The profile of women who died with a diagnosis of Gynecological Cancer at Charlotte Maxeke Johannesburg Academic hospital over a four-year period.

Mongezi James Siqana

Student number: 2336050

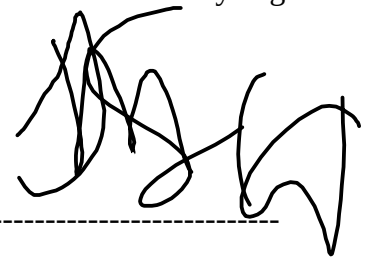
A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfillment of the requirements for degree of Master of Medicine in Obstetrics and Gynecology.

Johannesburg, 18 March 2022

DECLARATION

I, Dr Mongezi James Siqana, declare that this Research Report is my own, unaided work. It is being submitted for the degree

of Master of Medicine at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.



(Signature of candidate)

18/03/2022

DEDICATION

I dedicate this Master of Medicine Research Project to my late father, Mr. Themba Johny Siqana who always encouraged me to be the best that I can and not permit any circumstances limit my achievements. His spirit lives forever and his teachings will always guide me until eternity.

1964 -2020

PRESENTATIONS

The findings of this research report were presented at the Wits Post Graduate Research meeting held on 08/07/2020 at the Rahima Moosa Mother and Child Hospital.

ABSTRACT

Background: A substantial number of women die of gynecological cancer each year. The aim of the study was to investigate the profile and complications among women who died with a diagnosis of gynecological cancer while admitted in the gynecological oncology ward at Charlotte Maxeke Johannesburg Academic Hospital over a four – year period.

Objectives: To describe the demographic profile of these participants, to determine the common cancer type and medical complications at presentation, lastly to determine treatment related complications based on the treatment modality received among the study cohort.

Methods: This was a retrospective review of participant's records between 01 July 2015 to 31st July 2019. Data regarding variables mentioned above was extracted using the ward registry to identify files that met the inclusion criteria onto our data collection sheet. Descriptive statistic principles were applied during analysis.

Results: 48 files met the inclusion criteria of the 368 admissions. Mean age 53 years (SD) (19-88). South African (SA) citizens 41 (85%), non-SA were 7 (15%). Africans 44 (92%), whites 3 (6%) Coloureds 1 (2%). Cervical cancer 18 (37, 5%), 13 (27, 7%) ovarian cancer, 12 (25%) endometrial cancer and 5 (9.8%) others. Obstructive uropathy 12 (25%) at presentation, hemorrhage 14 (29%) and sepsis 15 (31) after or at surgery.

Conclusion: Most young women die from cancer and treatment related complications, commonly due to cervical cancer. Hemorrhage and sepsis were associated with death. More emphasis on gynecological cancers education, importance of screening, early presentation to healthcare facilities and availability of more facilities that offer gynecologic oncology treatment will benefit women in SA by decreasing the long waiting periods for theatre and chemoradiation.

ACKNOWLEDGEMENTS

I would like to extend my gratitude to the following entities and individuals:

- CMJAH National Health Laboratory Services for providing me with histologic results without which this MMed would not have been possible.
- To members of CMJAH medical record keeping department for providing me with files and records for this research report.
- Professor L Chauke who inspired and guided me to select this research topic.
- My supervisors, Dr L Mbodi and Prof L Chauke, for their patient mentorship and assistance through this project.
- My Clinical Mentor Dr ZIM Lenake for always being supportive.

TABLE OF CONTENTS **PAGES**

LIST OF FIGURES

LIST OF TABLES

LIST OF ABBREVIATIONS

CMJAH	Charlotte Maxeke Johannesburg Academic hospital
CEO	Chief Executive Officer
DM	Diabetes mellitus
ED	Emergency Department
HAART	Highly active antiretroviral therapy
HPV	Human Papillomavirus
HIV	Human immunodeficiency virus
HL	Hodgkin's lymphoma
HPT	Hypertension
HREC	Human Research Ethics Committee
ICU	Intensive Care Unit
Redcap	Research Electronic Data Capture
SA	South Africa
SAJOG	South African Journal of Obstetrics and Gynecology
WITS	University of the Witwatersrand

JOURNAL ARTICLE

The profile of women who died with a diagnosis of Gynecological Cancer at Charlotte Maxeke Johannesburg Academic hospital between 1 July 2015 and 31 July 2019.

Siqana Mongezi, [a] Mbodi Langanani, [b] Chauke Lawrence [c]

[a] Registrar(O&G), University of the Witwatersrand, Charlotte Maxeke Johannesburg Academic Hospital, MBCHB(UFS)

[b] Specialist Obstetrician/ Gynecologist, MBCHB(MEDUNSA), Dip. Obst (SA), FCOG(SA), MMed (WITS), MSc((Medicine)(WITS), Post Grad Dip Health Sc Ed (WITS), Cert Gynae Onc (SA), Department Obstetrics and Gynecology, Charlotte Maxeke Johannesburg Academic hospital

[c] Specialist Obstetrician/ Gynecologist, MBCHB(UCT), Dip HIV(SA), B.Th. (ATS), MMed (UP), FCOG(SA), MSc (Clinical research) (Liverpool), cert Maternal and Fetal medicine (SA), Head of the Department Obstetrics and Gynecology, Charlotte Maxeke Johannesburg Academic hospital.

[a] Corresponding author email: mongezisiqana@gmail.com

ABSTRACT

Background: A substantial number of women die of gynecological cancer each year. The aim of the study was to investigate the profile and complications among women who died with a diagnosis of gynecological cancer while admitted in the gynecological oncology ward at Charlotte Maxeke Johannesburg Academic Hospital over a four – year period.

Objectives: To describe the demographic profile of these participants, to determine the common cancer type and medical complications at presentation, lastly to determine treatment related complications based on the treatment modality received among the study cohort.

Methods: This was a retrospective review of participant's records between 01 July 2015 to 31st July 2019. Data regarding variables mentioned above was extracted using the ward registry to identify files that met the inclusion criteria onto our data collection sheet. Descriptive statistic principles were applied during analysis.

Results: 48 files met the inclusion criteria of the 368 admissions. Mean age 53 years (SD) (19-88). South African (SA) citizens 41 (85%), non-SA were 7 (15%). Africans 44 (92%), whites 3 (6%) Coloureds 1 (2%). Cervical cancer 18 (37, 5%), 13 (27, 7%) ovarian cancer, 12 (25%) endometrial cancer and 5 (9.8%) others. Obstructive uropathy 12 (25%) at presentation, hemorrhage 14 (29%) and sepsis 15 (31) after or at surgery.

Conclusion: Most young women die from cancer and treatment related complications, commonly due to cervical cancer. Hemorrhage and sepsis were associated with death. More emphasis on gynecological cancers education, importance of screening, early presentation to healthcare facilities and availability of more facilities that offer gynecologic oncology treatment will benefit women in SA by decreasing the long waiting periods for theatre and chemoradiation.

INTRODUCTION

Gynecological cancers are a major cause of morbidity and mortality worldwide. The International Agency for Research on Cancer estimates that 19% of the 5.1 million deaths from cancers are gynecological (1). Globally, cervical cancer is the most common gynecological cancer responsible for the high number of cancer related deaths among women (2). Cervical cancer related mortality varies between countries, varying age standardize mortality rate of 0.77/100 000 in Israel and 14.87/100 000 in Chile. In SA, the age-standardized mortality rate for cancer of the cervix was found to be between 3.6 in metropolitan Whites, 30.2 in non-metropolitan Coloureds and 25.7 in metropolitan Blacks. Coloureds and Blacks in SA were found to be at a higher risk of dying because of cancer of the cervix (2).

Globocan 2012 lists the mortality rate of female cancers in both less developed and more developed countries as listed on figure 1 below.

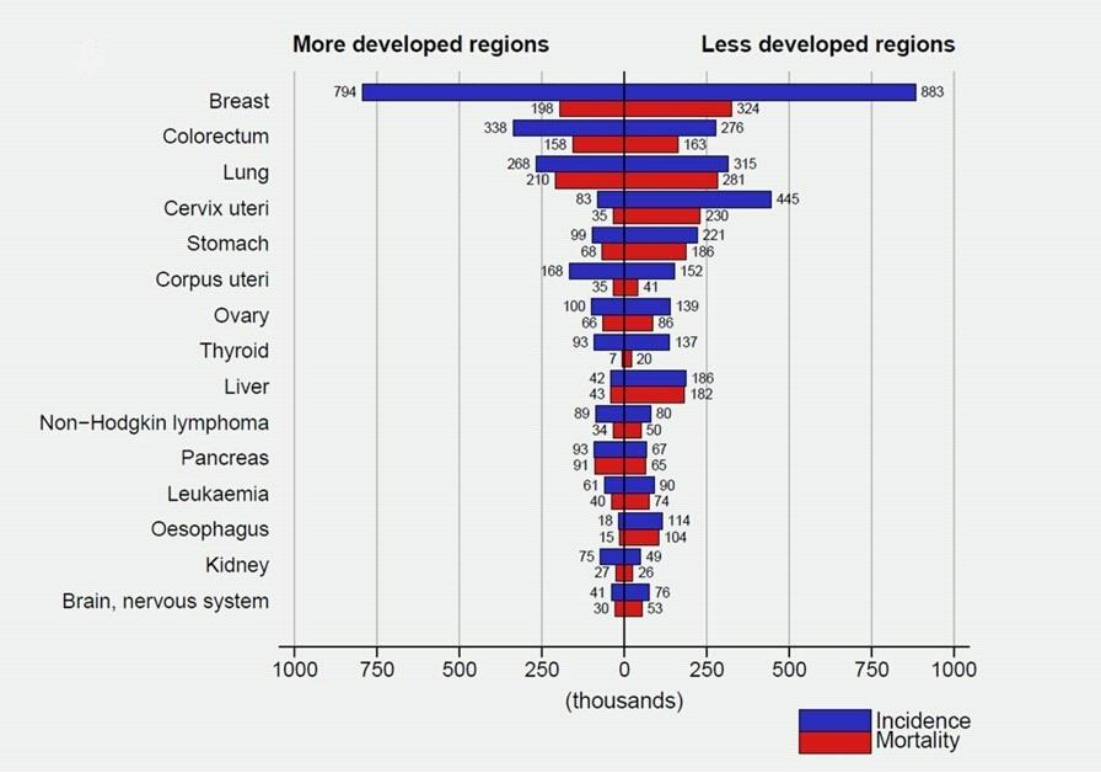


Figure 1. Incidence (in thousands) of cancer and mortality (in thousands) in females from more developed and less developed regions of the world in 2012. (3) (Used with permission from Ferlay et al).

The aim of the study was to investigate the profile and complications among women who died with a diagnosis of gynecological cancer while admitted in a gynecological ward at CMJAH over a four – year period. Identifying the common and preventable factors related to death in cancer women will help in designing programs that will aim at reducing cancer and cancer-related complications deaths.

METHODS

CMJAH is one of more than 400 National Hospitals in South Africa. The hospital is in the north of Johannesburg, provides services to two metros and one district, namely Ekurhuleni, City of Johannesburg, and the West Rand district. It is one of the three major training hospitals for the Faculty of Health Sciences, University of Witwatersrand.

It has 1088 beds, and the Department of Obstetrics and Gynecology shares these beds with other departments. The hospital has well-functioning ICU and High care facilities, radiology, Blood bank and National Health laboratory services.

It is also one of the two hospitals that provide radiation oncology services in the Gauteng province. It is the only accredited hospital to offer gynecologic oncology services for all patients with gynecologic malignancies with regards to all hospitals that has affiliation with the University of Witwatersrand. There is only one Gynecology oncology consultant and one registrar at any given time who takes care of all gynecologic malignancy cases. One clinic day a week is allocated to gynecology oncology.

This was a retrospective review and descriptive statistic principles were applied during analysis. We identified all participants who were admitted in the ward with a diagnosis of gynecological cancer during our study period by using a ward admission registry that is kept by the ward clerk. We identified all participants by using gynecological cancer diagnosis and the outcome of those

patients admitted during our study period as our selection criteria. Participants were searched using personal details, diagnosis, type of treatment received and outcomes. We then extracted basic demographic information, diagnosis, complications, and treatment modality using specially designed data collection sheet. Data was cleaned, coded, and transferred to an excel document. Data analysis was in the form of descriptive statistics (obsolete numbers and frequencies) using the Statistical Package for Social Science (SPSS). This study was approved by the University of Witwatersrand Human Research Ethics Committee (Medical) with clearance number M200880.

RESULTS

Demographics

There was 368 cancer related admissions and 51(13.8%) cancer-related deaths during the study period. However only 48 files were available.

Majority of women who died during the period of study were above 50 years of age and ranged between 19 and 88 years. Results shows the most affected age group were women between 51-60 years of age where 10 of 48 (20,8%) died together with those who were above 70 years where the same percentage of 20,8% died during the study period. The mean age of the participants was 52.7 years (SD ±16.92).

Most participants were of black race and of South African citizenship. We found that these participants were mostly unemployed and the most common comorbidities that these patients had was HIV and hypertension. Demographic details are described further on table 1 below.

Table 1: Demographic profile of participants who died with a diagnosis of gynecological cancer

Parameter	Number
Age	
Less than 30	6.3(13.1%)
30-40	18.8(39.2%)
41-50	18.8(39.2%)
51-60	20.8(43.3%)
61 -70	14.6(30.4%)
>70	20.8(43.3%)
Citizenship	
South Africans	41(85%)
Non -south African	7(15%)
Race	
Blacks	44(91.6%)
Whites	3(6.3%)
Coloured	1(2.1%)
Indians	0(0%)
Employment status	
Employed	11(22.9%)
Unemployed	37(77.1)

Co morbidities	
Hypertension	20(41.7%)
HIV	20(41.7%)
Others (PTB, Previous CVA, COPD, B-Cell Lymphoma)	9(18.8%)
Diabetes mellitus	7(14.6%)

Cancer type

Out of the 368 participants that were admitted in the gynecological ward, the most common cancer type that contributed significantly to the total number deaths (48) in women with a diagnosis of gynecological cancer was cervical cancer (14/ 48), followed by ovarian cancer (13/48) then endometrial cancer (12/48). Table 2 summarizes the cancer types, numbers admitted and deaths.

Table 2: Cancer types, numbers admitted and deaths

Cancer type	Cervical	Ovarian	Endometrial	Vulvar	Gestational trophoblastic neoplasia	Total
Admissions	144(39.9%)	77(20.9%)	78(21.2%)	64(17.0%)	5(1.6%)	368
Death (on included patients)	18(37.55%)	13(27.7%)	12(25%)	3(6.3%)	2(4.2%)	48

Complication at presentation

Obstructive uropathy was the most common complication related to the malignancy. This was more common in cervical cancer patients (16/18), Ovarian cancer (4/13), and Endometrial cancer (6/12). Thrombo-embolism was also observed in cervical cancer (2/18), Endometrial cancer (2/12), Ovarian Cancer (2/13) and Vulval cancer (1/3). Of all the 16 patients who had obstructive uropathy, 15 had advanced, non-operable stages 3B and greater and only 1 was a stage 1B.

Figure 2 below summarizes the complications at presentation. Figure 2 summarizes complications at presentation.

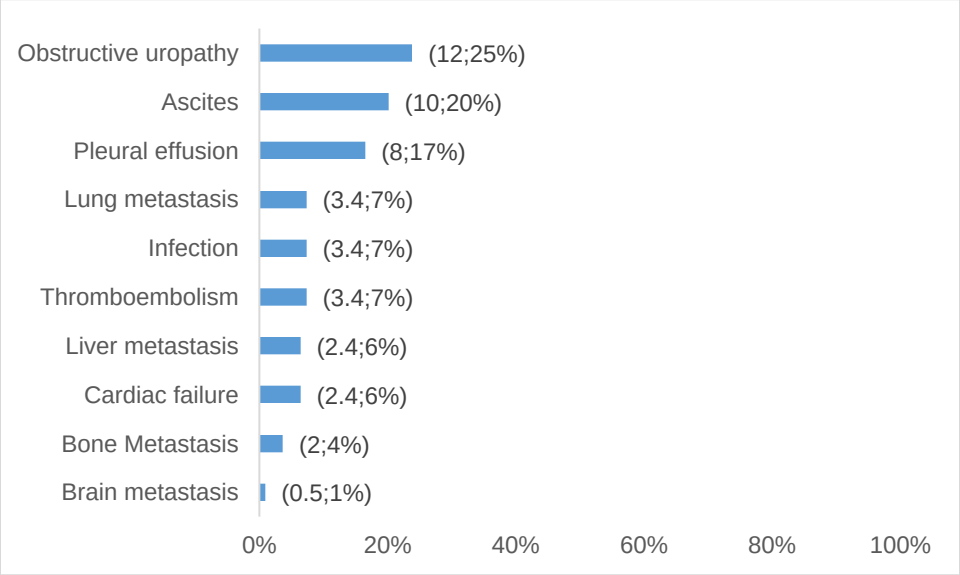


Figure 2: Medical complications among the participants at presentation

Treatment received

Majority of participants in our study received cancer specific treatment 26(54.2%) while 22(45.8%) did not receive treatment directed at treatment for cancer for different reasons. Surgery was the common treatment modality that these participants received followed by radiotherapy. None of the participants in this cohort received chemotherapy alone for the treatment of cancer.

Table 3: Types of treatment received

Treatment	Surgery	Radiotherapy	Chemotherapy	Combination (chemoradiotherapy)	Total

Number	20(76.9%)	5(19.2%)	0(0%)	1(3.8%)	26(100%)

Majority (25%) of the women underwent a minor surgery, biopsy for diagnosis. This was followed by total abdominal hysterectomy (TAH), bilateral salpingo-ophorectomy (BSO) and Omentectomy procedure with curative intent in 19%. Further details on the surgical intervention are described on Figure 3 below. The majority of participants presented with late-stage disease; hence biopsy was the most common surgical modality done as these patients were inoperable. An opportunity was missed for those participants who would benefit from radiation or chemotherapy, especially those with advanced disease because of late presentation or because of long waiting periods for radiotherapy and chemotherapy.

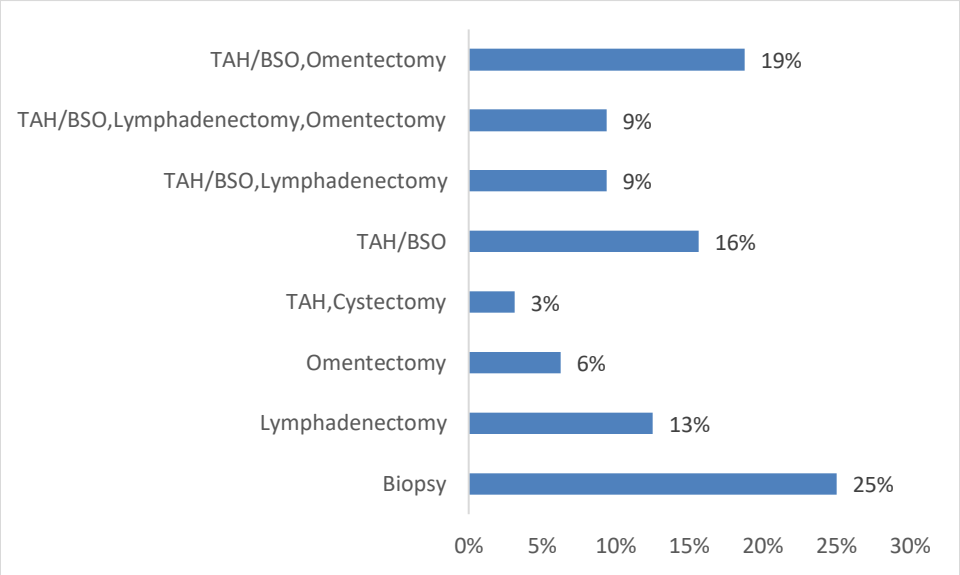


Figure 3: Surgery types received before death

Treatment related complications among the women in our study cohort.

The common complications recorded were sepsis (31%) and hemorrhage (29%) which were observed post-surgical intervention. None of the participants had thermal burns as a complication of surgical treatment modality. Figure 4 summarizes these findings. The majority of participants who demised due to hemorrhage demised due to continued hemorrhage and its sequelae. While participants who died from sepsis had long stay in hospital, failure of sepsis source control and complications of sepsis.

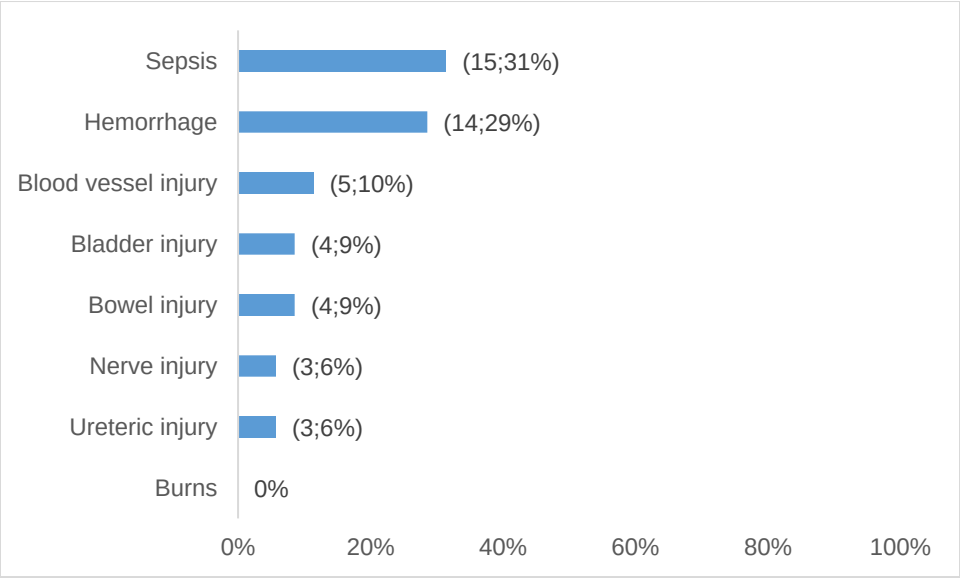


Figure 4: Complications related to surgery performed

DISCUSSION

The mortality rates for gynecological cancer in Denmark were reported to be 2-3-fold higher among women who are 70 + years-old than younger women. Even though over the years there was an observed decrease from 1980 to 2012, it is still 3-4 times higher among the elderly than young women. (4) Our study findings of a mean age of 52.7 years are not in keeping with the above study. However, the mortality in women above 30 years of age is three times more than those 30 years and younger. Even though South African population is still predominantly young compared to most European countries, mortality was increased in older patients. Stats SA also reported that the highest death rate in general in 2017 (not related to cancer) was observed in

ages 60-64 and 65-69 years (5). It is noted that our study was limited to those women who died with a malignancy diagnosis and hence this mean age is not representative of the general population or even the mean age at diagnosis of cancer.

The high mortality rate was commonly found among participants who were black (92%), and cervical cancer being the most common malignancy among these participants. This finding was similar to the reported prevalence in Globocan 2012 (3).

Majority of participants in our study cohort presented with late-stage diseases to healthcare facilities, at stage three (34%), which probably contributed to majority of these patients demising before treatment because of extensive disease at presentation. The most common complication at presentation was of obstructive uropathy (24%) was expected as most pathologies were those of cervical cancer presenting at late stages. Our findings were similar to studies conducted in Arab countries (6). However, lack of knowledge regarding screening and gynecological cancers and related mortality and long waiting periods for therapy after diagnosis may be contributing in our cohort.

The most common surgical complication was infection (31%) and hemorrhage (29%) in our study cohort. This is contrary to study findings by Allanson ER *et al* (7), although our study had a small sample size. Alexandra L *et al* also reported that the patients in their studies were at elevated risk of surgical site sepsis (11,5%) after undergoing vulvar surgery (8). Another study reported that sepsis (20.8%) and extensive bleeding (7.4%) were associated with mortality. However, this was in patients who underwent surgery with diagnosis of cervical cancer (9). It is unclear why patients in our study were dying from malignancy related and treatment related complications at an early age. Perhaps the prevalence of HIV played a role.

LIMITATIONS

This was a small study with a small sample size and the inherent shortcomings of a retrospective study. It was also done at a single center/hospital.

We were not able to account for those patients who demised in other words, or at home, namely those who might have been receiving therapy in other supporting departments.

Records keeping using manual files and books present a challenge in loss of data or reduced reliability. Three files were not retrieved because the names and hospital numbers were not legible.

All these factors did limit the findings of this study in shedding light on what gynecologic patients over this period died from.

RECOMMENDATIONS

- Patients records to be updated, and relevant information documented
- Better designed retrospective studies on larger populations are needed to evaluate the impact of gynecological cancer related mortality.
- We need more than one hospital that can manage women with gynecological cancer who need more than surgical treatment.
- More emphasis needs to be focused on education about cancers that kill women, importance of screening and early presentation to health facilities.

CONCLUSION

The average age of patients who die with a diagnosis of gynecological cancer is 53 years in our setting. Most of these patients are of South African citizenship, blacks are more affected as compared to other races. However, this could be related to the demographics of the population that the hospital services. The common malignancy in our setting is cervical cancer and these patients commonly presented with obstructive uropathy as a complication The likelihood is because they present with late stages of the disease. Most patients still demise prior to initiation of treatment due to long waiting periods for chemotherapy and radiotherapy. However, most participants with ovarian and endometrial cancer died after surgical intervention. The common complication after surgical intervention in our setting was sepsis followed by hemorrhage.

ACKNOWLEDGEMENTS

I would like to extend my gratitude to the following entities and individuals:

- CMJAH NHLS for providing me with histologic results without which this Mmed would not have been possible.
- To members of CMJAH medical records keeping department for providing me with files and records for this research report.
- Professor L Chauke who inspired and guided me to select this research topic.
- My supervisors, Dr L Mbodi and Prof L Chauke, for their patient mentorship and assistance through this project.
- My Clinical Mentor Dr ZIM Lenake for always being supportive.

DISCLOSURE

The author reports no conflict of interest in this study

REFERENCES

1. Sankaranarayanan R, Ferlay J. Worldwide burden of gynaecological cancer: the size of the problem. Best Pract Res Clin Obstet Gynaecol. 2006;20(2):207-225. doi:10.1016/j.bpobgyn.2005.10.007

2. Bailie RS, Selvey CE, Bourne D Bradshaw D. Trends in cervical cancer mortality in South Africa. Int J Epidemiol. 1996;25(3):488-493. doi:10.1093/ije/25.3.488

3. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2015;136(5):E359-E386. doi:10.1002/ijc.29210 9.

4. Ør Knudsen A, Schledermann D, Nyvang GB, Mogensen O, Herrstedt J; Academy of Geriatric Cancer Research (AgeCare). Trends in gynecologic cancer among elderly women in Denmark, 1980-2012. Acta Oncol. 2016;55 Suppl 1:65-73. doi:10.3109/0284186X.2015.1115119

5. Mortality and causes of death in South Africa, 2017: Findings from death notification. Accessed from: https://www.statssa.gov.za/ P030932017.pdf (statssa.gov.za)

6.Ortashi O. Gynecological cancer services in Arab countries: present scenario, problems and suggested solutions. Asian Pac J Cancer Prev. 2013;14(3):2147-2150. doi:10.7314/apjcp.2013.14.3.2147

7. Allanson ER, Powell A, Bulsara M, Lee HL, Denny L, Leung Y, et al. Morbidity after surgical management of cervical cancer in low and middle income countries: A systematic review and meta-analysis. PLoS One. 2019;14(7):e0217775. Published 2019 Jul 3. doi:10.1371/journal.pone.0217775

8. Martin AL, Stewart JR, Girithara-Gopalan H, Gaskins JT, McConnell NJ, Medlin EE. Trends and Complications of Vulvar Reconstruction After Vulvectomy: A Study of a Nationwide Cohort. Int J Gynecol Cancer. 2018;28(8):1606-1615. doi:10.1097/IGC.0000000000001332.

9. Zaczek T, Palczak R. Powikłania po operacjach radykalnych u chorych na raka szyjki macicy [Complications following radical surgery in women with uterine cervix cancer]. Ginekol Pol. 1978;49(3):223-227.

10. Llanos AAM, Warner WA, Luciani S, Lee TY, Bajracharya S, Slovacek S, et al. Gynecologic cancer mortality in Trinidad and Tobago and comparisons of mortality-to-incidence rate ratios across global regions. Cancer Causes Control. 2017;28(11):1251-1263. doi:10.1007/s10552-017-0961-4

11. Iyoke CA, Ugwu GO. Burden of gynaecological cancers in developing countries. World J Obstet Gynecol 2013; 2(1): 1-7. doi:10.5317/wjog.v2.i1.1

12. Mclaughlin ME, Suneja G, Chino JP. Incidence of comorbidities on death certificate data in women with gynaecological cancers. JCO.2019.37.15. doi:10.1200/JCO.2019.37.15

13. Khorana AA, Francis CW, Culakova E, Kuderer NM, Lyman GH. Thromboembolism is a leading cause of death in cancer patients receiving outpatient chemotherapy. J Thromb Haemost. 2007;5(3):632-634. doi:10.1111/j.1538-7836.2007.02374

14. Begoihn M, Mathewos A, Aynalem A, Wondemagegnehu T, Moelle U, Gizaw M, et al. Cervical cancer in Ethiopia - predictors of advanced stage and prolonged time to diagnosis. Infect Agent Cancer. 2019;14:36. Published 2019 Nov 11. doi:10.1186/s13027-019-0255-4

15. Zaorsky NG, Churilla TM, Egleston BL, Fisher SG, Ridge JA, Horwitz EM, et al. Causes of death among cancer patients. Ann Oncol. 2017;28(2):400-407. doi:10.1093/annonc/mdw604

16. Tapera O, Dreyer G, Kadzatsa W, Nyakabau AM, Stray-Pedersen B, Sjh H. Cervical cancer knowledge, attitudes, beliefs and practices of women aged at least 25 years in Harare, Zimbabwe. BMC Womens Health. 2019;19(1):91. Published 2019 Jul 8. doi:10.1186/s12905-019-0790-6

17. Denny L, de Sanjose S, Mutebi M, Anderson BO, Kim J, Jeronimo J, et al. Interventions to close the divide for women with breast and cervical cancer between low-income and middle-income countries and high-income countries. Lancet. 2017;389(10071):861-870. 1doi:10.1016/S0140-6736(16)31795-0

18. Dvoretsky PM, Richards KA, Angel C, Rabinowitz L, Beecham JB, Bonfiglio TA, et al. Survival time, causes of death, and tumor/treatment-related morbidity in 100 women with ovarian cancer. Hum Pathol. 1988;19(11):1273-1279. doi:10.1016/s0046-8177(88)80281

19. Zar N, Garmo H, Holmberg L, Hellman P. Risk of second primary malignancies and causes of death in patients with adenocarcinoma and carcinoid of the small intestine. Eur J Cancer. 2008;44(5):718-725. doi:10.1016/j.ejca.2007.12.003

20. Das S, Badhe B, Bibi A, Mohanty MK. Sudden death as a complication of choriocarcinoma. J Forensic Sci. 2015;60(1):236-239. doi:10.1111/1556-4029.12581

21. Stålberg K, Svensson T, Lönn S, Kieler H. The influence of comorbidity on mortality in ovarian cancer patients. Gynecol Oncol. 2014;133(2):298-303. doi:10.1016/j.ygyno.2014.02.024

22. Inagaki J, Rodriguez V, Bodey GP. Proceedings: Causes of death in cancer patients. Cancer. 1974;33(2):568-573. doi:10.1002/1097-0142(197402)33:2<568::aid-cncr2820330236>3.0.co;2-2

23. Cappel R, Klastersky J. Viral infections in patients with malignant diseases. Eur J Cancer. 1972;8(2):175-179. doi:10.1016/0014-2964(72)90041-2

24. Ward KK, Shah NR, Saenz CC, McHale MT, Alvarez EA, Plaxe SC. Cardiovascular disease is the leading cause of death among endometrial cancer patients. Gynecol Oncol. 2012;126(2):176-179. doi:10.1016/j.ygyno.2012.04.

25. Barbera L, Taylor C, Dudgeon D. Why do patients with cancer visit the emergency department near the end of life?. CMAJ. 2010;182(6):563-568. doi:10.1503/cmaj.

Appendix A: Approved Research Protocol

MMed research protocol

The profile of women who died with a diagnosis of Gynecological Cancer at Charlotte Maxeke Johannesburg Academic hospital over a four-year period.

Researcher name: Dr Mongezi James Siqana

MBCHB: (UFS) 2012

Student number: 2336050

Supervisor 1: Prof Lawrence Chauke

Head of Obstetrics and Gynecology at Charlotte Maxeke Johannesburg Academic hospital

Department of Obstetrics and Gynecology

University of Witwatersrand

Supervisor 2: Dr Langanani Mbodi
Academic Head of Unit: Gynecologic Oncologist, University of Witwatersrand:
Charlotte Maxeke Johannesburg Academic Hospital
Department of Obstetrics and Gynecology

TABLE OF CONTENTS

LIST OF ABBREVIATIONS

CMJAH	Charlotte Maxeke Johannesburg Academic hospital
CEO	Chief Executive Officer
DM	Diabetes mellitus
ED	Emergency Department
HPV	Human Papilloma-virus
HIV	Human immunodeficiency virus
HL	Hodgkin's lymphoma
HPT	Hypertension
HREC	Human Research Ethics Committee
ICU	Intensive Care Unit
Redcap	Research Electronic Data Capture
SA	South Africa
WITS	University of the Witwatersrand

1. INTRODUCTION

Cancer burden estimation is thought to be a pivotal instrument for countries and departments to set priorities for disease control. The International Agency for Research on Cancer estimates that 19% of the 5.1 million deaths from cancers are gynecological (1).

The mortality data used to estimate deaths from cancers in Europe and Americas are from comprehensive death registration systems whereas in regions such as Africa and Asia, such is obtained from statistics of sample surveys (2).

In the US and around the world a large number of deaths is as a result of carcinomas. In the US, during 2013, 611,105 deaths were due to heart diseases, 584,881 were due to cancer. In patients with oropharynx, larynx, Hodgkin's lymphoma and testis cancers, second cancers accounts for a significant number of deaths in these patients. More effective surveillance would be beneficial to this group of patients. Infection and heart failure were said to be the important cause of death (3).

2. LITERATURE REVIEW

MORTALITY ASSOCIATED WITH DIFFERENT GYNECOLOGICAL CANCERS

Cervical cancer: Globally, deaths due to cancer of the cervix when compared to all carcinomas common in women lead to a high number of years of life lost. It is said that cervical cancer mortality rates vary between countries, however the 1980 age-standardized rates in Israel were from 0.77/100 000 to 14.87/100 000 in Chile. In SA the age-standardized mortality rates for cancer of the cervix were found to be between 3.6 in metropolitan Whites to 30.2 in non-

metropolitan Coloureds and 25.7 in metropolitan Blacks. Coloureds and Blacks in SA were found to be at a higher risk of dying as a result of cancer of the cervix (4).

Globocan 2012 lists the mortality rate of female cancers in both less developed and more developed countries as listed on figure 1 below.

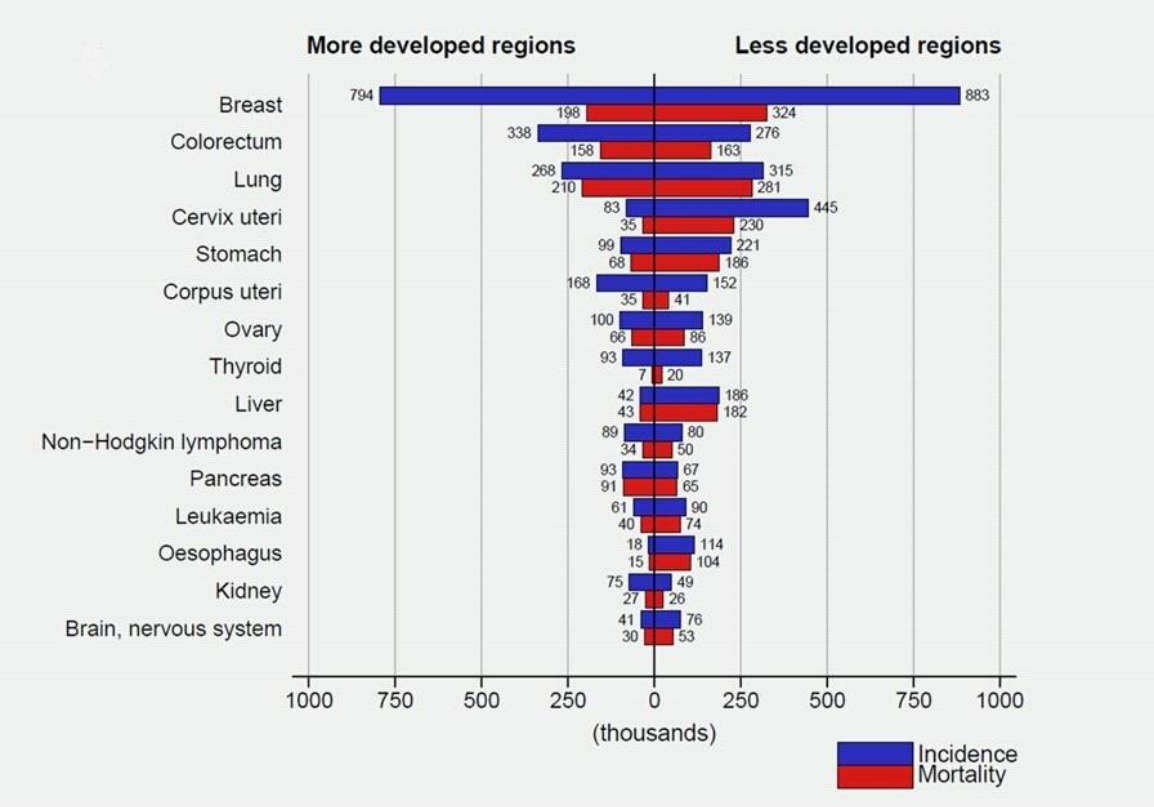


Figure 1. Incidence (in thousands) of cancer and mortality (in thousands) in females from more developed and less developed regions of the world in 2012. (3) (Used with permission from Ferlay et al).

Ovarian cancer: This is the seventh most common cause of deaths from cancer and the eighth most common cause deaths in women with 239 000 cases and 152 000 deaths.

Endometrial cancer: It is said to carry a larger burden with regards to new cases; with recorded 320 000 cases when compared to its mortality of 76000 deaths**.** Cancer of the endometrium

incidence rates are thought to be low especially in Northern Central Asia and most parts of Africa as compared to Northern America, Northern and Western Europe.

Carcinoma of the vulvar: Accounted for approximately 3% of all gynecological cancers with estimated; 26 800 cases. The incident rates of vulvar cancer are low in developing countries.

Vaginal cancer: These are generally very rare cancers and comprise about 2% of all gynecological cancers; with estimated 13 200 cases of which; 9000 cases are thought to be in developing countries.

Choriocarcinoma: It is said to be rare and; accounts for approximately 0.6% of all gynecological cancers; with 5800 cases; 5400 of those cases were in developing countries.

A study done in Zimbabwe suggests that information about causes and prevalence of cervical cancer was readily accessible via listening to the radio as compared to other methods of acquiring information. It is also said that despite fair knowledge of the prevalence of carcinoma of the cervix, screening, risk factors, treatment and accessing primary care and routine use of screening services is still suboptimal. It is suggested that using different methods like community campaigns, mobile messages and policies reiterated by health professionals to patients can help strengthen health education with regards to cervical cancer (5).

The mortality to incidence ratio of gynecologic caners in low-income countries compared to high income countries is high e.g., cervical, endometrial and ovarian cancers. Despite these findings, these ratios are still shockingly high in these high-income countries like the Caribbean where you would expect them to be low. It is therefore clear that it is important to improve on surveillance, screening and treatment of these cancers (6).

Gynecologic cancer survival rate is a global issue, especially in low resource settings. Cervical and breast cancer affect women at the peak of the lives, leading to substantial economic and social effects. Survival rate from these cancers is determined by where patients come from and where they stay. Strategies are needed to improve the lives of these women and to ensure that these diseases remain on the health care agenda of the nations that are burdened and globally (7).

Women in Arab countries seek medical assistance at late stages of the disease, reason being the stigma around reporting gynecological complains in these countries. It is suggested that poor resource countries invest more on HPV vaccine programs and find innovative ways of providing cancer services with the available resources (8).

There is recorded benefit in reducing the risk of co-morbid diseases such as diabetes, ischemic heart disease, and embolic disorders in women. In uterine and cervical cancers, stopping smoking and optimal control of HIV is beneficial for women with these cancers (9).

The mortality rates and survival in gynecological cancers are age-dependent; and survival is slightly shorter in the elderly. Mortality rate in women 70years and older is two to three times higher than in younger women, with shorter survival rates in all gynecological cancers. Elderly women are not well-represented in many clinical trials and it is suggested that randomized trials focusing on fit and frail elderly patients especially those with ovarian cancer is warranted; because prognosis is poor (10).

Developing countries fail to have effective nationally organized screening programs for cervix cancer and this malignancy continue to have high incidence and mortality from gynecologic cancers in these countries. It is suggested that subsidies for funding from governments and sponsorships are important to get nationally organized HPV vaccines and low costing screening programs (11).

CAUSES OF DEATH IN PATIENTS WITH GYYNECOLOGICAL CARCINOMAS

Malignant causes: Mortality due to cancer of the ovary lead to a mean survival time of less than 5years. A decreased survival time was associated with increase in histological grade and clinical stage at diagnosis. Mortality was always associated with cancer of the ovaries or its treatment. The most common cause of mortality was due to carcinomatosis (found to be true in almost half of these patients). However More than three quarters of deaths in these patients was due to a combination of infection and carcinomatosis (12).

Patients with adenocarcinoma of the small bowel are at a higher risk of getting gastrointestinal malignancy, genital or breast malignancy, while carcinoid tumor of the small intestine couple increased risk of prostate cancer, melanoma or malignancies of other endocrine organs (13).

The cause of immediate death was said to mostly involve the cardiovascular system in these cases. Infection and malignancy were the less common causes of sudden deaths (14).

Thromboembolism as a cause of death: Khorona et al (15) has studied relative contribution of thromboembolism to death in cancer patients with active disease on chemotherapy. Cancer-associated thrombosis was thought to be the probable leading cause of death in ambulatory patients receiving active therapy.

Thromboembolism, hematological complications and infections had a significant effect on the mortality rates in women with cancer of the ovary. The impact of comorbidity was mainly apparent among those with a more prosperous prognosis, such as longer period since cancer diagnosis, less aggressive tumors and younger age (16).

Infection as a cause of death: The results of the study by Inagaki et al (17) indicate that in patients with cancer the most common cause of mortality was due to gram- negative infections. Same findings were found to be true in acute leukemia patients.

Morbidity and mortality was said to be due to bacterial infections in cancer patients in these patients, however viral infection may also be a common cause, especially in patients with lymphoma. These patients had a depressed antibody-producing function. Immune response was thought to predispose cancer patients to severe viral infections in these patients.

Cancer patients are prone to have herpes zoster infection. Patients with Hodgkin's disease are found to frequently have herpes zoster and chickenpox infection, mortality of this disease was high especially in children with leukemia (18).

Cardiovascular diseases: The risk of dying from cancer of the endometrium decreases over time, while that of cardiac disease increases. It is recommended that work-up for cardiac disease in patients with a diagnosis of cancer of the endometrium forms part of routine work-up in patients diagnosed with this type of cancer (19).

Patients with terminal cancer visit the emergency department (ED) mainly because of uncontrolled symptoms, especially pain. Dyspnea and vomiting are second and third most common chief complaint among the patients with terminal cancer using ED (20).

CONCLUSION

A substantial number of women die of gynecological cancer to date. Cancer of the cervix is said to be the second most common cancer in developing countries, despite the availability of adequate screening tools. It is clear that more work needs to be done.

Availability of more funds from all public and private sectors to improve on screening and awareness campaigns should be put in place to address health challenges posed by gynecological cancers.

Medical conditions that these patients have or develop while being treated for gynecologic cancers also contribute to the increasing mortality rate in this population group. The complications of surgery and those of chemoradiation in these patients add a further risk of death in cancer patients. Identifying the common and preventable factors related to death in cancer women will help in designing programs that will aim at reducing cancer and cancer-related complications deaths.

3. AIM OF THE STUDY

To investigate the profile and complications among women who died with a diagnosis of gynecological cancer while admitted in a gynecology ward at CMJAH over a four-year period.

4. STUDY OBJECTIVES

1) To describe the demographic profile of women diagnosed with gynecological cancer who died while admitted in a gynecology ward at CMJAH during the study period.

2) To determine the related frequency of the different gynecologic cancers among the women who died.
3) To determine types of and frequencies of medical complications among the women at presentation.
4) To describe the type of treatment the women received before they died.
5) To determine treatment related complications among the study cohort.

5. SUBJECTS AND METHODS

5.1 SETTING

CMJAH is a hospital in Johannesburg, South Africa. The hospital is in the north of Johannesburg, provides services to two metros, namely Ekurhuleni and City of Johannesburg.

It is one of the University of Witwatersrand Health Sciences Faculty training institution. It has 1088 beds, of which Department of Obstetrics and Gynecology shares these beds with other departments.

The hospital has a well-functioning ICU and High care facilities, radiology, Blood bank and National Health laboratory services.

It is the only accredited hospital to offer gynecologic oncology services for all patients with gynecologic malignancies with regards to all hospitals that has affiliation with the University of Witwatersrand.

There is only one Gynecology oncology consultant and one registrar at any given time who takes care of all gynecologic malignancy cases. One clinic day a week is allocated to gynecology oncology.

5.2 STUDY DESIGN

This will be a retrospective review of patient's hospital records

5.3 STUDY POPULATION

All women who died with a histologically confirmed diagnosis of gynecological malignancy during the four- year study period

5.3.1 INCLUSION CRITERIA

All patients registered as diagnosed with any gynecologic malignancy, who subsequently died while still admitted **in a gynecology ward** at CMJAH from July 2015 and July 2019.

5.3.2 EXCLUSION CRITERIA

Patient who died before the study period of July 2015 to July 2019.

Those patients without histological confirmation of malignancy.

Patients who died at home or at palliative care facilities.

Patients who did not die in a gynecology ward.

5.4 SAMPLING AND SAMPLE SIZE

There will be no sample size calculations for this study. It will be a period-based study.

5.5 DATA COLLECTION

The researcher will collect all data from patient's record using a data collection sheet specifically designed for the study (Appendix B). The following data will be collected:

DEMOGRAPHICS

- Patient's age
- Parity
- Citizenship
- Marital status
- Income class

MEDICAL AND SOCIAL HISTORY

- HIV status
- Hypertension
- Diabetes mellitus
- Smoking history

CANCER DETAILS

- Type
- Stage at **diagnosis**
- Medical complications at presentations
- Treatment received surgical/Chemo/radiation/both
- Complications of treatment
- Death before/ after treatment
- Duration of hospital stay from admission till death

5.6 DATA ANALYSIS

This is a retrospective chart review and a descriptive statistic. With the help of a statistician research data will be uploaded from the excel sheet to the Redcap[R.]

Frequencies and percentages will be used to summarize categorical variables. Continuous variables will be summarized by means, standard deviation, median and interquartile range. After which will then be illustrated by means of bar charts, bar graphs or time charts.

We will manage precision by using 95% confidence interval and 5% significance level.

5.7 ETHICS

Permission to access patient clinical records will be sought from the from CMJAH CEO

Ethical approval from the Wits Human Research Ethics committee (HREC)

Registration of the study with the National health data Base

6. LIMITATIONS

In its nature, a retrospective study has limitation. Data/information from files may be incomplete and significant information required for analysis may not be available. The study will be limited to one hospital with a small sample size and hence likely to be less powered.

7. FUNDING

The cost of the study will be the responsibility of the researcher.

Activity	**Estimated Cost**
Photocopies, printing, stationery and binding.	R1000

All other costs will be borne by researcher

More Comments

8. TIMELINES

2019-2020	**Aug**	**Sep**	**Oct**	**Nov**	**Dec**	**Jan**	**Feb**	**Mar**	**Apr**	**May**	**Jun**
Develop protocol and literature review	*	*	*	*	*	*	*	*	*	*	
Submission to Assessor comm											*
Corrections											
2020-2021	**July**	**Aug**	**Sept**	**Oct**	**Nov**	**Dec**	**Feb**	**Mar**	**Apr**	**May**	**Jun**
Ethics	*	*	*								
Data - collection				*	*	*					

Analysis							*				
Write up								*	*		
Marking										*	
Corrections											*

9. REFERENCES

1. Sankaranarayanan R, Ferlay J. Worldwide burden of gynaecological cancer: the size of the problem. Best Pract Res Clin Obstet Gynaecol. 2006;20(2):207-225. doi:10.1016/j.bpobgyn.2005.10.007
2. Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2015;136(5):E359-E386. doi:10.1002/ijc.29210
3. Zaorsky NG, Churilla TM, Egleston BL, et al. Causes of death among cancer patients. Ann Oncol. 2017;28(2):400-407. doi:10.1093/annonc/mdw604
4. Bailie RS, Selvey CE, Bourne D, et al. Trends in cervical cancer mortality in South Africa. Int J Epidemiol. 1996;25(3):488-493. doi:10.1093/ije/25.3.488
5. Tapera O, Dreyer G, Kadzatsa W, Nyakabau AM, Stray-Pedersen B, Sjh H. Cervical cancer knowledge, attitudes, beliefs and practices of women aged at least 25 years in Harare, Zimbabwe. BMC Womens Health. 2019;19(1):91. Published 2019 Jul 8. doi:10.1186/s12905-019-0790-6
6. Llanos AAM, Warner WA, Luciani S, et al. Gynecologic cancer mortality in Trinidad and Tobago and comparisons of mortality-to-incidence rate ratios across global regions. Cancer Causes Control. 2017;28(11):1251-1263. doi:10.1007/s10552-017-0961-4
7. Denny L, de Sanjose S, Mutebi M, et al. Interventions to close the divide for women with breast and cervical cancer between low-income and middle-income countries and high-income countries. Lancet. 2017;389(10071):861-870. doi:10.1016/S0140-6736(16)31795-0
8. Ortashi O. Gynecological cancer services in Arab countries: present scenario, problems and suggested solutions. Asian Pac J Cancer Prev. 2013;14(3):2147-2150. doi:10.7314/apjcp.2013.14.3.2147

9. Mclaughlin ME, Suneja G, Chino JP. Incidence of comorbidities on death certificate data in women with gynaecological cancers. JCO.2019.37.15
10. Ør Knudsen A, Schledermann D, Nyvang GB, Mogensen O, Herrstedt J; Academy of Geriatric Cancer Research (AgeCare). Trends in gynecologic cancer among elderly women in Denmark, 1980-2012. Acta Oncol. 2016;55 Suppl 1:65-73. doi:10.3109/0284186X.2015.1115119
11. Iyoke CA, Ugwe GO. Burden of gynecological cancers in developing countries. World J Obstet Gynaecol 2013; 2(1): 1-7
12. Dvoretsky PM, Richards KA, Angel C, et al. Survival time, causes of death, and tumor/treatment-related morbidity in 100 women with ovarian cancer. Hum Pathol. 1988;19(11):1273-1279. doi:10.1016/s0046-8177(88)80281
13. Zar N, Garmo H, Holmberg L, et al. Risk of second primary malignancies and causes of death in patients with adenocarcinoma and carcinoid of the small intestine. Eur J Cancer. 2008;44(5):718-725. doi:10.1016/j.ejca.2007.12.003
14. Das S, Badhe B, Bibi A, et al. Sudden death as a complication of choriocarcinoma. J Forensic Sci. 2015;60(1):236-239. doi:10.1111/1556-4029.12581
15. Khorana AA, Francis CW, Culakova E, et al. Thromboembolism is a leading cause of death in cancer patients receiving outpatient chemotherapy. J Thromb Haemost. 2007;5(3):632-634. doi:10.1111/j.1538-7836.2007.02374.
16. Stålberg K, Svensson T, Lönn S, et al. The influence of comorbidity on mortality in ovarian cancer patients. Gynecol Oncol. 2014;133(2):298-303. doi:10.1016/j.ygyno.2014.02.024
17. Inagaki J, Rodriguez V, Bodey GP. Proceedings: Causes of death in cancer patients. Cancer. 1974;33(2):568-573. doi:10.1002/1097-0142(197402)33:2<568::aid-cncr2820330236>3.0.co;2-2
18. Cappel R, Klastersky J. Viral infections in patients with malignant diseases. Eur J Cancer. 1972;8(2):175-179. doi:10.1016/0014-2964(72)90041-2
19. Ward KK, Shah NR, Saenz CC, et al. Cardiovascular disease is the leading cause of death among endometrial cancer patients. Gynecol Oncol. 2012;126(2):176-179. doi:10.1016/j.ygyno.2012.04.

20. Barbera L, Taylor C, Dudgeon D. Why do patients with cancer visit the emergency department near the end of life?. CMAJ. 2010;182(6):563-568. doi:10.1503/cm

10. APPENDICIES

APPENDIX 1

Certificate of attendance of the research methods course.

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG | FACULTY OF HEALTH SCIENCES

UNIVERSITY OF THE WITWATERSRAND
DEPARTMENT OF

Certificate of Attendance

2020Research Methodology and Techniques Course

Dr Mongezi Siqana

31st January 2020
Date

Research Coordinator: Prof Deirdré Kruger

Professor & Head: Prof Martin Smith

APPENDIX 2

The profile of women who died with a diagnosis of Gynecological Cancer at Charlotte Maxeke Johannesburg Academic hospital over a four-year period.

DATA COLLECTION SHEET

Demographic factors

Age(years)		**Parity**	
Citizenship	South African	Non-South African	Unknown
Race	African	White	Coloured	Unknown
Marital status	Married	Never married
Employment	Yes	No
Smoking	Yes	No

Comorbidities

Diabetes mellitus	Yes	No	Treatment	Yes	No
Hypertension	Yes	No	Treatment	Yes	No
HIV	Yes	No	Treatment	Yes	No
Other	Yes	No	Treatment	Yes	No
If yes, specify:					

Imaging modalities

X-rays	**Yes**	**No**
Ultrasound	**Yes**	**No**
CT scan	**Yes**	**No**

MRI	**Yes**	**No**
V/Q scan	**Yes**	**No**

Cancer details

Date of first consultation to oncology					
Cancer type			Cervical		Ovarian
Vulvar	Vaginal		Endometrial		
Choriocarcinoma			Gestational trophoblastic neoplasm		
Stage at diagnosis					
FIGO					
Hospital stay(days)					
Type of treatment					
Surgical			TAH/BSO	Biopsy	Laparoscope / Cystectomy
			Lymphadenectomy		Omentectomy
Chemotherapy			Yes		No
Radiotherapy			Yes		No
Combination			Yes		No
			If yes:		

Specify		
Death		
Before treatment	Yes	No
After treatment	Yes	No
Cause of death known	**Yes**	**No**

Complications at presentation

Thromboembolism	Yes	No
Infection	Yes	No
Ascites	Yes	No
Pleural effusion	Yes	No
Cardiac failure	Yes	No
Obstructive uropathy	Yes	No
Brain metastasis	Yes	No
Bone metastasis	Yes	No
Liver metastasis	Yes	No

Lung metastasis	Yes	No

Complications of treatment

Surgery					
Hemorrhage	Yes	No	Blood vessel injury	Yes	No
Bowel injury	Yes	No	Bladder injury	Yes	No
Ureteric injury	Yes	No	Nerve injury	Yes	No
Sepsis	Yes	No	Burns	Yes	No
Chemo radiation					
Skin reactions	Yes	No	Weight loss	Yes	No
Nausea and vomiting	Yes	No	Hair loss	Yes	No
Radiation enteritis and diarrhea	Yes	No	Kidney injury	Yes	No

Appendix B: Letter of approval from the CMJAH CEO

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

CHARLOTTE MAXEKE JOHANNESBURG ACADEMIC HOSPITAL

Enquiries:
Ms. X Dhlamini
Office of the Clinical Director
Email: xolisane.dhlamini@gauteng.gov.za
Tel: (011): 488-3710
03 June 2020

Dear Dr, MJ Siqana

STUDY TITLE: Gynecologic Malignancy related mortality at Charlotte Maxeke Johannesburg Academic Hospital, Gauteng South Africa

Permission to conduct the above-mentioned study is provisionally approved. Your study can only commence once Ethics approval is obtained. Please forward a copy of your Ethics Clearance Certificate as soon as the study is approved by the Ethics Committee for the CEO's office to give you the final approval to conduct the study.

Supported / not supported

Dr. PN Africa
Acting Clinical Director
DATE: 05/06/2020

Approved / not approved

Ms. G. Bogoshi
Chief Executive Officer
DATE: 05.06.2020

Appendix C: Ethics clearance certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Dr MJ Siqana

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M200880

NAME: (Principal Investigator)	Dr MJ Siqana
DEPARTMENT:	School of Clinical Medicine Department of Obstetrics and Gynaecology Medical School University
PROJECT TITLE:	The profile of women who died with a diagnosis of gynaecological cancer at Charlotte Maxeke Johannesburg Academic Hospital over a four-year period
DATE CONSIDERED:	28/08/2020
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Professor L Chauke and Dr L Mbodi
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	2020/09/21

This clearance certificate is valid for 5 years from the date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the 3rd Floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.
I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to submit details to the Committee. **I agree to submit a yearly progress report**. When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **August** and will therefore reports and re-certification will be due early in the month of **August** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

20/07/21
Date

Appendix D: journal guidelines for SAJOG

Authorship

Named authors must consent to publication. Authorship should be based on: (i) substantial contribution to conceptualisation, design, analysis and interpretation of data; (ii) drafting or critical revision of important scientific content; or (iii) approval of the version to be published. These conditions must all be met for an individual to be included as an author (uniform requirements for manuscripts submitted to biomedical journals; refer to www.icmje.org)

If authors' names are added or deleted after submission of an article, or the order of the names is changed, all authors must agree to this in writing.

Please note that co-authors will be requested to verify their contribution upon submission. Non-verification may lead to delays in the processing of submissions.

Conflicts of interest

Conflicts of interest can derive from any kind of relationship or association that may influence authors' or reviewers' opinions about the subject matter of a paper. The existence of a conflict – whether actual, perceived or potential – does not preclude publication of an article. However, we aim to ensure that, in such cases, readers have all the information they need to enable them to make an informed assessment about a publication's message and conclusions. We require that both authors and reviewers declare all sources of support for their research, any personal or financial relationships (including honoraria, speaking fees, gifts received, etc) with relevant individuals or organisations connected to the topic of the paper, and any association with a product or subject that may constitute a real, perceived or potential conflict of interest. If you are unsure whether a specific relationship constitutes a conflict, please contact the editorial team for advice. If a conflict remains undisclosed and is later brought to the attention of the editorial team, it will be considered a serious issue prompting an investigation with the possibility of retraction.

Research ethics committee approval

Authors must provide evidence of Research Ethics Committee approval of the research where relevant. Ensure the correct, full ethics committee name and reference number is included in the manuscript.

If the study was carried out using data from provincial healthcare facilities, or required active data collection through facility visits or staff interviews, approval should be sought from the relevant provincial authorities. For South African authors, please refer to the guidelines for submission to the National Health Research Database. Research involving human subjects must be conducted according to the principles outlined in the Declaration of Helsinki. Please refer to the National Department of Health's guideline on Ethics in Health research: principles, processes and structures to ensure that the appropriate requirements for conducting research have been met, and that the HPCSA's General Ethical Guidelines for Health Researchers have been adhered to.

Protection of rights to privacy

Research Participants

Information that would enable identification of individual research participants should not be published in written descriptions, photographs, radiographs and pedigrees unless the information is essential for scientific purposes and the patient (or parent or guardian) has given informed written consent for publication and distribution. We further recommend that the published article is disseminated not only to the involved researchers but also to the patients/participants from whom the data was drawn. Refer to Protection of Research Participants. The signed consent form should be submitted with the manuscript to enable verification by the editorial team.

Other individuals

Any individual who is identifiable in an image must provide written agreement that the image may be used in that context in the SAJOG.

Copyright notice

Material submitted for publication in the SAJOG is accepted provided it has not been published or submitted for publication elsewhere. Please inform the editorial team if the main findings of your paper have been presented at a conference and published in abstract form, to avoid copyright infringement. The SAJOG does not hold itself responsible for statements made by the authors. The corresponding author should also indicate if the research forms part of a postgraduate short report, dissertation or thesis.

Previously published images

If an image/figure has been previously published, permission to reproduce or alter it must be obtained by the authors from the original publisher and the figure legend must give full credit to the original source. This credit should be accompanied by a letter indicating that permission to reproduce the image has been granted to the author/s. This letter should be uploaded as a supplementary file during submission.

Privacy statement

The SAJOG is committed to protecting the privacy of its website and submission system users. The names, personal particulars and email addresses entered in the website or submission system will not be made available to any third party without the user's permission or due process. By registering to use the website or submission system, users consent to receive communication from the SAJOG or its publisher SAMA on matters relating to the journal or associated publications. Queries with regard to privacy may be directed to publishing@samedical.org.

Ethnic/race classification

Use of racial or ethnicity classifications in research is fraught with problems. If you choose to use a research design that involves classification of participants based on race or ethnicity, or discuss issues with reference to such classifications, please ensure that you include a detailed rationale for doing so, ensure that the categories you describe are carefully defined, and that socioeconomic, cultural and lifestyle variables that may underlie perceived racial disparities are appropriately controlled for. Please also clearly specify whether race or ethnicity is classified as reported by the patient (self-identifying) or as perceived by the investigators. Please note thatit is not appropriate to use self-reported or investigator-assigned racial or ethnic categories for genetic studies.

Continuing Professional Development (CPD)

SAJOG is an HPCSA-accredited service provider of CPD materials. Principal authors can earn up to 15 CPD continuing education units (CEUs) for publishing an article; co-authors are eligible to earn up to 5 CEUs; and reviewers of articles can earn 3 CEUs. Each month, SAJOG also publishes a CPD-accredited questionnaire relating to the academic content of the journal. Successful completion of the questionnaire with a pass rate of 70% will earn the reader 3 CEUs. Administration of our CPD programme is managed by Medical Practice Consulting. To complete questionnaires and obtain certificates, please visit MRP Consulting

Manuscript preparation

Preparing an article for anonymous review

To ensure a fair and unbiased review process, all submissions are to include an anonymised version of the manuscript. The exceptions to this requirement are Correspondence, Book reviews and Obituary submissions.

Submitting a manuscript that needs additional blinding can slow down your review process, so please be sure to follow these simple guidelines as much as possible:

• An anonymous version should not contain any author, affiliation or particular institutional details that will enable identification.

• Please remove title page, acknowledgements, contact details, funding grants to a named person, and any running headers of author names.

• Mask self-citations by referring to your own work in third person.

General article format/layout

Submitted manuscripts that are not in the correct format specified in these guidelines will be returned to the author(s) for correction prior to being sent for review, which will delay publication.

General:

• Manuscripts must be written in UK English (this includes spelling).

• The manuscript must be in Microsoft Word or RTF document format. Text must be 1.5 line spaced, in 12-point Times New Roman font, and contain no unnecessary formatting (such as text in boxes). Pages and lines should be numbered consecutively.

• Please make your article concise, even if it is below the word limit.

• Qualifications, full affiliation (department, school/faculty, institution, city, country) and contact details of ALL authors must be provided in the manuscript and in the online submission process.

• Abbreviations should be spelt out when first used and thereafter used consistently, e.g. 'intravenous (IV)' or 'Department of Health (DoH)'.

• Numbers should be written as grouped per thousand-units, i.e. 4 000, 22 160.

• Quotes should be placed in single quotation marks: i.e. The respondent stated: '...'

• Round brackets (parentheses) should be used, as opposed to square brackets, which are reserved for denoting concentrations or insertions in direct quotes.

If you wish material to be in a box, simply indicate this in the text. You may use the table format –this is the only exception. Please DO NOT use fill, format lines and so on.

SAJOG is a general specialist obstetrics and gynaecology journal, therefore for articles involving genetics, it is the responsibility of authors to apply the following:

- Please ensure that all genes are in italics, and proteins/enzymes/hormones are not.

- Ensure that all genes are presented in the correct case e.g. TP53 not Tp53.

** NB: Copyeditors cannot be expected to pick up and correct errors wrt the above, although they will raise queries where concerned.

- Define all genes, proteins and related shorthand terms at first mention, e.g. ‘188del11’ can be glossed as ‘an 11 bp deletion at nucleotide 188.’

- Use the latest approved gene or protein symbol as appropriate:

o Human Gene Mapping Workshop (HGMW): genetic notations and symbols

o HUGO Gene Nomenclature Committee: approved gene symbols and nomenclature

o OMIM: Online Mendelian Inheritance in Man (MIM) nomenclature and instructions

o Bennet et al. Standardized human pedigree nomenclature: Update and assessment of the recommendations of the National Society of Genetic Counselors. J Genet Counsel 2008;17:424-433: standard human pedigree nomenclature.

Preparation notes by article type

Research

Guideline word limit: 3 000 words (excluding abstract and bibliography)

Research articles describe the background, methods, results and conclusions of an original research study. The article should contain the following sections: introduction, methods, results, discussion and conclusion, and should include a structured abstract (see below). The introduction should be concise – no more than three paragraphs – on the background to the research question, and must include references to other relevant published studies that clearly lay out the rationale for conducting the study. Some common reasons for conducting a study are: to fill a gap in the literature, a logical extension of previous work, or to answer an important question. If other papers related to the same study have been published previously, please make sure to refer to them specifically. Describe the study methods in as much detail as possible so that others would be able to replicate the study should they need to. Where appropriate, sample size calculations should be included to demonstrate that the study is not underpowered. Results should describe the study sample as well as the findings from the study itself, but all interpretation of findings must be kept in the discussion section. The conclusion should briefly summarise the main message of the paper and provide recommendations for further study.

• May include up to 6 illustrations or tables.

• A max of 20 - 25references

Structured abstract

• This should be no more than 250words, with the following recommended headings:

o Background: why the study is being done and how it relates to other published work.

o Objectives: what the study intends to find out

o Methods: must include study design, number of participants, description of the research tools/instruments, any specific analyses that were done on the data.

o Results: first sentence must be brief population and sample description; outline the results according to the methods described. Primary outcomes must be described first, even if they are not the most significant findings of the study.

o Conclusion: must be supported by the data, include recommendations for further study/actions.

• Please ensure that the structured abstract is complete, accurate and clear and has been approved by all authors. It should be able to be intelligible to the reader without referral to the main body of the article.

• Do not include any references in the abstracts.

Here is an example of a good abstract.

Scientific letters/short reports

These are shorter length, scholarly research articles of no more than 1500 words, and include case reports.

Guideline word limit: 1 500 words

• Abstract: Structured, of about 150 words, with the following recommended headings: Background, Objectives, Methods, Results, and Conclusion.

• May include only one illustration or table

• A maximum of 8 references

Editorials

Guideline word limit: 1 000 words

These opinion or comment articles are usually commissioned but we are happy to consider and peer review unsolicited editorials. Editorials should be accessible and interesting to readers without specialist knowledge of the subject under discussion and should have an element of topicality (why is a comment on this issue relevant now?) There should be a clear message to the piece, supported by evidence.

Please make clear the type of evidence that supports each key statement, e.g.:

• expert opinion

• personal clinical experience

• observational studies

• trials

• systematic reviews.

Review articles

Review articles should always be discussed with the Editor prior to submission.

Guideline word limit: 4 000 words

These are welcome, but should be either commissioned or discussed with the Editor before submission. A review article should provide a clear, up-to-date account of the topic and be aimed at non-specialist hospital doctors and general practitioners. They should be aligned to practice in South and/or sub-Saharan Africa and not a précis of reviews published in the international literature

Please ensure that your article includes:

• Abstract: unstructured, of about 100-150 words, explaining the review and why it is important

• Methods: Outline the sources and selection methods, including search strategy and keywords used for identifying references from online bibliographic databases. Discuss the quality of evidence.

• When writing: clarify the evidence you used for key statements and the strength of the evidence. Do not present statements or opinions without such evidence, or if you have to, say that there is little or no evidence and that this is opinion. Avoid specialist jargon and abbreviations, and provide advice specific to southern Africa.

• Personal details: Please supply your qualifications, position and affiliations and MP number (used for CPD points); address, telephone number and fax number, and your e-mail address; and a short personal profile (50 words) and a few words about your current fields of interest.

Correspondence (Letters to the Editor)

Guideline word limit: 400 words

Letters to the editor should relate either to a paper or article published by the SAJOG or to a topical issue of particular relevance to the journal's readership

• May include only one illustration or table

• Must include a correspondence address.

Obituaries

Guideline word limit: 400 words

Should be offered within the first year of the practitioner's death, and may be accompanied by a photograph.

Illustrations/photos/scans

• If illustrations submitted have been published elsewhere, the author(s) should provide evidence of consent to republication obtained from the copyright holder.

• Figures must be numbered in Arabic numerals and referred to in the text e.g. '(Fig. 1)'.

• Each figure must have a caption/legend: Fig. 1. Description (any abbreviations in full).

• All images must be of high enough resolution/quality for print.

• All illustrations (graphs, diagrams, charts, etc.) must be in PDF form.

• Ensure all graph axes are labelled appropriately, with a heading/description and units (as necessary) indicated. Do not include decimal places if not necessary e.g. 0; 1.0; 2.0; 3.0; 4.0 etc.

• Each image must be attached individually as a 'supplementary file' upon submission (not solely embedded in the accompanying manuscript) and named Fig. 1, Fig. 2, etc.

Tables

• Tables should be constructed carefully and simply for intelligible data representation. Unnecessarily complicated tables are strongly discouraged.

• Embed/include each table in the manuscript Word file - do not provide separately as supplementary files.

• Number each table in Arabic numerals (Table 1, Table 2, etc.) consecutively as they are referred to in the text.

• Tables must be cell-based (i.e. not constructed with text boxes or tabs) and editable.

• Ensure each table has a concise title and column headings, and include units where necessary.

• Footnotes must be indicated with consecutive use of the following symbols: * † ‡ § ¶ || then ** †† ‡‡ etc.

Do not: Use [Enter] within a row to make ‘new rows’:

Rather:

Each row of data must have its own proper row:

Do not: use separate columns for n and %:

Rather:

Combine into one column, n (%):

Do not: have overlapping categories, e.g.:

Rather:

Use <> symbols or numbers that don't overlap:

References

NB: Only complete, correctly formatted reference lists in Vancouver style will be accepted. If reference manager software is used, the reference list and citations in text are to be unformatted to plain text before submitting..

• Authors must verify references from original sources.

• Citations should be inserted in the text as superscript numbers between square brackets, e.g. These regulations are endorsed by the World Health Organization,[2] and others.[3,4-6]

• All references should be listed at the end of the article in numerical order of appearance in the Vancouver style (not alphabetical order).

• Approved abbreviations of journal titles must be used; see the List of Journals in Index Medicus.

• Names and initials of all authors should be given; if there are more than six authors, the first three names should be given followed by et al.

• Volume and issue numbers should be given.

• First and last page, in full, should be given e.g.: 1215-1217 not 1215-17.

• Wherever possible, references must be accompanied by a digital object identifier (DOI) link). Authors are encouraged to use the DOI lookup service offered by CrossRef:

o On the Crossref homepage, paste the article title into the ‘Metadata search’ box.

o Look for the correct, matching article in the list of results.

o Click Actions > Cite

o Alongside 'url =' copy the URL between { }.

o Provide as follows, e.g.: https://doi.org/10.7196/07294.937.98x

Some examples:

• Journal references: Price NC, Jacobs NN, Roberts DA, et al. Importance of asking about glaucoma. Stat Med 1998;289(1):350-355. http://dx.doi.org/10.1000/hgjr.182

• Book references: Jeffcoate N. Principles of Gynaecology. 4th ed. London: Butterworth, 1975:96-101.

• Chapter/section in a book: Weinstein L, Swartz MN. Pathogenic Properties of Invading Microorganisms. In: Sodeman WA, Sodeman WA, eds. Pathologic Physiology: Mechanisms of Disease. Philadelphia: WB Saunders, 1974:457-472.

• Internet references: World Health Organization. The World Health Report 2002 - Reducing Risks, Promoting Healthy Life. Geneva: WHO, 2002. http://www.who.int/whr/2002 (accessed 16 January 2010).

• Legal references

• Government Gazettes:

National Department of Health, South Africa. National Policy for Health Act, 1990 (Act No. 116 of 1990). Free primary health care services. Government Gazette No. 17507:1514. 1996.

In this example, 17507 is the Gazette Number. This is followed by :1514 - this is the notice number in this Gazette.

• Provincial Gazettes:

Gauteng Province, South Africa; Department of Agriculture, Conservation, Environment and Land Affairs. Publication of the Gauteng health care waste management draft regulations. Gauteng Provincial Gazette No. 373:3003, 2003.

• Acts:

South Africa. National Health Act No. 61 of 2003.

• Regulations to an Act:

South Africa. National Health Act of 2003. Regulations: Rendering of clinical forensic medicine services. Government Gazette No. 35099, 2012. (Published under Government Notice R176).

• Bills:

South Africa. Traditional Health Practitioners Bill, No. B66B-2003, 2006.

• Green/white papers:

South Africa. Department of Health Green Paper: National Health Insurance in South Africa. 2011.

• Case law:

Rex v Jopp and Another 1949 (4) SA 11 (N)

Rex v Jopp and Another: Name of the parties concerned

1949: Date of decision (or when the case was heard)

(4): Volume number

SA: SA Law Reports

11: Page or section number

(N): In this case Natal - where the case was heard. Similarly, (C) woud indicate Cape, (G) Gauteng, and so on.

NOTE: no . after the v

• Other references (e.g. reports) should follow the same format: Author(s). Title. Publisher place: Publisher name, year; pages.

• Cited manuscripts that have been accepted but not yet published can be included as references followed by '(in press)'.

• Unpublished observations and personal communications in the text must not appear in the reference list. The full name of the source person must be provided for personal communications e.g. '...(Prof. Michael Jones, personal communication)'.

From submission to acceptance

Submission and peer-review

To submit an article:

• Please ensure that you have prepared your manuscript in line with the SAJOG requirements.

• All submissions should be submitted via Editorial Manager

• The following are required for your submission to be complete:

o Anonymous manuscript (unless otherwise stated)

o Author Agreement form

o Manuscript

o Any supplementary files: figures, datasets, patient consent form, permissions for published images, etc.

• Once the submission has been successfully processed on Editorial Manager, it will undergo a technical check by the Editorial Office before it will be assigned to an editor who will handle the review process. If the author guidelines have not been appropriately followed, the manuscript may be sent back to the author for correcting.

Peer Review Process

All manuscripts are reviewed initially by the Editor-in-Chief and only those that meet the scientific and editorial standards of the journal, and fit within the aims and scope of the journal, will be sent for external peer review. Each manuscript is reviewed by two reviewers selected on the basis of their expertise in the field. A double-blind review process is followed at SAJOG.

Authors are expected to receive feedback from reviewers and an editorial decision within approximately 6 weeks of submission. The time period of the entire review process may vary however depending upon the quality of the manuscript submitted, reviewers' responses and the time taken by the authors to submit the revised manuscript.

Manuscripts from review may be accepted, rejected or returned to the author for revision or resubmission for review. Authors will be directed to submit revised manuscripts within two months of receiving the editor's decision, and are requested to submit a point-by-point response to the reviewers' comments. Manuscripts which authors are requested to revise and resubmit will be sent for a second round of peer review, often to the original set of reviewers. All final decisions on a manuscript are at the Editor's discretion

Production process

The following process should usually take between 4 - 6 weeks:

1. An accepted manuscript is passed to a Managing Editor to assign to a copyeditor (CE).

2. The CE copyedits in Word, working on house style, format, spelling/grammar/punctuation, sense and consistency, and preparation for typesetting.

3. If the CE has an author queries, he/she will contact the corresponding author and send them the copyedited Word doc, asking them to solve the queries by means of track changes or comment boxes.

4. The authors are typically asked to respond within 1-3 days. Any comments/changes must be clearly indicated e.g. by means of track changes. Do not work in the original manuscript - work in the copyedited file sent to you and make your changes clear.

5. The CE will finalise the article and then it will be typeset.

6. Once typeset, the CE will send a PDF of the file to the authors to complete their final check, while simultaneously sending to the 2nd-eye proofreader.

7. The authors are typically asked to complete their final check and sign-off within 1-2 days. No major additional changes can be accommodated at this point.

8. The CE implements the authors' and proofreader's mark-ups, finalises the file, and prepares it for the upcoming issue.

Changing contact details or authorship

Please notify the Editorial Department of any contact detail changes, including email, to facilitate communication.

Errata and retractions

Errata

Should you become aware of an error or inaccuracy in yours or someone else's contribution after it has been published, please inform us as soon as possible via an email to publishing@samedical.org,including the following details:

• Journal, volume and issue in which published

• Article title and authors

• Description of error and details of where it appears in the published article

• Full detail of proposed correction and rationale

We will investigate the issue and provide feedback. If appropriate, we will correct the web version immediately, and will publish an erratum in the next issue. All investigations will be conducted in accordance with guidelines provided by the Committee on Publication Ethics (COPE).

Retractions

Retraction of an article is the prerogative of either the original authors or the editorial team of SAMA. Should you wish to withdraw your article before publication, we need a signed statement from all the authors.

Should you wish to retract your published article, all authors have to agree in writing before publication of the retraction.

Send an email to publishing@samedical.orgincluding the following details:

• Journal, volume and issue to which article was submitted/in which article was published

• Article title and authors

• Description of reason for withdrawal/retraction.

We will make a decision on a case-by-case basis upon review by the editorial committee in line with international best practices. Comprehensive feedback will be communicated with the authors with regard to the process. In case where there is any suspected fraud or professional

misconduct, we will follow due process as recommended by the Committee on Publication Ethics (COPE), and in liaison with any relevant institutions.

When a retraction is published, it will be linked to the original article.

Indexing

Published articles are covered by the following major indexing services. As such articles published in the SAJOG are immediately available to all users of these databases, guaranteed a global and African audience:

• DOAJ

• AIM

• AJOL

• EBSCO

• EMBASE

• Scopus

• Crossref

• Sabinet

• Emerging Sources Citation Index (Web of Science)

Sponsored supplements

Contact the managing editor (claudian@samedical.org) for information on submitting ad hoc/commissioned supplements, including guidelines, conference/congress abstracts, etc.

Submission Preparation Checklist

As part of the submission process, authors are required to check off their submission's compliance with all of the following items, and submissions may be returned to authors that do not adhere to these guidelines.

Named authors consent to publication and meet the requirements of authorship as set out by the journal.

The submission has not been previously published, nor is it before another journal for consideration.

The text complies with the stylistic and bibliographic requirements in Author Guidelines.

The research was approved by a Research Ethics Committee (if applicable)

The authors are aware of the page fee costs associated with their submission. Please see Author Guidelines for more information.

Copyright Notice

Copyright of published material remains in the Authors' name. This allows authors to use their work for their own non-commercial purposes without seeking permission from the Publisher, subject to properly acknowledging the Journal as the original place of publication.

Authors are free to copy, print and distribute their articles, in full or in part, for teaching activities, and to deposit or include their work in their own personal or institutional database or on-line website. Authors are requested to inform the Journal/Publishers of their desire/intention

to include their work in a thesis or dissertation or to republish their work in any derivative form (but not for commercial use).

Material submitted for publication in the SAJOG is accepted provided it has not been published or submitted for publication elsewhere. Please inform the editorial team if the main findings of your paper have been presented at a conference and published in abstract form, to avoid copyright infringement.

Privacy Statement

The SAJOG is committed to protecting the privacy of the users of this journal website. The names, personal particulars and email addresses entered in this website will be used only for the stated purposes of this journal and will not be made available to third parties without the user's permission or due process. Users consent to receive communication from the SAJOG for the stated purposes of the journal. Queries with regard to privacy may be directed to publishing@hmpg.co.za.

Appendix E: Plagiarism declaration

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

FACULTY OF HEALTH SCIENCES

PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

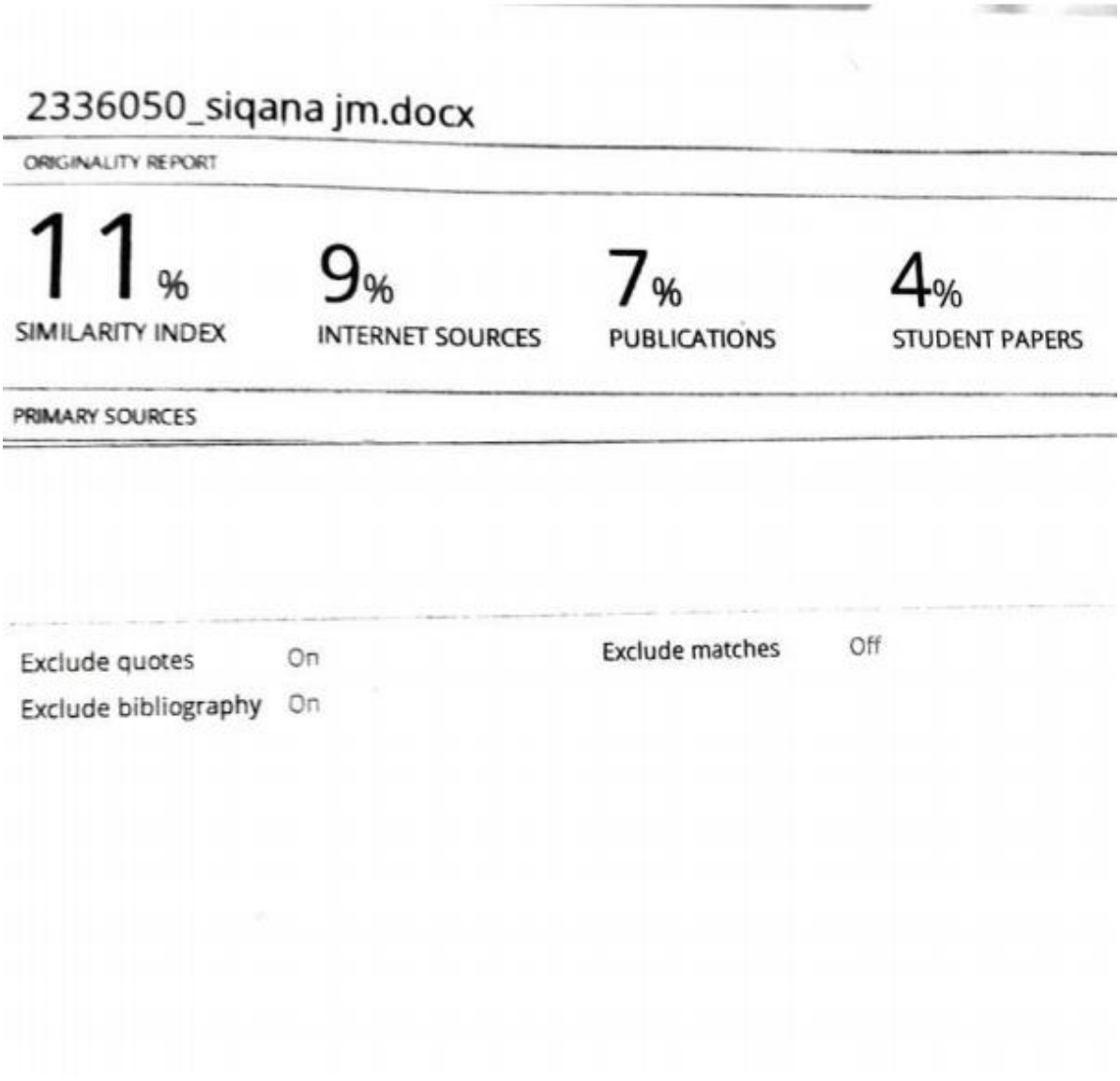
I J M Sipas (Student number: 2336050) am a student registered for the degree of MMed(O&G) in the academic year 3rd.

I hereby declare the following:

- I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.
- I confirm that the work submitted for assessment for the above degree is my own unaided work except where I have explicitly indicated otherwise.
- I have followed the required conventions in referencing the thoughts and ideas of others.
- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.
- I have included as an appendix a report from "Turnitin" (or other approved plagiarism detection) software indicating the level of plagiarism in my research document.

Signature: _____ Date: 20/07/2021

Appendix F: Turnitin



2336050_siqana jm.docx

ORIGINALITY REPORT

11%	9%	7%	4%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

Exclude quotes	On	Exclude matches	Off
Exclude bibliography	On		