Cervical cancer elimination in Africa: where are we now and where do we need to be?

International Agency for Research on Cancer
World Health Organization

AFRICAN CANCER REGISTRY NETWORK
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Answers for Cancer Control

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Introduction: Towards elimination of cervical cancer in the African Region

Every two minutes a life is lost to cervical cancer. In 2020, 342 000 women died from the disease and almost a quarter of these deaths (22.5%) occurred in Africa. It does not have to be this way. Cervical cancer is one of the most highly preventable and, if diagnosed early, one of the most treatable forms of cancer. We have a real opportunity to save millions of lives as we have the tools, the know-how and a path to follow to eliminate cervical cancer on the African continent and globally.

On November 17th 2020, the Director General of WHO, Dr Tedros Adhanom Ghebreyesus, launched the WHO Global Strategy to Accelerate the Elimination of Cervical Cancer. Elimination means that the cervical cancer incidence is reduced to four cases or less per 100,000 women per year. However, much remains to be done across the region, especially in Sub-Saharan Africa where incidence rates are 10 times higher than the elimination threshold set by the WHO Global Strategy. When talking about the elimination effort we cannot forget that behind the incidence and mortality data there are real people. The 76,745 women who died from cervical cancer across the African region in 2020 represent a huge loss to their families, communities and societies. These 76,745 individuals, daughters, mothers, grandmothers, sisters, aunts, friends, work colleagues, neighbours, career professionals, caretakers and breadwinners all died from a preventable disease that we know how to address. Therefore, we can no longer ignore cervical cancer as a global health issue and have a moral imperative to eliminate this preventable disease.

The WHO Global Strategy to Accelerate the Elimination of Cervical Cancer established global targets that should be reached by the year 2030 in order to be on track towards elimination and achieve it by the end of the century:

- 90% of girls fully vaccinated with HPV vaccine by 15 years of age
- 70% of women screened using a high-performance test by 35 years of age and again by 45 years of age
- 90% of women identified with cervical disease receive treatment (90% of women with precancer treated, and 90% of women with invasive cancer managed)

The Strategy will contribute to the attainment of the Sustainable Development Goals and targets, not only those that are specifically health related, but will help achieve the other development goals as well. By eliminating cervical cancer, countries in Africa will contribute to addressing gender inequality and poverty as well as make progress towards the goal of Universal Health Coverage, aligning with the overarching principle of the 2030 Agenda for Sustainable Development of 'leaving no one behind'.

However, the elimination of cervical cancer as a public health problem across Africa will only be possible with support from heads of governments, local leaders, international agencies, civil society and relevant private sector organisations. It is important for African countries to prioritise cervical cancer control in national cancer control plans and align them with the Global Strategy. To achieve the elimination of cervical cancer on the continent, there is an urgent need to increase access to prevention, early detection, treatment and palliative care services for women. African countries also need to provide financial protection for patients who face the risk of catastrophic spending through out-of-pocket payments for their cervical cancer treatment.

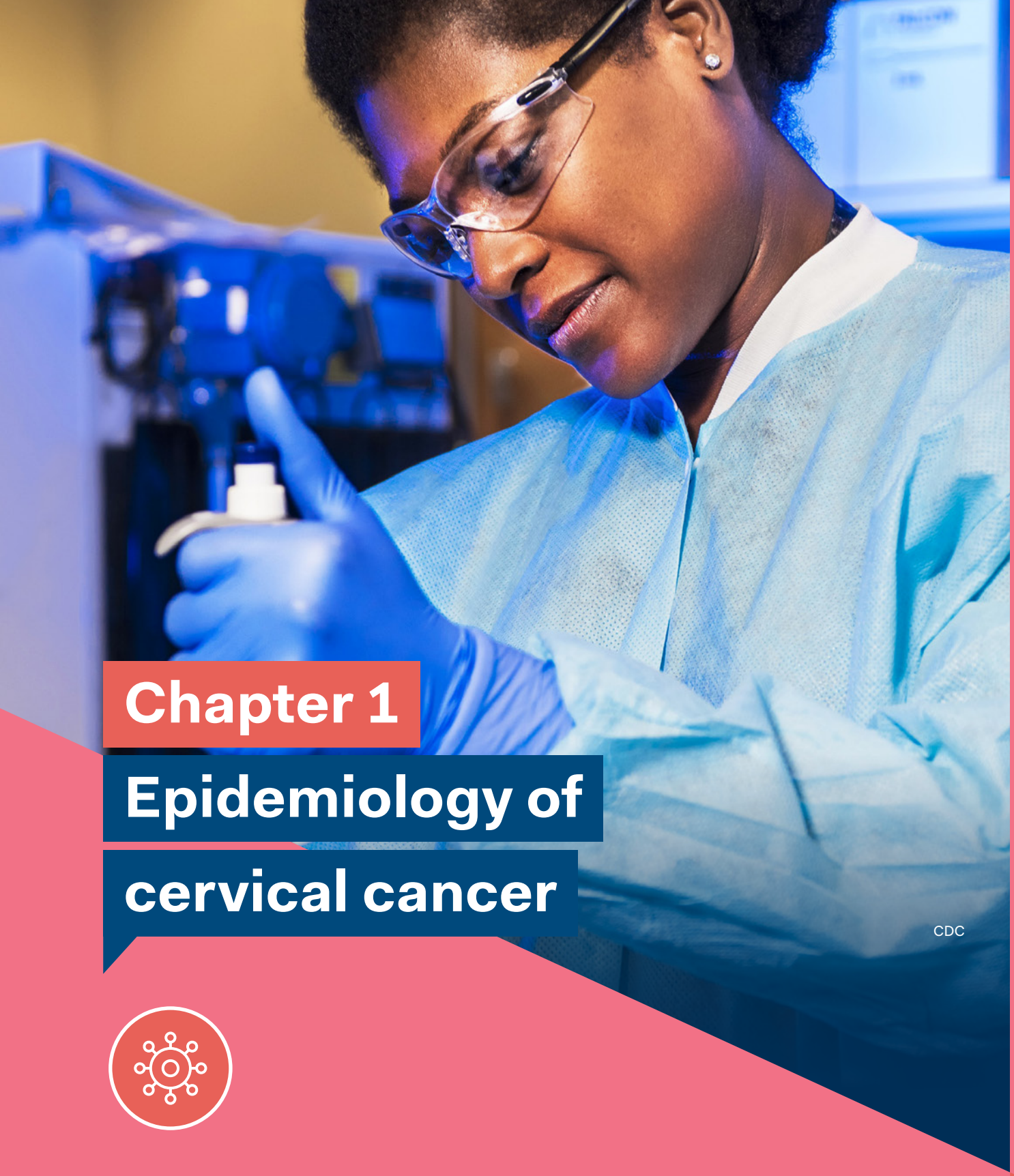
Across the continent, countries are facing a common challenge of developing the integrated services required to achieve the 90-70-90 targets, including their affordability, sustainability and scale-up. Several countries in the African region are working to introduce national coverage of HPV vaccination, with 45% of WHO member states in the region having introduced HPV in their immunisation programmes thus far. In addition to vaccination, screening, early diagnosis, treatment and palliative care are critical but equally challenging for countries to develop. Only 20% of the WHO member states in the region reported having a national cervical cancer screening programme, with almost all these programmes being opportunistic. Treatment options are limited and, in many cases, when offered, therapy does not have a curative potential. Palliative care service delivery for cervical cancer in the region remains limited, centralised at cancer care centres and not available at a community level. Much remains to be done but with clear targets and plans every country can make progress towards cervical cancer elimination.

To ensure that we are on the right course to meeting the elimination targets in Africa, we need robust monitoring and evaluation mechanisms. Monitoring the burden of cervical cancer in Africa and evaluating the impact of the interventions requires cancer surveillance systems at national level through cancer registries. There is an urgent need to improve the availability and quality of data from countries with the highest burden of cervical cancer as these data are crucial for establishing national priorities, decision making, and resource allocation by both local and international stakeholders, including donor organisations.

The availability and quality of cancer registries varies across the region and must be addressed in national elimination efforts. To measure progress towards the elimination targets, cancer registries need to produce data that are a reasonably accurate reflection of the true cancer profile of the country. This will require support for initiatives such as IARC's Global Initiative for Cancer Registry Development (GICR) and the African Cancer Registry Network (AFCRN) as its regional hub, as well as increased international donor assistance and national investment to develop local capacity for generating, analysing and interpreting data on cervical cancer occurrence and outcomes.

The following publication has been developed to reflect the status of current efforts towards elimination of cervical cancer in the African region. Each chapter describes the current situation, starting with epidemiology, progressing through an overall assessment of prevention (HPV vaccination and screening) efforts and treatment and palliative care. The focus of each chapter is on the coverage of key interventions as well as on data collection and monitoring systems required to track progress against the cervical cancer elimination targets across the African continent.

Our purpose is to provide readers: representatives of Ministries of Health, healthcare professionals and civil society organisations, researchers and others with a publication that points out areas that require urgent attention, research, development and improvement. The publication positions current public health programmes in the global context and encourages the audience to look at a bigger picture of cervical cancer elimination in Africa. With concerted efforts, political will and adequate financing, the elimination of cervical cancer can become a reality on the continent.



Chapter 1

Epidemiology of cervical cancer

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Effective disease control programmes require adequate information on the size, nature, and evolution of the health problem which they pose. At the population level, there are four key complementary measures for cancer, namely:

1. The prevalence of specific risk factors for cancer in the general population
2. Incidence (newly diagnosed cases of cancer)
3. Survival (percentage of patients surviving n years after the date of first diagnosis of cancer)
4. Mortality (number of cancer deaths).

In this chapter, we focus on describing and elucidating variations in the current patterns and recent trends in cervical cancer burden across Africa to build a contemporary epidemiologic profile in the region today. The data sources and methods for this purpose and the challenges in collecting this information and in developing national estimates of burden are described below. We then examine national variations in incidence estimates and recent trends based on recorded incidence, ending with a contemporary assessment of the stage at which cervical cancer is diagnosed in Africa, within defined populations and clinical series.

Sources of data on incidence, stage, and survival

The results provided below are based on the best data currently available and provide a reasonable appraisal of the cervical cancer situation in Africa. Nevertheless, there are still deficiencies in surveillance on the continent, with very few countries with well-functioning civil registration and vital statistics (CRVS) systems in Africa which record deaths. An essential and complementary component to CRVS, population-based cancer registries (PBCR), provide a unique source of incidence and survival (by cancer and stage) and a means to track progress in reaching the overall target of the Cervical Cancer Elimination Initiative (CCEI): an incidence rate of 4 per 100,000 women (or less). This is a major undertaking on a continent where cervical cancer incidence rates in many countries in Southern, Eastern and Western Africa are among the highest in the world [1] and where there is compelling evidence of increasing trends in a number of constituent countries.[2] It is therefore evident that a coordinated approach to implementing the 90-70-90 strategy in-country must equally set about improving national surveillance systems - from which the scale-up of interventions can be planned and progress monitored.

Population-based cancer registries (PBCRs) are the key providers of incidence and a prerequisite to national cancer control planning and evaluation. PBCRs comprise a continuous system of data collection, storage, validation and analysis that enables the dissemination of incidence and survival for the major types of cancer, and by stage at diagnosis. They are an essential foundation in planning and evaluating cancer prevention activities, informing the planning of cancer services, and benchmarking the effectiveness of cancer care delivery in different regions and countries through comparisons of the survival of cancer patients. As with any other public health surveillance strategy, the recording and reporting of data are undertaken in a standardised way to ensure maximum comparability.[3–5]

PBCRs are especially valuable in Africa given the lack of population-based data on cancer occurrence and outcome available from other sources.[6] To support the local planning and development of PBCRs in countries within defined regions, the International Agency for Research on Cancer (IARC) through the Global Initiative for Cancer Registry Development (GICR) has established a series of IARC Regional Hubs for Cancer Registration in Africa, as well as in Asia, and in Latin America. The African Cancer Registry Network (AFCRN) serves as the IARC Regional Hub in Sub-Saharan Africa, coordinating all cancer registration activities. An IARC Regional Hub based in Izmir, Turkey coordinates activities in Northern Africa and Western Asia. However, international donor assistance as well as national investments are critically needed to build sufficient capacity to generate, analyse and interpret quality-assured local data on cervical cancer occurrence and outcomes. General aspects of the surveillance, monitoring and evaluation of the disease in the context of the WHO Cervical Cancer Elimination Initiative have been developed.[5]

The results presented in this publication are from several sources. Numbers and rates were extracted from the GLOBOCAN 2020 database of IARC, which presents the estimates of incidence of, and mortality from, all cancers and 38 major types in 185 countries or territories worldwide for 2020. Cancer registry data are a key source for such national indicators [7,8] including high-quality cancer registry incidence data, as compiled in IARC's Cancer Incidence in Five Continents (CI5) series [9] as well as other registry data sources, most notably through a continued expansion of the members of the AFRCN.[6] The quality of national estimation depends upon the availability and quality of the source information in each country. The data sources and methods used to estimate incidence in each country are summarised in Table 1.

	Method						
Source	1	2	3	4	5 9	No method	Total
High Quality PBCR	1	4	1	0	0	1	7
PBCR	1	18	0	2	0	0	21
Registration activities	0	1	1	1	1	0	4
No information	0	0	1	1	15	0	17
Total	2	23	3	4	16	1	49

1. Observed notational incidence rates were projected to 2020 (2 countries).
2. The most recently observed incidence rates (notational or subnational) were used as proxy for 2020 (23 countries).
3. Rates were estimated from national mortality data by modeling, using morality-to-incidence ratios derived from the USA, Black population (see Methods).
4. Age-and sex-specific national incidence rates for all cancer combined were obtained by averaging overall rates from neighbouring countries. These rates were then partitioned to obtain the national incidence for specific sites using available cancer- specific relative frequency data in the country (4 countries).
5. Rates were estimates as an average of those from selected neighbouring countries (16 countries).

Table 1. **Data sources and methods used to estimate incidence**

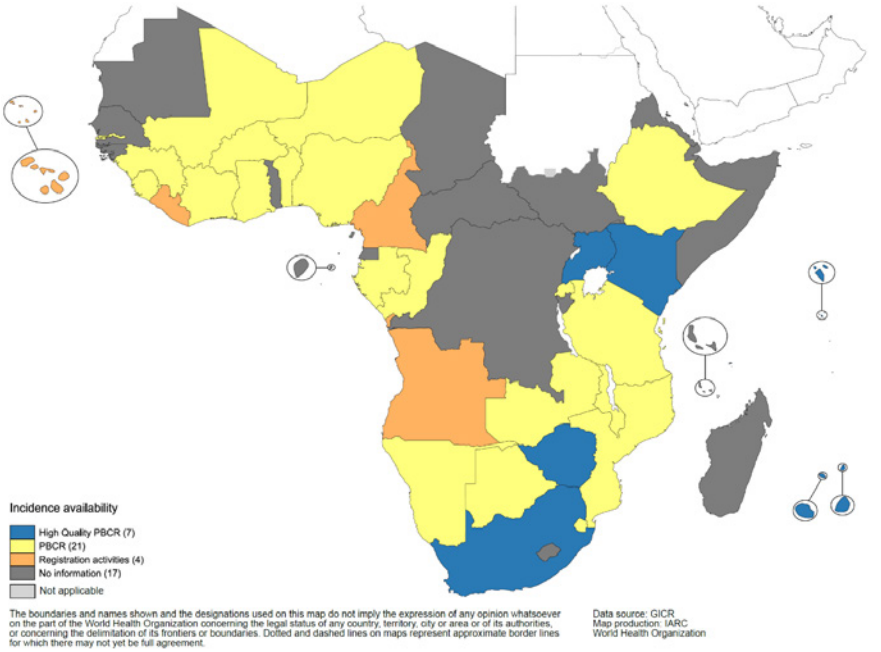
Of the 54 countries of Africa for which national estimates were made[1] (48 in Sub-Saharan Africa and six in Northern Africa), relatively recent cancer registry data were used for 32, while the absence of any recent data for 16 meant that estimates were based on data from neighbouring countries. Figure 1 depicts the data sources and methods used. Cancer registries covering the entire (national) population whose data were published in CI5 are present in Mauritius, La Reunion and Seychelles, and data in the former two were used to prepare national estimates of incidence. [10] In five other countries (Algeria, Kenya, South Africa, Uganda, and Zimbabwe) there were local ("regional") registries which cover less than 10% of the national population, but which were judged to be of sufficient quality for inclusion in the latest volume of CI5 (Volume XI).[9] Data from six registries were used to estimate national incidence (Method 2 in Table 1).

Cancer registries covering the entire (national) population are present in Botswana, Gambia, eSwatini and Namibia. In a further 16 countries there were local (subnational) registries which cover less than 10% of the national population; although none appeared in the latest volume of CI5 [9], incidence data appeared in the monograph "Cancer Incidence in Sub Saharan Africa Vol III (CinSSA) [11] and their data were used to estimate national incidence (Method 2 in Table 1). We report three studies examining secular trends in cervical cancer incidence in Africa where longer-standing data series from PBCR were available. These studies involved ten registry populations in Sub-Saharan Africa [2], and two populations in Northern Africa, namely Setif, Algeria (1986-2010) and Central Tunisia (1993-2006).[12,13]

To examine population-based variations in cervical cancer survival in Africa, we report results from a recent AFCRN study involving 13 PBCR in Sub-Saharan Africa [14], namely: Cotonou (Benin), Abidjan (Cote d'Ivoire), Addis Ababa (Ethiopia), Eldoret (Kenya), Nairobi (Kenya), Mauritius, Maputo (Mozambique), Namibia, Eastern Cape (South Africa), Seychelles, Kampala (Uganda), Bulawayo (Zimbabwe) and Harare (Zimbabwe). Five-year relative survival estimates (by age and stage at diagnosis) were obtained using a random sample of invasive cervical cancer cases diagnosed in black African women between 2005 and 2015 from each registry, with sample numbers determined by the ease of obtaining follow-up information. Survival time was measured from date of cancer diagnosis to the earliest of: (a) date of last contact and (b) date of death or date of study closure (31 December 2017). From the forthcoming "Survcan-3 project", we also included data from three PBCR in Algeria, Annaba, Batna and Setif, as part of the ongoing "Survcan-3 project" at IARC.

To examine stage distributions of cervical cancer at diagnosis, we used information from the above 13-registry study in Sub-Saharan Africa [14] from which clinical stage of cervical cancer cases was abstracted from patient records by registrars at the time of registration. Registries recorded stage according to either the International Federation of Gynaecology and Obstetrics (FIGO) staging system or UICC TNM system; the latter was converted to the equivalent FIGO stage. Information on stage at diagnosis was not available for Mauritius and Kampala registries. We also examined staging information in the three PBCR in Algeria.

1. Estimates for Seychelles do not appear in GLOBOCAN, despite the availability of a high-quality cancer registry, as the population in 2020 was below the minimum threshold of 150,000



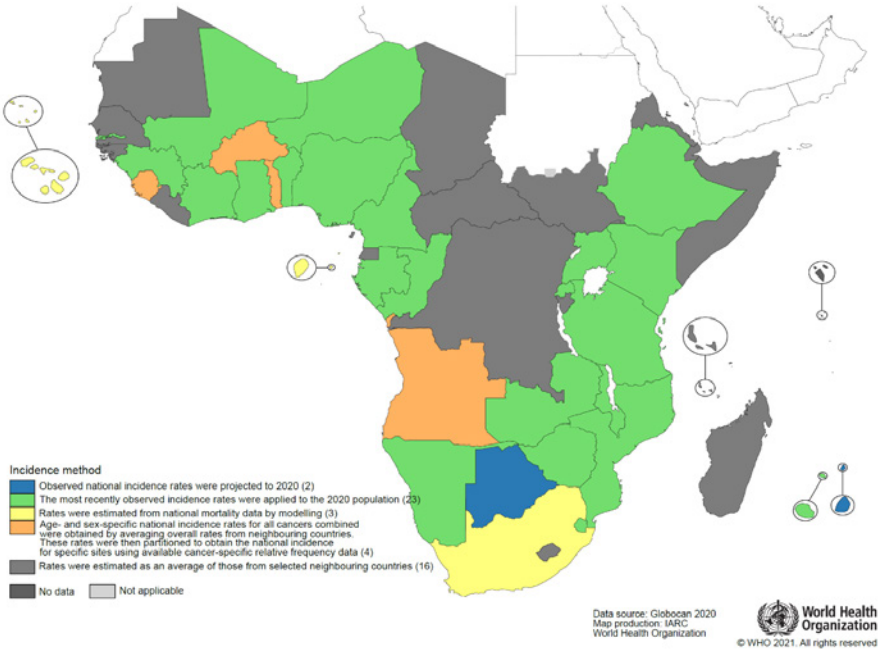
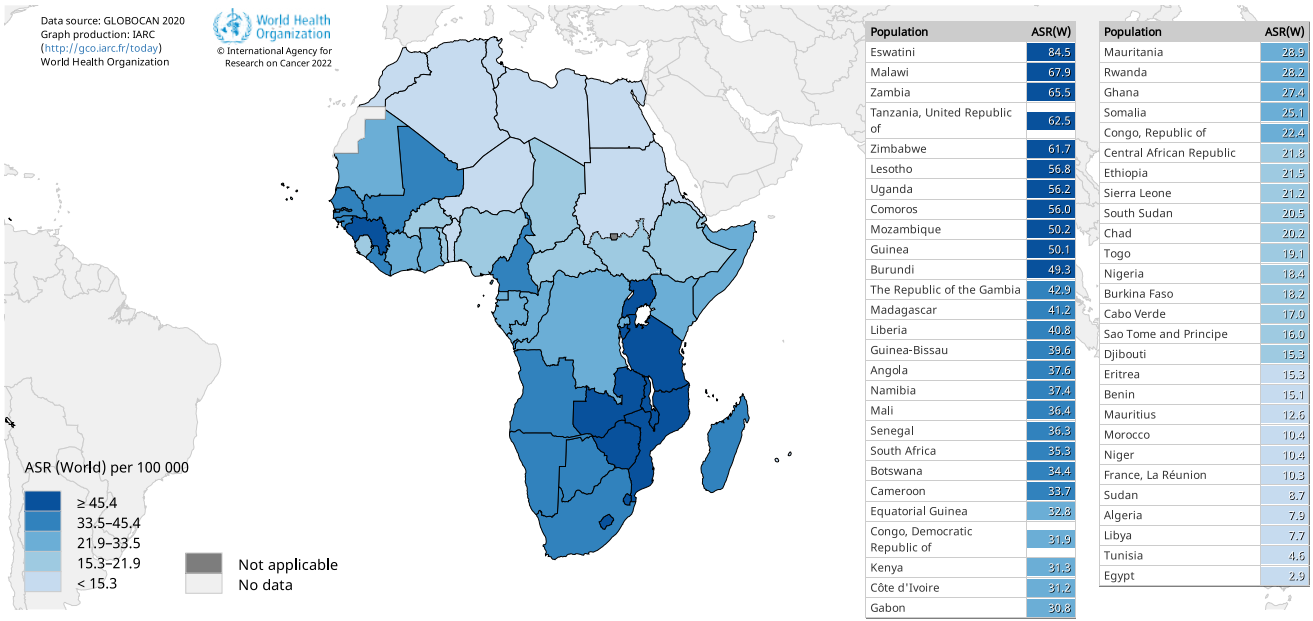


Figure 1. **Availability of cancer incidence data and method used to compile the national estimates in GLOBOCAN for the year 2020**

(Source: IARC)

Incidence of cancer of the cervix

In 2020, there were an estimated 604,000 new cases of cervical cancer and 342,000 cervical cancer deaths estimated worldwide, of which about one-fifth occurred in Africa (117,000 cases and 77,000 deaths).[8] While cervical cancer incidence rates in Northern Africa (defined here as Morocco, Algeria, Tunisia, Libya, Egypt and Sudan) are lower (ranging between 2.9/100,000 in Egypt and 10.4/100,000 in Morocco), Sub-Saharan Africa has the highest rates worldwide, in particular countries from eastern, southern, or western Africa (eSwatini, Malawi, Zambia, Tanzania, Zimbabwe, Lesotho, Uganda, Comoros, Mozambique, Guinea, Burundi, Gambia, Madagascar, Liberia), where incidence rates exceed 40 per 100,000 [1,8], (Figure 2), thus remaining over 10-fold higher than the elimination threshold set by the WHO Global Strategy.[15] Cervical cancer is the most common female cancer in 20 countries, and most common cause of female cancer death in 21 of 48 Sub-Saharan Africa countries.[8] The estimated incidence rates range between 12.6/100,000 in Mauritius to 84.5/100,000 in eSwatini.



Population	ASR(W)
Eswatini	84.5
Malawi	67.9
Zambia	65.5
Tanzania, United Republic of	62.5
Zimbabwe	61.7
Lesotho	56.8
Uganda	56.2
Comoros	56.0
Mozambique	50.2
Guinea	50.1
Burundi	49.3
The Republic of the Gambia	42.9
Madagascar	41.2
Liberia	40.8
Guinea-Bissau	39.6
Angola	37.6
Namibia	37.4
Mali	36.4
Senegal	36.3
South Africa	35.3
Botswana	34.4
Cameroon	33.7
Equatorial Guinea	32.8
Congo, Democratic Republic of	31.9
Kenya	31.3
Côte d'Ivoire	31.2
Gabon	30.8

Population	ASR(W)
Mauritania	28.9
Rwanda	28.2
Ghana	27.4
Somalia	25.1
Congo, Republic of	22.4
Central African Republic	21.8
Ethiopia	21.5
Sierra Leone	21.2
South Sudan	20.5
Chad	20.2
Togo	19.1
Nigeria	18.4
Burkina Faso	18.2
Cabo Verde	17.0
Sao Tome and Principe	16.0
Djibouti	15.3
Eritrea	15.3
Benin	15.1
Mauritius	12.6
Morocco	10.4
Niger	10.4
France, La Réunion	10.3
Sudan	8.7
Algeria	7.9
Libya	7.7
Tunisia	4.6
Egypt	2.9

Figure 2. Variations in age-standardised (world) incidence rates of cervical cancer incidence in Africa

(Source: Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.fr/today, accessed 15 August 2021)

There is considerable heterogeneity in the recorded cumulative incidence rates reported from AFCRN cancer registries,[11] ranging from 1.0% in the Reunion to 9.3% in Zimbabwe (Harare) and 10.8% in Tanzania (Mwanza), signalling that one in 10 women develop the disease in their lifetimes. Indeed, the highest cumulative incidence is predominantly observed in registry populations in Eastern Africa. (Figure 3)

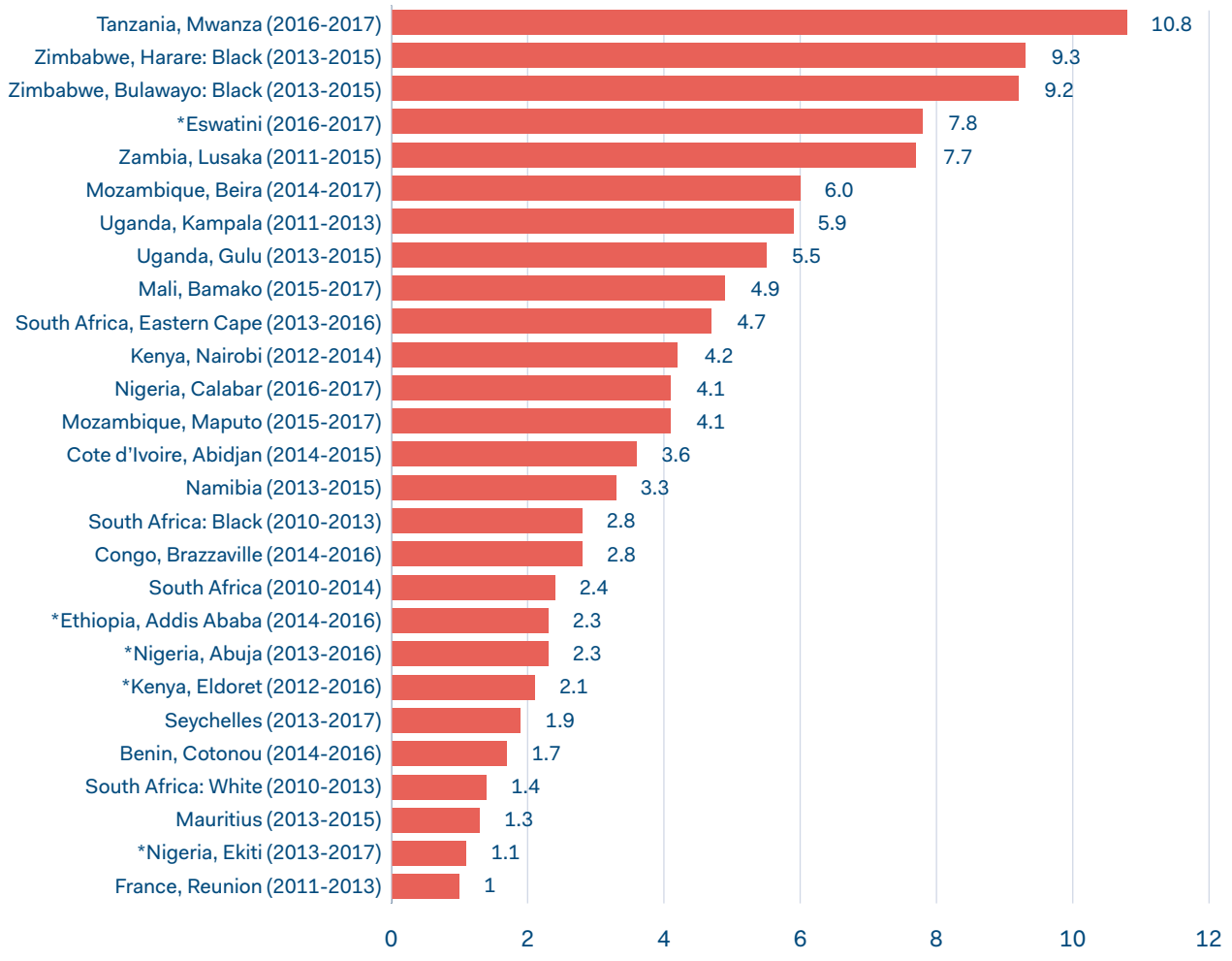


Figure 3. **Cumulative incidence (0-74) (%) of cervical cancer in Sub-Saharan Africa by registry population**

(Source: Parkin D, Jemal A, Bray F, Korir A, Kamaté B, Singh E, et al., editors. Cancer in Sub-Saharan Africa, Volume III [Internet]. Vol. III. Geneva: UICC; 2019 Available from: https://www.uicc.org/resources/cancer-sub-saharan-africa, accessed 18 August 2021)

Cervical cancer incidence: determinants and trends

Geographical patterns in cervical cancer incidence reflect the prevalence of risk factors (infection with high-risk HPV types as a necessary cause), as well as the extent to which cervical cancer control measures (including screening and vaccination, see Chapter 2 for details) are in place in the population.[16] In view of the mostly opportunistic screening programmes with poor population coverage, geographical differences in invasive cervical cancer incidence in Africa mainly reflect the prevalence of chronic HPV infection as the major risk factor, as well as of HIV which increases the risk in HPV-positive women.[2,17] Cervical cancer is the most common cancer in women living with HIV and is classified as an AIDS-defining illness.[18] The proportions of cervical cancer cases attributable to HIV were 53.2% in southern Africa, and 22.9% in eastern Africa. In eSwatini, Lesotho, Malawi, South Africa, Zambia, and Zimbabwe, ASRs of HIV-attributable cervical cancer only, were over 20 per 100,000.[19] In contrast, Northern Africa has a low prevalence of HPV [19], as well as HIV.[20]

Cervical cancer incidence rates have decreased dramatically in developed countries since the discovery of Pap-smear and subsequent introduction of organised population-based cytology screening programmes in the 1960s, and more recently, (HPV) DNA testing.[21–24] Due to the large population coverage by cervical cancer screening programmes in high-income countries, the peak of cervical cancer incidence rates is commonly attained at ages in the early forties.[1] Cervical cancer incidence rates have decreased dramatically in developed countries since the discovery of Pap-smear and subsequent introduction of organised population-based cytology screening programmes in the 1960s, and more recently, (HPV) DNA testing.[21–24]

In contrast, in the absence of early detection and removal of precancerous lesions in younger ages, cervical cancer incidence rates, at least in high-risk populations of SSA, continue to increase with age.[1] (Figure 4)

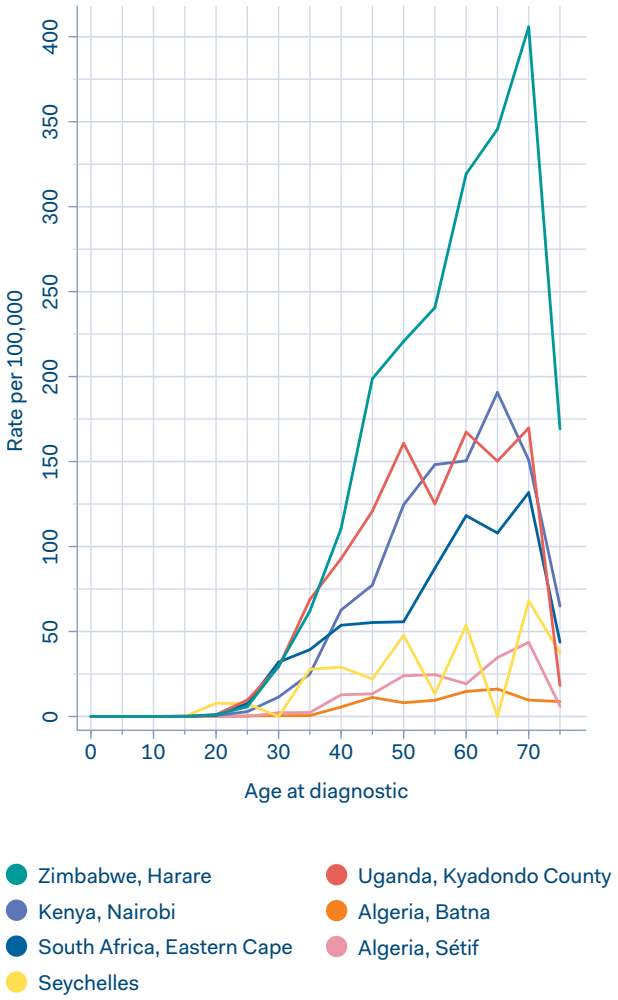


Figure 4. Age-specific rates of cervical cancer incidence in selected African populations (2008-2021)

(Source: Bray F, Colombet M, Mery L, Piñeros M, Znaor A, Zanetti R, et al. Cancer Incidence in Five Continents, Vol. XI (electronic version). Lyon; 2017. Available from: https://ci5.iarc.fr, accessed 18 August 2021)

Trends in the incidence of cervix cancer in Africa

In Northern Africa, a study from Sousse Cancer Registry in Central Tunisia [25] has shown a decreasing cervical cancer incidence trend in the period 1993-2006 (annual percentage change, APC: -6.1%).

These findings have been attributed to the national screening programme as well as a reduction in risk due to changes in sexual behaviour and use of barrier contraception. A more recent study from Setif Cancer Registry, Algeria (1986-2010) has also documented decreasing cervical cancer incidence rates in the period 1986-2010 (APC: -4.2%), also attributed to opportunistic cytology screening.[13] Both registries have documented decreases limited to squamous cell carcinoma, further substantiating the possible screening effect.[12,13] In Morocco, the only long-term data are from the Casablanca Cancer Registry, which reports increasing number of cervical cancer cases over the 2004-2012 period. However, the age-standardised rates are not available, thus it is not possible to control for demographic effects.[26] However, most North African registries have yet to accrue long-term annual data to enable time trend analyses. In Sub-Saharan Africa, a recent study examining cervical cancer incidence trends of over 10-25 years in 10 PBCR from eight SSA countries documented the increasing trends in most registry populations. The increases were most pronounced (Figure 5) in Blantyre, Malawi (APC: 7.9%) and Eastern Cape, South Africa (APC: 3.5%). In Eldoret, Kenya, a decrease was followed by a significant increase (APC: 9.5%) from 2002 to 2016, while in Kampala, Uganda an increase until 2006 was followed by a non-significant decline. The only population with clearly declining incidence trends in the study was Mauritius (Figure 5), where a population-wide cytology screening programme was introduced within the national cancer control programme 2010-2014.[2]

To measure progress towards cervical cancer elimination in Africa in meeting the target of an incidence rate of 4 per 100,000 women or less, cancer registries need to routinely produce incidence data that are a reasonably accurate reflection of the true cancer profile in all 54 countries. IARC's Global Initiative for Cancer Registry Development (GICR) and the Regional Hubs have been developed to build that needed capacity, via the AFCRN in Sub-Saharan Africa, and the Northern Africa/Western Asia Hub based in Izmir, Turkey.

Critically, such efforts will require international donor assistance as well as national investment to develop the local capacity to generate, analyse and interpret data on cervical cancer occurrence and outcomes.

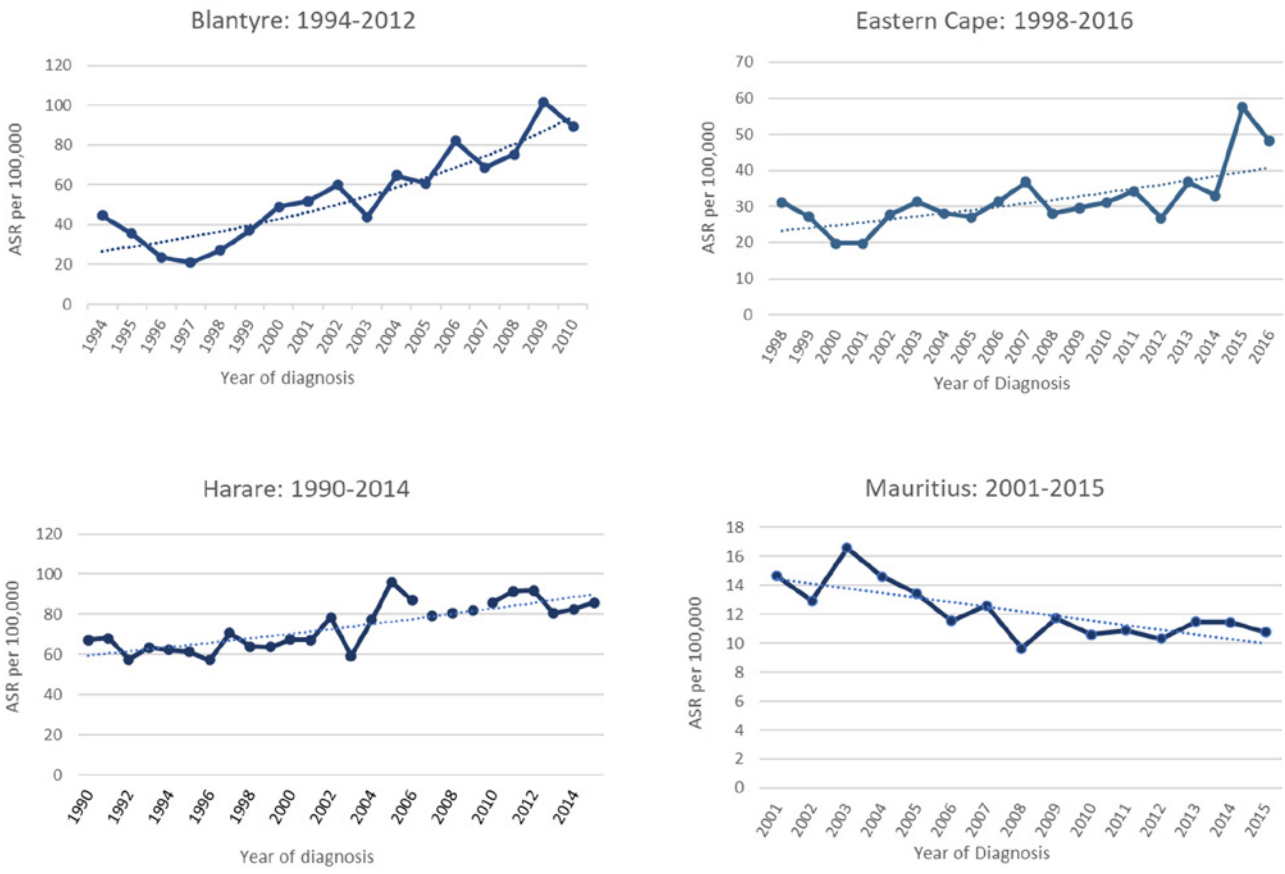


Figure 5. Incidence trends in four Sub-Saharan African populations
Cervix cancer ASR by year of diagnosis with best fitting regression line, and corresponding coefficient of determination (R2)

(Source: Jedy-Agba E, Joko WY, Liu B, Buziba NG, Borok M, Korir A, et al. Trends in cervical cancer incidence in Sub-Saharan Africa. British Journal of Cancer. 2020 Jul 7;123(1).)

Improving the availability of information: key population-based metrics

At the population level, three complementary measures are essential: (a) cervical cancer incidence (new cases of disease); (b) cervical cancer survival (percentage of patients surviving n years after date of diagnosis); and (c) mortality (number of cervical cancer deaths). These indicators, in addition to HPV prevalence (if the means to measure them are in place), are obtained through surveys (HPV), population-based cancer registries (incidence, survival) and vital statistics systems (mortality). Assessing whether cervical cancer is a local public health problem in the current year, or will be in the years ahead, requires an ongoing assessment of the magnitude of the cervical cancer burden using these metrics. The ultimate measure of elimination is the threshold incidence of 4 per 100 000 women-years, based on the incidence data calculated from population-based cancer registries.

Stage of cancer of the cervix

Stage at diagnosis for patients with cancer— i.e., the anatomical extent of the disease at the time of diagnosis—is a crucial component of clinical patient care, which helps guide the selection of appropriate treatments. It is also hugely important in epidemiological studies to evaluate effectiveness of healthcare systems in managing cancer patients. Cancer survival is a powerful measure to assess the overall effectiveness of a healthcare system and a cancer control programme. However, the stage of disease at the time of diagnosis is such an important determinant of prognosis, that survival by stage has much more value in assessing the effectiveness of treatment. The distribution of cases according to stage – either as proportions, or, more usefully, incidence rates by stage, are informative about how early in the course of disease it is detected and diagnosed. Advanced stage relates to delays in referral to, and diagnosis in hospital. Several studies have shown that this relates as much to delayed response to the presence of symptoms by primary health care providers, as to delay by the patients themselves.[27,28] Lack of knowledge of the symptoms and signs of cervix cancer among primary health care workers is surely a problem [29] arguing for the integration of primary level oncology training into the training curriculum of nurses and community health extension workers that form the core of health personnel at the primary healthcare level in SSA. Enhancing awareness and knowledge of symptoms among the population and implementation of specific measures to achieve diagnosis of cancer at a less advanced stage, including screening programmes, are also highly relevant.

The stage at diagnosis is optimal information when measured at the population level rather than single institutions, or a clinical series.[2] The latter are inevitably a selected group of patients that are unlikely to be a representative sample of the totality of cancer cases in a population. If they have reached a specialist facility, they are likely to be cases thought to be more amenable to treatment (and, quite possibly, able to afford to pay for it) or within easier access of a tertiary health care facility. However, selected case series can be informative about the variables related to early (or late) diagnosis.

Population-based cancer registries (PBCRs) are the most usual source of data on the distribution (or incidence) of specific cancers according to stage at the population level.[22] Because of the importance of information about cancer incidence by stage in public health, cancer registries are expected to record stage when it is available in the clinical record. Cancers of the cervix are nearly always staged according to the FIGO staging system, which allows incorporation of imaging and/or pathological findings, and clinical assessment of tumour size and disease extent.[30] Nevertheless, such data are often unavailable, or incomplete, and there are problems of access to, and ease of abstraction of, the necessary data from medical records. As a result, stage information has not been reliable or consistently recorded in cancer registries in Africa, as is seen in the following section.

2. A case series in which the patients receive treatment in a medical facility

Stage at diagnosis in population-based case series

There are few data on stage at diagnosis from population-based cohorts in SSA, and those that are available report a substantial proportion of cervical cancer cases diagnosed at late stages. For example, 30% of patients in Uganda presented with FIGO III-IV and 58% of patients in Zimbabwe with regional and metastatic disease.[27,31]

As part of the "SurvCan-3" project, coordinated by IARC, stage at diagnosis was available for a random sample of 2735 incident cervical cancer cases, diagnosed in 2005-2015, drawn from 13 population-based cancer registries in 11 countries (Benin, Cote d'Ivoire, Ethiopia, Kenya, Mauritius, Mozambique, Namibia, Seychelles, South Africa, Uganda and Zimbabwe).[14] Information on stage was abstracted from patient records by registrars at the time of registration, using various staging schemes (FIGO, TNM, and, occasional SEER "summary stage"). When available, stage was grouped into two categories, FIGO I-II and III-IV.

Stage had been recorded in just over one third of the cases (35%), but, for those in whom it was available, two thirds (66%) were in stage III-IV at the time of diagnosis. Stage at diagnosis was significantly related to age, with 56% of subjects aged less than 45 being in late stage (III/IV) compared with 71% of those aged 65 or more.

A more recent study [32] involving nine of these registries, supplemented the recorded data on stage by tracing the clinical records of registered cases (via the source(s) recorded in the registry), and verifying or updating stage at diagnosis, according to the FIGO (2009) classification. Of the 410 diagnosed between 2010 and 2016 whose records could be traced, the stage distribution is shown in Table 2.

As in the larger "Survcan-3" study, the majority of staged cases (61%) were in FIGO stages III and IV, and stage distribution was significantly related to age at diagnosis.

Stage	Age at diagnosis			Total	Percent of known stage
	15-39	40-59	60+		
I	17	25	7	49	14%
II	17	56	18	91	25%
III	27	62	34	123	34%
IV	18	53	28	99	27%
Unknown	6	22	20	48	

Table 2. Stage distribution

Hospital series from Africa

A comprehensive search of published literature describing clinical case series and population-based studies that have reported on stage at diagnosis of cervical cancer in Africa was carried out. The following electronic databases were searched: MEDLINE (via PubMed), Sciencedirect, Africa Wide Information, Web of Science and Google Scholar.

We included only studies for which the original article in an indexed journal was available. Case series that were selective according to stage (for example, early-stage cases only) or by age were excluded.

Table 1A (Appendix) shows the results from 22 studies from 14 countries meeting these eligibility criteria. As already noted, it is problematic to extrapolate the likely profile of stage at diagnosis in the populations of these countries (or, indeed, of the cities where they were performed) given the selection inherent in any case series. The factors influencing stage may, however, be informative, even in selected populations. Unfortunately, as can be seen from column 10 of Table 1A, few studies provided such information.

Stage distribution in high-income countries

In the 18 US SEER registries (2011-2017), overall, some 44% of cases were localised, 36% "regional" and 16% distant. Stage was associated with race, with 46% of cases in whites recorded as "localised" compared with 36% in blacks, and with age, with the proportion of localised cases declining with increasing age.

Determinants of stage in Africa

The population-based studies confirmed the observations made elsewhere (e.g., in the USA) that older women tend to present at a later stage of disease. Factors associated with late-stage disease in the case series (Table 1A) are rarely noted. However, several studies note that lower socio-economic status, HIV positivity and no previous screening are predictors of late-stage disease. Several studies have shown that advanced stage at diagnosis is associated with financial difficulties or being uninsured [33–35], resulting in women being more likely to avoid or delay their cancer care.

Stage and screening

Screening aims to detect pre-invasive lesions, and so prevent invasive disease (cancer). It will therefore reduce cancer incidence, but the invasive cancers that DO occur are often at a late stage, since they are found among women who have not attended screening, and are older, and less health conscious. As a result, the introduction of screening may paradoxically be associated with an increase in the proportion (but not incidence) of cases diagnosed at late stage.[36,37]

Improving availability of information on stage

As noted earlier, stage is poorly recorded by cancer registries in Africa, both because it may not be clearly documented in the clinical record, and because of lack of skill (or time) for the staff of cancer registries to extract the necessary information to assign a stage. To overcome these barriers, simplified staging systems, such as SEER Summary Stage [29] and – much more recently - Essential TNM [39] have been developed. The application of the Essential TNM staging system with training in its use [40], will allow cancer registrars in SSA to abstract cancer stage at diagnosis in a clinically recognised format, which is crucial information for cancer control and public healthcare policy making.

Survival from cancer of the cervix

Survival is a key indicator within the cervical cancer control continuum.[41] Cervical cancer survival is collectively influenced by population-level factors, health system factors, patient characteristics, tumour characteristics, in addition to the effectiveness of treatment.[35,42,43] Methods of data collection and analysis, tumour characteristics (histology, stage, method of detection), and patient characteristics (age, ethnicity, socioeconomic status, lifestyle) affect survival at the population level.[44] Survival data are more meaningful when measured at the population level rather than single institutions, or a clinical series[3]. The latter are inevitably a selected group of patients that are unlikely to be a representative sample of the totality of cancer cases in a population. If they have reached a specialist facility, they are likely to be cases thought to be more amenable to treatment (and, quite possibly, able to afford to pay for it) or within easier access of a tertiary health care facility. However, such studies can provide data on the influence of specific patient-related factors that may influence outcome. Until relatively recently, though, there have been very few data available on survival from cancer of the cervix from defined populations in Africa, and most published results are from clinical series in specific hospitals. Population-based cancer registries (PBCRs) are the main source of data on the incidence and survival of specific cancers according to stage at the population level.[45,46]

We present cervical cancer survival estimates and determinants of survival in Sub-Saharan Africa from PBCRs and clinical series and how they compare to higher income countries. We also highlight limitations of available information on survival and strategies to fill these gaps within the surveillance and monitoring cervical cancer elimination framework.[41,46]

Measuring survival

Survival is the *proportion (percentage)* of cases that are still alive at given intervals – usually 1, 3 or 5 years – after diagnosis (it is not a *"rate"*). Crude, or observed survival measures the proportion of cases who did not die of any cause, while net survival (relative or corrected (cause-specific) survival) measures the proportion who did not die from the cancer in question.

Determining which cases have or have not died can be done in two ways. In high-income settings, record linkage with the death register of the country is used. This is not feasible in many low-income countries, where death registration is incomplete or inaccurate. Active follow-up of cancer cases is needed, to find out whether they have died, and, if so, when.

This process inevitably leads to "loss to follow-up" – cancer cases that cannot be traced, so it is not known if they have died, or not. Losses to follow-up may cause bias in the estimate of survival IF the losses are frequent AND correlated with the patient prognosis or survival.

Survival in population-based case series

There are few data on survival from cancer of the cervix from population-based cohorts in Africa, and those that are available are handicapped by a substantial loss to follow-up of cases, as well as missing data on important determinants of survival, notably stage at diagnosis.

The first two population-based studies reported a 5-year relative survival of 17.7% and 26.5% in Kampala and Harare respectively, in the period 1993 – 1997.[47,48] As part of the "SurvCan-3" project, coordinated by IARC, survival from cancer of the cervix was studied in a random sample of 2735 incident cases, diagnosed in 2005-2015, drawn from 13 population-based cancer registries in 11 countries (Benin, Cote d'Ivoire, Ethiopia, Kenya, Mauritius, Mozambique, Namibia, Seychelles, South Africa, Uganda and Zimbabwe).[43]

3. A case series in which the patients receive treatment in a medical facility

The 1, 3 and 5-year observed and relative survival were estimated by registry, stage and country-level Human Development Index (HDI). Stage had been recorded in just over one third of the cases (35%), but, for those in whom it was available, two thirds (66%) were in stage III-IV at the time of diagnosis.[49]

The average relative survival from cervix cancer in the 11 countries was 69.8%, 44.5% and 33.1% at 1, 3, and 5 years, respectively, but there was considerable variation between them. (Figure 6)

Survival was significantly influenced by age at diagnosis, stage, and the HDI level of the country concerned. (Figure 7)

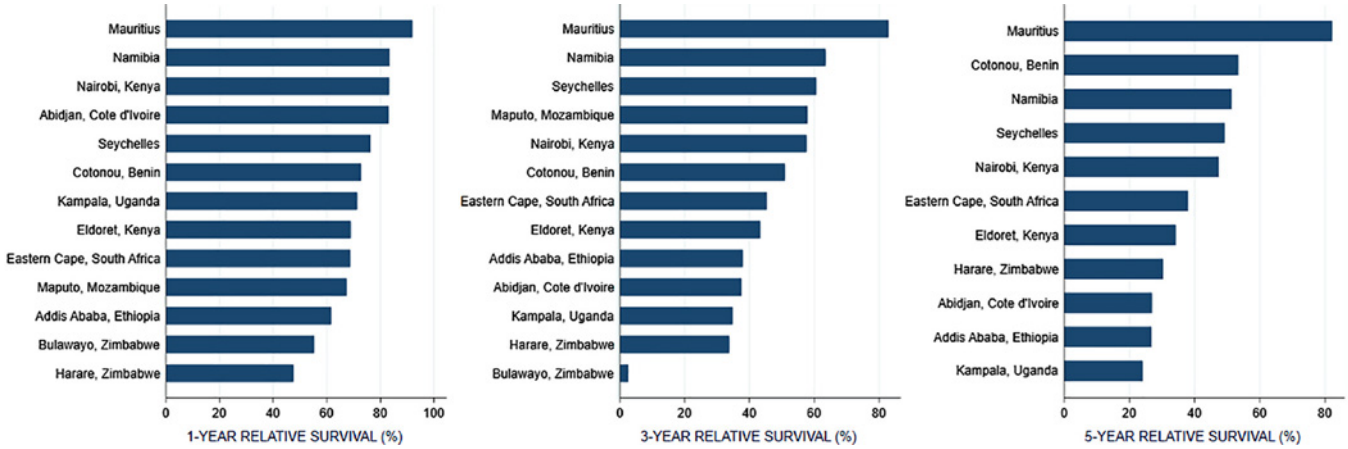


Figure 6. Relative survival from cervical cancer at 1, 3 and 5 years after diagnosis, by registry

(Source: Sengayi-Muchengeti M, Joko-Fru WY, Miranda-Filho A, Egue M, Akele-Akpo M, N'da G, et al. Cervical cancer survival in Sub-Saharan Africa by age, stage at diagnosis and Human Development Index: A population-based registry study. International Journal of Cancer. 2020 Dec 19;147(11).)

(A)
Observed survival by age at diagnosis

(B)
Observed survival by stage at diagnosis

(C)
Observed survival by country Human Development Index

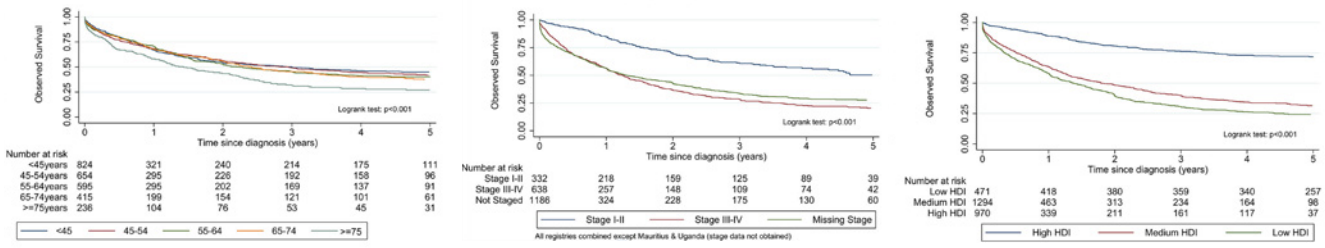


Figure 7. Observed survival for all registries combined, by age (A), stage (B), and country-level Human Development Index (C).

(Source: Sengayi-Muchengeti M, Joko-Fru WY, Miranda-Filho A, Egue M, Akele-Akpo M, N'da G, et al. Cervical cancer survival in Sub-Saharan Africa by age, stage at diagnosis and Human Development Index: A population-based registry study. International Journal of Cancer. 2020 Dec 19;147(11).

In the study by Griesel et al. [50] involving nine of these registries, additional information on stage at diagnosis, and on the treatment received by the cases, was obtained in a smaller sample of cases (632) diagnosed between 2010 and 2016, by tracing the clinical records of registered cases. As in the larger study, survival was significantly related to stage at diagnosis, but, in addition, in the subset of cases for which information on therapy was available, the degree of adherence to standard treatment guidelines was a strong predictor of outcome.

The CONCORD-3 study [51] published survival data for four centres: Algeria (Annaba, Setif, Tlemcen), Nigeria (Ibadan), Mauritius and South Africa (Eastern Cape Province) (Table 1). The validity of the results from all but Mauritius were considered to be questionable. (Table 3)

In a study from the cancer registry of Rabat (Morocco) [52] reported on survival of 191 women registered between 2005 and 2008. Survival at 5 years was 50% and was strongly related to stage (85.9% in stage I) and age, with the best survival in middle-age range [35-64].

Survival in high-income countries

In the 18 US SEER registries (2011-2017), overall 5-year relative survival was 66.3%, higher in whites (67.6%) than in blacks (56.3%) and survival was associated with age (better survival in young patients) and stage at diagnosis.[53] In England and Wales, 5-year net survival for cases diagnosed in 2010-2011 was similar (67.4%).[54] In the Nordic countries, 5-year relative survival in 2012-2016 ranged from 66% (Finland) to 73% (Norway) and was very strongly associated with age (>85% in women aged under 50 compared with ~35% in those over 80.[55] (Figure 8)

Five-year survival in high-income countries is much higher than survival in PBCRs in African and clinical series. (Table 1)

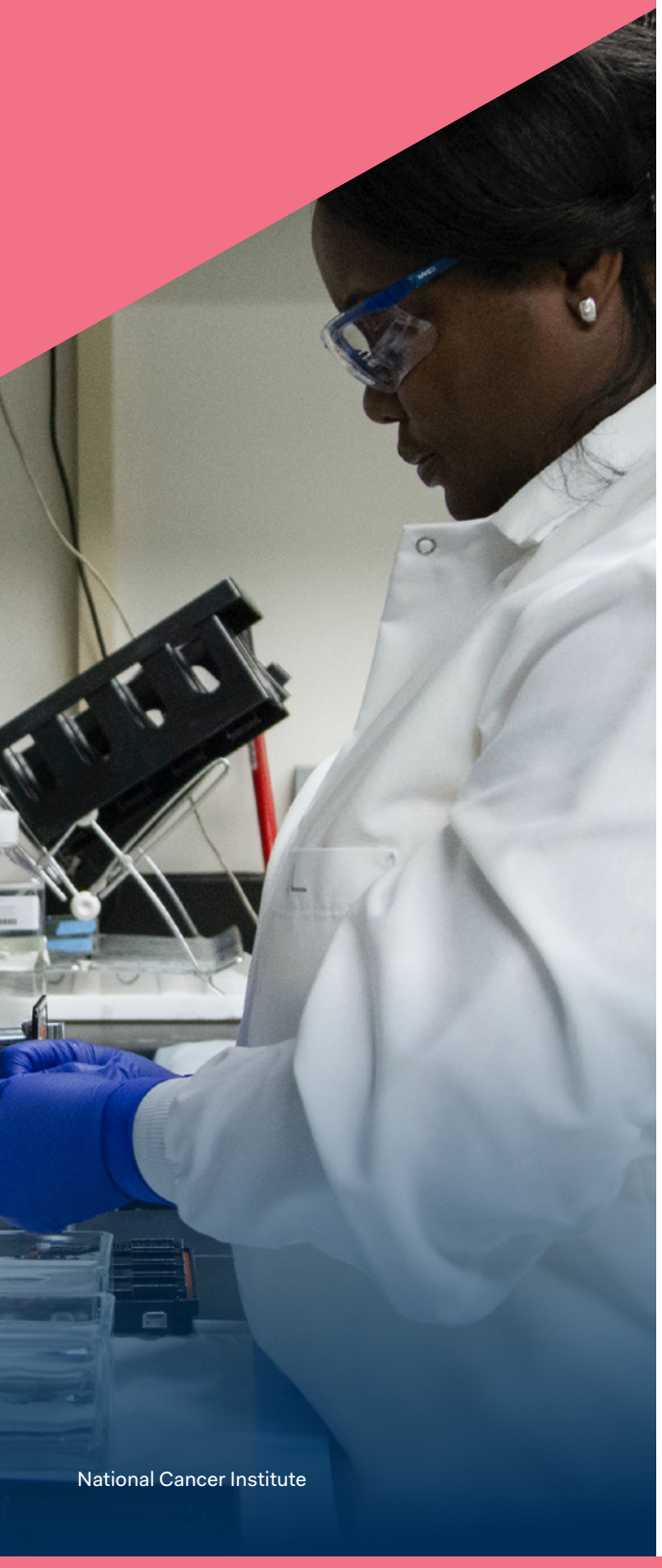
Stage and screening

As noted earlier, the introduction of screening programmes may be paradoxically associated with an increase in the proportion (not incidence) of cases diagnosed at late stage. Thus, there may be little or no improvement in survival at the population level, even though incidence (and mortality) will decrease.[56]

Algeria (three registries)		Mauritius*		Nigeria (Ibadan)		South Africa (Eastern Cape)	
2000-04	61.1§ (55.5-66.7)					2000-04	70.7§ (56.7-84.7)
2005-09	70.7§ (64.5-77.0)	2005-09	80.0 (76.0-85.6)	2005-09	58.6§ (46.5-70.7)	2005-09	40.2§ (32.2-48.1)
2010-14	72.4§ (66.0-78.7)			2010-14	49.8§ (36.5-63.1)	2010-14	37.1§ (31.4-42.9)

Table 3. **Age-standardised 5-year net survival (%) with 95% CI: women (15–99 years) diagnosed with cancer of cervix**

(Source: Allemani C, Matsuda T, di Carlo V, Harewood R, Matz M, Nikšić M, et al. Global surveillance of trends in cancer survival 2000–14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. The Lancet. 2018 Mar;391(10125))



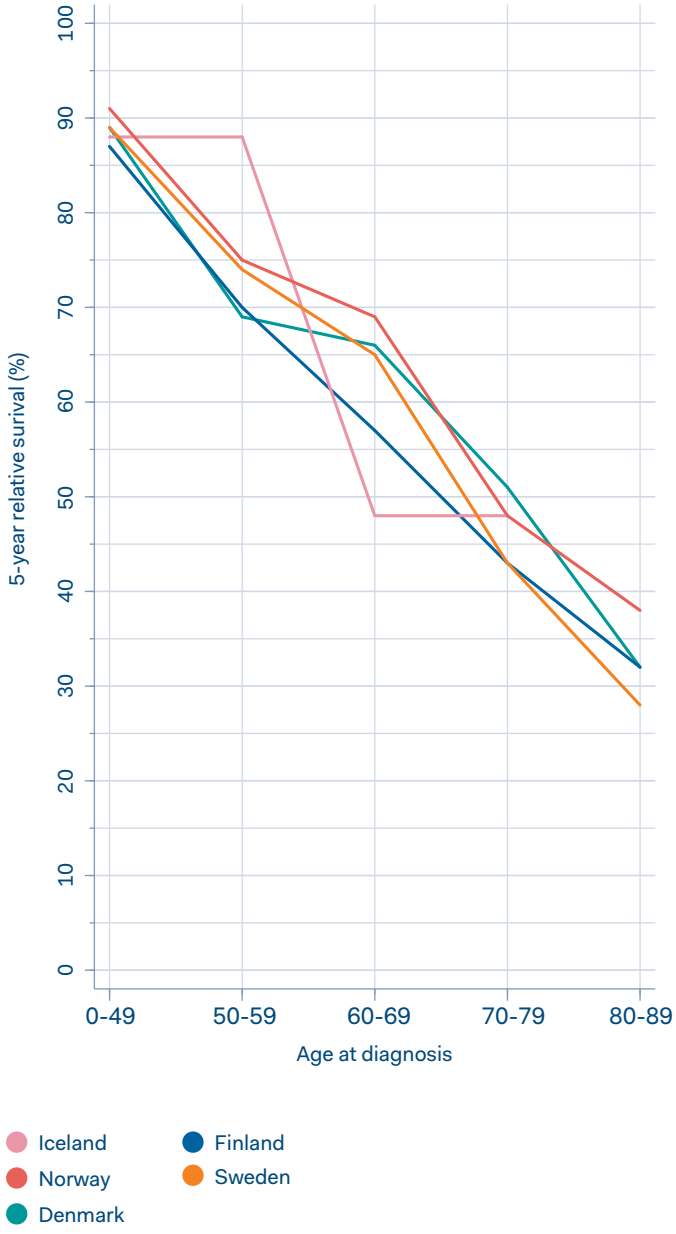


Figure 8. **Age specific relative survival from cancer of the cervix diagnosed 2012-2016 in five Nordic countries**

(Source: NORCAN 1.0, IARC) Five-year survival in high-income countries is much higher than survival in PBCRs in African and clinical series (Table 1).

Hospital series from Africa

Several clinical series and clinical trials have estimated survival in African women with cervical cancer (Table 1B in Appendix). One-year survival ranged from 31% in Malawi [57] to 92.1% in Ethiopia [58], two-year survival ranged from 5,2% in Malawi [57] to 86% in Ghana [59], and five-year survival ranged from 30% in Ghana [60] to 70.8% in Cape Town, South Africa [61]. Survival estimates in the clinical studies were slightly higher than those seen in PBCRs especially in clinical trial settings and in studies conducted at tertiary hospitals probably due to selection bias.[43,58,61–63] Survival of HIV positive women with cervical cancer was consistently lower than that in HIV negative women especially for early-stage disease.[64–66] HIV positive women had poorer survival than HIV negative women even in settings where HIV positive women had access to antiretroviral treatment. [64,66] Favourable survival estimates in clinical trials of HIV positive women with locally invasive cervical cancer demonstrated that treatment with curative intent is worthwhile even in the setting of HIV.[62,63]

There was incomplete or suboptimal treatment and sometimes no access to treatment for cervical cancer patients with a small proportion of patients getting access to the full stage-specific recommended surgical and/or radiation and adjuvant chemotherapy.(43,60,67,68) Clinical case-series remain critical for evaluation of adherence to treatment protocols and their impact on survival.

Determinants of survival

Population-level factors such as country-level human development index (HDI) affect survival. Women with cervical cancer living in low HDI African countries (such as Zimbabwe, Uganda, Mozambique, Cote d'Ivoire, Ethiopia and Benin) have five times excess hazard of dying compared to women in high HDI African countries such as Mauritius and Seychelles.[49]

Health system factors such as efficient referral systems, availability of working radiation infrastructure, skilled personnel, and chemotherapy also determine survival.[43,69] In Ethiopia, brachytherapy was not available and several patients diagnosed with cervical cancer never returned for treatment.[43] Long treatment waiting periods, frequent radiation machine breakdown, result in post-diagnosis disease stage progression which then affects survival.[43,69] As noted above, when diagnosis and treatment have to be paid for by the patient, those who cannot afford are more likely to present at a later stage, or not at all.

Consequently, strategies to improve survival need to include health systems strengthening and country development.

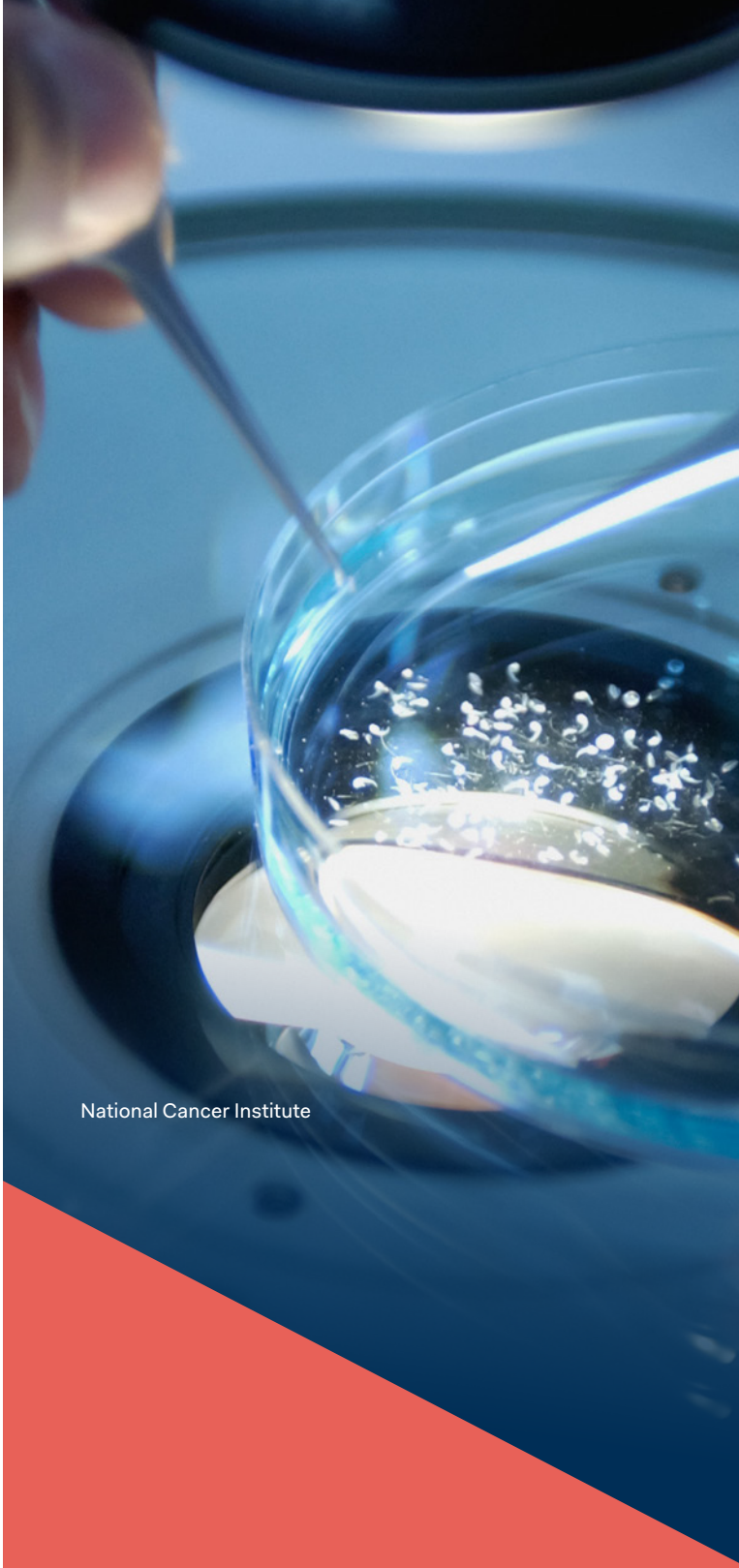
Patient characteristics such as older age, poor education, low socioeconomic status, substance use and co-morbidities such HIV and anaemia are associated with poor survival.[49,58,70] In Botswana, HIV infection doubled the risk of death, with excess risk highest at earlier disease stages. HIV positive women with cervical cancer had a 3-year survival of 35% vs 48% in HIV negative women.[64]

Tumour characteristics such as advanced disease stage and poor tumour differentiation are strongly associated with poor survival.[60,61,68] In Malawi, patients with adenocarcinoma had poorer survival than those with squamous cell carcinoma.[57] Poor access to timely surgical, radiation and chemotherapy in African women with cervical cancer has a profound effect on survival. When available, treatment is often late and incomplete. Often women with cervical cancer lack financial resources to return for treatment.[59] When they are able to return, factors such as surgical and radiation waiting periods, machine breakdowns, chemotherapy stock-outs and treatment toxicity often affect treatment completion and effectiveness.[43,69,71]

Improving availability of information on survival

Population-based surveillance indicators for evaluating the progress towards cervical cancer elimination include cervical cancer survival by type and stage, all-cause mortality and cancer-specific (net) mortality. [41,46] Weaknesses in available population-based survival estimates include poor ascertainment of vital status due to incomplete death registration, with consequent high loss to follow-up rates which bias survival estimates. [46,49] Only 28 of countries in Africa have functional PBCRs (Table 1) and morphological verification of cancers is limited by availability of histopathology services. Staging information is often lacking.[49] Despite the high HIV prevalence in Sub-Saharan Africa and its effect on survival, HIV status is often not documented in PBCRs. Most countries still use paper-based records making data collection tedious, expensive and inaccurate.

Strategies to improve cervical cancer survival data include raising awareness among clinicians to accurately document cause of death, staging, HIV status and treatment information. There is need to develop and harmonize electronic health information systems on clinical and laboratory patient records. Where electronic records exist, record linkage of cancer registries with HIV and death registries may help to fill gaps in HIV status, vital status and cause of death.



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Chapter 2

Cervical cancer prevention and screening

House of Life, Lalla Salma Foundation in Fes, Morocco

HPV vaccination in Africa

With the exception of the Eastern Mediterranean region, Africa is the region with the lowest rate of HPV vaccine introduction. This is despite some African countries having the highest cervical cancer burden in the world. As of December 2021, only 21 countries (45% of WHO member states in the African Region) have introduced HPV in their immunisation programmes. Of these, 14 countries have introduced HPV vaccination in the last 5 years.[1] In terms of regional population covered by HPV vaccination, currently 43% of all girls 9-14 years old in Africa live in countries that include HPV vaccination in their national schedule of immunisation. However, it is estimated that only 19% received the full course of 2 doses in 2020.[2]

While the high- income African countries introduced HPV vaccination (2 of 2, 100%), only 4 of the 7 upper- middle- income countries (57%), 9 of 19 low- and middle-income countries (47%) and 6 of 21 low-income countries (29%) in the region did so. A similar pattern is seen at the global level, with currently 22 of the global low-income countries having introduced HPV in 2020.[1]

Looking forward, several countries in the region have vaccination plans and Gavi support for the introduction of the HPV vaccine in the coming years.

If we consider those countries that have already been approved and those countries that have shown strong interest to apply for Gavi support in the next 2-3 years, the picture looks more encouraging, with potentially 75% of low-and middle-income countries and 60% low-income countries to have introduced HPV vaccination by 2025. This will, among other factors, depend on the evolution of the HPV vaccine supply situation and the budgetary realities of the current and post COVID-19 era. The countries currently planning to introduce HPV vaccination include some of the high population countries, which means that not only will more countries provide HPV vaccination, but also that a considerably larger share of the region's population of girls may have access to HPV vaccination.

The performance of HPV programmes in terms of coverage in Africa has been good relative to other regions, particularly considering the high proportion of low and lower middle-income countries. An analysis of 2019 coverage data showed nearly 60% average final dose coverage across countries.[2,3] However, the global COVID-19 pandemic in 2020 and the lockdown measures often with prolonged school closures have led to partial or full interruption of HPV vaccination and, as a result, many countries and the African region overall experienced the largest drop in coverage in 2020. (Figure 9)

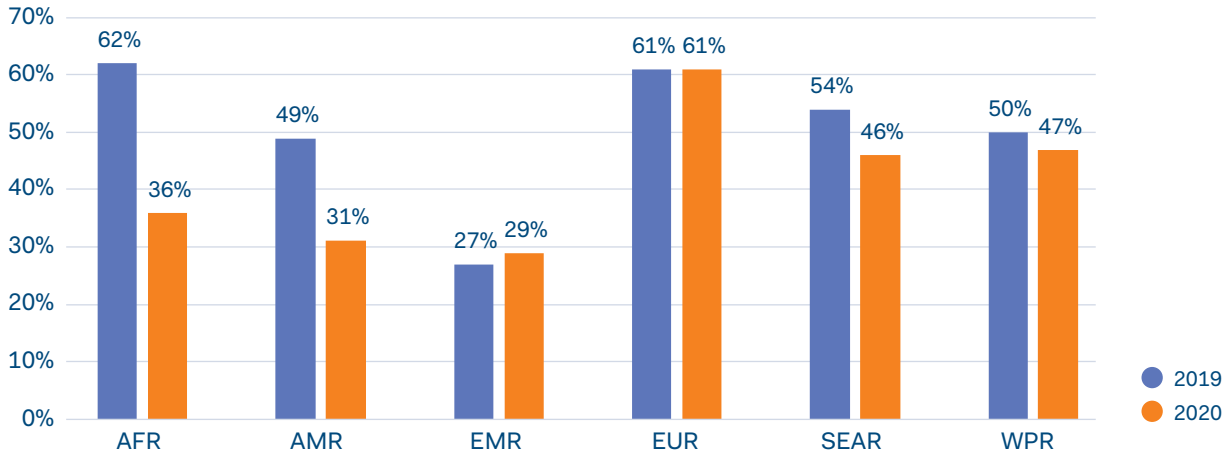

Figure 9. **Average HPV final dose coverage by WHO region**

Source: World Health Organization. Human papillomavirus (HPV) vaccination coverage Available from: https://immunizationdata.who.int/pages/coverage/hpv.html

Opportunities and challenges

Gavi support for HPV vaccination is an opportunity for countries in the African region that have not yet introduced HPV vaccination to do so. Gavi supports the lowest income countries through subsidising the HPV vaccine and financing planning efforts related to vaccine introduction. An acceleration in the pace of introducing HPV vaccination in countries has been visible in LMICs around the world over the last 5 years, particularly in the African region. Another opportunity is the high trust that generally exists in vaccination programmes in the region and has resulted in very high acceptance rates of the HPV vaccine where these have been introduced.[4] For example, between 2013 and 2016 when smaller scale Gavi HPV demonstration programmes were rolled out, countries such as Tanzania [5] reached coverage rates of over 90%. The first country to have introduced HPV vaccination in Africa, Rwanda in 2011[6], has been able to achieve coverage well above 80% for nearly a decade.[7] Several other countries that introduced HPV vaccination more recently, for example Zimbabwe, have also reached 80% (2018). [3] Other countries, however, have experienced more challenges. For example, a lack of trust in COVID-19 vaccines that emerged in 2020 has affected uptake in several recent HPV introductions in Western Africa, in particular.[2]

To monitor the achievement of the elimination target on vaccination, national immunisation monitoring systems will be essential to collect data to establish HPV vaccine coverage rates. In African countries, HPV doses delivered are being monitored using the same system used for childhood vaccines. Challenges exist in these systems, particularly with the absence of accurate local and, sometimes, national denominators due to the lack of recent census data. However, overall data availability among countries that have introduced HPV is higher in African countries reporting annually to WHO than among European countries.[2]

At the same time, many challenges exist for scaling up HPV vaccination programs to meet the elimination target of 90%. A consistent challenge is the identification of sustainable delivery strategies.

The high coverage often obtained with school-based delivery strategies is proving to be unsustainable in several of the LMICs that do not have functioning school health delivery platforms that can be leveraged. Consequently, some countries are currently developing "hybrid systems" whereby the vaccine delivery strategy is labeled as "routine" and hence available in health facilities and through regular community outreach, while at the same time including schools among these community outreach strategies or finding other ways of collaborating with the education sector to boost vaccination coverage. A recent evaluation in Senegal showed how the country transited from a school based, campaign style (short duration) approach during the demonstration phase to a more routine way of delivering the HPV vaccine throughout the year.[8]

Reaching "out-of-school" girls - a group that now is a minority in most countries in the African region but still a sizeable population at the typical HPV vaccination age of 10 years old - remains a big challenge, even more so for hard-to-reach groups, such as nomadic populations.[9] In many countries, monitoring systems do not capture delivery sites making it difficult to monitor the coverage among such populations. The transition towards electronic immunisation registries (EIR) is less advanced in Africa than in other regions. In some countries like Zambia and Tanzania, important projects are ongoing to establish such EIRs that could be linked to handheld devices and change the quality and use of data in vaccination.[10] Other gaps include the systematic exclusion of certain groups due to programme design, for example, the exclusion of girls attending non-governmental schools in South Africa.[11]

While several evaluations of national scale HPV vaccine introductions have taken place in Senegal[8], Zimbabwe [12] and Tanzania [13] providing important lessons learned for other countries, there is a lack of implementation research to identify delivery and communication strategies adapted to the different settings and populations in the African region.

Finally, one of the largest gaps is in addressing the HIV+ population of girls. The WHO recommends a three-dose schedule of the HPV vaccination for those known to be immunocompromised and/or HIV-infected. Countries in Africa have yet to develop protocols to ensure those girls that are HIV+ are provided with an additional dose of HPV vaccine. This is challenging in various ways, such as avoiding disclosure of the HIV+ status of girls in school settings and the need to work with HIV programmes to identify girls in need of a third dose- and provide it. While higher income level countries in other regions have often included immunosuppressed, HIV+ (as well as MSM[4]) populations among the special groups that can access HPV vaccines for the additional dose or for catch-up at higher ages, this is not the case in Africa, despite the continent having the highest HIV burden countries.

Screening for cancer of the cervix: current situation and challenges in achieving elimination targets in Africa

In most African countries, the foremost challenge in achieving the targeted 70% coverage of screening is the absence of a national cervical cancer screening programme targeting the general population. The World Health Organization (WHO) conducted a non-communicable disease (NCD) country capacity survey in 2019 in which all member countries (47) from the Africa region participated.(14) Of these, only 20% reported having a national cervical cancer screening programme, and almost all these programmes were opportunistic. The capacity assessment also revealed that many African countries having national cancer plans (which included cervical cancer screening) did not allocate budget for implementation of the plan. A National Cancer Control Plan (NCCP) is a strategic plan to reduce cancer burden based on the country's cancer profile, prevalence of cancer risk factors and the resources available to implement the plan in the context of the health care system in that country.

Without financial allocation, an NCCP is difficult to operationalise. A recently conducted survey by IARC among the cancer screening programme coordinators of 12 African countries claiming to have cervical cancer screening included in national cancer policies corroborated the findings of the WHO survey. (Table 4)

Less than half of these countries allocated budget for cervical cancer screening. The survey also revealed that cervical cancer screening is offered free of charge to women in all countries except two, but diagnostic and/or treatment services are chargeable in most of them. It is impossible to achieve a high participation of women in the cervical cancer screening care cascade without provision of adequate financial resources within the programme to provide services free of charge.

A major hindrance to monitor progress towards the elimination target is that very few countries in the region systematically collect population level data to estimate cervical cancer screening coverage and other performance indicators. WHO and the World Bank aim to collect information on cervical screening coverage as one of the 16 tracer indicators to monitor progress towards universal health coverage (UHC).(15) Data is collected through household sample surveys and the screening coverage is calculated as the percentage of 30-49 year old women ever screened for cervical cancer. Such an estimate is not based on real data from the programmes and is often unreliable. The majority of African countries either do not have the data or have an estimated coverage of below 20% (Figure 10).

4. Men who have sex with men

	Documented cancer screening policy*	Dedicated budget for cervical cancer screening programme	Screening tests provided free of charge	Diagnostic tests provided free of charge	Treatment services provided free of charge
Botswana	✓ *	✗	✓	✓	✓
Cameroon	✓ **	✓	✓	✗	✗
Cape Verde	✓ **	✗	✓	✓	✓
Côte d'Ivoire	✓ **	✗	✓	✓	✓
Ethiopia	✓ **	✓	✓	✗	✗
Kenya	✓ *	✓	✗	✗	✗
Malawi	✓ **	✗	✓	✗	✗
Mozambique	✓ *	✓	✓	✓	✓
Rwanda	✓ *	✓	✓	✗	✗
South Africa	✓ *	✗	✓	✓	✗
United Republic of Tanzania	✓ **	✗	✓	✗	✗
Zimbabwe	✓ *	✗	✓	✗	✗

Table 4. **Outcomes of a survey among cancer screening programme coordinators from selected African countries claiming to have documented cancer screening policies** (*The policy is in the form of a notification from the Health Ministry/Health Authority published in a government official publication; **The policy is in the form of a recommendation developed by a public health institution or a professional organisation in the country)

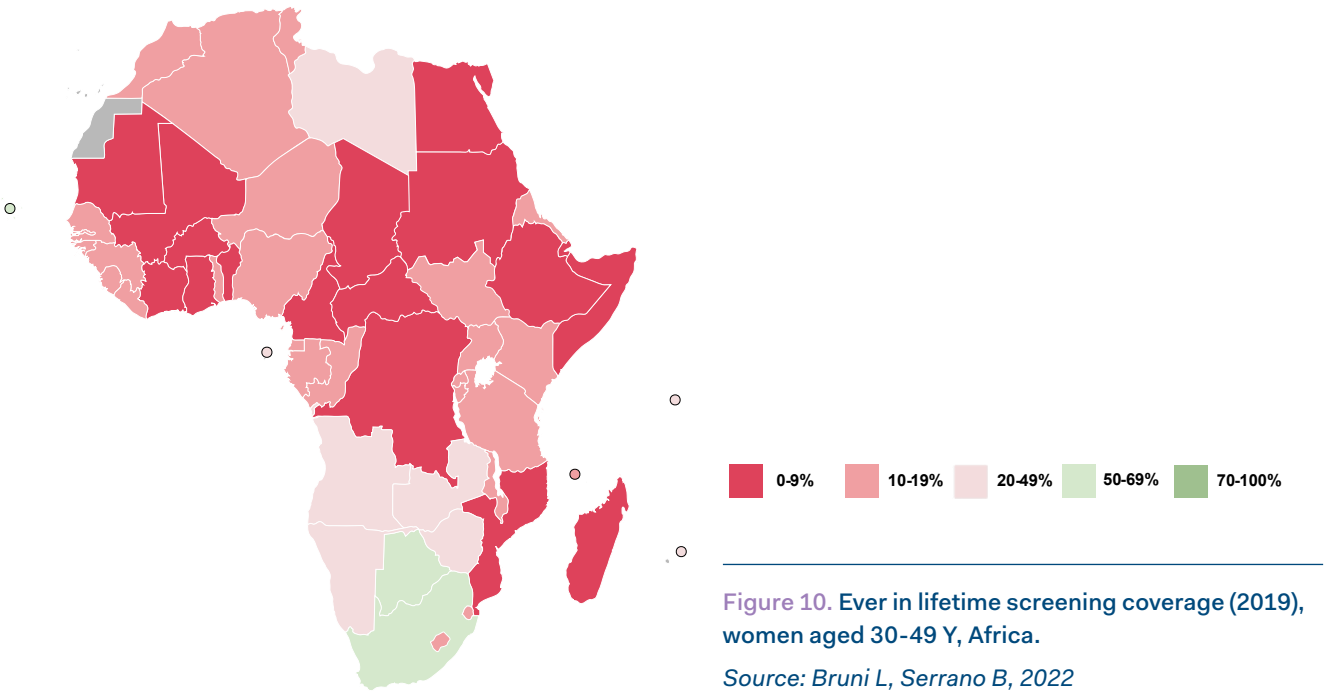

Figure 10. **Ever in lifetime screening coverage (2019), women aged 30-49 Y, Africa.**

Source: Bruni L, Serrano B, 2022

Burkina Faso, Côte d'Ivoire, Kenya, Malawi, Senegal and Tunisia reported an estimated screening coverage of 10-50% with only South Africa and Mozambique reporting a coverage between 50-70%. A meta-analysis of 26 studies published between 2009 and 2019 observed the pooled screening coverage to range from 7.6% in southern SSA to 14.1% in eastern SSA with considerable heterogeneity among the studies.[16] The low coverage can be ascribed to barriers related to service users, service providers, and health systems.[17] Service-user level barriers to high screening uptake include lack of formal education, low level of awareness of cervical cancer, preference for female providers, fear and stigma associated with getting a cancer diagnosis and low perceived susceptibility to the disease. Overburdened healthcare providers and a lack of training opportunities for them are the key provider level barriers. The Pap smear is unimplementable in almost all countries of SSA due to shortages of cyto-technicians and cyto-pathologists. Setting up colposcopy and excision treatment facilities is quite challenging due to the lack of trained manpower. Major health system level barriers are lack of political commitment, low prioritisation, limited resources for preventive healthcare, lack of access to affordable services and low empowerment of women.[17]

Since 2006, Zambia has demonstrated an effective implementation model of leveraging the resources available to HIV/AIDS programmes to build infrastructure for cervical cancer screening.[18] Though initially targeting women living with HIV (WLHIV) in the capital city of Lusaka, the programme was gradually scaled up nationwide as part of routine healthcare for all women in the target age range. The Zambian programme is currently the largest public sector screening programme in Sub-Saharan Africa, in which nurses screen women with visual inspection with acetic acid (VIA) assisted by digital cervicography and the model has been emulated in other neighbouring countries such as Zimbabwe. Even in Zambia, however, the proportion of women in the target age group ever screened for cervical cancer is only 21.1% from 30-49 years.[19] The program initially had a wide screening age range.

Eligibility for screening was anybody who was sexually active, which included lower ranges of below 18 years old and upper limit of 70+ years old; when the age range of 30-49 is used, the screening coverage drops. This has now changed and has been aligned with WHO guidelines for WLHIV and the general population. The guidelines are finally under review to align with the WHO recommendations.

Screening programmes in Africa

In terms of screening methods, visual inspection with acetic acid (VIA) is the most frequently practised screening test in Africa. Pap smear cytology is widely used in South Africa as a screening test with the national policy still recommending it as the test of choice.[20] Both VIA and cytology are available in a few other countries such as Botswana and Namibia. Though widely used, VIA is far from being an ideal test to achieve cervical cancer elimination. The test is moderately sensitive at best. Ensuring a sufficient level of competence of a large number of providers to perform the subjective test and implementing quality assurance are major programmatic challenges. IARC recently completed a demonstration project to implement VIA-based screening in the public sector in Benin, Côte d'Ivoire and Senegal. Nurses and general practitioners screened 16,530 women in primary health centres. VIA positivity varied widely, ranging from 0.7% to 17.6% across the facilities, demonstrating the difficulties in ensuring quality.[21]

At least one study has shown that with a nurse-led VIA screening intervention implemented as part of a routine health service programme which combined the use of a telecommunications matrix, advanced cervix screening technology (digital cervicography), peer review, continuing medical education, quality assurance, proper documentation, access to expert opinion when needed and linking screening to treatment in a single visit, the uptake for screening improved for women in the 25-49 years age bracket.

Notably, with training and supervision of service providers, the VIA positivity rate reduced from about 46% positivity rate at the beginning of the program to about 12% seven years later. In other words, the more healthcare workers screen with supportive supervision, the accuracy of the screening programme improves.[18]

Moving from VIA to HPV testing

In the 2021 "WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention", the World Health Organization recommends an HPV DNA-based test as the preferred screening method instead of the VIA or cytology for the general population and women living with HIV. VIA should be replaced with a more sensitive, objective and robust test such as the HPV DNA-based test. Self-collection of upper vaginal samples is likely to be the preferred approach over provider-collection, since the accuracy of both methods of collection is the same (when PCR based tests are used), and the former is highly acceptable to women in Africa.[22,23] Due to these reasons, in the recently published guidelines, the WHO has strongly recommended to switch to HPV detection-based screening from VIA even in countries with limited resources. HPV detection involves less frequent screening (once every 10 years) and this is more feasible, efficacious and cost-effective compared to 3 or 5 yearly VIA screening in African countries. However, until now, HPV testing is scarcely available in African countries and performed at private facilities only against payment.[24]

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Screen and treat strategy

Cryotherapy or thermal ablation of the VIA-positive women eligible for ablative treatment as a single visit approach (screen and treat strategy) is the preferred management algorithm in most African countries as it reduces loss to follow-up. This approach minimises the number of visits women need to make to a health facility thus reducing the cost and time requirements including transportation, childcare, time taken off work, among others. Studies have shown that a multiple visit approach leads to significant loss to follow-up. For example, the national cervical cancer screening programme of Morocco recommends colposcopy and biopsy for all VIA positive women, for which the women are referred from a primary health centre to designated colposcopy clinics. An evaluation of the programme in 2015 revealed that 43% of the VIA-positive women never attended the colposcopy clinics.[25] The proportion of women undergoing treatment was extremely low due to a multiple visit approach. Consequently, the management algorithm of HPV detection-based screening should also rely on a single visit approach to ensure high compliance to treatment. This may be difficult with the currently available HPV tests as not all of them have a rapid turnover time.

While achieving the WHO goal of 70% coverage of the screen-eligible women with a high-performance test like the HPV test and ensuring treatment of the 90% of screen detected precancers and cancers by 2030 is a huge challenge for Africa, it is not insurmountable with high focused and coordinated investment. The fact that 10% to >50% of cervical cancers in Sub-Saharan African countries are attributable to HIV infection [26] necessitates prioritising cervical cancer screening among women living with HIV and a greater effort to integrate cervical cancer prevention and screening with HIV programmes. HIV positive women visit antiretroviral therapy (ART) clinics at least a few times a year and this provides an opportunity to screen them with an HPV test, triage those who are HPV positive with VIA and treat VIA-positive women, as per the new WHO guidelines.[27] The standard HPV tests are positive in more than half of HIV positive women. Treatment and follow-up of so many women is not sustainable for any health system and that is why WHO has recommended to use a triage test (e.g. VIA) for HPV positive women before deciding on treatment. Studies have indicated that an LMIC-adapted HPV test with a smaller number of genotypes (current tests have 13/14 genotypes) may have a better balance of sensitivity and specificity in the African context [28] and this alternative needs to be further explored.

Moving towards achieving the elimination target

To achieve the elimination target, countries in Africa need to improve the organisation of their screening programmes, which requires improved leadership and governance, good coordination, pragmatically costed action plans with additional vertical investments, development of a skilled workforce in adequate numbers, improved healthcare infrastructure and realistic monitoring and evaluation plans. Cervical cancer screening programmes should be well-funded with a budget line created within the national cancer control programme. In terms of screening infrastructure, the capacity to perform molecular tests has been significantly augmented in most African countries to mitigate the COVID-19 pandemic. Equally, many platforms that are currently in use for HIV and TB testing can be used for HPV testing. However, there is an urgent need for national multi-disease testing guidelines to ensure effective use of all the available platforms.

The price of HPV tests can be reduced through regional pooled procurement which will promote access to HPV tests and significantly facilitate rapid transition from VIA-based to HPV DNA test-based screening. Careful planning is required to ensure uninterrupted supply of the consumables (self-collection devices, collection media and HPV test kits), transfer of the collected samples to the laboratories and delivery of the reports to the women. Innovative approaches of community-based self-sampling may reduce costs for the women as well as their risk of and exposure to COVID-19 infection at health facilities.

Careful planning is required to ensure access to ablative or excisional treatment services (with or without triage) for the HPV-positive women. Navigation of the screen positive women through community health workers, primary care providers or mobile applications may be considered.

The investments made to improve electronic disease surveillance, telehealth and m-Health in response to the COVID-19 pandemic can be gainfully used to build back cervical cancer screening programmes better.[15] An electronic information system will be essential to register women, track the samples, deliver test reports, and send reminders to HPV-positive women more efficiently. Leveraging the existing electronic HIV linked specimen courier systems might circumvent the anticipated challenges. HIV services have been using laboratory hubs to increase access to laboratory services, where the specimens are transported to laboratories with testing capacity and are tracked electronically, and the results are returned to the laboratory hubs electronically. These are then downloaded and sent back to the facilities that submitted the specimens. Similar to the approach employed for COVID-19, national cervical cancer screening programmes may work with telecommunication providers (who have detailed population level data) for demand generation and directing traffic to the health facilities that provide HPV detection test and treat services.

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Chapter 3
Treatment of cervical cancer

Aga Khan Hospital in Nairobi, Kenya

Current status of cervical cancer diagnosis and treatment in Africa

In Sub-Saharan Africa (SSA), health systems have traditionally prioritised infectious diseases, paediatric conditions, and wider maternal health services, leaving cancer management largely based on symptomatic treatment rather than primary or secondary prevention. Despite their limitations, cervical cancer prevention programmes in SSA using visual inspections with acetic acid or Lugol's iodine (VIA/VILI) have shown some measurable success.[1,2] In well-organised screening clinics, particularly those well integrated with human immunodeficiency virus (HIV) clinics, these programmes are able to offer same-day treatment or referral of women with pre-cancerous lesions, and serve as important entry points to the health care system for asymptomatic and symptomatic patients with invasive disease.[2] However, for screening services to translate into reduced morbidity and mortality at the patient and population levels, strong linkages must be established in parallel between screening programmes and referral to diagnostic (laboratory, pathology, imaging), treatment, social, and palliative care services.[3]

The two main pathways for entry into invasive cervical cancer management are asymptomatic screening and symptomatic presentation[4]. Symptomatic patients may present with intermenstrual or postmenopausal vaginal bleeding, postcoital vaginal bleeding, foul-smelling vaginal discharge and, in more advanced cases, lower abdominal pain, debilitating back pain, passage of urine and/or faecal material through the vagina, and leg swelling.

Beliefs, knowledge, financial, cultural, and social capacity all require redress if the WHO 90-70-90 cervical cancer elimination targets are to be met in SSA.[3,5,6] Even in the face of a confirmed cervical cancer diagnosis, women's preference for alternative medicine is common due to mistrust and misunderstanding of the conventional healthcare system and unreliability of the latter to deliver services in a timely and effective manner, leading to further delays in accessing the care pathway.[7–9]

Gynaecologic oncology and radiotherapy services are often centralised to urban areas, requiring rural women to travel to seek specialised cancer care, away from their livelihoods and families, which leads to social and financial disruption that need to be addressed through policy and dedicated financing. There is also great need for patient navigation, post-treatment follow-up, and financing for direct medical costs as well as indirect costs associated with cervical cancer care.[10–14] The WHO cervical cancer elimination strategy includes the three pillars of cancer control; primary prevention, secondary prevention or screening, and treatment.[6] Harmonisation of the three pillars could lead to equitable access to cervical cancer care services for women in SSA countries and, over time, strengthening of overall cancer management capacity in SSA countries. Countries need to establish clinical practice guidelines in oncology tailored to their health system and resources. Sustainable cervical cancer management programmes must be prioritised in countries' National Cancer Control Plans (NCCP), National Health Plans (NHP), and National Development Plans (NDP), all of which should be in alignment with the United Nation Sustainable Development Goals.[15–17]

Diagnosis, staging, and treatment

Diagnosis and staging

The cornerstone of optimal management of malignancy is the ability to accurately determine the pathological tumour type and extent of disease in the patient. In 2018, revision of cervical cancer staging guidance by the International Federation of Gynecology and Obstetrics (FIGO) incorporated advanced imaging results from computed tomography (CT) scans, magnetic resonance imaging (MRI) and positron emission tomography (PET).[18] Staging converges and synergises clinical examination, pathology and imaging services. However, there is relative scarcity of imaging capability in SSA compared to other world regions, as documented in the International Atomic Energy Agency (IAEA) Medical imAGIng and Nuclear mEdicine (IMAGINE) database.[19,20]

For example, the number of CT scanners per million population in SSA is 1.0 as opposed to 55.2 in Australia and New Zealand. There is even greater disparity in the availability of PET and MRI scanners. The reality in most SSA countries is continued reliance on the basic imaging modalities available, such as ultrasound and chest X-ray, if available.

Cervical cancer staging entails clinical, pathological and imaging examinations, guided by a multidisciplinary team to determine the extent of cancer spread.[21] Combined information from these examinations contributes to the most accurate diagnosis, staging, and prognosis, and guides decision-making regarding appropriate treatments and, ultimately, leads to optimal patient outcomes beyond prolonged survival. This evidence-based approach promotes the most appropriate use of limited resources. The inability to accurately determine the extent of disease hinders the rational use of scarce treatment resources, contributing to poorer outcomes at both the population- and individual-patient levels. As well, the direct role of imaging in treatment planning cannot be understated.

Multimodality imaging services play a crucial role in the evaluation and staging of cervical cancer. Pelvic imaging assesses tumour size, presence or absence of tumour invasion such as possible extension to the vagina, parametrium, adjacent organs (bladder and rectum), and/or pelvic side wall. Imaging techniques also evaluate lymph node chains typically affected by advanced cervical cancer, and assess anatomic areas commonly affected by cervical cancer metastases. These imaging findings dramatically alter both prognosis and treatment recommendations. Table 2.2 of the WHO Framework for strengthening and scaling-up services for the management of invasive cervical cancer provides a summary of medical imaging and endoscopy interventions in the management of cervical cancer.[4] Furthermore, imaging can facilitate treatment monitoring and patient follow-up, enabling identification of cancer recurrence in a timely fashion for palliation. However, advanced technologies such as MRI are not always feasible or available in SSA.

Ultrasound is low-cost, easy to use and implement, and can serve multiple purposes for cervical cancer patients in low- and high-income settings alike. Ultrasound can be used to assess tumour and local spread, as well as hydronephrosis.[4] It is also a useful tool for the guidance of applicator insertion during brachytherapy treatment. With the advent of low-cost portable ultrasound devices, many rechargeable, the ability to expand access to ultrasound has grown significantly. The availability of such interventional, image-guided radiology procedures is pivotal to management of advanced cervical cancer. For example, ultrasound can diagnose hydronephrosis, a common complication when advanced cervical cancer encases and obstructs the ureters. Ultrasound can guide percutaneous nephrostomy and/or ureteral stent placement; critical to patient-centred, personalised palliation of many patients.

The lack of cervical cancer staging information is an urgent need that must be addressed in order to achieve the WHO cervical cancer elimination strategy goals in SSA. Lack of staging information leads to the inability to properly diagnose and treat cervical cancer patients, and not being able to measure the impact of cervical cancer prevention interventions in reducing cervical cancer incidence, stage of disease at diagnosis, mortality, and increasing survival. Moreover, where resources are scarce, patient flow and management must be optimised to offer those with early cancers and the highest probability to cure; this is not possible without precise staging.

Treatment

A recent multi-country study[22] found that, in eight SSA countries, as many as two-thirds of cervical cancer patients diagnosed between 2010-2016 did not have documented cancer directed therapy (defined by surgery, external beam radiation, brachytherapy, or chemotherapy). Moreover, of the one-third of patients with treatment documented, only half of them received therapy with curative potential. These findings, together with advanced stages at diagnosis due to the lack of organised cervical cancer screening, contribute to low cervical cancer survival rates observed in SSA. The dearth of specialists trained in surgical and gynaecological oncology, lack of opportunities for and access to surgery, diagnosis and treatment facilities, radiologic imaging and therapy, and drug shortages all lead to deficits in effective care.[23,24] In many SSA countries, the lack of radiation therapy renders patients with palliative chemotherapy as the only treatment available.[25–27]

Primary cervical cancer

Surgery is the standard of care for early-stage cervical cancer (FIGO 2018 Stage IA1- IB2, IIA1), while radiotherapy is recommended for early and advanced disease (FIGO 2018 Stage IB3, IIA2-IVA).[28–30] Treatment options for most SSA women depend on the availability of services. In regions with no radiotherapy or long waiting lists, it is common for physicians to modify the standard of care to match the resources available; for example, the use of a combination of neoadjuvant chemotherapy and surgery is offered as an alternative treatment for locally advanced disease.[30] Besides the known health system challenges due to the lack of specialised workforce, operating theatre space, availability of chemotherapy and radiotherapy machines, more complex societal and patient-based issues must be considered. The multidisciplinary nature of treatment must also be taken into account as treatment planning hinges directly upon combined clinical, laboratory, pathology, and imaging services.

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The open abdominal approach is the historical standard and recommended approach to radical hysterectomy for early-stage cervical cancer.[30, 31] The most extensive surgery for cervical cancer is pelvic exenteration which is performed for select cases of recurrent disease and includes resection of a central lesion with bowel, and/or bladder resection, and excision of a portion of the vagina. This surgery will require reconstruction and assistance from plastic surgeons, urologists, and other surgeons.

For very early disease (Stage IA1 cancer with stromal invasion ≤ 3 millimetres in depth), an extrafascial hysterectomy (also called simple hysterectomy, includes resection of the uterus and cervix with preservation of the parametria and upper vagina) is recommended.[28] A vaginal hysterectomy can be offered for early, low-risk stages of cervical cancer, or cervical conisation if patients wish to preserve fertility options. For Stage IA2 (>3 to ≤5 mm invasion), typically a radical hysterectomy is recommended though recent studies indicate that a simple hysterectomy with pelvic node dissection may be sufficient.[32] If patients are unable to have surgery, primary radiation therapy is a valid alternative treatment.

When Stage IB1 cancer is diagnosed (<2 cm lesion on exam), a radical hysterectomy (removal of more vagina and parametria) is planned.[28] For patients with larger disease such as Stage IB2 cervical cancer (clearly invasive disease on exam that is > 2 centimetres and ≤ 4 centimetres at its greatest dimension), a radical hysterectomy is also recommended. Pelvic lymphadenectomy is recommended at the time of all radical hysterectomies, and ovarian preservation can be offered in selected cases.

For more extensive tumours, such as Stage IB3 with a tumour on exam measuring >4 centimetres, Stage II tumour extending beyond the cervix but not to the pelvic sidewall, Stage III disease extending to the sidewall or involving lower third of the vagina or involving regional lymph nodes, or Stage IV with invasion of the bladder, rectum, or distant metastasis, the treatment of choice is primary radiation therapy with chemosensitisation (the addition of lower doses of chemotherapy to boost the effect of radiation therapy).[33] Adding chemosensitisation to primary radiation therapy resulted in a 19% reduction in risk of death (hazard ratio 0.81) and 12% improvement in 5-year survival.[33]

Radiation therapy is a key pillar in the treatment of invasive cervical cancer. Radiation therapy for cervical cancer in most cases should include the two main techniques of treatment, known as, external beam radiotherapy or teletherapy, and brachytherapy.[20,34,35] External beam radiotherapy is treatment given with the radiation source located distant from the patient, given traditionally with Cobalt source treatment machines or Linear accelerators. Cervical cancer radiotherapy treatment consists of 20-25 daily fractions of external beam therapy to the cervix and areas at high risk of involvement such as nearby lymph nodes. Brachytherapy is radiation therapy delivered by positioning the radiation source in close proximity to the tumour, providing a high dose of radiation in the tumour and a low dose to the healthy tissues surrounding the tumour. Cervical cancer treatment can be delivered with either low- or high-dose rate brachytherapy.

Basic parameters for radiation therapy include delivery of 45- 50 Gray (Gy) to the pelvis with a brachytherapy boost to bring the total dose to 80-90 Gy, and chemosensitisation with cisplatin at 40 mg/m^2.[18] It is important to note that primary radiation therapy must include cervical brachytherapy to improve local control.[34] If extra-pelvic nodal (para-aortic) disease is documented on imaging, radiation therapy should be extended to include these areas. Treatment should be completed in a timely fashion, usually within 8 weeks.

Women living with human immunodeficiency virus (HIV) are at substantially higher risk of developing invasive cervical cancer, particularly those younger than age 35 years.[36,37] Recent studies suggest that curative standard of care treatment for locally advanced cervical cancer should be prescribed for women living with well-managed HIV infection, as no difference was seen in five-year overall survival or acute toxicity between HIV uninfected and infected women with HIV well managed.[38,39]

Radiation therapy plays an important role in palliative care for cervical cancer as an effective treatment in case of obstruction of the ureter or bleeding. Interventional radiology procedures should be considered among requisite palliative care modalities, especially percutaneous nephrostomies and ureteral stents. Such procedures can prevent death by uremia when the tumour has encircled the ureters, deep in the pelvis. Image-guided palliative procedures are commonly required in the setting of advanced cervical cancer.

Achieving the WHO cervical cancer elimination target of getting 90% of patients diagnosed and treated appropriately requires significantly increased access to radiotherapy treatment, particularly in SSA.[26,27] The IAEA DIrectory of RAdiotherapy Centres (DIRAC) database allows close monitoring of the number of treatment machines within SSA and is a resource for countries in the planning and development of national radiotherapy programmes.[20–22,24] The number of machines per million population and machines per 1000 cancer cases can be extracted from DIRAC, and serve as rough indicators of access to radiotherapy in countries. Together with WHO, IAEA provides guidance on training, education of the human resources needed, and helps countries identify their gaps and find step by step solutions. Currently only about 50% of the countries in Africa have external beam treatment machines and only 39% have brachytherapy treatment machines.[23,24] This directly impacts the expected outcomes and overall survival of SSA cervical cancer patients. Significant effort is needed in global radiotherapy market shaping to find robust and sustainable solutions, especially for low-income countries. Given that establishing new radiotherapy services in low-income countries will remain challenging in the foreseeable future, models for regional care delivery centres that build on cross-country cooperation and innovative business solutions are needed.

Additional urgent needs include human resource capacity building, including training at primary care level for appropriate and timely referral, patient navigation as a core component of service delivery, survivorship care, rehabilitation and supportive oncology, as well as providing information and building communication skills of health care workers.

Recurrent cervical cancer

Equal emphasis should be placed on metrics of enhanced palliation and patients' quality of life. Chemotherapy is recommended for recurrent metastatic cervical cancer or palliation of advanced disease. Numerous studies have shown the importance of adding platinum to any cervical cancer chemotherapy regimen.[40] Gynecologic Oncology Group Study Protocol 240 showed an improvement in overall survival of 3.3 months with a hazard ratio of 0.77 when bevacizumab was added [41]. In high-income countries, a common regimen for first line treatment of recurrence is paclitaxel, cisplatin, and bevacizumab. However, the regimen is not commonly used in LMIC with the highest cervical cancer burden because of its unaffordable cost; this is particularly true for targeted agents but, in some settings, also for basic drugs and commodities. Second line treatment can be offered for patients who progress after first line treatment, however, the response rate is low and enrolment in a clinical trial is recommended. Second line treatment is usually a single agent therapy and includes: nanoparticle albumin-bound paclitaxel, vinorelbine, pemetrexed, ifosfamide, topotecan, paclitaxel. Most recently pembrolizumab, a checkpoint inhibitor, has demonstrated significant activity for recurrent disease.[42] Due to their unaffordably high cost, these regimens are not commonly used in LMIC that bear the highest cervical cancer burden. It should be noted that bevacizumab and pembrolizumab are not included on the WHO List of Essential Medicines based on review of scientific evidence for comparative effectiveness, safety and cost-effectiveness.

It is recognised that, while much research is needed to identify cost-effective solutions in SSA, including treatment of curable cancers, currently there is limited opportunity for SSA patients to participate in clinical trials or even afford the medication at market price.

Clinical research needs

Clinical research is an important component of the WHO cervical cancer elimination strategy. Key elements that enable clinical research include hospital-based cancer registries and treatment information, vital registration data, as well as hospital information systems with routine collection of data on all cervical cancer cases, in accordance with the African Cancer Registry Network standards.[43] Data should include imaging findings at time of diagnosis, FIGO staging, receipt of primary treatment, and disease status. Patient follow-up and linkage to vital status are critical to ascertain patient outcomes, both for monitoring patient care and for research. There must be a process in place to contact individual patients through mobile phone, through friends and family members, or primary health clinics.

Leadership of health care institutions should promote clinical research and recognise the contributions of health care providers who conduct clinical research, which are effective and critical means to improve the quality of care and patient outcomes. Developing a supportive environment for clinical research is important. Both national and institutional policies should facilitate clinical research. Training programmes for doctors, nurses, and pharmacists should include principles of clinical research. Ethical review should be informed and timely.

Priorities for clinical research span the cancer continuum from screening, diagnosis, through treatment, symptom management, survivorship, and end-of-life care. For patients with invasive cervical cancer, research priorities include identifying the most accurate and cost-effective imaging regimen to guide initial treatment. Surgical research questions include identifying resource-sparing surgical approaches, and best ways to teach surgical techniques.

In radiation therapy, we need to identify and make accessible resource-sparing chemosensitising agents, such as those which could be given orally rather than intravenously. Similarly, identifying effective resource-sparing approaches to chemoradiation should be a high priority.

Clinical research includes implementation science, where research questions include ways to optimise workflow in imaging and radiation oncology departments to deliver safe and effective treatments to as many cancer patients as possible each day, week, and month. Of particular interest is learning the most effective and efficient approaches to provide patients with information and counselling during and after cancer diagnosis, in settings with limited human resources. To increase the proportion of women with abnormal screening results linked to appropriate treatment, identifying the best strategies to build and improve the cervical cancer referral pathways represents another implementation science priority in SSA. Clinical research that addresses these issues has the potential to improve quality of care for women and accelerate the translation of research findings to improve the standard of care.

Optimising the patient experience must be a high priority for clinical research, questions include identifying optimal approaches to symptom evaluation and management at the time of diagnosis, during and after treatment. This requires developing and validating short questionnaires that can be administered in patients' native languages, in a way that is understandable to patients. Questionnaires should evaluate physical symptoms common to cancer patients, such as pain and depression, as well as symptoms more common in women with cervical cancer, including bowel, bladder, and vaginal dysfunction. The adaptation and use of existing tools [44] to capture patients' experience represent additional areas of research.

Psychosocial issues after treatment, such as intimacy and family interactions, are also important to evaluate and address. Research priorities should include identifying optimal interventions for cancer survivorship and quality of life. Implementation science questions include finding optimal times throughout the care continuum to ask women about symptoms, how best to ask them and ensure women receive appropriate follow-up for issues identified.

In SSA hospitals and other settings where women with cervical cancer are screened, diagnosed, or treated, clinical research should not be considered a luxury, reserved for high-income and high-resource settings. Rather, clinical research in SSA must be considered a necessity, to ensure that all women receive the best possible care.

National Research Fund of Kenya

In 2013, the Kenyan government passed the Science, Technology and Innovation Act and established the National Commission for Science, Technology and Innovation (NACOSTI) to promote, coordinate, and regulate progress in science, technology and innovation (ST&I) in the country. NACOSTI works with the Kenya National Research Fund to ensure funding and implementation of prioritised research programs. NRF targets funding of scientific research in priority areas to support the development agenda of the Government. In recent years, the NRF has issued calls for proposals that address the cancer burden in Kenya. This is an excellent example of national government funding cancer research and the translation of research findings into policy and practice.

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Information systems needed

Among health care providers and policy makers, there is acute recognition of the need to implement high quality and interoperable information systems for health and cancer surveillance in SSA. In addition to forming effective policies for prudent use of scarce resources, setting up robust monitoring and evaluation systems for each component of the cervical cancer care continuum is equally important.[17] Currently, unacceptably high numbers of women are lost to follow up along the continuum of care, in part due to lack of referral or tracking systems. Innovative approaches must be deployed by designing and testing feasible local solutions such as using mobile phones for text messaging follow-up reminders to women. Outreach through religious groups, traditional leaders, and other influencers may also be effective in addressing the well-documented challenges faced in SSA.[45]

As described in Chapter 1, SSA bears the highest and increasing burden of cervical cancer worldwide,[46,47] estimated in 2018 to account for 20% of the world's newly diagnosed cervical cancer and 24% of cervical cancer deaths.[48] SSA also has the lowest population coverage of population-based cancer registries globally. The lack of reliable cervical cancer reporting is a barrier to fully understanding the true magnitude of this problem in SSA. In order to reach the WHO targets, urgent action and innovative approaches must be developed and implemented for patient-centred monitoring systems to ensure communication with women throughout the care continuum. The WHO initiative provides the opportunity for such innovation in SSA.[4,6,49,50]

Again, to measure achievement towards the WHO target of reaching coverage of 70% in screening and 90% in treatment of pre-invasive lesions and invasive cervical cancer, evidence and benefits of treatment will need to be documented at the population-level.[4,51,52] This requires surveillance and monitoring systems to measure the success of the recommended and intended treatment, or modification of existing information systems to link information from screening, diagnostic, and multiple treatment services at the health facility and population levels.[52]

Important elements of successful monitoring include population-based surveillance and health facility-based programme monitoring that are interoperable with other information systems.

For population-based cancer surveillance, it is critical to record all new cases of invasive cervical cancer diagnosed, with stage of disease, first course treatment received, and follow-up on survival and mortality. Population-based cancer registries with high data quality and completeness in coverage are needed to collect such data and, ultimately, measure and report progress towards achieving WHO targets.[43,49] Facility-based programme monitoring, feedback to health care providers, and documentation of the receipt, timeliness, outcome, complications, and quality of diagnostic and therapeutic services are critical to ensure the quality of services, adherence to medical standards, as well as patients' quality of life.[4] It is essential, yet challenging, to implement surveillance and monitoring systems with limited resources and sustain them over time in SSA.

Some SSA health ministries are actively working to improve health management information systems throughout various levels of the healthcare system. In order to measure countries' current status and progress towards achieving WHO 90-70-90 targets, careful planning and national investment in information systems are urgently needed even at the primary care level where cervical cancer screening takes place and where women enter the care pathway. Such systems need to be interoperable with those at the secondary and tertiary care levels that provide specialised cervical cancer diagnosis and treatment services. Information systems must ensure data security and confidentiality, be able to communicate with women on test results and next steps in care, and provide data for reporting and feedback to improve care on a routine and timely basis. Information systems need to capture measurable indices of quality and timeliness of screening, diagnosis, imaging studies, pathology, surgery, radiation therapy, and palliative care services at the individual patient level, within and among various levels of care where cervical cancer patients access services.

In SSA, reaching women using ubiquitous mobile phones to send reminders, test results, and inform next steps is feasible and economical. Mobile technology can be used to list communities to establish the population of women eligible for cervical cancer screening, and track the use of cervical cancer management services, outcomes, and linkage to services. Cervical cancer screening programmes urgently need to implement cervical cancer screening and care registries that can enrol eligible women at entry, whether through asymptomatic screening or presenting with symptoms, and track women's journey throughout the cervical cancer care pathway.[51] Cervical cancer screening and treatment registries should be linkable with data in population-based cancer and death registries to measure the impact of interventions and treatment success on a population level over time, including documenting changes in cervical cancer incidence, disease stage, survival, and mortality.[52] Information systems and service delivery registries are needed to capture the numerator of events of interest and the denominator of the number of women eligible to receive cervical cancer services; these numbers are essential for monitoring progress towards reaching the WHO 90-70-90 targets.

An important premise for the establishment of interoperable surveillance systems is that the various systems must cover the same well-defined population, and that all systems capture and are linkable by unique patient identification numbers. Currently, in SSA, cervical cancer screening programmes are not always implemented in geographic regions covered by population-based cancer and death registries, making it impossible to measure the impact of screening in reducing incidence, mortality, and progress towards WHO targets. Changes are needed at the global, national, and local levels in the design, funding, and implementation of programmes and services. Given that achieving global cervical cancer elimination as a public health problem will require focused effort in the coming decades and century,[53] it is imperative to invest now and implement monitoring and information systems that can meet the needs now and in the future as prevention, screening, and treatment services are scaled up in SSA.

Key policy and programmatic next steps

The challenges of implementing a cervical cancer control programme in SSA are well documented. Innovative steps forward must be taken by SSA governments with global partners to interrupt the status quo in order to achieve the WHO 90-70-90 cervical cancer elimination targets. Such steps should be guided by evidence in the published literature as well as unpublished experiences and best practices.

One fundamental recommendation going forward is to ensure equity in investments made to advance each of the cervical cancer control pillars. While primary prevention remains the focus of most programmes, a significant number of women who are not HPV vaccinated and do not have reliable access to health care will continue to present with invasive cervical cancer requiring surgery, radiotherapy and palliative care services. Moreover, investments are needed in auxiliary infrastructure such as boarding facilities for women forced out of their homes. In the fragile economies of SSA, where many women survive hand to mouth, the social and financial needs of women on their cervical cancer journey cannot be overlooked. Simply providing medical care without social or supportive services creates insurmountable bottlenecks as women try to access cervical cancer care. Another critical need to safeguard equity for future generations is to ensure financial literacy is embedded in prevention programmes.

A second recommendation to accelerate achieving the WHO 90-70-90 targets in SSA is to explore and foster public private partnerships (PPP) for the treatment of invasive cervical cancer. For national governments facing massive responsibilities in environments without universal health coverage, investments in treating gynaecological cancers tend to take a back seat not only for capital programmes but also for their maintenance. Radiotherapy, while cost effective over time, requires significant upfront investments that then last up to fifteen years. In addition, maintenance, operational costs, and maintaining quality assurance may be challenging in unstable or unpredictable economic environments, such as in low-income countries. PPPs may provide the necessary stability so that cancer prevention, control, and treatment can operate under viable business models with an ethical orientation, rather than be dependant only on the political will or prevailing policies.

A third recommendation is to accelerate human resource development in SSA by innovative training and education, as well as support to and funding of regional high volume cancer centres to function as training institutions for south-to-south capacity building. Support and identification of highly motivated and skilled professionals who can drive the programmes is critical. The gains may take several years to be realised, yet continued support is essential to prevent the brain drain, as medical professionals are often unable to operate or achieve stated goals for the programme in an unsupportive working environment. This highlights the need for SSA governments to ensure that well-trained professionals can work in a favourable working environment with opportunities for continuing medical education and appropriate compensation and job security. This is another example of the need for governments to make investments in a holistic rather than a siloed approach to addressing the myriad challenges.

A fourth recommendation is for greater coordination and investments in information systems at the global, national, and local levels to monitor current status and progress over time. Such information systems must meet the needs of today and those in the coming decades as prevention, screening, and treatment services are scaled up in SSA. Investments should prioritise interoperable surveillance systems that cover the same well-defined populations to enable documentation of quality, outcomes, and the impact of interventions. Governments and other partners must work together to ensure that the limited global resources are maximised for the equitable benefit of all in SSA.

The final recommendation is for national governments to work closer with governments across borders, and with the World Health Organization (WHO), IAEA, IARC, and other partners such as International Cancer Control Partnership (ICCP) to develop and implement a national cancer control plan (NCCP), to make the investment case and use the WHO cancer prioritisation tool for rational allocation of resources for cancer care,[54–56] including developing action plans and setting milestones for inclusion of radiotherapy as an essential NCCP component. Such a prioritisation process should contribute toward establishing universal health coverage that includes cancer primary prevention, treatment, palliation, rehabilitation, and associated indirect costs. The input of cancer patients, survivors, and caregivers is critical in the development of the NCCP and the prioritisation of resources. SSA governments joining forces to establish regional networks would increase negotiation power through pooled procurement and access to regional hubs for cancer treatment, equipment maintenance, and training.

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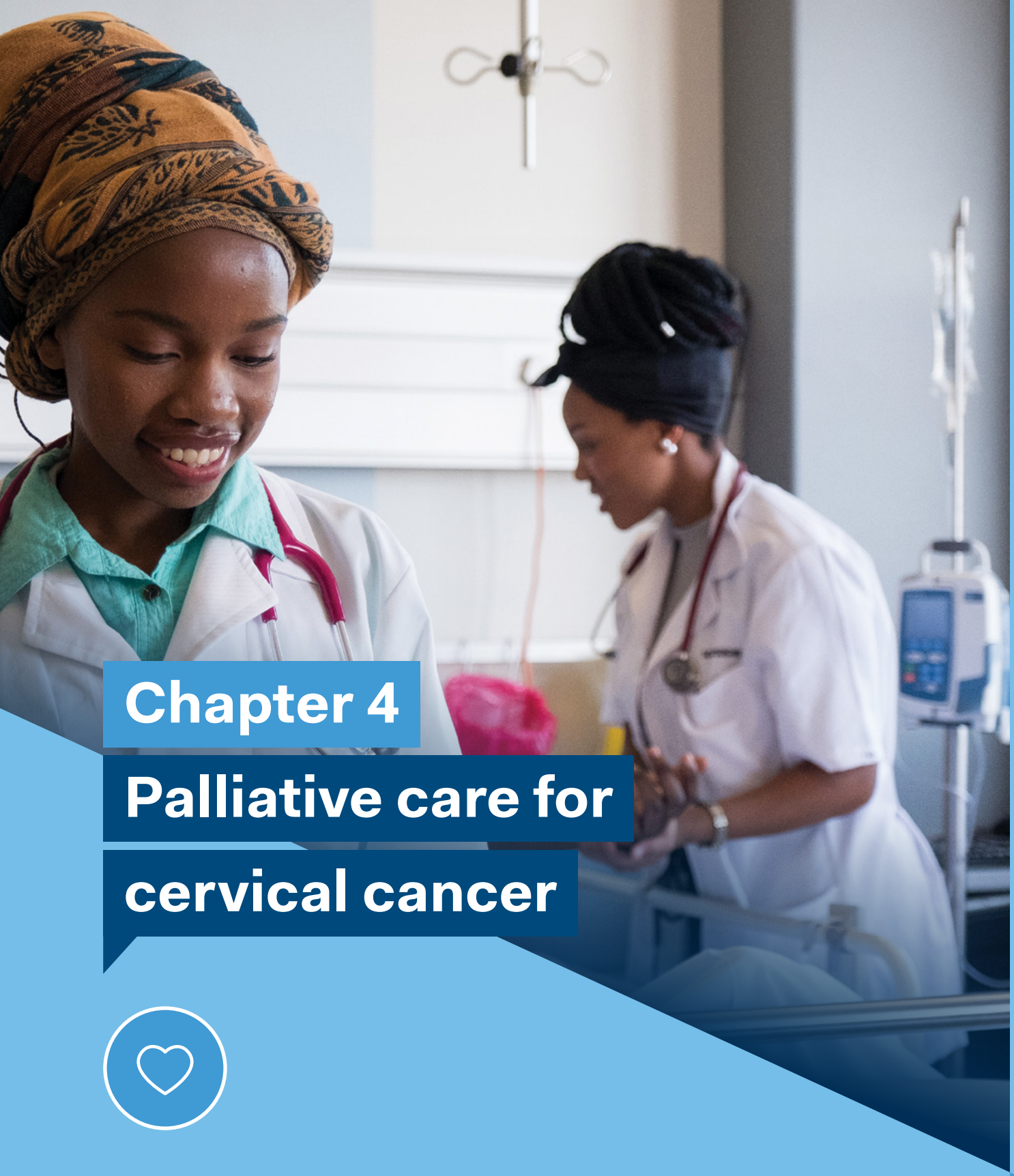

Chapter 4
Palliative care for cervical cancer

Definitions and overview of palliative care for cervical cancer

The World Health Organization (WHO) defines Palliative Care as an approach that improves the quality of life of patients and their families when facing the challenges associated with life-threatening illness, through the prevention and relief of suffering by means of early identification, assessment and treatment of pain and other physical, psychosocial and spiritual problems. Palliative care can relieve these symptoms to improve patient quality of life and compliance with treatment. To further increase access to palliative care for cervical cancer patients, palliative care should be integrated within health systems and covered under Universal Health Care plans. The WHO has endorsed the need to achieve 70% coverage for cervical cancer screening targeting the whole population.[1] Evidence from a policy mapping analysis in 12 African countries showed that cervical cancer screening was commonly available as a free service while diagnostic and treatment services required payment.[2] In the region, women frequently present with advanced cervical cancer disease and require diagnostic and treatment services, including palliative care. As described in Chapter 1, cervical cancer remains a leading cause of death in Africa. Therefore, there is a need to ensure the availability of these services as coverage increases to meet the 70% screening target.

To achieve the cervical cancer elimination target in relation to treatment and care, it is urgent that African member states capture data on key indicators which include integrated cervical cancer palliative care services and where these are located, use of essential medicines including opioids for pain relief, education for health workers to build their capacity to deliver care, and research and training in palliative care,[3] as it relates to cervical cancer. Notably, the need to empower patients and communities to participate in prevention and treatment initiatives is also worth emphasising as by involving them, health systems can develop appropriate programmes which are aligned to their needs and priorities.[4,5] This can also enhance the integration and continuity of care through supporting patients and communities to identify barriers to access care and other structural barriers such as access to education and essential medicines such as oral morphine.

Patients presenting with advanced disease often have complex physical, psycho-social, and spiritual pain and concerns.[6] Therefore, interdisciplinary palliative care must be available close to the patient. Palliative care for women with cervical cancer must be available at primary, secondary and community levels of health service delivery for equitable access. These include hospices, home/community-based care, health centres, hospitals and tertiary care facilities. Currently, within the public health system in African countries, palliative care service delivery for cervical cancer remains limited. This may be explained by the slow progress in integrating palliative care within the public health frameworks, which makes access difficult.[7] Progress in integrating palliative care within private for profit and not-for-profit hospitals is even slower given the limited influence of government in these sectors. In most African countries, it is difficult to access a comprehensive package of cervical cancer care which comprises palliative care because oncology care remains largely centralised at specialist cancer care centres and not integrated within hospitals.

Radiotherapy is another treatment modality that is central in treatment and palliation of some cancers including cervical cancer. It is also very useful in the management of palliative care emergencies such as superior vena cava syndrome, malignant spinal cord compression and bleeding from tumours.[8] According to the International Atomic Energy Agency Directory of Radiotherapy Centres, at the beginning of 2021, there were over 21 African countries with no access to radiotherapy whatsoever though there are also countries such as Egypt, Morocco, South Africa, Kenya and Tanzania that have several radiotherapy centres. Statistics from The Directory of Radiotherapy Centres show that the number of radiotherapy machines per million population stands at 1.207 for North Africa, and 0.078 for middle Africa,[9] a finding which highlights the significant unmet need.

The lack of access to radiotherapy services is a major problem especially for women in low-resource countries such as Burundi, Sierra Leone and Benin.[5]

Women experiencing cervical cancer face complex multi-dimensional symptoms and concerns associated with the malignancy itself, its treatment, treatment-associated side effects, and the effects of serious illness, death, and bereavement on their families.[10] These must be assessed and managed effectively to lessen the associated distress and improve the quality of life of patients and their families. As described in Chapter 3, physical symptoms associated with cervical cancer include; pain, vaginal discharge, [11] nausea, vomiting, diarrhoea, frequent passing of urine, tight and shorter vagina, leaking of urine [12] intermenstrual bleeding and post menstrual bleeding and offensive vaginal discharge.[6] Cervical cancer is also associated with psychosocial symptoms including fear for children's wellbeing after the mother's death, and loss of faith[11] and it negatively impacts on women's quality of life and quality of intimate relationships.[13] Many partners abandon women and their children, adding to financial and emotional stress.

Palliative care policy development in Africa

Several African countries are developing standalone palliative care policies to create enabling policy environments for palliative care to thrive. [2] As of 2016, six African countries had standalone palliative care polices including: Malawi, Mozambique, Rwanda, eSwatini (Swaziland,) Tanzania, and Zimbabwe.[8] Botswana launched its palliative care policy after 2016, Kenya in October 2021 and Uganda is yet to launch hers, which is in the final stages of development.

Palliative care should be reflected in national health strategies, including national cancer control plans (NCCPs). A recent national cancer control plan global analysis showed that 35% of the 23 low-income countries analysed had national cancer control plans that address palliative care, 26% address paediatric palliative care, 43% address WHO essential medicines, 26% address National treatment guidelines. Only 13% of plans addressed survivorship.[14]

Many African countries have adopted the WHO Essential Medicines list including palliative care medicines such as oral morphine. However, access to these medicines varies from country to country. For example, in South Africa, Seychelles and Tunisia, patients have access to these medicines at the nearest health unit. In Uganda, morphine is provided free to patients as the government meets the costs, whilst in the Democratic Republic of Congo patients have difficulty accessing essential controlled medicines and have to purchase these from private pharmacies. Despite these system arrangements, effective access to opioids still remains a challenge due to other structural barriers such as lack of prescribers, supply chain related barriers[15] and logistical challenges. Where access to essential controlled medicines is a problem, the plight of health-related suffering faced by women with cervical cancer cannot be underestimated.[16]

Palliative care education

Education is pivotal to palliative care service development and sustainability. Palliative care providers have a right to be trained, to empower them with skills to deliver the best quality of care and it is important that they continue to train peers and support each other through Continued Medical Education. To scale up access to palliative care, WHO recommends that palliative care should be integrated within the training curriculums in every medical and nursing school. In addition, short term courses should be available for members of multi-disciplinary teams who may wish to strengthen their skills. Over the years, the status of palliative care education in the region has improved greatly. As of 2021, several institutions across Africa provide standard courses in palliative care.[17] Examples of such institutions include universities such as Makerere University, University of Tanzania, University of Cape Town Kenya Medical Training College, and Malawi University.[17]

There are also several organisations, health worker training institutions, and national associations that provide short-term palliative care courses, for example, Hospice Africa Uganda, Island hospice, Nairobi hospice, and Mildmay Uganda. In most African countries, accreditation remains a barrier, as trained staff are often not compensated for their newly acquired credentials if the national medical associations have not recognised palliative care as a specialty or essential primary health care service.

To address the lack of prescribers as a structural barrier to accessing opioids, Hospice Africa Uganda offers a 9-month prescriber's course for nurses and clinical officers, who can then prescribe morphine for medical use. In Uganda, Zimbabwe, Botswana, and Rwanda, trained nurses are allowed to prescribe opioids for pain management.[18] An evaluation of palliative care nurse prescribing which was conducted in Uganda concluded that palliative care nurses can effectively assess and manage pain in palliative care patients and can prescribe morphine appropriately.[19]

Developing a minimum palliative care package at national level

The African Palliative Care Association has developed a minimum Universal Health Care package for palliative care.[20] This is meant to give practical guidance on how palliative care can be integrated within the Universal Health Care package as a public good. A minimum package for women with cervical cancer designed to be safe and effective for alleviating pain, symptoms, concerns, and health-related suffering in these patients has been proposed and includes essential medicines, simple equipment, social support, and human resources [21] The proposed package is centred on a multi-dimensional approach to care, affordable medication, and interventions that require only basic training[21] making it a feasible package to be incorporated into the Universal Health Care package. For example, human resources required include doctors, nurse practitioners, nurses, and community health workers with training in palliative care.

The package also provides key information required by policymakers and care providers to effectively integrate palliative care within their services. According to the Africa Scorecard on Domestic Financing for Health, government expenditure on health should be greater than $86.3 per capita (target 1) and 5% of their GDP (target 2).[22] Reaching these targets is key to protect people from catastrophic financial expenses and could increase the availability of cervical cancer palliative care within the public health services.

Due to the strong interconnection between HIV and cervical cancer[23], PEPFAR, one of the leading donors for HIV care in Africa has begun working on cervical cancer,[24] which is an opportunity to accelerate service development across the region through increased collaboration and partnerships. Screening services are becoming increasingly available at health centres and in hospitals. Patients with cervical cancer risk are treated on-site and those that have cancer are referred to cancer care centres. This presents an opportunity to engage governments to provide cervical cancer palliative care at the hospital level to ensure access for patients that need it within proximate locations. There are promising models of hospice care that are now supporting palliative care for patients with cervical cancer, as shown in case study 1.

These hospices are also involved in the screening and detection of cervical cancer and hence support timely referrals to cancer care centres alongside the provision of palliative care to relieve any distressing symptoms and concerns, as described in case study 2.

Case study 1: palliative home-based care in Uganda

Rays of Hope Hospice Jinja (RHHJ) is providing palliative home-based care to people with life-limiting diseases, mainly cancer and severe HIV/AIDS in Busoga Region and Kayunga District, Uganda, an area of 10,000 km^2 and a population of 3.5 million people (2014). In 2020, the organisation cared for 1133 patients and had 6650 patient contacts. On a monthly basis, RHHJ had on average 578 patients enrolled. RHHJ uses a holistic model that includes offering pain relief, symptom management, and psychosocial support. This includes treatment support for patients in need of treatment but unable to access it due to financial constraints, as well as prevention of cervical cancer through community education and screening.

Due to the very high number of advanced cervical cancer patients being enrolled in the programme (41% of all women enrolled with cancer), RHHJ started in 2018 to offer free screening and treatment for cervical cancer through mobile screening clinics. This programme was met with great interest from women and health centers as there is very limited or no access to free screening for cervical cancer in the rural areas. All the Visual inspection of the cervix with acetic acid (VIA) positive women are treated on site, and if further testing or treatment are needed, the women are supported financially if they cannot afford to travel. All patients in need of ongoing treatment are enrolled in the programme, and they are helped to get the care they need at Uganda Cancer Institute in Kampala. Of the 122 patients in 2020 being helped with treatment support, 24 (19.7%) had cervical cancer.

In any given month, 21% of all patients enrolled with RHHJ are suffering from cervical cancer. Most of them arrive when they are in advanced stages where they can only be helped with pain and symptom control as well as with re-usable diapers and mattress covers to help them live in dignity until the last day.

Case study 2: palliative care during COVID-19 pandemic in Zimbabwe

Providing quality palliative care services during the COVID-19 pandemic has been challenging for the Cancer Association of Zimbabwe (CAZ). There has been a reduction in visits to palliative care services by patients, as well by nurses. Most patients stayed at home for fear of being infected by the virus.

The lockdown and travel restrictions which were imposed by the government also contributed to the reduction in the number of visits. Since nurses could not monitor patients closely and maintain physical presence, cervical cancer patients faced a number psychosocial challenges. However, the Cancer Association of Zimbabwe maintained contact with cervical patients through remote follow-up through phone calls and WhatsApp messages.

	Challenges faced	Proposals for improving quality of life of cervical cancer patients
1	**COVID-19** COVID-19 disrupted the support groups and patient home visits which are main modes of palliative care support	• Set up a WhatsApp chat board and a toll-free line for continued engagement with cancer patients during the COVID 19 crisis. • Support cervical cancer patients through providing COVID-19 prevention utilities such as masks and sanitisers, sanitary pads, home based care kits and training of home-based care givers. This recommendation is based on the December 2020 assessment which found out that some patients had no home-based care items such as pain killers, soap, bandages etc.
2	**Medication related challenges** Cost of palliative care medication and cancer medication is unaffordable	• Provision and administering of palliative care medication to cervical cancer patients for the relief of pain and other symptoms. This also entails training of health workers in safe prescribing for rational use, and supply chain strengthening and improving availability, accessibility, and affordability of internationally controlled essential medicines in countries with limited resources.
3	**Livelihood challenges for patients and family**	• Basic food handouts or food vouchers to cushion selected cervical cancer patients during the COVID-19 period. This recommendation is based on the December 2020 assessment, and it can be limited to elderly cervical cancer patients depending on the availability of resources.
4	**Shortage of financial and human resources to carry out palliative care**	• Funds for supporting existing staff (palliative care nurse, driver and monitoring and evaluation officer) and recruitment of staff and volunteers in carrying out planned palliative cancer activities. Include capacity building for staff and volunteers.
5	**High demand for palliative cancer services among cervical cancer patients**	• Design and implementation of large-scale palliative care interventions among cancer patients in both rural and urban areas starting with PEPFAR, USAID districts with intensive cervical cancer screening. • These cervical cancer screening and education interventions by the Government and partners (PEPFAR, USAID) despite being offered at large scale, do not have the palliative care component to cater for those already having cervical cancer or those who, after screening, will progress to advanced cervical cancer stages.
6	**Palliative care data management, reporting gaps**	• Strengthen organisational capacity and data management.

Table 5. Challenges faced and proposed solutions for improving quality of life of cervical cancer patients

Responding to the development of cervical cancer services requires a public health system strengthening approach, focusing on the WHO health system building blocks of services, health service delivery, health workforce, health information systems, access to essential medicines, health systems financing, and leadership and governance.[3,25] A high symptom burden remains a challenge for cervical cancer patients. There is loss to follow-up for patients still in the pathway whilst others die. [17] Person-centred interventions are urgently needed to address the unmet palliative care symptoms and concerns and hence optimize outcomes of care.

Although radiotherapy is a known essential and cost-effective treatment for cancer, its availability remains sub-optimal, with over half of the countries in the region not having any radiotherapy service. [26] Advocacy at regional and national levels should be prioritised to address the inequities in access to radiotherapy services to effectively meet the needs of cancer patients. It is important that training for health workers in delivering comprehensive person-centred care is also prioritised to build a critical mass of service providers. Investment in strengthening networking, collaborations, partnerships, and increasing government funding for prevention, treatment, and palliation should be considered for sustainable financing of cervical cancer care.

Cervical cancer screening outreach to rural areas – Goromonzi Rural Clinic, March 2020

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Recommendations

Recommendations

1. Include cervical cancer services: screening, diagnosis, prevention, treatment, and palliative care as part of the basic healthcare package under UHC
2. Include cervical cancer control strategy in the NCCP or develop a standalone strategy that addresses each of the cervical cancer elimination pillars, and is costed and budgeted, with adequate funding available for operationalisation
3. Advocate for inclusion of cervical cancer in the WHO AFRO Integrated Disease Surveillance and Response (IDSR) technical guidelines as a priority disease for reporting
4. Use existing testing platforms for other disease areas (HIV, TB) and investments made in response to the COVID-19 pandemic (expanded molecular diagnostics, electronic disease surveillance, telehealth and m-Health) to improve cervical cancer surveillance, screening and management
5. Integrate cervical cancer prevention, early detection, and palliative care into other health programmes particularly at primary health level (adolescent health, maternal health, sexual and reproductive health, HIV and TB programs)
6. Explore pooled procurement in the region for diagnostics and treatment technologies and products and consider public private partnerships for treatment of invasive cervical cancer across treatment modalities
7. Strengthen adolescent and school health services to increase uptake of HPV vaccination and raise awareness of cervical cancer
8. Reduce HPV and cervical cancer stigma through working with communities to address discriminatory attitudes and/ or misconceptions that prevent women from accessing screening and treatment
9. Put in place resources and infrastructure to enable the transition from VIA and Pap smear to HPV DNA testing depending on feasibility and resource availability. Consider self-sampling as a more feasible and acceptable approach
10. Follow WHO guidelines to screen the general population every 5 to 10 years starting at 30 years and women living with HIV (WLHV) every 3 to 5 years starting at 25 years. Promote screen and treat strategy for general population and screen, triage and treat strategy for WLHV to minimise loss to follow-up
11. Improve access to oral morphine and adopt a minimum palliative care package at national level that is funded, with training for healthcare workers and integrated in the national health strategy
12. Invest in and establish cervical cancer screening registries able to track screening episodes, outcomes, link women to treatment, and capture treatment outcomes
13. Build capacity of cancer registries to collect stage data (Essential TNM) to ensure staging information is available and comparable
14. Ensure that cervical cancer screening and treatment information management systems are interoperable with population-based cancer registries to measure the impact of interventions and to observe changes in incidence, disease stage, survival and mortality, and ensure these surveillance systems cover the same well-defined populations to enable documentation of program quality, outcomes, and impact

Examples of cervical cancer elimination initiatives in the region

African Cancer Registry Network

Since 2012, the African Cancer Registry Network (AFCRN) has partnered with the International Agency for Research on Cancer Global Initiative for Cancer Registry Development (GICR) to provide a network Regional Hub for cancer registration in Sub-Saharan Africa (SSA). The Network is a consortium of 35 SSA population-based cancer registries (PBCRs).

In SSA, where information on cancer mortality is sparse, data on cancer incidence and survival from PBCR are essential for estimating cancer burden and monitoring the impact of cancer control programmes. AFCRN has been working with the SSA PBCRs to improve the quality and availability of the information on incidence, stage at diagnosis and survival of all cancers – with several special research project focusing on cervical cancer; advocating the cause of using cancer surveillance data for planning, monitoring and evaluation of programme of prevention, early detection and treatment of cervical cancer; and seeking funding to implement linkage of registers of vaccination and screening programmes and population-based cancer data to provide evidence of their efficacy.

International Atomic Energy Agency (IAEA)

IAEA Director General Rafael Grossi has affirmed, "The fact that millions of women die from a preventable disease, often in what should be their most productive years, is a great tragedy and the IAEA is doing everything it can to change that." For example, the IAEA participated in a United Nations Joint Global Programme on Cervical Cancer Prevention and Control in response to the global crisis, to reduce cervical cancer mortality. In addition, the IAEA, in part through collaboration with partners like the WHO and UNAIDS, helps countries to develop comprehensive cancer control plans and safely set up and use medical imaging (radiology and nuclear medicine) and radiotherapy services. Even during the Covid pandemic, the IAEA has managed to provide this support.

An example is a workshop on education in cervical cancer: Brachytherapy training for radiation oncologists and medical physicists in Morocco. The IAEA is also involved in technical support to the cervical cancer elimination initiative. Other IAEA activities include AFRONET, Nuclear Safety initiatives, Brachytherapy education (e.g. UN Joint programme and in-country technical cooperation projects) and Coordinated Research Projects for treatment and health economics. However, greater collaboration is necessary to provide the funds, training and equipment needed to continue to decrease mortality from cervical cancer, a preventable and curable disease. The IAEA is prioritizing initiatives that can impact cervical and other cancers. In 2022, the IAEA launched the "Rays of Hope" initiative, aiming to support Member States in establishing or expanding radiotherapy, medical imaging, dosimetry and medical physics, with a special focus on low- and middle-income beneficiary countries where radiotherapy services remain insufficient. Twenty-two African countries do not yet have radiotherapy and all have less than optimal access to this treatment. For cervical cancer patients, this is a challenge which we can address together. Collaboration as a global community will aim to achieve measurable improvements in patient outcomes
on a population-based level.

Commonwealth Task Force on Cervical Cancer

In May 2021, The Commonwealth Secretariat and UICC launched a new taskforce to step up efforts towards preventing and treating cervical cancer. The 'International Taskforce on Cervical Cancer Elimination in the Commonwealth' aims to encourage and facilitate cooperation between countries, support the Commonwealth Secretariat cervical cancer elimination initiative and build synergies with UICC's cervical cancer programme.

The Task Force focuses on three thematic areas i) HPV vaccination; ii) screening and treatment of precancerous lesions and iii) early detection, treatment and palliative care of cervical cancer.

The Task Force members provide guidance to the Commonwealth Secretariat as they develop an action plan with key milestones up to 2030 and by supporting the development of advocacy messages and actions on cervical cancer at the Commonwealth Heads of Government Meeting (CHOGM) and ministerial meetings of the Commonwealth. The Task Force members also engage in cervical cancer advocacy in their own countries and regions, including youth-led activities to encourage greater awareness and uptake of the HPV vaccine.

Go Further

The United States President's Emergency Plan for AIDS (PEPFAR) Relief Go Further initiative was launched in 2018 to reduce new cervical cancer cases by 95% among women living with HIV in twelve African countries with some of the highest rates of HIV prevalence and cervical cancer incidence in the world. Go Further is a public-private partnership among PEPFAR, the George W. Bush Institute, the Joint United Nations Programme on HIV/AIDS, and Merck. It invests in the integration and scale-up of cervical cancer screening and treatment services within existing platforms for HIV treatment and women's health.

Union for International Cancer Control (UICC)

As part of its role to unite the cancer community, UICC has committed to leverage its convening platforms, including the World Cancer Congress, World Cancer Leaders' Summit, Virtual Dialogues and World Cancer Day to maintain a spotlight on cervical cancer elimination and progress towards the achievement of the global targets. As an organisation and community that is committed to and believes in the power of multi-sectoral action, UICC is also engaging and showcasing the role of all sectors in its efforts to support the elimination agenda.

UICC has developed a set of resources and provides tailored support to UICC members to develop national advocacy capacity on cervical cancer and encourage organisations to join forces with others for greater impact in their advocacy efforts. Alongside this, through UICC's established Technical Fellowships, which are approaching their 50-year anniversary, UICC seeks to help fill the health workforce gaps and build skills and knowledge in cervical cancer prevention and control. Furthermore, in conjunction with its broader ambition to strengthen leadership in cancer control, UICC is committed to raising the profile of emerging leaders in cervical cancer, to ensure that the current momentum on cervical cancer continues in years to come.

Globally, from the advocacy perspective, UICC has been closely working with the WHO from the Director General's call to action since 2018 and represent its members. Specifically, bringing attention to the critical topic of health financing to achieve the elimination targets, UICC commissioned a report published in 2021 by The Economist Intelligence Unit entitled Global action on financing cervical cancer elimination: funding secondary prevention services in low resource settings.

Many elements of this work have been achieved as a result of the SUCCESS (Scale-up Cervical Cancer Elimination with Secondary prevention Strategy) project, which is funded by Unitaid, led by Expertise France and implemented in collaboration with Jhpiego. Through this project, UICC is working to help increase access to screening and treatment in four target countries (Burkina Faso, Ivory Coast, Guatemala and the Philippines), with the learning, resources and expertise gained to be shared to support action in other countries in the respective regions, and globally. Through UICC's work, the SUCCESS project is mobilising and supporting civil society to raise awareness and advocate for improved cervical cancer screening and treatment and bring attention to the need for increased financing for cervical cancer. This is essential to long-term sustainability and the implementation of the Strategy at the national level.

Appendix

Table 1A. Clinical series describing stage at diagnosis of cervix cancer in African women.

Reference	Year of publication	Time period under review	Study design	Mean (SD) or median age (IQR)	Sample size	Number with known stage	Stage distribution	% Late stage	Determinants of stage
Algeria									
(1)	2013	2006-2010	Case series (Tlemcen province)	48.5 (SD=NA)	196	NA	IV=43 (22.3%)*		Not provided
Benin									
(2)	2013	2000-2008	Cross sectional (2 hospitals), l'hôpital de la Mère et de l'Enfant-Lagune (HOMEL) & clinique universitaire de gynécologie et d'obstétrique (CUGO) de Cotonou	43.6 (SD=NA)	56	56	I=6 II=14 III=17 IV=19	64%	Not provided
Botswana									
(3)	2016	2010-2015	Retrospective cohort, Princess Marina Hospital, Gaborone Private Hospital, Nyangabgwe Referral Hospital, Botswana	45.1 (38.8-54.4)	327	327	I=37 II=123 III=124 IV=33	49.5%	
(4)	2019	2010-2017	Retrospective cohort, 4 oncology centres in Botswana	47.9 (For all women with cancer)			NR	~55%	
(5)	2018	2016-2017	Retrospective review (1 hospital-Princess Marina Hospital)	49.5	149	149	NR	89.2%	Lack of previous CC screening, presentation with vaginal bleeding and unmarried status were associated with advanced stage presentation
Burkina Faso									
(6)	1998	1993-1995	Case series (Ouagadougou National Hospital Center)	48.0 (3.7)	46	46	I=3 II=5 III=22 IV=16	82.6%	Not provided
Ethiopia									
(7)	2020	Jan-June 2018	Hospital Based, Cross Sectional Study, Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.	52.1 (10.4)	405	394	I= 10 II= 132 III= 108 IV=144 Unknown=11	64%	Not provided
(8)	2020	Jan 2017-Jun 2018	Hospital based, retrospective cohort, 7 major hospitals or diagnostic centres in Addis Ababa	52.9 (13.1)	212	212	I=8 II= 76 III=49 IV=79	60.4%	Paying medical bills out of pocket, Diagnostic interval >90 days, visiting more than 3 health providers before a diagnosis was made, practising religion as a remedy.
(9)	2019	2008-2012	Retrospective cohort, Tikur Anbessa Specialized Hospital (TASH), Addis Ababa, Ethiopia	49 (11.6)	1575	1575	I-IIa= 191 IIb=497 III= 731 IV= 156	56.3%	Longer patient intervals, HIV positivity associated with more advanced stage at diagnosis

Appendix

Table 1A. Clinical series describing stage at diagnosis of cervix cancer in African women. *Continued.*

Reference	Year of publication	Time period under review	Study design	Mean (SD) or median age (IQR)	Sample size	Number with known stage	Stage distribution	% Late stage	Determinants of stage
(10)	2017	2008-2012	Retrospective cohort, 1 hospital Tikur Anbessa Specialized Hospital (TASH), Addis Ababa	49 (11.6)	1655	1110	I-IIA= 164 IIB-IIIA= 256 IIIB-IVA= 664 IVB= 26		HIV positive patients had more late-stage disease (IIb – IV) than those who were HIV negative
Ghana									
(11)	2017	2010-2013	Retrospective cohort (2 hospitals), Komfo Anokye and Korle Bu Teaching Hospitals	56.9	1725	1311	I=90 II=428 III=631 IV=162 Missing= 414	60.5%	NR
(12)	2018	2012-2016	Retrospective cohort (1 hospital, Catholic Hospital, Battor)		159	157	NR	66%	Poor education or lower educational level, no previous screening for cervical cancer
Kenya									
(13)	2013		Retrospective cohort		355	209	NR	80.5%	
Malawi									
(14)	2017	Jan-July 2015	Prospective cohort (1 hospital Queen Elizabeth Central Hospital)	44.9	300	300		56%	
Morocco									
(15)	2010	2006	retrospective cohort (1 hospital, National institute of oncology)	50.0 (min=23;max=85)	646	555	I=90* (14%) II=227* (35.1%) III=227* (35.1) IV=11* (1.7%)	57%	Not provided
Nigeria									
(16)	2018	2012-2016	Retrospective review, 1 hospital Ahmadu Bello University Teaching Hospital, Zaria, Nigeria)	50.5	1639	1467	I=52 IIA=52 IIB=400 III & IV=963	93%	NR
Senegal									
(17)	2008	1977-1999	Retrospective cohort (l'Institut du cancer de Dakar).[† squamous cell carcinomas only]	35 (SD=NA)	616		NA	419 (68%)	

Table 1A. Clinical series describing stage at diagnosis of cervix cancer in African women. *Continued.*

Reference	Year of publication	Time period under review	Study design	Mean (SD) or median age (IQR)	Sample size	Number with known stage	Stage distribution	% Late stage	Determinants of stage
Sudan									
(18)	2011	2007	Retrospective cohort (Radiation & Isotope Centre, Khartoum)	54.5 (range 25-76)	197	197	I=17 (8.7%) II=39 (19.8%) III=27 (13.7) IV= 114 (57.9%)	71.5%	Age >55, African ethnicity (v Arab), rural (v urban) residence, no health insurance
Tanzania									
(19)	2012	2010-2011	Retrospective cohort, 1 hospital Bugando Medical Centre and Teaching hospital, Tanzania [†Results for histologically confirmed cases only]	50.5 (12.5)		74	IB= 24 IIA= 15 IIB= 11 IIIA= 6 IIIB= 10 IV=8	52.7%	
(20)	2016	2013-2014	Cross sectional (1 hospital), Bugando Medical Centre and Teaching hospital, Tanzania [†Population based study]	50.5 (13.3)	202	202	I-IIA=3 IIB-IV=129	63.9%	
Uganda									
(21)	2016		Cross Sectional (1 hospital), St Mary's Hospital Lacor Uganda	48 (13)	149	149	I=17 II=29 III=67 IV=31 Missing= 5	66%	Early sexual debut in women of low socio-economic status, financial difficulties, low education levels, referral delays from primary health care centres.
(22)	2017	2003-2010	Retrospective cohort, Kampala cancer registry-population-based study	43 (20-84)	315	315	I=13 II=76 III=162 IV=27	68%	
Zambia									
(23)	2021	2014-2018	Retrospective cross sectional (1 hospital), Cancer Diseases hospital, Zambia		2121		I=162 II=941 III=771 IV= 103	44%	

* Total number calculated based on given percentages and total number of patients included in the study.
NA= not available

Appendix

Table 1B. Cervical cancer survival in clinical studies in Sub-Saharan Africa.

Population	Reference	Study period	N	Stage	1-year survival	2-year survival	3-year survival	5-year survival	Median survival	Treatment	Factors associated with mortality	Prognostic factors for good survival
Botswana												
Princess Marina Hospital, Gaborone Hospital, Nyangabgwe Referral Hospital, Botswana	(3)	2010 - 2016	327	IA-IVB			HIV positive :35% (27-44) HIV negative: 48% (35-60)		HIV positive: 21.7 months HIV negative: 30.5 months	EBRT, brachytherapy with concurrent cisplatin chemotherapy, ART for HIV positive patients	HIV status doubled risk of death, excess risk greater at in earlier stages Advanced stage, and poor treatment completion	
Gaborone, Botswana	(24)	2013 - 2015	182	85% had stage II/III		HIV positive: 65 %(54 - 74) HIV negative: 66% (49 - 79)				Curative chemo-radiation therapy, ART for HIV positive patients		Total radiation dose 75Gy, age<40, baseline Hb>10
Gaborone, Botswana (HIV positive only)	(25)	2015 - 2018	231	Locally invasive cervical cancer					Nadir CD4 count: 633 days Delta CD4 count: 569 days	EBRT, brachytherapy and cisplatin based chemotherapy		Higher CD4 count
Ethiopia												
Tikur Anbessa Specialized Hospital (TASH), Addis Ababa University, Ethiopia	(10)	2008 - 2012	1655	I-IV					38 months	Only 13.5% received curative radiotherapy doses	Older age, advanced disease, baseline anaemia	
TASH, Addis Ababa University, Ethiopia	(26)	2008 - 2012	1059	47% were IIB-IIIA, 34.6% IIIB	90.4%	73.6%				Radiation and/or surgery, no brachytherapy		Earlier stages
TASH, Addis Ababa University, Ethiopia	(27)	2008 - 2012	788	70% were IIIB - IVA at RT	84%	64%			33 months	EBRT without brachytherapy, 15% received chemotherapy		Adherence to guideline-conforming radiation treatment
TASH, Addis Ababa University, Ethiopia	(28)	2014-2016	634	65.1% were stage III & IV	92,11%	75,29%	52,92%	38,20%	37 months	Surgery and/or chemotherapy and/or radiation	Stage IV, advanced age, baseline anaemia, substance use, comorbidities	
Ghana												
Komfo Anokye and Korle-Bu Teaching Hospitals,Kumasi, Ghana	(29)	2010 - 2013	821	I-IV	62%		39%	30%		Radiation and/or surgery and/or chemotherapy, 32% received no treatment	Advanced stage, adenocarcinoma, poor differentiation, not receiving treatment	
The National Centre for Radiotherapy, Accra, Ghana	(30)	2006 - 2011	250	Stage IIB or more in 80% of patients			86%			EBRT, brachytherapy and chemotherapy		

Table 1B. Cervical cancer survival in clinical studies in Sub-Saharan Africa. *Continued.*

Population	Reference	Study period	N	Stage	1-year survival	2-year survival	3-year survival	5-year survival	Median survival	Treatment	Factors associated with mortality	Prognostic factors for good survival
Kenya												
Kenyatta National Hospital, Nairobi, Kenya	(13)	2008 - 2010	355	80% advanced IIB or above		<20%			15 months	6.7% got optimal EBRT, brachytherapy and adjuvant chemotherapy	Poorly differentiated SCC, advanced disease stage	Optimal treatment
Malawi												
NdiMoyo Palliative Centre, Salima District, Central Malawi	(31)	2006 - 2013	125	Not available	31%	10,3%	5,20%					
Morocco												
National Institute of Oncology of Rabat, Morocco	(32)	2006	646	Locally advanced stages (88%)				63%		Two thirds received chemo-radiation therapy	Poor response to radiation, late stage, anaemia, tumour size, lymph node involvement	
South Africa												
Baragwanath Hospital, Soweto, South Africa	(33)	1981 - 1982	210	IA - IV	50% (36-64) at 1,6 years follow-up					Extended hysterectomy for IA,IB surgery/EBRT and brachytherapy, II-IV full course RT		
Groote Schuur Hospital, Cape Town, South Africa	(34)	1993 - 2008		IB2				70,8		Radical radiation vs radical surgery	Larger tumour size, Surgical treatment was protective	
Radiation Oncology Division, Tygerberg Hospital, Cape Town, South Africa	(35)	2007 - 2011	492	Locally advanced cervical cancer IB1 - IIIB (69.5% were IIIB)		HIV positive: 41,6% (29,5 - 53,7) HIV negative: 62% (57,2 - 66,7) All: 59,1%		HIV positive: 35,9% (23,9 - 48,0) HIV negative: 49,5% (44,6 - 54,4) All: 47,6%		EBRT, platinum-based chemotherapy	HIV, Stage IIIB vs IB1-IIIA, Hydronephrosis	
Phase III RCT, Johannesburg, South Africa (HIV positive only)	(36)	2014 - 2017	206	IIB-IIIB		82,2% (standard care) 87,1% mEHT) at 6 months				Chemoradiotherapy +/- modulated electrohyperthermia		mEHT had better outcomes at 6 months than standard care
Phase II AIDS Malignancy consortium trial , Harare Zimbabwe, Johannesburg, SA **(HIV positive only)**	(37)	2014 - 2017	38	Locally advanced cervical cancer IB2 - IVA (70% were Stage IIB)	HIV positive : 81.6% (65.2 - 90.8)					EBRT, brachytherapy, cisplatin, ART		

Table 1B. Cervical cancer survival in clinical studies in Sub-Saharan Africa. *Continued.*

Population	Reference	Study period	N	Stage	1-year survival	2-year survival	3-year survival	5-year survival	Median survival	Treatment	Factors associated with mortality	Prognostic factors for good survival
Uganda												
Kenyatta National Hospital, Nairobi, Kenya	(38)	2000	36	Mostly Stage IIB and above	HIV positive: 67%	HIV positive: 40%	HIV positive: 27%			60% received both EBRT and brachytherapy	HIV	
Uganda Cancer Institute, Kampala, Uganda	(39)	2013 - 2015	149	I-IV	HIV positive: 65% (51-77) HIV negative: 69% (58-77)	HIV positive: 30% (17-44) HIV positive: 51% (39-62)			HIV positive: 13,7 months HIV negative: 24,3 months			

Abbreviations:

ART – antiretroviral treatment
EBRT – external beam radiation treatment
MEHT – modulated electrohypothermia treatment
RT – radiation treatment

Appendix

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