Spatial Distribution of Cancer Cases Seen in Three Major Public Hospitals in KwaZulu-Natal, South Africa

Mpho KTN Motlana1,2, Themba G Ginindza1, Aweke A Mitku1,2,3 and Nkosana Jafta2

1Discipline of Public Health Medicine, School of Nursing and Public Health, University of KwaZulu-Natal, Durban, South Africa. 2Discipline of Occupational and Environmental Health, School of Nursing and Public Health, University of KwaZulu-Natal, Durban, South Africa. 3Department of Statistics, Science College, Bahir Dar University, Bahir Dar, Ethiopia.

ABSTRACT

BACKGROUND: Noncommunicable diseases (NCDs) like cancer are posing a challenge in the health system especially in low- and middle-income countries (LMICs). In South Africa, cancer is under-reported due to the lack of a comprehensive cancer surveillance system. The limited knowledge on the extent of cancer burden has led to inaccurate allocation of public health resources. The aim of this study was to describe cancer incidence and spatial distribution of cancer cases seen at 3 main public oncology facilities in KwaZulu-Natal.

METHODS: In this retrospective study, cases of cancer observed from year 2015 to 2017 were extracted from medical records. The crude incidence rate was estimated for the total cancer cases and for different type of cancer reported over that period. Age-standardised incidence rates (ASR) per 100 000 was calculated per year using age groups and sex according to the district population data of KwaZulu-Natal. The comparisons of cancer diagnosed incidences were made between 11 districts using the ASR. Choropleth spatial maps and Moran’s Index were used to assess the ASR cancer spatial distribution along with geographical patterns among the districts. One sample chi-square test was used to assess the significant increase/decrease over time.

RESULTS: The study lost numerous cases due to incompleteness. A total of 4909 new cases were diagnosed with cancer during 2015 to 2017, 62% of which were female. Both uMngundlovu and eThekwini districts had the highest ASR among district municipalities of KwaZulu-Natal for both male and female (93.6 per 100 000 per men year for men, 158.2 per 100 000 women per year, and 60.1 per 100 000 men per year and 96.9 per 100 000 women per year, respectively). Random distribution of reported cancer cases in KwaZulu-Natal was observed with a high concentration being in and around 2 metropolitan districts. Spatial variation showed a significant difference from year to year between the districts with the random spatial distribution. Overall, there was a significant decline of cancer incidences observed from 2015 to 2017 (P < .05) in the province.

CONCLUSION: The overall cancer incidence in the study shows that female cancers (breast and cervical) are still on the rise and still need to be given priority as they were most prevalent in KwaZulu-Natal. Spatial analysis (choropleth maps) was used to show a pattern of higher concentration of cancer incidence in the north-western parts of the province.

KEYWORDS: Cancer incidence, spatial variation, age-standardised incidence rates, Moran Index, KwaZulu-Natal

Background

The International Agency for Research on Cancer (IARC) estimated the global burden of cancer at 18.1 million new cases and 9.6 million deaths in 2018.1 The report further estimated that about 1 049 800 (5.8%) of all the new cancer cases were from Africa,1 and this is an increase from 847 000 new cases observed in 2012.1,2 Several countries in Africa provide sufficient data to be used to estimate national incidences while some such as South Africa, the accuracy of cancer data remains a huge challenge, and the reported incidence is not used to estimate the burden of cancer in the country.1

Low- and middle-income countries (LMICs) including South Africa are experiencing increased migration to urban areas and uptake of western practices4,5 that led to many risk factors including changes in lifestyle,6 behavioural factors such as unhealthy diets, use of tobacco,7 lack of physical activity,8 and risky reproductive behaviours.3 In addition, HIV/AIDS epidemic and prevalent oncogenic infections have a significant contribution to the rise of cancer burden.9

The increasing concern for environmental issues and their relation to the health of individuals has sparked an increase in the use of spatial epidemiology methods to this relationship.10,11 The commonly used spatial techniques for health research include disease mapping, distance calculations, spatial aggregation, clustering, spatial smoothing, and spatial regression.12,13 Measuring the true spatial heterogeneity and quantifying...
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disease burden can be achieved by using disease mapping to summarise spatial variation of disease risk.10
The current South African cancer registry is pathology-based resulting in it having a limitation in providing geographical cancer estimations for different areas in the country.14 This shortcoming has led to the inaccurate allocation of public health resources for different populations.15 The aim of the study was to determine incidence and spatial distribution of cancers over period of 3-years (2015-2017) attended in 3 main oncology public hospitals.

Materials and Methods
Study area and design
The study area was the province of KwaZulu-Natal, the second most populated province in South Africa, with an estimated population of 11.3 million.16 The province is further divided into 10 municipality districts and 1 metropolitan as shown in Figure 1.

This retrospective study was a 3-year (2015-2017) medical records review observing cancer incidence from 3 public hospitals providing oncological services in KwaZulu-Natal namely Addington hospital and Inkosi Albert Luthuli Central hospital (IALCH) situated in eThekwini Metropolitan municipality and Greys hospital in uMgungundlovu municipality.

Data collection
Medical records of cancer patients who were attended to in the oncology clinics of the 3 facilities between January 1, 2015 and December 31, 2017, were identified, and relevant information was extracted from them using standardised hard copy form/tool. The data extracted were classified into different sections namely (1) demographics, (2) clinical symptoms presented by the patient, (3) diagnosis as per laboratory report, and (4) risk factors that are reported by the patient. The information collected were the hospital details (hospital identifier, name of
referring hospital, name of receiving hospital, date of initial encounter at the oncology department), demographics of the patient (sex, date of birth, age at diagnosis if documented, race, area of residence at a district/magisterial level), self-reported risk factors (smoking status and long-term disease); and clinical/laboratory diagnosis details. Cancer confirmation methods that included different clinical methods (X-ray and computerised tomography [CT] scan) and laboratory tests (blood tests and histopathology/cytology) were also documented.

Data management

Abstracted data were captured onto Redcap database and then exported to Microsoft Excel for management. Disease diagnosis was coded according to the International Classification of Disease (ICD-10), excluding codes from D03 to D48 which are diseases not classified as malignant. The age was categorised into 5-year age groups except for lower age bands merged to 0 to 14 and upper bands of over 80 years fused to one age band.

The data set had missing observations on several essential variables. Mitigations were taken to avoid extensive data loss by introducing imputation measures for sex and age variables. Out of the 131 cases which were not sex specified, 48 of the cases were assigned sex based on the type of cancer presented provided that the cancer was unique for the specific sex. The age at diagnosis was generated using the date of birth alongside the date of diagnosis, and where the date of birth was missing, we used age recorded in the medical records. This resulted in the imputation of age for 290 cases, and for the rest of the missing age observations (n = 69), we used a mean computed from existing data. The remainder of the cancer cases with missing information on these 2 variables were omitted from the database.

One hundred and sixty-three (163) cases were duplicates, and 10.6% (n = 811) were diagnosed outside the study's time scope and, therefore, were dropped from the data set. We further excluded 1784 cases that had at least one incomplete or missing observation in variables of interest, 907 cases had missing date of diagnosis, 150 cases had incomplete type of diagnosis and 306 cases had missing residential information. Finally, we excluded 93 cases of nonmelanoma (C43).

Data analysis

After cleaning data on Microsoft Excel, it was exported to STATA version 15 for data analysis. Descriptive statistics were used to summarise the data and describe distribution by socio-demographic characteristics. We used population statistics requested from the country’s official vital statistics institution, Statistics South Africa (Stats SA), to calculate incidence of cancer in the province over the 3-year period (2015-2017). The population at risk was estimated using the census data of 2015, 2016, and 2017 by sex and 5-year age group (except for 0- to 14-year and over 80-year bands). To estimate the age-standardised incidence rate (ASR), the world standard population structure was used as reference population, and ASR were presented as number of cancer cases per 100 000 persons. After computing different ASR for the different age bands of each cancer, we summed them to achieve the overall ASR for the different districts.

Chi-square test and trends test were used to evaluate the statistical significance of the average annual change of cancer incidence (P value < .05 was considered significant). Spatial and temporal analyses of ASRs across the 11 districts were performed using Arc GIS software package 10.6 (Esri, Redlands, CA, USA). Thematic mapping was the best suit for the study, as the residency information collected was documented at the district level. Global Moran’s I was used to determine the presence of spatial autocorrelation. Trends of cancer incidence between years were tested using time trend analysis and a significant change was when P < .05.

Results

Over the 3-year period (2015-2017), 4909 cancer cases were diagnosed, treated, and/or managed in the 3 public hospitals (IALCH, Addington, and Greys), providing oncology services in KwaZulu-Natal were eligible for inclusion in the analysis. Of the total number of cancer cases, females were more than males (3054 and 1855, respectively). The mean (SD) age of the patients at diagnosis was 52.9. Most (44%) cases were between the ages of 50 to 69 years old. The mean (SD) age of cases was slightly younger in males (52.6 [SD]) than females (53.5 [SD]).

Table 1 and 2 show the number of cancer cases stratified by primary site, age group, and sex, together with the total frequency, crude rates, and ASRs. During 2015 until 2017, 44 types of cancers were recorded ranging from oral cavity (C00-C08) to leukaemia (C91-C95) in the 3 health facilities. The total crude incidence rate and ASR were calculated accordingly. The crude incidence rate was 11.8; ASR 48.6 per 100 000 men and 17.8; ASR 83.9 per 100 000 women in the province. When trend test was used, there was a significant decline in cancer incidences observed in these 3 health institutions from 2015 to 2017 (P < .05) [data not shown].

Figure 2 shows a random geographical spread of seen cancer incidence in KwaZulu-Natal. Higher spatial concentrations were marked in and around eThekwini and uMgungundlovu municipalities, where the 3 referral (Addington, IACLH, and Greys) hospitals are located. Temporal trends over the 3 years show that uMkhanyakude consistently had the lowest incidence rate (2015: 73, 2016: 55, and 2017: 22). For uThungulu (rural district situated in the north–eastern region) and Ugu (predominantly rural situated in the south coast), a decline was noted over the 3 years (from 114 to 36 cancer incidences), whereas Amajuba (rural district situated in the north western region) and uMzinyathi (urbanised district situated in the north-central areas of KZN) had an increase over time. Some districts such as iLembe (rural district situated in east coast
Table 1. Number of male cancer cases reported in the period 2015 to 2017 in the health facilities in KZN stratified by primary site and age group.

| SITE | ICD 10 | 0-14 | 15-24 | 25-39 | 40-49 | 50-59 | 60-64 | 65-74 | 75-84 | 85+ | TOTAL | CRUDE | ASR |
|------|--------|------|-------|-------|-------|-------|-------|-------|-------|-----|--------|-------|-----|
| Oral cavity | C00-C08 | 0 | 1 | 0 | 0 | 4 | 4 | 8 | 12 | 22 | 27 | 21 | 22 | 9 | 6 | 6 | 142 | 7.7 | 0.9 | 2.5 |
| Other pharynx | C09-C10, C13 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 5 | 13 | 15 | 10 | 2 | 7 | 4 | 2 | 61 | 3.3 | 0.4 | 1.0 |
| Nasopharynx | C11 | 1 | 1 | 2 | 0 | 0 | 0 | 1 | 2 | 2 | 2 | 2 | 3 | 0 | 1 | 0 | 15 | 0.8 | 0.1 | 0.6 |
| Oesophagus | C15 | 0 | 0 | 0 | 0 | 1 | 2 | 2 | 5 | 12 | 25 | 13 | 22 | 7 | 4 | 2 | 95 | 5.1 | 0.6 | 1.5 |
| Stomach | C16 | 0 | 0 | 1 | 3 | 1 | 4 | 3 | 7 | 6 | 6 | 12 | 11 | 7 | 5 | 0 | 66 | 3.6 | 0.4 | 1.3 |
| Colon, anus, and rectum | C18-C21 | 0 | 0 | 0 | 6 | 8 | 13 | 22 | 14 | 21 | 24 | 35 | 30 | 22 | 3 | 6 | 204 | 11.0 | 1.3 | 4.2 |
| Liver | C22 | 2 | 0 | 0 | 2 | 3 | 1 | 3 | 7 | 6 | 7 | 6 | 3 | 2 | 3 | 0 | 45 | 2.4 | 0.3 | 1.4 |
| Gallbladder | C23-C24 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 1 | 0 | 1 | 4 | 0.2 | 0.0 | 0.0 |
| Pancreas | C25 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 2 | 1 | 1 | 3 | 0 | 0 | 0 | 0 | 8 | 0.4 | 0.1 | 0.2 |
| Nasal cavity | C30 | 0 | 0 | 0 | 1 | 1 | 0 | 5 | 1 | 2 | 3 | 1 | 1 | 0 | 1 | 0 | 16 | 0.9 | 0.1 | 0.4 |
| Accessory sinuses | C31 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 2 | 0 | 1 | 0 | 0 | 7 | 0.4 | 0.0 | 0.1 |
| Larynx | C32 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 7 | 21 | 8 | 23 | 14 | 9 | 2 | 0 | 86 | 4.6 | 0.5 | 1.4 |
| Bronchus and lung | C33-C34 | 0 | 1 | 0 | 1 | 1 | 5 | 10 | 15 | 28 | 42 | 42 | 52 | 25 | 8 | 6 | 236 | 12.7 | 1.5 | 3.7 |
| Thymus | C37 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0.1 | 0.0 | 0.1 |
| Heart, mediastinum, and pleura | C38 | 3 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 5 | 0.3 | 0.0 | 0.7 |
| Bones | C41 | 2 | 1 | 4 | 2 | 0 | 1 | 2 | 1 | 1 | 1 | 3 | 1 | 0 | 0 | 0 | 19 | 1.0 | 0.1 | 1.1 |
| Skin and other | C44 | 1 | 1 | 1 | 1 | 4 | 6 | 0 | 2 | 4 | 2 | 4 | 5 | 2 | 2 | 4 | 39 | 2.1 | 0.2 | 1.2 |
| Kaposi sarcoma | C46 | 1 | 3 | 8 | 41 | 59 | 69 | 52 | 24 | 18 | 11 | 7 | 5 | 2 | 1 | 2 | 303 | 16.3 | 1.9 | 12.6 |
| Nervous system | C47 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 2 | 0.1 | 0.0 | 0.0 |
| Connective and other soft tissues | C49 | 0 | 4 | 4 | 1 | 4 | 4 | 3 | 3 | 6 | 2 | 3 | 2 | 0 | 2 | 1 | 39 | 2.1 | 0.2 | 1.4 |

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### Table 1. (Continued)

| SITE                        | ICD 10 | 0-14 | 15-19 | 20-24 | 25-29 | 30-34 | 35-39 | 40-44 | 45-49 | 50-54 | 55-59 | 60-64 | 65-69 | 70-74 | 75-79 | 80+ | TOTAL (%) | CRUDE | ASR |
|-----------------------------|--------|------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|----|---------|-------|-----|
| Breast                      | C50    | 0    | 0     | 0     | 0     | 1     | 1     | 3     | 0     | 2     | 4     | 3     | 2     | 0     | 0    | 16 | 0.9      | 0.1   | 0.3 |
| Prostate                    | C60    | 0    | 0     | 0     | 1     | 0     | 3     | 6     | 6     | 3     | 0     | 0     | 0     | 0     | 1    | 0   | 20       | 1.1   | 0.6 |
| Penis                       | C61    | 0    | 0     | 0     | 0     | 0     | 1     | 5     | 6     | 16    | 33    | 41    | 37    | 25    | 14   | 178| 9.6      | 1.1   | 1.8 |
| Testis                      | C62    | 1    | 2     | 4     | 4     | 2     | 4     | 3     | 1     | 1     | 0     | 1     | 0     | 1     | 0    | 26 | 1.4      | 0.2   | 1.3 |
| Kidney and renal pelvis     | C64-C65| 5    | 0     | 0     | 0     | 0     | 0     | 1     | 1     | 1     | 4     | 2     | 1     | 1     | 0    | 16 | 0.9      | 0.1   | 1.2 |
| Bladder                     | C67    | 0    | 0     | 0     | 0     | 1     | 1     | 3     | 0     | 11    | 1     | 3     | 5     | 3     | 1    | 29 | 1.6      | 0.2   | 0.4 |
| Eye                         | C69    | 2    | 0     | 0     | 0     | 4     | 1     | 2     | 2     | 2     | 3     | 2     | 0     | 1     | 1    | 0   | 20       | 1.1   | 0.9 |
| Brain                       | C70-C72| 1    | 2     | 2     | 2     | 1     | 0     | 2     | 1     | 2     | 1     | 1     | 0     | 0    | 0    | 18 | 1.0      | 0.1   | 0.9 |
| Thyroid                     | C74    | 3    | 0     | 0     | 0     | 0     | 2     | 1     | 1     | 2     | 1     | 2     | 0     | 0    | 0   | 12 | 0.6      | 0.1   | 0.8 |
| Other endocrine glands      | C75    | 2    | 1     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0    | 3  | 0.2      | 0.0   | 0.5 |
| Neck, face, and head        | C76-C77| 1    | 0     | 2     | 2     | 1     | 4     | 4     | 2     | 4     | 6     | 2     | 2     | 1     | 3    | 1  | 35       | 1.9   | 0.2 |
| Unknown primary site        | C80    | 1    | 0     | 0     | 0     | 0     | 1     | 0     | 0     | 2     | 0     | 1     | 3     | 0     | 1    | 0  | 9        | 0.5   | 0.1 |
| Hodgkin's disease           | C81    | 0    | 0     | 1     | 1     | 2     | 1     | 1     | 0     | 1     | 4     | 1     | 0     | 0     | 0    | 0  | 12       | 0.6   | 0.4 |
| Non-Hodgkin's lymphoma      | C82-C86| 0    | 4     | 1     | 3     | 3     | 3     | 8     | 5     | 4     | 0     | 3     | 3     | 3     | 1    | 2  | 43       | 2.3   | 0.3 |
| Multiple myeloma            | C88-C90| 0    | 0     | 0     | 0     | 1     | 3     | 4     | 1     | 4     | 0     | 2     | 0     | 1     | 0    | 0  | 16       | 0.9   | 0.1 |
| Leukaemia                   | C91-C95| 2    | 2     | 2     | 1     | 0     | 1     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0    | 0  | 8        | 0.4   | 0.1 |
| Total                       |        | 28   | 23    | 30    | 73    | 106   | 132   | 149   | 141   | 196   | 229   | 242   | 234   | 146   | 77   | 49 | 1855     | 100   | 11.8 | 48.6 |

Abbreviations: ASR, age-standardised incidence rates; ICD, International Classification of Disease; KZN, KwaZulu-Natal.
Table 2. Number of female cancer cases reported in the period 2015 to 2017 in the health facilities in KZN stratified by primary site and age group.

| FEMALE 2015-2017 | AGE | SITE | ICD 10 | 0-14 | 15-24 | 25-34 | 35-44 | 45-54 | 55-64 | 65-74 | 75-84 | 85+ | TOTAL | TOTAL (%) | CRUDE | ASR |
|------------------|-----|------|--------|------|-------|-------|-------|-------|-------|-------|-------|-----|-------|-----------|-------|-----|
| Oral cavity      | C00-C08 | 0 | 1 | 3 | 4 | 5 | 8 | 8 | 6 | 13 | 13 | 11 | 11 | 11 | 11 | 103 | 3.4 | 0.6 | 2.5 |
| Other pharynx    | C09-C10, C13 | 0 | 0 | 2 | 0 | 0 | 1 | 2 | 3 | 0 | 4 | 4 | 2 | 1 | 1 | 0 | 20 | 0.7 | 0.1 | 0.5 |
| Nasopharynx      | C11 | 0 | 1 | 1 | 0 | 0 | 1 | 1 | 1 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 7 | 0.2 | 0.0 | 0.2 |
| Oesophagus       | C15 | 1 | 1 | 0 | 2 | 1 | 1 | 4 | 6 | 19 | 19 | 15 | 15 | 11 | 8 | 6 | 109 | 3.6 | 0.6 | 2.3 |
| Stomach          | C16 | 0 | 0 | 0 | 1 | 0 | 2 | 3 | 6 | 3 | 12 | 7 | 8 | 7 | 2 | 3 | 54 | 1.8 | 0.3 | 1.1 |
| Colon, anus, and rectum | C18-C21 | 0 | 0 | 5 | 8 | 13 | 24 | 28 | 17 | 21 | 12 | 20 | 27 | 12 | 7 | 9 | 203 | 6.6 | 1.2 | 1.4 |
| Liver            | C22 | 0 | 0 | 2 | 1 | 3 | 4 | 1 | 3 | 1 | 0 | 5 | 2 | 1 | 2 | 1 | 26 | 0.9 | 0.2 | 0.7 |
| Gallbladder      | C23-C24 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 2 | 0 | 2 | 0 | 0 | 1 | 1 | 0 | 5 | 0.2 | 0.0 | 0.1 |
| Pancreas         | C25 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 2 | 1 | 1 | 0 | 0 | 1 | 7 | 0.2 | 0.0 | 0.1 |
| Nasal cavity     | C30 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 2 | 2 | 1 | 1 | 1 | 3 | 12 | 0.4 | 0.1 | 0.2 |
| Accessory sinuses | C31 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 1 | 1 | 0 | 1 | 1 | 6 | 0.2 | 0.0 | 0.1 |
| Larynx           | C32 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 2 | 3 | 3 | 1 | 1 | 1 | 0 | 14 | 0.5 | 0.1 | 0.3 |
| Bronchus and lung | C33-C34 | 0 | 0 | 0 | 0 | 1 | 4 | 4 | 4 | 9 | 11 | 12 | 7 | 12 | 6 | 0 | 70 | 2.3 | 0.4 | 1.4 |
| Thymus           | C37 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 3 | 0.1 | 0.0 | 0.1 |
| Heart, mediastinum, and pleura | C38 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 4 | 0.1 | 0.0 | 0.1 |
| Bone             | C41 | 3 | 1 | 2 | 1 | 3 | 2 | 1 | 3 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 19 | 0.6 | 0.1 | 1.1 |
| Skin and other   | C44 | 0 | 0 | 0 | 1 | 2 | 1 | 4 | 2 | 1 | 7 | 1 | 1 | 1 | 1 | 0 | 1 | 22 | 0.7 | 0.1 | 0.6 |
| Mesothelioma     | C45 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0.1 | 0.0 | 0.1 |
| Kaposi sarcoma   | C46 | 2 | 0 | 18 | 40 | 49 | 26 | 19 | 12 | 7 | 3 | 2 | 0 | 2 | 2 | 4 | 186 | 6.1 | 1.1 | 8.0 |
| Nervous system   | C47 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0.0 | 0.0 | 0.1 |
### Table 2. (Continued)

| SITE                                       | ICD 10 | 0-14 | 15-24 | 25-34 | 35-44 | 45-54 | 55-64 | 65-74 | 75-79 | 80+ | TOTAL (%) | CRUDE | ASR |
|--------------------------------------------|--------|------|-------|-------|-------|-------|-------|-------|-------|-----|-----------|-------|-----|
| Connective and other soft tissues         | C49    | 0    | 1     | 1     | 1     | 0     | 5     | 2     | 6     | 6   | 4         | 2     | 4   |
| Breast                                    | C50    | 0    | 1     | 2     | 8     | 31    | 41    | 73    | 77    | 80  | 78        | 70    | 71  |
| Female genital and other                  | C51-C52| 0    | 1     | 3     | 14    | 22    | 38    | 22    | 10    | 6   | 9         | 3     | 9   |
| Cervix uteri                              | C53    | 1    | 3     | 2     | 15    | 70    | 82    | 122   | 96    | 128 | 102       | 59    | 75  |
| Corpus uteri                              | C54    | 0    | 0     | 0     | 1     | 0     | 5     | 6     | 20    | 30  | 28        | 19    | 20  |
| Ovary                                     | C56    | 4    | 3     | 4     | 1     | 2     | 3     | 6     | 11    | 13  | 11        | 3     | 4   |
| Placenta                                  | C58    | 0    | 0     | 0     | 1     | 0     | 0     | 0     | 0     | 0   | 1         | 0     | 0.1|
| Kidney and renal pelvis                   | C64-C65| 8    | 1     | 0     | 0     | 0     | 2     | 1     | 2     | 0   | 6         | 3     | 1   |
| Bladder                                   | C67    | 0    | 0     | 0     | 1     | 1     | 0     | 0     | 2     | 0   | 1         | 3     | 3   |
| Eye                                       | C69    | 3    | 0     | 0     | 2     | 2     | 3     | 2     | 1     | 3   | 3         | 0     | 1   |
| Brain                                     | C70-C72| 1    | 1     | 1     | 1     | 3     | 0     | 1     | 1     | 0   | 0         | 0     | 2   |
| Thyroid                                   | C74    | 1    | 2     | 1     | 1     | 4     | 4     | 4     | 7     | 7   | 9         | 5     | 6   |
| Other endocrine glands                    | C75    | 1    | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0   | 0         | 0     | 1   |
| Neck, face, and head                      | C76-C77| 1    | 0     | 1     | 2     | 1     | 1     | 1     | 3     | 0   | 1         | 3     | 5   |
| Unknown primary site                      | C80    | 0    | 0     | 0     | 0     | 2     | 0     | 1     | 1     | 1   | 1         | 1     | 1   |
| Hodgkin’s disease                         | C81    | 0    | 3     | 1     | 2     | 1     | 0     | 3     | 1     | 3   | 0         | 1     | 0   |
| Non-Hodgkin’s lymphoma                    | C82-C86| 0    | 2     | 2     | 2     | 4     | 6     | 8     | 6     | 5   | 4         | 3     | 2   |
| Multiple myeloma                          | C88-C90| 0    | 0     | 0     | 0     | 1     | 0     | 1     | 0     | 1   | 0         | 1     | 1   |
| Leukaemia                                 | C91-C95| 2    | 1     | 2     | 1     | 1     | 0     | 0     | 0     | 0   | 0         | 0     | 8   |
| **Total**                                 |        | 28   | 24    | 54    | 112   | 224   | 262   | 326   | 288   | 340 | 344       | 282   | 289 |

Abbreviations: ASR, age-standardised incidence rates; ICD, International Classification of Disease; KZN, KwaZulu-Natal.
region) had a low incidence for 2015 to 2016 and increased in 2017. When tested for randomness with Moran's Index, a random geographical distribution was found for all cancers, and it was noticed that the northern districts of the province seem to have lower ASR of cancer throughout the 3 years (Figure 2).

Female cancers (cervical and breast) ranked highest in cancer incidence in the 3 facilities over the 3-year period (2015-2017), and most of these cases were in 50- to 54-year age band (Table 2). The spatial variation of cervical and breast cancer shows urban municipality (uMgungundlovu) to have a high ASR of 43.8 per 100,000 and 35.5 per 100,000, respectively. However, the lowest rates were observed in rural municipalities for cervical cancer were in Zululand; 11.4 per 100,000 and for breast cancer in uMkhanyakude; 2.3 per 100,000 (Figures 4 and 5).

Kaposi sarcoma was more common in males than females across the province with the highest incidence rates observed in the 35 to 39 age range. Figures 3 and 4 illustrate that the highest ASRs of Kaposi sarcoma for both males and females were observed in uMkhanyakude (17.5 per 100,000 persons per year and 11.9 per 100,000 persons per year) followed by uMgungundlovu (9.3 per 100,000 persons per year and 11.3 per 100,000 persons per year). The lowest incidence rates were observed in uMzinyathi (2.1 per 100,000 males per year and 3.3 per 100,000 females per year). Figures 5 and 6 provide geographical variation and the spread of the top cancers by sex.

The only exclusive male cancer in the top 5 of the cancers was prostate cancer, and the highest rate was observed in Amajuba district (ASR of 8.6 per 100,000) and lowest in Ugu (ASR of 0.1 per 100,000) (Figure 4).

**Discussion**

Our study established a decrease in the estimated overall ASR over the 3-year period both in males and females. Even though
a random spatial distribution of cancer among the districts of the province was observed, high levels of cancer reported in urban districts and low levels of cancer reported in the districts that are mainly rural.

The incidence rates of cancer reported in our study are lower than the national estimates reported by the South African National Cancer Registry (NCR) in 2014 for both males and females (131.16 and 137.84 per 100 000, respectively), and this could be that the results of this study are an estimation of one province over the 3-year study period using data from public hospitals only. There may be changes as there are no recent cancer estimates in the country, but NCR does not stratify the results by province therefore making difficult to compare at the provincial level. Our findings on standardised incidence rates are also lower in comparison to Bray et al results showing for both males and females in Southern Africa having (230.5 per 100 000 and 196.1 per 100 000, respectively).

Missing data are problematic especially in epidemiologic studies. The study lost a sufficient number of data due to incomplete or missing observations in variables of interest. Imputation merges were taken to minimise further loss of data. The results of the study may not show a true reflection of malignant cancers which are more aggressive as cancer patients may succumb to cancer while in the process of localising the
disease resulting to incomplete diagnosis. The shortcoming demonstrates the cracks in the health system from timely diagnostic procedures and treatment as well as complete documentation of all-important information. It was noted in the manuscript that the focus was on medical records of cancer patients who were seen in the oncology departments of the 3 facilities. It was realised upon data collection that paediatric patients and patients with blood-related cancers were referred or seen at special clinics and not all of them were seen at the oncology department. These cancers are not well represented in the study.

Our findings demonstrate substantial decline of cancer cases in the 3 hospitals over time (3-year period). In 2017, the provincial Department of Health in KZN initiated another cancer treatment site that caters to the management of breast and cervical cancer patients in Ngwelezane, the Northern part of the province24; therefore likely resulting in low number of cases from that area having presenting in the 3 health facilities. Preventive campaign strategies such as hepatitis B and human papillomavirus virus (HPV) vaccination programmes that are part of the Extended Programme of Immunisation and policies on breast and cervical cancer that are carried out by the government and nonprofitable organisations may have also influenced the decline of cancer incidence over time.25-27 Based on this study, breast and cervical cancers were leading cancers in KwaZulu-Natal, and this trend is similar to the global cancer data presented in the Global Cancer Incidence, Mortality, and Prevalence (GLOBOCAN) report (2018) that shows Africa having these 2 cancers leading in incidence and mortality.1,28

The ASR for both males and females displayed a high degree of cancer distribution among magisterial districts of the province, with high levels found in mainly urban areas of the province. A study conducted in KwaZulu-Natal by Scott et al suggested that socio-economic factors could be the reason for inconsistency in cancer distribution because of the difference in accessibility to cancer care facilities.13,29 Another likely factor contributing to the high concentration of patients residing in districts that are largely urban is that patients from remote areas often use an address of a relative or friend that lives around the health facilities, therefore, leading to the elevation of cancer incidences around the 3 hospitals.13,30 Furthermore, the lack of cancer awareness, interventions, and proper surveillance systems in rural settings may affect the trends and distribution of cancer locally and nationally.27,29

Colorectal cancer and Kaposi sarcoma were the most common cancers for both sexes. Colorectal cancer cuts across as the third leading cancer and was more prevalent in urban areas (uMgungundlovu and eThekwini); however, in comparison to

Figure 6. Female top cancers by district of the KwaZulu-Natal province: (A) cervical, (B) breast, (C) Kaposi sarcoma, (D) colorectal, and (E) female genital, other.
national statistics, it was the fourth leading for men and not in the top 10 cancers for females in 2014.28 The province of KwaZulu-Natal has a consistent high prevalence of HIV in South Africa which could be the reason for the high incidence of Kaposi sarcoma.27,31,32 UMkhanyakude, the rural district with the highest incidence rate of Kaposi sarcoma, is surrounded by multiple borders with large areas that are socio-economically deprived; ultimately this becoming one of the reasons behind the population being susceptible to HIV/AIDS and eventually having high cases of Kaposi sarcoma according to the results of the study.33,34

This study provides information on incidence of cancer seen 3 major public oncology facilities in the province over time and their geographical distribution. To avoid major loss of data, we managed to incorporate stringent measures such as imputation. In most north-west regions of KZN with low population density, cancer incidence trend was increasing, and it is expected that the cancer ASR will rise even more in the future adoption of westernisation increasing ageing population. Cancer-preventive initiatives can be informed by the findings especially with the high incidence rate of cervical and breast cancer in the province.

A limitation of the study was evident in the underestimation of some cancers (blood cancers) as a result of barriers affecting patients accessing health systems. Data collected in the study was primarily from oncology departments in public hospitals, whereas other facilities or private hospital data were not included. Although the goal of the study was to show spatial variation of cancer in the province, it rather provides a geography of accessibility of cancer treatment.

Conclusion
The overall cancer incidence in the study shows that female cancers still need to be given a priority as they were that most prevalent with cervical and breast cancer at the top in the province of KZN. Other common cancers such as colorectal and oral cavity require further research to better understand and inform cancer policies. Health policymakers need to prioritise the development and implementation of comprehensive cancer control programmes which include population-based cancer registries that are vital to providing complete quality data as a measure towards producing realistic estimates.

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Author Contributions
All authors (M.M., T.G., A.M., and N.J.) designed the study. M.M. collected the data. M.M. and A.M. analysed the data. M.M. and N.J. organised the manuscript, and all authors reviewed the paper and revised the manuscript.

Availability of Data and Materials
Data from this study are the property of KZN-DOH and the University of KwaZulu-Natal and cannot be made publicly available. All interested readers can access the data set from the DOH Research ethics committee and University of KwaZulu-Natal Biomedical Research Ethics Committee (BREC) from the following contacts: The Health Research and Knowledge Management, 330 Langalibalele Street, Private bay X9051, Pietermaritzburg, 3200, Tel: +27 33 3952805 Fax: +27 33 3943782 Email: hrk@kznhealth.gov.za. The Chairperson Biomedical Research Ethics Administration Research Office, Westville Campus, Govan Mbeki Building University of KwaZulu-Natal/Bag X54001, Durban, 4000 KwaZulu-Natal, South Africa Tel: +27 31 260 4609 Email: BREC@ukzn.ac.za.

Ethics Consideration
Full ethical approval was obtained from the Biomedical Research Ethics Committee (BREC) at the University of KwaZulu-Natal (Ref no: BE553/18). Permission to conduct this research was sought from the Provincial Department of Health (DOH) Ref: KZ_201810_050 and the 3 hospitals to ensure all ethical considerations were met.

ORCID iD
Mpho KTN Motlana https://orcid.org/0000-0002-5989-5545

REFERENCES
1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jamal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68:394-424. doi:10.3322/ casc.21492.
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:E39-E186. doi:10.1002/ijc.29290.
3. Parkin DM, Bray F, Ferlay J, Jamal A. Cancer in Africa. 2012. Cancer Epidemiol Biomarkers Prev. 2014;23:953-966. doi:10.1158/1055-9965.EPI-14-0281.
4. Bello B, Fadahun O, Kielkowsk D, Nelson G. Trends in lung cancer mortality in South Africa: 1995-2006. BMC Public Health. 2011;11:209. doi:10.1186/1471-2458-11-209.
5. Mayouzi BM, Flisher AJ, Lalloo UK, et al. The burden of non-communicable diseases in South Africa. Lancet. 2009;374:934-947. doi:10.1016/S0140-6736(09)61087-4.
6. Stefan DC. Cancer care in Africa: an overview of resources. J Glob Oncol. 2015;1:30-36. doi:10.1200/JGO.2015.00406.
7. Norman B, Bradshaw D, Schneider M, et al. A comparative risk assessment for South Africa in 2000: towards promoting health and preventing disease. S Afr Med J. 2007;97:637-641.
8. Tabish SA. Lifestyle diseases: consequences, characteristics, causes and control. J Cardiovasc Care Rev. 2017;9:2-6. doi:10.15406/jccr.2017.09.00326.
9. Coghill AE, Newcomb-Pa, Madeleine MM, et al. Contribution of HIV infection to mortality among cancer patients in Uganda. AIDS. 2015;27:2933-2942. doi:10.1097/01.aids.0000432326.55937.cb.
10. Best N, Richardson S, Thomson A. A comparison of Bayesian spatial models for disease mapping. Stat Methods Med Res. 2005;14:35-59. doi:10.1191/0962280205sm388oa.
11. Kirby RS, Delmelle E, Eberth JM. Advances in spatial epidemiology and geographic information systems. Ann Epidemiol. 2017;27:1-9. doi:10.1016/j. annepidem.2016.12.001.
12. Tsai PJ. Application of Moran’s test with an empirical Bayesian rate to leading health care problems in Taiwan in a 7-year period (2002-2008). Glob J Health Sci. 2012;4:63-77. doi:10.5539/gjhs.v4n5p63.

13. Scott D, Curtis B, Twumasi FO. Towards the creation of a health information system for cancer in KwaZulu-Natal, South Africa. Health Place. 2002;8:237-249. doi:10.1016/S1353-8292(02)00009-6.

14. Singh E, Ruff PP, Babb C, et al. Establishment of a cancer surveillance programme: the South African experience. Lancet Oncol. 2016;16:e414-e421. doi:10.1016/S1470-2045(15)00162-X.

15. Made F, Wilson K, Jina R, et al. Distribution of cancer mortality rates by province in South Africa. Cancer Epidemiol. 2017;51:56-61. doi:10.1016/j.canep.2017.10.007.

16. Statistics South Africa. Mid-Year Population Estimates. Pretoria, Republic of South Africa: Department of Statistics South Africa. https://www.statssa.gov.za/publications/P0302/P03022019.pdf. Published 2019. Accessed September 23, 2019.

17. National Government of South Africa. KwaZulu-Natal municipalities. Municipalities.co.za. https://municipalities.co.za/provinces/view/4/kwazulu-natal. Accessed January 16, 2021.

18. World Health Organization (WHO). The International Classification of Diseases, 10th Revision (ICD-10). 5th ed. Geneva, Switzerland: WHO Press; 2015.

19. ESRI. ArcGIS Desktop. Redlands, CA: Environmental Systems Research Institute. https://www.esri.com/en-us/home. Published 2019. Accessed July 20, 2019.

20. Rytkonen MJ. Not all maps are equal: GIS and spatial analysis in epidemiology. Int J Circumpolar Health. 2004;63:9-24.

21. Stefan DC. Why is cancer not a priority in South Africa? South African Med J. 2015;105:103-104. doi:10.7196/SAMJ.9501.

22. Perkins NJ, Cole SR, Harel O, et al. Principled approaches to missing data in epidemiologic studies. Am J Epidemiol. 2018;187:568-575. doi:10.1093/aje/kwx1348.

23. Parliamentary Monitoring Group. ATC171101: report of the Portfolio Committee on Health on the South African Human Rights Commission’s Report Investigation into Oncology Services in Kwa-Zulu Natal Province. Dated 01 November 2017. Report of the Portfolio Committee on South Africa. https://pmn.org.za/tabled-committee-report/3253/. Published 2017.

24. National Department of Health. Breast Cancer Control Policy. Pretoria, South Africa: National Department of Health; 2017. doi:10.1074/mcp.R300003-MCP200.

25. National Department of Health. Cervical Cancer Prevention and Control. https://www.westerncape.gov.za/text/2020/February/cervical_cancer_preven_ tion_and_control_policy.pdf. Published 2017.

26. Department of Health. National Cancer Strategic Framework for South Africa 2017-2022. Vol. 54. Pretoria, South Africa: National Department of Health, 2017. http://www.health.gov.za/policies-and-guidelines/.

27. National Institute for Communicable Diseases. Cancer in South Africa 2014. Full Report National Cancer Registry. https://www.nicd.ac.za/wp-content/uploads/2019/12/2014-NCR-tables.pdf. Published 2014.

28. MacDonell S, Low M. Graphs that tell the story of HIV in South Africa’s provinces. Spotlight. August 5, 2019. https://www.spotlightnsp.co.za/2019/08/05/graphs-that-tell-the-story-of-hiv-in-south-africas-provinces/. Accessed January 14, 2021.

29. Barron P, Day C, Monticelli F. District Health Barometer2006/07. https://www.hst.org.za/publications/DistrictHealthBarometers/DHB_2006_07.pdf. Published 2006.

30. Department of Health. Umkanyakude District Health Plan 2018/19 – 2020/21. Vol. 21. https://www.spotlightnsp.co.za/wp-content/uploads/2020/12/Umkhanyakude_DHP_2018.19.pdf. Published 2018.