CANCER EPIDEMIOLOGY



Trends in the incidence of ovarian cancer in sub-Saharan Africa

Muluken Gizaw^{1,2} | Donald Maxwell Parkin^{3,4} | Ole Stöter^{2,5} | Anne Korir⁶ | Bakarou Kamate⁷ | Biying Liu⁸ | Lamin Bojang⁹ | Guy N'Da¹⁰ | Shyam S. Manraj¹¹ | Phiona Bukirwa¹² | Eric Chokunonga¹³ | Tatenda Chingonzoh¹⁴ | Jean-Félix Peko¹⁵ | Anne Finesse¹⁶ | Nontuthuzelo Somdyala¹⁷ | Akinade Ladipo¹⁸ | Eva Johanna Kantelhardt^{2,5}

¹Department of Preventive Medicine, School of Public Health, Addis Ababa University, Addis Ababa, Ethiopia

²Institute for Medical Epidemiology, Biometrics and Informatics, Martin Luther University Halle Wittenberg, Global Health Working Group, Halle, Germany

⁴International Agency for Research on Cancer, Cancer Surveillance Unit, Lyon, France

⁵Department of Gynaecology, Martin-Luther-Universitat Halle-Wittenberg, Halle, Germany

⁶Nairobi Cancer Registry, Kenya Medical Research Institute, Nairobi, Kenya

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<sup>7</sup>Bamako Cancer Registry, Bamako, Mali
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⁸African Cancer Registry Network, Oxford, UK

⁹Gambia National Cancer Registry Medical Research Council Unit, Fajara, Gambia

¹⁰Abidjan Cancer Registry, Abidjan, Côte d'Ivoire

¹¹Mauritius National Cancer Registry, Port Louis, Mauritius

¹²Kampala Cancer Registry and Department of Pathology, School of Biomedical Sciences, College of Health Sciences, Makerere University, Kampala, Uganda

¹³Zimbabwe National Cancer Registry, Harare, Zimbabwe

¹⁴Bulawayo Cancer Registry, Bulawayo, Zimbabwe

¹⁵Brazzaville Cancer Registry, Brazzaville, Congo

¹⁶Seychelles National Cancer Registry, Victoria, Seychelles

¹⁷Burden of Disease Research Unit, South African Medical Research Council, Eastern Cape Cancer Registry, Tygerberg, South Africa

¹⁸Ibadan Cancer Registry, Department of Pathology University College Hospital, Ibadan, Nigeria

Correspondence

Eva Johanna Kantelhardt, Magdeburgerstrasse 8, 06097 Halle, Germany. Email: eva.kantelhardt@uk-halle.de

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Abstract

Ovarian cancer (OC) is one of the commonest cancers of women in sub-Saharan Africa (SSA), although to date no data have been available on time trends in incidence to better understand the disease pattern in the region. We estimate time trends by histological subtype from 12 population-based cancer registries in 11 countries: Kenya (Nairobi), Mauritius, Seychelles, Uganda (Kampala), Congo (Brazzaville), Zimbabwe (Bulawayo and Harare), Cote d'Ivoire (Abidjan), The Gambia, Mali (Bamako), Nigeria (Ibadan) and South Africa (Eastern Cape). The selected registries

Abbreviations: AAPC, Average Annual Percentage Change; AFCRN, African Cancer Registry Network; ASR, age-standardised rate; CI, confidence interval; DCO, death certificate only; ICD-10, International Classification of Diseases 10th revision; ICD-O-3, International Classification of Diseases for Oncology 3rd revision; MV, morphological verification; OC, ovarian cancer; SSA, sub-Saharan African.

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³Nuffield Department of Population Health, Oxford University, Oxford



were those that could provide consistent estimates of the incidence of ovarian cancer and with quality assessment for periods of 10 or more years. A total of 5423 cases of OC were included. Incidence rates have been increasing in all registries except Brazzaville, Congo, where a nonsignificant decline of 1% per year was seen. Statistically significant average annual increases were seen in Mauritius (2.5%), Bamako (5.3%), Ibadan (3.9%) and Eastern Cape (8%). Epithelial ovarian cancer was responsible for the increases observed in all registries. Statistically significant average annual percentage changes (AAPC) for epithelial OC were present in Bamako (AAPC = 5.9%), Ibadan (AAPC = 4.7%) and Eastern Cape (AAPC = 11.0%). Creating awareness among professionals of the growing importance of the disease is surely an important step to improving availability of, and access to, diagnosis and treatment of OC in SSA. Support must be given to the cancer registries to improve the availability of good-quality data on this important cancer.

KEYWORDS

epithelial, incidence, ovarian cancer, sub-Saharan Africa, trends

What's new?

Ovarian cancer is one of the most common cancers in sub-Saharan Africa. Here, the authors investigate changes in ovarian cancer incidence over time. They analysed data from 12 population-based cancer registries representing multiple regions, for a total of 5423 cases of ovarian cancer over a period of at least 10 years. Incidence rates, they found, have increased in all regions except Brazzaville, Congo. These trends point to the need for improving ovarian cancer care in Africa, as well as improvements to cancer registries to expand the areas where strong epidemiological data is being collected.

1 | INTRODUCTION

Worldwide, ovarian cancer (OC) was the eighth most commonly diagnosed cancer among women in 2020, with an estimated 314 000 new cases, and the eighth most common cause of cancer death, with 207 000 deaths in the same year.^{1,2} The incidence and mortality rates of OC vary between different regions, with the highest age standardised incidence rates observed in Europe and North America.²⁻⁵

Almost 18 000 cases and 13 000 deaths from ovarian cancer were estimated to have occurred in the sub-Saharan African (SSA) region in 2020, constituting 2.2% of all cancer cases (both sexes), with the disease ranking the fourth most frequent neoplasm in women.^{1,5} The cumulative incidence (0-74) varies at least 10-fold among the registry populations in the region although risks of 1% or greater—equivalent to those seen in the highest risk populations in Europe—are observed only in Zimbabwe (Bulawayo and Harare Blacks), Nairobi (Kenya) and Mali (Bamako).⁵ Incidence rates have been observed to be rising in many populations, although there is no information on trends in populations of SSA.⁶⁷

Most ovarian cancers are epithelial in origin, with a number of reproductive and hormonal factors shown to confer protection (eg, parity,⁸ oral contraceptive use⁸ and lactation⁹), while others increase risk (eg, late age at menopause and hormone replacement therapy^{8,10}). More controversially, the risk of ovarian cancer is also associated with height, and with body mass index.¹¹ In the United States, genetic predispositions are responsible for one-fifth of ovarian cancer cases.¹²

It remains largely unknown as to whether the interplay between a higher or lower prevalence of these determinants relates to the present cancer profile in SSA. But in any case, ongoing changes in reproductive and behavioural factors in these populations would be expected to result in rising incidence rates of ovarian cancer in future years in many populations. The African Cancer Registry Network (AFCRN), which includes all population-based cancer registries in SSA with relatively complete recording, provides a good source of data to determine the epidemiology of cancer in SSA.⁵ In the present study, we examine trends in ovarian cancer incidence in 12 cancer registries from four regions in SSA for periods between 10 and 34 years, with particular interest in the trends by histological subtype. Given the limited data on OC incidence in SSA, the current study will provide useful information on this important cancer of women, to inform policy makers and health professionals on the current burden of the disease and its likely future evolution, and so help in the development of strategies for early diagnosis and clinical care of OC.

2 | METHODS

Twelve population-based cancer registries in 11 countries, members of AFCRN, were included in the study: Kenya (Nairobi), Mauritius, Seychelles, Uganda (Kampala), Congo (Brazzaville), Zimbabwe (Bulawayo and Harare), Cote d'Ivoire (Abidjan), The Gambia, Mali

1 Carcinoma	8010-8231, 8246-8576, 9014-9015, 9110
1.1 Serous carcinoma	8441, 8460-8463, 9014
1.2 Mucinous carcinoma	8470-8490, 9015
1.3 Endometrioid carcinoma	8380-8383, 8560, 8570
1.4 Clear cell carcinoma	8310-8313, 9110
1.5 Adenocarcinoma, NOS	8140-8147, 8170-8190, 8211-8231, 8260, 8384, 8440, 8576
1.6 Other specified carcinoma	
1.7 Unspecified carcinoma	8010-8035
2 Sex cord-stromal tumours	8590-8671
3 Germ-cell tumours	8240-8245, 9060-9102
4 Other specified malignant neoplasm (including Mullerian mixed tumour, carcinosarcoma)	
5 Unspecified malignant neoplasm	8000-8005

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TABLE 1Histologically definedsubgroups of ovarian cancers, with thecorresponding codes in the ICD O 3

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Source: Ferlay J, Rous B. Histological Groups. IARC Scientific Publications; 2014.

(Bamako), Nigeria (Ibadan) and South Africa (Eastern Cape). All are population-based, recording data in defined populations whose composition by age, and sex is known. The methods of data collection, validation and storage in these registries are described elsewhere.⁵

The registries selected for the study were those that could provide estimates of the incidence of cancer of the ovary of consistent quality for periods of 10 or more years. Quality of the registration process was evaluated as described in Chapter 3 of Parkin et al.⁵ Cases of ovarian cancer (ICD-10, C56.9) were abstracted from the database of the AFCRN, along with the estimated populations at risk by age group, and ethnicity, where appropriate. Population data were derived from census estimates, and inter-censal estimates were calculated assuming an exponential growth rate between censuses. Annual age specific, crude and age standardised rates were calculated, with age standardisation carried out by the direct method using the "world standard population."¹³

Ovarian cancers were further classified as Epithelial, Germ Cell tumours, Sex cord-stromal tumours, Other specified types and Unspecified, according to the ICD O-3 morphology codes, as described in table 4.9 of chapter 4 (Histological Groups) of Bray et al (Table 1).¹⁴ Cases without morphological proof of diagnosis were classified as Unspecified (Group 5), although in some registries, some of these cases had been coded as "Carcinoma NOS" (ICD-O 3 code 8010).

For those datasets/periods retained, we investigated trends in annual age standardised rates, fitting regression lines to determine whether the trends (best fit of the regression) were best explained as linear, exponential or polynomial. For registries for which there was a poor fit of a simple exponential trend ($R^2 < .5$), due to a change in the trend during the period examined, we analysed trends in incidence using the Joinpoint Regression Program version 4.7.0.0 (2019) developed by the US National Cancer Institute (NCI). The point(s) [years] at which statistically significant change(s) in trends occurred are identified by the Joinpoint regression. The average rate of change (annual percent change) in each trend segment was calculated using a Monte Carlo permutation method.¹⁵

For two datasets with discontinuous data over a very long time period (Bulawayo and Abidjan) we compared incidence rates for two separate time periods. For Seychelles, although data were available for a continuous 13-year period, numbers were sparse (45 cases in total), so we present age specific rates for two adjacent time periods. We calculated some conventional indicators of data quality^{16,17}—the percentage of cases with morphological verification (histology or cytology) of diagnosis (MV%) and the percentage of cases registered by death certificate only (DCO%)—for the time periods under review. Results are presented for the individual cancer registries.

3 | RESULTS

The cancer registries included in the study are shown in Table 2, grouped according to the regions of SSA as defined by the United Nations. Of the 12 registries, Mauritius, Seychelles and The Gambia had national coverage, Eastern Cape covered a rural area and the rest covered populations that are predominantly urban. Bulawayo registry, active in the 1960 s,¹⁸ was reactivated recently after a gap of 40 years, with rates available for 2011 to 2015. For Abidjan registration was interrupted for the period (1999-2011) due to political instability.⁵ The longest case series was from The Gambia, with 34 years observation and followed by Bamako, Mali, with 31 years. A total of 5423 cases of OC were registered, and, except for three registries (Kampala, Brazzaville and The Gambia), all reported >50% MV% of cases (Table 2). The median age of all cases at diagnosis was 50 years (IQR = 24 years).

Table 3 shows the average annual percentage change (AAPC) in the ASRs over the whole period of observation for each registry. Incidence rates have been increasing in all registries except Brazzaville, Congo, and The Gambia where nonsignificant declines of 1% and 0.1% per year were seen respectively. Statistically significant average annual increases were seen in Mauritius (2.5%), Bamako (5.3%), Ibadan (3.9%) and Eastern Cape (8.0%).





TABLE 2 Ovarian cancer cases (C56) by time period, total number of cases and most valid basis of diagnosis by cancer registry and region of SSA

SSA region	Cancer registry	Time period	Female population (average in period)	No. cases	DCO ^a	MV ^b
East Africa	Kenya, Nairobi	2003-2016	1 558 000	672	6%	68%
	Mauritius (national)	2001-2018	635 000	906	1%	88%
	Seychelles (national)	2008-2020	46 000	45	7%	82%
	Uganda, Kampala	1991-2015	927 000	626	3%	46%
	Zimbabwe, Bulawayo	1964-1972 2011-2015	74 000 355 000	10 77	0% ^c 16%	90% 62%
	Zimbabwe, Harare	1991-2017	702 000	678	13%	57%
Middle Africa	Brazzaville, Congo	1998-2019	788 000	384	0%	37%
Western Africa	Abidjan, Cote d'Ivoire	1995-1998 2012-2017	1 337 000 2 246 000	62 243	0% 14%	68% 47%
	The Gambia (national)	1986-2019	767 000	172	0.6%	40%
	Bamako, Mali	1987-2017	675 000	626	1%	65%
	Ibadan, Nigeria	1995-2015	1 253 000	736	1%	73%
Southern Africa	South Africa, Eastern Cape	1998-2017	581 000	186	0%	88%

^aDCO: Cases registered based on information contained on a death certificate only.

^bMV: Cases for which diagnosis was based on cytology or histology.

^cNumber of cases by year were too few hence rates were calculated by time period and not annually.

TABLE 3 simple trend analyses in all years of observation for all registries

Cancer registry	Time period	AAPC ^a (%)	95% CI of AAPC
Kenya, Nairobi	2003-2016	2.3	-1.2 to 5.8
Mauritius	2001-2018	2.5	0.0 to 5.0
Seychelles	2008-2020		n/a ^b
Uganda, Kampala	1991-2015	1.3	-0.2 to 2.8
Zimbabwe, Bulawayo	1963-1972; 2011-2015		n/a
Zimbabwe, Harare	1991-2017	0.03	-1.6 to 1.7
Brazzaville, Congo	1998-2019	-0.98	-2.6 to 0.6
Abidjan, Cote d'Ivoire	1995-1998; 2012-2016		n/a
The Gambia	1986-2019	-0.1	-1.6 to 1.6
Bamako, Mali	1987-2017	5.3	3.7 to 6.9
Ibadan, Nigeria	1995-2015	3.9	1.4 to 6.5
South Africa, Eastern Cape	1998-2017	8.0	4.6 to 11.5

^aAverage annual percentage change.

^bNumber of cases by year were too few hence rates were calculated by time period and not annually.

TABLE 4Joinpoint analyses: Timetrends in two separate periods

Registry	Time periods	AAPC (%)	95% CI of AAPC	P value
Bamako	1987-2004	+0.8	-3.6 to 5.4	
	2004-2017	+9.2	5.4 to 13	<.001
Ibadan	1995-2013	+4.7	1.3 to 8.2	<.01
	2013-2015	-12.4	-62.7 to 106	
Mauritius	2001-2015	0.2	-2.9 to 3.4	
	2015-2018	18.7	-5.4 to 48.8	
Eastern Cape	1998-2002	-6.1	-47.3 to 67.1	
	2002-2017	9.9	4.7 to 15.4	.001



FIGURE 1 Ovarian cancer age standardised incidence rate (ASR) (with 95% confidence intervals) in Abidjan, Seychelles and Bulawayo, by period of diagnosis

Table 4 shows a joinpoint analysis results for two periods in four registries, Bamako, Ibadan, Mauritius and Eastern Cape. The registries were selected based on the statistically significant changes in a simple trend analysis. In three registries (Bamako, Eastern Cape and Mauritius) there were increases in incidence in the second half of the period. For Bamako, a nonsignificant average annual increase of 0.8% during the period 1987 to 2004 was followed by a statistically significant increase from 2004 to 2017 (AAPC = 9.2%; 95% confidence interval [CI]: 5.4-13). For Ibadan, there was a statistically significant increase in the first part of the period (AAPC = 4.7%; 95% CI: 1.3-8.2). In Eastern Cape, there was a nonsignificant decline until 2002 (AAPC = -6.1%), which was followed by a statistically significant increase from 2002 to 2017 (AAPC = 9.9%; 95% CI: 4.7-15.4).

Figure 1 compares ASRs (with their 95% Cls) in two periods for three registries (Abidjan, Bulawayo and Seychelles). In Abidjan, there was a slight increase in the ASR (3.0 vs 3.6) a period between 1995 to 1998 and 2012 to 2017, and a similar small increase (ASR = 5.4 vs 6.6) in Seychelles between 2008 to 2013 and 2014 to 2020. However, the incidence in Bulawayo declined between 1963 to 1972 and 2011 to 2015. None of these changes was statistically significant.

Figure 2 shows the proportionate distribution of OC by histological subtype for the overall period in all 12 registries. The percentage of cases with unspecified histology ranged from 12% to 70%—these were very largely cases where there had been no pathological (or cytological) diagnosis (Table 2). Of those with a morphological diagnosis, the largest component was the epithelial cancers—85% overall, ranging from 62% in Abidjan to 99% in Brazzaville. Most of these epithelial cancers had a rather nonspecific histological diagnosis—carcinoma or adenocarcinoma—but of the remainder, serous cell carcinomas comprised the majority. Otherwise, of the cases with specified histology, sex cord-stromal tumours comprised at least 10% of cases in Seychelles (11%) and Harare (10%), and germ cell tumours at least 10% of cases in Bamako (15%), Bulawayo (14%), Kampala (13%) Abidjan (12%), Harare 12% and Seychelles (11%).

Figure 3 shows the trends by histological subtype for the four registries that had significantly increasing rates of OC (in Table 2). Visually, it appears that the increase in incidence is greater for epithelial cancers than for other histological subtypes—except in Mauritius. Indeed, the trends for epithelial OC were statistically significant in three registries: Bamako (5.9% annually, 95% CI: 3.7-8.1), Ibadan (3.9% annually, 95% CI: 1.4-6.5) and Eastern Cape (8% annually, 95% CI: 4.6-11.5). In Mauritius (2001-2018), there was a nonsignificant increase for epithelial OCs (AAPC = 1.6%, 95% CI: -1.5 to 4.8). There were no statistically significant trends for any of the other histological subtypes.

4 | DISCUSSION

Data on ovarian cancer incidence in SSA are sparse, and, to date, there has been no systematic investigation of time trends in incidence. Our study examines trends in incidence from 12 population-based cancer registries in SSA. Overall, the findings from our study suggest that ovarian cancer incidence is increasing. This was clearly true for by the applicable Creative Commons



FIGURE 2 Ovarian cancer: Histological subtypes as a percentage of all cases for overall period included

Bamako, Ibadan, Mauritius and Eastern Cape. These registries represent three different regions in the SSA. Moreover, nonsignificant increases are seen in Nairobi, Kampala, The Gambia, Harare, Abidjan and Seychelles. There were nonsignificant declines in Brazzaville and Bulawayo.

This current study also looked at the incidence of ovarian cancer by histological subtype. Although, as in other published studies, ^{19,20} the proportion of unspecified cancers was relatively high (40% overall, ranging from 12% to 70%), epithelial ovarian cancers were still more common compared to other subtypes in all of the registries. The increasing trends in ovarian cancer incidence in Bamako, Ibadan and Eastern Cape were clearly due to increases in epithelial cancers. There was also a nonsignificant increasing trend of epithelial OCs from Mauritius.

Ovarian cancer needs a surgical approach to achieve histological diagnosis and at least ultrasound or CT/MRI imaging with specific tumours markers such as Ca125 and HCG for a clinical diagnosis, so it is possible that the incidence rates reported from the registries in our study were underestimated due to the lack of necessary diagnostic capacity. However, seven of the registries selected for our study are in the two highest quality categories in IARC's GLOBOCAN estimates programme, having been published in at least one of the last three volumes of the "Cancer Incidence in Five Continents" series. The data selected for analysis were carefully examined to detect changes in any of the indicators of data quality over time. Of particular concern to the study of time trends is the possibility of increasing diagnostic capacity over time, due to the introduction of increasingly powerful imaging technology (ultrasound, CT scans, MRI scans, etc). To see if this had influenced ascertainment, we examined trends in the

proportion of cases being diagnosed with and without a histological diagnosis in those registries showing increasing trends in incidence. No apparent trend in the proportion of cases diagnosed morphologically was evident (Figure S1).

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Several factors have been associated with the risk of ovarian cancers. The risk increases with higher parity, while oral contraceptive use and tubal ligation decrease risk.⁴ The relationship between risk and overweight and obesity (as measured by BMI) is complex, with some studies suggesting that this applies only to certain histologic subtypes (low-grade serous and invasive mucinous tumours), or only premenopausal ovarian cancers (which are more likely to be of these subtypes).²¹ Genetic predisposition also plays a role in the risk of developing the OCs,^{12,22} with the risk of developing epithelial OCs increasing when first-degree family members are affected.²³ Although many genes are associated with the hereditary OC risk, *BRCA1* and *BRCA2* are the main genes involved in Hereditary Breast and Ovarian Cancer syndrome (HBOC).²² We were unable to find published data on the prevalence of known mutations of these genes in the countries we studied.

In SSA, the rising trend of OCs incidence may be associated with changes in fertility, increasing age at menopause, and, possibly, increases in body mass index. According to population-level surveys, fertility rates are declining in all 11 nations included in our study.^{24,25} Trends in BMI for sub-Saharan African populations are increasing, with greater increases reported from southern and central Africa.^{26,27} In South Africa, an increase of 1.82 kg/m² per decade was reported among adult women, which was higher than in the male population.²⁸ Mean BMI tends to be greater in countries with higher HDI such as Seychelles and Mauritius.²⁹ There are no reports or available data on



FIGURE 3 Trends of ovarian cancer by histological subtypes in Bamako, Ibadan, Eastern Cape and Mauritius

trends in age at menopause at population-level among sub-Saharan African women.

The increasing ovarian cancer incidence in SSA suggests the need to strengthen prevention and treatment services. However, preventive strategies are hardly feasible, since the only clear risk factorsrelated to fertility-are inappropriate targets for action. Genetic counselling and testing followed by risk-reducing surgery for women with a high-risk family history or early onset/high-risk breast cancer would theoretically be an option for a small proportion of women. Still, neither genetic testing facilities nor culturally appropriate counselling concepts and ethical guidelines are available. Early diagnosis should improve patient survival, but there is no conclusive evidence to promote OC screening at population level so that early detection remains the only feasible approach to improve patient survival. However, given the vague and nonspecific symptoms of early ovarian cancer,³⁰ late-stage diagnosis has been a critical problem in OC care everywhere, not only in SSA. Therefore, treatment with specialised surgery and systemic therapy are the pillars of ovarian cancer care. The considerable and increasing proportion of histologically verified diagnoses is encouraging since those rely on a surgical approach, which clinical colleagues seem to increasingly attempt in the lowresource settings. The amount of residual intra-abdominal tumour material determines prognosis, and clinical reports from the region still show low proportions of macroscopic surgical resection.^{31,32} Even in the presence of active surgeons, capacity building is needed to assure specialised oncologic surgery, equip operating theatres and to invest in other relevant services such as high-quality anaesthesia, intensive care units and blood banks.³³ In view of the rising numbers of patients diagnosed with ovarian cancer, access to systemic therapy—specifically platinum-based chemotherapy—is essential. This adds to the global demand for chemotherapy, which is projected to increase between 2018 and 2040 by 53%.³⁴

Special attention must be given to the higher proportion of nonepithelial cancers in the relatively young population, compared to what is observed in high-resource settings. These cancers require less extensive surgery and may allow fertility-sparing surgery. Management requires frozen section facilities with diagnosis followed by a radical operation. Younger women in particular need thorough counselling and close follow-up.

The findings in our study underline the importance of continued monitoring of trends in incidence and survival, and this in turn requires that the coverage (and quality) of cancer registration should be improved, to provide the evidence to plan strategies for OC control. Data from only 12 cancer registries was available to study trends of OC incidence from the whole of SSA. Although this situation may improve as some newer cancer registries mature, and acquire longer case series, there remains an urgent need for support from all key stakeholders so that best available epidemiological data is generated from all cancer registries in SSA to inform the required interventions.

AUTHOR CONTRIBUTIONS

Muluken Gizaw: Conceptualization; formal analysis; methodology; software; validation; visualisation and writing-original draft. Donald Maxwell Parkin: Conceptualization; formal analysis; methodology; supervision; validation; writing-review and editing. Ole Stöter: Conceptualization; formal analysis; methodology; software; validation; visualisation: writing- review and editing. Anne Korir, Bakarou Kamate, Lamin Boyang, Guy N'Da, Shym S. Maraj, Phiona Bukirwa, Eric Chokunonga, Tatenda Chongonzah, Jean-Felix Peko, Anne Finesse, Nontuthuzelo Somdyala, Akinande Ladipo: Data curation; investigation; resources; writing-review and editing. Biying Liu: Conceptualization; project administration; writing-review and editing. Eva Johanna Kantelhardt: Conceptualization; formal analysis; funding acquisition; methodology; project administration; supervision; writingreview and editing. The work reported in the article has been performed by the authors, unless clearly specified in the text.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of our study are available on request. All data requests will be evaluated by the AFCRN research committee. Details of the data application process are outlined on the AFCRN website http://afcrn.org/index.php/research/how-to-apply/76-research-collaborations. Further information is available from the corresponding author upon request.

ETHICS STATEMENT

Our study was approved by the AFCRN and anonymised secondary data was used. Informed consent was not feasible as we used the secondary collected data. Permission was obtained from each participating registry.

ORCID

Muluken Gizaw ^(b) https://orcid.org/0000-0002-6500-5852 Donald Maxwell Parkin ^(b) https://orcid.org/0000-0002-3229-1784 Nontuthuzelo Somdyala ^(b) https://orcid.org/0000-0001-6564-8754 Eva Johanna Kantelhardt ^(b) https://orcid.org/0000-0001-7935-719X

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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