







RESEARCH ARTICLE

The state of cancer in Meru, Kenya: a retrospective study

[version 1; peer review: 1 approved with reservations, 1 not approved]

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Abstract

Background: It is projected that by 2030, 70% of all cancer related deaths will occur in low-middle income countries. However, data on the state of cancer in most African countries is scanty. Cancer estimates for Kenya are based on the Nairobi and Eldoret cancer registries, leaving most parts of the country unrepresented. Lacking national coverage, these data do not accurately reflect Kenya's cancer burden. The paucity of reliable data impedes formulation of effective cancer control strategies and cancer research prioritization. Here, we report the findings of a retrospective study of the cancer state in Meru County, Kenya.



Methods: A retrospective analysis of patient files at Meru hospice was carried out. 2349 cancer cases seen at the Meru hospice between 2003 and 2018 were analyzed. Data abstracted from the records included patient age, gender and cancer type. The abstracted data was analyzed by descriptive statistics.


Results: Our results indicate that cancer is almost evenly distributed across genders, with men accounting for 49% and women 51%. Stomach cancer rates are strikingly elevated and equal to those in countries with the highest stomach cancer rates globally – making it the commonest cancer in this region (14%). Among men, the most common cancers affect the prostate (18%), stomach (17%), esophagus (14%), head & neck (12%), liver (8%) and colorectum (5%). Among women, the commonest are cancers of the breast (22%), cervix (20%), stomach (11%), esophagus (8%), head & neck (6%) and liver (5%). Breast cancer occurs at a notably early age, with 20% of those affected aged below 40. Lung cancer rates are notably low in this region (1.3%) relative to world estimates.

Conclusion: Cancer distribution in Meru is nearly even between sexes.

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Any reports and responses or comments on the article can be found at the end of the article.

Our analysis suggests that the Meru region is a stomach cancer hotspot and that it also experiences elevated esophageal cancer levels.

Keywords

Cancer incidence, Cancer burden, Kenya, Africa, Stomach cancer, Esophageal cancer

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Introduction

Accounting for over 70% of all global deaths annually, non-communicable diseases (NCDs), including cancer, are the world's leading cause of mortality^{1,2}. The bulk of NCD global burden is borne by low and middle-income countries (LMICs), where greater than 75% of all NCD-associated deaths occur¹. After cardiovascular complications, cancer is the second leading cause of mortality globally – causing more than 9 million deaths annually^{1,3}. In 2018, there were 18 million new cancer cases and 9.6 million cancer deaths worldwide⁴. These numbers are projected to rise to 29.5 million new cancer cases and 16.5 million cancer deaths by the year 2040⁵. Cancer is projected to be the leading cause of death worldwide within the 21st century⁴. It is estimated that 70% of cancer deaths occur in LMICs^{6,7}.

Comprehensive data on cancer incidence and mortality is sparse in most African countries⁸. Nonetheless, it is estimated that by 2030, the number of new cancer cases will rise most rapidly in Africa, with a projected 70% increase in cancer rates on the basis of demographic changes alone^{8,9}.

Cancer incidence data provided by the World Health Organization's (WHO) International Agency for Research on Cancer (IARC) are derived from population-based cancer registries (PBCRs). While PBCRs have national coverage in some countries, in many parts of the world, including Africa, they are subnational and cover a few urban areas⁴. Only 1% of Africa is covered by high-quality cancer registries^{4,10,11}. Hence, estimates of cancer incidence and mortality in most African countries are likely to be significantly underestimated due to a range of factors including a lack of cancer registries⁸. For instance, IARC's 2018 comprehensive report on cancer in Sub-Saharan Africa (SSA) is based on 25 cancer registries in 20 countries⁹. This report's data on cancer in Kenya is based on two cancer registries; the Nairobi cancer registry and the Eldoret cancer registry⁹, which may not accurately portray the country's cancer burden. This paucity of reliable information about cancer incidence, distribution and mortality greatly limits the country's ability to develop effective cancer control and prevention programs.

Nonempirical observation indicates that the Meru region of Kenya has one of the highest cancer rates in the country^{12,13}. Here, we present data from the Meru hospice in Eastern Kenya and describe the pattern of cancer in the greater Meru region of Kenya for the period between 2003 and 2018 (Figure 4). We contend that in the absence of a comprehensive cancer registry, the data we present here provide a valuable resource to guide cancer control policy and prioritize cancer research efforts. We report that for some cancer types, incidence rates in the greater Meru region markedly differ from GLOBOCAN's cancer rate estimates for Kenya, East Africa, Africa and globe.

Methods

Ethical clearance

Ethical clearance for this study, approval number 908, was obtained from the Institutional Research Ethics Committee of

Mount Kenya University (IREC-MKU). Because this retrospective analysis of Hospice cancer records (2003–2018) did not directly involve patients or pose any risks, a patient consent waiver was requested and granted by IREC-MKU. To protect patient privacy, redacted cancer records with all personal identifying information removed, were obtained from Meru Hospice. Permission to analyze redacted patient records was granted by the Meru Hospice administration.

Geographical area of the study

This retrospective study investigated cancer cases affecting residents of the larger Meru region in Eastern Kenya. The larger Meru region encompasses Meru County and the neighboring Tharaka Nithi County. Residents of this region have similar economic and cultural practices and therefore, they may likely share environmental and genetic drivers of cancer.

Meru region is located in eastern Kenya, on the eastern slopes of Mount Kenya at coordinates 0° 3' 0" N, 37° 38' 0" E. According to the 2019 Kenya population and housing census, Meru County has a land area of 7,006.3 km² and a population of 1,545,714. This population consists of 767,698 males and 777,975 females. Tharaka-Nithi County has a land area of 2,564.4 km² and 393,177 inhabitants. The population of Tharaka Nithi is made up of 193,764 males and 199,406 females¹⁴. The Ameru people are dominant in the region. The main economic activities in the larger Meru region are commercial farming of *khat*, cash crop farming, floriculture, horticulture, and subsistence farming of bananas, maize, beans and livestock keeping. The county literacy rate for Meru was 53% by 2012¹⁵ and the poverty level was at 15.5% as of 2016¹⁶. The county literacy rate for Tharaka Nithi is 69.75% and poverty rate is about 40%^{17,18}.

Data source and collection

For this study, we used all cancer cases data recorded by the Meru Hospice from 2003 to 2018. The Hospice began providing palliative care on 21st January 2003 and has records for 2003 to 2018, the latest year with complete annual data. Meru Hospice provides palliative care services to residents of the wider Meru region, covering Meru and Tharaka Nithi Counties. We considered Meru Hospice cancer records to be representative of the cancer burden in this region. Being the only palliative care provider in the Meru region, the hospice sees most of the region's cancer cases. The hospice also sporadically cares for cases from regions beyond the larger Meru region. A few patients from Embu, Nyeri, Laikipia, Marsabit, Samburu, Kirinyaga and Kitui county were also attended to at Meru Hospice during the study period. The data analyzed was collected during patient admission and included the following information: patient sex, age, diagnosis, area of residence and year of admission.

Data analysis

A de-identified patient register, with a total of 2424 entries was obtained from Meru Hospice. The file was first cleaned-up to exclude incomplete and non-cancer entries, a total of 39 entries. Because this analysis aimed to describe cancer patterns in the larger Meru region only, cases from

Embu, Nyeri Laikipia, Marsabit, Samburu, Kirinyaga and Kitui county, 36 cases in total, that were seen at the Hospice during the study period were excluded from the analysis. This left 2349 cancer cases eligible for further analysis.

To make analysis uniform, we categorized cancer cases by type based on the diagnosis entry in the hospice cancer patient register. Cases whose raw data diagnosis column indicated colon cancer, rectal cancer or Ca rectal were together categorized as colorectal cancers. Cases affecting the head and neck region and whose raw data diagnosis column indicated tonsillar cancer, throat cancer, nasopharyngeal cancer, oral cancer, tongue cancer, laryngeal cancer, mandible cancer, squamous cell carcinoma (SCC) of the mouth, SCC of the throat, palate cancer, SCC of the hypopharynx, lip cancer, oropharyngeal carcinoma or another site in the head & neck region, were collectively grouped as the head and neck cancers. Other cancer types that were analyzed included bile duct cancer, bladder cancer, bone cancer, brain cancer, breast cancer, cancers of the uterus, cervical cancer, gall bladder cancer, Kaposi sarcoma, liver cancer, lung cancer, lymphoma, melanoma, multiple myeloma, esophageal cancer, pancreatic cancer, prostate cancer, stomach cancer and ovarian cancer. Because cancer in Kenya is often diagnosed late^{19,20}, we considered year of admission to be same as year of diagnosis.

Of the 2349 cancer cases eligible for further examination, entries that were incomplete for particular forms of analysis were

excluded from those analysis only. For instance, entries lacking the age were excluded from age-distribution analysis but included in other forms of analysis. Cancer entries whose site was not clearly recorded, e.g. those entered as SCC without indication of the affected site, were excluded from the analysis of cancer incidence by type. Statistical analysis and graphs were done using GraphPad® Prism 6 statistical software. Analysis was done to describe cancer incidence in Meru by age, sex, type and age-distribution. Incidence refers to the number of cancer cases recorded at Meru Hospice between 2003 and 2018. Incidence is conveyed here as a proportion (%) of the total number of cases under consideration, i.e. the total male and female cases combined, total male cases only or total female cases only. For the age at diagnosis analysis, all cancer records were used except where the age was missing in the register.

Results

Cancer cases are distributed evenly between genders

To characterize the patterns of cancer distribution in the larger Meru region, Kenya, we analyzed cancer records at Meru Hospice for the years 2003 to 2018. In total, after excluding incomplete entries, cases from outside the larger Meru region and non-cancer cases, 2349 out of the 2424 cases seen at Meru Hospice from 2003 to 2018 were analyzed. Of the 2349 cancer cases, 1151 (49%) were male and 1198 (51%) were female (Figure 1A), indicating an about equal distribution of cancer cases across sexes²¹.

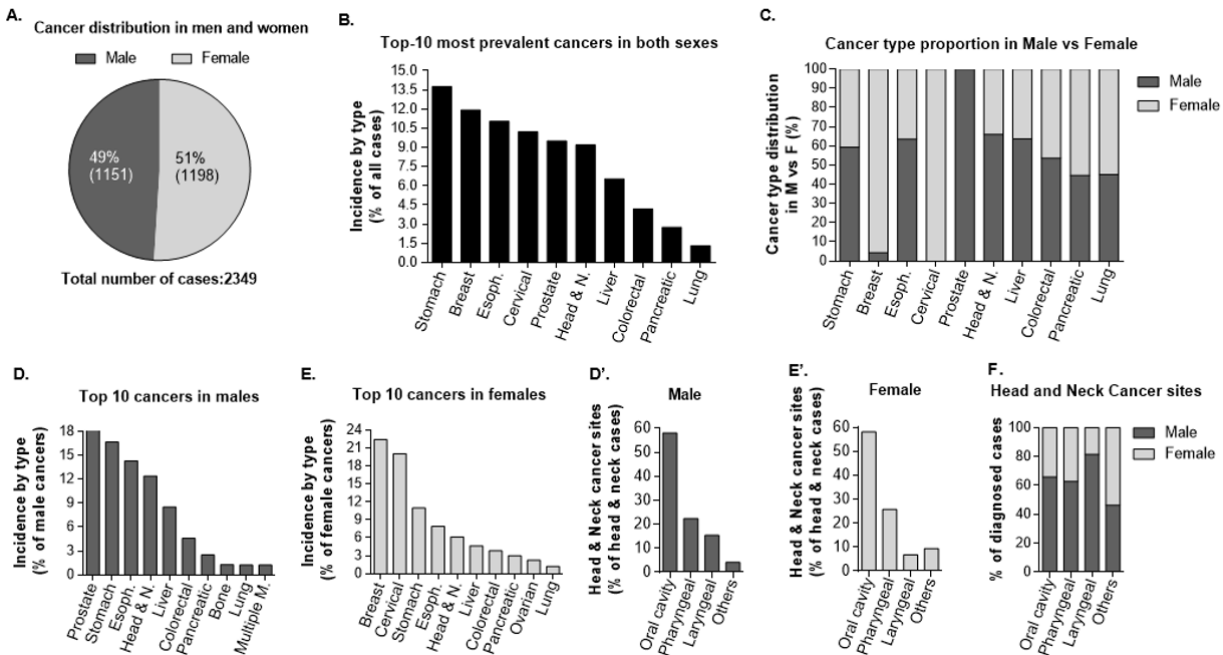


Figure 1. Cancer cases admitted to Meru hospice in 2003 – 2018. Cancer incidence in Meru county, 2003–2018. All cancer cases seen at the Meru hospice in the 15 years from 2003–2018 were analyzed. **A)** After exclusion of incomplete entries, non-cancer cases and cases from outside the larger Meru region, 2349 cases were analyzed, revealing an almost equal split of cancer cases between men and women. **B)** The 10 most frequent cancer types in both sexes combined are shown. **C)** Stomach cancer, esophageal cancer, head and neck cancers occur more frequently in men than women. Colorectal cancer affects men slightly more frequently than women. Pancreatic and lung cancer rates are slightly higher in men than women. **D)** The 10 most frequent cancer types in men only are shown. **E)** The 10 most frequent cancer types in women only are shown. **D' and E')** The most common head and neck cancers types in men only and women only are shown. **F.)** The various head neck cancer types affect men more frequently than women.

Prevalence of cancer cases by type in both sexes

We next analyzed the distribution of cancer cases by type in both sexes. From this analysis, the 10 most frequent cancers in both sexes combined, were stomach cancer (13.76%), breast cancer (11.93%), esophageal cancer (11.03%), cervical cancer (10.23%), prostate cancer (9.51%), head & neck cancers (9.21%), liver cancer (6.54%), Colorectal cancer (4.2%), pancreatic cancer (2.76%) and lung cancer (1.32%) (Figure 1B). 30 male and 20 female cases lacking information on the cancer type or the affected site and whose diagnosis was recorded only as SCC were excluded from this analysis.

Cancer distribution in men vs women

Next, we analyzed the cancer types to establish their proportions in male vs female patients. This analysis does not apply to the sex-specific cancers, i.e. prostate cancer, cervical cancer and ovarian cancer. Stomach cancer, which is the most common cancer type in this region (Figure 1B), was found to affect men more frequently than women, with 60% of cases occurring in men. Expectedly, our analysis revealed that breast cancer mostly affects women, with 95.7% of breast cancer cases afflicting women. Our analysis also revealed that esophageal cancer affected men more frequently than women, with 63% of cases occurring in men. Head and neck cancers are also more common in men, in whom 66% of cases occur. Likewise, liver cancer affects men more frequently than women, with 64% of cases being in men. Colorectal cancer is only slightly more frequent in men, who are affected in 54% of cases. Together, these data indicate that, as in other world regions, most cancers affect men more frequently than women²². The reasons for this gender bias are unclear. However, pancreatic and lung cancer appear to occur in women slightly more frequently than in men, with 55% of pancreatic and lung cancer cases affecting women (Figure 1C). It should also be noted that our data show that the rates of these two diseases are relatively low in the Meru region. 50 cases whose diagnosis was recorded only as SCC without indication of affected site were excluded from this analysis.

Cancer distribution by type in men and women

We next analyzed the distribution patterns of cancer types among men and women separately. To do this, the data on cancer cases diagnosed in men were first analyzed and ranked by cancer type frequency. Frequency is expressed as the percentage of a cancer type out of the total number of male or female cancer cases seen at Meru Hospice from 2003–2018. From this analysis, prostate cancer is the most frequent in men, accounting for close to 20% of all cancers in men (Figure 1D). It is followed by stomach cancer (17%), esophageal cancer (14%), head and neck cancers (12%), liver cancer (8%) and colorectal cancers (5%) (Figure 1D). Other cancer types in the top 10 most frequent cancers in men are pancreatic cancer (2.52%), bone cancer (1.3%), lung cancer (1.22%) and multiple myeloma (1.22%) (Figure 1D). 30 male cases recorded only as SCC and whose type/site was unknown were not analyzed. Among women, breast cancer was the most frequent cancer type, accounting for 22% of all cancer cases in women. It is followed by cervical cancer (20%), stomach cancer

(11%), esophageal cancer (8%), head and neck cancers (6%) and liver cancer (5%) (Figure 1E). Other cancers in the top 10 most frequent cancers in women are colorectal cancer (4%), pancreatic cancer (3%), ovarian cancer (2%) and lung cancer (1.22%) (Figure 1E). 20 female cases recorded only as SCC and whose type/site was unknown were not analyzed. Head and neck cancer collectively refers to cancers affecting various sites in the head and neck region – including the oral cavity, nasal cavity and the pharynx²³. To establish the incidence of specific head and neck cancers in men, we broke down the cases by site. It was found that 58% of head and neck cancers in men affect the oral cavity (Figure 1D'). Cancers affecting the pharynx and larynx account for 22% and 15% of all head neck cancers in men, respectively (Figure 1D'). A similar analysis of head and neck cancer cases in women revealed that 58% of the cases affect the oral cavity, while 25% and 6% affect the pharynx and larynx, respectively (Figure 1E'). However, the incidence of head and neck cancers is almost twice as high in men than in women (Figure 1C).

Age distribution of cancer in the Meru region

Next, we analyzed cancer distribution by age in both sexes together as well as separately. We first analyzed all cancer cases to establish the mean age of cancer occurrence in men and women combined. The average age of cancer diagnosis in both sexes combined is 58 years. In men and women separately, the average age of cancer diagnosis is 61 and 56 years, respectively (Figure 2A). We next analyzed the age of diagnosis for the top six cancer types (each responsible for $\geq 5\%$ of the total cancer cases) in men. The average age of diagnosis for prostate cancer, stomach cancer, esophageal cancer, head and neck cancers, liver cancer and colorectal cancer was 72, 61, 65, 51, 55 and 60 years, respectively (Figure 2B). In women, the average age of diagnosis for breast cancer, cervical cancer, stomach cancer, esophageal cancer, head and neck cancers and liver cancer was 51, 55, 61, 63, 58 and 58 years, respectively (Figure 2C).

We then analyzed the distribution pattern of the top six cancer types (each responsible for $\geq 5\%$ of total cancer cases) by age of diagnosis in both sexes as well as in men and women separately (Figure 3). In men, cancer diagnosis peaked in age group 60–69, at which age 25% of all cancers in men were diagnosed (Figure 3A). 19% of all cancers in men were diagnosed in age group 50–59 and 23% were diagnosed in age group 70–79. Together, 66% of all cancers in men were diagnosed in these three decades of life (Figure 3A).

Next, we analyzed the age distribution of the top six cancers in men by type. The most frequently diagnosed cancer among men was prostate cancer, which accounts for 19% of cancers in men (Figure 1D). Analysis of the age-distribution of prostate cancers indicated that its diagnosis peaked in age group 70–79, which comprised 28% of the cases (Figure 3A–I), with 24% of prostate cancer cases diagnosed in age group 60–69 and 22% in age group 80–89. No prostate cancer cases were diagnosed in patients below 40 years (Figure 3A–I). Only 2% and 8% of prostate cancers were diagnosed in age groups 40–49 and

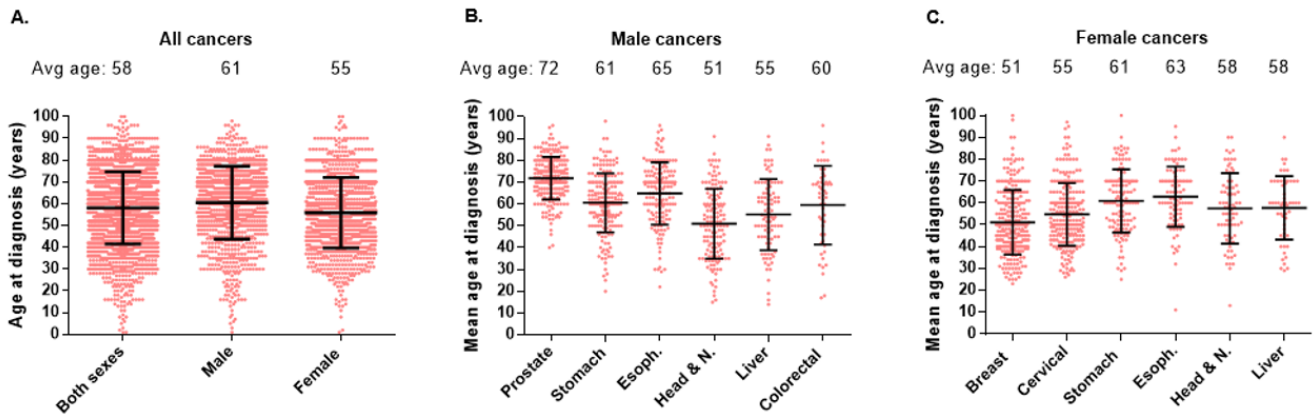


Figure 2. Age at cancer diagnosis. Age at cancer diagnosis in Meru county. **A)** Analysis of the age at cancer diagnosis in Meru county revealed that in both sexes combined, the average age of cancer occurrence is 58 years. In men and women only, the average age of cancer occurrence is 61 and 56 years, respectively. **B)** Analysis of the age at cancer diagnosis of the most frequent cancers (rate $\geq 5\%$ of all cancers) among men revealed that the average age of prostate, stomach, esophageal, head and neck, liver and colorectal cancer diagnosis was 72, 61, 65, 51, 55 and 60 years, respectively. **C)** A similar analysis of cancers in women revealed that the average age of breast, cervical, stomach, esophageal, head and neck and liver cancer diagnosis was 51, 55, 61, 63, 58 and 58 years, respectively.

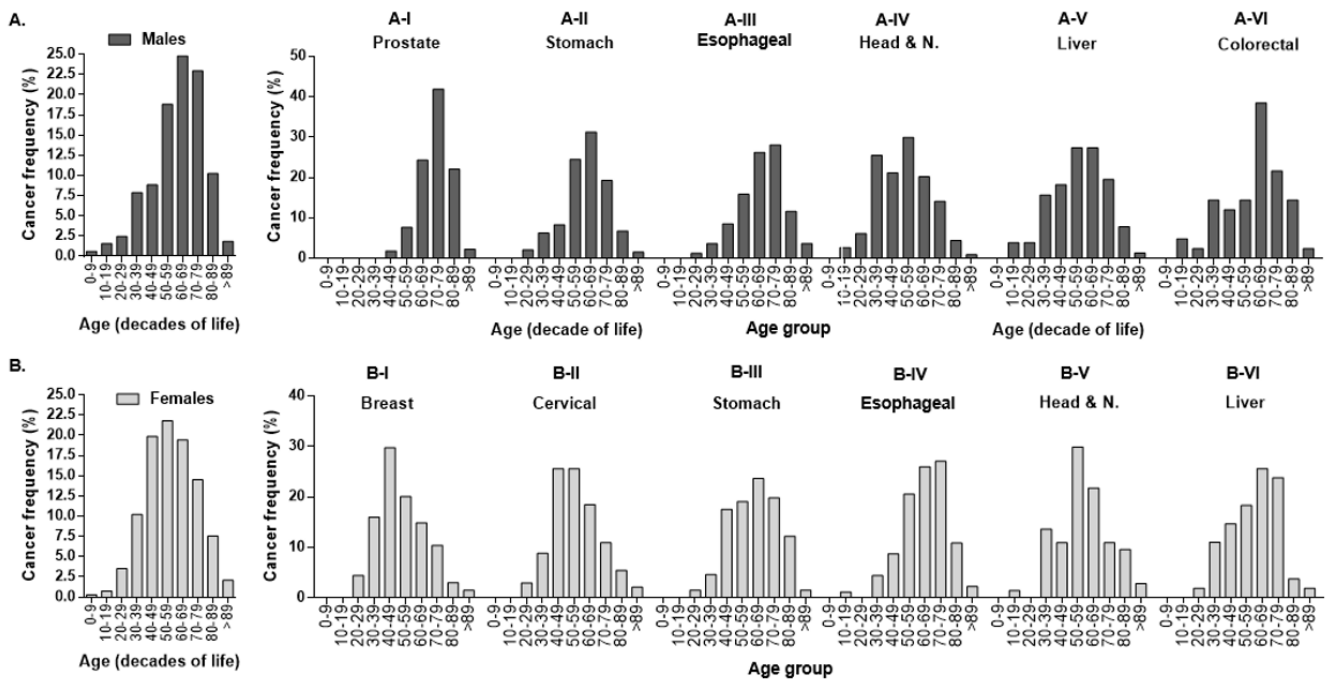


Figure 3. Age distribution of cancer in Meru county. Age distribution of cancer in Meru county. **A)** Analysis of the age distribution of cancer in males showed that most cancer cases occur between 50 and 80 years of age, peaking in the seventh decade of life. A-I to A-VI) Analysis of the age distribution of the most frequent cancers (rate $\geq 5\%$ of all cancers) in men shows that: prostate cancer cases peak in the eighth decade of life, with most cases occurring between 60 and 90 years of age. Stomach cancer cases peak in the seventh decade of life, with most cases occurring between 50 and 80 years of age. Esophageal cancer cases peak in the seventh and eighth decades of life, with most cases occurring between 50 and 80 years of age. Head and neck cancer cases peak as early as at 30–40 years of age, peaking between the fourth to the seventh decade of life. Liver cancer cases peak in the sixth and seventh decades of life but cases start rising at 30–40 years of age. Colorectal cancer cases peak in the seventh decade of life. **B)** Analysis of the age distribution of cancer in females showed that most cancer cases occur between 40 and 80 years of age - peaking in the fifth, sixth and seventh decade of life. A-I to A-VI) Analysis of the age distribution of the most frequent cancers (rate $\geq 5\%$ of all cancers) in women reveals that: breast cancer peaks between 40 and 50 years of age and majority of the cases occur from the fourth to seventh decade of life. Cervical cancer cases peak between 40 and 60 years of age and most cases occur in the fourth, fifth and sixth decades of life. Stomach cancer cases in women are highest in seventh decade but are almost Equally distributed between 40 and 80 years of age. Esophageal cancer in women peaks between 60 and 80 years of age and the most cases occur between 50 and 80 years of age. Head and neck cancers in women peak at 50–60 years of age, with most cases occurring between 50 and 70 years. Liver cancer in women steadily rises from 30 years of age and peaks at 60–80 years of age.

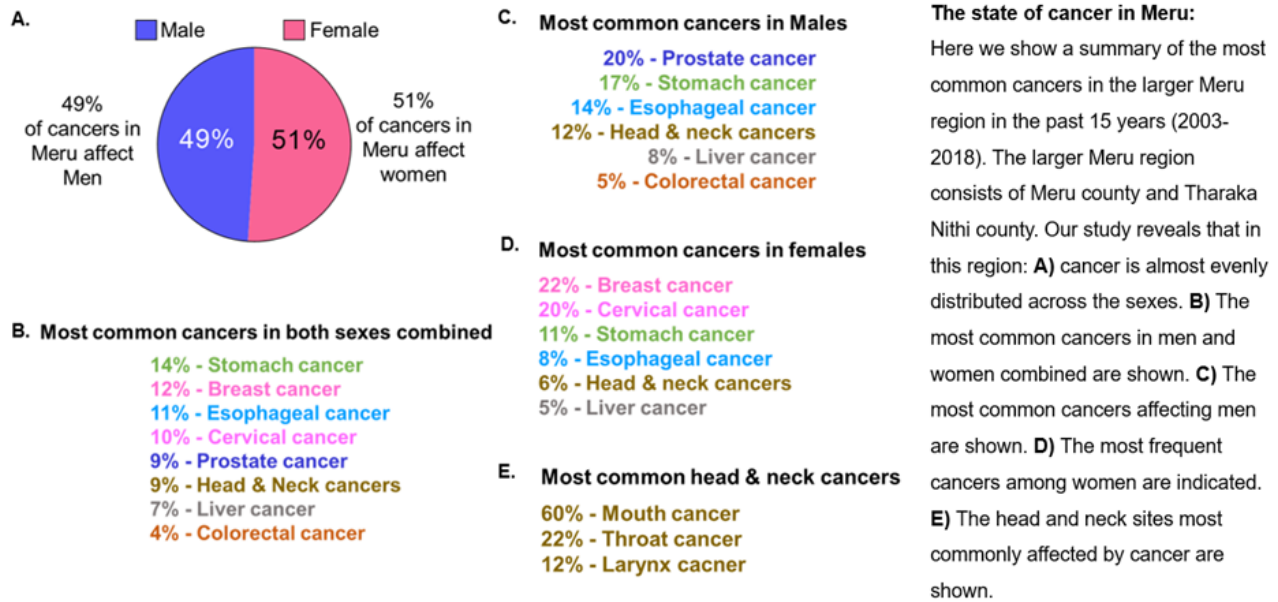


Figure 4. A summary of the state of cancer in Meru county, Kenya.

50–59, respectively (Figure 3A–I). Together, 90% of the prostate cancer cases were diagnosed after the age of 60 (Figure 3A–I).

Stomach cancer accounts for 17% of all cancers in men (Figure 1D). The age distribution analysis revealed that stomach cancer peaked in age group 60–69, in which 31% of the cases were diagnosed. 25% of stomach cancer cases in men were diagnosed in age group 50–59 (Figure 3A–II), 56% were diagnosed between 50 and 69 years of age, 16% of all stomach cancer cases were diagnosed before 50 years of age (Figure 3A–II) and 28% after the age of 70 (Figure 3A–II).

The frequency of esophageal cancer diagnosis in men peaks in age groups 60–69 and 70–79, in which 54% of all male cases were diagnosed (Figure 3A–III). 30% of esophageal cancers in men were diagnosed before age 60 (Figure 3A–III) and 15% after the age of 80 (Figure 3A–III).

Diagnosis of head and neck cancers in men peaked in age group 50–59, in which 24% of the cases were diagnosed. 37% of head and neck cancers occurred before 50 years and 16% in age group 60–69 (Figure 3A–IV). 7% of head and neck cancers in men were diagnosed before 30 years of age and 15% past 70 years.

Liver cancer diagnosis in men peaked in age groups 50–59 (22%) and 60–69 (22%), in which 44% of liver cancers were diagnosed (Figure 3A–V). 34% of liver cancers in men were diagnosed before the age of 50 (Figure 3A–V) and 23% past 70 years of age.

Finally, colorectal cancer diagnosis among men peaked in age group 60–69, in which 31% of cases were diagnosed (Figure 3A–VI). 28% of all colorectal cancers in men were

diagnosed before age 50 and 31% of all colorectal cancers in men were diagnosed after 70 years of age (Figure 3A–VI).

Age-distribution analysis revealed that cancer among women peaks a decade earlier than it does in men (Figure 3B). 20% of cancers diagnosed in women occur in age group 40–49, 22% in age group 50–59 and 20% in age group 60–69. Together, 62% of all diagnosed cancers in women occur in these three age groups. 34% of all cancers in women were diagnosed under the age of 50 and 23% after the age of 70.

We next analyzed the age-distribution of the top six cancers in women. The most frequently diagnosed cancer in women was breast cancer, which accounts for 22% of all diagnosed cancer cases in women (Figure 2E). Analysis of breast cancer age distribution indicated that its diagnosis peaked in age group 40–49 (30%) and age group 50–59 (20%), with 50% of all breast cancer in women diagnosed in these two age groups (Figure 3B–I). 20% of all female breast cancer cases were diagnosed before 40 and 30% after age 60 (Figure 3B–I).

Cervical cancer diagnosis peaked in age groups 40–49 (24%) and age group 50–59 (25%), with 49% of all cervical cancers diagnosed in these two decades (Figure 3B–II). 12% of all cervical cancer cases were diagnosed before age 40 and 38% of cervical cancer cases were diagnosed after 60 years of age (Figure 3B–II).

Stomach cancers in women peaked in age group 60–69 at 24%. 18% of all stomach cancers in women fell in age group 40–49, 19% in age group 50–59 and 20% in age group 70–79 (Figure 3B–III). 7% of stomach cancer cases in women were diagnosed before 40 years of age (Figure 3B–III). 14% of

stomach cancer cases in women occurred after the age of 80 (Figure 3B–III).

Diagnosis of esophageal cancer cases in women peaked in age groups 60–69 and 70–79, in which 53% of the cases were diagnosed. Of all esophageal cancer cases in women, 20% were diagnosed in age group 50–59 and 26% in age group 60–69 (Figure 3B–IV). 13% of esophageal cancer cases were in women younger than 50 and 13% were diagnosed after 80 years of age (Figure 3B–IV).

Head and neck cancer diagnoses in women peaked at age groups 50–59 and 60–69, in which 52% of the cases were diagnosed (Figure 3B–V). 25% of head and neck cancers in women occurred before 50 years of age and 23% after the age of 80 (Figure 3B–V).

Liver cancer in women peaked in age groups 60–69 and 70–79, in which 48% of liver cancer cases were diagnosed (Figure 3B–VI). 28% of liver cancer cases in women occurred before 50 years of age and 18% in age group 50–59. 6% of all liver cancers in women were diagnosed after the age 80 (Figure 3B–VI).

Five cases, one male and four female, that lacked age information were not included in the analysis of cancer distribution by age.

Rare cancer types seen at the Meru hospice

Outside of the top 10 most frequent cancer types, there were various other cancer types seen at the Meru hospice during the study period. These rare cancer types (responsible for ≤1.2% of cases) include bone cancers, ovarian cancer, melanoma,

multiple myeloma, leukemia, lymphoma, Kaposi sarcoma, kidney cancer and uterine cancer (Figure 5).

Discussion

African countries are experiencing an increasingly heavy cancer burden⁸. This is attributable to multiple factors including lifestyle changes, aging populations and increased proliferation of cancer risk factors²⁴. Despite the grim statistics, cancer in most African regions receives limited public health resources^{8,25}. This is partly due to a lack of comprehensive information on the cancer burden in these countries. This deficiency hampers effective cancer control and prevention policy as well as cancer research prioritization. The most comprehensive cancer incidence and mortality reports on cancer in SSA are produced by the IARC. These reports are based on the PBCRs of the respective countries⁴. However, most African countries lack high-quality PBCRs^{4,24,25}. According to volume XI of IARC’s Cancer Incidence in Five Continents report, only 1% of Africa is covered by high-quality PBCRs^{4,11}. In addition, where PBCRs are available, they are often subnational and usually based on one or few major cities. For instance, IARC’s 2018 report on cancer incidence in SSA is based on just 25 cancer registries from 20 countries^{4,9}. As cancer distribution may vary widely even within the same country^{25–29}, reliance on few subnational PBCRs may significantly underestimate cancer incidence and distribution in these countries.

IARC’s report on cancer incidence in Kenya is based on the two main cancer registries in the country; the Nairobi cancer registry and the Eldoret cancer registry. The other operational PBCR in the country is the Kisumu cancer registry, in western Kenya^{30,31}. The Nairobi cancer registry consists of data from hospitals within Kenya’s capital, while the Eldoret

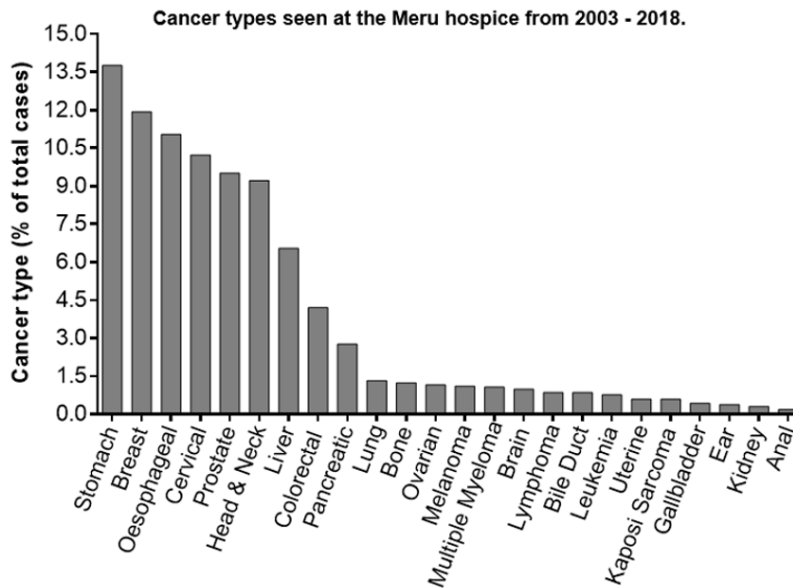


Figure 5. Cancer types seen at the Meru hospice from 2003 – 2018. The various cancer types seen at the Meru Hospice between 2003 and 2018 are shown in order of frequency.

registry covers parts of the Rift Valley region of Kenya³¹. The lack of quality PBCRs with national coverage means that most parts of Kenya are unrepresented in national cancer estimates. However, most public hospitals and hospices possess low-quality cancer patient registers that can partially remedy the deficiency in PBCRs. While such registers do not meet the standards of quality PBCRs, they are unbiased indicators of cancer incidence in their respective populations. In this retrospective study, using data from the patient register at the Meru hospice, we report the state of cancer in the Meru region of Eastern Kenya. Paying greater attention to the most common cancers in this region, we discuss how our cancer incidence observations deviate from GLOBOCAN's national, regional and global cancer rate estimates.

Stomach cancer

Cancers of the stomach are responsible for almost 800,000 annual deaths worldwide⁴. According to GLOBOCAN's estimates, it is the fifth most common cancer globally, making up 5.7% of all cancers. Its incidence is reportedly highest in Eastern Asia (11% of cancers in both sexes combined) and lowest in Africa, where it constitutes only 3% of cancers in men and women combined^{4,32}. Our data show that in this region of Kenya, stomach cancer is the commonest cancer in both sexes combined, constituting 14% of all cancers. This rate is similar to its rates in countries in Eastern Asia with the highest stomach cancer incidence globally, including Japan, Republic of South Korea and Mongolia where it constitutes 13.1%, 13.4% and 14.4% of all cancers, respectively^{4,32}. From our analysis, this disease is the second most common in men, making up 17% of cancers in men and third most common in women, constituting 11% of cancers in women. These rates are markedly elevated relative to the global stomach cancer rates in men (7.2%) and women (4.1%)³². Together, this indicates that stomach cancer incidence is surprisingly elevated in Meru to a rate that equals stomach cancer incidence in countries with the highest rates worldwide. Interestingly, elevated stomach cancer rates were observed in this region as early as in the early 1990s³³. Globally, stomach cancer rates are two-fold higher in men than women⁴. Consistent with this observation, our analysis shows a 1.5-fold higher stomach cancer rate in men than in women.

Helicobacter pylori (*H. pylori*), which infects more than 50% of the world's population, is an established major risk factor for stomach cancer^{34–37}. However, only a small proportion of *H. pylori* positive individuals go on to develop stomach cancer and the carcinogenicity of *H. pylori* seems to be strain specific. While *H. pylori* infection rate is high in Kenya³⁸, the role of this pathogen in Kenyan stomach cancers has not been investigated. There is a need to establish if and how *H. pylori* contributes to stomach cancer in this region. Epstein-Barr virus has been associated with increased stomach cancer risk. EBV-associated gastric cancers comprise about 10% of all stomach cancer cases³⁹. The role of EBV in stomach cancer is poorly investigated in African populations⁴⁰. Given the high prevalence of EBV infection in all human populations⁴¹, and the high prevalence of *H. pylori* in Kenyan populations³⁸, it is

curious whether co-infection with both pathogens contributes to the high stomach cancer rates seen in this population. The roles played by other risk factors, including genetic, dietary and environmental risk factors, also warrant comprehensive examination. From our analysis, the average age of stomach cancer diagnosis is 61 years in both men and women – almost a decade earlier than the world average of 69 years⁴². Considering that in general, cancer is diagnosed late in Kenya, stomach cancer onset is probably much earlier than revealed by our data. The reasons for the earlier age of diagnosis in Kenya are unknown and merit investigation.

Prostate cancer

In 2018, about 1.3 million new prostate cancer cases and 359,000 prostate cancer deaths were recorded worldwide⁴. Globally, prostate cancer is the fourth commonest cancer in men and women combined, constituting 7.1% of all cancers. It is the second commonest cancer in men, making up 13.5% of cancers affecting men³². Prostate cancer is the most frequently diagnosed cancer in men of most SSA countries and the leading cause of cancer mortality⁴. Our study shows that prostate cancer is the most common cancer in Meru men, constituting 19.4% of all cancers in men. This is a higher rate than globally estimated. The rate is also elevated when compared to GLOBOCAN's estimates for Kenya, which reports that prostate cancer constitutes 14.9% of all cancers in Kenyan men³². As in other parts of the world, our analysis shows that prostate cancer manifests itself in advanced age and is on average diagnosed at 71. Despite the high incidence rates, little is understood about the etiology of prostate cancer. The best understood prostate cancer risk factors are advanced age, ethnicity and genetic predisposition^{4,43,44}. Prostate cancer rates are highest in men of African descent^{4,45}. There is compelling evidence that obesity is an important risk factor^{4,46} but the importance of body weight in SSA prostate cancer is not evident. The factors leading to high prostate cancer rates in Kenya are unknown and further investigation into its etiology is required.

Esophageal cancer

In 2018 there were close to 600,000 new esophageal cancer cases worldwide, resulting in over half a million deaths. This disease is the leading cause of cancer mortality in Kenya and the third leading cause of cancer deaths in East Africa. It is the sixth leading cause of cancer deaths worldwide^{4,32}. Our study ranks it the third most frequent cancer, making up 11% of all cancers in men and women combined. This is a markedly elevated rate relative to its global rate (3.2% incidence; seventh most common;³². Our data reveal a marked esophageal cancer elevation in both men (14.3% of cancers in men; third most common) and women (7.9% of cancers in women; fourth most common) when compared to the global rates of the disease in men (4.2% incidence; seventh most common) and women (2% incidence; 13th most common)³². Esophageal cancer incidence displays a markedly variable geographic distribution^{4,47}. Kenya lies along Africa's esophageal cancer corridor but as currently defined, the corridor runs from Ethiopia through Western Kenya to South Africa²⁶ and does not include the Eastern Kenya region that includes Meru. All of Africa's

esophageal cancer hotspots, including the only characterized Kenyan esophageal cancer hotspot (Tenwek – Eldoret) lie along the Rift Valley. Our study suggests that in addition to Tenwek, there may be other high esophageal cancer incidence regions in the country, including the Meru region. Such regions may be inadequately accounted for in national esophageal cancer estimates as these estimates are based on the Nairobi and Eldoret registries. Esophageal cancer falls into two histological subtypes; esophageal adenocarcinoma (EAC) and esophageal squamous cell carcinoma (ESCC)^{27,48}. ESCC forms about 90% of esophageal cancers and is the predominant subtype in SSA^{47,48}. Although our study does not demonstrate the relative proportions of the two subtypes, it is probable that most esophageal cancers in this population are ESCCs. Future studies should investigate the relative proportions of EAC and ESCC in this and other Kenyan populations. While comprehensive research on the drivers of esophageal cancer in Kenya are lacking^{4,49}, several risk factors have been proposed. They include hot beverage consumption, poor oral hygiene and consumption of *mursik* – a fermented milk beverage popular in the rift valley region^{50–52}. To the best of our knowledge, all esophageal cancer studies in Kenya have been carried out in the Rift Valley region esophageal cancer hotspot. Studies of the etiological drivers of esophageal cancer in this high-incidence region are warranted.

Breast cancer in women

Breast cancer is the commonest cancer in women worldwide, constituting 24.2% of cancers in women, and the leading cause of cancer deaths among women. It is the second commonest cancer in both sexes combined, making up 11.6% of all cancers. In 2018, there were over 2 million new breast cancer cases globally and more than 600,000 breast cancer deaths^{4,32}. According to GLOBOCAN estimates, this disease is the most common cancer in Africa and the second commonest in East Africa³². In our study population, breast cancer closely mirrors these trends. It is the commonest cancer among women, making up 22.4% of cancers in women. It is second commonest in men and women combined, comprising 11.9% of all cancers. These figures also conform with GLOBOCAN's breast cancer estimates for Kenya, which rank it the most common cancer in women, with a 20.9% incidence³². We observe that breast cancer is frequently diagnosed at a young age (<40 years) in our study's population. It is estimated that only about 7% of breast cancer cases are diagnosed before the age of 40^{53,54}. However, our analysis shows that over 20% of breast cancer cases in this study's population are diagnosed before 40 years of age. Considering that in Kenya cancer is often diagnosed late, the rate of breast cancer onset before age 40 could be higher. Drivers of breast cancer in Kenya are poorly investigated. Studies carried out in other regions on migrant groups indicate that non-genetic factors account for the bulk of breast cancer cases, while familial and genetic risks contribute <10% of breast cancers⁴. Known non-genetic breast cancer risks include early age at menarche, late age at menopause, nulliparity, late age of first child, high body weight and high alcohol consumption^{4,55–58}. Well characterized genetic risks for breast cancer include mutations in BRCA1, BRCA2 and

p53^{4,59}. Because breast cancer risks are not well investigated in many African regions, the roles played by these factors in Kenya's breast cancer cases are not clear. Future research should seek to better characterize the genetic and non-genetic risk factors driving this disease, given that breast cancer incidence is climbing fastest in African countries^{4,60}.

Cervical cancer

In 2018, there were 570,000 new cervical cancer cases and 311,000 cervical cancer deaths worldwide. It is the fourth most common cancer among women globally, at a 6.6% incidence rate^{4,32}. The highest cervical cancer incidence and mortality rates are seen in Africa⁴. Our analysis shows that cervical cancer is strikingly elevated in women from the Meru region in relation to the disease's global estimates. Our analysis ranks this disease fourth commonest in both sexes together (10.2% of all cancers) and second most common among women (20% of cancers in women). These rates are consistent with GLOBOCAN's estimates, which rank cervical cancer the second most common cancer in Kenyan women (18.3% of cancers in women)³². The vast majority of cervical cancer cases are linked to persistent infection by at least one high-risk human papillomavirus (HPV)^{61,62}, mainly HPV16 or HPV18⁶³. It is estimated that 9.1% of Kenyan women carry cervical HPV/16 infection and more than two thirds of invasive cervical cancers are attributable to HPV16 and/or HPV18 infection⁶⁴. However, HPV infection alone is not sufficient to induce cervical cancer and additional risk factors influence cervical carcinogenesis^{4,65,66}. Principal cofactors include cigarette smoking, multiparity, immunosuppression and the use of oral contraception^{4,67,68}. While it is likely that majority of cervical cancers in Meru women are HPV-associated, further studies are needed to establish this. Comprehensive research is required to uncover the cofactors driving the high incidence of this disease and their roles.

Head and neck cancers

Head and neck cancer broadly refers to malignancies that affect one or more sites of the head and neck region. This region includes the oral cavity, paranasal sinuses, pharynx, larynx, thyroid, associated lymph nodes, soft tissues and bone⁶⁹. Globally, head and neck cancers account for about 8% of all cancers in both sexes combined and about 5% of all cancer deaths⁴. Head and neck cancers disproportionately affect more men than women⁷⁰. From our analysis, head and neck cancers are the sixth commonest cancer type, comprising 9% of all cancers in men and women combined. This group of cancers is fourth most common in men (12.4% of cancers) and fourth most common in women (7.9% of cancers). Our study shows that the rate of these cancers is twice as high in men than women and that the oral cavity is the most frequently affected site, accounting for about 60% of all head and neck cancers in men or women. Multiple factors, including HPV infection, EBV infection, cigarette smoking, high alcohol consumption, poor oral hygiene and chewing leaves from certain plants have been implicated as head and neck cancer risk factors^{71–77}. Several genetic risks, including aberrations in the Notch pathway and chromatin factors^{78,79}, have also been implicated in

the development of head and neck cancer. Further research is needed to establish the involvement of these and other factors in the etiology of head and neck cancers in this and other Kenyan regions.

Liver cancer

In 2018, there were an estimated 841,000 new liver cancer cases worldwide and more than 780,000 liver cancer deaths. Globally, this disease ranks sixth most common in both sexes combined, making up 4.2% of all cancers, and is the fourth leading cause of cancer deaths^{4,32}. Accounting for 6.5% of all cancers in men and women combined, our analysis reveals a moderate elevation in liver cancer rates in the Meru region. Globally, liver cancer is the fifth commonest cancer in men (6.3% of cancers in men) and sixth commonest among women (2.8% of cancers in women)³². Relative to global rates, our analysis reveals a moderate elevation of liver cancer incidence among men (8.5% of cancers in men) and women (4.7% of cancers in women). The major risk factors for liver cancer include chronic hepatitis B or hepatitis C infection, aflatoxin ingestion and high alcohol consumption^{80,81}. Given the high prevalence of these risk factors in Kenya⁸²⁻⁸⁵, they are likely to be important drivers of liver cancer in the Meru region. However, further research is necessary to establish how liver cancer incidence in Meru correlates with these and other probable risk factors.

Colorectal cancer

In 2018, there were close to 1.8 million new colorectal cancer cases worldwide and nearly 900,000 colorectal cancer deaths. Globally, colorectal cancer ranks third commonest in men and women combined (10.2% of all cancers), third most common in men (10.9% of cancers in men) and second most common in women (9.5% of cancers in women)³². Conforming with reports that colorectal cancer rates are low in African regions, our study reveals a much lower colorectal cancer rate than estimated globally. Our analysis ranks colorectal cancer eighth most common in men and women combined (4.2% of all cancers), sixth most common in men (4.6% of cancers in men) and seventh most common in women (3.8% of cancers in women). These rates conform with GLOBOCAN's assessment of colorectal cancer in Kenya, which estimates a 4.8% incidence in men and women combined, 5.9% incidence in men and 4.1% incidence among women³². However, GLOBOCAN ranks colorectal cancer the fifth most common in Kenya³², compared to our observation of eighth most common in the Meru region. According to GLOBOCAN, colorectal cancer ranks third and fourth most common in Kenyan men and women, respectively³²; above its rank of sixth and seventh most common cancer in the Meru region in men and women respectively. The lower ranking of colorectal cancer in our analysis is due to elevated rates of stomach, head and neck and liver cancer. Advanced age, sedentary lifestyles, familial predisposition, cigarette smoking, heavy alcohol consumption and diet have been proposed as major colorectal cancer risk factors^{4,86}. The roles of these and other risks in the etiology of this disease have not been investigated in Kenyan populations. Nonetheless, we observe that most colorectal cancer cases occur after the age of 50, indicating that, as in other parts

of the world, advanced age may be an important risk factor. Consistent with global reports that colorectal cancer afflicts men more than women^{32,87}, we observe more cases of the disease in men (54% of colorectal cases) than women (46% of colorectal cases). Comprehensive studies are warranted to establish the roles played by various risk factors in the etiology of this disease in Kenyan populations.

Pancreatic cancer

In 2018, there were over 450,000 new pancreatic cancer cases worldwide and more than 430,000 pancreatic cancer deaths³². Global pancreatic cancer incidence is estimated at 2.5% of cancers in both sexes combined (12th most common), 2.6% of cancers in men (12th most common) and at 2.5% of cancers in women (11th most common)³². Consistent with global estimates, we observed that pancreatic cancer comprised 2.7% of cancers in both sexes combined (ninth most common), 2.5% of cancers in men (seventh most common) and 3% of cancers in women (eighth most common). However, these rates are about twice as high as the national pancreatic cancer estimates for Kenya. According to GLOBOCAN 2018 estimates for Kenya, pancreatic cancer makes up 1.5% of all cancers in both sexes combined (14th most common), 1.8% of cancers in men (13th most common) and 1.4% of cancers in women (14th most common). The distribution of pancreatic cancer in Meru men and women is consistent with the global distribution pattern, which shows a moderately higher incidence in men than women³². It is thought that most pancreatic cancer cases are driven by environmental risks⁸⁸. Suspected risk factors for this disease include advanced age, cigarette smoking, high body weight, diet, diabetes and ethnicity^{88,89}. As with most cancer types, the causes of pancreatic cancer in Kenyan populations have not been investigated. Future research will elucidate the role played by these factors in Kenyan pancreatic cancers.

Lung cancer

It is estimated that in 2018, there were about 2.1 million new lung cancer cases worldwide and close to 1.8 million lung cancer deaths^{4,32}. Globally, lung cancer is the leading cancer type in men and women combined, constituting 11.6% of all cancers. It is the leading cancer type in men, making up 14.5% of cancers in men and the third most common in women, accounting for 8.4% of cancers in women^{4,32}. Curiously, our analysis ranks lung cancer 10th most common in men and women combined, constituting only 1.3% of all cancers. Among men it is ninth most common, making up only 1.2% of cancers in men. It is the 10th most common cancer among women and makes up just 1.2% of cancers in women. The low incidence of lung cancer emerging from our study is consistent with GLOBOCAN's low lung cancer rates estimated for Kenya in 2018³². In Kenya, this disease is ranked 15th most common in men and women combined, at less than 1.4% of all cancers³². In Kenya, lung cancer constitutes 2% of cancers in men and less than 1.3% of cancers in women. According to GLOBOCAN cancer estimates, lung cancer rates are also low in Eastern Africa (1.8% of all cancers) and Africa (3.7% of all cancers)³². Cigarette smoking is considered to be the most important risk factor for lung cancer and can explain up to 90% of lung

cancers⁹⁰. Because reliable data on cigarette smoking in Kenya is not available, it is difficult to judge whether the low lung cancer incidence we report is reflective of a low prevalence of cigarette smoking. The curiously low lung cancer rates in Kenyan populations warrant further research into the etiology of this disease.

This study sought to describe the pattern of cancer in the larger Meru region. This region is thought to bear one of the heaviest cancer burdens in the country, although this has not previously been supported with empirical data. Because of limited cancer research in Kenya, the etiologies of this region's high-incidence cancers are uncharacterized. This report offers a framework for cancer research prioritization in the region. It calls for more concerted epidemiological and basic cancer research efforts that will guide the formulation of effective cancer care and control programs.

Because the study relied on patient records, it contained only information that the hospice deems necessary during patient visits, i.e. age, sex, diagnosis, date of admission and area of residence. According to the Global Cancer Observatory, ideally, PBCRs should provide information about cancer burden as well as relevant information to facilitate the evaluation of cancer etiology in the study population and hence support studies of cancer care, screening, early detection and prevention⁹¹. As opposed to quality PBCRs, the patient register we analyzed

does not capture important information like occupation, lifestyle (e.g. smoking or drinking) and therapeutic interventions, thereby limiting its capacity to inform about possible cancer causes and support early cancer detection, screening and prevention. Nonetheless, in the absence of quality PBCRs in most of Kenya, hospital and cancer care registers hold crucial information on the burden of cancer in the country, meeting a crucial goal of PBCRs. Evaluating the data contained in cancer patient registers can greatly inform cancer research priorities to elucidate underlying causes and formulate effective screening, early detection and prevention strategies.

Data availability

Underlying data

Open Science Framework: The state of cancer in Meru, Kenya - a retrospective study. <https://doi.org/10.17605/OSF.IO/KH649>²¹.

This project contains the following underlying data:

- Raw data_The state of cancer in Meru, Kenya – a retrospective study.xlsx (de-identified data file containing the following information from the patient records analyzed: year, age, sex, diagnosis and sub-county).

Data are available under the terms of the [Creative Commons Zero “No rights reserved” data waiver](#) (CC0 1.0 Public domain dedication).

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General Comments

This report on the state of cancer in Meru has good intentions but its methods and conclusions are misleading. As the authors correctly noted, the lack of data hampers effective cancer control and prevention policy, as well as cancer research prioritization. It is also important to call for more concerted epidemiological and basic cancer research to guide formulation of effective cancer care and control programs. However, patient data from one hospice in Meru county do not provide information on the state of cancer in Meru.

The study data are interesting if presented appropriately as data from 2003-2018 on cancer patients admitted to the Meru Hospice serving residents of the larger Meru region in Eastern Kenya. The data could answer questions about change in hospice admissions over time, characteristics of cancer patients admitted to hospice, and could provide information for planning of hospice and cancer services in the region. These data should not be interpreted as cancer incidence observed in Meru county; they are not the appropriate data needed to support conclusions about the burden of cancer in Meru.

The computation of cancer incidence rates requires data from population-based cancer registries that capture data on all newly diagnosed cancers (numerator) among residents in a well-defined population (denominator). Hospices or hospitals do not capture information on all incident cancers diagnosed in a well-defined population. The numerator does not include all newly diagnosed cases and likely includes recurrent cases, and the denominator is unknown. This report does serve to highlight the urgent need for a population-based cancer registry in Meru County that collects and reports high quality data for policy, research, and planning of services.

Specific comments and questions:

1. The report refers to 'rates' and 'incidence' of various cancers, these should be correctly referred to as proportions throughout.
2. It would be helpful to know the hospitals or clinics in the larger Meru region that diagnose and treat cancer patients, and to know the proportion and type of cancer patients that are referred to hospice. For example, compared to all patients diagnosed with cancer in Meru, what is the profile of cancer patients referred to and admitted to hospice? Are they usually diagnosed with later stage disease? Could patient with earlier stage disease get referred for treatment elsewhere? Do patients of some cancer sites get referred more often than patients of other sites? Are hospice patients usually older in age? Could some of these be cases of metastatic cancer?
3. To be more informative and to help readers better interpret the data, suggest presenting data on cancer cases admitted to hospice by year (2003-2018) and stratified by age, sex, cancer site.
4. In the second paragraph of the discussion, authors state that low quality patient registers in hospitals and hospices are unbiased indicators of cancer incidence in their populations. This statement should be omitted.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

No

Are sufficient details of methods and analysis provided to allow replication by others?

Partly

If applicable, is the statistical analysis and its interpretation appropriate?

No

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

No

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Epidemiology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Reviewer Report 12 February 2020

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This is an interesting study on hospice cancer data from Meru county in Kenya.

A few comments and observations:

The title should reflect that this is Hospice data. The methodological approach and conclusions are flawed specifically the fact that comparisons are being made with the Globocan estimates and the Kenya cancer registry data based solely on hospice data. As an example, stomach cancer by virtue of the nature of the disease and its late presentation at diagnosis is likely a hospice case whereas this is not generally true for prostate, cervix or breast cancer. There are too many generalizations; as an example, the year of admission is the same as the year of diagnosis. Also not convinced about the methodology used for assigning a diagnosis. Cancer registry data is based on a strict methodological approach to ascertain diagnosis from multiple sources. Using a hospice register may be too simplistic, I thought. However, in the absence of much data in the region, it is "interesting to know the **trends**". So the paper may still be indexable but with modifications. Making general statements on trends but without the **detailed** comparison of Meru stats with Globocan stats. Authors can discuss the trends in what they have found. Pages 9-12 can be consolidated. Referencing and comparing their findings with that of Nairobi and Eldoret is probably more appropriate for trends rather than world stats.

The Discussion section on the various cancers can be further enriched by referencing local studies and published data. As an example the statement in the manuscript "While it is likely that majority of cervical cancers in Meru women are HPV-associated, further studies are needed to establish this" Do the authors expect cervical cancer etiology to be different from what is already an established fact? Was the intention to state that there may be regional differences in HPV genotypes? Some important work around prevalence and risk factors for certain cancers has already been published from Kenya and for others work is ongoing - this has not been mentioned in the manuscript- Some important work the authors may wish to reference include the following:

1. Human papillomavirus correlates of high-grade **cervical** dysplasia in HIV-infected women in Mombasa, **Kenya**: a cross-sectional analysis¹.
2. Prevalence of Human Papillomavirus Genotypes among African Women with Normal **Cervical** Cytology and Neoplasia: A Systematic Review and Meta-Analysis².
3. Dental fluorosis and oral health in the African **Esophageal Cancer** Corridor: Findings from the **Kenya** ESCCAPE case-control study and a pan-African perspective³.

4. Traditional and commercial alcohols and **esophageal cancer** risk in **Kenya**⁴.
5. The African **Esophageal Cancer** Consortium: A Call to Action⁵.

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6. Sayed S, Moloo Z, Wasike R, Bird P, et al.: Ethnicity and breast cancer characteristics in Kenya. *Breast Cancer Res Treat*. **167** (2): 425-437 [PubMed Abstract](#) | [Publisher Full Text](#)

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Partly

Are sufficient details of methods and analysis provided to allow replication by others?

Partly

If applicable, is the statistical analysis and its interpretation appropriate?

I cannot comment. A qualified statistician is required.

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Breast Cancer

We confirm that we have read this submission and believe that we have an appropriate level

of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.
