

https://dspace.org/

An assessment, with nice guidelines as a benchmark, of delay to care in a cohort of colorectal cancer patients seen in the Witwatersrand university academic complex

Singh, Kimisha

2022
https://hdl.handle.net/10539/34412

Downloaded from a DSpace repository. https://dspace.org/



An Assessment, with NICE Guidelines as a Benchmark, of Delay to Care in a Cohort of Colorectal Cancer patients seen in the Witwatersrand University Academic Complex

KIMISHA SINGH

Student Number: 1828913

A research article submitted to the Faculty of Health Sciences, University of the Witwatersrand, in partial fulfilment of the requirements for the degree of Master of Medicine. Written in the submissable format according to SAJS guidelines

Johannesburg, 2022

DECLARATION

I declare that this research is my own, unaided work. It is being submitted for the Degree of Mastery of Medicine at the University of the Witwatersrand, Johannesburg in the submissable format according to SAJS guidelines. It has not been submitted before for any degree or examination at any other University.



_____ _____

(Signature of candidate)

_____28_____day of
_____January_____20_22_____at____14:00_____

In loving memory of

Che^ Freddy

1994 – 2009

Farewell, my friend till we meet again, someday, somewhere

Abstract

Background

Colorectal cancer (CRC) in South Africa is the second most common in women and the third in men. According to GLOBOCAN data CRC is the second most deadly cancer worldwide. As a subset, colon cancer is the fifth most deadly with an estimated 551 000 deaths in 2018. CRC makes up 5.8% of all cancer related deaths globally. Despite this, there are no screening programmes in South Africa, diagnosis of this cancer being largely dependent on symptomatic presentation. Additionally, there is no clear understanding of the significance to outcome imposed by delay to referral and delay to treatment. Unlike countries in Europe, South Africa has no guidelines defining cut-offs for acceptable delays in this context. This belies a paucity of research done around the pathways to care in this setting.

Objectives

To determine extent of delays to referral and treatment of CRC patients by benchmarking these timelines against the NHS two-week-rule and the European provision of no more than one month to treatment. Evaluate the variables that impact 90-day mortality post therapeutic surgery and define the significance of the delays against the identified confounders.

Methods

A retrospective study was done on the delay to referral, diagnosis and treatment of CRC patients. The outcome measure used was 90-day mortality post definitive treatment. A cohort of patients who presented to Witwatersrand Academic Hospitals was studied. Data from MRC CRECSA study for colorectal cancer was studied. Patients in which surgery was the primary treatment were assessed.

Delays in these patients were benchmarked against fourteen days from primary contact to consultation with a treating specialist and consultation to treatment delay of more than 31 days. Further, definitive treatment delay was defined as time from referral to treatment centre and tumour resection. This was benchmarked against a cut-off of 62 days. Outcomes were then evaluated by defining the 90-day mortality in each group.

Results

The median referral delay was 78 days and for treatment delay was 54 days in 587 patients. Definite treatment delay median was 175 days. Of the 587 patients analysed, 341 had therapeutic surgery, of which 17 demised within 90 days post-surgery. Longer delays and higher mortality rates were seen in the public sector and lower socio-economic group of patients.

Conclusion

Delay in referral and treatment of colorectal cancer patients in South Africa does not meet the goals of the European time parameters set out. There were greater delays seen in patients with a lower socio economic background and in those attending the public sector. The effect of delays on 90-day mortality is doubtful. Delays to care both outside of hospitals and in hospitals may be a point of investigating in future studies. The complexity of the circumstance that gives rise to poor outcomes is highlighted by the effect of socio-economic status on 90-day mortality. This further suggests poor outcome is not driven by delay to referral or delay to treatment.

AKNOWLEDGEMENTS

To my sister Sharista Singh for your unyielding support throughout this process

To my parents Rabindranath and Rakee Singh for your endless love and encouragement

TABLE OF CONTENTS

Title Page	1
Declaration	2
Dedication	3
Abstract	4
Acknowledgements	5
Table of contents	6
List of figures	7
List of tables	8
List of abbreviations	9
Introduction	10
Methods	11
Data analysis	12 -14
Results	14 -22
Discussion	22 -24
Conclusion	24
References	25 -26
Appendix 1	29-32
Appendix 2	33-50

LIST OF FIGURES

Figure 1: Timelines to treatment Page 12

Figure 2: Percentage of patients delayed to referral Page 16

Figure 3: Cumulative incidence to treatment delay Page 18

Figure 4: Cumulative incidence to definitive treatment delay Page 20

LIST OF TABLES

Table 1: Demographic characteristics of CRC patients Page 14-16

Table 2: Referral Delay Page 17

Table 3: Treatment Delay Page 18 – 19

Table 4: Definitive Treatment Delay Page 20-21

Table 5:90 Day Mortality Page 21-22

List of abbreviations

CRC – colorectal cancer

SA- South Africa

NHS- National Health Society

MRC- Medical Research Counsel

CANSA – Cancer association of South Africa

NCR- National Credit Regulator

UK- United Kingdom

CMJAH – Charlotte Maxeke Johannesburg Hospital

CHBAH- Chris Hani Baragwanath Hospital

WDGMC- Wits Donald Gordan Medical Centre

SES- Socio economic Status

HLOE- Highest level of education

AJCC- American Joint Committee on Cancer

ECOG- Eastern Cooperative Oncology Group

GP- General Practioner

PCA- Principle component analysis

HR – Hazard Ratio

IQR-Interquartile range

Introduction

The incidence of colorectal cancer (CRC) in the developing world has been shown to increasing each year. Demographic trends have reflected an expected increase in incidence by 80% within the next two decades. Most of this increase has been expected to occur in less developed regions (62%).[14] This has been accompanied by a proportional increase in the yearly reported mortality rates reflecting the inability of health services to deal with the demand of the burgeoning incidence in the circumstance of poverty.[14] In 2018 alone, over 1, 8 million new cases were identified and 881 000 deaths occurred world-wide. This ranks CRC globally as the third most common cancer in terms of incidence and the second most common cause of cancer related death globally[1]

In South Africa we have no convincing data on the yearly change in the incidence of colorectal cancer nor the change in associated mortality rate.[13] the national cancer registry (NCR) which provides statistical updates has not up to date.[2] However in the last updated registry NCR pined this malignancy as the third most common in women and the second most common in men.[2] At present, the population-based data regarding colorectal cancer in South Africa has been scanty. In the absence of national data, it has been the clinician's responsibility to use hospital-based data to determine current statistics and to monitor outcome within their institution

With this in mind, we were interested to identify possible management deficiencies in the pathways to care in CRC. Using United Kingdom (UK) and European guidelines for treatment quality. We have subjected our cohort of patients to an evaluation of various delays in management to see if this has had a bearing of outcome.

The direct comparison of these patients with those in the UK and Europe was not feasible but, we attempted to see how the delays in our pathways to care in CRC compare with the stipulated requirements of best quality of management defined by the National Health Service(NHS) and services in the European union.

In South African Health care facilities there have been no attempts made to determine indices of best practice in CRC treatment pathways. Interruptions incurred both in getting into the health system as well as delays within the system may be worth exploring in this context. Internationally, the effect of delays to referral and treatment on outcome has shown mixed results.[15] Most research on this topic from Europe has shown that diagnostic and

treatment delay has not shown to decrease survival.[16] In the United States some components of delay were examined with similar findings[3]. However, in developing countries, where CRC treatment pathways are new or poorly developed lengthy delays have been commonplace. From Taiwanese data, treatment within 30 days of confirmed diagnosis questionably decreased the risk of death while delays beyond 90 days unfavourably impact outcomes[4].

Despite these discrepancies, the Cancer Research Society UK has produced three broad time periods. If we followed the recommendations of Cancer Research UK, patients with suspected cancer were to be seen within 2 weeks of referral/presentation by a specialist. This time interval supports early diagnosis and improved survival of patients. Once the decision to treat cancer is made, first cancer treatment was to be started within the first 31 days of this decision. First definitive treatment of cancer was to occur within 2 months/62days from initial GP referral/presentation of the patient. [5]These time frames have been used as targets in the UK and European Union. They are not official targets at local hospitals. We have hoped to compare the local data in our cohort of patients used in this study to these.

The primary aim of this study is to determine if time delays to care in our population compares to that in the UK as benchmarked against the stipulated NHS standards. The secondary aim of this study is to determine 90-day mortality of colorectal cancer post major resection. This may provide some insight into the circumstances of a cohort of South African CRC patients as they pass through care and whether delays as describe have any bearing on these outcomes.

Methods

Data sources and study population Ethics approval was obtained from the University of Witwatersrand, Johannesburg, South Africa, and Human Research Ethics committee (Certificate number M1811110). Subjects used were enrolled on the REDCap database: MRC Prospective Colorectal Cancer Database. Data obtained was on 587 adult patients (>=18y at enrolment) with histologically confirmed colorectal cancer (CRC). Only patients with adenocarcinoma were selected. Enrolment for the study was over the period 1 Jan 2016 – 31 Dec 2019 (last follow-up on 31 Mar 2020). The following study centres were included: Charlotte Maxeke Johannesburg Academic Hospital, (CMJAH), Chris Hani Baragwanath Academic Hospital (CHBAH), Wits Donald Gordon Medical Centre (WDGMC) and Edenvale Hospital, which are part of the major centres in the circuit that treat colorectal cancer. CMJAH and CHBAH are tertiary institutions within public service, whereas WDGMC is a tertiary university hospital within private practice. Edenvale Hospital is a public based

secondary treatment hospital that refers to CMJAH. Patients with recurrent cancer, patients with synchronous lesions, patients with anal carcinoma, patients who had received treatment before being seen at the specialist centre, patients diagnosed more than 1 year before presentation at the specialist centre were excluded from the study. In order to define the population and for reasons of analysis, the independent variables analysed were derived from demographic domains, socioeconomic status, treatment intent and tumour / patient specific data. Demographic data analysed from the database included: age at first visit, gender and ethnicity. Instruments pertinent to socioeconomic status (SES) that were used include: centre at which treatment was received, healthcare sector (public/private), number of people per household, employment status, highest level of education (HLOE) and SES assets score (range 0-11). Tumour specific data included was defined by location/sidedness of malignancy, AJCC staging of the CRC. The patient's clinical makeup was determined by: ECOG status and initial definitive treatment received (therapeutic surgery / radiation / chemotherapy).

The dependant variables measured in this study are specific time lines which included: date of primary consult (with GP/at primary care centre), date of first visit to specialist centre, date of first definitive treatment (if any), date of first therapeutic surgery (if applicable), date of death / date last seen. The timelines used are illustrated in the diagram below.



Figure 1: Timeline to treatment

Data Analysis

Patients recruited at Edenvale hospital were grouped with the CMJAH patients. An overall SES score was derived from employment status, HLOE, number of people in household,

and the 11 assets (for data collected from Nov 2016 onwards) using Principal Component Analysis (PCA) (ref: Vyas, 2006). The first component was used as the SES score, which was then categorised as: lowest 40% of households as 'poor', the highest 20% as 'rich' and the rest as the 'middle' group (Filmer and Pritchett, 2001).

Initial treatment (date and type) was derived from treatment after the first specialist centre visit: Therapeutic surgery was taken as surgery done to resect tumour in its entirety for cure. Palliative procedures were not considered as therapeutic surgery. The earliest treatment (of surgery / chemo / radiation) was taken as the initial treatment. Some patients therefore had no treatment and this study only considers those patients managed with curative intent.

90-day mortality was determined for all therapeutic surgeries (as defined above) carried out prior to 31 Dec 2019. Where a patient had more than one therapeutic surgery, the first surgery was considered. The p-values provided in the tables are the p-values for the overall analysis of the different groups. If the p-value is >=0.05 nothing further was done. If the p-value was <0.05, then the significant differences where determined. If the overall test was significant, then the following was done.

Referral delay (percentage exceeding 14 days), as well as 90-day mortality after definitive surgery, was compared between groups (age, gender, ethnicity, centre, healthcare sector) using the X^2 test (Fisher's exact test was used for 2 x 2 tables or where the requirements for the X^2 test could not be met). Treatment delay and Definitive treatment delay were compared between groups using competing-risks Cox Proportional Hazards regression analysis, with death as competing event and censoring for those who had neither had definitive treatment nor died.

Data analysis was carried out using SAS version 9.4 for Windows. A 5% significance level was used.

Sample size

As a starting point, we assumed definitive treatment delay of 75% within 62 days. Based on a prevalence of a risk factor (e.g. age > 50y) of 50%, the detection of a hazard ratio of at least 1.3 with 80% power at the 5% significance level required a minimum sample size of 608 patients. (or HR 1.35 requires 465 patients)

Inclusion/exclusion criteria

716 patients were enrolled onto the MRC Prospective Colorectal Cancer Database between 1 Jan 2016 and 31 Dec 2019. All patients had histologically confirmed primary

adenocarcinoma of the colon or rectum. All patients were aged 18y or older. The following patients were excluded from our analysis of the MRC database, we excluded: 1 from a non-qualifying centre, 1 with unknown date of first visit to the specialist centre, 81 who had received treatment before being seen at the specialist centre, 36 with recurrent cancer, 8 with synchronous lesions, 2 with missing referral date

A total of 129 patients was excluded, leaving 587 patients included in the study.

Results

Study Sample

Of all the 587 patients analysed, 264 were diagnosed with either left or right sided colon cancer and 323 had rectal cancer. Of the greater than fifty age group 73.8% of the population were analysed. There was an almost even distribution between male and female patients.

Characteristics of the study sample s and cancer location is provided in the table below:

		Overall	
n		587	
Variable	**Category**	**n**	**%**
Age at first visit (y)	<=50y	154	26,2
	>50y	433	73,8
Gender	male	301	51,3
	female	286	48,7
Ethnicity	black	307	52,3
	white	206	35,1
	Indian	38	6,5
	coloured/ mixed race	33	5,6
	east Asian (e.g., Chinese)	2	0,3

	other	1	0,2
Study site (recruitment)	CHBAH	216	36,8
	WDGMC	190	32,4
	CMJAH	181	30,8
Study site (recruitment) (grouped)	State	397	67,6
	Private	190	32,4
SES class (from PCA) (recruitment 1 Nov 2016 onwards; n=481)	Wealthy	95	20,0
	Intermediate	191	40,1
	Poor	190	39,9
	Unknown	5	
SES class - STATE	Wealthy	18	5,6
	Intermediate	121	37,9
	Poor	180	56,4
	Unknown	4	
SES class - PRIVATE	Wealthy	77	49,0
	Intermediate	70	44,6
	Poor	10	6,4
	Unknown	1	
Location of malignancy	Colon: right	112	19,1
	Colon: left	152	25,9
	Rectum	323	55,0
AJCC staging	stage 1	40	7,6
	stage 2a	73	13,9
	stage 2b	14	2,7

	stage 2c	13	2,5
	stage 3a	7	1,3
	stage 3b	82	15,6
	stage 3c	122	23,1
	stage 4a	112	21,3
	stage 4b	64	12,1
	unable to stage	60	
AJCC staging (grouped)	Stage 1 or 2	140	26,6
	Stage 3 or 4	387	73,4
	Unable to stage	60	
ECOG status	grade 0 - Fully active, able to carry on all pre-disease performance without restriction	128	26,7
	grade 1 - Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work	208	43,4
	grade 2 - Ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours	98	20,5
	grade 3 - Capable of only limited self-care; confined to bed or chair more than 50% of waking hours	42	8,8
	grade 4 - Completely disabled; cannot carry on any self-care; totally confined to bed or chair	3	0,6
	test not done/ not recorded	108	
ECOG status (grouped)	Grade 0-2	434	90,6
	Grade 3-4	45	9,4
	not done / not recorded	108	
Initial Treatment	Surgery	229	39,0

	Radiation	171	29,1
	Chemotherapy	99	16,9
	None	88	15,0

Table 1: *Selected characteristics of colorectal cancer patients included in*

**Age of first visit is tabulated in years(y) as either less than or equal to fifty (<=50) or more than fifty (>50)*

**The standard deviation of age of first visit was 13.5 and the range was 18-91*

Referral delay

The median referral delay was 78 days (IQR 23-201 days) (range 0-1319 days). The distribution of the data is shown below.

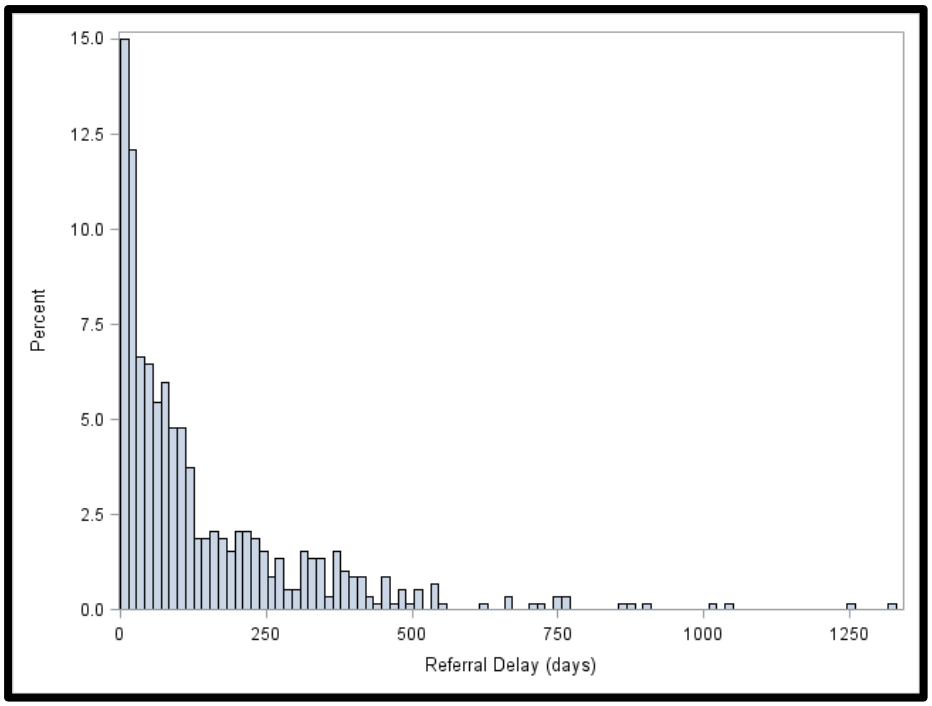


Figure 2: *Percentage of patients delayed to referral*

The data below in table 2 shows the following:

Overall, 83.3% of the patients in the study had a referral delay in excess of 14 days. This percentage was significantly higher for:

- Black compared to white patients
  *there was no significant difference found between the other ethnicities
- CHBAH patients compared to WDGMC patients
- State patients compared to private patients
- Intermediate/Poor SES patients compared to Wealthy SES patients

There were no significant differences with regard to age and gender (table 2).

Variable	Category	n	Referral delay > 14 days	
			% of patients	p-value for between-group test
Overall		587	83,3	
Age at first visit (y)	<=50y	154	81,2	0,45
	>50y	433	84,1	
Gender	male	301	85,4	0,18
	female	286	81,1	
Ethnicity	black	307	87,0	0,022
	white	206	77,2	
	Indian	38	89,5	
	coloured/ mixed race	33	81,8	
	east Asian (e.g. Chinese)	2		>0.05
	other	1		
Study site (recruitment)	CHBAH	216	93,5	<0.0001
	WDGMC	190	73,2	
	CMJAH	181	81,8	
Study site (recruitment) (grouped)	State	397	88,2	<0.0001
	Private	190	73,2	
SES class (from PCA) (recruitment 1 Nov 2016 onwards; n=481)	Wealthy	95	73,7	0,0004
	Intermediate	191	90,6	
	Poor	190	87,4	
	Unknown	5		

Table 2: *Referral Delay*

Treatment delay

88 patients had no treatment; of these 68 died (competing risk which is an event which precluded the occurrence of the primary event of interest) and 20 are still awaiting treatment (or had refused treatment) (censored time to treatment). All these patients and both of these factors are taken into account in the subsequent analysis and were excluded from the analysis

The median treatment delay was 56 days (IQR 20-125 days). The cumulative incidence function for treatment is shown below

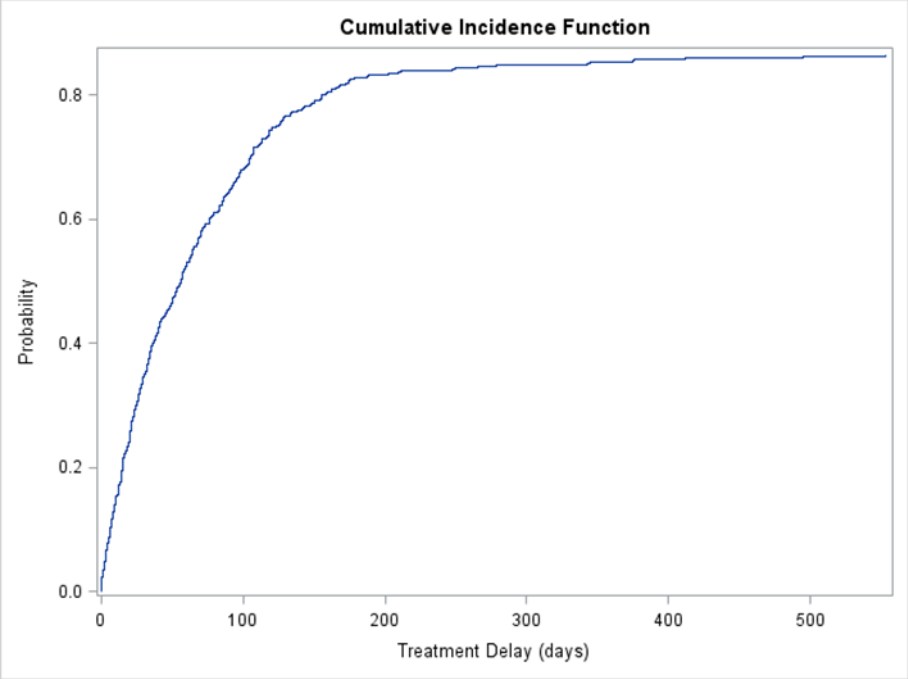


Figure 3: Cumulative incidence of treatment delay

Overall, 64.5% of patients had a treatment delay in excess of 31 days this percentage was significantly higher for:

- Black compared to white and Indian patients
  * there was no significant differences found between the other ethnicities
- Patients from different hospitals in the order CHBAH > CMJAH > WDGMC
- State patients compared to private patients
- SES in the order Wealthy > Intermediate > Poor

There were no significant differences with respect to age and gender.

Variable	**Category**	**n**	**Treatment delay > 31 days**	
			% of patients	**p-value for between-group test**
Overall		587	64,5	
Age at first visit (y)	<=50y	154	62,6	0,37
	>50y	433	65,1	
Gender	male	301	63,7	0,52
	female	286	65,3	

Ethnicity	black	307	71,1	<0.0001
	white	206	55,7	
	Indian	38	59,0	
	coloured/ mixed race	33	66,7	>0.05
	east Asian (e.g. Chinese)	2		
	other	1		
Study site (recruitment)	CHBAH	216	78,9	<0.0001
	WDGMC	190	44,6	
	CMJAH	181	68,1	
Study site (recruitment) (grouped)	State	397	74,4	<0.0001
	Private	190	44,6	
SES class (from PCA) (recruitment 1 Nov 2016 onwards; n=481)	Wealthy	95	49,6	<0.0001
	Intermediate	191	63,1	
	Poor	190	72,6	
	Unknown	5		

Table 3: Treatment delay

Definitive Treatment delay

Definitive treatment delay was calculated by adding, referral delay to the Treatment delay and applying a cut off of 62 days.

88 patients had no treatment; of these 68 died (competing risk) and 20 were still waiting for treatment (or had refused treatment) (censored time to treatment). All these patients and both of these factors are taken into account in the subsequent analysis.

The median definitive treatment delay was 172 days (IQR 78-406 days). The cumulative incidence function for definitive treatment is shown below.

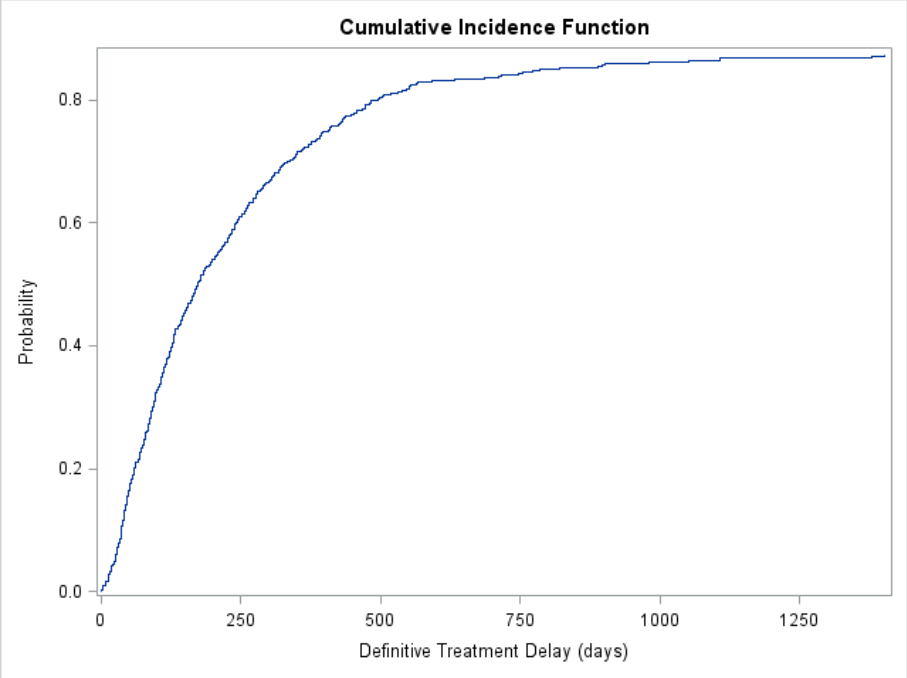


Figure 4: Cumulative incidence of definitive treatment delay

Overall, 79.0% of patients had a treatment delay in excess of 62 days. This percentage was significantly higher for:

- Black compared to white and Indian patients; Mixed race compared to white patients
  *no significant differences were found between the east asia and other ethnicities
- Patients from different hospitals in the order CHBAH > CMJAH > WDGMC
- State patients compared to private patients
- SES in the order Wealthy > Intermediate > Poor

There were no significant differences with respect to age and gender.

Variable	**Category**	**n**	**Definitive Treatment delay > 62 days**	
			% of patients	**p-value for between-group test**
Overall		587	79,0	

Age at first visit (y)	<=50y	154	78,3	0,64
	>50y	433	79,2	
Gender	male	301	78,4	0,52
	female	286	79,5	
Ethnicity	black	307	84,8	<0.0001
	white	206	70,7	
	Indian	38	74,1	
	coloured/ mixed race	33	79,2	<0.0001
	east Asian (e.g. Chinese)	2		>0.05
	other	1		
Study site (recruitment)	CHBAH	216	89,1	<0.0001
	WDGMC	190	61,8	
	CMJAH	181	83,6	
Study site (recruitment) (grouped)	State	397	86,8	<0.0001
	Private	190	61,8	
SES class (from PCA) (recruitment 1 Nov 2016 onwards; n=481)	Wealthy	95	66,8	<0.0001
	Intermediate	191	82,3	
	Poor	190	87,0	
	Unknown	5		

Table 4: Definitive treatment delay

90-day mortality after therapeutic surgery

There were 341 therapeutic surgeries in the study period which had at least a 90-day follow-up period.

The overall 90-day mortality was 17/341=5.0%. This percentage was significantly higher for:

- Patients from CHBAH and CMJAH compared to WDGMC
- State patients compared to private patients

There were no significant differences with respect to age, gender, ethnicity or SES.

The selected characteristics of patients that underwent surgery are in the table below:

Variable	**Category**	**n (surgeries)**	**90-day mortality**

			Mortality (%)	p-value for between-group test
Overall		341	5,0	
Age at first visit (y)	<=50y	85	2,4	0,26
	>50y	256	5,9	
Gender	male	171	6,4	0,32
	female	170	3,5	
Ethnicity	black	134	7,5	0,27
	white	157	3,8	
	Indian	27	0,0	
	coloured/ mixed race	20	0,0	
	east Asian (e.g., Chinese)	1		
	other	2		
Study site (recruitment)	CHBAH	76	13,2	<0.0001
	WDGMC	170	0,6	
	CMJAH	95	6,3	
Study site (recruitment) (grouped)	State	171	9,4	<0.0001
	Private	170	0,6	
SES class (from PCA) (recruitment 1 Nov 2016 onwards; n=279)	Wealthy	78	1,3	0,18
	Intermediate	112	6,3	
	Poor	87	6,9	
	Unknown	2		

Table 5: 90-day mortality

Discussion

The delay in diagnosis and treatment of colorectal cancer in the South African population is largely unexplored. Most studies from developed countries suggest that prognosis is not worsened with delay in diagnosis and treatment[3]. However, newer international studies from less developed countries showed that delay does in fact increase risk of mortality. The study described above done in Taiwan showed that the risk of death increased 1.5 times if treatment is delayed by 31-150 days post diagnosis and is 1.6 times higher if delay was more than 150 days.[4] This study however did not clearly differentiate patients managed with curative intent and those managed with a view to cure which will fundamentally effect outcomes defined by mortality. They did point out, timely treatment is found to decrease patient anxiety and improve quality of life but this was not substantiated in the data.[4]

Against this background of uncertainty, there has been no international or South African guidelines for acceptable delays in referral and treatment in this setting.

Our study clearly showed substantive higher referral delays and treatment delays when

compared with the NHS and European equivalent. Despite this poor outcome is driven by poverty and low SES scores. Prehospital delays are probably playing a much greater role in unfavourable outcomes. Prehospital delays can be patient related, or physician related.[7] in the context of developed nations, it would appear patient related delays are significant. Patients do not recognise symptoms of concern in the unfolding natural history of CRC. They tend to self-medicate and out of fear of possible tests and interventions that might be required avoid medical attention[7]. Physician related factors included lack of recognition of symptoms, inadequate investigations and avoidance of digital rectal examination[7]. All of these prehospital events were unexplored in this study, but certainly need to be evaluated in future research.

Importantly, approximately 85% of the South African population are dependent on public health care.[10] Understanding and exploring the differences in access to care between private and public health sectors has been pertinent. In this study it has been found that patients from state sector and of lesser socio-economic status (SES) backgrounds had longer delays to referral and treatment. This has buried deeper issues in access to care. In other studies, unfavourable access to care was dependent on socio-economic status, insurance status and geographic location. ethnicity, the poor, the uninsured and rural residence.[10] Poor access immediately has its roots in long travel distances and high travel costs, high out of-pocket payments for care; long queues; and patient disempowerment.[8] In our setting the cause of preadmission delays in the care of the poorer patient desperately needs exploration.

As noted by the NHS “where patients wait longer, this should be because of the diagnostic process or their personal choice, not because of built in delays in the system of care”.[9] .Delays to referral and treatment was clearly demonstrated in our study. If this in itself was considered a reason for action there is much that could be done. In a study from Minnesota, Canada, overall delay to treatment was found to be the consequence of delays in diagnosis. Simplification of steps in well-structured diagnostic pathways were seen as the solution to this issue. This is a course we could well imitate .[9]

Finally, 30-day mortality has conventionally been used to reflect peri-operative outcome. By extending mortality reporting to 90-days, this study set out maximise the number of patients with an unfavourable outcome and a greater number of mortality outliers.[11] Internationally, 90-day mortality was also used as a surrogate of surgeon’s outcome and is a quality metric system by which hospitals are benchmarked.[11] Within this study group 5% of patients demised within a 90-day period post therapeutic resection. Using this as a quality metric system in South Africa has not been explored. However, with significant differences found between the three study sites, it can be assumed that implementing such a system could

benefit the future care of colorectal patients. Better service may be driven by implementing ongoing quality assessments, forcing us to reflect on management techniques and identifying areas of need.

Limitations

The data collected for the study was done retrospectively. Therefore data was collected with convenience sampling , and are thus not representative of the general population .Additionally, only information of the patients that presented to the four Witwatersrand Hospitals ,used in the study was utilised. Patients seen outside of these hospitals was not included in the study. Therefore the sample of patients used does not represent Gauteng as a whole. Secondly there are no reliable registries to utilise for patient recruitment. Recruitment was only possible through activity of a research nurse, which introduced bias to the sample. Thirdly the sample size used in the study was small, when sub categorising the patients for the sub group analysis the power of prediction was further decreased. Finally extended delays may contribute to other patient outcomes other than death. Future research could explore the effect of delays on outcomes such as postoperative complications, hospital stay, hospital readmission, cost, quality of life, and psychosocial outcomes such as anxiety.

Conclusion

This study is one of the first studies in South Africa to look at delay in treatment pathways and 90-day mortality in colorectal cancer. We found that most patients did not meet the time parameters recommended by the NHS guidelines. With greater delay times seen in lower socio-economic subgroups and within the public sector. The effects of this on prognosis and mortality were not directly explored in this study. However, when looking at 90-day mortality post-surgery, it was found that a similar distribution of results was seen within the subcategories. With such discrepancies found within the subgroups it can be assumed that developing a treatment pathway guideline would be of benefit in this setting in an attempt to improve and equalise standard of care. In addition, monitoring 90-day mortality post major resection could also help us reflect on institutional based outcomes and ultimately improve overall management of colorectal cancer patients in South Africa

REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394-424. DOI:10.3322/caac.21492

2. Singh E, Underwood JM, Nattey C, Babb C, Sengayi M, Kellett P. South African National Cancer Registry: Effect of withheld data from private health systems on cancer incidence estimates. S Afr Med J. 2015;105(2):107-9. DOI:10.7196/SAMJ.8858

3. Pruitt SL, Harzke AJ, Davidson NO, Schootman M. Do diagnostic and treatment delays for colorectal cancer increase risk of death? Cancer Causes Control. 2013;24(5):961-77.

   DOI: 10.1007/s10552-013-0172-6

4. Lee YH, Kung PT, Wang YH, Kuo WY, Kao SL, Tsai WC. Effect of length of time from diagnosis to treatment on colorectal cancer survival: A population-based study. PLoS One. 2019;14(1): e0210465. DOI: 10.1371/journal.pone.0210465

5. Cancer Research UK. Bowel Cancer 2015 [updated 30 September 2015. Available from: http://about-cancer.cancerresearchuk.org/about-cancer/bowel-cancer

6. Redaniel MT, Ridd M, Martin RM, Coxon F, Jeffreys M, Wade J. Rapid diagnostic pathways for suspected colorectal cancer: views of primary and secondary care clinicians on challenges and their potential solutions. BMJ Open. 2015;5(10): e008577.DOI:10.1136/bmjopen-2015-008577

7. Mitchell E, Macdonald S, Campbell NC, Weller D, Macleod U. Influences on pre-hospital delay in the diagnosis of colorectal cancer: a systematic review. Br J Cancer. 2008;98(1):60-70. DOI: 10.1038/sj.bjc.6604096

8. Harris, Bronwyn & Goudge, Jane & Ataguba, John & McIntyre, Diane & Nxumalo, Nonhlanhla & Jikwana, Siyabonga & Chersich, Matthew. (2011). Inequities in access to health care in South Africa. Journal of public health policy. 32 Suppl 1. S102-23. 10.1057/jphp.2011.35. doi:10.1057/jphp.2011.35.

9. Singh H, De Coster C, Shu E, Fradette K, Latosinsky S, Pitz M, et al. Wait times from presentation to treatment for colorectal cancer: a population-based study. Can J Gastroenterol. 2010;24(1):33-9. https://doi.org/10.1186/s12913-016-1590-4

10. Crawford SM, Sauerzapf V, Haynes R, et alSocial and geographical factors affecting access to treatment of colorectal cancer: a cancer registry studyBMJ Open 2012;2: e000410. doi: 10.1136/bmjopen-2011-000410

11. Byrne BE, Mamidanna R, Vincent CA, Faiz O. Population-based cohort study comparing 30- and 90-day institutional mortality rates after colorectal surgery. Br J Surg. 2013;100(13):1810-7. doi: 10.1002/bjs.9318

12. Arnold M, Sierra MS, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global patterns and trends in colorectal cancer incidence and mortality. Gut. 2017;66(4):683–91. DOI:10.1136/gutjnl-2015-310912

13. Burger EH, van der Merwe L, Volmink J. Errors in the completion of the death notification form. South African Med J. 2007;97(11 I):1077–81. PMID: 18250917

14. Karsa LV, Lignini TA, Patnick J, Lambert R, Sauvaget C. The dimensions of the CRC problem. Best Pract Res Clin Gastroenterol. 2010 Aug;24(4):381-96. doi: 10.1016/j.bpg.2010.06.004. PMID: 20833343.

15. Neal RD. Do diagnostic delays in cancer matter? Br J Cancer. 2009 Dec 3;101 Suppl 2(Suppl 2):S9-S12. doi: 10.1038/sj.bjc.6605384. PMID: 19956171; PMCID: PMC2790696.

16. Ramos M, Esteva M, Cabeza E, Campillo C, Llobera J, Aguiló A. Relationship of diagnostic and therapeutic delay with survival in colorectal cancer: a review. Eur J Cancer. 2007 Nov;43(17):2467-78. doi: 10.1016/j.ejca.2007.08.023. Epub 2007 Oct 10. PMID: 17931854.

APPENDIX 1

SAJS Guidelines for research article

General specifications of manuscripts

Format of text: Manuscripts should be typed in Arial font 11 point with one and a half line spacing. Please save manuscripts for upload in MS Word format, not in PDF format. Please ensure authors' names and affiliations and any acknowledgements are omitted [and provided on the title page] to facilitate the double-anonymous review process.

Length requirements:

Type	Word count (including abstract, significance and references)	References	Figures and/or tables
Research Article	6000	60	10

Unique fonts: If these are necessary, they should be embedded in the document in order to ensure they display correctly.

Layout: Start each paragraph at the margin (no tabs to indent first line). Include a line space between paragraphs to separate. Numbered paragraphs/sections are not permitted.

Heading styles: First level headings: boldface, normal case, centred, on a separate line, 14pt. Second level headings: boldface, normal case, justified at left margin, on a separate line, 14pt. Third level headings: boldface, normal case, justified at left margin, on a separate line, 12pt. Fourth-level headings: underlined, not bold, normal case, justified at left margin, on a separate line, 12pt.

Spelling: Please use UK spelling and not US spelling. Use IUPAC nomenclature recommendations for chemical elements and compounds.

Quotations in the text: Single quotation marks are used for all quotations; to highlight a quote within a quote, please use double quotation marks. If citations are longer than 30 words, please do not use single quotation marks; rather indent the quotation and italicise it.

Footnotes may not be used in the text but may be used for Tables and Figures.

Equations: Use English Equation Editor if you have equations in your manuscript; other versions will not convert correctly.

Acronyms: If a phrase with an established acronym or abbreviation is used, and appears more than five times in your article, please include the acronym/abbreviation in brackets after first mention of the phrase, then use the acronym/abbreviation only. Please note that you should not define acronyms or abbreviations in any of your headings. If either has been used in your abstract/summary, you need to define them again on their first use within the main text. Abbreviations/acronyms used in figures and tables must be explained in the heading/legend or footnote.

Units: The use of units should conform to the SI convention and be abbreviated accordingly. Metric units and their international symbols are used throughout, as is the decimal point (not the decimal comma), and the 24-hour clock.

Spacing and punctuation: There should be one space (not two) between sentences; one space before unit terms (e.g. 5 kg, 5 mm, 5 mmol, 5 days, 5 °C); but no space before %. Thousands/millions are marked with a space, not a comma, from 10 000 (e.g. 10 000, 1 000 000 but 1000). Ranges are expressed with an extended hyphen, not with a short hyphen (e.g. 1990–2000).

Dates: Dates must be written as: 12 July 2012.

Figures and Tables: Figures and Tables must be included in the Main Document at the end together with the captions. Abbreviations/acronyms used in figures and tables must be explained in the captions or footnotes.

Submission of manuscripts for consideration

Manuscripts for peer review must be submitted online. Please ensure that you have complied with the guidelines and completed the Publishing Agreement before you start the

submission process. Submissions that are incomplete or do not comply with the instructions will be returned.

Fees

There are no submission fees or article-processing charges.

Readability

As the journal has a multidisciplinary focus, manuscripts must be written in a manner and style that is intelligible to specialists and non-specialists alike. Articles are judged by reviewers at the discretion of the editors. Contributions should therefore be written clearly and simply so that they are accessible to readers in other disciplines and those for whom English is not a first language.

Plagiarism

Plagiarism is when you use someone else's work (book, article, website, etc.) or idea without acknowledging them as the source, whether it be copied verbatim or paraphrased. Manuscripts submitted online will be screened for potential plagiarism before peer review using similarity detection software. All cases of suspected or alleged plagiarism are considered very seriously in accordance with the journal's Plagiarism Policy.

Permissions

Permission must be obtained from the copyright owner for the use of quotations, illustrations, tables and other materials taken from previously published works that are not in the public domain. The author is responsible for the payment of any copyright fee(s) if these have not been waived. The letters of permission must accompany the manuscript. The original source(s) must be mentioned in the figure legend or as a footnote to a table.

Ethical guidelines

Submissions involving research conducted on human or non-human vertebrates must meet the highest standards regarding both the ethical consideration given and reporting of the procedures followed. Full details are necessary so that a non-specialist reader can appreciate the need for the research undertaken.

All reported research involving humans or other animals must be approved prior to commencement of the study by an institutional ethics committee. The name of the approving body and a reference number (if provided) must be included in the Methods section of the manuscript.

In addition, all manuscripts describing research involving human subjects, tissue or data must also indicate that informed consent was obtained and that the principles of the Declaration of Helsinki were adhered to. All manuscripts describing research involving non-human animals must also indicate that the ARRIVE guidelines for reporting in vivo animal experiments were adhered to. Proper reporting should include the number, sex, age, weight, health status and source of the individuals used, as well as full details of anaesthesia and surgical procedures. The Declaration of Helsinki and the ARRIVE guidelines are also available from the Editorial Office. Manuscripts failing to adhere to these instructions will not be considered for publication.

Deposition of new sequences and structures

The reporting of new or not previously reported structures or sequences (such as chemical and crystallographic structures, synthetic compounds, genes and proteins) must include the accession numbers of the relevant database in which they have been deposited. Details of the synthesis of new structures and compounds must also be given. See Data sets for deposition of other data.

Authorship

Authorship of a manuscript should be agreed upon by authors prior to submission. Generally, a person attributed as an author should have contributed to (1) the conception and design of the study and data collection or data analysis; (2) writing or revising the manuscript; and (3) final approval of the version to be published. The corresponding author is responsible for ensuring that all listed authors have agreed to: (1) the authorship as listed and in the order given by the submitting author; (2) the content of the manuscript; and (3) its submission to the journal. All authors are required to sign the Publishing Agreement before submission. Any requests for changes in authorship prior to publication should be accompanied by a new Publishing Agreement.

Authors' contributions

The contributions of each author should be listed and submitted as a separate file. Contributions should be specified along the lines of: conceptualisation; methodology; data collection; sample analysis; data analysis; validation; data curation; writing – the initial draft; writing – revisions; student supervision; project leadership; project management; and funding acquisition. For a brief description of each contribution please click here.

Author information

This section may be included should you wish to provide information on the author(s) that may be directly relevant to readers, such as qualifications, and positions or appointments.

If a group is given as the author, the individual members of the group can be listed in this section.

Reviewers

Authors must suggest three potential reviewers to evaluate their work. The names and full contact details (including email) of the suggested reviewers must be provided in the cover letter. Suggested reviewers should not be people with whom the authors have recently collaborated or published. Authors may also indicate if they oppose any potential reviewers. The final selection of reviewers is, however, at the discretion of the editors. Please see Peer-review Process for more information on the peer-review process.

APPENDIX 2

An Assessment, with NICE Guidelines as a Benchmark, of Delay to Care in a Cohort of Colorectal Cancer patients seen in the Witwatersrand University Academic Complex

CANDIDATE: Kimisha Singh (MBCHB KZN)

Student Number: 1828913

Protocol for Mmed (Surg)

Supervisors: Dr Brendan Bebington MBChB; FCS(SA)

Specialist Colorectal surgeon WDGMC

Dr Daniel Surridge MBBcH (UP); FCS (SA); MMed (surg)(Wits)

Cert. Gastroenterology Surg (SA)

Table of Content

1. List of abbreviations …….
2. Abstract ……..…
3. Introduction/background ……..……
4. Study objectives ……..……
5. Methods ……..……
6. Data analysis ……..……
7. Benefit ……..……
8. Ethics ……...
9. Timing ….....
10. Cost ……..……
11. References ……..…
12. Appendix A ……..….

List Of Abbreviations

MDT – multi-disciplinary team

CRC- Colorectal cancer

ASR- Age standardised rates

CHBAH – Chris Hani Baragwanath Academic hospital

CMJAH – Charlotte Maxeke Johannesburg Academic Hospital

WDGMC- Wits Donald Gordan Medical centre

MRC – Medical research council

ABSTRACT

Colorectal cancer is one of the commonest cancers in South Africa. Early identification and initiation of treatment is linked to increased survival rate, while delay in treatment is associated to poorer outcomes of affected patients. Currently there is no available screening or standardised time parameters defining acceptable progression of investigationary and treatment related events in the management of patients with colorectal cancer for South African patients.

A retrospective case control study on a prospective database will be conducted to determine the delay in presentation, diagnosis and treatment of colorectal cancer in CMJAH, CHBAH, WDGMC and Edenvale. Using a database created for the Wits Academic hospitals by the MRC Colorectal Cancer Group. The data base includes patient records, histology results and treatment details of colorectal patients from each hospital. All confirmed colorectal cancer patients treated during the period 1 Jan 2016 – 31 Dec 2019 (last follow-up on 31 Mar 2020), will be reviewed and results compared between respective hospitals.

INTRODUCTION

Colorectal cancer is one of the commonest cancers in the world. According to Globacan 2012 it is the third commonest cancer in men affecting 10% of the total 746 000 cases reported. It is the second most common in female affecting 9.2% of the total 614000 cases worldwide. Incidence rates were found to be highest in Australia and New-Zealand with an ASR 44.8 per 100 000 in men and 32.3 in females per 100 000. The lowest incidence was found in Western Africa 4.5 and 3.8 per respectively for males and females.[17] Mortality rates have been decreasing through the years at a rate of 3% per year [14]In the developing world, however, there is a noticeable increase in age stanerdised incidence rate, accompanied with a concurrent increase in mortality from colorectal cancer[23] . Poorer survival was found in less developed regions according to Globacan with a reported 52% of 694 000.[17] The National Cancer registry of South Africa reports, colorectal cancer is the second most common cancer in males. With an estimated lifetime risk of 1:81.[11] It makes up 4.98% of all cancers affecting males. In females it is the fourth commonest cancer, with a lifetime risk of 1:135 and makes up 4.14% of all cancers affecting females. [11]All these trends suggest colorectal cancer may need to be taken into consideration when planning for future health care in South Africa.

Because malignant progression in CRC may take up to 5 to 8 years, timeous detection of asymptomatic lesions and prompt management of established cancer may impact favourably on the incidence and mortality associated with this disease.[5] In South Africa no screening program for Colorectal cancer has ever been implemented. Without screening tests available the vast majority of colorectal cancers present on the basis of their symptoms alone.[5] For this reason patients with colorectal cancer tend to present with advanced disease as might be apparent in this cohort of patients sampled[5] Stage of diagnosis is an important indicator of outcome in this disease.[11] Screening programmes for CRC, if deemed of economic value, could help reduce mortalities . There is no clarity in this regard in South Africa hence prompt symptom identification and diagnosis may be important if the outcome of care is hoped to be improved.[11]

This conjecture is questionable. The effect of delay in diagnosis occurs against a background of multiple unexplored variables effecting outcome of care in the South

African context.[8] Decrease in mortality rate through screening programmes show benefit in early diagnosis in asymptomatic patients; there is uncertainty whether early diagnosis in symptomatic patients improves overall survival in CRC.[1] There is belief that prognosis in these patients is largely dependent on the delay in presentation, diagnosis and treatment.[1] Some studies however suggest that delay from referral to diagnosis showed no correlation with later stage disease and poorer prognosis.[12]

Factors associated with delay

There are many attributable factors to delay in diagnosis. An important consideration is CRC symptoms are non-specific, hence early detection and recognition of symptomatic colorectal cancer by both the patient and physician is often a challenge.[2,5]Delays to care could broadly divided as follows:

1. Patient delay – time of first symptom to first consultation.[1,3,6]
2. Referral delay- date of first consultation to referral to another hospital/unit [3]
3. Diagnostic delay- time from seeking medical advice/referral to histopathological diagnosis of CRC[1,3]
4. Treatment delay – If time taken between diagnosis and treatment [3]

Patient Delay

Patients may delay reporting symptoms because of ignorance of their significance of their symptoms, embarrassment of consulting a doctor or even fear of cancer diagnosis.[2,3,4] Low socio economic status, patients living in rural areas and health care costs may also contribute to delay and hence is associated with later stage diagnosis.[7]

Hospital and GP delay

GP, primary care clinic and hospital delays may be due to inadequate investigations , wrong diagnosis and false negative results from investigations.[1] Long waiting periods for patients will also inevitably impact outcomes.[5] Waiting periods are

influenced by various factors such as time taken to conduct appropriate testing , surgical consultation , pre-operative assessments in terms of staging , discussion at MDT and finally waiting for actual surgery.[21] Other factors include volume of patients , requiring pre-op testing and surgery, limited availability of physical and paucity of human resources.[21]

Diagnostic Delay

Diagnostic delay is defined as the time from first symptom to initiation of treatment or decision not to treatment.[3]As the first of the potential delays it is the most difficult to assess and is likely to be the most difficult to alter, where not clear structured health care systems for colorectal cancer patients exist.[3]

Treatment Delay

Until recently (2011) Netherlands ,like South Africa at present, had no CRC screening program, with diagnosis of CRC being largely based on symptomatic presentation in that country. In this period of the Dutch past it was noted that a third of patients diagnosed with colorectal cancer only began treatment in 3 months of diagnosis.[3] Similarly in a Canadian study of patients with rectal cancer, if delay in treatment from onset of symptoms is more than 60 days the risk of presenting advanced rectal cancer is doubled, which is likely to impact on local recurrence and overall survival.[5]There is one proviso when considering rapid provision of therapy: emergency presentation of colorectal cancer usually suggests advanced disease with a short diagnostic delay in CRC patients. These patients are likely to have a poor overall survival despite their truncated route to care.[1l] Despite this there is no optimal time to elective colon resection but surgery within a 6 week interval has not worsened CRC survival or mortality rates.[15]Not withstanding the controversies surrounding delay in presentation of symptomatic patients in the developed world all , the situation with regards the barriers to care in South African CRC patients is largely unexplored and as they invariably present unscreened and as a consequence of symptoms the assessment of what defines outcome is even more contentious.

CRC related mortality has shown to be reduced in early detection of (pre) malignant lesions in the asymptomatic , average risk group.[1] However controversial studies exist between early diagnosis and treatment in the symptomatic group of patients.[1]

The complex relationship between duration of CRC symptoms, stage of cancer and survival rate have brought about conflicting evidence.[1]

No standardised time frame is currently available internationally with regard to these delay parameters.[18] However the cancer research society UK has produced three broad time periods as to which times patients should be referred , when initial treatment should begin and by when definitive treatment should be implemented.[18] It is this time frame that will be used to compare the equivalent in the study sample

According to cancer research UK, suspected cancer should be seen within 2 weeks of referral/presentation by a specialist.[18] This time interval supports early diagnosis and improved survival of patients.[18] Once the decision to treat cancer is made , first cancer treatment should be started within the first 31 days of this decision.[18] First definitive treatment of cancer should occur within 2 months/62days from initial GP referral/presentation of the patient.[18]

Health services internationally varies structurally hence different definitions of delay are noted in different studies however there is some broad consensus.[19]Despite uncertain evidence the NHS still has strict targets in the referral , diagnosis and treatment in CRC patients, in an attempt to decrease delays in these periods this is guideline based and patient driven.[10] In 2000 the NHS had concerns about delay in diagnosis of CRC and the two week rule was passed.[13] It proposes patients with high risk symptoms would be seen within two weeks by a specialist.[13]Also recommended was, a guideline, which includes the urgent symptoms that warrant referral and is believed to identify 90% of patients with colorectal cancer.[13]

Summary and reason for study?

Properly implemented screening programs are probably in part responsible for a decrease in Mortality rate reported in developed nations.[13,18] Currently there is no recognised screening programme for CRC available in South Africa. Diagnosis of CRC is dependent on symptom presentation of patients.[22] Delay in diagnosis, stage of disease and treatment is therefore critically important when screening is not standard policy. Assessment of these delays is made benchmarked with the NICE guidelines.[22]There is no clarity whether South Africa should implement screening for

colorectal cancer and for this reason care in insuring prompt attention to the symptomatic patient, punctual implementation of investigation and treatment gives the impetus to this study.[18]

Delay in treatment in CRC has not been explored in South Africa. Therefore, this study aims at identifying treatment delay and compare this to an established guideline as provided by the NHS. This may give some insight into the circumstance of a cohort of South African CRC patients as they pass through care.

STUDY OBJECTIVE

1. To determine if there is a comparative difference in the delays in the course of patient care for CRC treatment in the four medical centres of Wits when evaluated against international standards i.e., NHS guidelines
2. Within the sub-groups (private/public, race, age, genders, regional/tertiary and quaternary care) of the sample analysed are their differences in these management delay with reference to the NICE guidelines
3. To determine 90 mortality outcome for these patients after major surgical resection

3.Methods

3.1 Study design

Retrospective , case control study on a prospective database

3.2 Site of study

CMJAH (quaternary hospital), CHBAH (tertiary hospital), WDGMC(private) and Edenvale Hospital)

3.3 Study population

All patients histologically diagnosed with adenocarcinoma of the colon and rectum, seen by clinicians at the study sites and brought to the attention of the research sister attached to the MRC research project.

3.4 Sampling

Subjects' data will be used from the existing database in WDGMC, which is dependent on referral by the treating clinician to the research body of the four hospitals involved in the study

Time period of review is 1 Jan 2016 – 31 Dec 2019 (last follow-up at 31 Mar 2020).

Sample Size: 716 patients

Inclusion criteria

- All patients diagnosed with CRC symptomatic and asymptomatic and presenting at any malignant stage or point of care.
- Histologically proven adenocarcinoma of the colon.
- Presenting within 1 year of diagnosis over the age of 18 and derived from both public and privately treated patients

Exclusion criteria

- Patients with recurrent cancer
- Patients with synchronous lesions
- Patients with anal carcinoma
- Patients who had received treatment before being seen at the specialist centre
- Patients diagnosed more than 1 year before presentation at the specialist centre

3.5 Measuring tool

Patient data will be accessed via the electronic data base, the MRC prospective colorectal Redcapp data base which collectively has data on all

CRC patients within the 4 institutions. Data is collected using a questionnaire which is attached

3.6 Data collection

Collected data will be recorded on data sheets on Excel . The data is subject to stats evaluation and addition to the redcap database . The accuracy of the data is verified by the WDGMC research team in conjunction with the research staff attached to the MRC project.

3.7 Sources of bias

The data is questionnaire based and is therefore subject to interpretation
Only patients presented to the four Wits centres are recorded and data on the patients are only captured if data capturers are told about each patient. This then is a sample of patients in Gauteng and is in effect not a true reflection of that Provinces total number of cases and certainly represents only a small fraction of South Africa's burden.

4.Data Analysis

Statistical analysis will be conducted to identify if there is a significant delay in presentation, diagnosis and treatment when compared to NHS standards of CRC. Regressional analyses of the subgroups will define the differences in intervals to care as well as outcomes. Outcomes will be measured using 90 days mortality. Comparative assessment of these delays and parameters of outcome will also be made between the public and private sector

5.Benefits

The study will reflect the delay in presentation , diagnosis and treatment of CRC in patients at our facilities . This will, through identifying the extent of the delay, hopefully benchmark efforts in improving access to care and implementation of vital services. This may help in initiating guidelines for standards of care in the management of CRC in South Africa

6.Ethics

Clearance to proceed with the retrospective study will be obtained from the ethics committee of the University of the Witwatersrand

7. Time Line

	Mar	April	May	June	Jul	Aug	Sept	Oct	Nov	Dec	Jan	Feb	Mar	Apr
Literature review	x	x												
Preparing protocol			x	x	X									
Protocol assessment						x								
Ethics application							X							
Collecting data								x	X	x				
Data analysis											x	x		
Writing up – thesis													x	x
Writing up – paper													x	x

8. Cost

No major expenses are expected

REFERENCES

1.Abu-Helalah MA, Alshraideh HA, Da'na M, Al-Hanaqtah M, Abuseif A, Arqoob K, et al. Delay in Presentation, Diagnosis and Treatment for Colorectal Cancer Patients in Jordan. Journal of gastrointestinal cancer. 2016;47(1):36-46.

2. National Institute for Health and Care Excellence. Improving outcomes in Colorectal cancers 2004 [updated 04 February 2016. Available from: https://www.nice.org.uk/guidance/csg5/resources/improving-outcomes-in-colorectal-cancer-update-pdf-773376301.

3. Terhaar sive Droste JS, Oort FA, van der Hulst RW, Coupe VM, Craanen ME, Meijer GA, et al. Does delay in diagnosing colorectal cancer in symptomatic patients affect tumor stage and survival? A population-based observational study. BMC Cancer. 2010;10:332.

4. Ortiz-Ortiz KJ, Rios-Motta R, Marin-Centeno H, Cruz-Correa MR, Ortiz AP. Emergency Presentation and Short-Term Survival Among Patients With Colorectal Cancer Enrolled in the Government Health Plan of Puerto Rico. Health services research and managerial epidemiology. 2016;3:2333392816646670.

5. Tomlinson C, Wong C, Au HJ, Schiller D. Factors associated with delays to medical assessment and diagnosis for patients with colorectal cancer. Canadian Family Physician. 2012;58(9):e495-501.
6. Pedersen AF, Hansen RP, Vedsted P. Patient Delay in Colorectal Cancer Patients: Associations with Rectal Bleeding and Thoughts about Cancer. PLOS ONE. 2013;8(7):e69700.
7. Forbes LJ, Warburton F, Richards MA, Ramirez AJ. Risk factors for delay in symptomatic presentation: a survey of cancer patients. British journal of cancer. 2014;111(3):581-8.
8. McLachlan S, Mansell G, Sanders T, Yardley S, van der Windt D, Brindle L, et al. Symptom perceptions and help-seeking behaviour prior to lung and colorectal cancer diagnoses: a qualitative study. Family Practice. 2015;32(5):568-77.
9. National Institute for Health and Care Excellence. Colorectal Cancer: Diagnosis and management [updated December 2014. Available from: https://www.nice.org.uk/guidance/cg131.
10. Murchie P, Raja EA, Brewster DH, Campbell NC, Ritchie LD, Robertson R, et al. Time from first presentation in primary care to treatment of symptomatic colorectal cancer: effect on disease stage and survival. British journal of cancer. 2014;111(3):461-9.
11. The Cancer Association South Africa Fact Sheet on Cancer 2011 [updated August 2016. Available from: http://www.cansa.org.za/files/2016/08/Fact-Sheet-Cancer-NCR-2011-web-Aug-2016.pdf.
12. Elferink MA, Pukkala E, Klaase JM, Siesling S. Spatial variation in stage distribution in colorectal cancer in the Netherlands. European journal of cancer (Oxford, England : 1990). 2012;48(8):1119-25.
13. Shabbir J, Vijayan V, Silavant M, Fowler AL, Cook TA, Lucarotti ME. Two week rule referral for patients with colorectal cancer below the age of 50; Are we being ageist? The Surgeon. 2009;7(5):276-81.
14. Aakif M, Balfe P, Elfaedy O, Awan FN, Pretorius F, Silvio L, et al. Study on colorectal cancer presentation, treatment and follow-up. International journal of colorectal disease. 2016;31(7):1361-3.
15. Compton CC, Greene FL. The Staging of Colorectal Cancer: 2004 and Beyond. CA: A Cancer Journal for Clinicians. 2004;54(6):295-308.

16. de Sousa JB, Souza CS, Fernandes MB, de Castro Duraes L, de Almeida RM, Dos Santos AC, et al. Do young patients have different clinical presentation of colorectal cancer causing delay in diagnosis? International journal of colorectal disease. 2014;29(4):519-27.
17. World Health Organisation. Globocan 2012: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2012 2012 [Available from: http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx?cancer=colorectal
18. Cancer Research UK. Bowel Cancer 2015 [updated 30 September 2015. Available from: http://about-cancer.cancerresearchuk.org/about-cancer/bowel-cancer.
19. Pruitt SL, Harzke AJ, Davidson NO, Schootman M. Do diagnostic and treatment delays for colorectal cancer increase risk of death? Cancer causes & control : CCC. 2013;24(5):961-77.
20. Simunovic M, Gagliardi A, McCready D, Coates A, Levine M, DePetrillo D. A snapshot of waiting times for cancer surgery provided by surgeons affiliated with regional cancer centres in Ontario. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne. 2001;165(4):421-5.
21. Gillis A, Dixon M, Smith A, Law C, Coburn NG. A patient-centred approach toward surgical wait times for colon cancer: a population-based analysis. Canadian Journal of Surgery. 2014;57(2):94-100.
22. American Cancer Society. Early detection, diagnosis and staging 2017 [Available from: https://www.cancer.org/cancer/colon-rectal-cancer/detection-diagnosis-staging.html.
23. Arnold M, Sierra MS, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global patterns and trends in colorectal cancer incidence and mortality. Gut. 2016.