A COST - COMPARISON OF THE USE OF INFLUENZA VACCINE IN OLD AGE HOME RESIDENTS IN JOHANNESBURG

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master of Family Medicine

Declaration

I, Dr. Hugh Cobb, declare that this research report is my own work. It is being submitted in partial fulfilment for the degree of Master of Family Medicine in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other university.

This study has received ethical clearance from the University of the Witwatersrand's Committee for Research on Human Subjects (Medical) and the clearance certificate number is: M01-05-35

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Abstract

Residents of old age homes are at increased risk for the complications of influenza. Studies in developed countries have consistently shown that influenza vaccination of old age home residents and staff can significantly decrease morbidity and mortality rates and that influenza vaccination is one of the most cost effective interventions possible in this population. No studies have been done on the cost benefit of using influenza vaccine in old age home residents in South Africa. The aim of this study was to evaluate the costs of treating influenza and influenza-like illnesses in old age home residents, and to compare the costs in people who had received the influenza vaccine to those who had not.

The study population comprised 151 people residing in two old age homes in Johannesburg, namely Sandringham Gardens and Nazareth House. The study population was divided into two groups- those who received influenza vaccine and those who had not been vaccinated. The residents of Nazareth House who gave consent had all been vaccinated. The subjects at Sandringham Gardens were sub- divided into two groups, namely: “Residents” and “Frail care / wards” section. The general health of the “Frail care” people was poorer than that of the “residents”.

Medical records were reviewed, and details of the number of doctor consultations, medication and physiotherapy prescribed, special investigations performed and hospital referrals related to influenza and influenza-like infections were recorded. The costs were then calculated using “medical aid rates”. There were no significant differences in the treatment costs, comparing those who had been vaccinated to those who had not been vaccinated. There are a number of possible explanations for this. These include, most importantly, a low to moderate epidemic activity of influenza in the season that the study was conducted. Other explanations are low patient numbers, the use of symptoms for diagnosis and the use of over the counter therapy.

Despite the findings in the present study, the international literature supports the view that influenza vaccination is a cost-effective intervention in the older adult population, particularly those at higher risk. These findings have been implemented in the official guidelines of many countries, including the South African Adult Influenza Vaccination Guideline.

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CHAPTER 1

Introduction

1.1. Background

Influenza is an important acute respiratory infection that causes significant preventable morbidity and mortality. Influenza viruses cause disease among all age groups. Rates of infection have been reported to be highest among children, but rates of serious illness and death are highest among persons aged ≥65 years and in persons of any age who have medical conditions that place them at increased risk for complications from influenza.[1] Old age home residents and others living in closed communities are more likely to be infected, because virus transmission is facilitated by living in close proximity.[2] This is shown in table 1:

Table 1.1: Incidence of clinical influenza in various studies from the USA[2]

a) General Population

Population	Rate (%)
children	37
people aged > 20 years	4-15
elderly (aged ≥ 60 years)	10

b) Closed Environments

Population	Rate (%)
Nursing homes	43-60
US military bases	30-87
Families of infected individuals	10

Influenza can produce repeated infections throughout life, is highly communicable, and is responsible for annual community epidemics of varying severity. In addition

to its acute respiratory presentation, influenza is also a systemic infection that predisposes particularly to pulmonary and cardiac complications.[3]

1.2. Molecular Epidemiology of Influenza

"Influenza viruses are members of the Orthomyxoviridae family. The designation of influenza viruses as type A, B, or C is based on antigenic characteristics of the nucleoprotein (NP) and matrix (M) protein antigens.

Influenza A viruses are further subdivided (subtyped) on the basis of the surface haemagglutinin (H) and neuraminidase (N) antigens; individual strains are designated according to the site of origin, isolate number, year of isolation, and subtype-for example, influenza A/Sydney/5/97 (H3N2).

Influenza B and C viruses are similarly designated, but H and N antigens from these viruses do not receive subtype designations, since intratypic variations in influenza B antigens are less extensive than those in influenza A viruses and may not occur with influenza C virus."[4]

Influenza A has 2 subtypes which are important for humans: A (H3N2) and A (H1N1), of which A (H3N2) is currently associated with most deaths.[5] Influenza C virus infection does not cause classic influenza illness.[6] Wild birds are considered the natural hosts for influenza A virus and the influenza viruses that infect birds are called "avian influenza viruses". These viruses do not usually directly infect or circulate among humans, however there have been several reports of human infections with avian influenza A since 1997.[7] Avian influenza A (H5N1) is commonly known as "bird flu". Influenza A (H5N1) was first isolated from terns, which are aquatic birds, in South Africa in 1961.[8]

An influenza pandemic is caused by antigenic shift of influenza A resulting in the appearance of an influenza virus with a novel haemagglutinin (H antigen), together

with or without a novel neuraminidase (N antigen) subtype. There have been three global pandemics of influenza in the 20th century.[7] "Experts agree that another influenza pandemic is inevitable and possibly imminent."[9]

Immunity to these antigens, especially the haemagglutinin, reduces the chance of infection as well as the severity of the infection if it does occur. Both influenza A and B undergo antigenic variation. The antigenic characteristics of the currently circulating strains provide the basis for selecting the virus strains to be included in each year's vaccine,[10] and therefore monitoring the antigenicity of viruses circulating each year is necessary to ensure the best possible match between the prevailing viruses and the vaccine strains.

During interpandemic periods, outbreaks of influenza A or B infection are reported nearly every winter and vary in severity. Antigenic variability during interpandemic periods is less marked and is caused by antigenic drift. This describes a process of minor antigenic changes resulting from the accumulation of random point mutations. These mutations lead to alterations in the amino acid composition of haemagglutinin and neuraminidase. New strains of influenza A and B are constantly being generated by antigenic drift, and epidemics arise if circulating strains are significantly different from previous strains encountered by the population.[11]

1.3. Symptoms of Influenza

Influenza is characterized by sudden onset of high fever, myalgia, headache and severe malaise, non-productive cough, sore throat, and rhinitis. Most people recover within one to two weeks without requiring any medical treatment. In the very young, the elderly and people suffering from medical conditions such as lung diseases, diabetes mellitus, carcinoma and renal or cardiac failure, influenza poses a serious risk. In these people, the infection may lead to severe complications of underlying diseases, pneumonia and death.[5]

Influenza can resemble numerous other acute winter respiratory infections, all casually referred to as the “flu”. As a consequence, its potential severity often goes unappreciated by the lay population and even some doctors. This lack of awareness of its potential to produce serious disease is a barrier to implementing a successful vaccination program.[3]

1.4. Control of Influenza

The occurrence and impact of influenza can be reduced by immunoprophylaxis with inactivated (killed) virus vaccine and chemoprophylaxis with influenza specific antiviral drugs.[10]

Vaccination is the principal measure for preventing influenza and reducing the impact of epidemics. Various types of influenza vaccines have been available and used for more than 60 years. They are safe and effective in preventing both mild and severe outcomes of influenza. Constant genetic changes in influenza viruses mean that the vaccines' virus composition must be adjusted annually to include the most recent circulating influenza A (H3N2), A (H1N1) and influenza B viruses.[5]

There is evidence that widespread use of influenza vaccine can produce what has been proposed as “herd immunity” that limits the spread of viruses during influenza epidemics.[3]

Antiviral drugs for influenza are an adjunct to influenza vaccine for the treatment and prevention of influenza in certain circumstances. However, they are not a substitute for vaccination. There are four antiviral drugs that act by preventing influenza virus replication. For several years, amantadine and rimantadine (not available in South Africa) were the only antiviral drugs. However, whilst relatively inexpensive, these drugs are effective only against type A influenza, and may be

associated with severe adverse effects, mostly in elderly persons on higher doses. In addition, the virus tends to develop resistance to these drugs.

A new class of antivirals, the neuraminidase inhibitors, has been developed. Such drugs, including zanamivir (which is available in South Africa) and oseltamivir, have fewer adverse side effects and the virus less often develops resistance to these drugs. However, these drugs are expensive and currently not available for use in many countries.[5]

The major goal of the influenza vaccine policy is to protect individuals from complications of influenza. Many of the highest risk individuals are at the end of the transmission chain, and therefore immunization of these groups cannot be expected to alter the course of an epidemic.[3]

Influenza remains a major cause of morbidity and mortality, especially in the geriatric population. While influenza vaccination is a low cost and effective method of preventing illness and reducing productivity losses, its level of use in society has been too low to achieve more than a small portion of its potential benefit.[12] South Africa as a country is well behind the developed world in its usage of influenza vaccine[13] and there is in South Africa a pervasive apathy and lack of awareness of the benefits of influenza vaccination compared with developed countries.[14]

1.5. The economic cost of Influenza

Influenza epidemics and pandemics have a huge impact on both society and individual sufferers. Scarce resources and increasing medical costs highlight the need to quantify the burden of diseases such as influenza and subsequently to make accurate economic assessments of the available interventions.

Direct costs relating to hospitalisation and treatment are greater for high-risk patient groups. In general, the highest hospitalisation rates occur in infants (<1 year old) and the elderly, with pneumonia being the major reason for hospitalisation.[2]

Only a limited amount of information is available regarding the economic benefits of influenza vaccination of the elderly in South Africa. This research work will hopefully begin filling the void. The South African studies that have been undertaken were performed in an occupational and general population setting, and did not determine the cost-effectiveness of influenza vaccination in the elderly, or in those with chronic illness or other high risk groups.[15, 16]

1.6. Aim and Objectives

The aim of this study was to evaluate the costs of treating influenza and influenza-like illnesses in old age home residents in Johannesburg, comparing people who received the influenza vaccine with those who had not.

The objectives of the study were to:

a. Describe the demographic profile of the subjects in terms of age and gender
b. Record existing co-morbid medical conditions
c. Record which subjects were vaccinated for influenza
d. Record the number of influenza and influenza- like illnesses during one Winter season
e. Record direct medical resources consumed:
    - Number of doctors' visits
    - Type and number of laboratory tests and chest radiographs performed
    - Types and amount of medications consumed

- Amount of chest physiotherapy used
- Hospitalisation and length of stay

f. Calculate the costs of medical resources consumed, and comparing the costs of those who were vaccinated for influenza with those who were not.

CHAPTER 2

Literature Review

2.1. Overview

Although only a small portion of older individuals live in old age homes, much of the literature on influenza in this age group describes outbreaks in such facilities. Old age home residents are uniquely vulnerable to influenza morbidity and mortality. Although independently living older persons actually experience relatively low rates of clinical influenza compared with younger persons, this is not always true in the elderly residing in old age homes. Once introduced into a facility, usually by staff or visitors, influenza can spread rapidly because of close contact among residents and because of their overall health status. The latter element is clearly involved in the severe manifestations of influenza illness, which can cause serious medical complications or death.[17]

Concerns about the safety, efficacy and cost-effectiveness of influenza vaccination have resulted in it being underutilised. The vaccine has been shown to be highly effective in preventing infections in young healthy individuals, but because of availability and cost considerations, most international recommendations and the South African Guidelines[10] for vaccine use target the elderly and certain other groups of patients who are at increased risk of acquiring influenza and its complications.[17]

2.2. Influenza Vaccine Effectiveness in the Elderly

Vaccine effectiveness is one of the crucial parameters in the economic evaluation of influenza vaccination in the elderly. If an estimate of effectiveness comes from a controlled clinical trial, it is actually efficacy that is being measured. Most of the literature being reviewed assumes that effectiveness equals efficacy.

The effectiveness of the influenza vaccine can be assessed in terms of:

a. Prevention of influenza-like illness in healthy adults younger than 65 years or in nursing home residents older than 65 years.
b. Prevention of hospitalisation because of pneumonia.
c. Prevention of death in the elderly.
d. Reduction of other negative consequences such as work or school absenteeism, visits to doctors' offices because of upper respiratory diseases, and so on.

Studies in students, military recruits, healthy working adults, and health care workers have established a vaccine efficacy of about 70% to 90% in reducing cases of influenza and laboratory-confirmed illness, principally during years when there is a good antigenic match between vaccine and circulating strains. When there was a poor match, the vaccine efficacy was 40% to 60%.[18]

Questions have been raised about the effectiveness of influenza vaccination in the elderly, because influenza outbreaks occur even in nursing homes with high rates of vaccination, in years when there is little difference between the circulating strain and the vaccine.[18]

A cohort study of influenza vaccine effectiveness among elderly nursing home residents was published by Monto, *et al*, in 2001.[17] The study population were residents aged 65 years and older, living in participating nursing homes. The eligible population numbered 2 351 residents.

Influenza vaccine was found to be:

- 35% effective in preventing total respiratory illness (influenza- like illness and clinically diagnosed pneumonia),
- 55% effective in preventing pneumonia alone.

A clinical definition of influenza was used in this study, although additional data on influenza virus activity was generated from virus isolation from throat cultures.

Nichol *et al*[19] evaluated the benefits of influenza vaccination in the elderly, comparing these benefits in three subgroups of people, as defined by co-morbid medical conditions. In this cohort study, subjects were grouped according to risk status: high risk (having heart or lung disease), intermediate risk (having diabetes mellitus, renal disease, stroke and/or dementia, or rheumatologic disease), and low risk.

Vaccination was associated with an overall reduction of:

- 39% for pneumonia hospitalisation
- 32% decrease in hospitalisations for all respiratory conditions
- 27% decrease in hospitalisations for congestive heart failure

Vaccination was also associated with a 50% reduction in all-cause mortality.

Within the risk subgroups, vaccine effectiveness was 29%, 32%, and 49% respectively for high-, intermediate-, and low-risk senior citizens for reducing hospitalisations for pneumonia and influenza. Effectiveness was 19%, 39%, and 33% respectively, for reducing hospitalisations for all respiratory conditions and 49%, 64%, and 55% respectively for reducing deaths from all causes. This study concluded that healthy senior citizens as well as senior citizens with underlying medical conditions are at risk for the serious complications of influenza and benefit from vaccination.

Drinka *et al* [20] demonstrated that large outbreaks of influenza may occur in old age homes, despite high resident vaccination rates, even when the vaccine strain is matched to the circulating strain. In this study, 85% of residents were vaccinated. Prospective surveillance was carried out, and cultures were performed even on those with mild symptoms.

Two seasons were studied, and both outbreaks were associated with non-significant increases in pneumonia and influenza mortality. The authors comment that although vaccination may not prevent illness, it can reduce the severity of illness and complications.

To quantify the protective efficacy of influenza vaccine in elderly persons, Gross and colleagues[21] did a meta-analysis on 20 observational studies, all except one consisting of institutionalised elderly. Only cohort observational studies with mortality assessment were included in the meta-analysis. In addition, 3 case-control studies, 2 cost-effectiveness studies, and 1 randomised, double-blind, placebo-controlled trial were reviewed.

The pooled estimates of vaccine efficacy were:

- 56% for preventing respiratory illness
- 53% for preventing pneumonia,
- 50% for preventing hospitalisation
- 68% for preventing death

Vaccine efficacy in the case-control studies ranged from:

- 32% to 45% for preventing hospitalisation for pneumonia
- 31% to 65% for preventing hospital deaths from pneumonia and influenza
- 43% to 50% for preventing hospital deaths from all respiratory conditions
- 27% to 30% for preventing deaths from all causes.

The randomised, double-blind, placebo-controlled trial showed a 50% or greater reduction in influenza-related illness. The authors of this meta-analysis and review make an important comment: “Studies on vaccine efficacy, therefore, need to be evaluated with caution. Standard definitions for influenza-like illness, influenza-related pneumonia, hospitalization, and death do not exist, and this confounds comparisons among studies”.

2.3. Pharmacoeconomics of influenza vaccination in the elderly and in the general population

As expenditure in healthcare increases, interest in the efficiency of certain interventions in healthcare has also increased. South Africa is one of many countries trying to balance the seemingly unlimited demand for health care with limited resources. From a pharmacoeconomic point of view, it is relevant to consider whether influenza vaccination in the elderly is worthwhile, namely, whether the benefits of vaccination surpass the costs, or if not, whether the net investment "buys sufficient health gains".[22]

No data on the pharmacoeconomics of vaccination in the elderly in South Africa are available. A study by Schoub and Martin[15] had two arms, an occupational setting and the general population. In the occupational study (ESKOM study), it was found that the benefit: cost ratio (BCR) was 5:1. The benefits were those of reduced absenteeism, as well as reduced medical costs. This was assuming that the vaccine was 43% effective in reducing absenteeism, and that there was 100% vaccination rate. The population (medical aid study) found that in 1995, if all people with access to medical aid had been vaccinated, and assuming an 80% vaccine efficacy, the medical aid industry would have saved approximately R53 million rand. A clinical diagnosis of influenza was used, and for other respiratory illnesses, a proportion of 25% was assumed to be influenza related.

A retrospective study by Boorman,[16] of about 700 manufacturing industry employees, found that the non- vaccinated group were twice as likely to be off work for illness compatible with influenza, compared with employees who were vaccinated. This study also used clinical diagnoses, but included other respiratory infections, such as sinusitis, as surrogate markers of influenza.

A review of the available evidence related to the pharmacoeconomics of vaccination in the elderly was published by Postma and his colleagues.[22] Their

selection criteria included studies published between 1980 and 1999, and excluded cost-of-illness and burden-of-illness assessments, such as this study. Of the ten studies that were selected, 6 refer to the USA, 2 to the Netherlands, 1 to Canada and 1 to New Zealand. None of the studies took place in a developing country. The subjects were not institutionalised, except for one study. Four studies found benefit: cost ratios of 5 or more, three studies found benefit: cost ratios ranging from 1.5 to 5, and 3 studies found benefit: cost ratios ranging from 0.7 to 1.2. In all these studies, only direct costs were measured. This was justified on the basis that most elderly people would not be in paid jobs.

Nichol and Goodman[23] describe both health and economic benefits of influenza vaccination in the elderly. Data from 6 seasons was pooled. They examined claims from a managed healthcare organisation in the USA, and included both direct and indirect costs. They included indirect costs, because more than 40 % of all persons aged 65-74 years may have several types of unpaid jobs, such as housekeeping and taking care of children, which deserve monetary valuation. Two thirds of subjects were healthy, and one third was at increased risk of complications of influenza. They showed that the total net savings per person vaccinated was US $ 39.34 for healthy people and US$ 34.50 for at-risk people.

In a population-based, case-control study,[24] Mullooly *et al* showed that in an American Health Maintenance Organisation (HMO), the net savings to the HMO per vaccination was $6.11 for high-risk elderly persons and $1.10 for all elderly persons. The HMO incurred a net cost of $4.82 per vaccination for non-high-risk elderly persons. They concluded that the medical care costs saved by preventing pneumonia and influenza through vaccination of high-risk elderly persons provide compelling reasons to increase compliance with recommendations for annual influenza vaccination. Indirect benefits, such as prevention of suffering, incapacity, and lost wages, are likely to compensate for the small net cost of vaccinating non-high-risk elderly persons.

2.4. Safety and Adverse Side Effects of Influenza Vaccination

Several studies have shown that the vaccine lacks severe adverse effects.[18] In placebo-controlled studies among adults, the most frequent side effect of vaccination is soreness at the vaccination site (affecting 10%–64% of patients) that lasts <2 days.[1] These local reactions typically are mild and rarely interfere with the person's ability to conduct usual daily activities.

Fever, malaise, myalgia, and other systemic symptoms can occur after vaccination and most often affect persons who have had no prior exposure to the influenza virus antigens in the vaccine (e.g., young children).[1] These reactions begin 6–12 hours after vaccination and can persist for 1–2 days. It has also been reported that "vaccine side-effects are more common in the elderly."[14] Acute, severe, anaphylactic reactions are rare.[1]

2.5. Influenza vaccination in Developing Countries

There are significant variations in influenza vaccination rates between different countries, despite similar vaccination guidelines.[25] One important factor, is whether or not recipients have to pay for the vaccine themselves.[26]

Van Essen *et al*[25] summarised information on recommendations for influenza vaccination in 50 developed and rapidly developing countries, including South Africa in the year 2000. These countries included 2 in North America, 17 in western Europe, 11 in central Europe, 6 in the western Pacific, 7 in Latin America and 7 in the Middle East and Africa. Of the 50 countries reviewed, South Africa ranked 37 in the doses of influenza distributed per 1000 population, with a figure of 43 doses/1000 population. The highest was in Canada, where 350 doses/1000 population were distributed, and the lowest was Morocco, with 7 doses/1000 population.

2.6. Summary of literature review

Studies of influenza vaccine efficacy differ in their matching of virus strains and they are confounded by the presence of other respiratory pathogens that cause illness. Reasons for death are also difficult to determine, which further compounds the difficulty of attributing death to influenza.

Appropriate laboratory studies should be done to fully characterize the causative infectious microorganisms responsible for an epidemic of respiratory illness. Without these determinations, attribution of morbidity and mortality may be imprecise. Vaccine efficacy, therefore, may be underestimated, and case-mortality rates in vaccinated persons are overestimated.

Although it is not possible to make direct comparisons between studies of vaccine effectiveness because of the above limitations, annual influenza vaccination is effective in preventing influenza and its complications in old age home residents. There are also economic benefits associated with the routine annual vaccination of old age home residents.

CHAPTER 3

Research Methods

3.1 Methodology

3.1.1. Design

A cohort, observational study design was used

3.1.2. Sites of Study

The study was conducted at two old-age homes, Nazareth House (NH) and Sandringham Gardens (SG) in the North Eastern suburbs of Johannesburg. At the time of this study, the population of these homes were White, and can be classified as being from a middle income level. The two old age homes are similar, in that they are privately funded.

It was planned to include two old age homes in Alexandra Township, where the residents of these homes at that time were Black, but it was not possible to obtain permission for this. These two homes are subsidised financially by the state, and the residents are from a lower income group.

There are permanent full-time and part- time doctors at Sandringham Gardens and part time physiotherapists. There are no full time doctors or physiotherapists at Nazareth House.

3.1.3. Study Population

The target population was all the residents of Nazareth House and Sandringham Gardens. Consent to participate in the study was obtained for 298 of the 340 residents at Sandringham Gardens. Accurate records of who received influenza

vaccine were available for only 117 subjects at Sandringham Gardens, of whom 42 received influenza vaccine. Only these 117 people were included in the study.

Nazareth House had 84 residents, of whom 34 gave informed consent to participate in the study. The response rate was 40 %. All of these 34 people had been vaccinated. The population who gave consent were ambulatory, and independent with regard to their activities of daily living.

The population at Sandringham Gardens was subdivided into “residents” and “wards/ frail care”. The ward population were generally frailer, and the residents were ambulatory and more independent. The control group was the unvaccinated residents at both homes. Those not vaccinated were people who had contra-indications to the vaccine and those who choose not to have it.

3.1.4. Ethical Issues

The researcher was known to the Medical Director of Sandringham Gardens and to the Matron at Nazareth House. The aim of the study was explained to them at the beginning of the year (2001) and their permission to use their facilities was requested. They were given the Case Report Form (CRF), shown in appendix B, and were given an opportunity to ask questions about the study, and suggest changes to the CRF. The confidentiality of the information gathered and anonymity was explained to them, and they were provided with informed consent forms to give to the subjects. They were requested to ask their staff, who were well known to the subjects, to obtain informed consent. The informed consent form is shown in Appendix A.

No interference was made in the normal running of the old age homes. Informed consent was needed, as access to confidential medical records was required. For those people who could not give informed consent, for example, people with dementia, it was requested from those who have legal permission to give informed consent for the subjects.

Permission to conduct the study was obtained from the Committee for Research on Human Subjects, now called the Human Research Ethics Committee, of the University of the Witwatersrand.

3.1.5. Data Collection

In December 2001, all the medical records were reviewed by a final year medical student, and the information was recorded on a Case Report Form.
The data recorded consisted of:

a. Demographic information (Age, Gender)
b. Vaccination history
c. Presence or absence of co-morbid medical conditions
d. Review of symptoms related to influenza and influenza-like illness (ILI)
e. Review of interventions (including doctor consultations, hospital referral, special investigations, chest physiotherapy and nebulisations)
f. Review of medications prescribed
g. Details of hospitalisation (if relevant)

3.1.6. Methods of Data Analysis

The observations were captured onto spreadsheets (Microsoft Excel 2000, Microsoft Office), and then analysed using a statistics computer program, “GraphPad InStat” (GraphPad Software Inc, San Diego, CA, USA). Means and Standard deviations were used, and the unpaired t test was used to determine if differences were significant. Costs were calculated in Rands, using the “Medical Aid” rate. This is the amount that medical aids would pay for medical services, and is lower than the tariff recommended by the South African Medical Association. When costs differed for drugs as a result of package size (bulk packs versus standard), an average price was used.

CHAPTER 4

Results

4.1. Introduction

The sample population consisted of a total of 151 subjects.
These were made up of:

a. Sandringham Gardens “Residents”: 85
b. Sandringham Gardens “Wards”: 32
c. Nazareth House: 34

As the subjects in the wards at Sandringham Gardens had significantly higher costs, for both vaccinated and unvaccinated groups, than those ambulatory subjects (residents) at both Sandringham Gardens and Nazareth House, they were analysed as a separate group.

4.2. Number of people vaccinated

In total, 80 people (52%) were vaccinated. Less people were vaccinated in the Sandringham Gardens “Residents” category, compared to the “Wards”. This is shown in table 4.1.

Table 4.1: Number of people vaccinated

(a) SG Residents (Total 85)

Parameter	Number
Vaccinated	24 (28 %)
Not Vaccinated	61 (72%)

(b) SG Wards (Total 32)

Parameter	Number
Vaccinated	18 (56%)
Not Vaccinated	14 (44%)

(c) NH Residents (Total 34)

Parameter	Number
Vaccinated	34 (100%)

4.3. Age distribution

The mean ages of the subjects are shown in Table 4.2. As can be seen, the mean age for all groups was approximately 82 years and the average age for Sandringham Gardens Ward subjects was slightly lower.

Table 4.2: Mean ages of subjects

Parameter	Mean age (years)	SD
SG Residents: Vaccinated (n=24)	82.67	10.97
SG Residents: Not Vaccinated (n=61)	82.15	7.55
NH Residents: Vaccinated (n=34)	82.06	15.87
SG Wards : Vaccinated (n=18)	82.59	10.13
SG Wards : Not Vaccinated (n=14)	79.80	9.65

The variation in the ages between the subgroups was not significantly different.

4.4. Gender distribution

As shown in Table 4.3, 33% of the Sandringham Gardens Residents were male, but all of the Sandringham Gardens Wards subjects were male. The reason for this is that accurate vaccination records were not kept for the females in the wards at Sandringham Gardens, and these females were therefore not included in this study.

Table 4.3: Gender distribution

(a) SG Residents (n=85)

Parameter	Males (%)
Vaccinated	33
Not Vaccinated	67

(b) SG Wards (n=32)

Parameter	Males (%)
Vaccinated	32 (100)
Not Vaccinated	0

(c) NH Residents (n=34)

Parameter	Males (%)
Vaccinated	21 (61.7)

4.5. Co-morbid conditions

In the tables below, lung disease includes chronic obstructive pulmonary disease and asthma. Diabetes mellitus includes non-insulin dependent diabetes and insulin dependent diabetes. The conditions reported under the heading “other” included a large number of conditions, such as arthritis and prostatism.

Heart disease refers specifically to congestive cardiac failure. Neurological conditions include cerebrovascular accidents, Parkinson’s disease and dementia. Many subjects had more than one co-morbid condition. Information on the severity and degree of control of the co-morbid conditions was not available.

In the Sandringham Gardens “residents” subgroup of subjects who were vaccinated, 26 out of 27 people had co-morbid conditions documented in their records (96.3 %). These are shown in table 4.4 (a)

Table 4.4: Co-morbid conditions

(a) Sandringham Gardens – residents: vaccinated n=27

Condition	lung disease	diabetes mellitus	heart disease	renal disease	neurological disease	other
Number	4	3	8	0	2	26
%	14.8	11.1	29.6	0	7.4	96.3

In the Sandringham Gardens residents subgroup of subjects who were not vaccinated, all 61 people had co-morbid conditions documented in their records.

(b) Sandringham Gardens – residents: not vaccinated n=61

Condition	lung disease	diabetes mellitus	heart disease	renal disease	neurological disease	other
Number	8	2	12	1	10	61
%	13.1	3.2	19.6	1.63	16.39	100

In the Sandringham Gardens wards subgroup of subjects who were vaccinated, all 17 people had co-morbid conditions documented in their records.

(c) Sandringham Gardens – wards: vaccinated n=17

Condition	lung disease	diabetes mellitus	heart disease	renal disease	neurological disease	other
Number	4	3	2	0	0	17
%	23.5	17.6	11.7	0	0	100

In the Sandringham Gardens wards subgroup of subjects who were not vaccinated, all 15 people had co-morbid conditions documented in their records.

(d) Sandringham Gardens – wards: not vaccinated n=15

Condition	lung disease	diabetes mellitus	heart disease	renal disease	neurological disease	other
Number	4	1	42	2	8	15
%	26.6	6.6	26.6	13.3	53.3	100

In the Nazareth House subgroup of subjects, all of whom were vaccinated, 14 out of 34 people had co-morbid conditions documented in their records.

(e) Nazareth House: vaccinated n= 34

Condition	lung disease	diabetes mellitus	heart disease	renal disease	neurological disease	other
Number	4	2	4	0	2	34
%	11.8	5.9	11.8	0	5.9	100

4.6. Symptoms

On the case report form (appendix B), 18 different symptoms related to influenza and influenza-like conditions were listed. Some of the symptoms recorded were specific, such as presence of a productive cough or sore throat, while others were less specific, such as fever or myalgia or a general deterioration in condition. At Nazareth House, a diagnosis was recorded with the monthly symptom review, but this was not done at Sandringham Gardens. At Sandringham Gardens, information on the diagnosis was available from the record of medications, where the indication for the medication was recorded.

At Nazareth House, the following diagnoses were made:

a. Influenza - 8 episodes
b. Bronchitis - 5 episodes
c. Cold - 1 episode
d. Lower respiratory tract infection - 1 episode
e. Upper respiratory tract infection - 1 episode

Some subjects had more than one episode of influenza or influenza like illness.
Of all the subjects, one resident at Sandringham Gardens, who was not vaccinated, was admitted to hospital. No details regarding the duration of hospitalisation or treatment were available.

The numbers of subjects having symptoms are shown in table 4.5. The Sandringham Gardens Wards group who were not vaccinated had lowest percentage of recorded symptoms, although there were only 7 subjects in this group.

Table 4.5: Number of subjects having symptoms

Group	Number	Percentage
SG Residents: vaccinated (24)	15	62.5 %
SG Residents: not vaccinated (61)	43	70.5 %
SG Wards: vaccinated (18)	12	66.7 %
SG Wards: not vaccinated (14)	7	50.0 %
NH: vaccinated (34)	16	47.1 %

There was no significant difference between the number of Sandringham Gardens Residents in the vaccinated group who had symptoms, compared to the non-vaccinated group. The two-tailed p value was 0.4821

There was no significant difference between the number of Sandringham Gardens Ward subjects in the vaccinated group who had symptoms, compared to the non-vaccinated group. The two-tailed p value was 0.3570

4.7. Cost of interventions

The following interventions were recorded, and the costs thereof calculated, in Rands:

a. Doctors' visits
b. Radiographs
c. Chest physiotherapy
d. Blood tests
e. Drugs

Additional costs, in the form of increased nursing care needed, were not included.

The costs were calculated using the "medical aid" for the year 2001. This is the fee that the Representative Association of Medical Aids (RAMS) pays a doctor for a consultation. The "private" rate is determined by the South African Medical Association, and is higher than the RAMS fee. The cost for a doctors' visit was that of a consultation at a doctors offices, rather than for a house-call, because Sandringham Gardens has it's own doctors, and at Nazareth House, it was not specified whether the doctor visited the site, or whether the patient went to the consulting rooms.

The costs used were:

1. Doctors' visit: R80.10
2. Physiotherapy (Physio), per session: R115.00 (assumed to be 7 sessions in 5 days)
3. Radiographs (CXR): R128.90

d. Blood tests (Lab)

   i. Full Blood Count (FBC) : R58.10
   ii. Erythrocyte Sedimentation Rate (ESR): R14.00
   iii. Urea and Electrolytes (U&E): R 90.70

e. Drug costs. Calculated individually.

The mean costs of medical intervention in the five subgroups are shown in table 4.6**.** The costs were calculated as mean for the entire subgroup. For example, in the group of Sandringham Gardens Residents who were vaccinated, 15 out of 24 subjects accounted for 22 doctors visits. The mean cost of doctors' visits for the 15 subjects was R117.48, and the mean cost calculated for the 24 subjects was R70.01.

As shown in table 4.6, in all groups except Nazareth House subjects, the single most costly intervention was for drugs.

Table 4.6: Cost of Interventions

Group	Doctor	CXR	Physio	Lab	Drugs	**Total**
S G Residents vaccinated (24)	R70.01	R10.78	R33.54	R6.20	R204.99	**R328.16**
S G Residents not vaccinated (61)	R65.66	R27.47	R0.00	R7.85	R228.99	**R319.75**
SG–Wards: vaccinated (18)	R66.75	R57.29	R0.00	R13.26	R732.06	**R869.36**
SG–Wards not vaccinated (14)	R97.26	R73.66	R115.00	R7.48	R462.15	**R755.55**
NH: vaccinated (34)	R42.41	R0.00	R118.38	R0.00	R66.20	**R230.15**

A summary for the total cost of interventions, in Sandringham Gardens residents, based on table 4.6, is shown in table 4.7.

Table 4.7: Summary for total cost of interventions - SG Residents, vaccinated and not vaccinated.

Parameter	Vaccinated	Not Vaccinated
Mean	328.16	319.75
Number of points	24	61
Std. deviation	495.30	667.91
Std error	101.10	85.517
Minimum	0.000	0.000
Maximum	2011.0	4337.0
Lower 95% CI	118.98	148.72
Upper 95% CI	537.34	490.78

Using an unpaired t test, the difference between the means of the cost of treating vaccinated Sandringham Gardens residents to non-vaccinated residents was not

significantly different. The two-tailed P value is 0.9556. The minimum cost in both groups is 0, as all subjects in the group were included.

A summary for the total cost of interventions, in Sandringham Gardens ward subjects, based on table 4.6, is shown in table 4.8.

Table 4.8: Summary for total cost of interventions - SG Ward subjects, vaccinated and not vaccinated.

Parameter	Vaccinated	Not Vaccinated
Mean	869.36	755.55
Number of points	18	14
Std. deviation	1173.5	1061.9
Std error	276.61	283.81
Minimum	0.000	0.000
Maximum	4356.1	2972.9
Lower 95% CI	285.72	142.53
Upper 95% CI	1453.0	1368.6

The difference between the means of the cost of treating vaccinated Sandringham Gardens wards subjects to non-vaccinated wards subjects was not significant. The two-tailed p value is 0.7787, t=0.2835 with 30 degrees of freedom (table 4.8).

The difference between the mean cost of intervention in the Sandringham Gardens Residents who were vaccinated from the cost of intervention in the Nazareth House residents, all of whom were vaccinated was not significant. The two-tailed P value was 0.5237.

The costs for the Sandringham Gardens ward subjects, in both the vaccinated and unvaccinated groups, were significantly higher than the healthier ambulatory subjects, in the residents subgroup.

CHAPTER 5

Discussion

5.1 Overview

The aim of the study was to compare the costs of treating influenza and influenza-like illnesses in old age home residents in Johannesburg, comparing people who had received the influenza vaccine with those who did not. The study took place at two sites, and over one season, namely April to October 2001. All the subjects were White.

The literature supports the view that vaccination of the elderly, as well as old age home residents, both of whom are high risk groups for complications of influenza, is cost effective. In keeping with this, the South African guidelines recommend that old age home residents should have an annual influenza vaccination. Despite this, the vaccine is underutilised, and a number of reasons have been suggested for this. These include a lack of awareness both in doctors and in the general public of the benefits, as well as concerns about side effects in patients.

Although serious side effects are rare, pain at the site of injection is common. Systemic flu-like effects are much less common in the general population, but are more common in the elderly.

The subjects in this study who chose not to be vaccinated were asked to give a reason for their choice. A common answer was that the vaccine gave them "'flu" in the past. This is not possible, as the vaccine described in this study were inactivated. Nevertheless, symptoms evoked by the vaccine may suggest to the patient that they have symptoms of 'flu and it is very important to warn patients about this.

The effectiveness of the vaccine is queried by patients who develop other respiratory illnesses in winter, including more common upper respiratory tract infections following influenza vaccination. These other illnesses may be diagnosed as influenza by doctors, due to symptoms and signs being common to both.

Most individuals who die from complications of influenza have underlying diseases that place them at high risk for complications of influenza. The most prominent high-risk conditions are chronic cardiac and pulmonary diseases. Mortality among individuals with chronic metabolic, renal, and certain immunosuppressive diseases has also been elevated, although lower than that among patients with chronic cardiopulmonary diseases. In this study, co-morbid conditions existed in all the subjects.

The mean age of subjects in this study was 81.85 years. Although influenza vaccination is effective in the elderly, the mistaken belief that it is not effective in this age group may be one of the reasons for its underutilisation in old age home residents. In this study, 52 % of subjects were vaccinated for influenza. It would be expected that higher rates of vaccination would have provided herd immunity, and help protect the unvaccinated.

This study did not show a significant cost saving in those ambulatory residents who were vaccinated. In the frail care subjects, there was a non-significant increase in costs. The limitations of this study which may explain these findings are discussed below.

5.2. Limitations of the Study

5.2.1. Sample size

The sample size was relatively small, and could have been increased by including other old age homes in the study.

5.2.2. Seasonal variation in influenza morbidity

The severity of influenza morbidity varies from season to season, and with a particularly severe influenza season, the benefits of vaccination may be more pronounced. Influenza during the 2001 winter season in South Africa was mild to moderate.[27] Studies over a number of seasons are needed to assess the amount of bias created by this factor. Unfortunately there is no scientific and reliable way of forecasting beforehand whether the forthcoming winter will bring a mild or severe epidemic.

5.2.3. Diagnosis of Influenza

Clinical signs and symptoms were used in this study. A specific diagnosis can only be made definitively by isolating virus. Virological studies were not done for this study, as they are expensive, and funding was not available. Some studies have shown that cough and fever are the only factors significantly associated with a laboratory diagnosis of influenza.[28, 29] An influenza-like illness can be caused by a variety of viral and nonviral pathogens, including influenza viruses, parainfluenza viruses, adenoviruses, respiratory syncytial virus, rhinovirus, *Chlamydia pneumoniae* and *Mycoplasma pneumoniae*. In the nursing home population, studies have shown that both influenza viruses and respiratory syncytial virus were associated with a flu-like illness and were among the leading causes of viral pneumonia. [28, 29]

One approach to this problem, used by other researchers was to assume that a specific percentage of all respiratory illness during the influenza season, for example 25 %, could be attributed to influenza. According to the World Health Organisation, during laboratory-confirmed influenza outbreaks, the majority of persons seeking medical advice for upper respiratory tract infections are likely to be infected by influenza. Some researchers used clinical indicators to make a diagnosis of influenza in old age home residents, but correlated this with virological evidence of a concurrent influenza epidemic in the general population. [5]

5.2.4. Use of over the counter medication

Some ambulatory subjects may have used over the counter influenza medication to treat themselves, and this may cause an underestimation of costs. The findings in this study show that in most cases, the most expensive intervention was that of drug costs.

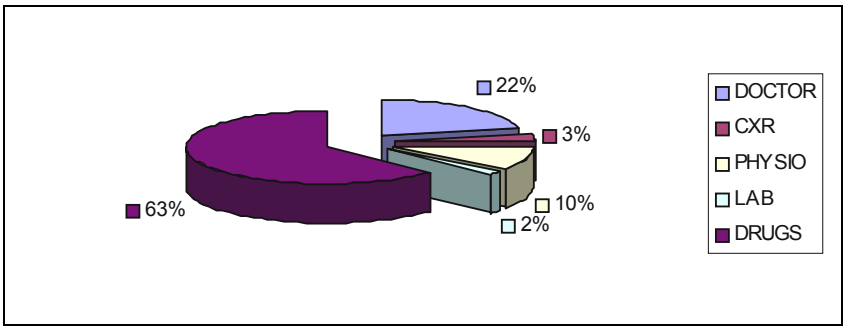

FIGURE 5.1: Relative costs of interventions. SG residents - not vaccinated

5.2.5. Poor record keeping

Accurate records of who received influenza vaccine were available for only 117 subjects at Sandringham Gardens and only these were included in this study.
Consent to participate in the study was obtained for 298 of the 340 residents at Sandringham Gardens.

If a subject had died during the duration of the study, for any reason including influenza, the file was removed, and was not available for review. This problem could have been averted by reviewing the records on a monthly basis, instead at the end of the season.

5.2.6. Population group studied

The population group studied was limited to White subjects, with financial resources to afford a private old age home. It was planned to include two other sites, both old age homes in Alexandra. This was not done, as permission could not be obtained to do so.

5.2.7. Cost of hospitalisation

Only one subject was hospitalised, and as no details were available, these costs were not included. Subjects at Sandringham Gardens who needed treatment with intravenous antibiotics received this at the home. In other old age home settings, this may not have been possible, and the patient would have needed hospitalisation.

5.2.8. Pneumococcal vaccination

Records giving information on which subjects had received pneumococcal vaccine for the season studied or in previous years were not available. Previous records are relevant because the protection provided by the vaccine against pneumococcal infections lasts a number of years.

5.3. Relative costs of interventions

A significant percentage of direct costs related to treatment of respiratory infections are for drugs. In the case of Sandringham Gardens residents who were not vaccinated, 63 % of total costs were for medication (figure 5.3, page 33). Antibiotics were the most expensive drugs prescribed. If a reliable and rapid diagnostic test for influenza was available, it may prevent the unnecessary use of antibiotics.

CHAPTER 6

Conclusion

This study measured the costs of treating influenza and influenza like illness in 151 old age home residents in Johannesburg. The costs were compared between two groups, those who received influenza vaccine, and those who did not. The control group was made up of those who were not vaccinated, which was slightly over 50 % of the total. The costs of medical intervention were found to be similar in both groups of people in this study. There are a number of possible explanations for this, as described in the limitations of the study. Despite the findings of the study, influenza vaccination is still currently recommended for the elderly.

Numerous studies have been published regarding cost evaluations of influenza vaccination in the United States of America, United Kingdom and other European countries. These studies conclude that in comparison with other health care interventions, influenza vaccination is one of the most cost-effective interventions possible in the older adult population, particularly those at higher risk, such as the elderly with chronic illness. In addition to cost benefits, there are also substantial health benefits to routine influenza vaccination.

These findings have been implemented in the official guidelines of many countries, including the South African Adult influenza Vaccination Guideline. The findings of this study do not affect these local guidelines, due to the limitations which were described. Further studies in South Africa, including studies of old age homes where the residents are of lower socioeconomic groups, would be valuable. In this setting, it would be expected that less resources would be available for funding influenza vaccination.

In order to increase influenza vaccination utilisation, medical practitioners need to be convinced of the benefits of annual influenza vaccination. Inaccurate beliefs about influenza vaccination persist in the community, and health care

professionals need to correct these misconceptions in order that those most at risk can benefit from influenza vaccination.

APPENDIX A

INFLUENZA SURVEY - INFORMATION LEAFLET AND INFORMED CONSENT

2001

Dear Resident

We would like to invite you to participate in study concerning the use of the **'flu vaccine** ('flu shots') in residents of old age homes in Johannesburg.

We would simply like to monitor the health of all residents in the home, both those who have the 'flu vaccine and those who do not. We will not be changing anything whatsoever in the running of the home, or the administration of the 'flu shots.

If you do take part in the study, we would like to have access to your medical records for the duration of the study. (From April 2001 until the end of October 2001). We would like you to report any episodes of illness during the duration of this study to the nursing staff who are responsible for your care. This is in addition to you seeing your usual doctor.

Please note that the survey is completely anonymous and you cannot be identified in any way. Permission to carry out this study has been obtained from the Committee for Research on Human Subjects, of the University of the Witwatersrand. ("Ethics Committee")

Dr. Hugh Cobb is doing this study as part of the requirements for obtaining a Masters degree from the University of the Witwatersrand, together with the pharmaceutical company "Aventis Pasteur", who make a 'flu vaccine'.

If you have any questions which are not fully explained in this leaflet, please contact Dr. Cobb for an explanation (Tel: 487-1714 or 082-344-5976).

You do not have to take part in this study. If you change your mind at any time later you have the right to leave the study. If you choose to leave the study, it will not be detrimental to you in any way and you will still be treated to the best of the attending doctors' ability.

Your right as a Participant

You have the right to privacy, and all information that is collected during this study is confidential. No study documentation that identifies you personally will ever be passed outside those directly involved in the study. Only the Ethics Committee will be granted direct access your records to verify study procedures or data.

You do not have to take part in this study. If you change your mind at any time later you have the right to leave the study. If you choose to leave the study, it will not be detrimental to you in any way and you will still be treated to the best of the attending doctors' ability.

Informed Consent

"I declare to have understood the objectives and the aim of the study, and to have obtained satisfactory answers to all of my questions. I have been informed that I can choose to withdraw my self from the study at any time, without affecting any future medical care to myself. I authorise Dr. H. Cobb, the Ethics Committee and Aventis Pasteur, to review my medical data. I am voluntarily participating in this study."

Subject's last and first names : ……..... Inclusion number in the study : |___|___|___|___|___|	Date : _____/_____/_____ Signature*:
Last and first name of a Witness: (unrelated to the investigator team if subject is unable to read and sign the form) .....……	Date : _____/_____/_____ Signature :
Last and first name of individual obtaining consent : .....……	Date : _____/_____/_____ Signature :

Thank you for your time and assistance.

Dr. Hugh Cobb
MB. B.Ch (Witwatersrand); DA (SA); DFM (Jer); MFGP (SA)
35 Bedford Road
Yeoville
Johannesburg Tel: 487-1714

APPENDIX B

CASE REPORT FORM: COST ANALYSIS OF INFLUENZA VACCINE

Subject inclusion number: |__|__|__|__|__|

Site: Nazareth House ☐

Sandringham Gardens ☐

Subject Initials: |__|__|__|

Gender: F ☐ M☐

Date of Birth: |__|__| |__|__| |__|__|__|__|
d d m m y y y y

Informed consent obtained: YES ☐ NO ☐

If yes, Date of informed consent: |__|__| |__|__| |__|__|__|__|
d d m m y y y y

1. Vaccination History:

Vaccine received	Yes			No
	Yes	If Yes, what date received	Commercial name of vaccine received	
Influenza				
Pneumococcal				
Other (specify)				
Other (specify)				

2. Review of Contraindication to Influenza Vaccine

Contraindication	Yes	No
Anaphylactic hypersensitivity to eggs		
Allergy to other components of the vaccine		
Acute severe febrile illness		
No informed consent		
Other reason (besides below)		
Subject chooses not to be vaccinated. If possible, state reason.		

3. Review of Medical History from Records

Date of review: |__|__| |__|__| |__|__|__|__|
d d m m y y y y

Presence or absence of condition	Yes	No
1. Emphysema / Chronic Obstructive Airway Disease		
2. Asthma		
3. Diabetes Mellitus (Insulin Dependent)		
4. Diabetes Mellitus (Non Insulin Dependent)		
5. Congestive Heart Failure		
6. Hypertension		
7. Previous Pneumonia		
8. Previous vaccination with pneumococcal vaccine		
9. Neurological disease Type: (eg. Parkinson's disease)		

3 Monthly record review of symptoms during the past month

Syptom	April		May		June		July		Aug		Sep		Oct		Nov		Dec	
Date of record review (dd/mm/yy)																		
	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N
Malaise																		
Cough																		
Rhinorrhoea																		
Sore throat																		
Chills																		
Headache																		
Anorexia																		
Myalgia																		
Productive cough																		
Dizziness																		
Hoarseness																		
Chest pain																		
Vomiting																		
Diarrhoea																		
Abdominal pain																		
Diagnosis E.g. URTI / FLU / LRTI / Pneumonia	April		May		June		July		Aug		Sept		Oct		Nov		Dec	

3. Record review of interventions

	Apr		May		Jun		Jul		Aug		Sep		Oct		Nov		Dec	
Date of record review (dd/mm/yy)																		
INTERVENTION	**Y**	**N**	**Y**	**N**	**Y**	**N**	**Y**	**N**	**Y**	**N**	**Y**	**N**	**Y**	**N**	**Y**	**N**	**Y**	**N**
Doctor Consultation																		
Referral to hospital (please complete hospitalisation section if hospitalised)																		
FBC																		
Other blood tests (please specify)																		
Chest x-ray																		
Antibiotics (please give dose and duration)																		
Symptomatic medication (please specify under medications section)																		
Chest physiotherapy																		
Nebulisations (please specify under medications section																		

6. Record of medications

Drug Name	Indication	Dosage	Route	Date started	Duration of treatment

7. Hospitalisation

Reason for Hospitalisation	Name of Hospital	Special transport required (e.g. ambulance) Y / N	Date admitted	Date discharged	ICU required (Y / N)

APPENDIX C

APPENDIX D

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