





RESEARCH ARTICLE

Cancer Epidemiology

Ovarian cancer survival in sub-Saharan Africa by human development index and histological subtypes: A population-based registry study

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Abstract

Ovarian cancer (OC) is the fourth most common cancer of women in sub-Saharan Africa (SSA), although few data have been published on population-level survival. We estimate ovarian cancer survival in SSA by human development index and histological subtype, using data from seven population-based cancer registries in six countries: Kenya (Nairobi and Eldoret), Mauritius, Uganda (Kampala), Cote d'Ivoire (Abidjan), Ethiopia (Addis Ababa) and South Africa (Eastern Cape). A total of 644 cases diagnosed during 2008–2014 were included, with 77% being of epithelial subtypes (range 47% [Abidjan]–80% [Mauritius]). The overall observed survival in the study cohort was 73.4% (95% CI: 69.8, 77.0) at 1 year, 54.4% (95% CI: 50.4, 58.7) at 3 years and

Abbreviations: AFRCN, African Cancer Registry Network; ASR, age-standardized rate; CI, confidence interval; DCO, death certificate only; HDI, human development index; ICD-10, International Classification of Diseases 10th revision; ICD-O-3, International Classification of Diseases for Oncology 3rd revision LMICs Lower and middle-income countries; MV, morphological verification; OC, ovarian Cancer; SSA, sub-Saharan African; TNM, tumour, node and metastasis.

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45.0% (95% CI: 41.0, 49.4) at 5 years. Relative survival at Year 1 ranged from 44.4% in Kampala to 86.3% in Mauritius, with a mean for the seven series of 67.4%. Relative survival was highest in Mauritius at 72.2% and lowest in Kampala, Uganda at 19.5%, with a mean of 47.8%. There was no difference in survival by age at diagnosis. Patients from high and medium HDI countries had significantly better survival than those from low HDI countries. Women with cancers of epithelial cell origin had much lower survival compared to women with other histological subtypes ($p = .02$). Adjusted for the young age of the African patients with ovarian cancer (44% aged <50) survival is much lower than in USA or Europe, and underlines the need for improvements in the access to diagnosis and treatment of OC in SSA.

KEYWORDS

epithelial, HDI, ovarian cancer, sub-Saharan Africa, survival

What's new?

Ovarian cancer is among the most common cancers affecting women in sub-Saharan Africa (SSA). Little is known, however, about ovarian cancer survival rates across populations in SSA. In this study, data from seven population-based cancer registries in SSA was analyzed to estimate net survival by age, histological subtype, and human development index (HDI) level. The findings reveal significant differences in survival across and within countries. Overall, survival in SSA is relatively poor, especially in low and medium HDI countries and for epithelial cancers. The study emphasizes the need for earlier diagnosis and prompt, effective treatment for ovarian cancer in SSA.

1 | INTRODUCTION

Worldwide, ovarian cancer (OC) is among the 10 most commonly diagnosed cancers among women, with an estimated 314,000 new cases and 207,000 deaths globally in 2020.^{1,2} Incidence and mortality rates of OC vary between different regions and although the lowest incidence rates are observed in Africa,^{3,4} it was the fourth most common cancer of women in the sub-Saharan African (SSA) region in 2020, responsible for about 18,000 cases (3.8% of all cancers) and 13,000 deaths.¹

Survival inequalities have been documented for various cancer types across different countries, with developing countries having a low survival rate for major cancer types.⁵ Although there has been some progress in improving the survival of cancer patients in low and middle income countries (LMICs), the ratio of deaths to cases remains disproportionately high.¹ In most LMICs, including those of SSA, ovarian cancer is diagnosed at an advanced stage, due to vague presentation symptoms.⁶ Generally, survival from ovarian cancer is rather poor—even in the United States, survival at 5 years is only about 50%.⁷ Studies in UK,⁸ USA⁹ and Australia¹⁰ have shown that ovarian cancer survival varies according to histological type, with epithelial subtypes having a worse prognosis. We have previously reported increasing trends in the incidence of ovarian cancer in SSA and identified changes in fertility, increasing age at menopause, and, possibly, increases in body mass index as likely to be responsible for such trends.¹¹ Moreover, the data suggested that the increase was due to

increasing trends of the epithelial ovarian cancers.¹¹ However, very limited data are available on survival from ovarian cancer in populations in sub Saharan Africa.

Evaluation of the effectiveness of services for cancer diagnosis and treatment at the population level requires outcome data from population-based cancer registries. For sub Saharan Africa (SSA) 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 survival of cancer in unselected (representative) patient populations.⁴ In the present study, we examine the survival of ovarian cancer patients, using data from seven population-based cancer registries in SSA, members of the AFCRN. Given the limited data on OC survival in SSA, the current study will provide useful information on this important cancer of women, to inform policymakers and health professionals on the effectiveness of current OC care, and so help in the development of strategies for early diagnosis and clinical management of this cancer.

2 | METHODS

2.1 | Study population

Data were obtained from seven population-based cancer registries in six countries, members of AFCRN: Cote d'Ivoire (Abidjan), Ethiopia (Addis Ababa), Kenya (Nairobi and Eldoret), Mauritius, South Africa

TABLE 1 Total number of ovarian cancer diagnosis, included and excluded cases, and data quality indicators by population-based cancer registry.

Country	HDI 2015	Registry	Period of diagnosis	Total number of ovarian cancer cases during study period	Included for survival analyses N (%)	Histologically verified ^a N (%)	Epithelial cancers ^a N (%)	Other specified types ^a N (%)	Unspecified types N (%)
Cote d'Ivoire	Low	Abidjan	2012–2013	61	34 (56)	19 (56)	16 (47)	3 (9)	15 (44)
Ethiopia	Low	Addis Ababa	2012–2013	175	163 (93.2)	117 (72)	105 (64)	12 (7)	46 (29)
Kenya	Medium	Eldoret	2008–2012	38	25 (65.8)	25 (100)	20 (80)	5 (20)	-
Kenya	Medium	Nairobi	2009–2013	58	56 (96.6)	45 (80)	41 (73)	4 (7)	8 (20)
Mauritius	High	Mauritius	2010–2014	254	247 (97.3)	211 (85)	190 (77)	21 (8.5)	36 (14.5)
South Africa	Medium	Eastern Cape	2008–2013	70	64 (91.4)	54 (84)	46 (72)	8 (12.5)	10 (15.5)
Uganda	Low	Kyadondo (Kampala)	2012–2013	78	55 (70.5)	29 (53)	28 (51)	1 (2)	26 (47)
Total cases				734	644 (87.7)	500 (77.6)	446 (69)	54 (8.4)	141 (22)

Note: MV: Cases for which diagnosis was based on cytology, or histology.

Abbreviation: HDI, human development index. Source: United Nations Development Program. Human Development Report 2016.

^aPercentage of cases included in the study.

(Eastern Cape) and Uganda (Kampala). We included all ovarian cancer cases (ICD-10: C56) diagnosed among black African females in these registries for periods of 2–6 years, around 2012. These registries had national coverage in Mauritius and covered an urban area for all the other registries except for the Eastern Cape registry which covers a rural area. The methods of data collection, validation and storage of these registries are described elsewhere.¹² The follow-up time was measured from the date of incidence until the date of last contact, the date of death or until the end of the study (31 December 2014), whichever occurred first.

2.2 | Vital status

This was obtained by active methods for all but one registry (Mauritius). In active follow-up, clinical records are traced and the patient's vital status at the closing date recorded. Cases whose vital status could not be confirmed at the end of this procedure were called when a mobile number was registered in the registry record. When no further information could be obtained, home visits were made by the registry staff. Patients whose vital status (alive/dead) could not be ascertained by the closing date of the study were censored "alive." In Mauritius, passive follow-up was done to ascertain the vital status of patients; this involves linkage of the list of registered cases with the population death records held in the vital statistics office. Patients not found to have died are assumed to be still alive.

2.3 | Data analyses

We excluded cases diagnosed based on a death certificate only (DCO), with no follow-up information (cases with <7 days of follow-up) and with incoherent follow-up dates. We present Kaplan–Meier (KM) survival

curves and estimate the observed and Ederer II relative survival (RS) at 1, 3 and 5 years after diagnosis.¹³ Mid-year (June 30) was used for 55 cases from Mauritius in 2014 where no exact day and month of the diagnosis had been recorded in the registry. The RS is the ratio of the "observed" survival in the study population to the "expected" survival. The expected survival derived from country-specific life tables is the survival experience of the general population of the same age, sex and period.¹² This corrects for background mortality (not due to cancer of the ovary) in the patient cohort. Abridged life tables by sex, age group and country were obtained from the WHO Global Health Observatory data repository. Age-specific death rates were obtained, calculated from the number of deaths among persons in a given age group during a given time period, and the total person-years for the population in the same time period. The number of deaths and person-time by sex, year and country were used to estimate mortality rates using a Poisson regression with a flexible function to expand the abridged age groups (0–4, 5–9, 10–14, ... 80+) to single ages (0, 1, 2, 3, ... 99) based on methods first described by Rachet et al.¹⁴

The human development index (HDI) is a composite measure developed by the United Nations Development Programme that aims at assessing the level of development of countries.¹⁵ It has three main components: life expectancy at birth, the educational attainment of citizens and the Gross National Income (GNI) per capita. We used the HDI 2015 classification to categorize the six countries and compared survival within SSA by HDI.¹⁶

We also estimated survival of ovarian cancer according to histological subtype. The ovarian cancers were classified as epithelial, other specified types and unspecified, according to the ICD O-3 morphology codes.¹⁷ Cases with no morphological proof of diagnosis were classified as Unspecified (Group 5).

We used univariable and multivariable Cox Hazard regression models adjusted for age at year of diagnosis, histology type and HDI to study the influence of these variables on observed survival.

3 | RESULTS

The cancer registries included in the study are shown in Table 1. Of the seven registries, three were from low HDI countries (Cote d'Ivoire, Ethiopia and Uganda), two from a medium HDI country (Kenya) and two were from high HDI countries (Mauritius and South Africa). We excluded 90 (12.2%) cases with no follow-up information or with inconsistent follow-up dates (Table 1). Finally, 644 (87.8%) incident cases diagnosed during the period of 2009–2014 were included. Except for two registries (Kampala and Abidjan), all reported >60% morphological verification (MV%) of diagnosis of cases. Among cases included in the study, the proportion of epithelial OC cases was 69%, ranging from 47% in Abidjan, Cote d'Ivoire to 80% in Eldoret (Table 1).

Of the 644 cases included for survival analyses (Table 2), the mean age at diagnosis ranged from 43.4 years in Eldoret, Kenya to 53.1 in Mauritius, with a median duration of follow-up ranging from 0.1 years in Kampala, Uganda to 2.7 years in Eastern Cape, South Africa. The highest proportion of cases of LFU was seen in the first year of follow-up in Eldoret (56% [14/24]) and Kampala (31% [17/55]). The LFU was much less in years 2 and 3—<10% in all registries except in Nairobi (24%[6/25]). The proportion of cases with 5-year complete FU ranged from 56% (19/34) in Abidjan to 100% in Mauritius (Table 2).

3.1 | Survival statistics

In the study cohort, the overall observed survival in SSA women with ovarian cancer was 73.4% (95% CI: 69.8, 77.0) at 1 year, 54.4% (95% CI: 50.4, 58.7) at 3 years and 45.0% (95% CI: 41.0, 49.4) at 5 years (Figure 1A). Figure 1B shows the KM survival by registry, the 5-year observed survival was lowest in Kampala (17.9% [8.9–36.3]) and highest in Mauritius (65.2% [59.5–71.4]). There were no statistical differences in age-specific survival ($p = .9$) (Figure 1C). Patients from high and medium HDI countries had the highest survival, while the lowest survival was found in low HDI registry areas ($p < .0001$; Figure 1D).

Relative survival at Year 1 ranged from 44.4% in Kampala to 86.3% in Mauritius (Figure 2). Similarly, at 5 years after diagnosis, relative survival was highest in Mauritius at 72.2% and lowest in Kampala, Uganda at 19.5% (Figure 2).

Of the total 579 (79%) histologically verified cases, 446 (77%) cases were epithelial ovarian cancer. The highest proportion of epithelial ovarian cancer was seen in Ethiopia 105/124 (85%) and Mauritius 190/238 (80%). However, only 47% and 54% in Cote d'Ivoire and Eldoret, Kenya, respectively. There were statistically significant differences in the survival by histological subtypes. The survival of women with epithelial ovarian cancer was significantly lower than that of women with ovarian cancers of other histological subtypes ($p = .022$) (Figure 1E).

TABLE 2 Patients characteristics: mean age at diagnosis, median years of follow-up and observed (all cause) survival and lost to follow-up.

Registry	Mean age at diagnosis years (SD)	No. of cases	Median follow-up time, Years (IQR)	Year 1		Year 2 and 3		Year 4 and 5	
				No. of deaths (%) year 1	Observed 1-year-survival % (95% CI)	No. of deaths (%) years 2–3	Observed 3-year-survival % (95% CI)	No. of deaths (%) Years 4–5	Observed 5-year-survival % (95% CI)
Cote d'Ivoire Abidjan	45.9 (14.4)	34	0.2 (3.3)	10 (29.4)	60.8 (44.3–83.4)	14 (41.2)	43 (26.9–68.5)	17 (50)	26.2 (12.4–55.2)
Ethiopia Addis Ababa	47.2 (15.9)	163	0.7 (2.6)	47 (28.8)	68.5 (61.5–76.4)	92 (56.4)	37.3 (30.2–46.1)	111 (68.1)	21.7 (15.7–30.1)
Kenya Eldoret	43.4 (12.4)	25	0.3 (0.5)	5 (20)	71.3 (52.2–97.4)	8 (32)	35.6 (15.1–84.1)	8 (32)	35.6 (15.1–84.1)
Kenya Nairobi	50.5 (19.4)	56	1 (1.7)	21 (37.5)	57.2 (44.8–73.2)	30 (53.6)	32.9 (20.9–51.6)	32 (57.1)	25.9 (14.8–45.4)
Mauritius	53.1 (14)	247	-	95 (38.5)	85 (80.7–89.6)	70 (28.3)	71.7 (66.3–77)	86 (34.8)	65.2 (59.5–71.4)
South Africa Eastern Cape	51.2 (17.4)	64	2.7 (3.2)	14 (21.9)	75.7 (65.4–87.7)	19 (29.7)	66.3 (54.9–79.9)	24 (37.5)	53.5 (40.9–69.9)
Uganda Kampala	49.4 (16.4)	55	0.1 (0.1)	22 (40)	43.5 (30.2–62.5)	28 (50.9)	26.9 (15.8–45.8)	31 (56.4)	17.9 (8.9–36.3)

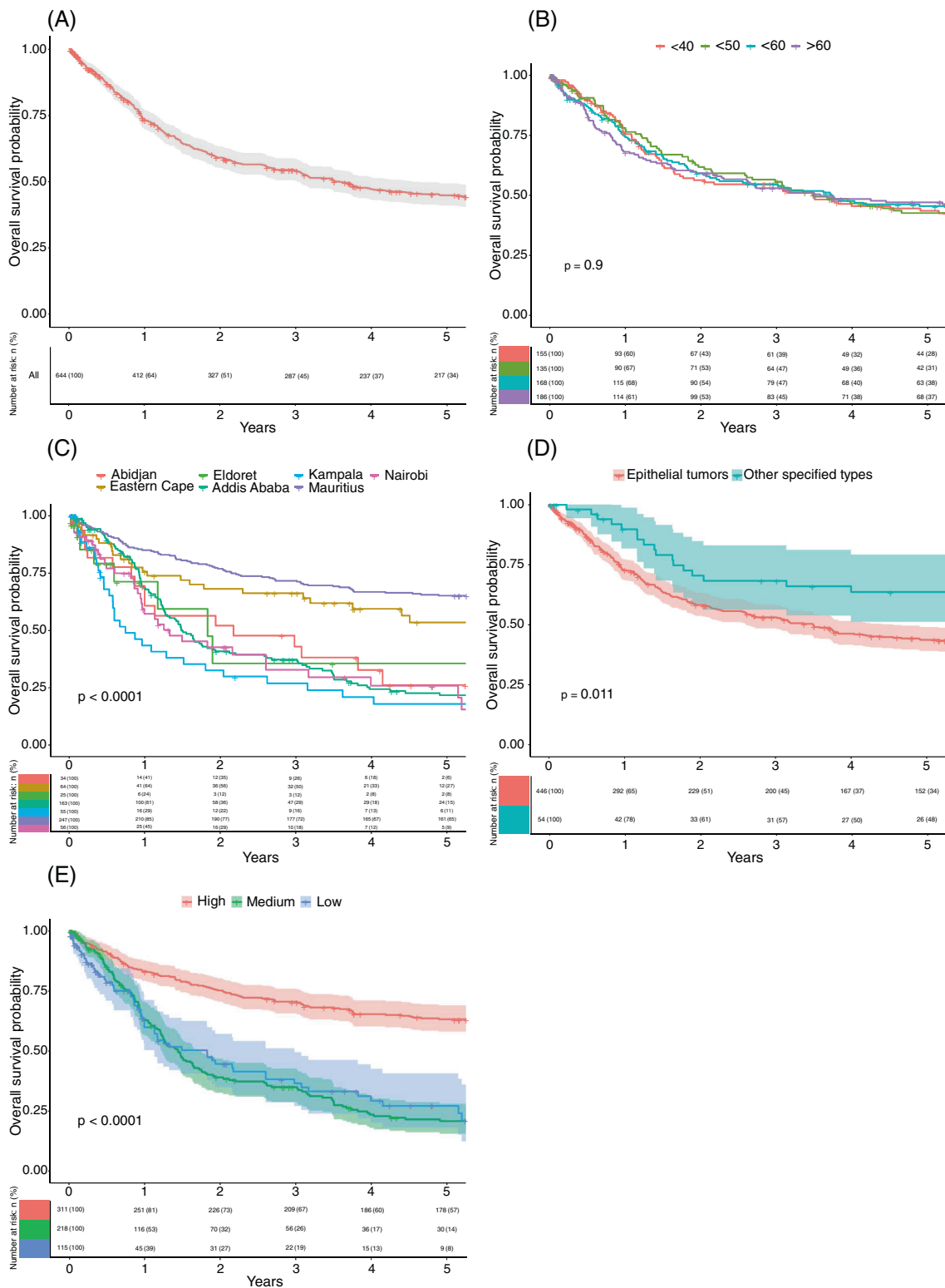


FIGURE 1 Observed (all-cause) survival for the entire study cohort (A), by age group (B), by registries (C), histological types (D) and human development index (HDI) (E).

3.2 | Excess hazard ratio

After adjusting for age at diagnosis and histology type, countries with low and Medium HDI were associated with a threefold risk

of death compared to countries with high HDI (Table 3). A 44% (95% CI: 34–90%) lower hazard was seen among other specified ovarian cancer, hazard ratio 0.56 (95% CI: 0.34, 0.90) compared with epithelial cancers. Age at diagnosis was not associated with

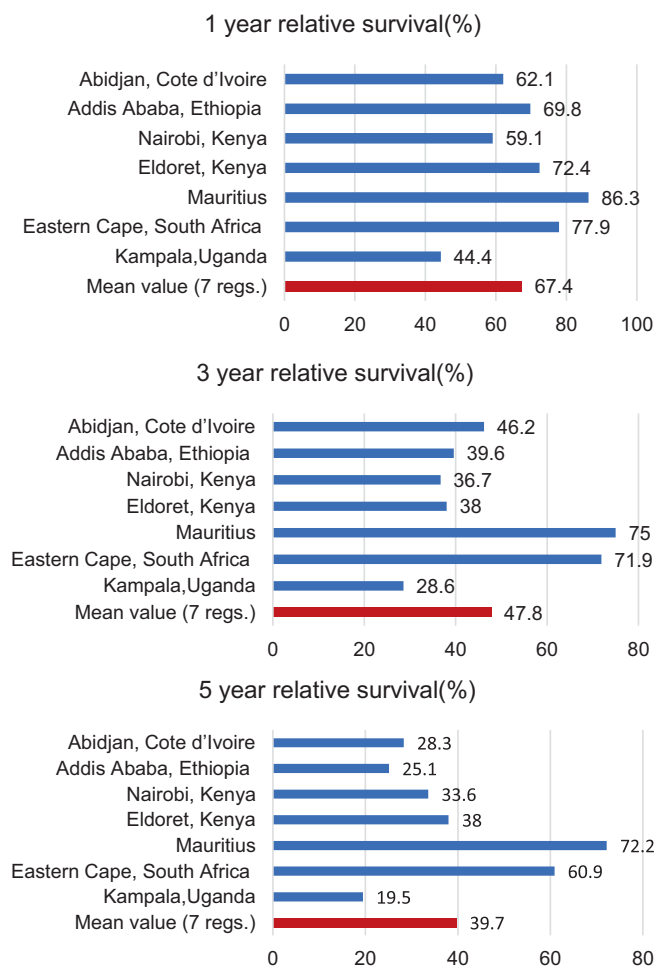


FIGURE 2 Relative survival (RS) from ovarian cancer at 1, 3 and 5 years after diagnosis, by registry.

TABLE 3 Ovarian cancer excess mortality hazard by age and histology type and HDI.

Variables	No. cases	Univariable analysis		Multivariable model ¹	
		Excess hazard ratio (95% CI)	p value	Excess hazard ratio (95% CI)	p value
Age at diagnosis (years)					
<40	155	Reference			
40–49	135	1.0 (0.72, 1.38)	.983	1.04 (0.75, 1.45)	.7818
50–59	168	0.9 (0.67, 1.24)	.569	1.10 (0.80, 1.52)	.5257
≥ 60	186	1.0 (0.74, 1.36)	.940	1.17 (0.86, 1.61)	.3008
HDI level					
High	311	Reference			
Medium	218	3.14 (2.29, 4.28)	<.001	3.40 (2.47, 4.68)	<.001*
Low	115	3.04 (2.38, 3.88)	<.001	3.09 (2.40, 3.97)	<.001*
Histology type					
Epithelial	446	Reference			
Other specified type	54	0.55 (0.34, 0.87)	.0123	0.56 (0.34, 0.90)	.0184*
Unspecified type	141	1.1 (0.85, 1.44)	.4385	0.95 (0.72, 1.24)	

Note: *Statistically significant. Adjusted for age at diagnosis, histology type and HDI. Abbreviations: CI, confidence interval; HDI, human development index.

the hazard of death even after adjustment for HDI and histological subtype.

4 | DISCUSSION

Cancer survival is one of the key indicators for evaluating the effectiveness of cancer prevention and treatment interventions in a country. For this purpose, data from population-based cancer registries are essential. Results from individual hospitals, or clinical series, are unlikely to be representative of the general experience of the population.¹⁸

Data on ovarian cancer survival in SSA are sparse, and, to date, there are few data on long term follow up of ovarian cancer in the region. This study examines 5 year survival of 644 cases from seven population-based cancer registries in SSA, and investigates the influence of age, Human Development Index and histological subtype.

Overall, the findings from this study suggest that, in most of the populations studied, more than half of the ovarian cancer patients died within 3 years of diagnosis. For all seven registries combined the 1-, 3- and 5-year observed (all-cause) survival (95% CI) was 73.4% (69.8, 77.0), 54.4% (50.4, 58.7) and 45.0% (41.0, 49.4), respectively. However, the survival estimates varied across the countries, with higher survival in Mauritius and South Africa. Although there are differences in survival from ovarian cancer between developed and developing countries, the net survival difference was not as high as for other cancer types.⁵

Previous studies based on cancer registry data from sub Saharan Africa have included results from Mauritius, Addis Ababa and Eastern Cape (South Africa) for earlier and/or shorter time periods.^{3,16} Five year relative survival (age adjusted) in Ibadan (Nigeria) for the period

2010–2014 was reported as 49.1%¹⁶ although this figure was considered to be “unreliable”.

This study identified a statistical significant difference in survival according to the countries human developmental index. Countries with low development index such as Ethiopia, Cote d'Ivoire and Uganda had the lowest relative 5 years survivals: 25.1%, 28.3% and 19.5%, respectively. Better relative 5 years survival was reported from the middle and higher HDI countries such as Kenya (35.1%), South Africa (71.9%) and Mauritius (75.0%). This finding was consistent with previous studies reports that the income level directly associated with the better cancer outcome.^{5,19,20} Although it seems surprising that residents of the only rural population studied (Eastern Cape in South Africa) had a relatively good survival, almost all of these women had been treated in major hospitals outside of the registry area, and rural residents did not have an inferior outcome in a study in the USA.²¹

Stage at diagnosis is a very strong predictor of outcome for ovarian cancer, and, within stage, younger patients have a more favourable prognosis than older women.²² In the present study, only limited data were available on stage at diagnosis, since this is poorly routinely recorded by cancer registries in Africa.²³ As a result, we were not able to adjust our survival estimates by stage, which may account for the lack of any difference in survival by age. African populations are relatively young, and so was our cohort of ovarian cancer patients, with 59% aged <54, compared with 26% in Europe (2000–2007), and 30% in the eight SEER registries of the USA in 2008–2012.^{24,25} Thus, although the average relative survival at 5 years for the seven African registries in our study—39.7% (Figure 2)—was not grossly inferior to that of the US SEER cancer registries, or the cancer registries of Europe (48.1% and 40.8%, respectively), this is largely due to the age differential. If the US and European figures are standardised to have the same age distribution as our African cases, the relative survivals would have been 60% and 52%, respectively—much higher than the African survival.

We did observe a significantly poorer survival among women with epithelial carcinomas, which is consistent with study reports from United Kingdom, USA and Australia.^{8–10}

Studies from elsewhere have reported that a higher Body Mass Index (BMI) is associated with poor ovarian cancer survival.^{8,26} Trends in BMI in sub-Saharan African populations are increasing, with higher increases reported from southern and central Africa.^{27,28}

Because of the powerful influence of stage on survival, there has been much interest in the feasibility of early diagnosis and screening. However, to date, there is no concrete evidence that show that mortality would be reduced by implementation of organized ovarian cancer screening at the population level, and early diagnosis is difficult, given the vague and non-specific nature of symptoms of the disease. Hence, improvement of the diagnostic capacity—including histology—and access for specialized radical surgery and systemic therapy might be the best options for improving survival from this disease.²⁹

The strength of this study lies in the use of the population based cancer registries from six countries in SSA. Most of the cases included in this analysis were morphologically verified and, as a result, the histological subtypes was identified for most of the cases. The limitations lie

in the lack of data on stage, completeness of surgery (presence of residual tumour) and the problems in getting complete follow-up of cases. Only in Mauritius was follow up complete, because of the use of passive follow up by linkage of registry records to the death register, and the assumption that cases not known to have died are still alive. This method may overestimate survival, if deaths among the cancer cases are missed because of failure of record linkage, or migration of cancer cases out of the registry area prior to death.³⁰ With active follow up, despite all attempts to trace cancer patients, a varying proportion are lost to follow up before the closing date of the study. In survival analysis, patients lost to follow up are censored at the date of their last follow up—an approach that gives accurate results if loss to follow up is random (i.e., for reasons not related to survival).³¹

While death registration in many African countries remains incomplete, follow up in the African context will continue to require efforts to trace patients at home. However, there have been actions taken by the AFCRN to improve the staging for major cancer types by introducing a simplified staging system (Essential TNM) and providing training in its use.^{32,33}

In conclusion, a huge difference in ovarian cancer survival across countries by HDI shows the need to strengthen cancer care programs and the importance of monitoring survival data as an indicator of their success. This is even more important given the large proportion of young patients with high probability of non-epithelial tumours and curable disease. The limited number—and quality—of the current data also underlines the need for improvements of the coverage and quality of cancer registration and follow up. Of the total 35 cancer registries that were members of AFCRN at the time of this study, only seven could provide follow up data on sufficient numbers of cases for this study of OC. This suggests there is still a need for support from all key stakeholders, including governments, academia, and other donors, to support cancer surveillance in sub Saharan Africa.

AUTHOR CONTRIBUTIONS

Muluken Gizaw: conceptualization; formal analysis; methodology; software; validation; visualization and writing-original draft. **Donald Maxwell Parkin:** conceptualization; formal analysis; methodology; supervision; validation; writing-review and editing. **Ole Stöter:** formal analysis; software; validation; visualization; writing- review and editing. **Phiona Bukirwa, Edom Seife, Gladys Chesumbai, Anne Korir, Shyam S. Manraj, Guy NDa and Nontuthuzelo I. M. Somdya:** 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; writing-review 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 STATEMENT

No conflict of interest to declare.

DATA AVAILABILITY STATEMENT


The data that support the findings of this study (including the population life tables) 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 anonymized secondary data was used. Informed consent was not feasible as we used the secondary collected data. Permission was obtained from each participating registry.

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