar nature in the NHREC 2015 guidelines. Although this sections states that prospective observational studies may also be eligible if they meet the same conditions, it is clear that it does not address waivers relevant to clinical interventions in an emergency care research context.

6.2.1.5. Proxy Consent

NHREC 2024 covers proxy consent in section 3.1.10.2 b) which is very similar in content to the analogous section from NHRC 2015, including the same ethical justification for a form of research consent that is not compliant with the National Health Act. There is no further clarification in NHREC 2024 of the situation where an adult participant lacks capacity but a proxy decision-maker is not available and the therapeutic window for an intervention is narrow.

6.2.1.6. Deferred Consent

Several conditions for the use of deferred consent in research with incapacitated adults in section 3.1.10.2 c) of NHREC 2024 are the same or very similar to those in the analogous section of NHREC 2015. However, several new subsections have been added:

- A requirement that deferred consent should only be acceptable if the cause of incapacitation is temporary and is a '*reasonably held prognosis*' that the participant will regain capacity within a '*predictable period*'.
- A statement regarding death of the participant where deferred consent was planned – in such cases data already collected should not be used without the wishes of a proxy decision-maker being considered.
- A note added on p27 that '*deferred consent is personal consent, with an alteration of the requirement of prospective consent (see also 3.1.10.1). Deferred consent is not an example of fully waived consent*'.
- A statement at the top of p28, that '*urgency is not by itself sufficient justification: all relevant principles must be observed as well as the individual circumstances of the patient…*'

There is also a noteworthy absence in this section of NHREC 2024, when compared to NHREC 2015. That is any statement about the risk level considered to be acceptable in justifying deferred consent. In NHREC 2015 this was minimal risk.

6.2.1.7. Research Involving Incapacitated Adults

This is covered in section 3.2.5.3 of NHREC 2024 and is mostly the same as the analogous section in NHREC 2015, including the statements on various acceptable benefit: risk ratios. However, there is one important omission in this section of NHREC 2024 – that a proxy

decision-maker must agree to participation. A note has also been added to this section of NHREC 2024 regarding '*refusal or resistance*' to participation and that this takes precedence over permission by a proxy (which is not listed as a requirement).

6.2.1.8. Patients Highly Dependent on Medical Care

The first paragraph of section 3.2.7 dealing with this subset of patients in NHREC 2024 is very similar to the analogous section in NHREC 2015. The paragraph deals with some of the risks associated with research involving this population and important factors to consider regarding understanding of information and consent. However, after this paragraph (at the bottom of p40) no further guidance is provided. In NHREC 2015, this was followed by a list of conditions to be met when considering research with this population.

6.2.1.9. Major Incidents and Research

Section 3.3.2 of NHREC 2024 deals with research during major incidents, a section also covered by NHREC 2015. This section does not deal directly with emergency care in the broader sense because it concerns itself with what in most other contexts are referred to as disasters – situations so large and complex that they constrain local resources to deal with them. There may be some overlap into emergency care, however the vast majority of '*everyday*' emergencies do not fit this description and therefore this section is not of direct relevance to them. The first three paragraphs of this section in NHREC 2024 are very similar to the analogous parts of NHREC 2015, but NHREC 2024 adds quite an extensive range of new material on public health emergencies which are categorised under major incidents.

On p46, towards the end of an introductory section on major incidents, the following note appears, quoted in whole below which presumably is intended to refer to the major incident context but seems to focus more on other (non-major incident) emergency care research: '*Sometimes researchers appear to assume that people caught up in 'emergency circumstances' in any context should be enrolled in research projects. For example, circumstances that include incapacitated patients, austere and under-resourced clinical environments (including pre-hospital patient care), complicating factors (for patients with capacity) such as acute pain, physiological derangements, anxiety, risky clinical contexts due to the pathophysiological effects of severe illness or injury, time-sensitive interventions and*

(often) no available proxy decision-makers within intervention time-frames present logistical and ethical challenges.
Researchers must remember that expedience is not an ethical principle and that sometimes the perceived opportunity for research is not appropriate due to challenges. The ethical and other regulatory requirements for sound ethical research are more important than a lost opportunity for a research project.'

6.2.1.10.Intensive Care Research

Ethical considerations for research in the intensive care (sometimes called critical care) environment are covered in section 3.3.3 on NHREC 2024. With the exception of some altered wording here and there, which is not of key importance, this section is the same as the analogous section in NHREC 2015. While there are some similarities between emergency care research and intensive care research (mainly, that most patient lack capacity) the two environments are not very similar and little guidance form this section can be transferred to the emergency care context other than guidance in section 3.2.5 in NHREC 2024 on research with those who lack capacity.

6.2.1.4. Critique of the NHREC 2024 Guidelines

The NHREC 2015 guidelines did contain some contradictions with regard to research ethics and incapacitated patients, however these guidelines were a significant improvement over local guidance in this area prior to their publication. The NHREC 2024 guidelines offered an opportunity to improve on the previous version in a few specific areas:

- Defining emergencies and emergency care and resolving the confusion between '*everyday*' emergency care, major incidents and public health emergencies.
- Acknowledgement of the importance of emergency care research in providing possible direct benefits for patients, but also importantly the generation of new knowledge that could improve outcomes across a broad range of conditions frequently associated with high levels of morbidity and mortality.
- Provision of clear guidance for (i) emergency care research where patients have capacity for consent but may have acute severe pain or other distractors, (ii) emergency care research where patients do not have capacity but a proxy decision-maker is available and (iii) emergency care research where there is a narrow therapeutic window and this

together with the nature of the condition investigated make the availability of proxy decision-makers unlikely.

- Linked to the above, a formal set of conditions for (ii) and (iii) and clarity regarding whether such an approach constitutes a waiver or exception from the requirement of informed consent under these conditions.
- Guidance for situations where patients might be included in emergency care research without consent, but never regain capacity and a proxy decision-maker never becomes available.

Unfortunately, the NHREC 2024 guidelines did not improve guidance related to any of these and in some respects, made certain areas of guidance less coherent then than they were in the NHREC 2015 guidelines. These problems will be discussed below.

6.2.1.5. Proxy Consent

As mentioned above, the assumption is made that a proxy decision-maker will always be available. While this may certainly be the case in many studies, in some – particularly interventional research where the intervention must be administered in a narrow time-frame – it is unlikely to be. As discussed in Section 7.2.2 of Chapter 7, many national regulations (certainly most of those discussed as subsections of 3.2) do provide guidance on this eventuality and it is a weakness of NHREC 2024 that it does not.

6.2.1.6. Deferred Consent

Conceptually, it is unfortunate that the term '*deferred consent*' is still used without qualification. In its fully valid form, consent cannot be deferred. Wording of the note referred to in Section 6.2.1.9 above seems to deepen the perception that there is such a misunderstanding. To state that deferred consent merely has '*an alteration of the requirement of prospective consent*' is quite puzzling. While the principle of a participant being approached for consent when they regain capacity to do so is contained in many other guidelines and regulations under these circumstances, it should be quite clear that this can only be consent for participation from that point forward.

Removal of the condition for deferred consent related to risk, as described in Section 6.2.1.9 above, seems to lack a rationale. The NHREC 2015 guidelines required risk no greater than that '*inherent in the patient's condition or alternative methods of treatment*'. In its current form, there is only a statement of benefit – that it must be more than that offered by standard care – but nothing about risk, which leaves researchers and RECs to try and navigate assessment of the risk: benefit ratio with insufficient guidance.

The statement on urgency, referred to in Section 6.2.1.9 above, is new although the last part of this sentence does appear in the NHREC 2015 guidelines. This statement lacks clarity and should be explained in more detail, as it is not very clear how urgency might relate to a proposal for deferred consent. If a patient in an urgent situation has capacity to consent, it should be self-evident from the preceding conditions, that urgency would not be grounds for deferred consent. Alternatively, this statement may have some intended bearing on situations where a proxy decision-maker is not available due to urgency of a research intervention. However, it is difficult to tell whether this is the intention when the urgency in question is not described adequately.

6.2.1.7. Research Involving Incapacitated Adults

The absence of a condition specifying that an incapacitated patient must be assisted by a proxy decision-maker is also seemingly without a rationale. This would appear to be an important condition and certainly one that is generally present in other national regulations and guidelines when considering the inclusion of incapacitated adults who themselves cannot consent (as described in Section 7.2.2 of Chapter 7). Linked to this, the note below this section stating that that a participant who is capable should assent only serves to deepen this inconsistency – a participant would not be able to assent without the assistance of a proxy decision-maker. It seems possible that this condition – of proxy decision-maker to assist the incapacitated participant – may have simply been removed in error.

6.2.1.8. Patients Highly Dependent on Medical Care

In the 2015 NHREC guidelines the conditions for deferred consent were linked to, and included under, this section. These conditions have been removed and are discussed elsewhere, under the broader section on research with incapacitated adults. This represents

an improvement in the 2024 guidelines as it removed any possible misunderstanding that deferred consent can be justified simply by a situation where a prospective participant is highly dependent on care.

6.2.1.9. Major Incident Research

While some changes to this section have clarified what major incident research is, the note on p46 reproduced above is both contradictory in this respect but also worrying for the tone that it adopts towards (what seems to be) emergency care research in general. The note starts by stating an assumption that, in all likelihood, probably does not reflect what many researchers actually assume about what is referred to as '*emergency circumstances*' and what it entitles them to do regarding enrolment of participants. However, the second part of the note adopts a negative – and perhaps even hostile – tone towards associating emergency care researchers with expedience and opportunism. The note ends off by clearly conveying the view that '*ethical and regulatory requirements*' outweigh lost opportunities for research.

While the importance of ethical and regulatory requirements is clear, there seems to be a form of zero-sum logic being applied in the wording of this note – that if the requirements are abided by then we cannot have opportunities for emergency care research. Contrast this with a statement from Guideline 16 of the Council for International Organizations of Medical Sciences research ethics guidelines: '*Adults who are not capable of giving informed consent must be included in health-related research unless a good scientific reason justifies their exclusion*'.(Council for International Organizations of Medical Sciences (CIOMS), 2016:61) It is unfortunate that the position in the NHREC's note has been taken and it is unclear what has informed it. As discussed in Section 7.2.2 of Chapter 7, many national regulations have acknowledged the importance of emergency care research along with a realisation that its ethical complexities cannot be avoided and, in fact, can be suitably addressed in a way that supports the principle of justice in access to both research benefits for incapacitated participants but also new knowledge with social value that may benefit others. However, this message does not seem to be conveyed in this part of the NHREC 2024 guidelines.

6.2.1.5. National Department of Health: Good Clinical Practice Guidelines

The National Department of Health's Good Clinical Practice (GCP) guidelines were revised and updated in 2020 (the preceding version was published in 2006).(Department of Health, 2020) The guidelines are intended to promote good practice in the conduct of clinical trials and compliance with them is required by parts of the National Health Act (71 of 2003) and Regulation 30 of the Medicine and Related Substances Act (101 of 1965) (as amended). The most recent GCP guidelines have been written to closely align with the NHREC 2015 guidelines.

The approach to informed consent with incapacitated patients in the GCP guidelines (dealt with in section 2.5 on informed consent and section 3.3 on vulnerability) is to simply refer to the relevant section of the NHREC 2015 guidelines (section 3.2.4.3). There is no further discussion about such situations. Consequently, no further analysis of the GCP guidelines within this context is possible.

6.2.1.6. Health Professions Council of South Africa

The Health Professions Council of South Africa (HPCSA) is a statutory body provided for by s2 of the Health Professions Act 56 of 1974 and functions as the regulator for a broad range of health professions, each represented by a professional board (in some instances several professions are represented by a single board). In its role as regulator the HPCSA has wide ranging powers in relation to many aspects of practice, qualification structure, scopes of practice and professional conduct among others. The HPCSA also publishes guidelines on a range of topics, one of them being ethical practice and good conduct. These guidelines span a total of 17 booklets, each devoted to a specific practice context (in addition to some booklets of a more general nature).

Of the 17 booklets referred to above, booklet 13 – General Ethical Guidelines for Health Researchers – deals with research ethics.(Health Professions Council of South Africa, 2016) The booklet covers a wide array of topics relevant to research ethics, beginning with the principles of research ethics (respect for persons, beneficence, non-maleficence and justice) and continuing to cover a series of subsections each detailing professional duties to research participants (including animals), other professionals, researchers and society.

Informed consent is discussed under a section (section 6.3) on duties to research participants. There is only a brief mention of situations where research is considered with incapacitated adults. Here, the guidelines recommend that the consent of legally authorised representatives should be obtained if participants themselves cannot consent (the guidelines give examples of children and the mentally challenged, elderly or unconscious). There is a further statement in this section that research should not be considered with these populations unless (i) the research promotes their health and (ii) the research cannot be conducted in a population with the capacity to consent.

The guidance on research with incapacitated patients provided by the HPCSA's booklet 13 is limited and consistent with but does not add to the guidance provided be the NHREC 2015 guidelines discussed above. It follows a similar line of reasoning, that research with incapacitated adults is ethically justified if the consent of a proxy decision-maker can be obtained even though there is no legal provision for such an approach for the purposes of research. This will be discussed in greater detail in the sections below.

6.2.2. Legislation

6.2.2.1. The Constitution

The Constitution of South Africa (1996) is one of the few in the world to include a section about consent for research participation. Signifying the transition to democracy and replacing an interim constitution which came into force on the day of South Africa's first democratic election (27 April 1994), the constitution was signed into law on 10 December 1996 and came into force on 4 February 1997.(South African History Online, 2019) The constitution consists of 14 chapters with chapter 2 setting out the bill of rights in sections 9 to 37. Since 1997 the constitution has undergone 17 amendments.

Of primary importance in the consideration of research ethics, and specifically the principle of autonomy, is the bill of rights. Section 12 of the bill of rights refers to freedom and security of the person and states, in subsection 2(c), that "*Everyone has the right to bodily and psychological integrity, which includes the right not to be subject to medical or scientific experiments without their informed consent*." This is the only direct reference to research participation and informed consent in the bill of rights. However, section 10 – which refers

to the right to human dignity and the right to have their human dignity respected and protected – could also be interpreted as having a bearing on research. If research with incapacitated adults without their consent is considered a threat to the dignity of such individuals, then section 10 reinforces section 12 although section 10 might also have application to a broader range of researcher conduct than just that related to the informed consent of participants.

6.2.2.2. National Health Act and Associated Regulations

The National Health Act (NHA) (61 of 2003) was commenced in 2005, however section 71 (dealing with research on human subjects) was commenced in 2012. The purpose of the act is to provide for a health care systems framework and a system of co-operative governance and management of health care at national, provincial and district level. As described under 2.1.1 above, the NHA (in section 72) requires establishment on the NHREC. Several other sections relate to health research, namely section 11 (health services for research purposes), section 16 (access to health records for research purposes), sections 55-57 (removal of tissue) and sections 62-65 (use of human organs and bodies).

Section 71(1)(b) of the NHA, which deals with research involving humans, states that "*research or experimentation on a living person may only be conducted with the written consent of the person after he or she has been informed of the objects of the research or experimentation and any possible positive or negative consequences on his or her health*". No exceptions to this subsection are given for research that may, of necessity, include persons not capable of providing the required consent.

Regulations associated with the NHA, and specifically research with human participants, were published in September 2014.(Department of Health, 2014) The regulations cover a range of research-related subjects with several subsections providing more detail on informed consent. Section 4.2 of the regulations deals with "*adults with decision-making incapacity*". According to 2.1, research with such adults is "*appropriate*" if:

(a) "the research cannot be conducted with adults who have decision-making capacity;
(b) the research poses no more than a minimal risk; or

(c) the research poses more than a minimal risk, but holds out the prospect of direct benefit to the participant; or

(d) the research poses a minor increase over minimal risk, and holds out no prospect of direct benefit but is anticipated to yield generalizable knowledge about the condition under study."

The regulations define minimal risk as "*the probability and magnitude of harm or discomfort anticipated in the research is not greater than that ordinarily encountered in daily life in a stable society or in routine medical, dental, educational or psychological tests or examinations*".

6.2.2.3. Critique of the Constitution and National Health Act and Associated Regulations

The constitution, together with the NHA, effectively prohibits a significant proportion of emergency care research because this would involve patients unable to comply with the requirement set out in section 71 of the NHA. It would appear that both the constitution and the NHA have drawn inspiration from the Nuremberg Code (discussed in more detail below) and its insistence on consent as an absolute requirement for human research. While this was no doubt done (as it was after Nuremberg) to prevent abuses committed in the past, it does create difficulties in a range of situations where research is needed to improve patient care, but prospective participants are incapacitated and thus cannot give consent.

Neither the constitution nor the NHA provides any alternative to participant consent for research. The NHA does, in section 7, allow for consent to be given by a legally authorized representative or proxy decision makers where a patient is incapacitated and requires treatment. However, this does not apply to research. As discussed above in 2.1.1, this has necessitated a situation where the NHREC guidelines have attempted, through the suggestion that treatment proxies could also be utilised in research, to mitigate this strict limitation on research participation by incapacitated adults.

The regulations discussed above (related to the NHA, and specifically research involving human participants) appear to be an attempt to recognise and remedy the NHA's strict exclusion of incapacitated research participants through an unconditional requirement of

informed consent. The regulations at least recognise the possibility of research involving incapacitated adults, however there are four main problems with the very short section 4.2. Firstly, it is unclear what '*appropriate*' means in the first line. Secondly, the wording in subsections (c) and (d) is difficult to understand – how much more is '*more than a minimal risk*' and what constitutes '*a minor increase over minimal risk*'? Thirdly, the standard of '*no more than minimal risk*', although similar to regulations in other countries for research with incapacitated adults, seems out of place in emergency care research. Emergencies are, by definition, not 'daily life' – for most patients requiring emergency care the day they require this may well be the riskiest and most challenging day of their lives. Emergency procedures and treatments, provided within this context are often invasive and associated with risks greater than '*routine medical,… tests or examinations*'. Setting minimal risk defined in this way as the default threshold for acceptability of research with incapacitated adults seems contradictory, as argued in Section 5.4.2 of Chapter 5. Lastly, section 4.2 of the regulations offers no guidance, and makes no reference to lawfulness of any other approach to informed consent such as proxy or delayed consent. It also is silent about the possibility of any type of exception from or waiver of the requirement of informed consent. In leaving this void, section 4.2 not only offers little clarification but actually adds to the confusion surrounding research with incapacitated adults.

6.2.2.4. Other Legislation

The Protection of Personal Information Act

The Protection of Personal Information Act (POPIA) (4 of 2013) came into force on 1 July 2020 with a grace period to allow compliance. It has thus been in full force since 1 July 2021. The POPIA governs data privacy and protection and also provides for the establishment of an Information Regulator. While the main thrust of the POPIA is regulation of commercial processing of personal information, it also applies to data collected and processed for the purposes of research.

In s11(1)(a) of the POPIA several legal justifications are given of which at least one must apply for lawful processing of personal information. Of these, two are relevant to research: that the individual whose personal information is processed consents to this or, if this is not applicable, that the research constitutes a legitimate interest of the responsible party (i.e.

the researcher(s)). There is no provision in the POPIA for a proxy decision-maker. Thus, in research with the incapacitated that requires processing of personal information in which consent from the research participant is not possible, researchers could only argue that benefits arising from their research – either for the participant or in the form of new knowledge with social value – represent a legitimate interest as a legal justification. It is not clear at this point if such an argument would be seen as a convincing legal justification.

The Children's Act and Mental Health Care Act

The Children's Act 38 of 2005 gives effect to the rights of children in the Constitution and deals with many different principles of the care and protection of children and related legislation. The Mental Health Care Act 17 of 2002 provides for the care, treatment and rehabilitation of the mentally ill and related legislation. Considering the focus of both of these acts, it might be anticipated that they could enlighten the problem of a lack of capacity for research consent – both due to maturity and mental state. However, both of these acts are silent regarding consent in such situations for research participation. As mentioned above under 2.1.1, the NHREC 2015 guidelines refer to the list of proxy decision-makers in s27(1)(a) of the Mental Health Care Act, however this list is for proxy decision-making for treatment only. The guidelines argue that the list should also be used for decisions about research participation.

6.3. Conclusion

In this chapter I have critically analysed both South African research ethics guidelines and statute as this applies to research and specifically research with the incapacitated. The most important guidelines are those published by NHREC and my analysis of these shows that they contain many inconsistencies and gaps. This was the case with the 2015 version of the guidelines, but the most recent version published in 2024 seems to have exacerbated this rather than improved it. The NHREC guidelines do not offer clear nor coherent guidance for researchers wishing to engage in research in an emergency setting with incapacitated adults. Analysis of the legal framework in the latter part of this chapter shows that all applicable law requires written informed consent as an absolute requirement for any form of health research. While regulations published in 2014 do seemingly allow research with incapacitated adults, they do not set out what the requirements are regarding consent in

such instances. This is a significant legal barrier to research with those incapable of giving such consent – a problem which the NHREC guidelines tries to address but with very limited success. In the next chapter I continue to analyse the available research ethics guidance, but I focus on what is available internationally.

CHAPTER 7: EMERGENCY CARE RESEARCH AND INCAPACITATED ADULTS: AN ETHICO-LEGAL ANALYSIS OF INTERNATIONAL GUIDELINES AND REGULATIONS

7.1. Introduction

Following on from the previous chapter, in this one I continue to critically analyse research ethics guidelines and regulations but in this case from sources other than South Africa. In the first section I focus on international guidelines from the Nuremberg Code of 1947 to the most recent updated version of the Declaration of Helsinki in 2024. After this I critically discuss research ethics regulations from several countries and regions – the USA, Canada, the European Union, the UK and some of the BRICS countries. In each case I focus specifically on regulations for research in emergencies with the incapacitated and I highlight the positive aspects of the regulations and some of their weaknesses or contradictions.

7.2. International Guidelines and National Regulations

7.2.1. International Guidelines

7.2.1.1. The Nuremberg Code

The origins of the Nuremberg Code, from a set of principles derived from the testimony of Andrew Ivy and Leo Alexander the two US medical expert witnesses at the Nuremberg Trial, had a major influence on its content. With the suffering of prisoners who were experimented on without their consent fresh in the minds of the world at the time, a natural response was to make sure that this type of abuse would never happen again. Consequently, the Code sets as its first point: '*The voluntary consent of the human subject is absolutely essential*'.(Shuster, 1997)

Although not directly invoked anymore in relation to the conduct of researchers, the Code has immense historical significance. Its origins are important both because of the historical context and also because of its source – it was a legal code. Although it is true that several important principles of research ethics were cemented by the Code, and many of these principles re-emerge in future research ethics guidance, it is the Code's formulation of informed consent that is considered its greatest strength and most lasting influence.(Annas and Grodin, 2008:138)

7.2.1.2. Critique of the Nuremberg Code

The Code has been criticised for a number of reasons. Perhaps the most frequent criticism relates to how its important message was initially ignored by researchers. This is often attributed to the *modus operandi* of the prosecutors and expert witnesses, insisting that the requirement of informed consent for medical research with humans was a widely accepted norm at the time which it was not. Consequently a perception, at least partially attributed to this, existed amongst researchers in the US that the Code had little to no relevance for them.(Miller, 2014) Considering the further occurrence of ethically questionable conduct that occurred after the War in the US, as highlighted by Beecher,(Beecher, 1966) this is a significant shortcoming. While having been devised to prevent a recurrence of the Nazi atrocities, the Code seemed ineffective in preventing further unethical research conduct.

Within the context of this thesis, however, the main focus of a critique of the Code is related to its elevation of informed consent to an unconditional requirement for human research. Historical significance of the Code, and the embedding of many of its principles in other documents such as the International Covenant on Civil and Political Rights, has meant that this idea has found expression in a very broad range of legislation and material on research conduct (s12 of the South African Constitution is another example).(Annas and Grodin, 2008:138) In principle one of the Code, the requirement of informed consent is associated with human participation in '*an experiment*'. No doubt the originators of the code had in mind the experimentation conducted in the concentration camps. However, the term '*experiment*' is quite narrow in the broader cross-section of research methods. Regardless of this, what the Code says about informed consent has been extended to apply to all research involving humans.

It is possible that, from an emergency care perspective, limitations of the strict requirement of informed consent were not considered to be significant at the time of drafting of the code. The key feature of the Nazi experiments was not that the victims were incapacitated (i.e. could not consent, in the conventional sense) but rather that their capacity for choice was ignored.(Annas and Grodin, 2008:139) The difference between a real lack of capacity and the abuses identified during the Doctors Trial seems to not have been taken into account in the desire to put in place a safeguard against future abuses of the latter kind.

Only much later, with the advent of legitimate and potentially widely beneficial research that of necessity involved patients that could not consent, did the complications brought about by the code in this area become apparent.

In conclusion, the thinking of the Nuremberg judges seems to have been captured quite clearly in the late 1990s by Katz in testimony to the Advisory Committee of Human Radiation Experiments, as described by Annas & Grodin (2008:139). His view is that attempting to balance different research ethics principles (for example, autonomy and beneficence) by placing them on an equal footing can lead to dangerous trade-offs. Katz believes that the requirement of informed consent should be the single, prime and non-negotiable requirement for research with humans and that only once this is in place can participant safety be assured. Any considerations of proceeding without informed consent can only be weighed, and must be relative to, the latter position. While this approach is not without debate, the difficulties brought about by the Code may be related less to its first principle than to the ways in which exceptions to the first principle have been approached.

7.2.1.3. The Belmont Report

The Belmont Report was officially published in 1979 by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, itself established in 1974. The National Commission's *raison d'etre* was growing concern in the US about what was often referred to as the utilitarian attitude in research ethics, something that had led to the Tuskegee syphilis study and a range of other scandals. The US Congress required of the National Commission to draft a report identifying ethical principles and providing guidance on the conduct of research involving humans.(Beauchamp, 2008:149)

The Belmont Report identified three core ethical principles – respect for persons, beneficence and justice. These have since been referred to as the '*Belmont principles*'.(Beauchamp, 2020) Respect for persons applies mainly to informed consent. Beneficence relates to participant benefit from research, taken together with the principle of non-maleficence, and applies to the risk/benefit ratio and analysis thereof. Justice applies to the fair selection of research participants. Thus, each of the moral principles put forward in the Belmont Report links to an area of application in research ethics. Of the three

principles, the first – respect for persons – is most applicable here. The National Commission deviated from prior positions about informed consent and held that it was not so much about protection from risk but rather about the protection of autonomy and personal dignity.(Beauchamp, 2008:151) This principle was, by its definition, extended to those unable to act autonomously, thus marking a departure from the Nuremberg Code's exclusive focus on those who are able to consent.

The Belmont Report specifically mentions those with diminished autonomy, either due to maturity or due to other forms of incapacitation, as requiring protection.(Lysaught, 2004; Beauchamp, 2008:151) The extent of protection is described as being dependent on the risk of harm and the likelihood of benefit. Under the principle of beneficence, further detail is added regarding the balancing of risk and benefit, although there is no specific focus on those who lack autonomy. The principle of justice cites the vulnerable, and specifically the institutionalised and those dependent on care, as deserving of particular protection.(National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979)

In the Belmont Report, description of the three principles is followed by a section detailing application of the principles. Respect for persons is applied as informed consent, beneficence as risk/benefit analysis and justice as fair selection of research participants. Informed consent is split into three components; information, comprehension and voluntariness.(National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979) Under the discussion of comprehension, specific mention is made of those lacking capacity and the measures that should be put in place to safeguard their interests. Here, the involvement of '*other parties*' as proxy decision-makers is proposed as a way of protecting participants from harm and the ability of these parties to observe the research and intervene by terminating participation if this is considered to be in the best interests of the participants is also proposed. Notably, under the discussion of comprehension, there is no mention or consideration of distractors such as severe pain as barriers to comprehension of informed consent.(National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979)

7.2.1.4. Critique of the Belmont Report

Several criticisms have been levelled at both the National Commission and the Belmont Report.(Beauchamp, 2008:152-154) The Report has been said to be too abstract and not practical enough and to be lacking in specificity of the priority order of its principles. However, two criticisms stand out that have relevance to consideration of incapacitated adults in research. The first criticism is that there is a confused distinction between the principles of respect for persons and beneficence. The basis for this criticism lies directly with the Report's attempts to respect both autonomous individuals and those lacking in their ability to act autonomously – the incapacitated. The principle of respect is invoked in the protection of both, but it has been pointed out that this is contradictory.(Beauchamp, 2008:152)

It has been argued that those incapable of autonomous actions can only be protected, in their incapacitated state, by application of the principle of beneficence.(Beauchamp, 2008:152) While this may at first sound odd, it should be remembered that the Belmont principle of beneficence contains a component of avoiding harm – what Beauchamp and Childress would later tease out separately as non-maleficence.(Beauchamp, 2020) Taking this into account, the Report appears to be contradicting itself in holding that respect for persons and beneficence are separate principles when, in fact, they are two sides of the same coin that applies to protection of all – regardless of capacity. While this is a valid point about principles, it doesn't necessarily detract from the Report's attempts to correct the Nuremberg Code's exclusion of the incapacitated in research.

While the Belmont Report's inclusion of incapacitated adults in considerations of research participation was a step forward from Nuremberg, the Report has been criticised for signalling a departure from a more moderate form of protectionism in research ethics towards what some consider to be an overly protective approach.(Moreno, 2001; Beauchamp, 2008:152) As Beauchamp suggests, the Report's default position of health research being a potentially dangerous hardship from which participants must be protected may have been shaped by a variety of scandals that motivated establishment of the National Commission.(Beauchamp, 2008:152) The Report's main response to this was to draw attention to the plight and protection of the vulnerable research participant and to

emphasise that the vulnerable required a greater level of protection.(National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979)

Initially, the Belmont Report confined the definition of vulnerability to a small list of groups; racial minorities, the economically disadvantaged, the very sick and the institutionalised.(National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979) However, this list was set to grow with future guidelines (including the future revisions of the Declaration of Helsinki and the Council for International Organisations of Medical Sciences (CIOMS) guidelines, which are discussed below) and to explicitly include incapacitated adults. Views differ on whether the focus on research participant vulnerability since publication of the Belmont Report constitutes over-protection or whether it simply facilitates an appropriate level of protection which had been overlooked before the report's publication.(Moreno, 2001; Beauchamp, 2008:152; Friesen *et al.*, 2017) The classification of incapacitated adults as vulnerable certainly has heightened awareness about protection of this participant group.

7.2.1.5. The Declaration of Helsinki

The Declaration of Helsinki was adopted by the General Assembly of the World Medical Association (WMA) in 1964 and has since then become one of the most frequently cited health research ethics guides. The WMA's origins in 1947 were largely in response to the Nazi atrocities committed in the name of medical science during World War II. The Association's origins were more or less co-existent with the other post-War attempts to protect human rights; the Nuremberg Trial, the establishment of the United Nations and enactment of the Universal Declaration of Human Rights.(Ashcroft, 2008:141)

Despite the timing of the WMA's establishment during a period a rapid development of human rights, it took more than decade for the Association to finally produce the Declaration of Helsinki. Precursors, in the form of statements on medical ethics in general, include the Declaration of Geneva (1948) and the International Code of Medical Ethics (1949), neither of which made any reference to research. Five years after adoption of the International Code of Medical Ethics, the WMA adopted a resolution on '*human experimentation*', followed by a draft Declaration in 1961 and final adoption of the

Declaration of Helsinki in 1964.(Ashcroft, 2008) Little is known about the reason for the protracted time course of final adoption, which seems contradictory to the obvious need for health research regulation following Nuremberg, 17 years before. Once again, views of the US health establishment that the Nuremberg code was not intended for them – and the belated revelations of Beecher in 1966 - may have played a role.(Beecher, 1966)

The 1964 Declaration represented a change from the strict legalistic Nuremberg Code in that it allowed consideration by the physician of a patient's capacity (what the Declaration refers to as legal capacity and '*physical*' capacity) when deciding whether informed consent is necessary.(Ashcroft, 2008:142-144) Furthermore, the Declaration suggests for the first time that in situations where patients lack capacity for informed consent a '*legal guardian*' could replace the patient as a decision-maker for therapeutic research. Together with the preamble which described the aim of medical science as balancing the need for human research with the need for human protection, the 1964 Declaration seemed to mark a clear conceptual departure from Nuremberg and the insistence that human experimentation was a fundamentally questionable activity contrary to human dignity with an unconditional requirement for patient consent. Importantly, the Declaration was not written as a statement of patient's rights but rather as a statement of the responsibility of physician-investigators.(Ashcroft, 2008:142-144)

The Declaration was revised in 1975 further clarifying statements regarding the balance between research risks and progress in biomedical research which depended on this research. Two changes to the 1975 Declaration were important for research with incapacitated adults. The first was wording to the extent that the interests of the individual (patient) should always take precedence over the interests of science and society.(Ashcroft, 2008:144) This suggested a subtle shift towards a focus on the interests of patients rather than the conduct of physicians although in general the Declaration remained a guide for physician conduct in research. This wording, along with detail in the 1975 Declaration on informed consent and research risks,(Ashcroft, 2008:144) highlighted the primacy of informed consent more than the 1964 Declaration. The second change in 1975 was inclusion for the first time of a section describing the mandatory requirement of a research protocol and the review and approval of a protocol by an independent research ethics

committee.(Ashcroft, 2008:144) This has relevance for decisions regarding informed consent in cases of incapacity which were now considered up to the research ethics committee rather than the judgement of the physician-investigator.

7.2.1.6. The 2013 Declaration of Helsinki and Research with Incapacitated Adults

The Declaration of Helsinki has been further revised (after the 1975 revision) in 1983, 1989, 1996, 2000, 2004, 2008, 2013 and 2024. Seemingly, revision after 1996 became a more complex process that attracted criticism from researchers and the pharmaceutical industry with debates emerging related to ethical relativism of research conducted in high-income countries and middle- and low-income countries, among others.(Ashcroft, 2008:145-146) This led to notes of clarification being added in 2002 and 2004. With regard to research involving incapacitated adults these revisions slowly added greater detail to guidance including decisions about the acceptability of such research and associated conditions, how such decisions should be made and the use of proxy decision-makers. A summary of the relevant sections in the 2013 version of the Declaration(World Medical Association, 2013a) is given below. This is followed by a description of revisions relevant to research with the incapacitated from the 2024 version of the Declaration in the next section (7.2.1.7). Very little of relevance to this population was added in the 2024 revision, thus most of the focus is on the 2013 Declaration below.

General Principles

The 2013 Declaration continues the trend established in revisions before 2000 that firmly establish the rights of the individual participant above those of science and society in paragraph 8 and to describe an approach of proportionality between the necessity of research involving human participants, risk and safety in paragraphs 5 and 6. The Declaration also clarifies in paragraph 10 that, from a moral and legal perspective, it is not put forth merely as guidance but rather as a way of setting a minimum standard of conduct that deficient local regulations cannot undermine. In paragraph 13 the Declaration states that underrepresented groups should be given adequate access to research – an important consideration in the context of emergency care research.

Risks, Burdens and Benefits

In paragraphs 16 – 18 the Declaration emphasises the required balance between importance of the research objective, benefits and risk in all research and the researcher's duty to minimise and monitor risks. Risks are presented in the paragraphs in a general sense – risks specific to research with incapacitated adults is briefly mentioned in paragraph 28 and is discussed further below.

Vulnerable Groups and Individuals

The Declaration highlights the protections that should be offered to vulnerable groups and individuals, and it does stress, in paragraph 20, that vulnerable participants should only be included in research if this can be justified because it is '*responsive to the health needs*' of a vulnerable group by generation of beneficial knowledge. Vulnerability is, however, not defined.

Informed Consent

The section of the Declaration on informed consent holds the most important information of relevance to research with incapacitated adults. After stating clearly in paragraphs 25 – 27 that informed consent for research participation is mandatory for all patients capable of giving it, the Declaration deals with those lacking capacity in paragraphs 28 – 30. The following requirements are set out:

- A legally authorised representative must decide about participation on behalf of the incapacitated adult.
- The research must have some likelihood of benefit for participants or, if not, it must promote the health of the group of which the incapacitated participants are representative, and the same research must not be possible with participants who have the capacity to consent.
- The research must pose only a minimal risk and minimal burden.
- The participant must assent to participation when this is possible, and dissent must be respected.

Unconsciousness is dealt with specifically in paragraph 30; once again, a legally authorised representative must be consulted about the participant's inclusion and the condition (unconsciousness) that causes the lack of capacity must be a necessary inclusion criterion for the research. This paragraph further deals with situations where a legally authorised representative is not available. In such situations the Declaration allows inclusion of the incapacitated adult provided that (i) the research protocol (stating the necessity of including incapacitated adults) has been approved by an ethics committee and (ii) that consent to remain in the research is given by the participant if possible or by a legally authorised representative if not possible.

7.2.1.7. The 2024 Declaration of Helsinki and Research with Incapacitated Adults

An updated version of the Declaration was released in 2024 after adoption at the 75th World Medical Association General Assembly in Helsinki. Very few changes were made in the updated version with respect to paragraphs relevant to research with the incapacitated. Paragraph 19, one of three on vulnerability, was changed to emphasise the importance of considering the implications of excluding the vulnerable with the wording: '*harms of exclusion must be considered and weighed against the harms of inclusion*'. However, following this, the paragraph reiterates the conditions for considering inclusion of vulnerable populations and has also undergone some changes highlighting the role of exclusion and its exacerbation of disparities between vulnerable and other populations in guiding decisions about participation. Thus, overall in these two paragraphs there seems to be a greater emphasis on care being taken to not over-protect vulnerable groups, such as those incapable of independent decision-making.

Apart from the above changes, none of the other paragraphs discussed above under 2.1.6 have undergone substantive revision in 2024.

7.2.1.8. Critique of the Declaration of Helsinki

Seen from a broad health professions perspective, the Declaration has a narrow focus on medicine and physicians (or, perhaps more correctly, physician-investigators). This is understandable considering its source – the WMA – however it seems to create the impression that only physicians conduct health research. Or that only physicians should

heed the guidance of the Declaration. Paragraph 2 of the current Declaration acknowledges the narrow focus on medical research and physicians and encourages others to adopt the principles contained in it. While other research ethics guidelines, most notably those from the Council for International Organizations of Medical Sciences, have more recently filled the gap of applicability to the broader spectrum of health research, relevance of the Declaration to non-medical (and perhaps more specifically non-clinical trial) research is arguably still limited by its narrow focus.

Some critics of the Declaration (especially the earlier versions) have seen it as an attempt by the medical profession to erode the sanctity of informed consent established by the Nuremberg Code in order to allow a broader scope of medical research.(Ashcroft, 2008:147) That the Declaration has weakened the requirement for unconditional consent progressively, over its many revisions since 1964, is not in question. However, the view that this is wrong or possibly harmful to research participants or that it merely represents an ever-expanding and questionable influence of medicine over the practice of research is open to question. When the principle of autonomy is elevated above all others, something that builds on a fundamental assumption that research involving human participants is inherently morally questionable, then the Nuremberg Code's insistence on consent might be justified. However, when human research is seen as an activity with inherent potential for good and something that should not unjustly exclude participants who stand to benefit from it (or whose participation may produce new knowledge with the potential for future benefit) such an insistence seems to be unjustifiable. From the perspective of emergency care research, the existence of which would be rendered unviable by the Nuremberg Code, the Declaration therefore represents a step forward rather than a step back.

Paragraphs of the Declaration dealing with research participants incapable of informed consent (summarised above) are, in some respects, contradictory or lacking important detail. Both paragraph 28 and paragraph 30 refer to research participants unable to give consent. In paragraph 28 the expression '*incapable of giving informed consent*' is used, followed by a description of conditions for inclusion of such participants (the same as those listed under *Informed Consent* above). In paragraph 30, the expression '*physically or mentally incapable of giving consent'* is used with an example of unconscious patients. It

isn't very clear how the conditions referred to in these two paragraphs differ, nor exactly what is meant by '*physically or mentally incapable*'. The conditions for inclusion of patients in both cases are the same. The only difference in paragraph 30 is that further detail is added for situations where a legally authorised representative is not available. Thus, it seems that the Declaration intends to emphasise some difference between paragraphs 28 and 30 but it is unclear what this difference is.

With regard to detail, the Declaration does not provide sufficient guidance with terms used in paragraph 28, referring to conditions for the inclusion of incapacitated patients in research – specifically the terms '*minimal risk'* and '*minimal burden'*. Although these terms are defined in other guidelines describing the acceptable risk level for research with incapacitated adults,(Council for International Organizations of Medical Sciences (CIOMS), 2016) their contextual meaning should be clarified in this paragraph because the accepted meaning of '*minimal risk*' may not be easy to understand in its application to some settings in which incapacitated adults are encountered (including the Declaration's own example of unconsciousness). Typically, minimal risk refers to risk equivalent to activities of daily life or routine physical examinations or tests.(Council for International Organizations of Medical Sciences (CIOMS), 2016) However, being unconscious is not a daily activity nor comparable to a routine physical examination. Considering that the context in which a clinical intervention is used might also contribute to its risk, the minimal risk standard seems to be a difficult one to apply simply to at least some emergency settings or conditions, as discussed in Section 5.4 of Chapter 5. It is therefore important for minimal risk as it applies to research with the incapacitated to be carefully explained (along with '*minimal burden'*), however this explanation is missing in the Declaration.

7.2.1.9. The Council for International Organisations of Medical Sciences Guidelines

The Council for International Organisations of Medical Sciences (CIOMS) was established in 1949 under the auspices of the WHO and the UN Educational, Scientific and Cultural Organisation (UNESCO).(Idänpään-Heikkilä and Fluss, 2008:168) In 1982, following work started in the 1970s, CIOMS published their first guidance on research ethics. The aim of doing so was to provide more detailed information on application of the 1975 version of the Declaration of Helsinki, particularly with regard to research in low-resource settings. The

1982 guidelines were revised in 1993 in response to several new challenges in the broader field of biomedical research ethics, including the HIV/AIDS pandemic and were called the *International Ethical Guidelines for Biomedical Research Involving Human Subjects*. The 1993 guidelines were updated again in 2002 with the most recent version dating to 2016 (referred to here as CIOMS 2016).(Idänpään-Heikkilä and Fluss, 2008:168-169) CIOMS 2016 has been broadened in scope to now apply to health research rather than biomedical research, a term that was considered to be too narrow.

In the preamble to CIOMS 2016 this broader health research scope is described in further detail. This section refers to '*generalisable health knowledge*' as the end product of the type of research, with human participants, that is envisaged. Examples provided are observational research, clinical trials, biobanking and epidemiological studies. Importantly, this description of health research also includes '*accumulation of information on which they [the examples] are based, related to health*'. Although perhaps not a significant limitation, the CIOMS 2016 definition of health research speaks exclusively to quantitative research designs and seemingly does not include other approaches such as qualitative or mixed methods research.

7.2.1.10.The 2016 CIOMS Guidelines and Research with Incapacitated Adults

Of all the sources discussed in this section so far, CIOMS 2016 contains the most detailed information and guidance on research with incapacitated adults. This includes guidance of particular relevance to emergency care research when research may focus on treatments that must be delivered in a very short period of time after onset of the emergency condition. Apart from sections on informed consent, part of other guidelines in CIOMS 2016 contain information of relevance to research with incapacitated adults and emergency care research. These are discussed below.

Guideline 3: Fair Distribution of Benefits and Burdens

This guideline touches on what is referred to as equity in benefits and burdens of research; that no particular group of individuals is exposed unfairly to burdens of research or deprived of potential benefits. This idea, based on the principle of distributive justice and incorporating consideration of vulnerability, is not new. However, the guidance emphasises

that protection from injustice in the past tended to exclude some groups identified as vulnerable and that this in itself led to an unfair deprivation of such groups from the potential benefits of research participation. This is important in relation to emergency care research, where restrictions associated with informed consent in patients lacking capacity may tend to make researchers avoid this kind of research and deprive patients (and others, who may benefit from future generalisable knowledge) of potential benefit. On the other hand, the same guideline warns that achieving a fair balance might be difficult as the populations that emergency care researchers often look to for participants (those highly dependent on care, lacking capacity or possibly in pain or anxious about their precarious condition) can become over-utilised due to their compromised positions and inability to protect their own interests. The theme of incapacitated patients having a right to participate in research, and not being over-protected, is picked up again in greater detail in Guideline 16.

Guideline 4: Potential Individual Benefits and Risks

Guideline 4 gives a detailed account of how researchers and research ethics committees, prior to enrolment of research participants, must evaluate the risks and benefits of the proposed research and how the risks and benefits should be balanced so as to minimise harm. In considering an appropriate balance of risks and benefits, the approach adopted is to consider each research intervention and to place it into one of two benefit categories; interventions with possible benefits for participants and interventions with no possible benefits for participants. In the former case, risks must be minimised and counterposed by potential benefits for the individual (this also relates to the choice of control in a trial) and in the latter case risks must again be minimised and commensurate with the anticipated societal benefits resulting from the production of generalised knowledge. Once each research intervention has been assessed in this way, the guidelines recommend an overall assessment of risk and benefits ensuring that the accumulated risk is appropriate relative to the benefits, that research ethics committees consider further steps to minimise risk if relevant and that an evaluation of risk and benefit must take place with communities in which the research takes place.

This guideline also gives specific attention to risk and benefit evaluation in situations where research participants do not have the capacity for informed consent. In such situations, the acceptable risk level depends on the possibility of benefits for research participants and an interpretation of how '*compelling*' the value (i.e. future potential benefit) of the research is in its ability to produce generalisable knowledge. If the research will not yield individual participant benefits, then the guideline states that only minimal risk is acceptable (the minimal risk standard is discussed in greater detail below). However, if the research has what is judged by a research ethics committee to be compelling social and scientific value, and it is not possible to access the required data from an alternative (less vulnerable) population or in a less risky way, then then a '*minor increase*' above the minimal risk standard is considered acceptable.

The commentary on Guideline 4 provides further detail on what is meant by the minimal risk standard, the standard that applies to the risk to benefit ratio in research involving incapacitated participants. Minimal risk is defined as the probability and magnitude of harm '*ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests*.' This definition simply compares research activities or interventions to the risks that an individual would be assumed to normally be exposed to in '*daily life*' and concludes that, if the these are the same or very similar, then the minimal risk standard applies. The guideline adds, somewhat redundantly, that this implies the risk of harm is '*very unlikely*' and that the possibility of harm from adverse events is '*small*'.

One obvious weakness of the above definition is its reliance on a rather abstract existence termed '*daily life*'. This seems to assume that all research participants '*daily life*' experiences are more or less similar when it is obvious that this cannot be the case. Hence, the guideline goes on to add some detail with respect the evaluation of minimal risk as it may apply to individuals who experience a '*daily life*' that may involve something other than good health. The detail offered is simply to state that research ethics committees should be careful not to permit research risks that are greater than minimal because of on increased '*background risk*' in the population of interest. This is attributed mainly to inequality with a brief mention of environments (other than those brought about directly by inequality) that might increase '*background risk*'. Similarly, the guidelines urge vigilance by research ethics committees in

not allowing the exposure of patients to more risky treatments or diagnostic procedures to alter their understanding or application of the minimal risk standard as defined (i.e. greater research risks should not be allowed in populations with greater '*background risk*'). Lastly, the guideline warns that minimal risk comparisons must not be made with activities involving inherently greater risk (presumably than '*daily life*', as defined) or with activities that may be risky but that are chosen by individuals because of associated personal benefits. Notably, as discussed in the critique below, having provided several cautions to research ethics committees about what the guideline considers to be asymmetrical risk comparisons there is no suggestion as to how research in populations of greater '*background risk*' could be approached other than disapproval.

Guideline 10: Modifications and Waivers of Informed Consent

Guideline 10 deals with situations where modifications or waivers of informed consent might be justifiable and related conditions and considerations. In both cases, the guideline emphasises the mandatory requirement for research ethics committee approval in any situation where participant inclusion is considered without informed consent from the participant themselves or their legally authorised representative. The guideline specifies that researchers should first consider modification of the informed consent process before making a case for a waiver of informed consent, with modification preserving as much of the participant's understanding and related decision-making ability as possible. A waiver, if modification of informed consent is not possible, is conditional upon (i) clear evidence that participants would not be able to consent (i.e. the research would not be feasible if informed consent were a requirement), (ii) important social value of the research and (iii) minimal risk (presumably defined the same way as that discussed above).

In commentary following the main body of the guidelines, some additional detail is given to the notion of a consent modification – that it most often involves modification of information provided to participants and how consent is recorded or documented. After this, a description of a waiver is given as allowing '*researchers to conduct studies without fully informed consent*'. Considering that this is the only real explanation of the word waiver in Guideline 10, it creates some confusion. Referring to research being conducted without

fully informed consent sounds more like a modification than a waiver which is usually used to describe proceeding with research in the absence of informed consent.

Three main situations that modifications and waivers of consent, as defined, could apply to are defined most clearly in this guideline and it seems that the main intention is to provide guidance related mainly to these. The first situation is one where information may be withheld from research participants at the beginning of the consent process for a legitimate reason related to validity of the research. One example used is withholding information about the purpose of tests so that participants do not modify their behaviour and in turn influence test outcomes. The second situation relates to the use of deception when this is seen as necessary to carry out valid research. In both these cases, the guidelines cover recommended approaches to information given and measures to be taken on completion of the research when participants are provided with information that was withheld at the outset. While this part of the guideline is of relevance under the broader heading of modification of consent, it is not very applicable to emergency care research with incapacitated adults and will not be discussed further in detail here.

The third situation relevant to modifications of consent discussed in this guideline is the use participant biological specimens or data contained in databases or registries. In such cases, whether data are identifiable or not, the guidelines specifies that the same three conditions described above apply if a waiver of informed consent is to be considered (in addition to the other requirement of research ethics committee review and approval). Special mention is made of population-based registries used for public health purposes and mandated by law. In such cases, neither ethical approval or informed consent are necessary, although in situations where research activities depart from being public health orientated then use of such data should be with the consent of the individuals from whom it was obtained unless the three conditions above apply, and a waiver of consent is justified.

In describing both modifications of consent and waivers of consent, Guideline 10 addresses some important detail relevant to emergency care research. In the last sentence of this guideline, before the subsections providing commentary, there is a reference to '*additional provisions*' which may apply (to modifications and waivers) in other contexts. It is not

immediately clear why the guidance in this section is separated from that in Guideline 16 which deals specifically with research involving those incapable of informed consent. There are several points throughout this section where mention is made of a lack of capacity to give consent as also being relevant, but it seems as though the main theme here is not a lack of capacity but rather a desire of the researcher to not fully inform research participants of all information although they do have the capacity for consent. Stating this clearly at the beginning of Guideline 10 would make its intended application easier to understand.

Guideline 15: Research Involving Vulnerable Persons and Groups

The problem of fair distribution of research benefits and burdens was briefly touched on in the discussion of Guideline 3. In that section, brief reference was made to vulnerability as a potential source of maldistribution of research burden. In Guideline 15, vulnerability is dealt with in greater detail (although the statement of Guideline 15 is quite short there is a lot more detail on vulnerability in the commentary that follows it). In essence, Guideline 15 highlights the duty of research ethics committees and researchers in safeguarding the rights and welfare of the vulnerable. In so doing, the definition of vulnerability is the definition from the Declaration of Helsinki that characterises vulnerable groups (and individuals) as those '*may have an increased likelihood of being wronged or of incurring additional harm*'. While many possible sources of this likelihood are discussed, the one that is of most interest within the context emergency care research is the characteristic of impaired decisional capacity producing a situation in which research participants are unable to protect their own interests and are thus, at least potentially, at risk of harm. Guideline 15 defers a more detailed discussion of this situation to Guideline 16, which will be discussed below.

Although this guideline does not deal in much detail with diminished decisional capacity as source of vulnerability, it does provide some general guidance on what it refers to as special protections for vulnerable groups or individuals. Two of these are in the form of restrictions aimed at reducing research with the vulnerable to the bare minimum as a way of reducing risk. These restrictions include the condition that only research meeting the minimal risk standard (as defined above) is acceptable and that only health conditions tightly associated with the source of vulnerability may be researched. The other form of special protection is a requirement of proxy or surrogate consent from a legally authorised representative or other

representative to replace the research participant's own decision regarding participation. This guideline concludes by reiterating that care should be taken not to over-protect and thus unfairly exclude the vulnerable from research that may hold potential benefits for them or that may have social value.

Guideline 16: Research Involving Adults Incapable of Giving Informed Consent

Guideline 16 is the most important part of CIOMS 2016 when considering emergency care research specifically, and research with incapacitated adults more generally. While Guideline 10, discussed above, mentions the incapacitated when describing the application of modified consent and waivers of consent, this guideline deals in detail with such situations. The tone of Guideline 16 is, from the outset, an enabling one with the opening statement that '*Adults who are not capable of giving informed consent must be included in health-related research unless a good scientific reason justifies their exclusion'*. This is quite a radical departure from the Nuremberg Code which all but forbade such inclusion and builds upon the incremental loosening of this stance brought about by successive versions of the Declaration of Helsinki and by the Belmont Report. At the same time, Guidelines 16 also notes that the incapacitated are due special protections and much of the rest of this guideline is devoted to describing these measures in some detail.

Guideline 16 begins by providing guidance on situations where patients may not be able to give informed consent, but a legally authorised representative is available to give permission based on perceived wishes of the patient. This part of the guideline refers to obtaining patient assent where possible (this might apply to situations where patients are incapacitated with respect to consent but are possibly of sufficient mental status to assent). Importantly, this guideline acknowledges the role played by others (referred to as '*socially acceptable*') who may not be legally authorised to act as surrogate decision-makers, especially when time constraints make accessing a legally authorised representative difficult. Mention is also made of advance directives that, if available, should be respected.

The next part of Guidelines 16 deals with benefits and risks. The main differentiator seems to be whether there is a reasonable prospect of any benefits. If this is the case, then this guideline recommends only that the risks must be minimised and '*outweighed*' by the

possible benefits. This is a subtle difference compared to Guideline 4 (discussed above) which states with reference to incapacitated patients that if benefits are possible, and if the research has compelling social value, a '*minor increase*' above the level of minimal risk is warranted. With regard to research that holds no prospect of benefits for patients, only minimal risk is allowed but if the social value of the research can be considered compelling then a '*minor*' increase above minimal risk is permitted. This part of the guideline also emphasises the general rule that, where research benefits are not likely, the research should always be done with participants who can consent before those who cannot, if this is possible.

A natural question, having considered the above, is how to proceed in situations where the time-sensitive nature of an intervention may mean that seeking the permission of a legally authorised representative is less feasible – a problem unique to emergency care research. Under such circumstances, Guideline 16 recommends several possible approaches. The first, which is rarely feasible in emergency care research especially that conducted in the pre-hospital environment, is to identify the relevant population and to obtain prior consent (that is, prior to incapacitation when patients are able to consent). If this is not possible, then reasonable efforts must be made to access a legally authorised (or other) representative. If this, in turn, is not possible then this guideline suggests that a maximum allowable time should be determined by the research ethics committee approving the research for involvement of the researcher with the patient (who, at this point would be a participant). Once this time has been exceeded, without the patient having capacity for consent or access having been gained to a legally authorised representative, the participant should be withdrawn from the research (unless there is reason to believe that this will leave the patient in a worse state). The final suggestion (actually a requirement) is for community consultation.

The last commentary on Guideline 16 refers to a waiver of the requirement to obtain permission from a legally authorised representative (as described above). This is considered acceptable if the conditions for waiving informed consent from participants who <u>are capable</u> of giving it also apply in this circumstance. These conditions were discussed under Guideline 10 above and are repeated here; (i) that the research would not be feasible without such a

waiver, (ii) that the research has important social value and (iii) that the research is considered to be minimal risk.

7.2.1.11.Critique of CIOMS 2016

One of the great strengths of CIOMS 2016, from the perspective of guidance on emergency care research, is its anticipation of the problems that this kind of research will pose for researchers and participants. Over time, most guidance on research ethics has slowly relaxed the very narrow restrictions on informed consent imposed by the Nuremberg Code. While the Declaration of Helsinki currently does provide guidance on research with the incapacitated, including situations where a legally authorised representative is not available, CIOMS 2016 provides greater detail – which was, from the outset of the CIOMS guidelines, its intention.

For the individual seeking clear guidance on research with the incapacitated patient, and specifically in the most challenging circumstances with time-sensitive interventions, CIOMS 2016 does provide this but there are several weaknesses in how the guidelines are structured and, in some cases, contradictory guidance. To some, these may seem like very small problems that could perhaps be labelled as irrelevant, but they relate to some very important considerations such as acceptable risk, evaluation of capacity and application of the word '*waiver*'. It may well be that some of these weaknesses and contradictions are rooted in the Declaration of Helsinki itself and not necessarily in CIOMS 2016.

Benefit and Risk

In Guideline 4, CIOMS 2016 clearly sets out the standard for minimal risk, as described above. Then, in Guidelines 10, 15 and 16 this risk standard is applied to vulnerable participants and those lacking capacity. In summary, two instances are described. Firstly, a situation where no benefits to participants are expected – here research interventions may only be allowed that are judged to be at the minimal risk level. Secondly, a situation where benefits to participants are possible or, when participant benefits are not possible but new knowledge with compelling social value is likely, a '*minor increase*' above the minimal risk level is permissible. From the perspective of research with incapacitated patients, there are

two main critiques of CIOMS 2016 focusing on the relevant risk standard and also the balance of risks and benefits. These are most closely related to Guidelines 4 and 16.

While the minimal risk standard is referred to in multiple parts of CIOMS 2016, it is discussed in some detail in Guideline 4 where the minimal risk standard is explicated. It is very difficult to understand what the minimal risk standard means when it applies to emergency care research. Minimal risk has, as its standard, the normal, healthy individual engaging in daily life and from a health perspective being exposed to the exemplars of routine medical or psychological tests. If this standard is applied to many research interventions or procedures relevant to emergency care where patients lack capacity, the problem is that these interventions and procedures will very likely be the sorts of things to be used in a context which is very different from '*normal*', *healthy*', 'routine' or '*daily life*'. As argued in the previous chapter, this conception of minimal risk applied to all research interventions in an emergency care setting with incapacitated patients may prove to be a significant limitation. In addition, the notion of '*a minor increase above minimal risk*' is very difficult to apply. For a start, this is an increase above minimal risk which, as already argued in Section 5.4.2 of Chapter 5, is difficult to apply to emergency care research with the incapacitated. Thus, uncertainty about the baseline meaning and application of '*minimal*' in this context would mean that any increase from this baseline would be equally uncertain. Moreover, there is no guidance regarding that magnitude of risk increment a '*minor increase*' might constitute. This is left entirely to research ethics committees to determine in any way they choose.

With regard to balancing risks and benefits, CIOMS 2016 departs from the Declaration of Helsinki's guidance on this for research with incapacitated adults and suggests a lower threshold for elevating acceptable risk. The Declaration of Helsinki states that only minimal risk is permissible for such research. Furthermore, it states that there should be a likelihood of therapeutic benefit, but in the absence of this the research must at least promote the health of the group being researched. This latter requirement does not alter the acceptable risk level, which remains nothing beyond minimal. Guidance from CIOMS 2016 related to capacity, social value of new knowledge associated with research, risk and benefit spans Guideline 4 and Guideline 16. This information is summarised below in Table 7.1.

Table 7.1: Capacity, Social Value, Risk and Benefit: Guidelines 4 and 16

Guideline	Capacity	Benefit[1]	Social Value[2]	Risk Standard
4	Has Capacity	Likely	Not Stated[3]	Benefit: Risk > 1, Minimised Risk[4]
	Has Capacity	Unlikely	Likely	Knowledge: Risk > 1, Minimised Risk
	Incapacitated	Likely	Not Stated[3]	Not Stated[5]
	Incapacitated	Unlikely	Unlikely	Minimal Risk
	Incapacitated	Unlikely	Compelling	Minor Increase Above Minimal Risk[6]
16	Incapacitated	Likely	Not Stated[3]	Benefit: Risk > 1, Minimised Risk
	Incapacitated	Unlikely	Unlikely	Minimal Risk
	Incapacitated	Unlikely	Compelling	Minor Increase Above Minimal Risk[6]

1=Individual participant benefit, 2=Social value of new knowledge generated by the research, 3=Where individual benefit is likely, social value of new knowledge generated by the research is typically not stated presumably because it is implied that such research is highly likely to produce new knowledge with significant social value, 4=Benefit: Risk > 1 means benefit outweighs risk, 5=Guideline 4 does not specifically identify the case of lack of capacity and likely benefit, however this could be inferred by the case of likely benefit which may be intended to include both capacity and lack of capacity for informed consent (although this is not clear – see discussion below), 6= It must be noted that the paragraph explaining the above in CIOMS 2016 is not clearly written and there is a possibility that this is not what was intended. The wording refers to 'studies with such interventions' mentioned in the section above, but in the section referred to both studies with and without benefit are described. Thus, the 'minor increase above minimal risk' may be in either or both situations – where benefits are possible or not. However, considering that in the case of likely benefit the applicable risk standard is simply that risk must be 'outweighed' by benefit, it seems unlikely that a 'a minor increase above minimal risk' would refer to this situation.

Several departures from guidance in the Declaration of Helsinki with regard to capacity, social value, risk and benefit are apparent from Table 7.1:

a) *Guideline 4*: The situation where a patient lacks capacity but the research is likely to produce individual benefit is not clearly defined in this guideline. This may be implied from the description of research with likely individual benefit – which states that risks should be minimised and outweighed by potential benefits – however it is not clear whether this applies specifically to incapacitated patients. If this is the intention, the risk standard is different to that in The Declaration of Helsinki for the same case (minimal risk only).

b) *Guideline 4*: Research with the incapacitated that is unlikely to produce individual benefit or new knowledge with social value is still permissible, but the minimal risk standard applies. For such a case, the Declaration of Helsinki is silent – it allows only research with likely individual benefit or the likelihood of promotion of health of the incapacitated group (see further comments on this definition vs. the social value of new knowledge below).

c) *Guideline 16*: Research with the incapacitated that is associated with likely individual benefit is permissible provided that risks are minimised, and benefits outweigh risks. The Declaration of Helsinki allows only minimal risk research in such a case.
d) *Guideline 16*: The same as b) above for research with the incapacitated unlikely to produce individual benefit or new knowledge with social value.
e) *Guideline 16*: Research with the incapacitated that is unlikely to produce individual benefit but is likely to produce new knowledge with '*compelling*' social value is permissible at a risk standard of a '*minor increase*' above minimal risk. The Declaration of Helsinki does not allow any increase of risk above the standard of minimal risk for research with the incapacitated under any conditions, not even likely individual benefit.
f) *Both Guidelines*: In several instances of both Guideline 4 and Guideline 16, CIOMS 2016 refers to '*social value*' or '*social and scientific value*' of new knowledge generated by research. These terms clearly suggest value of new and generalisable knowledge broadly applied and beyond the research participants themselves – to society in general and (where '*scientific value*' is referred to), the scientific community. The Declaration of Helsinki, under similar circumstances, refers only to value in the form of health promotion applicable to '*the group represented by the potential subject*' meaning a group characterised by the same or similar clinical conditions as the individual research participant in question. This latter group is much narrower, and arguably easier to define, than the very broad reference to society at large in CIOMS 2016.

The points a) - f) described above provide details of instances where CIOMS 2016 differs from the Declaration of Helsinki with regard to permissible risk and the risk: benefit ratio in the context of research with incapacitated adults. The fact that such differences exist is not necessarily a negative critique, considering the original goal of CIOMS in offering more detailed information to guide application of the Declaration of Helsinki. However, if such differences are to be helpful in an applied sense they should (i) not contradict each other and (ii) be based upon a principled justification, especially considering that in the above guidelines CIOMS 2016 suggests a lowering (albeit a seemingly small one) of the risk threshold for research with incapacitated adults and most notably where there is no likelihood of individual benefit.

While there are no glaring contradictions between the guidance given in Guideline 4 and Guideline 16, there are some inconsistencies between the guidelines. For research involving patients both with (Guideline 4) and without capacity (Guideline 16), where benefits are likely the risk standard is the same (a benefit: risk > 1 with minimised risk). One might expect the heightened vulnerability of incapacitated patients to perhaps be aligned with a lower risk threshold (perhaps minimal risk) yet the risk threshold for patients with and without capacity is identical. In Guideline 4, in the case of an incapacitated patient where individual benefits are likely the risk standard is not stated (only the case of an incapacitated patient where benefits are unlikely or impossible is discussed). In Guideline 16, acceptable risk for the same case is described as minimised with benefits outweighing risks. In both of these cases, the inconsistencies may not be material but rather a case of the way the information is communicated – in the latter case above the information that is omitted from Guideline 4 (regarding incapacitated patients and research likely to have individual benefits) is covered in Guideline 16. Thus, there appears to be a gap in Guideline 4 but the information is not absent from CIOMS 2016 as a whole.

Departures from the Declaration of Helsinki described above may be seen by researchers as helpful in the practical conduct of their research with incapacitated adults mainly because they place greater emphasis on the social value of new knowledge as a moderator of risk, whereas the Declaration of Helsinki is quite restrictive in its approach to risk. This favours researchers in certain disciplines, such as emergency care. However, CIOMS 2016 provides no principled position on why such an approach is morally acceptable. It might be argued that this is consistent throughout CIOMS 2016, which is a concise set of guidelines supporting research ethics practice rather than a more detailed document spelling out details of the primary moral principles. Nevertheless, lack of justification for this particular guidance in a contentious area of research ethics – research with the incapacitated not able to give informed consent – does not assist researchers in understanding why their actions in following CIOMS 2016 might be defensible.

Capacity

Guideline 16 provides a brief overview of capacity for informed consent, beginning from the position that capacity should be assumed unless the opposite can be proven. This guideline

gives as examples of situations where capacity might be expected to be lacking: *'dementia, some psychiatric conditions and accidents*'. It is not quite clear what is meant by '*accidents*' and what the nature of the lack of capacity might be in such circumstances. It is unfortunate that factors negatively affecting capacity in a clinical context such as acute severe pain, severe dyspnoea, the effects of psychoactive medication and anxiety among others – are not mentioned here. They occur commonly in clinical research and particularly in emergency care research and referring to them would be more accurate than using the word '*accidents'.*

Guideline 16 further recommends that, in situations where potential research participants are expected to lack capacity, they must be routinely screened. While this guidance looks reasonable, the problem is that there does not exist a valid and reliable screening tool that is widely recommended for this purpose. Added to this is the problem in some emergency care research contexts of significant time limitations for enrolment of research participants and thus screening. The problem is not so much the patients who obviously lack capacity due to unconsciousness but rather those who are conscious but affected by the factors mentioned above (pain etc). Thus, routine screening is a sound recommendation but lacking in a practical and valid implementation at present.

Modification of Informed Consent

In Guideline 10 modifications of informed consent are described, however these are applicable only to withholding of information so as to not negatively affect the validity of research (i.e. deception, where this can be defended) and the use of biological specimens or data in registries and databases without informed consent (if the specimens or data are deidentified). It might be expected that under the broad heading of modifications of informed consent, some consideration would be given to situations where research participants can be classified as having capacity for informed consent but exist in the capacity penumbra described in Section 3.4.4 of Chapter 3 – those affected by acute severe pain, anxiety or other acute factors distracting participants or otherwise negatively affecting decision-making ability. Several suggestions have been made regarding modification of informed consent to make it simpler and more suited to such acute situations while still facilitating the understanding required to make an informed decision.(Bromwich and Rid,

2015) While it is acknowledged that this is an uncertain area of research ethics and may be lacking meaningful research on which to base guidance, it is unfortunate that it is completely ignored given the frequency with which such situations are encountered in clinical research and emergency care research in particular.

Assent and Dissent

Guideline 16 provides guidance on the role of assent and dissent in participation of incapacitated patients in research. Assent is described as a way of obtaining agreement for participation when a patient does not have full capacity for informed consent or in response to changes in cognitive status and capacity. While no further detail is given about the application of assent, this might be a strategy that could be effectively used in situations such as those described above where factors such as acute severe pain or other distractors may interfere with capacity for informed consent. However, this important application is not elaborated on in Guideline 16.

Guidance related to dissent states that any '*explicit objection*' (a term not defined) must be respected and can only be overruled if the incapacitated patient requires beneficial treatment '*not available outside the research context*'. This approach to dissent seems to overlook the fact that patients to whom it is applied do not have a normal mental status and that this factor may contribute to their dissent. Such a problem is likely to occur in an emergency care setting more often, where patients of this type may suffer from acute derangements of physiology (e.g. cerebral hypoxia, hypercapnia and acidosis) rendering them anxious, confused and often agitated or combative. For example, the effects of acute pain, hypoxia, traumatic brain injury and post-insult delirium may render patients disorientated, agitated or frankly combative.(Melamed *et al.*, 2002; Aubanel *et al.*, 2020) The question to ask when dissent is noted, is whether the dissent is in itself rational or irrational. In other words, is the dissent based on a reasoned desire to refuse an intervention or is it simply a product of pathophysiological derangement caused by the patient's condition, resulting in irrational refusal? The fact that this part of the guideline is concerned with patients lacking capacity suggests that, by definition, dissent in such circumstances cannot be considered to be a reasoned refusal. If it was, we would have to consider the patient to have capacity in making a reasoned choice. Consequently, this

section on dissent is contradictory and offers little to assist researchers in clarifying how to approach this kind of difficult situation.

Emergency Care Situations with Many Participants Unable to Consent

Guideline 16 contains a section with specific guidance regarding research with incapacitated patient in situations where (i) interventions must be given rapidly and (ii) a legally authorised representative may not be available. There a few elements of this section that are either of limited practical application or unclear.

a) The idea that populations can be identified prior to the existence of emergency conditions, allowing prospective informed consent, is so rarely applicable as to be practically futile. The very nature of an emergency means that it (as an acute event) is unexpected and involves the chance interaction of an individual patient and health care team that cannot be predicted or planned for in advance.
b) This section of the guidelines recommends a maximum '*time of involvement*' after which, if the patients has not been able to consent or a legally authorised representative cannot be found, the patient is withdrawn from the study. This section further suggests that such withdrawal should not be done if it would leave the participant '*worse off*'. It is not clear what such an approach would achieve, compared to not doing this and following other guidance in the same section that participants are to be given information about the research and requested to provide consent to continue (or to opt out) if and when they recover and regain capacity. If the research is testing an intervention then, in order to have justified the inclusion of incapacitated patients, there must have been in many cases at least a potential for direct benefit – thus, it would not reasonably be the case that any participant would be withdrawn because they would be left '*worse off*'. If the reason for suggesting withdrawal of participants from research after a specific time is to mitigate risk, this doesn't seem logical because the intervention would have already been administered and thus the participant would have already been exposed to any extant risk. Withdrawing a participant after the intervention could not be seen to lessen risk, unless a specific circumstance clearly involves risk that accumulates over time. Finally, the term '*worse off*' is not very clear partly because it is unknown whether this refers to benefit or risk or both but also because it is typically very difficult to know whether withdrawing a participant suffering from a complex and

rapidly evolving condition will leave them better or worse off within a certain time frame. It is often not possible to predict this with any clinical certainty.

Waivers

Commentary at the end of Guideline 16 mentions that research ethics committees may grant a waiver of the requirement for permission from a legally authorised representative if a patient is incapacitated and cannot consent themselves. However, this only applies under conditions identical to those in which a waiver of informed consent for a patient with capacity to do so would apply under Guideline 10 (i.e. the research could not be conducted without a waiver, the research has important social value and the research constitutes minimal risk). Although this section is clear enough, it remains less clear – under the heading of emergency care research which this section deals with – whether a waiver of the requirement for informed consent for research involving incapacitated patients in emergencies exists and what the conditions for this might be.

From the various guidelines above it is evident that a waiver of the requirement for informed consent for research involving incapacitated patients in emergencies can be supported by CIOMS 2016, under specific conditions as summarised in Table 7.2.

Table 7.2: Conditions for a Waiver of Informed Consent

Guideline	Context	Conditions	Comment
10	General – does not specify a particular context but research involving deception and use of data in registries or biological specimens are emphasised in the commentary.	▪ Research cannot be conducted without the waiver. ▪ Research has important social value. ▪ Research is minimal risk.	Does not exclude emergency care research with incapacitated patients.
16	Adults incapable of giving informed consent	▪ A legally authorised representative must give permission (and assent of patient if applicable). ▪ A favourable risk: benefit ratio if direct benefit is likely, a minor	

Guideline	Context	Conditions	Comment
		increase above minimal risk if there is compelling social value (but direct benefit is unlikely) or otherwise minimal risk.	
16	Emergency care situations, especially those with time-sensitive interventions – a subset of the above.	▪ Community engagement prior to the research, with '*substantial support*' of the community. ▪ Waiver of permission by a legally authorised representative is possible under Guideline 10 conditions (above).	

From Table 7.2 it can be seen that a researcher may enrol an incapacitated adult in research without their informed consent if (i) the risk: benefit ratio is favourable (if there are direct benefits) or the research has compelling social value (in which case a minor increase above minimal risk is acceptable) or the risk is minimal (if there are no direct benefits or social value) and (ii) there is permission from a legally authorised representative. If permission from a legally authorised representative is not possible then the research may proceed only if it is of minimal risk. Furthermore, if the research occurs within the context of an emergency with a time-sensitive intervention there must be prior community engagement.

There are two main problems with the guidance on research with incapacitated adults in emergency care situations. Firstly, the applicable conditions are spread over two guidelines and are not easy to understand the way they are presented. A table summarising this information or a diagrammatic presentation would make it easier to understand and apply correctly. Secondly, there seems to be a contradiction regarding waivers of the requirement for permission of a legally authorised representative and social value of the research. On the one hand, research being of minimal risk and having important social value are both conditions for such a waiver (these conditions come from Guideline 10). However, in Guideline 16 '*compelling*' social value of research is suggested as justifying research at a minor increase above minimal risk. Thus, it seems that research associated with '*important*'

and '*compelling*' social value allows two different levels of risk to be considered at the same time. It is not clear whether a difference is intended between '*important*' and '*compelling*' as descriptors of social value, but this is not explained in either Guideline 10 or Guideline 16. Notwithstanding the ambiguity above, one thing that CIOMS 2016 as a whole does not support is research with incapacitated adults under a waiver of the requirement for informed consent without the permission of a legally authorised representative and at a level of risk beyond minimal, even in emergency care situations where legally authorised representatives are unlikely to be accessible. Several other national regulations do allow such waivers – these will be discussed below in Section 7.2.2.

With the focus in this section on fine detail, it is possible to miss the important longer-term progression across all of the guidelines presented here. That is, an evolving facilitation of research with the incapacitated and – in more recent years – acknowledgement of the unique context and challenges constituted by emergency care research. In ending this section, Table 7.3 below provides a historical summary of the key features illustrating the progress made in this area of clinical research between 1946 and 2024.

Table 7.3: Historical Guideline Progression: Research with Incapacitated Adults

Source of Guidance	Year	Key Points: Research and Incapacitated Adults
Nuremberg Code	1946	No research with incapacitated adults was permitted, as emphasised by the wording of point 1: '*The voluntary consent of the human subject is absolutely essential*'. This made emergency care research under such conditions impossible.
Declaration of Helsinki	1964	Beginning in 1964, the Declaration permitted both therapeutic and non-therapeutic research with incapacitated adults provided that the permission of a '*legal guardian*' is obtained. A favourable risk: benefit ratio was seen as required for all research. This was a significant departure from the Nuremberg Code.
	1975	In 1975, permission of a '*responsible relative*' replaced that of the legal guardian for those with '*physical or mental incapacity*'.
	2000	In 2000, more detail is added in relation to research with those physically or mentally incapable of giving consent: permission from a '*legally authorised representative*' (as opposed to a responsible relative) is required, the condition preventing informed consent

Source of Guidance	Year	Key Points: Research and Incapacitated Adults
		must be a necessary characteristic of the population, health of the group to be included must be promoted, research should be conducted with those able to consent first (if possible), participant assent should be obtained (if possible) and permission to remain in the research should be obtained as soon as possible (if possible) from the participant or a legally authorised representative.
	2008	In 2008, vulnerable populations are highlighted, and it is emphasised that research if they should only be included in research that is responsive to their needs and likely to benefit them. For the first time, the requirement of minimal risk for research with the incapacitated is made mandatory and the requirement of likely benefit is stated, unless the research promotes the health of the population studied. Also for the first time, '*unconscious*' patients are specifically mentioned as an example of those incapable of giving informed consent and allowance is made for situations where a legally authorised representative is not available and the '*research cannot be delayed*'. In such cases the research may proceed if the reasons for including such participants have been stated in a research protocol that has been approved by a research ethics committee.
	2013	In 2013, the need to respect dissent shown by incapacitated research participants was added.
	2024	Modification of Paragraph 19 on vulnerability, emphasising the balancing of considerations regarding inclusion and exclusion of vulnerable groups.
Belmont Report	1979	The Belmont Report identified the three principles of respect for persons, beneficence and justice. Respect for persons was seen as respect for and protection of autonomy and personal dignity. Importantly, respect for persons extends to those with diminished autonomy which the Report states are *'entitled to protection*' dependent on the risk of harm and likelihood of benefit. The Belmont Report also, under the principle of justice, highlights the notion of vulnerability and the role of researchers in protecting the vulnerable (the Report identified several vulnerable groups, those highly dependent on care are probably most applicable to the incapacitated). In a section dealing with application of the principles, the Report suggests the use of '*other parties*' as proxy decision-makers for those who lack the ability to comprehend

Source of Guidance	Year	Key Points: Research and Incapacitated Adults
		relevant information about research. Thus, the Belmont Report also signifies an important movement away from the absolutism of the Nuremberg Code with regard to informed consent, extends consideration of respect for persons to the incapacitated and puts forward important considerations about their protection.
CIOMS	1982	In 1982, informed consent for research participants was required '*where feasible*' and it was recognised that not all potential research participants will have the capacity to consent. Included under this broad heading are children, pregnant and nursing women, the mentally ill and prisoners, but no mention of other causes of incapacity. In the case of research with the mentally ill, perhaps the closest approximation to those lacking capacity due to emergency conditions, the consent of a legal guardian was considered mandatory. Notably, on p25, emergency treatment of children is suggested as a possible scenario for proceeding without the '*agreement*' of parents or guardians in the section on research involving children. No further detail or conditions are added to this, and no mention is made of research involving emergency treatment in any other population.
	1993	In 1993, there was greater emphasis placed on vulnerability of various groups with emphasis on their protection. Those lacking capacity for informed consent are broadly described as vulnerable and proxy consent of a '*legal guardian or other duly authorized representative*' is considered mandatory. There is no detailed description of emergency care research as a context for incapacity, but '*patients in the emergency room*' are mentioned under the section on equitable distribution of burdens and benefits of research and vulnerability. Minimal risk research is allowed with waived consent (or with modification of consent) if authorised by a research ethics committee (the example of accessing medical records is given as a form of '*minimal risk*').
	2002	In 2002, specific guidance on situations where research is planned with adults incapable of consenting – extending beyond the narrower category of those with mental illness – was described for the first time. This included more detailed guidance on considerations applicable to research in emergency situations with time-sensitive interventions. This information is placed

Source of Guidance	Year	Key Points: Research and Incapacitated Adults
		under Guideline 9 – '*Obtaining informed consent: Obligations of sponsors and investigators*'. The guidance presented here is substantially the same as that discussed above under Guideline 16 of CIOMS 2016. However, one notable difference is the subtitle of this section. In 2002, wording of the subtitle begins '*Exception to the requirement of informed consent…*'. In CIOMS 2016 this wording has been removed, perhaps so as not be confused with US Federal Regulations using the same expression (see 3.2.1 below). Another omission from 2002 is a subsection in the commentary of Guideline 6 following the section dealing with informed consent and incapacitated adults in emergency situations. This subsection deals specifically with participation of incapacitated adults with acute conditions in clinical trials and emphasises that clinical trials may sometimes include a mix of participants with and without capacity for informed consent and describes relevant considerations of this situation. Lastly, Guideline 9 in 2002 introduces the notion of a '*slight increase above minimal risk*' that carries through to CIOMS 2016 and is discussed above. However, the conditions for permitting research at such a risk level are different to what is seen in CIOMS 2016 with the role of social value not featuring,
	2016	The features of CIOMS 2016 relevant to research with incapacitated adults and research in emergency situations have been described in 7.2.1.10 above. Differences between 2002 and CIOMS 2016 are also summarised in the row above.

7.2.2. National Regulations

7.2.2.1. USA: Code of Federal Regulations: Title 21: 50.24 Exception from Informed Consent Requirements for Emergency Research

Human resuscitation research, that is research investigating various aspects of the practice of resuscitation and generally involving patients who are in cardiac arrest, has most of its historical origins in the USA. For this reason, it was the early pioneers of resuscitation research in the USA who first grappled with the ethical problems of incapacitated patients, time-sensitive interventions and a frequent lack of access to proxy decision-makers.(Biros, 2005) Current Federal Regulations governing emergency research under such conditions, now referred to as the exception from informed consent for emergency research, or Final

Rule, have a long and somewhat difficult historical background. While the main purpose of this section is to provide an overview of the regulations, their history contains many insights and lessons about the pitfalls of emergency care research conducted in a setting of inadequate regulatory oversight and guidance. For this reason, a brief background to the origins of these regulations will be given before discussing their characteristics.

The Situation in the U.S. Before 1993

In 1981 the Department of Health and Human Services (DHHS) published regulations on human participants research, and these served as a basis for a federal Policy for the Protection of Human Subjects, generally referred to as the Common Rule. The Common Rule was subsequently adopted as an ethical standard by all US government agencies involved in research funded by the federal government.(Biros *et al.*, 1998) The DHHS regulations of 1981 made an allowance for situations where research participants could not give informed consent.(Biros *et al.*, 1998; Foex, 2001) Accordingly, a waiver of informed consent could be granted by an Institutional Review Board (IRB) if (i) it did not seriously affect the rights and welfare of the patient, (ii) withholding of the waiver rendered the research impossible or impractical, (iii) '*pertinent information*' would be given to participants after their participation and (iv) the research involved no more than minimal risk to the participants.(Biros *et al.*, 1998) Similarly, the Food and Drug Administration's slightly different regulations allowed for the use of a test article or investigational product in an emergency where consent could not be given. This amounted to a once-off form of treatment in an emergency and was not intended to justify treatment in a clinical trial or ongoing research study without consent.(Biros *et al.*, 1998; Foex, 2001)

It became clear in the late 1980s and early 1990s that the DHHS regulations seemed to rule out research in an emergency setting.(Biros *et al.*, 1998; Richardson, 2005) In response to this problem, researchers and IRBs tried to find a way to make the existing requirements for a waiver of consent fit research participants in an emergency setting. Complying with three of the four requirements for the granting of a waiver of consent under the DHHS regulations was possible for many emergency medicine research studies, but the requirement of minimal risk presented a problem. Researchers argued that the everyday meaning of minimal risk had little relevance in an emergency situation. They contended that the idea of

minimal risk should be seen against the background of risks faced by the critically ill or injured patient.(Biros *et al.*, 1998; Richardson, 2005) When viewed this way the vast majority of emergency medicine research studies did indeed pose no more than '*minimal risk*' to participants. This changing of the definition of minimal risk was applied and waivers of consent were authorised by IRBs on this basis.(Biros *et al.*, 1998) Additionally, the practice of '*deferred consent*' – where researchers enrolled patients into studies without consent and then obtained consent later from either the patient or a legally authorised representative – was used in several large studies.(Abramson and Safar, 1990) Although often seen as attempts to subvert normal ethical research practices, these efforts were really attempts to balance patient protection and autonomy with scientific progress in emergency care in the face of inadequate regulations. Evidence has been presented strongly suggesting that even representatives of the Office for Protection from Research Risks (OPRR) and the FDA found these two measures acceptable, at least in the short term.(Biros *et al.*, 1998)

The US Moratorium on Emergency Care Research in 1993

In August 1993 the Director of the OPRR sent a letter to IRBs stating that, with immediate effect, all human research studies approved by them, and all National Institutes of Health-funded studies would require prospective informed consent from each patient (or a legally authorised representative) as a prerequisite for approval. The letter left no doubt that the previous strategies involving alternative definitions of minimal risk and deferred consent were no longer acceptable. Furthermore, the letter declared that all existing (previously approved) studies involving either deferred consent or the alternative minimal risk definitions should be stopped immediately. (Biros *et al.*, 1998; Biros, 2003; Richardson, 2005)

Even after this letter had been circulated, effectively halting most forms of emergency medicine research, the tension between regulatory authorities and researchers seemed to escalate. Staff of the US House Subcommittee on Regulation of Small Business and Technology published a document severely criticising existing consent-related practises in emergency care research. Two emergency care-related studies started in 1992 and 1993 (by now halted) were specifically cited as enrolling participants inappropriately, without

informed consent.(Biros *et al.*, 1998; Richardson, 2005) The emotive nature of this publication can be gauged by its title: '*Human Guinea Pigs in the Hospital Emergency Rooms: How Some Drug and Device Manufacturers Use Patients Who Can't Say No*'.(Biros *et al.*, 1998; Richardson, 2005) In this document there was allegedly free use of uncorroborated statements from participants and witnesses which created the impression that researchers had taken advantage of compromised patients, particularly those in disadvantaged communities, in pursuit of personal advancement.(Biros *et al.*, 1998; Biros, 2003; Richardson, 2005) This created a charged atmosphere in which US emergency care researchers saw their ability to scientifically improve patient care through research being threatened.

The Final Rule of 1996

The situation described above was brought to the attention of the US Society for Academic Emergency Medicine (SAEM) in 1994 and it was discussed at the Society's annual general meeting the same year. Representatives of the OPRR and the FDA attended this meeting and consensus was reached that SAEM representatives should approach the US House Subcommittee referred to above in order to put across the academic side of the debate. A Subcommittee hearing was held and was attended by senior OPRR and FDA officials who acknowledged that there were major problems with the 1981 DHHS regulations. These officials undertook to hold a public meeting to obtain input on the problem from the research community.(Biros *et al.*, 1998; Biros, 2003; Richardson, 2005)

Because of repeated delays in arranging the public meeting referred to above, the SAEM and American Heart Association (AHA) arranged a conference of emergency medicine researchers to draft a consensus statement in October 1994. This conference gave rise to the Coalition of Acute Resuscitation and Critical Care Researchers.(Biros *et al.*, 1998) After much input, review and discussion a Coalition Consensus Statement was presented to the FDA and US National Institutes of Health. This consensus statement contained the Coalition's views on the informed consent problem, related comments and a set of seven recommendations.(Biros *et al.*, 1995)

From these inputs, the FDA formulated a Proposed Rule for Waiver of Informed Consent for Emergency Research Circumstances. Known as the Final Rule, this document was published on 21 September 1995. After a 45-day public comment period, 90 comments were received. Sixteen opposed the regulation and the remainder supported it. Many of the comments of support were also requests for clarification of requirements cited in the document. After due consideration of all comments, the Final Rule went into effect in November 1996.(Biros *et al.*, 1998; Biros, 2003) The Final Rule does not allow a waiver of informed consent under any circumstances. It allows an exception from informed consent for life-threatening conditions and emergency research (research in emergency circumstances).(Biros, 2003) Hence, it is often referred to as the exception from informed consent (EFIC) regulations.

The Final Rule attempted to correct deficiencies in the 1981 DHHS regulations governing informed consent in human research when applied in emergency situations. Its creators and proponents argued that although restrictive, it at least is true to the principles embodied in the Belmont Report, particularly that of beneficence.(Richardson, 2005) Critics of the Final Rule have either seen it as too liberal in allowing exception from informed consent or too strict in not allowing meaningful scientific investigation in aspects of emergency medicine where more effective and safe forms of treatment are needed.(Richardson, 2005) The view has even been expressed that the Final Rule makes resuscitation research '*very difficult*' to carry out in the US,(Kowey and Ornato, 2000) that the Final Rule is leading to resuscitation research being conducted mainly outside the US (Cone and O'Connor, 2005) and that it is time for change.(Moler, 2004) Regardless of which of these problems is perceived as more of a threat to participant autonomy on the one hand or science on the other hand, the Final Rule resulted in a lot of important dialogue in the US between the two factions in this debate and stimulated an unprecedented degree of interest and investigation in all aspects of informed consent applicable to emergency medicine research after 1996.

The Final Rule

As mentioned above, the Final Rule was published in November 1996. The Final Rule deals only with a subset of situations specific to emergency care research, where patients are incapacitated and a proxy decision-maker is not available and cannot be accessed due to the intervention in question being time-sensitive (there are other conditions, these are

explained in greater detail below). In other situations, where patients are capable of providing informed consent, The Common Rule (45 CFR 46, criteria for IRB approval in subpart 111a) applies.

The conditions for IRB approval of research in line with The Final Rule have been summarised by McRae and Weijer (2008) and are listed below:

1. "*The human subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence is necessary to determine the safety and effectiveness of particular interventions.*
2. *Obtaining informed consent is not feasible because:*
    a. *Subjects will not be able to give informed consent because of their medical condition;*
    b. *The intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible; and*
    c. *There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.*
3. *Participation in the research holds out the prospect of direct benefit to the subjects because:*
    a. *Subjects are facing a life-threatening situation that necessitates intervention;*
    b. *Animal and preclinical studies support the potential for the intervention to provide a direct benefit to the individual subjects; and*
    c. *Risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.*
4. *The clinical investigation could not practicably be carried out without the waiver.*
5. *The protocol defines the length of the therapeutic window, and the investigator has committed to attempting to contact a legally authorized representative for each subject within that window of time and to ask for consent within that window rather than proceeding without consent.*
6. *The institutional review board has reviewed and approved an informed consent procedures and an informed consent document consistent with the Common Rule.*

7. *Additional protections will be provided, including, at least:*
    a. *Consultation with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn;*
    b. *Public disclosure of plans for the investigation and its risks and expected benefits;*
    c. *Public disclosure following completion of the clinical investigation to apprise the community and researchers of the study and its results;*
    d. *Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation; and*
    e. *If a legally authorized representative is not available, the investigator will attempt to contact another family member for permission to enroll the subject.*"

7.2.2.2. Critique of The Final Rule

Although it represented a solution to the impasse of 1993 regarding emergency care research, the Final Rule was criticised by researchers active in the field of emergency care research in the US as being too restrictive and posing a barrier to the conduct of very necessary research.(Biros, Fish and Lewis, 1999; Biros, 2003, 2007) Reasons for this view included problems with the interpretation of terminology (e.g. '*life-threatening situation*'), interpretation and implementation of requirements for community consultation and public notification and IRBs that varied in their interpretation of the Final Rule and their degree of comfort in considering applications requesting an exception from informed consent, among others. Efforts have been ongoing, including a public meeting arranged by the FDA in 2007 on the Final Rule, to clarify the Rule's details.(Biros, 2007) Additional guidance has been provided by the FDA (US Food and Drug Administration, 2013) and a consensus conference on ethical conduct of resuscitation research convened by the Society for Academic Emergency Medicine.(McGee *et al.*, 2005)

The Final Rule does add clarity to the principled position that emergency care research is necessary to establish the safety and efficacy of interventions for common and serious conditions that could lead to the reduction or morbidity and mortality for many. The idea that this public good must be of sufficient weight to set aside the otherwise ironclad requirement of individual informed consent was not new at the time of deliberation about the Final Rule. The National Commission for the Protection of Human Subjects of Biomedical

and Behavioral Research had considered this in the 1970s yet had not adequately dealt with the questions of (i) balancing research risk with individual benefit and the broader benefit of new knowledge generation and (ii) how to interpret the existing requirement of minimal risk for waivers of informed consent. While the events leading up to publication of the Final Rule were seen as an opportunity to do this, it seems that this opportunity was missed.(Karlawish, 2008) Consequently, one of the greatest criticisms of the Final Rule is its articulation of permissible risk for emergency care research.(Karlawish, 2008; McRae and Weijer, 2008) The Final Rule also requires an open, community-orientated assessment of research risk and benefit, something that was not required by any previous regulations. Here too, a lack of clarity has attracted significant criticism.(Biros, 2003, 2007; Baren and Biros, 2007) Both of these criticisms will be briefly outlined below.

The minimal risk standard has been associated with research permissible under a waiver of informed consent since the 1980s. Conceptually, this has been intended to convey the premise that it is only acceptable for incapacitated patients to be enrolled as research participants if among other safeguards they are exposed to the lowest level of risk. While the term '*minimal risk*' now has a standard definition in the Common Rule (and much the same definition in the CIOMS guidelines and Declaration of Helsinki), this definition has not always been comparatively anchored by reference to '*normal*' and '*healthy*' participants and '*daily life*'.(Department of Health and Human Services National Institutes of Health and Office for Human Research Protections, 1980) Early attempts to capture the nature of emergencies as inherently riskier episodes than '*normal*' life and to incorporate this into the definition of minimal risk ultimately did not carry through to regulations that were in operation at the time of the moratorium on emergency care research, declared in 1993.(McCarthy, 1995) However, a consensus statement from the Coalition of Acute Resuscitation and Critical Care researchers published in 1995 seemed to be once again moving in this direction. Termed '*appropriate incremental risk*' by the Coalition, this risk standard took into account the '*natural consequences*' of the relevant emergent condition and risk of the experimental intervention relative to the standard of care for the same condition.(Biros *et al.*, 1995) Perhaps unsurprisingly, something very similar to this risk standard found its way into the Final Rule as a definition of an acceptable level of risk for an exception from informed consent, the only difference being that '*natural consequences*'

became '*what is known about the medical condition of the potential class of subjects*' under consideration.

Arguments that the minimal risk standard of activities of '*daily life*' and '*healthy*' individuals do not reflect the context of emergencies seem valid because there appears to be a mismatch in comparing the risks faced by a seriously ill or injured patient to those of a healthy person when determining minimal risk. However, the incremental risk standard as currently expressed in the Final Rule, which recognises this mismatch, has been criticised for allowing riskier interventions in sicker or more severely injured patients.(McRae and Weijer, 2002; Karlawish, 2008) This has been argued to be at odds with the principle of respect for persons, and specifically the Belmont Report's directive to offer those lacking capacity additional protection.(McRae and Weijer, 2002) Finally, although not directly related to the definition or application of minimal risk directly, the Final Rule does not provide any guidance at all on the balancing of risk with the generation of new knowledge having social value as a benefit, rather than (or in conjunction with) direct participant benefit.(Karlawish, 2008)

Since its inclusion in the Final Rule in 1996, the requirement that researchers must consult '*representative communities*' prior to initiation of research requiring an exception from informed consent has been criticised. These criticisms were loudly voiced immediately after implementation of the Final Rule and relate mainly to the perceived complexity, time and cost of community consultation – mainly in the area of resuscitation research.(Kremers *et al.*, 1999; Shah and Sugarman, 2003; Salzman *et al.*, 2007) However, there are also difficulties interpreting what is required from the Final Rule's wording. First and foremost of these difficulties is understanding what constitutes '*the community*' because it appears that the emergency care context significantly complicates what is meant and understood by '*community*'.

The FDA suggests in wording of the Final Rule that a community (to be consulted) is defined by the population of interest in a particular study.(McRae and Weijer, 2008:97) However, McGee *et al*. point out that in emergency care research such populations may include subcategories that do not fit the traditional conception of a community as they may reside

far away from where a study is being conducted yet find themselves meeting the inclusion criteria.(McGee *et al.*, 2005) The example of research on victims of motor vehicle accidents, who may be passing through a geographic area and would not be considered part of the community, is relevant along with the recognition that emergency services and emergency departments serve anyone requiring their care in a geographic area, not just more enduring residents. Moreover, when community members were asked in a focus group discussion to define a '*community*' they were not able to provide a coherent definition.(Richardson *et al.*, 2005a) Among the various proposed definitions included were individuals in a neighbourhood, city or state, those with shared interests, those with shared religious beliefs or those with a communal feeling of belonging among others. No focus group participants proposed a definition of community in any way similar to that suggested by the Final Rule. Thus, what exactly constitutes the community for consultation remains unclear.(Tisherman, 2018; Largent *et al.*, 2024)

Finally, there remain just below the surface of the Final Rule unresolved tensions that cut to the deeper conceptual question about emergency care research and the ethical justifiability of proceeding without informed consent. The Rule claims to have resolved this question, however it has actually failed to offer an unequivocal position. This can be seen from the Rule's requirement that, even if an exception form informed consent is granted, researchers must still have a consent form prepared and available for the participant or a legally authorised representative in the event that it turns out to be feasible to obtain informed consent from either.(McRae and Weijer, 2008:93) While seemingly pragmatic, this weakens the argument that the balance of benefit and risk and additional protections justifies such research without consent in the first place.(Karlawish, 2008:286)

7.2.2.3. Canada: Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans

Canada's Tri-Council Policy Statement (TCPS) on Ethical Conduct for Research Involving Humans has its origins in work done by the Tri-Council Policy Working Group on Ethics, established at the behest of the Canadian Ministry of Health and Ministry of Industry and Commerce in 1994.(Onyemelukwe and Downie, 2011) The work was done by representatives of the three major federal research funding bodies in Canada – the Medical

Research Council (now called the Canadian Institutes of Health Research), the Social Sciences and Humanities Research Council of Canada and the Natural Sciences and Engineering Research Council of Canada. Initially, the aim was to develop research ethics guidelines, and this culminated in the publication of a discussion paper in 1994, a Code of Ethics in 1997 and eventually – after broad stakeholder consultation and input – the TCPS in May 1998. This has subsequently undergone major revision leading to updated versions in 2010, 2018 and the most recent version in 2022 which is referred to in the discussion below.(Onyemelukwe and Downie, 2011)

Consent for Research in Individual Medical Emergencies (Article 3.8)

Considerations relevant to emergency care research are set out in Article 3.8, referred to in the introduction to this article as an '*exception to consent*' under conditions where prospective research participants require emergency care (the term used is '*urgent medical care*') and are not able to provide informed consent. This inability is described on p52 as being due either to unconsciousness or a lack of decision-making capacity. The conditions for an exception of this nature are set out in the Article 3.8, reproduced below:(Canadian Institutes of Health Research; Natural Sciences and Engineering Research Council of Canada and Social Sciences and Humanities Research Council of Canada, 2022:53-54)

"Subject to all applicable legal and regulatory requirements, research involving medical emergencies shall be conducted only if it addresses the emergency needs of the individuals involved, and then only in accordance with criteria established in advance of such research by the REB. The REB may allow research that involves medical emergencies to be carried out without the consent of

participants, or of their authorized third party, if all of the following apply:

a. *A serious threat to the prospective participant requires immediate intervention.*
b. *Either no standard efficacious care exists, or the research offers a realistic possibility of direct benefit to the participant in comparison with standard care.*
c. *Either the risk is not greater than that involved in standard efficacious care, or it is clearly justified by the prospect for direct benefits to the participant.*
d. *The prospective participant is unconscious or lacks capacity to understand the risks, methods and purposes of the research project.*

e. Third party authorization cannot be secured in sufficient time, despite diligent and documented efforts to do so.

f. No relevant prior directive by the participant is known to exist.

When a previously incapacitated participant regains decision-making capacity, or when an authorized third party is found, consent shall be sought for continuation in the project, and for subsequent examinations or tests related to the research project."

7.2.2.4. Critique of the TCPS Article 3.8

Like the Final Rule, Article 3.8 does focus specifically on research in the emergency care context and specifically addresses situations where the intervention under investigation is time-sensitive, the prospective participant cannot consent, and a legally authorised representative is not available to act as a proxy decision-maker. It spells out the conditions for an exception to the usual requirement for informed consent, all of which must be met, concisely. The introductory paragraph just before the conditions of Article 3.8 are given contains a broad statement about the application of an exception of consent and, among other characteristics (echoed later in the article's conditions), the delay in obtaining consent from a legally authorised representative is mentioned. This delay is described as being one that '*could seriously compromise that individual's health*'.(Canadian Institutes of Health Research; Natural Sciences and Engineering Research Council of Canada and Social Sciences and Humanities Research Council of Canada, 2022:52) There seems to be an element of therapeutic misconception in this wording, as it assumes that an experimental intervention would be effective. In reality, because efficacy of an experimental intervention is yet to be established, delays in application of such an intervention may only exceed the therapeutic window and jeopardise validity of the research rather than comprise the health of participants. Some uses of terminology in wording of the article itself and its conditions is inconsistent, as discussed further below.

There is some ambiguity regarding the conditions under which an exception from consent is justified, as described in different parts of the document. The wording of Section a of Article 3.8. states that there must be '*a serious threat to the participant*' that requires '*immediate intervention*'. However, the Application section on the following page gives the purpose of Article 3.8 as the facilitation of improvements in the treatment of '*life-threatening*

conditions'. While these two expressions may sound similar, they are not necessarily the same. For example, a long bone fracture with compromised distal circulation may well be seen as a threat to the participant but may not necessarily qualify (at the time it happens) as life-threatening. Indeed, as was the case with the Final Rule, '*life-threatening*' requires more accurate definition. Unfortunately, using these expressions interchangeably does not aid in clarifying the meaning intended with regard to application of Article 3.8. In a similar vein, and also under the Application section on p54, with reference to the details of Article 3.8 the term '*research in emergency medicine*' is used which is even broader and creates even more uncertainty. Article 3.8 certainly does not seem to apply to all research in emergency medicine, rather a small subset of this where a prospective participant's condition is urgent, application of the intervention must occur within a narrow therapeutic window and a legally authorised representative is unlikely to be available.

Section c of Article 3.8 deals with risk and what is considered acceptable risk to justify an exception from consent. The expression *'risk [is] not greater than that involved in standard efficacious care*' is used to convey this. Here too there is some ambiguity, because it is not clear whether '*standard efficacious care*' refers to standard care in an emergency context for the relevant condition or whether it refers to something similar to the minimal risk standard anchored to a healthy individual and routine tests. It is likely that the latter is not what is intended, however this is not explicitly stated which leaves this section open to interpretation. If '*standard efficacious care*' does refer to standard care in an emergency context, this risk standard would be open to the same criticism as that of the Final Rule which is held to imply that sicker patients may, by application of the standard, be exposed to greater research risk.

Lastly, the final paragraphs of the Application section on p54 contain a statement about the vulnerability of prospective participants that Article 3.8 may refer to and the consequent need for special protections. A list of possible additional protections is listed, one of which is '*consultation with former and prospective participants*'. This latter statement may be a reference to community consultation, but it is hard to tell exactly what it refers to. Consequently, it is worth noting that unlike the Final Rule, Article 3.8 does not require community consultation or notification.

7.2.2.5. Australia: National Statement on Ethical Conduct in Human Research

Like the TCPS above, the Australian National Statement on Ethical Conduct in Human Research (the National Statement) was compiled by collaborative effort of the Australian National Health and Medical Research Council, the Australian Research Council and Universities Australia. The discussion below is based on the latest version, released in 2023 and taking effect on 1 January 2024, which replaces the previous 2007 version (updated in 2018).(National Health and Medical Research Council; Australian Research Council and Universities Australia, 2023) Unlike the Final Rule or the TCPS, there is no separate top-level section dealing with research in emergencies. Rather, the National Statement has a section devoted to ethical considerations specific to defined categories of participants and one of these – people highly dependent on care who may be unable to give consent (Chapter 4.4) – contains guidance on emergency care research along with research involving neonates, terminal care, intensive care and unconscious people. One other section of the National Statement is also important (and is referred to specifically) and that is the section on risk and benefit.(Chapter 2.1)

Chapter 4.4 starts with an outline of conditions making research involving individuals highly dependent on care, and particularly those who may not be able to give consent, justifiable. These include the requirement of potential for new knowledge with relevance to the particular population being studied and a favourable risk: benefit ratio if there is no capacity for consent or the latter plus a risk level which is accepted by those with capacity for consent. This is followed by a series of subsections based on three of the four principles of research ethics (justice, beneficence and respect) into which the categories above are placed and discussed. Emergency care research is discussed under the heading of '*respect*'. This short subsection states that recruitment in emergency care research must often be done rapidly and that, provided the conditions given above are met, and those of section 2.3.10 of the National Statement, a waiver of consent may be applied.

Section 2.3.10 is a subsection of Chapter 2.3 of the National Statement which deals with situations where consent may be waived – this subsection focuses specifically on waivers of consent and the conditions that justify this. It appears that the conditions in section 2.3.10

are actually intended to apply to waivers of consent for the use of personal information, because section 2.3.9 specifies this quite clearly. Nevertheless, the conditions include impracticability in obtaining consent, no existing reason to believe that participants would object to being enrolled, adequate protection of privacy and confidentiality and others related to important information being made available to participants and financial interests of participants in relation to their data. When it comes to risk and benefit in section 2.3.10, there is a clear statement about research being limited to '*low risk*' and benefits outweighing the potential harm of not seeking consent. What constitutes '*low risk*' in the National Statement is described in Chapter 1.2 as '*no risk of harm*' only risk of discomfort (examples of the latter provided include minor-side effects of medications, discomfort related to non-invasive examinations or tests, or mild anxiety from an interview).

Processes to be followed in obtaining consent amongst individuals highly dependent on care are set out in 4.4.9 – 4.4.14 of the National Statement. According to these sections, wherever possible, the legally authorised representative of an individual incapable of consenting should be obtained, Failing this, for whatever reason, an REC may approve research provided:(National Health and Medical Research Council; Australian Research Council and Universities Australia, 2023:73-74)

"(a) there is no reason to believe that, were the participant or the participant's representative to be informed of the proposal, he or she would be unwilling to consent;
(b) the risks of harm to individuals, families or groups linked to the participant, or to their financial or social interests, are minimised;
(c) the project is not controversial and does not involve significant moral or cultural sensitivities in the community;
and, where the research is interventional, only if in addition:
(d) the research supports a reasonable possibility of benefit over standard care;
(e) any risk or burden of the intervention to the participant is justified by its potential benefits to him or her; and
(f) inclusion in the research project is not contrary to the interests of the participant."

Additionally, section 4.14.14 requires that the individual concerned, if they have capacity, or a legally authorised representative must be informed as soon as practicable about research inclusion and consulted with regard to further participation. If a decision is made not to continue this must not negatively affect ongoing quality of care.

7.2.2.6. Critique of the National Statement Chapter 4.4 and Related Sections

The fact that the National Statement contains a section devoted to those highly dependent on care as a special population, including specific reference to emergency care research, is positive and recognises the special challenges presented by this research context. However, several parts of this section (and other related sections, especially related to risk and harm) are inconsistent and others lack a clear set of delimiters regarding conditions under which they should be applied. These will be discussed below.

Broadly speaking, Chapter 4.4 (dealing with those highly dependent on care as a whole) attempts to address both situations where individuals have capacity for consent and where there is a lack of capacity. While this is necessary – because the main criterion for the chapter is dependence on care rather than capacity for consent in a binary sense – it does make the chapter less coherent. The chapter would be easier to understand if it was perhaps limited to those with no or impaired capacity. Similarly, in terms of structure, the top-level organisation according to principles of research ethics seems to be rather simplistic – the subcategories included in this chapter (e.g. neonatal intensive care, emergency care) all have many considerations cutting across the full set of principles, yet most are discussed under only one or two of them. For example, emergency care research only features under the principle of 'respect'. However, this seems to have been a pattern decided on for all parts of Section 4 and not just Chapter 4.4.

Perhaps the greatest critique of the National Statement, and specifically Chapter 4.4, is about risk as this applies to emergency care research involving both those with and without capacity. The National Statement's approach does not use any descriptor of severity of clinical condition as an entry point to its section on waivers of consent. Rather, it merely delimits emergency care research as research requiring '*emergency treatment*'. Provided this (extremely broad and poorly defined) criterion can be met, a waiver of consent may be

considered by a REC. At this point, the National Statement has radically departed from both the Final Rule and the TCPS which both require the existence of a life-threatening condition (along with some other conditions) for a waiver to be considered (the Final Rule only refers to exceptions and not waivers, however with respect to an individual qualifying case these are very similar). Thus, the aim seems to have been to make a potentially very large pool of prospective participants accessible to researchers with a possible waiver of consent if a reasonably small set of other conditions are satisfied.

Whether the above very broad potential application of waivers is positive or negative is debatable. It may be argued that waivers of consent should be possible for only the smallest subset of prospective participants in emergency care research – in the other regulations above, typically those in life-threatening condition who do not have capacity for consent and where a legally authorised representative is not available within the therapeutic window. However, taking into consideration the effect that many factors associated with the emergency care context – such as anxiety or acute severe pain – may have on capacity, it could also be argued that applying the potential for a waiver of consent so broadly is quite progressive. Nevertheless, broad application would necessitate very careful consideration of the other conditions for such a waiver in order to avoid problematic situations where the autonomy of those who have capacity may be negated by a waiver. This is a complex balance to achieve, both at the level of REC approval and application in the field.

When considering these further conditions for a waiver of consent there is substantial inconsistency in Chapter 4.4, particularly with regard to acceptable risk. Section 4.4.1 (c)(i) starts out by stating that one of the conditions justifying research involving individuals highly dependent on care (of which emergency care research is a subset) is that risk is justified by potential benefit. However, for emergency care research to qualify for a waiver of consent (not necessarily implying a lack of capacity) the conditions of section 2.3.10 must apply, one of which is that the level of risk can be no greater than low risk, described as a situation where there is only a possibility of discomfort and not harm. The statements of acceptable risk in these two sections are not necessarily inconsistent, because the first one applies to the broader category of those highly dependent on care and the second one

applies to emergency care research which might be expected to be associated with a lower risk level.

The inconsistency is apparent later in section 4.4.13 which describes the process to be followed when consent cannot be obtained from either a prospective participant or their legally authorised representative in the case of interventional research. In such cases, research may proceed '*without prior consent*' provided (amongst other conditions) the risk of the intervention is justified by its potential benefits. For research to proceed '*without prior consent*' is effectively equivalent to a waiver of consent, however when a waiver is obtained (as set out in 4.4.6, as described above) the condition is that the research risk must be no greater than low risk. Thus, there exist two contradictory levels of acceptable risk for what is essentially the same set of circumstances – emergency care research without prior consent. In addition to this inconsistency, section 2.3.10 (referred to in section 4.4.6), which describes the conditions for a waiver of consent, seems to be written for a context very different to the one intended by section 4.4.6. Wording used in this section, and in section 2.3.9 which introduces it and explains its application, makes it clear that the waivers referred to here are for the use of personal information. On the whole, sections 4.4.6 and 4.4.13 seem to be in conflict with each other because in many situations they may both apply (i.e. research involving emergency treatment and consent cannot be obtained from the prospective participant or a legally authorised representative) but the relevant conditions specify different allowable level of risk.

Chapter 4.4 of the National Statement includes, as one of the subcategories of individuals highly dependent on care, '*unconscious people*'. It is unclear what the intention is in referring to this group – whether this means individuals who are unconscious in an acute care setting (e.g. after a stroke or severe traumatic brain injury) or a longer-term care setting (e.g. rehabilitation). Because emergency care research is described in the same chapter as a separate category, it may be reasonable to assume that the acute care setting of unconsciousness is not included in '*unconscious people*', however this is not clearly stated. Making this distinction is important because section 4.4.8 limits research with unconscious people to being '*minimally invasive*' – a term not defined but possibly different

from what is encompassed in low-risk research (as required for a waiver of consent in emergency care research in section 4.4.6).

As a summary of the above discussion, the different sections and risk levels are tabulated below.

Table 7.4: National Statement Chapter 4.4: Research Without Consent and Risk

Section	Scope	Risk Level
4.4.1	People highly dependent on care (broad category) – conditions for approval of research.	Risk justified by benefits. If there is capacity – risk must be acceptable to participant.
4.4.6	Emergency care research (research involves emergency treatment) – conditions for a waiver of consent.	Refers to 4.4.1 but '*low risk*' is also a condition ('low risk' is risk of discomfort only, no risk of harm).
4.4.13	People highly dependent on care – conditions for interventional research without prior consent.	Risk justified by benefits.

Finally, section 4.4.13 states as a condition of research involving individuals highly dependent on care without prior consent that the research is '*not controversial and does not involve significant moral or cultural sensitivities in the community*'. This is a very broad and ill-defined condition that would be very difficult for researchers to demonstrate that they have met. Considering the difficulties in establishing what constitutes a community in emergency care research (as discussed in Section 7.2.2 above) and the lack of certainty regarding what may qualify as a valid objection from such a community, this condition may be at best ineffectual and at worst possibly antithetical to the aim of facilitating meaningful research in this population.

7.2.2.7. European Union: Regulation 536/2014 – Articles 31 and 35

The European Union (EU) regulations governing clinical trials contain information and conditions relevant to research conducted in emergency situations where it may not be possible to obtain informed consent due to the lack of capacity of prospective participants and unavailability of a legally authorised representative within a specified therapeutic window.(European Parliament and of the Council, 2014) Two articles are of greatest relevance – Article 31 which covers clinical trial research with incapacitated individuals

(defined as those lacking capacity other than for reasons of age of legal capacity) and Article 35 which covers clinical trials in emergency situations. Clinical trials are defined in Article 2 of the regulations as clinical research where a therapeutic strategy is decided in advance and '*does not fall within normal clinical practice*' or a decision is taken to prescribe research interventions at the same time as inclusion of the participant or diagnostic or monitoring procedures in addition to normal clinical practice are used. Articles 31 and 35 will be discussed below.

Article 31 has intended application to clinical trials with incapacitated individuals but not those conducted in '*emergency situations*'. While some additional detail on what is meant by '*emergency situations*' is given in Article 35 (discussed below), there is no detailed definition provided in the regulations. Thus, in the absence of emergency conditions, clinical trial research may only include the incapacitated if informed consent is obtained from a legally authorised representative. Other conditions include that the research is directly related to a condition that the participant suffers from and cannot be meaningfully conducted with participants capable of consenting, that participants must be provided with information relevant to their ability to understand it and have the right to refuse participation if able to form such an opinion and that no incentives or inducements for the participant or legally authorised representative are permitted. In terms of benefit and risk, there must be scientific grounds for a direct benefit outweighing risk or future benefit from new knowledge with social value in the case of a '*life-threatening or debilitating condition*' and the risk level is minimal compared to standard treatment of the relevant condition.

Article 35 deals directly with clinical trials in emergency situations, and specifically those where prospective participants are incapacitated and the therapeutic window is narrow, not allowing consent to be obtained from a legally authorised representative. In addition to the broad term '*emergency situations*' this article further specifies the applicable context as one where there is '*a sudden life-threatening or other sudden serious medical condition*' and the research is limited to that conducted '*exclusively in emergency situations*'. Provided that the decision to enrol a participant is taken at the time the participant is first exposed to the intervention under investigation, the following conditions (if all are complied with) allow

inclusion in a clinical trial without consent:(European Parliament and of the Council, 2014:33-34)

"(a) due to the urgency of the situation, caused by a sudden life- threatening or other sudden serious medical condition, the subject is unable to provide prior informed consent and to receive prior information on the clinical trial;
(b) there are scientific grounds to expect that participation of the subject in the clinical trial will have the potential to produce a direct clinically relevant benefit for the subject resulting in a measurable health-related improvement alleviating the suffering and/or improving the health of the subject, or in the diagnosis of its condition;
(c) it is not possible within the therapeutic window to supply all prior information to and obtain prior informed consent from his or her legally designated representative;
(d) the investigator certifies that he or she is not aware of any objections to participate in the clinical trial previously expressed by the subject;
(e) the clinical trial relates directly to the subject's medical condition because of which it is not possible within the therapeutic window to obtain prior informed consent from the subject or from his or her legally designated representative and to supply prior information, and the clinical trial is of such a nature that it may be conducted exclusively in emergency situations;
(f) the clinical trial poses a minimal risk to, and imposes a minimal burden on, the subject in comparison with the standard treatment of the subject's condition."

Article 35 further states that consent must be obtained as soon as possible after inclusion in a clinical trial subject to the above conditions from either the participant or a legally authorised representative, depending on the capacity of the participant. Furthermore, if a legally authorised representative has given consent and the participant on whose behalf they have consented regains capacity, the participant must be approached as soon as possible for consent. If, after inclusion in a clinical trial without consent, neither the participant not their legally authorised representative (whichever applies) does not give consent, they must be informed of their right to object to their data being used in the clinical trial.

7.2.2.8. Critique of Articles 31 and 35

These two articles, parts of Regulation 536/214 direct specific attention to situations where prospective participants (i) lack capacity for consent and (ii) are in an emergency situation where application of a research intervention must be done rapidly, making consent non-feasible. As is the case with the regulations above, the fact that these two circumstances are specifically provided for in the two articles is of assistance to researchers active in this type of research. However, the Regulation as a whole is written for application to clinical trials specifically and not other types of research. Clinical trials are defined in the Regulation as a subtype of clinical study, itself described within the confines of investigation of various forms into '*medicinal products*'. A clinical trial is further defined as a clinical study that allocates participants to therapeutic groups in advance which are not considered to constitute normal practice, or one where the decision to prescribe the treatment ('*medicinal products*') is taken at the same time as the decision to include the participant, or one where diagnostic or monitoring procedures beyond normal clinical practice are used. Any one of these conditions may apply to a clinical trial. This definition seems to be much broader than, for example, the WHO definition of a clinical trial which emphasises group allocation (usually random) as a major feature.(World Health Organization, no date) Thus, despite the narrow term, it seems that the Regulation is applicable to various forms of clinical research and not only randomised trials.

Many of Article 31's conditions for research involving the incapacitated are not unusual when compared to other regulations of a similar nature above. For example, the need for consent from a legally authorised representative, the requirement that the research and the need to specifically recruit incapacitated participants is essential and that the trial relates directly to a condition relevant to the specific population of incapacitated participants are similar. However, Article 31 attempts to accommodate consideration of the wishes of incapacitated participants who are capable of forming an opinion into the decision-making process in the form of refusal or withdrawal. Identifying the participant who is capable of forming an opinion is a very difficult judgement for researchers to make without more specific guidance. In addition, as argued in Section 7.2.1.10 above, in the presence of altered physiology such as that encountered in many emergency situations it may be very difficult

to differentiate patient behaviours driven by involuntary combativeness and those driven by a rational desire to refuse interventional care.

Article 35 is derived by derogation from the first two points (a) and (b) of Article 31 (and two others), which require the consent of a legally authorised representative and information to be provided to participants in a form that is commensurate with their capacity to understand it. In other words, the application of Article 35 begins with the incapacitated prospective participant (derogation from Article 31). The presence of an urgent situation brought about by a life-threatening condition then provides the context for Article 35 allowing the inclusion of such an individual without consent. While this is clearly indicated, having the two Articles completely separate (with three other intervening Articles in the document) linked only be a statement of derogation does not make practical application to the context of incapacitation and emergency situation easy to understand.

Although the basic meaning of Article 35 is clear enough, the wording of paragraph 1 suggests that consent to participate can be given retrospectively – the section states that '*informed consent to participate in a clinical trial may be obtained, …, after the decision to include the subject in the clinical trial*.' This wording is contradicted by paragraph 2 of the same Article which states that '*informed consent in accordance with Article 29 shall be sought to continue the participation of the of the subject*'. This latter wording is more accurate and seemingly what the Article attempts to convey – that consent obtained after inclusion can only logically be for continued participation and not for anything that has occurred up until that point. At no point in regulation 636/2014 is the word '*waiver*' or '*exception*' used with reference the provisions of Article 35 in allowing inclusion of a prospective participant in a clinical trial without consent.

Article 35 assumes that in all cases either the participant will regain capacity and make a decision about continued participation, or a legally authorised representative will be available to make such a decision. It is silent regarding situations where neither are possible. This leaves open to question whether data collected in such situations may be used for research. While not explicitly stated, given the wording of Article 35 the assumption would be that in the absence of consent this could not be justified. Explicit identification of such

situations, possibly incorporating the role of benefit from new knowledge with social value as a means to informing decisions about data use in the absence of consent, would have added value to this regulation.

Lastly, the statement of acceptable risk justifying Article 35's inclusion of prospective participants without consent refers to '*minimal risk*' but invokes the comparator of risk associated with '*standard treatment of the subject's condition*'. This is similar to the risk level defined in the Final Rule ('*the risk…of standard therapy*') and the TCPS ('*not greater than that involved in standard efficacious care*').

7.2.2.9. UK: The Medicines for Human Use (Clinical Trial) Regulations and Mental Capacity Act

The Medicines for Human Use (Clinical Trial) Regulations

The UK Clinical Trails Regulations govern clinical trials on '*medicinal products*' and were amended in 2006 and 2008 to bring them in line with the EU Clinical Trails Directive.(United Kingdom, 2004) The 2006 amendments were specific to situations where a prospective participant can be entered into a clinical trial without consent – prior to this amendment such a step was not possible.(Pattinson, 2012) The relevant section of the Regulations relating to clinical trials with incapacitated adults include Schedule 1, Part 1, paragraph 1 (6)-(7) and Part 5, paragraphs 1-15. A clinical trial is defined in these Regulations as an investigation in human subjects (not including a '*non-interventional trial*') aimed at determining the effects, adverse reactions or pharmacokinetic characteristics of a '*medicinal product*'.

Part 5 of the regulations lists conditions and principles applicable to clinical trial research involving incapacitated adults in general. Most of these conditions are the same as those listed in Article 21 of the EU Clinical Trial Regulation discussed above. However, there are some differences in the conditions related to risk, when compared to the EU Regulations. The (UK) Regulations refer to an expectation that benefit will outweigh risk, which is very similar to 1(g)(i) of the EU regulations. However, the UK Regulations then add in paragraph 9 that if this is not the case there should be '*no risk at all*' for the participant. The EU Regulations describe an alternative (if direct participant benefit does not outweigh risk)

involving some benefit to the population represented by the participant ('*if the condition is life-threatening or debilitating*') and minimal risk in comparison to standard treatment of the participant's condition. The UK Regulations also add two principles in Part 5 related to risk that do not have equivalents in the EU Regulations. The first is that the clinical trial must be designed to '*minimise pain, discomfort, fear and any other foreseeable risk in relation to the diseases and the cognitive abilities of the patient*'. The second principle is that '*the risk threshold and the degree of distress have to be specially defined and constantly monitored*'.

One other condition relevant to the inclusion of incapacitated adults in clinical trials exists in the UK Regulations but not in the EU Regulations. This condition states that the clinical trial must be essential to validate other data obtained in other clinical trials where consent was obtained, or other data obtained in research using other methods.

Paragraph 1(6) of Part 1 in Schedule 1 sets out the conditions for including incapacitated adults in a clinical trial without consent when time constraints prevent the otherwise essential condition of consent from a legally authorised representative. These conditions are that (i) the prospective participant must be provided with (or about to be provided with) treatment '*as a matter of urgency*' and (ii) the intervention being investigated must also be provided as a matter of urgency and (iii) it is not practicable to obtain informed consent (as set out in Schedule 1 of the regulations). Paragraph 1(7) of the same Part specifies that if these conditions are met then paragraphs 1(1)-(5) of Schedule 1 (dealing with informed consent) will not apply provided the clinical trial has been approved by REC. What constitutes treatment or any other intervention provided '*as a matter of urgency*' is not defined in the regulations.

The Mental Capacity Act

The UK Mental Capacity Act (2005) contains, under Part 1, several sections dealing with research involving incapacitated adults. While it might seem that there is a conflict between the UK Clinical Trial Regulations and these parts of the Mental Capacity Act (MCA), S30(3) of the MCA clarifies that these sections do not apply to clinical trials but rather to what the MCA refers to as '*intrusive research*', defined in s30(2) as research that would be considered unlawful if it was conducted without the consent of a person who had capacity to consent.

The MCA therefore applies to all non-clinical trial research where participants are incapacitated. Many of the conditions for allowing research with incapacitated adults, in the absence of consent, are similar to those of the UK Clinical Trial Regulations including that:

- The research must be related to the impairing condition (the condition bringing about the impairment leading to a lack of capacity for consent).
- The research cannot be conducted with participants capable of consent.
- The research must be approved by a research ethics committee.

However, with respect to some other conditions there are differences when compared to the UK Clinical Trial Regulations. Firstly, with regard to acceptable risk both the MCA and the UK Clinical Trials Regulations require direct participant benefits to outweigh risk. If there are no direct participant benefits but potential for new knowledge relevant to the population from which the participant has been drawn, then the UK Clinical Trials Regulations allow '*no risk at all*' while under the same circumstances the MCA allows '*negligible risk*' – presumably a slightly higher level of risk. The MCA also requires under these circumstances that a researcher must ensure that nothing will interfere with the prospective participant's freedom of action, or privacy or be unduly invasive or restrictive.

Secondly, there are differences in who must be consulted and how when an incapacitated adult is to be included in research. The UK Clinical Trials Regulations require a '*legal representative*' to give consent for any incapacitated prospective participant to be included. The MCA requires researchers to identify a person who is '*engaged in the caring for' or 'interested in [the] … welfare*' of a prospective participant or, failing this, a person nominated by the researcher to consult on the prospective participant's inclusion in the research. This consultation is not referred to as the giving of consent but rather as '*advice*' on the prospective participant's likely wishes with respect to research participation.

The above conditions are related only to research where time permits consultation of the type described in the MCA. Under conditions typical of those in an emergency, the MCA sets out very similar conditions to those found in the UK Clinical Trails Regulations. The MCA uses identical wording in its description of the requirement of treatment and a research intervention that must be provided '*as a matter of urgency*'. However, in such situations the MCA specifies that the agreement of a medical practitioner not connected to the research is

required for inclusion of the prospective participant. Failing this, for reasons of urgency, the prospective participant may be included without the medical practitioner's agreement.

Finally, in s34 of the MCA provision is made for a situation where a participant who has given consent while capacitated to do so loses capacity '*to continue to do so*' before the end of the research project. This section states that, provided the '*prescribed requirements*' are in place (i.e. approval by a research ethics committee) an '*appropriate authority*' may produce regulations allowing that the research may still be carried out, but that information or material obtained from the participant must have been obtained prior to the loss of capacity. These regulations may also include provisions similar to those discussed above but for application to a participant who has become incapacitated rather than a participant who is incapacitated from the outset. There is no equivalent provision in the UK Clinical Trials Regulations.

7.2.2.10.Critique of the UK Clinical Trial Regulations and Mental Capacity Act

The UK Clinical Trials Regulations share the EU Clinical Trials Regulation's strong points and limitations as described above in Section 7.2.2.7. However, there are a few differences between the two which create some uncertainty in application. The most significant of these differences relates to the acceptable risk level in situations where direct benefits do not outweigh risk. As described above in Section 7.2.2.7, under these circumstances the EU Regulations allow research of minimal risk while the UK regulations allow only research with no risk at all. While '*no risk at all*' is a clear definition, it will unfortunately rule out any and all research, particularly when applied in an emergency care context. This level of risk is quite unique in the guidelines and regulations covered in this chapter – nowhere else is '*no risk at all*' cited as a risk level. Moreover, under similar circumstances, the MCA allows negligible risk. Thus, for the same basic situation – one where direct participant benefit does not outweigh risk – between the EU Regulations, UK Regulations and the MCA there are three different allowable levels of risk: minimal (in relation to standard care), none at all and negligible.

In addition to the above, the term used to denote application in an emergency - '*matter of urgency*' – lacks a useful and precise definition. It could be applied to a broad range of

situations and seems to be less specific than terms such as '*life-threatening*' that are used in the Canadian, Australian and European regulations (admittedly '*life-threatening*' is also open to interpretation but would seem to encompass a narrower range of emergency situations). Finally, while both the EU and UK Clinical Trial Regulations require consent for continuation to be obtained from an incapacitated participant once they regain capacity (or from a legally authorised representative if they do not) the MCA, which in all other respects attempts to stay as close as possible to the Clinical Trials Regulations with conditions regarding research with the incapacitated, does not. It is not clear why this is the case.

7.2.2.11.BRICS Countries

The BRICS countries (Brazil, Russia, India, China and South Africa) all have established and active biomedical research institutions and related industries with applicable research ethics regulations. Relevant South African research ethics-related statute and guidelines have been covered above in Chapter 6 in detail. Obtaining detailed regulatory information from the remaining BRICS countries is challenging because these are published in languages other then English. However, the US National Institute of Allergy and Infectious Diseases maintains an online database of country-specific clinical research regulatory information called ClinRegs.(National Institute of Allergy and Infectious Diseases, no date) While the research ethics regulatory information available via ClinRegs is not as detailed as the regulatory information referred to above, it does cover Brazil, India and China. Information for ClinRegs relevant to these countries and related to research ethics regulations with incapacitated participants and emergency contexts is summarised in Table 7.5 below.

Table 7.5: Summarised Research Ethics Guidelines: Brazil, China and India

Country	Incapacitated	Emergency
Brazil	Inclusion requires justification and prior approval by a REC. Prospective participants must be informed to the extent possible (depending on their capacity) and should give written consent if possible. A legally authorised representative must also '*be present*' during the consent	The consent of a legally authorised representative is required. If this is not possible, prior approval from a REC must be in place in order to include the prospective participant without consent. Consent of the participant or a legally authorised representative must

Country	Incapacitated	Emergency
	process and sign the consent form.	be obtained as soon as possible after inclusion.
China	National regulations list the incapacitated ('*mentally impaired*') as a vulnerable group, however there are no special consent procedures for their inclusion in research. The Chinese National Medical Products Association and International Council for Harmonisation's Guideline for Good Clinical Practice (ICH-GGCP) makes provision for the inclusion of incapacitated participants provided the consent of a legally authorised representative is obtained.	National regulations state that research in the context of an emergency may only be conducted with the prior approval of an REC, however no other information is given. The ICH-GCCP is cited as providing for research under emergency conditions. According to the ICH-GCCP if a legally authorised representative is not available for consent, inclusion of a participant is permissible if an effective treatment is '*lacking*' and the experimental intervention could '*save the participant's life*'. The participant or a legally authorised representative must be consulted as soon as possible after inclusion and consent obtained for continuation in the study.
India	National regulations state that research with the incapacitated should be kept to a minimum, clearly motivated and requires prior approval from a REC. Most emphasis seems to be on '*mental illness*' rather than lack of capacity for other reasons, with linkage to the Indian Mental Health Act which contains further detail. In line with the act, research involving those with a mental illness who are incapable of consent may be authorised by the relevant '*State Authority*' if set of conditions are met and a '*nominated representative*' can give consent.	ClinRegs only contains information on research in emergency conditions involving minors, not adults. There is also a reference to research in humanitarian emergencies, however humanitarian emergencies are a different context compared to acute emergencies of the type relevant to this discussion. The National Regulations do identify '*patients in emergency situations*' and those '*incapable of making a voluntary informed decision for themselves … if their autonomy is compromised temporarily or permanently*' as vulnerable groups. The Regulations require that all vulnerable groups are protected from exploitation and

Country	Incapacitated	Emergency
		that research involving the cognitively impaired should be done '*carefully*'. No further or specific details are provided that might be relevant to emergency situations, particularly those with a narrow therapeutic window when a legally authorised representative may not be available.

7.3. Conclusion

In this chapter I have critically analysed international research ethics guidelines and regulations relevant to emergency care research with the incapacitated. I have highlighted how, over several decades in varying degrees, the Declaration of Helsinki and the CIOMS guidelines have adopted a more permissive stance towards research with those incapable of giving informed consent including under emergency conditions. The regulations discussed in this chapter are all notably different to those in South Africa in the sense that they recognise emergency care research as an entity unique enough for specific consideration, they take into consideration the lack of capacity inherent in many of these instances and they also recognise and provide for some quite unique limitations of the emergency setting such as narrow therapeutic windows and the absence of proxy decision-makers.

While this chapter deals with a lot of detailed information in the various guidelines and regulations, three main themes emerge that are of relevance in this thesis. Firstly, that all the regulations in Sections 7.2.2.1 – 7.2.2.9 contain specific guidance for emergency care research with the incapacitated and not just the incapacitated in broader terms. The emergency care context is seen as unique and treated as such. Secondly, while details vary, all these regulations – along with The Declaration of Helsinki and the CIOMS 2026 guidelines – allow for informed consent to be waived or for an exception of the requirement of informed consent dependent on a set of conditions. This typically includes situations where proxy consent is not possible. Thirdly, there are generally clear statements about acceptable risk for the latter – these vary, with some guidelines and regulations using an absolute interpretation of minimal risk while others favour a more contextual risk standard. With the

exception of the 2016 CIOMS guidelines, which seem to advocate adopting the Net Risks Test in Guideline 4 (discussed in Section 7.2.1.10 of Chapter 7), none of the regulations go as far as specifying a risk assessment methodology.

These three themes will be taken up and expanded on in the next and final chapter, along with elements of the previous chapters on autonomy, emergency care research, informed consent, human dignity, vulnerability, risk and benefit in a proposed normative framework favouring waivers of informed consent for emergency care research with incapacitated adults in South Africa.

CHAPTER 8: EMERGENCY CARE RESEARCH AND INCAPACITATED ADULTS IN SOUTH AFRICA: A PROPOSED NORMATIVE FRAMEWORK

8.1. Introduction

In this final chapter I present the normative framework referred to in the study aim articulated in Section 1.5 of Chapter 1. I begin with a recap of the main motivation for doing so – deficiencies in local research ethics guidelines regarding emergency care research with incapacitated adults. Already seen as a somewhat ethically controversial and a challenging area of clinical research, I argue these deficiencies have a chilling effect on the interests of research participants, the confidence of researchers and the ability of emergency care research in general to deliver on its promise of advances in care that have the potential to positively affect many in society.

After this recap I present the normative framework in three parts. The first two of these are related to: (i) the assessment of research risk in emergency care research with the incapacitated and (ii) what I have referred to as the capacity penumbra where prospective research participants are not incapacitated but in which decision-making is complicated by factors commonly encountered in emergencies such as acute severe pain, anxiety or the effects of sedative or analgesic drugs. The third part, which is the focal point of this thesis, is a normative argument for waivers of informed consent in emergency care research with the incapacitated followed by a statement of scope and a set of conditions relevant to the proposed waiver. I end the chapter by returning to Figure 1, presented in Section 1.5 of Chapter 1, and updating it with the relevant components of the proposed framework.

8.2. Summary: Critique of South African Research Ethics Guidelines and Statute Regarding Emergency Care Research with Incapacitated Adults

Research ethics guidelines and statute in South Africa currently do not facilitate emergency care research with incapacitated adults. Both s12(2) of the Constitution and s71(1)(b) effectively render research participation without informed consent of the participant unlawful. Although regulations on research with those lacking decision-making capacity exist, they refer only to levels of risk in such research and offer little clarity regarding consent. Recognising the unjust nature of this situation, the National Health Research Ethics Council's (NHREC's) guidelines attempt to offer a framework that researchers can use in

order to include incapacitated adults in research in a way that protects their interests and is ethically justifiable. However, as described in Chapter 1 and in greater detail in Chapter 6, these guidelines currently contain contradictions and do not constitute a coherent framework. In summary (from Chapter 6), the guidelines are deficient in the following areas:

- The definition of '*emergency*' which conflates emergencies, as defined in Chapter 3, with public health emergencies and disasters.
- No clear specification that proxy consent is or is not a condition for the inclusion of incapacitated adults in research.
- Absence of any guidance for research with incapacitated adults where proxy decision-makers are not available. This would be of particular relevance in interventional emergency care research with narrow therapeutic windows. Existence of this gap in the guidelines suggests that under these circumstances inclusion of incapacitated patients is not ethically justifiable, but this is not made explicit.
- A lack of conceptual clarity regarding deferred consent both in the meaning of the term and in its lack of admissibility when incapacitation may not be transient and what other strategies may be considered in such cases. Also, the lack of any conditional statement of research risk deemed acceptable for the consideration of deferred consent as a strategy.
- Insistence that deferred consent – the way it is described in the guidelines – is not a waiver of the requirement for informed consent when it seems to be exactly that because it allows inclusion of incapacitated patients in research without their consent and because deferred '*consent*' obtained when participants regain capacity cannot retrospectively authorise this and so cannot truly be considered consent.
- A piecemeal approach where proxy consent and deferred consent are described separately as different '*formats*' of consent while minimum requirements for research with the incapacitated are described in a different section and are not connected to the latter. There is no coherence to the guidelines with respect to research involving incapacitated adults.
- A difficult to apply formulation of risk – including an absolute interpretation of minimal risk – in the description of the minimum requirements for research with the incapacitated.

These deficiencies in the NHREC's guidelines will undoubtedly create uncertainty for researchers considering emergency care research with incapacitated adults and will, for this reason, very likely discourage this type of research. Considering the legal position on informed consent and those lacking capacity, it is particularly important for research ethics guidelines to offer a clear, coherent and robust framework for researchers to operate within and one that both facilitates important research and offers protection to this vulnerable population. Examples of guidelines and regulations that go a long way to achieving this in the international arena have been discussed in detail in Chapter 7 and include those from the USA, Canada, Australia, the EU and the UK. While it is possible to critique all of these, as I have done in Chapter 7, I believe there are three broad themes that can be identified in all of them that seem to be important as part of a basic normative framework supporting emergency care research with the incapacitated.

a) Identification of emergency care research with the incapacitated as a specific subset of (i) clinical research and (ii) clinical research with the incapacitated having unique characteristics justifying equally unique research ethics considerations.
b) Explicit waiving of the requirement for informed consent with a clear description of the scope for such waivers and applicable conditions taking a) into consideration.
c) Clear statement of the risk-benefit ratio considered acceptable for the consideration of b).

The historical progression of emergency care research with the incapacitated in the USA, as outlined in Section 7.2.2.1 of Chapter 7, is a cautionary tale that should and can be avoided in South Africa. In the USA example, a lack of clear guidance for researchers over the preceding decade led to a three-year moratorium on emergency care research involving the incapacitated significantly affecting both the development of emergency care research and related interventions along with the confidence of researchers to engage in this kind of research. Thus, the crucial role of clear and unambiguous research ethics guidance is clear.

To this end, I propose a normative framework below for emergency care research. The primary focus of this framework is emergency care research with incapacitated adults.

However, the framework will also include research with those in the capacity penumbra as defined in Section 1.2.6 of Chapter 1.

8.3. A Proposed Framework: I – The Assessment of Research Risk

There is ongoing debate regarding the fundamental goal of clinical research and its ethical justification (the ethics of care vs. ethics of research as discussed in Section 5.3.1 of Chapter 5). While, as a normative argument, this remains unsettled it is self-evident in research ethics guidelines – both local and international – that the ethics of care position and its related importance of individual care and benefit as a primary goal of research is ubiquitously adopted. The assessment of research risk (and benefit), as discussed in detail in Chapter 5, is central to ethics review and approval of research by Research Ethics Committees (RECs). This analysis becomes even more crucial when the protection of participant choice is removed due to a lack of capacity for informed consent and when the research context may be one characterised by heightened risk.

Rather than adopt an agnostic approach to the assessment of research risk based on vague references to '*weighing risks and benefits*' or similar expressions, I believe that the normative framework referred to above should adopt a position on a risk assessment method that is clearly described, has a defensible normative grounding and is practically applicable. In Chapter 5 I described and critiqued five different risk assessment methods and concluded that there is no perfect method for the assessment of research risk. However, on the basis of both a sound normative footing and practical application, in Section 3.11 of Chapter 5 I argued that component analysis was the best suited for clinical interventional research including emergency care research of this nature and I propose that for application in the assessment of risk in emergency care research, particularly with the incapacitated, it should be adopted uniformly. I return to this point in Section 8.5.3.3 below when discussing the assessment of research risk in the context of a waiver of informed consent.

8.4. A Proposed Framework: II – The Capacity Penumbra and Informed Consent

The capacity penumbra, described in detail in Section 1.1.1.5 of Chapter 1 and Section 3.4.4 of Chapter 3, presents a problem for researchers and research participants. Factors that may influence capacity for informed consent in the penumbra – such as acute severe pain or

anxiety among others, all of which may be exacerbated by time pressure – represent a poorly understood and vaguely represented body of knowledge in the research ethics literature and in research ethics guidelines. As discussed in Section 3.4.1 of Chapter 3, very little is known about the effects of pain on capacity with only a single example of empirical research investigating this. Other empirical research discussed in Section 3.4 of Chapter 3 has focused on clinical conditions during which symptoms such as pain and anxiety are prevalent and has identified negative effects of these factors on capacity, although not many of these studies have been done.

Perhaps because of this lack of empirical data, research ethics guidelines are mostly silent regarding the effects of such factors on capacity. For example, the National Health Research Ethics Council (NHREC) 2024 guidelines refer only to incapacity resulting from '*a variety of causes*' taking '*various forms*' but contain no further detail about these.(Department of Health, 2024:38-39) The Council for International Organizations of Medical Sciences (CIOMS) 2016 research ethics guidelines, in Guideline 9 which deals with capacity for informed consent,(Council for International Organizations of Medical Sciences and World Health Organization, 2016:32-36) do not mention the role of penumbral factors, how they might affect capacity or how researchers should approach such contextual situations. Australia's National Statement on Ethical Conduct in Human Research does refer to '*discomfort or distress*' as factors negatively affecting capacity for informed consent however there is little detailed guidance available in this section other than a requirement for the relevant REC to ensure that researchers clearly state how capacity will be determined.(National Health and Medical Research Council; Australian Research Council and Universities Australia, 2023:75-76)

Despite lacking clarity on the penumbral factors mentioned above, research ethics guidelines do in a number of instances emphasise the importance of careful deliberation by prospective research participants prior to consent being given. This can be seen by the emphasis on prospective participants being given sufficient time for decision-making. As examples, the NHREC 2024 guidelines state that the informed consent process should '*permit sufficient time for consultation*' and that '*no person should be required to make an immediate decision*'(Department of Health, 2024:21) and the CIOMS 2016 guidelines require

researchers to ensure '*that the potential participant has been given sufficient opportunity and time to consider whether to participate*'.(Council for International Organizations of Medical Sciences (CIOMS), 2016:33) This emphasis on careful and cogent deliberation militates against the acceptance of consent obtained under conditions where factors such as those described above negatively influence thoughtful decision-making. If consent obtained under conditions of anxiety or acute severe pain does not measure up to what research ethics guidelines suggest as adequate conditions to facilitate comprehension, then how ought researchers to proceed in such situations? There are three possible approaches to this problem.

a) Waive Consent

If a determination can be made that prospective participants who find themselves in the capacity penumbra are not capable of sufficiently autonomous action, then arguably researchers should proceed as they would in the case of an incapacitated individual. If Beauchamp and Childress' (2013) principle of respect for autonomy is applied as described in Section 2.3.4 of Chapter 2 then there is no obligation to respect the autonomy of those who cannot act in a *sufficiently* autonomous manner and consequently an argument could be made that informed consent – which according to this principle is a way of respecting autonomy – could be waived. In such cases then, researchers could apply to an REC for a waiver of the requirement to obtain informed consent if certain conditions are met such as those set out in the Australian National Statement on Ethical Conduct in Human Research, (National Health and Medical Research Council; Australian Research Council and Universities Australia, 2023:72-74) for example (or others, described in Section 7.2.2 of Chapter 7).

While the argument above is a logical application of the principle of respect for autonomy and how the principle applies to the incapacitated, it depends on a binary interpretation of *sufficient* capacity. That is, an interpretation that there is a well-defined dividing line between an individual having sufficient capacity for autonomous decision-making and not having such capacity, at which point they are incapacitated. The dependence of this argument on a binary interpretation of sufficient capacity arises because waiving the usual requirement of obtaining informed consent is a binary decision – either we must insist on informed consent or forego it as a requirement. The argument further depends on an

interpretation that the presence of the penumbral factors identified above (such as acute severe pain, anxiety etc.) are sufficient to interfere with decision-making capacity to the point of crossing the line into a state of incapacity. However, this does not seem to be the interpretation of decision-making capacity that Beauchamp and Childress (2013:114-125) put forward, nor does it seem to be the approach taken by research ethics guidelines.

Beauchamp and Childress (2013:114-125) promote the idea put forward by Faden, Beauchamp and King (1986:237-241) that decision-making capacity exists on a spectrum determined primarily by degrees of two of the three conditions for autonomous action – understanding and non-control (this interpretation is described in Section 2.3.4 of Chapter 2). They argue that in practice identifying the kind of dividing line referred to above is unimportant because, based on varying degrees of participant understanding and non-control, decisions about *substantial* capacity can be made on a case-by-case basis depending on a particular objective and context. Decision-making capacity therefore exists on a context-specific spectrum and all that is required is *substantial* capacity in a particular context – similar to the idea that in other areas of decision-making in life '*full*' capacity (i.e. complete understanding) is rarely or ever achieved but meaningful decisions can still be made. Thus, in line with the principle of respect for autonomy, facilitating the decision-making of an individual who has context-specific *substantial* capacity even if this does not meet an objective context-free definition of capacity, is a way of respecting that person's autonomy as understood in the decisional and self-determinant way described in Section 2.3.4 of Chapter 2.

Research ethics guidelines seem to align with this normative definition of a context-specific capacity spectrum rather than a well-demarcated dividing line between capacity and incapacity. They further seem to support the normative position that respect for autonomy should not be seen as an idealised prescription anchored to an equally idealised definition of capacity but rather that it should be seen as a principle applied to whatever degree the context allows. For example, the NHREC 2024 guidelines state that incapacity must be determined on a '*case-by-case basis*' and that even those considered to be legally incompetent '*may retain the capacity to make decisions*'.(Department of Health, 2024:38-39) As another example, the CIOMS 2016 guidelines suggest that when prospective

participants are incapacitated '*they must be engaged in the research discussion at the level of their capacity to understand*' and given an opportunity to agree with or decline participation.(Council for International Organizations of Medical Sciences (CIOMS), 2016:62) The Declaration of Helsinki refers to this as assent and requires that it is sought wherever possible and takes into account the '*preferences and values*' of the prospective participant.(World Medical Association, 2024:5)

Thus, from the above discussion, there does not seem to be a strong case to be made for waivers of informed consent that could be applied in a coherent way to those in the capacity penumbra. A convincing counterargument to this position would require an alternative conception of capacity incorporating a clear demarcation of when an individual in the capacity penumbra is incapacitated. It would further require an argument as to why an individual capable of contributing to decisions about their research participation to some degree should be ignored and how this might align with the principle of respect for autonomy. On the first count, there is no way of clearly demarcating capacity from incapacity under penumbral conditions in such a way that could map to a binary decision to waive the requirement of informed consent (although this is entirely feasible under different conditions which are dealt with below in Section 8.5). On the second count, I believe a split counterargument could be given. Decision-making abilities of prospective participants that might be constrained under penumbral conditions should still be taken into consideration as a way of allowing them to protect their interests but, as I have argued in Section 5.2.2 of Chapter 3, there are convincing arguments that this does not necessarily entail respect for autonomy. Consequently, rather than an elaborate information-laden ritual inevitably ending in the researcher's '*lapse into hypocrisy*'(Sreenivasan, 2003:2018) the focus of decision-making under such conditions should simply be the avoidance of coercion and manipulation. I argue in Section c) below that this can likely be done in ways that do not place an unfair burden on prospective participants.

b) Use Proxy Decision-makers

Proxy decision-makers are recommended, in fact mandated in many cases, by various research ethics guidelines and regulations when prospective participants are incapacitated as described in Section 6.2.1 of Chapter 6 and Sections 7.2.1 and 7.2.2 of Chapter 7. In many

cases, proxy consent is '*packaged*' as one of the conditions of a waiver of informed consent for emergency care research with the incapacitated. For example, Paragraphs 28 and 30 of the Declaration of Helsinki make proxy consent for research with the incapacitated mandatory where consent is waived, unless a proxy is not available and other conditions for a waiver of informed consent have been met.(World Medical Association, 2024:5) This approach is also contained in the CIOMS 2026 guidelines.(Council for International Organizations of Medical Sciences (CIOMS), 2016:61) The NHREC 2024 guidelines only describe proxy consent in the broader context of research with the incapacitated but do not provide any guidance (formally) for a waiver of informed consent.(Department of Health, 2024:26-27)

While proxy consent is a common feature of research with the incapacitated, the notion of respecting the autonomy of a non-autonomous individual through the decision-making of others is complicated. Empirical data suggests several problems with the operationalisation of proxy consent not the least of which are the burden that it places on proxy decision-makers and the uncertainty regarding what frame of reference proxies should adopt – the incapacitated individual's best interests or a substituted judgement of what they would have wanted.(Torke, Alexander and Lantos, 2008; Shepherd *et al.*, 2021) I will expand on some of these problems with proxy consent in Section 8.5.3.1 below, however for now I focus on the question of what role proxy consent could play in the capacity penumbra and how this might be justified.

Clearly, in the capacity penumbra proxy consent should not fully substitute the decision-making of a prospective participant because the latter still has some degree of decision-making capacity. In addition, I have argued above that waiving the requirement of informed consent in the capacity penumbra does not seem justifiable. If this is true, then it follows that a proxy decision-maker to fully substitute decision making of the prospective participant is also not justifiable because this would be contingent on a situation where the participant does not make any decisions, in other words under the conditions of a waiver. However, there may be scope for a proxy decision-maker to play a more supporting role in this penumbral context and, in addition, to have the prospective participant retain their decision-making role in the sense that they can decide on the extent of this support. For

example, if a proxy is available under penumbral conditions the researcher could first ask the prospective participant to what extent they would like to allow the proxy to support them in deciding about participation. This support could range from none to substantially assisted, stopping short of fully substituted decision-making. Assistance by a proxy to the prospective participant could entail emotional support, simplifying information or providing another opinion about participation based on the information provided.

The approach suggested above has the advantage that it aligns with the principle of respect for autonomy by preserving the prospective participant's ability to make decisions about research participation to the extent possible in a particular context and as assessed by the participant themselves. While this approach does to a certain extent address the problem of factors in the capacity penumbra interfering with decision-making, because this is now assisted by another individual who is not susceptible to them, a proxy under these circumstances would still need to grapple with the burden of two factors which would be, in effect, '*transferred*' to them. The first is anxiety, which a proxy in such a situation would undoubtedly experience partly from the emergency care context and partly from concerns about supporting the prospective participant and expectations of contributing to them reaching the '*right*' decision. The second is the volume and complexity of information about research participation that the proxy will most likely now be in the front line of dealing with. These two factors are related, as exposure to the first would be expected to make the second more difficult to process and understand while simultaneously communicating with and supporting the prospective participant.

c) Rethink Consent

The factors described in Section 1.2.6 of Chapter 1 that characterise the capacity penumbra vary in extent from case to case, but their influence cannot be removed entirely. I have argued above that to waive the requirement for informed consent under such conditions cannot be justified, neither can fully substituting decision-making of the prospective participant with that of a proxy. While there may be a role for proxy decision-makers in supporting prospective participants as outlined above, a proxy would still be faced with the burden of fulfilling this role under difficult circumstances a significant component of which is contributed to by the volume and complexity of information typically constituting what

Miller and Wertheimer (2011:202-205) referred to in Chapter 3 as the autonomous authorisation model of informed consent. I believe that the main positive effect in facilitating informed consent in the capacity penumbra can be obtained through a fundamentally different approach to the consent process itself. This approach should move away from placing the protective burden of understanding extremely complex information and its consequences on prospective participants to the important but more feasible primary goal of protecting participants from coercion and manipulation as suggested by O'Neill (2002:73-95).

Several possible approaches to modifying the current information-laden approach to informed consent in the penumbra can be found in the literature. Although none of them are yet implementable some may, with more development and particularly more empirical study, improve the validity of consent in this neglected area:

a) Appelbaum (2014:223-225) suggests an alternative approach to informed consent that moves away from transmission of information to adopting an approach similar to that of educating students – an activity focused on understanding rather than disclosure and shallow acknowledgement. While the education analogy has several strong points, including that the volume of information typically underpinning informed consent must be reduced to the absolute minimum, it would not be feasible for the capacity penumbra where the potential '*students*' are far too distracted to be teachable in a meaningful way.

b) In the context of randomised trials, it may be possible to reduce the number of prospective participants that need to be put through the trial informed consent process by using Zelen's method sometimes also called the randomised consent design.(Zelen, 1990) In this approach instead of random participant allocation to either a standard of care or experimental intervention group followed by informed consent, participants are randomised first without consent. Those in the control (standard of care) group are not subjected to informed consent for the research while those in the experimental group are. Two advantages of this approach are that (i) the number of participants subjected to trial informed consent procedures is reduced (possibly halved if equal group

allocation is assumed) and the risk of therapeutic misconception may be similarly reduced, although other factors may predispose participants to therapeutic misconception. While this design has some important limitations and has been ethically questioned because of the deceptive use of randomisation, it also has several advantages from an informed consent perspective and may be justified in this sense for those in the capacity penumbra (together with other approaches that simplify the informed consent process).(Allmark, 1999; Simon, Shortreed and DeBar, 2021)

c) Approaches to the simplification of informed consent may vary and include simply cutting down on the volume and complexity of information presented to prospective participants as part of the process,(Appelbaum, 2014:225) utilizing verbal consent instead of written consent and basing this on shorter verbal explanations rather than requiring prospective participants to read lengthy information letters,(Noë, Vaillancourt and Zawati, 2025) and making more use of innovative technology such as electronic media or visual representations of consent information.(Lie and Witteveen, 2017; Manda-Taylor *et al.*, 2019; Gisladottir *et al.*, 2022; Schears and Bellolio, 2023) While these approaches may all hold some promise, the greatest obstacle to their use in emergency care research is the principle that consent based on reduced information is currently only seen as being justified in contexts of lower research risk. The Fair Transaction Model of informed consent described in Section 3.5.2.4 of Chapter 3 promoted this position, mirrored by the Consent Continuum of Tunzi, Satin and Day (2021). Acceptance of these approaches make it more likely that researchers will choose conventional informed consent methods with dense information in situations of greater risk, even if these will not lead to more valid consent, particularly in the capacity penumbra.

d) Finally, at a more abstract level O'Neill (2003) – whose conception of principled autonomy as a defence of a modified consent process without resorting to respect for autonomy was discussed in Section 3.5.2.3 of Chapter 3 – suggests two broad approaches. Firstly, to significantly reduce the amount of information that prospective participants need to grapple with and to reduce the number of propositions that they need to consider but at the same time provide them with easy access to extensible

> information should they want it. O'Neill sees this as the primary way of avoiding deception. Secondly, coercion can be prevented by providing prospective participants with an easy way to rescind their decision at any time. Taken together, these two features constitute what O'Neill refers to as a *veto* of participation.(O'Neill, 2003:6)

Perhaps because the autonomous authorisation model of informed consent has become so entrenched, along with the habitual transferring of more and more responsibility to prospective participants in the form of needing to understand ever more dense and complex research information, few alternatives have emerged in research ethics thus far. Normative arguments can only go so far in addressing the problem of consent in the capacity penumbra – more empirical studies are needed to clarify which of the innovative approaches above might translate into real change for those stuck in the unenviable position of having to make a difficult decision on what will in many cases be the worst day of their lives.

8.5. A Proposed Framework: III – The Incapacitated Adult in Emergency Care Research

Having proposed normative frameworks for the assessment of research risk and informed consent in the capacity penumbra, I now propose a normative framework for the focal point of this thesis – emergency care research with incapacitated adults. In Chapter 7 I described in detail and critiqued a number of international guidelines and regulations on emergency care research with incapacitated adults. The framework described below has drawn on some elements of these guidelines and regulations, however I am mindful of this possibly being interpreted as a variant of the fact/value or is/ought distinction in drawing normative conclusions from facts or, in this case, existing guidelines or regulations. Equally, as Sulmasy and Sugarman (2001:7-10) point out majority opinions, statute and expert opinion do not entail normative conclusions. While existing guidelines and regulations are informative (which was the purpose of analysing their content in Chapters 6 and 7) they only contain the conclusions of deliberative processes and typically do not illuminate the detailed legal or moral arguments and trade-offs that shaped them (one exception is the Final Rule that has a well-documented account of its development as described in Section 7.2.2.1 of Chapter 7). Consequently, I have consulted each of the guidelines and regulations from Chapter 7 is order to construct the basic elements presented below, but I have been mindful of their

limitations and transferability to a local research ethics context. In each subsection below, I provide a rationale that I believe fulfils the purpose of a normative grounding for each, drawing on analysis and arguments from previous chapters.

8.5.1. A Waiver of the Requirement for Informed Consent

The top-level component of this proposed normative framework is a waiver of the requirement for informed consent when emergency care research is conducted with incapacitated adults. A waiver means a conditional removal of the normal mandatory requirement that informed consent is obtained from every adult research participant. Emergency care research means research conducted with the aim of investigating an emergency condition as defined in Section 3.2 of Chapter 3 (p57). Incapacitated adults refers to prospective participants 18 years of age or older who lack the capacity for informed consent because of physical or physiological derangements caused by the emergency condition.

Rationale

Research in the field of emergency care is essential in order to test new interventions capable of reducing morbidity and mortality and alleviating suffering. Emergency care personnel, whether operating outside the hospital or in the Emergency Department (ED), constitute the front line of care for a large sector of the population affected by a very broad range of injuries and other conditions such as stroke and ischaemic heart disease, among others, which account for many potentially avoidable deaths and much disability annually. It is no exaggeration to state that the potential impact of improvements in emergency care interventions is very broad at population level and compelling in its importance.

The nature of these conditions on which emergency care research is focused is such that many prospective research participants are incapable of providing informed consent, a statutory requirement. Prohibiting emergency care research, with its associated potential benefits as outlined above, is morally untenable. In acknowledgement of this, the NHREC provide research ethics guidance suggesting various ways of conducting research with the incapacitated while protecting their interests and preventing exploitation of this vulnerable population. Unfortunately, as described in Section 2 above, these guidelines are deficient

and do not achieve the goal of balancing the facilitation of emergency care research with the incapacitated and adequate protection. The NHREC guidelines adopt a contradictory position claiming to prohibit waivers of informed consent in this context but actually allowing, under certain circumstances, incapacitated adults to be included in research without informed consent. I propose that a formal waiver of informed consent for emergency care research with incapacitated adults is preferable to the NHREC's current approach because it would provide the structure and clarity needed to protect both participants and researchers, the latter who are likely to be reluctant to do research in a context considered to be risky with vague and contradictory guidelines.

Apart from the argument above, I believe that a moral case can be made for such a waiver. This is grounded in the principle of respect for autonomy, as described in Section 3.4 of Chapter 2. Specifically, the argument put forward by Beauchamp and Childress (2013:108), that respect for individual autonomy is contingent upon the individual in question being able to act in a sufficiently autonomous manner along with its corollary that those in the complimentary condition of not being capable of autonomous action are not owed this respect. This argument, and the more foundational focus on respect for autonomy rather than respect for persons, has been criticised as being at odds with a deeper '*moral security of respect [for persons]*'.(Lysaught, 2004:676) However, as I have argued in Section 2.3.4.1 of Chapter 2, whether the frame of reference is respect for persons or respect for autonomy the important principle is that the incapacitated are protected at a time when they are not able to protect their own interests. These protections are grounded in the recognition of human dignity as an influence of researcher behaviour and the soft paternalism inherent in contemporary approaches to vulnerability and the role of RECs, as I have argued in Chapter 4. The conditions described in Sections 8.5.3.1 – 8.5.3.6 are a practical implementation of these protections.

8.5.2. Scope

The scope of a waiver of informed consent for emergency care research with incapacitated adults includes any clinical condition necessitating the waiver.

Rationale

In some regulations, such as the Final Rule and the EU Regulation 536/2014 as described in Sections 7.2.2.1 and 7.2.2.7 of Chapter 7, the scope of a waiver of informed consent is limited to research investigating an acutely life-threatening condition. However, the acutely life-threatening nature of any clinical condition leading to the incapacitation of a prospective participant in an emergency context is self-evident. It is difficult to argue that a line can be drawn, and to decide where that line may be, which differentiates acutely life-threatening from non-acutely life-threatening conditions in the set of those lacking capacity in emergency care research. Moreover, assuming that non-acutely life-threatening emergency conditions leading to incapacitation could be accurately defined, it seems counterintuitive to argue that scientific advances related to these conditions are not important enough to justify a waiver in order to facilitate research. The approach taken in the regulations mentioned above seems to be a trade-off of sorts, only allowing waivers when justified by the highest acuity emergency conditions. However, if the moral justification for waivers as they apply to the larger set of incapacitated adults in an emergency care context is valid, there seems to be little if any additional moral justification required for any smaller subset.

8.5.3. Conditions

The following conditions apply to any waiver of informed consent as described above.

8.5.3.1. The Role of Proxy Consent

When research is conducted under a waiver of informed consent with incapacitated adults in an emergency setting a proxy decision-maker should be consulted whenever possible and the proxy's decision should be regarded as substituting the prospective participant's decision if they had decision-making capacity. Proxy consent should be subject to the same considerations discussed in Section 4 above, with regard to simplification and avoidance or large volumes of complex information wherever possible. The need for proxy consent falls away in situations where a proxy decision-maker is not available within the timeframe required for administration or application of the intervention under study.

Rationale

Substituted judgement for those unable to make their own decisions in the form of surrogate or proxy consent is widespread in all the research ethics guidelines and regulations described in Sections 6.2.1 and 7.2.2 of Chapters 6 and 7. It is also an important legal principle, expressed in the South African health care setting in s7(1)(a)-(c) of the National Health Act (No 61 of 2003). As described in more detail in Section 6.2.2.2 of Chapter 6, the legal provision for proxy decision-makers extends only to health services and not to research highlighting the importance of guidelines in determining the role, scope and condition for proxy decision-making in research with the incapacitated. Despite its ubiquitous normative and legal role in determining how research with the incapacitated ought to proceed, empirical research has highlighted several unsettling limitations of proxy decision-making.

Shepherd *et al.* (2021) describe a disjuncture between normative accounts of proxy decision-making and the results of empirical research investigating its processes and outcomes. Normative accounts typically invoke a hierarchical approach with advance directives taking precedence, followed by substituted judgement and as a last resort the best interests standard. Both the qualitative study by Shepherd *et al.*(2021) and an earlier systematic review on proxy-decision making (Shepherd *et al.*, 2018) clearly show that the reality is more complex, with proxies seldom relying on either substituted judgement or best interests alone as framing criteria and drawing on several other normatively ill-defined factors in decision-making. Empirical research investigating the accuracy of proxy decision-making compared to patient decisions in hypothetical research scenarios shows that proxy agreement with patients on whose behalf they make decisions can vary considerably and may be less than moderate when expressed as inter-rater reliability.(Coppolino and Ackerson, 2001; Newman *et al.*, 2012; Bryant *et al.*, 2013) Other empirical research investigating proxy decision-making in treatment (rather than research) has shown that patient preferences change over time making proxy evaluation in the form of substituted judgement less likely to be accurate.(Torke, Alexander and Lantos, 2008) It is likely that a similar effect may be seen in patient decisions about research participation.

Aside from the above problems identified empirically with substituted judgement, the normative grounding of the best interests standard seems to also be unconvincing. Veatch

(1995:638-639) proposes that the best interests standard in proxy decision-making is '*terribly implausible*' because of both the complexity and subjectivity of these decisions and because of the difficulty faced by proxies in balancing many competing interests only one of which may be to decide on that fate of the patient. In fact, the best interest standard of the proxy decision-maker is a special case of a broader problem that Veatch (1995:638-641) argues is intractably difficult and should be abandoned. Berger (2011) further argues that research participation of any description can seldom be held to be in a patient's best interests due to its speculative nature. Like Veatch, he also argues that it is poorly defined in research ethics guidelines and presents an extremely challenging task for proxies. Much of Section 5.3 in Chapter 5 was spent describing the complexities of risk and benefit assessment in research by RECs. In trying to determine a patient's best interests, a proxy decision-maker would need to grapple with this question too and in the setting of emergency care research this would happen during a time of anxiety and time pressure. This plainly seems to be an unreasonable request of proxy decision-makers and an unattainable goal.

In light of the above then, why is there still such reliance on proxy decision-makers in research with the incapacitated? The argument put forward in the NHREC 2024 guidelines for proxy consent, while important because it fills a gap left by the National Health Act, seems weak. The argument is that disallowing research participation by incapacitated adults would be unconstitutional because it would be a form of unfair discrimination.(Department of Health, 2024:27) While this part of the argument may be valid, it is not an argument for the necessity of proxy consent. Alternative arguments omitting proxy consent could be made in favour of the same principle upholding the constitutional right of equality by inclusion of the incapacitated, subject to other conditions. Torke, Alexander and Lantos (2008:1515) argue that the bioethical primacy of the principle of autonomy (as discussed in Section 5 of Chapter 2) is probably the main reason for the durability of substituted judgement in the face of evidence calling its validity and reliability into question, along with a strong legal precedent. Their view is that, even in the absence of an individual's ability to act autonomously, the principle of respect for autonomy is so persistent that it is seen as transcending the boundaries of the incapacitated individual and extending vicariously to those around them. There may be other reasons, such as the belief that family members or

loved ones experience some relief from the burden of proxy decision-making by reconciling themselves to the idea that the decision is at least partially the patient's own choice or what they would have wanted – autonomy once again eclipsing the bounds of the incapacitated.

Despite the imperfect empirically demonstrated track record of proxy decision-making, its normative uncertainty and the unconvincing appeals to respect for autonomy as a motivation there is a disturbing sense of wrong at the thought of including an incapacitated adult in research in the presence of someone intimately related to them who might object to this but does not have an opportunity to intervene. Brock (1996) has suggested a set of moral grounds in favour of family members being considered as valid proxies for treatment decisions of incapacitated patients and I believe that some of these support the view above, that family members of the incapacitated have a legitimate claim to decision-making for their loved ones. These include democratic, patient-regarding and non-patient-regarding grounds. The first two grounds are centred on legal authority as a function of democratic political processes (assuming that a family member is a legal guardian) and patient self-determination based on the assumption that an incapacitated patient would have chosen a family member as a decision-maker. These grounds are not particularly compelling because in the former case it is a legal rather than a moral argument and in the latter case it attempts to invoke the autonomy of the incapacitated which, as mentioned above, seems contradictory. I find three of the non-patient-regarding grounds more compelling, perhaps because of their simplicity. These include arguments that (other than the patient) family proxies will be most affected by the decision and so have a legitimate interest in it, that distributive justice requires consideration of the family's decisions and that the family constitutes an independent moral unit with decision-making responsibility for its members.(Brock, 1996:608-615) These grounds do not directly address how such decisions should be made which is admittedly still a question without a clear answer. However, I think they do make a moral case for accepting the authority of family members as proxy decision-makers and could justify the waiver condition of taking their decisions into consideration if possible. At the very least, I believe that these grounds are compelling enough to constitute an argument against the removal of proxy decision-making as a condition for a waiver of informed consent. Naturally, this argument applies only to family members and would not

extend to some other proxy categories as set out in the NHREC 2024 guidelines.(Department of Health, 2024:26)

Because of the time-sensitive nature of many interventions in emergency care, it may be that a proxy decision-maker is not available prior to the time of intervention. In these situations, delaying an intervention until a proxy decision-maker is available may significantly affect research outcomes and bias the results. A secondary analysis of data from the CRASH-2 trial suggests that delaying the administration of tranexamic acid in cases of major trauma with uncontrolled haemorrhage by an average of 1 hour (the average time taken for proxy consent in an earlier trial was observed to have been 1.2 hours) would have reduced the number of participants benefiting from the intervention by 14% and increased the relative risk of mortality from 0.85 to 0.96.(Roberts *et al.*, 2011) In another secondary analysis of data from the ProTECT trial conducted under proxy consent, a hypothetical application of exception from informed consent reduced time to administration of progesterone in cases of moderate to severe traumatic brain injury by four hours with greater monthly recruitment rates due to lower exclusions from failure to locate proxies.(Wright *et al.*, 2008) Cardiac arrest and resuscitation research is another example of an emergency care research focus often involving highly time-sensitive interventions with known negative effects on outcomes brought about by even small delays.(Perkins *et al.*, 2020)

In sum, despite its wide application in research ethics guidelines where prospective participants are incapacitated the case to be made for validity of proxy consent does not appear to be very strong nor do its normative foundations. However, I believe that there are moral grounds to include the interests of decision-making by family members into account wherever this is possible and does not delay the administration or application of an intervention. Under a waiver of informed consent, in the absence of a proxy a defined above, the potential benefits of the intervention and scientific rigour of the study – which may affect future benefits in the form of generalisable knowledge – should take precedence.

8.5.3.2. Dissent and Refusal

When research is conducted with a waiver of informed consent with incapacitated adults in an emergency setting participant actions suggestive of dissent, objection or refusal of an intervention should be interpreted against the prevailing clinical situation and condition of the participant and do not necessarily require mandatory withdrawal of the intervention.

Rationale

Emergency care of higher acuity patients, in other words those likely to be incapacitated, is frequently characterised by factors that can result in restlessness, agitation and even combativeness as described in Section 7.2.1.11 of Chapter 7 (Assent and Dissent). Both local and international research ethics guidelines promote the idea that incapacitated participants may dissent or '*explicitly object*' to research interventions and that such dissent or objection must be respected. While the reasoning behind this position is not explicated and '*explicitly object*' is never defined, it may be based on the principle described above in Section 4 a) that capacity can be thought of as existing on a spectrum and being context-specific, requiring researchers to allow participants to make decisions as far as context-specific *substantial* capacity is judged to support them in doing so. This may only be overruled, according to the CIOMS 2016 guidelines, if the intervention in question potentially offers *significant* benefits not available outside of the research.(Council for International Organizations of Medical Sciences (CIOMS), 2016:62)

In the context of emergency care, as alluded to above, I believe that this is the incorrect interpretation. It is not plausible to interpret such responses in this kind of context as a rational or reasoned refusal of an intervention made with intent or understanding, even limited understanding. It also seems to make little sense to anchor the overruling of such responses to the benefit of an intervention because this would seem to apply to most experimental interventions meaning that in most interventional research (which would have to have at least some prosect of benefit to proceed) dissent or refusal could be overruled making the benefit condition somewhat of a *non sequitur* in such cases. The response of an incapacitated participant in dissenting to or rejecting research interventions with potential benefit in an emergency setting should be managed the same way as the same response to non-research interventions.

8.5.3.3. Risk and Benefit

In order to justify a waiver of informed consent for emergency care research with incapacitated adults, the intervention under investigation must offer a reasonable prospect of direct participant benefit and research risks should be justified by these benefits. As argued in Section 3 above, the assessment of risk and benefit in this context should use component analysis as described in Section 3.1 of Chapter 5.

Rationale

As I have argued in Section 3 above, the assessment of risk should adopt a specific methodology and the methodology that I believe to be best suited to this context is component analysis (described in Sections 3.1 and 3.2 of Chapter 5). One reason why I believe component analysis to be well-suited is that, through the construct of clinical equipoise and through its segregation of therapeutic and non-therapeutic procedures, it offers a clinically relevant and pragmatic way to balance clinical benefit and risk and avoid the problem described in Section 5.4 of Chapter 5 of an absolute interpretation of minimal risk for clinical (therapeutic) interventions in the emergency care setting. I have argued in Section 5.4.2 of Chapter 5 that an absolute interpretation of this nature regarding therapeutic procedures in the context of emergency care research is not justifiable. The application of an absolute minimal risk benchmark to non-therapeutic procedures, on the other hand, is not problematic because these types of procedures play a supporting role in answering the relevant scientific question and are not interventional.

Assessing risk (and benefit) in this kind of context but using a methodology other than component analysis will lead to intractable problems of the type already described in Section 5.3.11 of Chapter 5. The moment an absolute interpretation of minimal risk is set as the benchmark for therapeutic research procedures it becomes extremely difficult to interpret in an emergency care context as argued in Section 5.4.2 of Chapter 5. Moreover, with this benchmark, further difficulties arise in evaluating incremental concepts such as a '*minor increase above minimal risk*' (see Section 6.2.1.2 of Chapter 6 and Section 7.2.1.10 of Chapter 7). The adoption of component analysis effectively side-steps this problem and makes risk and benefit assessment less prone to differing interpretations of absolute risk levels and thus more reliable.

8.5.3.4. The Role of Deferred Consent

The terms '*deferred consent*' and '*delayed consent*' should be discontinued. Rather, in cases where an incapacitated adult has been included in emergency care research with a waiver of informed consent and the participant regains decision-making capacity at a later stage, the participant should be approached and asked for permission for continued inclusion after having been given information about the research. If the participant does not give permission for continued inclusion, permission should be requested from them to use their research data collected up until that point.

Rationale

Informing a research participant who has regained capacity that they have already been included in research and received one or more interventions without their consent cannot be considered to be any form of consent.(Beauchamp and Levine, 1980) Logically, if the inclusion was permitted under a waiver of informed consent, then consent has been waived – it cannot re-appear later in the process after exposure of a participant to an intervention which would have required consent. While it may be consistent to state that a participant could consent to ongoing inclusion from the point of regaining capacity and being informed of the research, placing the words '*deferred*' and '*consent*' in the same expression seems to only propagate the contradiction described above.

Permission for continued inclusion (as I have referred to it above) should not be seen as a surrogate for informed consent or an independent justificatory or motivating factor for a waiver of informed consent because it cannot compensate for the inability to obtain consent at the outset. It should be done, as a basic requirement, wherever participants who were included in research with a waiver of informed consent regain sufficient capacity.

8.5.3.5. The Role of Community Engagement

Community engagement can play an important role in showing respect for persons comprising a community and enriching research design and methods for emergency care research with the incapacitated proposed under a waiver of informed consent. However, several difficulties exist regarding the delimitation of and ideal approaches to engaging with

communities within the context of emergency care research. Insofar as prospective participants for this kind of research can be considered to comprise an identifiable and practically reachable community, researchers should engage with this community as early as possible in the planning phases of the research and on an ongoing basis during its execution using methods considered to be most practically effective.

Rationale

Community engagement is required in South Africa where research is conducted in '*a specific community*'.(Department of Health, 2024:15-16) While this requirement seems simple enough, it may be difficult to interpret within the context of emergency care research with the incapacitated. There are two main *loci* of participant recruitment in such research – one is in the ED, where incapacitated patients are transferred to either by members of the public or after treatment in the field by Emergency Medical Services. The other *locus* of patient recruitment is in the field itself, where incapacitated patients are first encountered, and an intervention is administered or applied before transfer to the ED.

It is unclear whether research recruiting participants in the ED would be considered to be research conducted in a specific community because patients meeting some set of clinical inclusion and exclusion criteria on arrival in the ED might come from a wide catchment area encompassing many different – and possibly quite diverse – communities, however a community might be defined. It seems more plausible perhaps that participants recruited in the field may be more community-based, however this could vary significantly depending on the scope of a particular study which may be narrow or very broad geographically. Clarity regarding whether emergency care research of this nature is considered to be taking place in a specific community is of primary importance, not only because of the mandated requirement for community engagement, but also because such a community would need to be defined in order to be engaged with. Thus, even at the outset when considering the basic question of whether community engagement is required, this question seems much more complex than those responsible for writing the guidelines appear to have anticipated.

Echoing the uncertainty hinted at above is the experience with community engagement in the USA as a requirement of the Final Rule (as described in Section 2.2.1 of Chapter 7).

Several studies have shown that there is a great deal of uncertainty mainly regarding (i) how to define a community for the purpose of engagement or consultation and (ii) how best to engage.(McGee *et al.*, 2005; Richardson *et al.*, 2005b; Baren and Biros, 2007; Salzman *et al.*, 2007; Flynn, 2008; Ragin *et al.*, 2008; Tisherman, 2018) In one instance, even a group of potential participants from a previously conducted clinical trial on public access defibrillation struggled to define how a community should be conceived, with many different views including geographical proximity, a shared sense of well-being, a sense of belonging, age, common interests or activities, religious groupings and shared experiences.(Richardson *et al.*, 2005:1086) As Largent *et al.*(2024) point out, much of the difficulty related to implementation of the Final Rule's requirements regarding community consultation is brought about by the very nature of emergencies – the fact that they are intermittent, cut across what might be considered to be community boundaries, place large sectors of diverse groupings at risk and may even involve individuals transiently passing through distant communities (e.g. victims of motor vehicle accidents in a location where a study is taking place but which is distant from their community of origin). The Final Rule itself lacks clarity about what a community is, suggesting both a geographical and a clinically defined population definition which adds to the uncertainty.(McRae and Weijer, 2008:93)

Despite these difficulties, Largent *et al.*(2024:3-5) set out a convincing argument in support of community engagement for emergency care research conducted under a waiver of consent. They argue that it may play an important role in overcoming possible negative public perceptions of emergency care research with the incapacitated under a waiver or informed consent. It may also bolster public perception that researchers are invested in the principle of respect for persons despite the research taking place under a waiver and some evidence exists to suggest that engagement may offer important opportunities for enriching research design and methods, particularly in ways related to communication and informational needs of those potentially affected. While they acknowledge the complex challenge of defining communities in emergency care research, they offer some useful suggestions in this regard one of which is that recovered patients who previously experienced a particular condition (e.g. stroke or a specific type of injury) may constitute a community whose views can provide important insights to researchers regarding methodological aspects of their research under a proposed waiver.(Largent *et al.*, 2024:5-6)

If there is one area of concordance in literature on community engagement for emergency care research with a waiver of informed consent it is that much more empirical research is needed to answer fundamental questions related to the best methods of engagement.(McGee *et al.*, 2005; Baren and Biros, 2007; Ragin *et al.*, 2008; Tisherman, 2018) Because there are still many questions in this regard, and because much of what is known empirically about community engagement in this context comes from North American data, it is difficult to make evidence-based recommendations. Researchers undertaking community engagement for emergency care research with a waiver of informed consent should be guided by an undertaking to reassure communities of their commitment to respect for persons, openness to community suggestions that may improve their research or prospective participant and community experiences of their research and practical methods tailored to the characteristics of specific communities.

8.5.3.6. Other Basic Conditions

In addition to the specific conditions discussed above, I propose several other conditions that should apply to a waiver of informed consent for emergency care research with the incapacitated. I have referred to these conditions as '*basic*' because I believe them to be fundamental and non-controversial.

a) Necessity

Obtaining a waiver of consent must be a necessity for the research to be conducted and in its absence the research would be impracticable to conduct. In addition, the research must require the study of incapacitated adults in order to answer a research question and generate new knowledge of relevance to this population. Taken together with Section 8.5.3.3 above, this condition means the intervention under investigation must potentially benefit the broader population of incapacitated adults from which the study sample is drawn.

b) Research Ethics Committee Review and Approval

Waivers of informed consent for emergency care research with incapacitated adults should only be approved after review by a REC registered with NHREC. The REC granting approval

must also be in a position to conduct or oversee monitoring of the research from inception until conclusion (see below).

c) Monitoring

Emergency care research with incapacitated adults under a waiver of informed consent must undergo active monitoring by the REC granting approval and an independent Data Monitoring and Safety Board must be established for additional oversight. Specific details regarding the implementation of monitoring is beyond the scope of this thesis, but should be in line with local guidelines.(Department of Health, 2020, 2024)

8.6. Factors and Zones Revisited: Informed Consent in Emergency Care Research

In Section 1.1.1.6 of Chapter 1 I presented a matrix-like arrangement of zones representing problem areas affected by several factors relevant to informed consent, decision-making capacity and several factors influencing these. In Section 1.3 I then identified the main problem areas in emergency care research with incapacitated adults as Zones C and D (what I referred to as the capacity penumbra) and Zones E and F (Figure 1). In summary of this final chapter, I now revisit Figure 1 and indicate for each zone the proposed approach described above, namely:

Zones C and D (the capacity penumbra): Modified consent, as described in Section 4, with assistance from a proxy decision-maker if available (Zone C).
Zones E and F: a waiver of informed consent, as described in Section 5, with proxy consent if allowed by the therapeutic window and availability of a proxy.

With Zones C-F taken together, Figure 2 is a high-level overview of the approach to informed consent in emergency care research with incapacitated adults contained within the normative framework described in this chapter, satisfying the aim of this thesis as stated in Section 1.1.7 of Chapter 1.

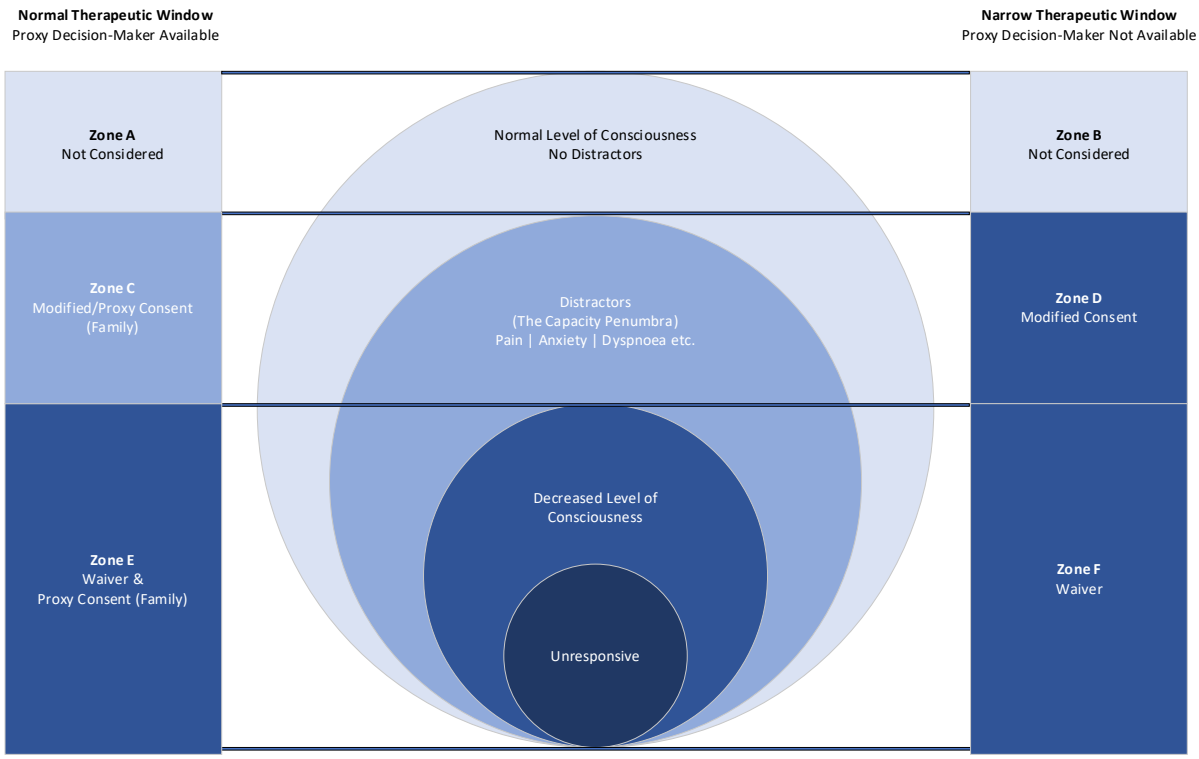

Figure 2: Factors and Zones Revisited: Informed Consent in Emergency Care Research

8.7. Conclusion

In this final chapter I have proposed a normative framework to guide emergency care research with incapacitated adults in South Africa. I have proposed this framework in response to several deficiencies in the prevailing research ethics guidelines the net effect of which is to make emergency care research of this nature, already perceived as ethically challenging, risky for both participants and researchers. This is a barrier to emergency care research fulfilling its promise of reducing morbidity and mortality across a wide range of diseases and disorder prevalent in large proportions of the population.

The normative framework I have proposed encompasses three main parts: (i) the assessment of research risk, (ii) informed consent in the capacity penumbra and (iii) emergency care research with the incapacitated. For (i) I have argued in favour of the adoption of a specific risk assessment method that is pragmatic to apply and overcomes the problem of an absolute interpretation of minimal risk for emergency care research procedures which I believe is not justified. For (ii) I have drawn attention to what I think is a neglected area of the emergency care context in research ethics guidelines and emphasised

the possible supportive role of proxy decision-makers but, more importantly, the need for a simplified approach to informed consent in such instances. I have also suggested possible approaches to this, although none of them are currently supported by enough empirical evidence to make a firm recommendation.

For (iii) I submit above that, contrary to what seems to be the current view in South Africa, a waiver of the requirement for informed consent in emergency care research provides much greater clarity, coherence and structure in terms of scope and conditions. I have proposed all of these, with a set of five conditions that I defend in detail and three others of a more fundamental nature. I end this chapter by referring back to the matrix-like schema presented as Figure 1 in Chapter 1 in updated form (Figure 2), with elements of the three parts described above showing how the normative framework addresses each specific cross-sectional requirement for informed consent affected by decision-making capacity and other factors specific to the emergency care research context.

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Appendix A: Ethics Waiver

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

Human Research Ethics Committee (Medical)

Research Office Secretariat:
Faculty of Health Sciences, Phillip Tobias Health Sciences Building, 3rd Floor, Office 301/2/4, 29 Princess of Wales Terrace, Parktown, 2193
Private Bag 3, Wits 2050
Office email: HREC-Medical.ResearchOffice@wits.ac.za
Website: www.wits.ac.za/research/about-our-research/ethics-and-research-integrity/

Ref: W-CBP-181207-2 07/12/2018

TO WHOM IT MAY CONCERN:

Waiver:	This certifies that the following research does not require clearance from the Human Research Ethics Committee (Medical)
Investigator:	Mr Christopher Stein (Student no. 324567)
Supervisor:	Prof Ames Dhai
School:	Clinical Medicine
Project title:	Acting Without Asking: An Ethico-Legal Analysis of the Problem of Emergency Care Research With Incapacitated Adults
Reason:	Study is purely normative in nature. No human participants will be involved in the study.

CB Penny

Dr CB Penny

Chairperson: Human Research Ethics Committee (Medical)

Copy – HREC (Medical) Secretariat: Zanele Ndlovu, Mapula Ramaila, Charmaine Khumalo, Josh Ndlangamandla and Rhulani Mkansi

Appendix B: Plagiarism Declaration

PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

I Christopher Owen Alexander Stein (Student number: 324567) am a student registered

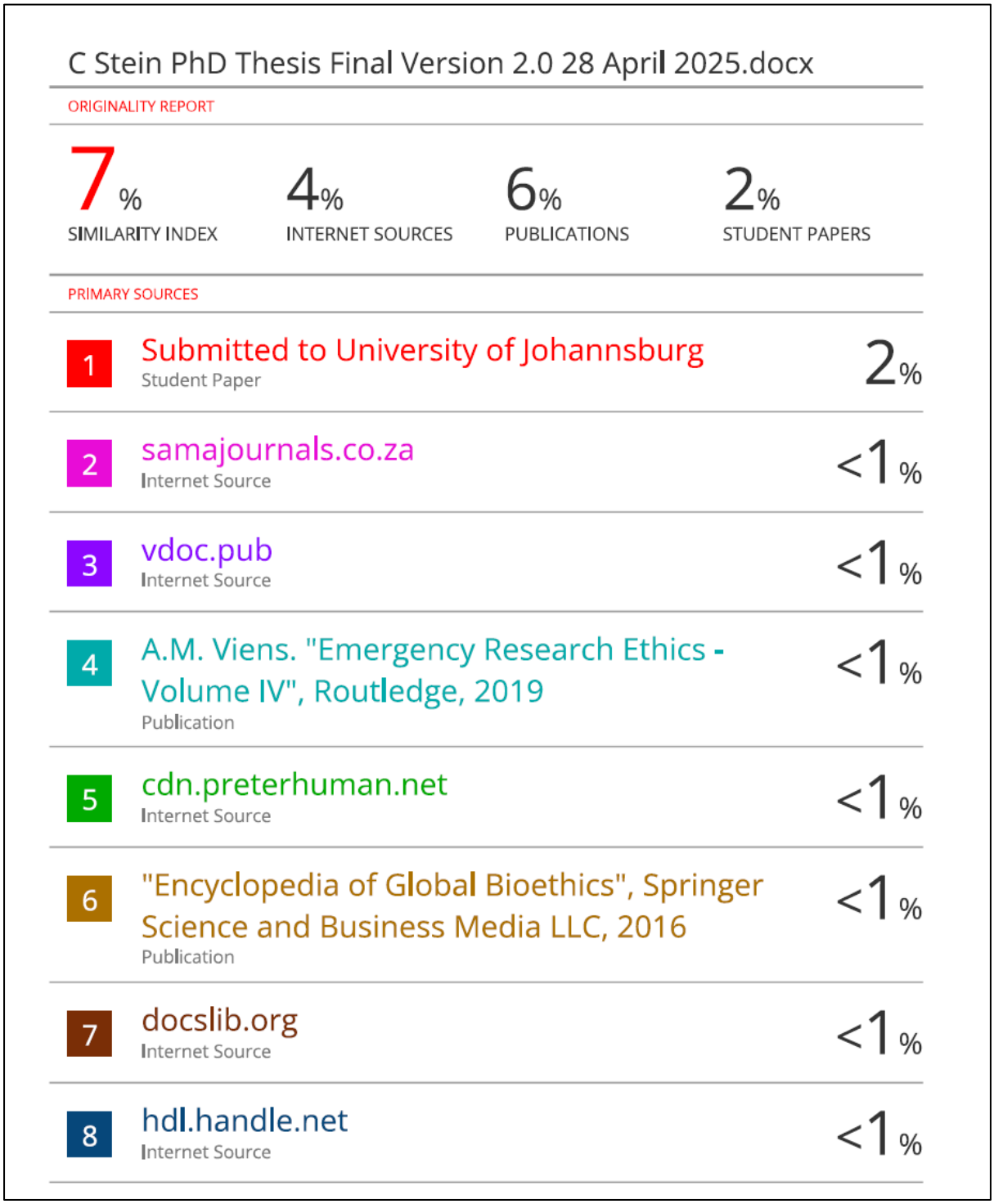
for the degree of PhD Bioethics & Health Law in the academic year 2025.

I hereby declare the following:

- I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.
- I confirm that the work submitted for assessment for the above degree is my own unaided work except where I have explicitly indicated otherwise.
- I have followed the required conventions in referencing the thoughts and ideas of others.
- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.
- I have included as an appendix a report from "Turnitin" (or other approved plagiarism detection) software indicating the level of plagiarism in my research document.

Signature:_____ Date: 7th October 2025

Appendix C: Turnitin Report



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