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Advancing the Elimination of Cervical Cancer Across Africa

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Abstract

Though cervical cancer is largely preventable, Africa faces a high burden with thousands of deaths. Highlighting the urgent need for action toward the WHO's 90-70-90 elimination strategy, this study presents the epidemiological burden of HPV and cervical cancer in Africa and advocates for decisive measures to improve screening and implement effective prevention through vaccination. Here, we discuss which is the better option for Africa: a single-dose or a two-dose vaccine regimen. Furthermore, we explore screening methods, such as methylation markers and AI-based screening, as well as treatment-related side effects and the prognosis of cervical cancer in Africa.

Keywords: Cervical cancer, Human Papillomavirus (HPV), Africa, Sub-Saharan Africa, Prevention, Vaccination, Screening, Primary HPV test, Treatment, Survival

1. Introduction

Cervical cancer remains a global public health concern. With millions of cases around the globe, the World Health Organization (WHO) has called for the elimination of cervical cancer as it is an almost entirely preventable disease by effective primary (prophylactic vaccines), secondary (screening), and tertiary (early treatment) prevention measures[1].

WHO developed the 90-70-90 strategy, which aims to (1) vaccinate 90% of girls with the HPV vaccine by age 15, (2) screen 70% of women by age 35 and again at 45 with a high-performance test, and (3) treat or manage 90% of diagnosed women[1]. Many developed countries have committed to achieving the 90-70-90 strategy, with countries such as the U.K., the USA, and European countries implementing widespread HPV vaccination and screening programs[2]. For example, Australia, the first country to initiate nationwide HPV vaccination, experienced a decline in high-grade cervical abnormalities after vaccination, halving from 2007 to reach 5.0 per 1,000 screened nationally by 2014 in women aged less than 20[3]. Also, a mathematical model estimated a reduction to six cases of cervical cancer per 100,000 by 2020 and a further decrease to four cases per 100,000 by 2028 in Australia[4]. In the U.K., a substantial reduction in cervical cancer (87%) and high-grade cervical abnormalities (97%) was observed after vaccination of women who were aged 12-13 during the period of immunization[5]. However, across low- and middle-income countries (LMICs), this remains a reality yet to be achieved. A mathematical model suggests that if LMICs attain the 90-70-90 strategy goal by 2030, the incidence of cervical cancer could fall by 42%, with over 62 million cases averted by 2120[6].

In this review, we aim to promote a deeper understanding and encourage prompt, decisive action to eliminate cervical cancer as a public health issue in Africa and to shed light on the current outlook for HPV and cervical cancer on the continent. We highlight epidemiology, prevention, screening, treatment, and prognosis.

2. Epidemiology

2.1 Cervical Cancer in Africa: A Public Health Concern

Globally, an estimated 660,000 new cases of cervical cancer and 350,000 deaths occurred in 2022, with 125,699 new cases and 80,614 deaths in Africa[1,7]. Cervical cancer has long been under-prioritized in developing countries, especially in Africa[8]. The highest age-standardized incidence rates were observed in Eastern Africa (40 [95% CI = 39.7–40.4]), followed by Southern Africa (36.4 [95% CI = 35.8–37.1]), and Central Africa (31.6 [95% CI = 31.1–32.1]). Mortality rates followed a similar pattern to incidence, with the highest recorded in Eastern Africa (28.6 [95% CI = 28.3–28.9])[9]. HPV infection and cervical cancer have become particularly worrying in terms of socio-demographic, economic, and health conditions. Campos et al. studied cervical cancer prevention in 50 LMICs. They discovered that implementing HPV vaccination and once-in-a-lifetime screening could prevent 5.2 million cases, 3.7 million deaths, and 22.0 million disability-adjusted life years (DALYs) over the lifetimes of the intervention cohorts. The total cost of the 10-year vaccination, screening, and treatment program was $3.2 billion, deemed cost-effective[10]. Figure 1 shows the estimated prevalence, and Figure 2 shows the incidence and mortality rates in Africa[7].

2.2 HPV Prevalence and Genotype Distribution

The prevalence and genotype distribution of HPV vary by geographic region, age, and HIV burden. Understanding the epidemiology of HPV in Africa is critical in developing a prophylactic HPV vaccination strategy and estimating the impact and resource planning for HPV screening, triage, and precancer treatment. In a five-continent meta-analysis among women with normal cytology, HPV prevalence ranged widely: 24% in sub-Saharan Africa, 21.4% in Eastern Europe, 16.1% in Latin America, 9% in Asia, and 5% in North America[11]; the highest prevalence was observed in studies conducted in Southern African countries. In the rural Eastern Cape Province of South Africa, the overall HPV prevalence in sexually experienced girls aged 15-22 was 76%, and the prevalence of carcinogenic HPV was 54.5%[12]. Also, HPV is among the most common sexually transmitted diseases in North Africa, with a prevalence of 23%[13]. In a meta-analysis covering the Middle East and North Africa (MENA), the study reported that the subgroup with abnormal cervical cytology in the MENA region with the highest HPV prevalence was found in Northeast Africa (94%; 95% CI = 91–96%), which was the same in the general population subgroup in the region (21%; 95% CI = 7–40%)[14].

Beyond overall prevalence, the distribution of specific HPV genotypes also exhibits distinct regional patterns. The five most common HPV types reported worldwide among women are HPV-16, -18, -52, -31, and -58[15]. Sub-Saharan African (SSA) trends diverge from these global averages; while HPV-16 and HPV-52 are the primary genotypes in Eastern and Southern Africa, HPV-16 and HPV-35 are the predominant genotypes in Western Africa[16-18]. In contrast to SSA, the most detected HPV types in the MENA region align more closely with global reports (HPV-16, -18, and -58)[14].

The prominence of genotypes like HPV-35 highlights a growing concern about Non-Vaccine-Targeted (NVT) carcinogenic genotypes (including HPV-39, -51, -56, -66, and -68) in Africa. HPV-35 is only associated with about 2% of global cervical cancer cases; however, in Africa, it occurs in about 10% of precancerous and cervical cancer cases[19]. An Ethiopian study showed that the prevalence of NVT HPV was 56 of 108 women (51.8%, 95% CI = 42–61%), of whom 28 (25.4%, 95% CI = 18–34%) had a single NVT HPV genotype infection. Also, HPV-35 accounted for the highest prevalence of NVT HPV cases (11 cases)[20]. Another study involving Kenyan and South African women showed that HPV-35 (8.4%) was as prevalent as HPV-18 (8.4%). In this study, a few (1.9%) had evidence of high-grade cervical abnormalities, among which HPV-35 was the most prevalent[21]. Supplementary Dataset 1 provides information on HPV prevalence and genotype distribution across multiple studies[20,22-79].

While demographic, socioeconomic, and lifestyle factors, geographic variations, and existing STI infections primarily influence HPV prevalence[80,81], it is crucial to acknowledge that methodological factors in HPV testing also contribute to variations in reported prevalence. For instance, a Malawian study observed differing prevalence rates when using the Xpert HPV test (Cepheid, USA) versus ScreenFire (Atila Biosystems) on the same population, reporting 100% and 90% prevalence, respectively. This may have resulted from storing specimens for 1 to 2 years before testing with ScreenFire[49].

2.3 The interplay of HIV and HPV

SSA has the highest cervical cancer rate worldwide. These rates are worsened by factors such as the high HIV prevalence, a high rate of unprotected sex, sexually transmitted infections, and

insufficient sexual and reproductive health education among young girls and women[82]. Both HPV and HIV infections share the same transmission route, and cervical cancer has been considered an AIDS-related disease since 1993. HIV infection is associated with an increased risk of acquiring new HPV infections and a reduction in the rate of HPV clearance[83].

The high burden of HPV among women living with HIV (WLWH) in Africa has significant implications for cervical cancer prevention, as the prevalence of single or multiple HPV infections is higher among WLWH [84]. This increased risk is further worsened by factors such as HIV viral load, as Akakpo and colleagues showed that WLWH with viral load ≥ 1000copies/ml (AOR = 5.58, 95% CI = 2.89-10.78, $p < 0.001$) had a higher likelihood of being co-infected with HIV and HPV[85]. Beyond the general prevalence, the most frequent carcinogenic HPV types among African WLWH were HPV 16 (18%), HPV 35 (10.12%), HPV 52 (9.98%), HPV 18 (9.7%), and HPV 45 (6.82%)[86]. Another study across three SSA countries demonstrated that the prevalence of single and multiple HPV infections, HPV 16, -18, -35, and -45, was higher and more common among WLWH than among HIV-negative women[87]. Although HPV 16 was the most frequently observed genotype, the significant prevalence of non-vaccine HPV 35 is evident. A recent study from the extensive African Cohort Study, which involved 12 clinics across Tanzania, Kenya, Uganda, and Nigeria, found a significant prevalence of HPV 35 at 9.3%[19]. Moreover, in 2022, a comparative study by Gilles et al. (2022) involving WLWH and HIV-negative controls specifically highlighted HPV 31, 33, and HPV 35 as more prevalent in WLWH[88]. This consistent and high prevalence of HPV-35 across multiple African settings, particularly among WLWH, shows a critical gap in the current vaccines available, which do not include this genotype. This justifies prioritizing its inclusion in future vaccine development or regional vaccination plans.

3. HPV Vaccination and the African Context

HPV vaccination is an essential preventive method for cervical cancer[89]. Boily et al. conducted a mathematical modeling study and found that implementing a program in which girls receive the HPV vaccine and participate in lifetime cervical cancer screenings could eliminate cervical cancer in the South African region by the end of this century[90]. 28 of 47 SSA countries have integrated HPV vaccination into their national routine immunization programs, with four

countries reaching 90% HPV vaccination coverage in 2023. Also, 17 SSA countries have incorporated HPV testing into cervical cancer screening programs[91,92]. Most of these countries are supported by the GAVI Alliance, a funding scheme aimed at achieving global vaccination equity[93]. However, not all GAVI-funded nations have incorporated vaccinations at the national level. Figure 3 shows countries with integrated national routine HPV vaccination programs and coverage, and Figure 4 shows GAVI-funded (eligible) countries in Africa, respectively[94-96].

Currently, six preventive HPV vaccines (Cervarix ®, Cecolin ®, Walrinvax ®, Cervavac ®, Gardasil ®, and Gardasil 9 ®) are licensed and widely recognized[97]. Girls aged 9-14 are recommended to receive the HPV vaccination as early as possible before their sexual debut[1]. Additionally, some middle- and high-income countries have implemented the "gender-neutral" vaccination program recommendation to immunize both boys and girls[98]. Due to resource limitations, only Cameroon, Cape Verde, and Mauritius have implemented "gender-neutral" vaccination programs[92].

In Africa, the HPV vaccination program mainly targets girls aged 9-14 through school-based HPV vaccination, which is integrated into school routine programs for adolescents[99]. This can be integrated with adolescent health services[100], as seen in Tanzania's HPV-Plus program, which provided additional services, including health education, deworming tablets, nutritional assessments, and vision screening[101]. However, school-based vaccination requires extra resources and costs, potentially limiting other school activities[102]. In addition to focusing on adolescents, a study suggests that combining cervical cancer screening for mothers with their daughters' HPV vaccination (Mother-to-daughter vaccination) in a single program can further enhance maternal knowledge of cervical cancer[103].

Furthermore, some countries have implemented community-based routine immunizations in which vaccines are delivered via mobile clinics, door-to-door campaigns, or community health workers. This strategy helps provide healthcare services to out-of-school girls and the community, including vaccinations at health facilities[104,105]. Some countries, such as Nigeria, use a mixed approach that combines school- and community-based vaccination strategies[93].

3.1 Efficacy and shortcomings of vaccination programs in Africa

There is substantial evidence supporting the effectiveness and safety of HPV vaccines[106,107]. As the first African country to implement an HPV vaccination program, Rwanda introduced a quadrivalent vaccine for girls aged under 15. This significantly reduced the prevalence of HPV types 6, 11, 16, and 18[108]. Moreover, a survey in Rwanda and Bhutan found that administering the quadrivalent vaccine in these regions provided cross-protection against five additional HPV types (HPV 31, 33, 35, 52, and 58)[109]. To offer faster herd immunity, HPV vaccination programs implemented in Africa typically follow a two-dose schedule. Although this improves cost-effectiveness, HPV vaccination rates in many African countries remain below WHO targets[110].

As a developing region, low vaccination rates are influenced by systemic barriers such as a lack of political will, limited vaccine supply, high costs, and scarce healthcare resources. Educational policies also pose challenges; in countries where compulsory education ends at primary school, ensuring full vaccination coverage may be particularly difficult for out-of-school or transferred children[111]. To improve coverage, support from national authorities and coordination among schools, communities, healthcare providers, and health ministries are essential[112].

Moreover, individual factors also play a role. In Uganda, financial constraints and a lack of education about HPV affected vaccination uptake[113]. Similarly, limited access to information has been cited as a barrier in North Africa[114,115]. Other personal factors include religious beliefs, fears of infertility or side effects, misinformation online, mistrust of healthcare systems, and attitudes of healthcare workers[116,117]. The COVID-19 pandemic further hampered vaccination efforts, as misinformation about the safety of COVID-19 vaccines increased vaccine hesitancy, delaying or preventing HPV vaccination even when services were available[104].

To address these challenges, Okunade et al. and Fokom Domgue et al. suggested adopting mobile health technologies or promoting communication between people and their communities to increase awareness of the HPV vaccine and reduce vaccine hesitancy, thereby improving HPV vaccination rates[118,119]. Furthermore, strengthening HPV vaccination programs is particularly crucial in countries with a high HIV burden, where WLWH face elevated risks. However, reports on the specific effects of HPV vaccination in this population remain limited[120].

Data from other countries suggests that a reduced-dose vaccination schedule may help prevent persistent HPV infection, lower costs, simplify vaccination processes, and increase coverage[121-123]. Specifically, two studies from Tanzania demonstrated that a single dose of the Cervarix® or Gardasil 9® HPV vaccine was well tolerated in healthy African girls aged 9-14[124,125]. Following WHO recommendations, 16 African countries are considering implementing a single-dose HPV vaccination program[92]. However, there are limited follow-up periods (approximately 24-36 months) in two key single-dose vaccine trials in Africa (KEN SHE and DoRIS), and the long-term protection over 10 years has not been validated[126]. Existing studies primarily assess the protective effect based on immunogenicity data rather than clinical endpoints, such as cervical cancer incidence.

Additionally, there is a large population of WLWH in Africa. Studies on the single-dose HPV vaccine for immunocompromised girls are limited[126]. Although a study in South Africa evaluated the impact of the single-dose vaccine on HIV-infected girls, concluding with a reduction in post-vaccine HPV 16/18, it has limitations, as it did not imitate all WLWH in Africa[127]. Currently, there are no large-scale, long-term prospective studies evaluating the protective effect of the single-dose HPV vaccine in HIV or HPV-infected populations.

Conversely, a mathematical modeling analysis indicated that an extended-duration two-dose HPV vaccination schedule might be easier to implement than a one-dose schedule, for which the ultimate protective efficacy remains uncertain. It may be more effective than the current two-dose schedule and can help prevent interruptions to vaccination programs[128]. For instance, during humanitarian crises, some refugees or nomadic groups may be forced to live a constantly mobile, transnational lifestyle, often lacking access to adequate medical personnel and vaccine supplies[129]. Additionally, severe infectious disease outbreaks, such as COVID-19, increased demand for healthcare workers and caused shortages of medical resources, potentially delaying or interrupting HPV vaccination programs during such emergencies[130,131]. In such situations, a two-dose HPV vaccination program with an extended schedule may be easier to implement than the current two-dose approach. Reduced-dose and extended-duration two-dose HPV vaccination schedules may become key preventive measures to significantly reduce cervical cancer incidence in LMICs in the future.

4. Cervical cancer screening

Persistent HPV infections, especially carcinogenic HPV types 16, 18, and 45, are the leading cause of cervical cancer globally. However, persistent infections last for many years before leading to abnormalities[132]. The time gap between infection and disease onset provides an opportunity for early detection and intervention, thereby potentially reducing the incidence and mortality of cervical cancer.

Screening is crucial as a secondary prevention measure in addition to increasing vaccination coverage. The main objective of cervical cancer screening is to identify treatable precancers that are likely to develop into invasive cancers. This proactive approach aids in reducing the incidence, mortality, and morbidity associated with cervical cancer. A secondary but important goal is the detection of early-stage cervical cancer, which helps with early treatment, hence reducing the mortality of cervical cancer[133]. Cytologic testing, including Pap testing and, more recently, liquid-based cytology, has served as the basis for primary cervical screening methods, effectively detecting cervical abnormalities in many developed countries over the years. Visual Inspection with Acetic Acid (VIA) and Lugol's Iodine (VILI) are also used for screening[133,134].

However, recognizing that carcinogenic (high-risk) HPV is the cause of cervical cancer is essential for screening. According to the WHO guidelines, women should be screened for cervical cancer every 5–10 years starting at age 30. WLWH should be screened every 3 years starting at age 25. The global strategy encourages at least 2 lifetime screens with a high-performance HPV test by age 35 and again by age 45[1].

HPV testing identifies the presence of carcinogenic HPV DNA in vaginal and cervical samples. WHO recommends primary HPV DNA testing and triage for women living with HIV, while suggesting optional triage for the general population[135]. Most HPV DNA assays are integrated with partial genotyping, which identifies the carcinogenic HPV types, mainly HPV 16 and 18, or extended genotyping, which detects a broader range of carcinogenic HPV types, enabling better risk stratification[136]. Women who are suspected to be at higher risk for cervical cancer are advised to undergo triage using either HPV genotyping or cytology.

WHO has set two screening approaches: "screen and treat" and "screen, triage and treat"[137]. In the "screen-and-treat approach," the treatment decision is based solely on a positive primary screening test, without a secondary test. A "visual assessment for treatment (VAT)" is performed after positive primary results using visual inspection to determine eligibility for ablative treatment[138]. When the patient is eligible for ablative treatment, it is ideally done immediately, at the same visit as the screening test (the single-visit approach)[137]. Whereas in the "screen, triage, and treat approach," the decision to treat is based on a positive primary screening test followed by a positive second test (a "triage" test). Also, a positive triage test may lead to biopsy and histopathological examination to diagnose and determine appropriate treatment. When the primary screening test is positive, and the triage test is negative, women need an appropriate follow-up evaluation at a specified date, according to the recommendations[137].

Africa, comprising numerous LMICs, faces resource constraints compared to developed countries or fast-growing economies. Due to these constraints, VIA or VILI is often used as the primary cervical cancer screening as it is a low-cost procedure[139]. A nine-year study in Zambia demonstrated the practical use and outcomes of VIA, tracking cervical cancer screening outcomes through Visual Inspection with Acetic acid and digital cervicography (VIAC)[140]. The study involved over 180,000 women and showed a 10.4% VIA positivity rate, with WLWH aged 30-39 exhibiting the highest rate. However, follow-up rates declined over time[140]. While VIA remains essential in resource-limited settings, it has limitations compared to advancements like HPV testing. For instance, a study in Eswatini with over 600 women supplemented VIA with HPV testing, which increased detection accuracy by identifying 223 women who tested negative on VIA but positive for HPV[34]. This shows that women unaware of their HPV status are at risk of late diagnosis if relying solely on VIA.

4.1 Enhanced Visual Assessment and the Potential Role of Artificial Intelligence in Screening

Technological advancements, such as computer-aided (smartphone-aided) methods and artificial intelligence (AI), are increasingly being integrated into VIA protocols in African countries[141]. A study in Eswatini confirmed a significant improvement in VIA using smartphone-aided screening, demonstrating greater diagnostic consistency than traditional VIA[142]. Benefits include

easier consultations among healthcare workers, better communication with patients, high-quality image assessment, and increased efficiency, reducing workload[143,144]. However, successful implementation requires proper technology management, including regulations, infrastructure, and training. Involving patients in the process can also help ensure these tools are widely adopted and effectively integrated into screening programs[144].

AI has the potential to significantly improve cervical cancer screening in Africa. Since 2017, the Enhanced Visual Assessment (EVA), a clip-on attachment for Android phones that functions as a mobile colposcope with integrated AI software, has been considered for use[145]. This AI, a Convolutional Neural Network (a type of machine learning) trained on over 100,000 cervical images from the U.S. National Cancer Institute, helps identify precancerous and cancerous lesions. Studies show that Automated Visual Evaluation (AVE) using EVA can accurately detect high-risk lesions, demonstrating strong correlation with expert evaluation[146], with one study in Zambia reporting sensitivities of 85% and specificities of 86%[147]. A recent prospective study evaluating the performance of the AVE tool for screening across five African countries found that AVE significantly outperformed VIA in sensitivity for detecting high-grade lesions, demonstrating its potential to improve screening effectiveness in resource-limited settings[148].

Beyond visual inspection, AI is also transforming cytology analysis. In rural Kenya, a trial with 740 HIV-positive women digitized cervical smear samples using a portable scanner, which were analyzed by a deep learning system (DLS) trained on over 350 images and validated on 361 images[149]. The system demonstrated high sensitivity (95.7% to 100%) and reasonable specificity (78.4% to 84.7%). Notably, the DLS accurately identified high-grade lesions and had no false negatives in cases rated high-grade by manual reading[149]. This shows AI's potential to enable early detection and improve cervical cancer screening in resource-limited settings.

4.2 Performance and Feasibility of Various Cervical Screening Methods

Vassilakos et al. conducted a Test-Triage-Treat (3T) study in Cameroon to compare the performance of commonly used screening methods. Women initially underwent HPV testing, with those testing positive subsequently proceeding to VIA and cytology examination (manual and automated). The sensitivity of single-test automated cytology was higher than that of the other systems (manual cytology and VIA). However, combining HPV-16/HPV-18/45 genotyping

and automated cytology yielded the highest sensitivity for CIN 2+ detection (91.2%, 95% CI = 74.8-97.3%)[28]. Another study in South Africa confirmed that a combination of HPV tests and other screening methods was the most effective in detecting cervical intraepithelial lesions. In this study, VIA performed poorly and did not meet the set standards. However, hrHPV testing was the most sensitive, while cytology showed the greatest specificity. The dual combination of hrHPV (HPV 16/18 genotyping) and cytology for ASCUS+ had the highest sensitivity amongst others. The study confirms that using hrHPV testing as the primary test with others (HPV-16/-18, cytology, and VIA) as the secondary test is the best strategy for screening in HIV-positive or HIV-negative people[64]. Furthermore, a similar study in Burkina Faso and South Africa also confirmed that hrHPV testing is more sensitive for CIN2+ detection, and triage of HPV-positive patients with cytology had optimal specificity, although with a slight loss in sensitivity[26]. Therefore, combining HPV tests and other screening methods may benefit low-resource countries.

Furthermore, adjusting the cut-off values for the cycle threshold (Ct) in HPV genotyping assays may enhance specificity while causing minimal sensitivity losses. The cycle threshold for HPV channels effectively predicted CIN2+, as Kuhn and colleagues showed[150]. Supplementary Dataset 2 details HPV testing assays, their genotype detection, and positivity cut-off limits, and Figure 5 illustrates the distribution of HPV testing techniques across Africa, as reported in various studies[20,22-79].

In recent years, alternative methods have been employed for cervical cancer screening in South Africa. Analysis of hypermethylation in specific host cell gene promoter regions is an increasingly intriguing method for identifying women at high risk of cervical cancer or advanced CIN lesions, as reported in recent studies[151-157]. One study aimed to validate the methylation markers ASCL1 and LHX8, identified in a genome-wide DNA methylation profiling study[158] as the primary screening method. The findings indicated that the sensitivity and specificity of ASCL1 and LHX8 as single markers were similar to those of HPV testing. However, combining both markers resulted in decreased sensitivity for CIN 3 detection but increased specificity compared to primary HPV testing without losing sensitivity. They suggested these combined markers might be better than primary HPV testing, potentially reducing referral rates and overtreatment[66]. Another study also used ASCL1 and LHX8 methylation analyses as post-

treatment monitoring markers for women treated for CIN 2/3. The study demonstrated that the ASCL1/LHX8 methylation test is associated with a low risk of recurrent CIN 2/3 after LLETZ (LEEP) treatment among test-negative individuals, while maintaining a high detection rate of recurrent CIN 2/3[159]. These studies emphasize methylation markers as a promising approach, providing potential for more precise cervical cancer screening and post-treatment monitoring.

Although several screening methods have been explored for use in Africa, their feasibility varies depending on factors such as cost and infrastructure. Visual Inspection with Acetic Acid (VIA) is inexpensive and requires minimal resources, but it has the lowest sensitivity for detecting dysplasia[160,161]. WHO recommends HPV DNA testing due to its higher sensitivity for detecting carcinogenic HPV. Although initially costly, recent studies show HPV testing is more effective and cost-efficient in the long run, especially when combined with single-visit "screen-and-treat" strategies[138,160,162-164]. Using existing nucleic acid testing platforms, such as Xpert HPV (Cepheid, USA) and AmpFire (Atila Biosystems), has further reduced costs and improved scalability[163]. Scaling up these methods could significantly enhance cervical cancer screening across Africa, provided a reliable supply of test cartridges is maintained[165].

Scaling up cytology-based screening in Africa is less likely to be practical. It is relatively costly and needs specialized infrastructure[160,161]. Additionally, methylation markers require expertise and specialized techniques, which can be difficult in low-resource settings[151-157]. Therefore, policies should evaluate the cost-effectiveness of methods and identify infrastructure gaps and other factors during decision-making for national screening programs.

5. Cervical Screening Coverage Rates in Africa

Cervical cancer is usually diagnosed in advanced disease stages among women in Africa[166-169]. A meta-analysis on survival revealed that 53.3% (95% CI = 50.9-55.6%) of cervical cancer cases in Africa were diagnosed at late stages (stage III-IV). This proportion varied significantly across countries and regions, ranging from 7.7% to 86.3%. Considering only SSA countries, the study showed that 56.3% (95% CI = 53.7-58.8%) of cervical cancer cases were presented in the late stages (stages III-IV)[170].

The observed high rates of late-stage diagnosis are directly related to persistently low cervical cancer screening coverage across Africa[166-169]. Screening coverage rates in Africa remain very low, ranging from 2% to 20.2% in urban areas and from 0.4% to 14% in rural regions[171], with an overall screening prevalence of merely 10%[172]. Examining trends in cervical cancer screening from 2000 to 2020, only Southern Africa experienced an increase in screening coverage among women aged 30-49, while Eastern Africa showed a slight rise, and Western and Central Africa showed slight declines[173]. Hailegebireal et al. and Yang et al. both highlighted Benin's low lifetime screening rates, with only 1% of women aged 30-49 screened, the lowest, while the highest proportion of women screened in a lifetime was in South Africa and Namibia[172,173].

Low screening rates and late-stage diagnoses across Africa stem from various barriers at individual, community, and systemic levels. At the individual level, factors such as rural residence, low education, and financial challenges limit access to care. Many women delay seeking healthcare due to a lack of awareness about cervical cancer, its symptoms, and the importance of early screening[166-169]. Notably, one study reported that HIV-negative women did not recognize the need to seek healthcare, which emphasizes the lack of awareness[167]. Furthermore, socio-cultural factors such as religious beliefs and negative partner involvement can deter women from accessing screening services[174]. Within healthcare systems, barriers include overburdened facilities, insufficient equipment, and staff shortages[175]. Healthcare providers may have limited knowledge of cervical cancer signs and hold negative attitudes toward screening[167-169,175], with some displaying implicit biases—nurses show the highest levels of bias[176]. Misconceptions among providers and policymakers about the acceptance of screening programs further hinder coverage[174,175]. Addressing these barriers could improve screening rates.

Self-sampling for primary HPV testing has increased screening coverage, with high acceptability shown in studies[177-179], including a systematic review across eight LMICs, mainly in Africa, where acceptability was 92.6%, even among WLWH (87-100%)[180]. A study on Catholic nuns in Ghana suggests that women with religious beliefs may prefer self-sampling, as it aligns with their privacy and beliefs[181]. Benefits include comfort, autonomy, and reduced fear of pain, while drawbacks include anxiety over sample quality[181-183]. The accuracy of self-sampled HPV tests compared to clinician-sampled HPV tests shows that the sensitivities and specificities of HPV testing for the CIN2+ and CIN3+ endpoints did not differ between the two, confirming that self-

sampling could be used for primary HPV screening[184]. The performance of self-sampling and clinician sampling was comparable across studies from Africa (concordance rates ranged from 79.7% to 94.2%)[180].

Self-sampling can help overcome some barriers to screening. Still, personal issues (such as lack of knowledge, fear, doubts about accuracy, and cost), environmental factors (such as discrimination and transportation), and structural problems (such as high costs, limited resources, and poor access) may limit its use[180]. Governments should incorporate self-sampling in national programs and work with agencies, donors, and NGOs to make kits more affordable and available. Increasing health insurance coverage for these kits could also boost participation. Expanding outreach through mobile clinics and community health centers, and mailing kits with phone support for results, can further reduce barriers[180].

5.1 Strengthening Screening Coverage, Capacity, and Sustainability

Evidence-based implementation approaches should be used to design and deliver patient awareness and education programs to enhance patient engagement and address issues such as treatment nonadherence, vaccine hesitancy, and refusal to be screened[185]. Additionally, educating healthcare professionals through training and hiring more lab workers is crucial to increasing in-country capacity and improving awareness[186,187]. Developing culturally relevant cervical cancer education interventions for women and healthcare providers in LMICs could be an effective strategy to reduce bias[176,188]. To further address patient disengagement, improve adherence, and overcome hesitancy, training on emotional intelligence, counseling, and effective communication between patients and healthcare providers may positively influence behaviors and outcomes[188,189].

The use of mobile health (mHealth) in oncology education and tele-mentoring can effectively enhance cancer screening knowledge among healthcare providers, as mobile technology is widely accessible and cost-efficient[190-192]. However, supervision and face-to-face interactions should be conducted in conjunction with mHealth services to ensure effectiveness. Training initiatives should prioritize developing competencies through sustained mentorship and supervision rather than relying solely on short-term lectures[193,194]. While support from international organizations may be crucial initially, reliance on external funding should decrease

over time as local capacity becomes sufficient. Providing funding for healthcare workers to pursue further studies can improve faculty retention, and local governments should take responsibility for maintaining these efforts, ensuring a long-term plan for recruiting and fairly compensating newly trained health professionals[193]. The C4P costing tool, developed by WHO, can assist national cervical cancer programs in estimating the financial resources required and the opportunity costs of reducing national cervical cancer incidence through primary, secondary, and tertiary prevention[195].

6. Treatment and Prognosis

6.1 Treatment

Cervical cancer is primarily a preventable disease, and early detection is strongly associated with significantly improved survival. Preventing cervical abnormalities from progressing into invasive cancer is crucial. The treatment (prevention) principle is to remove precancerous lesions and treat the transformation zone of the cervix[196]. This can be achieved through ablative procedures (thermal ablation and cryotherapy) and surgical procedures such as conization and Large Loop Excision of the Transformation Zone (LLETZ or LEEP)[196]. During screen-and-treat visits, women who test positive for pre-cancerous lesions and are eligible for treatment are subjected to either of the following: thermal ablation, conization, LLETZ (LEEP), cryotherapy, etc., to remove precancerous tissues[62,140,141,197,198]. Thermal ablation, an alternative to cryotherapy, may be a better choice for low-resource countries. Its advantages include portability (battery-powered), lower costs, and simpler operation. A limitation of thermal ablation is that it does not involve lesion biopsy[199]. Multiple studies showed that thermal ablation causes little or no pain during the treatment and no severe adverse events (AEs) weeks afterward, making it a safe option accepted by women in such settings[200,201]. One-year follow-up after thermal ablation, the successful cure rate was 96%[202], 39%[203] , and 39.0% among WLWH and 65.2% among women without HIV[62]. Overall, WLWH tend to have a higher risk of CIN2+ recurrence after thermal ablation[62,203]. Table 1 shows the acceptability and adverse effects of thermal ablation[62,200-202,204-206].

Cervical cancer treatment typically involves surgery, radiotherapy, and chemotherapy. Women with early-stage cancer usually undergo surgery[198,207], but many are diagnosed at advanced stages due to a lack of early screening[166-169]. Chemoradiation is crucial, especially for advanced cases[198,207]. In Africa, patients often receive radiotherapy, chemotherapy, or both, and brachytherapy is also used[198,207,208]. A recent Zimbabwean study utilized high-dose Cobalt-60 for brachytherapy, achieving a 75% complete tumor response at six weeks and a 23% partial response. At one-year follow-up, 40% showed a response, decreasing to 19% after two years[209]. However, there are more problems associated with treatment, such as financial burden, as reported by Rubagumya et al.[210], and access to radiotherapy, which has been extensively reviewed by Ponce et al.[211]. The waiting time for chemoradiation may be significantly associated with disease progression, as there is limited equipment. An Ethiopian study demonstrated that, compared to women who initiated radiotherapy ≤60 days after diagnostic confirmation, the odds of tumor progression to a higher stage were three times higher in women who commenced radiotherapy between 120-179 days and ≥180 days[212].

In addition to logistical challenges affecting treatment effectiveness, patients also endure significant physiological burdens from the therapies. Recent Zimbabwean studies on cisplatin in women with cervical cancer show peripheral neuropathy and ototoxicity as common AEs. These AEs risks are higher among those with existing conditions like high blood pressure or kidney disease[213]. In a South African study, patients experienced complete ototoxic hearing loss 1 month after treatment. The most common AEs were sensorineural hearing loss and high-frequency tinnitus[214]. These findings emphasize the need for clinicians to carefully monitor and manage treatment-related side effects to ensure patient safety and quality of life.

6.2 Prognosis

Quality care and management are usually associated with a good prognosis. A population study conducted in SSA revealed that countries with a lower Human Development Index (HDI) had a significantly poorer survival rate for stage I-II cervical cancer patients than those with a higher HDI[215]. An observational study examined treatment adherence and survival rates. It found that early-stage patients were more likely to follow guidelines than late-stage patients. Deviations from guidelines, whether minor or major, were linked to poorer survival in patients with FIGO

stage I-III. Additionally, cancer-directed therapy without curative intent, or no therapy at all, was associated with significantly worse outcomes[216].

Surgery or chemoradiation may improve survival rates, offering hope for some patients. DeBoer et al. found that the three-year event-free survival rates were 90% with radical hysterectomy (95% CI = 72-97%), 66% with chemoradiation (95% CI = 55-75%), and 12% with chemotherapy only (95% CI = 6-20%)[207]. Patients should be encouraged to receive chemoradiation as the first-choice therapy rather than radiation alone, as it has a relatively higher overall survival rate[217]. A meta-analysis of cervical cancer survival rates in East African countries showed pooled one-year, two-year, three-year, four-year, and five-year survival rates of 84%, 71%, 50%, 39%, and 36%, respectively[218]. Additionally, a Moroccan study concluded that the 5-year overall survival rate ranged from 41.3% to 73.6%, while the 3-year overall survival rate ranged from 64.9% to 78.3%. The study also linked survival to age, noting that older patients tend to have lower survival rates[166]. In a Botswana study, the 5-year overall survival rates after chemoradiation were 56.8% for women without HIV and 55.1% for WLWH. The study concluded that regardless of HIV status, hemoglobin levels and stage at diagnosis were associated with survival[219]. The above finding was also confirmed in the same country; well-managed HIV had no significant effect on either chemoradiation, “standalone” radiotherapy, or palliative radiotherapy[220]. Considering this, HIV patients should strictly adhere to antiretroviral therapy, as this increases their chances of survival.

The way forward for Africa

Achieving cervical cancer elimination in Africa requires moving from policy to action, addressing structural barriers, with future efforts grounded in feasible implementation. These efforts should address HPV vaccine delivery issues by adopting and exploring cost-effective vaccination schedules, developing nationwide distribution strategies, and partnering with vaccine manufacturers. Future research can focus on validating the long-term efficacy of the single- or extended-duration two-dose regimen in both the HIV population and the general population. Future efforts also require governments to integrate self-sampling into screening programs, introduce health insurance covering screening and treatment to address existing low screening rates, and strategically invest in decentralized diagnostics and treatment by equipping regional

hospitals with local radiation oncology centers and advanced diagnostic laboratories, thereby reducing reliance on external processing and improving availability and access. This infrastructure must be paired with specialized cancer care centers of excellence. These combined efforts will make elimination a tangible reality.

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Methods

This study analyzes population-level data extracted from the IARC Global Cancer Observatory, WHO Immunization Data Portal, and Gavi, the Vaccine Alliance. To ensure technical consistency, data were harmonized by standardizing country names using ISO-3 codes and age-standardizing cancer rates to the World Standard Population. Descriptive analysis and visualizations were conducted in R (v4.4.2) using the dplyr and ggplot2 packages. For full reproducibility, the processed datasets and custom analysis code are available (See Data and Code Availability).

Data Availability

The compiled and processed dataset generated from these sources for the analysis and visualizations in this study has been deposited in the Zenodo repository under accession code doi.org/10.5281/zenodo.17722637 (https://doi.org/10.5281/zenodo.17512055). Source data are provided with this paper.

Code Availability

R software (version 4.4.2) was used for all analyses and visualization. The custom code used in this study has been deposited in the Zenodo repository under accession code doi.org/10.5281/zenodo.17534613 (https://doi.org/10.5281/zenodo.17511134).

Statement of Competing Interests.

The authors declare no competing interests.

Author Contributions

K.S.O – conceptualization, drafting, tables, and figures, revision; Y.Z – drafting, tables, and revision; D.O.Y – revision; B.S – revision; H.Y – revision; P.M.S – conceptualization and revision.

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Legends

Figure 1. Five-Year Estimated Prevalence of Cervical Cancer in Africa

The figure displays the estimated prevalence in Proportion (World) per 100,000 women. The bar and pie charts show the prevalence of each country and region in Africa, respectively. Light yellow, Pale Pastel Blue, Pale Peach, Deep Red, and Light Lavender represent the Central, Eastern, Northern, Southern, and Western regions, respectively. Eswatini has the highest estimated prevalence, and Egypt has the lowest. Regionally, Eastern Africa (38.9%) has the highest estimated prevalence, followed by Western Africa (25.2%), Southern Africa (18.4%), and Central Africa (14.8%), while the lowest estimated prevalence is in Northern Africa (2.8%).

Source: Data for this figure were obtained from the Global Cancer Observatory 2022. The visual representations were created independently by the authors.

Figure 2. Incidence and Mortality Rates of Cervical Cancer in Africa

This figure shows the Age-Standardized Incidence Rates (ASIR) on the left and Age-Standardized Mortality Rates (ASMR) (per 100,000 women) on the right. The bar and pie charts show the rates of each country and region in Africa, respectively. Dark blue-green, Teal, Gold, Orange, and Coral represent the Central, Eastern, Northern, Southern, and Western regions, respectively. The incidence and mortality rates are highest in Eswatini and lowest in Egypt. Regionally, Eastern Africa (40.8% and 42.6%) has the highest rates, followed by Western Africa (26.8% and 26.3%), Southern Africa (15.5% and 14.4%), and Central Africa (14.7% and 14.9%), while the lowest are found in Northern Africa (2.1% and 1.8%).

Source: Data for this figure were obtained from the Global Cancer Observatory 2022. The visual representations were created independently by the authors.

Figure 3. HPV Vaccination Introduction and Vaccination Coverage in Africa.

This figure shows vaccination introduction in 2024 on the left, with very light gray representing "No introduction," steel blue representing "a full introduction," and light blue-gray representing

"partial introduction." The figure also shows vaccination coverage in 2024 on the right, with steel blue representing the first dose and orange the last.

Vaccination coverage is defined as the percentage of the target population that has received the final dose of the HPV vaccine in a given year. The target population who received the first and last doses of the HPV vaccine in the reporting year are identified as first and last dose, respectively.

Most countries have fully introduced HPV vaccination into their national immunization routines, whereas Nigeria has introduced it partially. Cape Verde and Burkina Faso achieved 99% coverage for the target of first and last doses of vaccines; though Morocco met its target, it has the lowest coverage. Botswana began with 93% first-dose coverage, but decreased by 59% in second (last)-dose coverage (34%), with several other countries also experiencing drops.

Source: Data were obtained from the World Health Organization Immunization Data Portal 2024. The authors created the figure by synthesizing regional datasets and visualizing them.

Figure 4. Eligibility for HPV support from GAVI in Africa.

This figure shows HPV support eligibility, with a very light blue green (Pale Turquoise) representing "Does not include HPV vaccine support", a light pastel blue (Light Blue) representing "Includes HPV vaccine support", and military blue green (Cadet Blue) representing "non-eligible".

Most countries eligible for the HPV vaccination fund have incorporated the HPV vaccination into their national immunization routines. Other countries, however, do not have a national HPV vaccination program despite GAVI support.

Source: Data were obtained from GAVI, The Vaccine Alliance 2025. The authors created the figure by synthesizing data from the country profiles and visualizing them.

Figure 5. Distribution of HPV testing techniques used across Africa.

This figure shows HPV testing techniques used in Africa, with near-white pink/lilac representing "Unavailable", light pastel pink representing "PCR-based", purplish-red representing "Non-PCR-based", and saturated pink-red representing "Both PCR- and Non-PCR-based".

This figure complements the detailed methodological data in Supplementary Dataset 2 by offering a high-level, comparative overview. It provides an immediate overview of the technological landscape in HPV research across Africa, highlighting the proportion of studies employing various methods. PCR-based methods use the classical PCR technique, while non-PCR-based methods use techniques such as isothermal amplification, signal amplification, chemiluminescent detection, etc. Unavailable indicates countries where no relevant HPV study was found or accessible during the literature search and drafting of this work.

Source: This figure was generated by synthesizing data from several primary studies. The full dataset, including individual study details and references, is available in Supplementary Dataset 2.

Table 1. Acceptability and Adverse Events of Thermal Ablation

This table shows that thermal ablation is acceptable (willingness to undergo, satisfaction, and willingness to recommend) and has mild to no adverse effects across studies in Africa.

Table 1. Acceptability and Adverse Events of Thermal Ablation

Country	Study Title	Acceptability Rate	Adverse Events	Ref.
South Africa	Point-of-care testing with Xpert HPV for single-visit, screen-and-treat for cervical cancer prevention	94.6% (same-day treatment)	No serious adverse events	62
Kenya	Safety and Acceptability of Thermal Ablation Among Women Living with HIV in Western Kenya	99.2% (satisfaction rate)	Mild pain (78.8%), vaginal discharge (98.5%), spotting (37.8%)	200
Cameroon	Acceptability and safety of thermal ablation to prevent cervical cancer in sub-Saharan Africa	99.6% (willingness to recommend)	Vaginal discharge (75.5% watery, 21.5% bloody, 14.5% malodorous), mild pain (2.5% severe pain)	201
Burundi	Evaluation of effectiveness, acceptability and safety of thermal ablation in the treatment of cervical neoplasia in Burundi	100% (high satisfaction)	Mild pain/cramps (33%), watery discharge	202
South Africa	Cervical Cancer Screening and Treatment Algorithms Using Human Papillomavirus Testing—Lessons Learnt from a South African Pilot Randomized Controlled Trial	Moderate to high (6/10)	Mild discharge (watery/brown)	204
Malawi	Uptake and safety of community-based "screen-and-treat" with thermal ablation preventive therapy for cervical cancer prevention in rural Lilongwe, Malawi	93% (treatment uptake)	Abnormal vaginal discharge (60%), light vaginal bleeding (52%)	205
Uganda	Experiences with thermal ablation for cervical precancer treatment after self-collection HPV-based screening in the ASPIRE Mayuge randomized trial	98% (willingness to recommend)	Mild pain during treatment (90%), recovery issues (37%: pain, discharge, bleeding)	206

Editor's summary:

Cervical cancer is a largely preventable disease that yet has a high burden and mortality rate in Africa. In here the authors review, the advancement in cervical cancer screening, treatment, and prognosis and advocate for decisive measures to enhance screening methods

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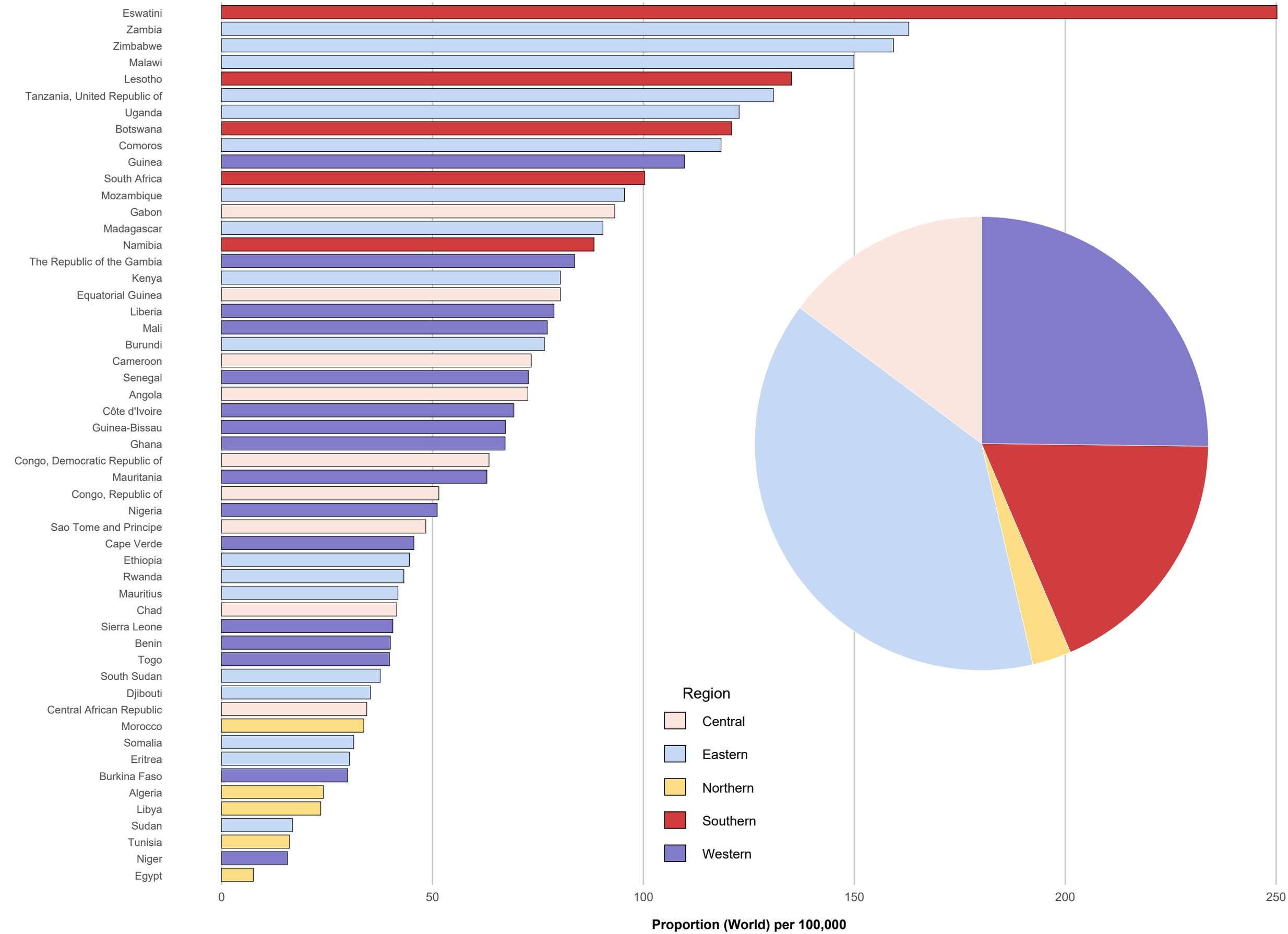
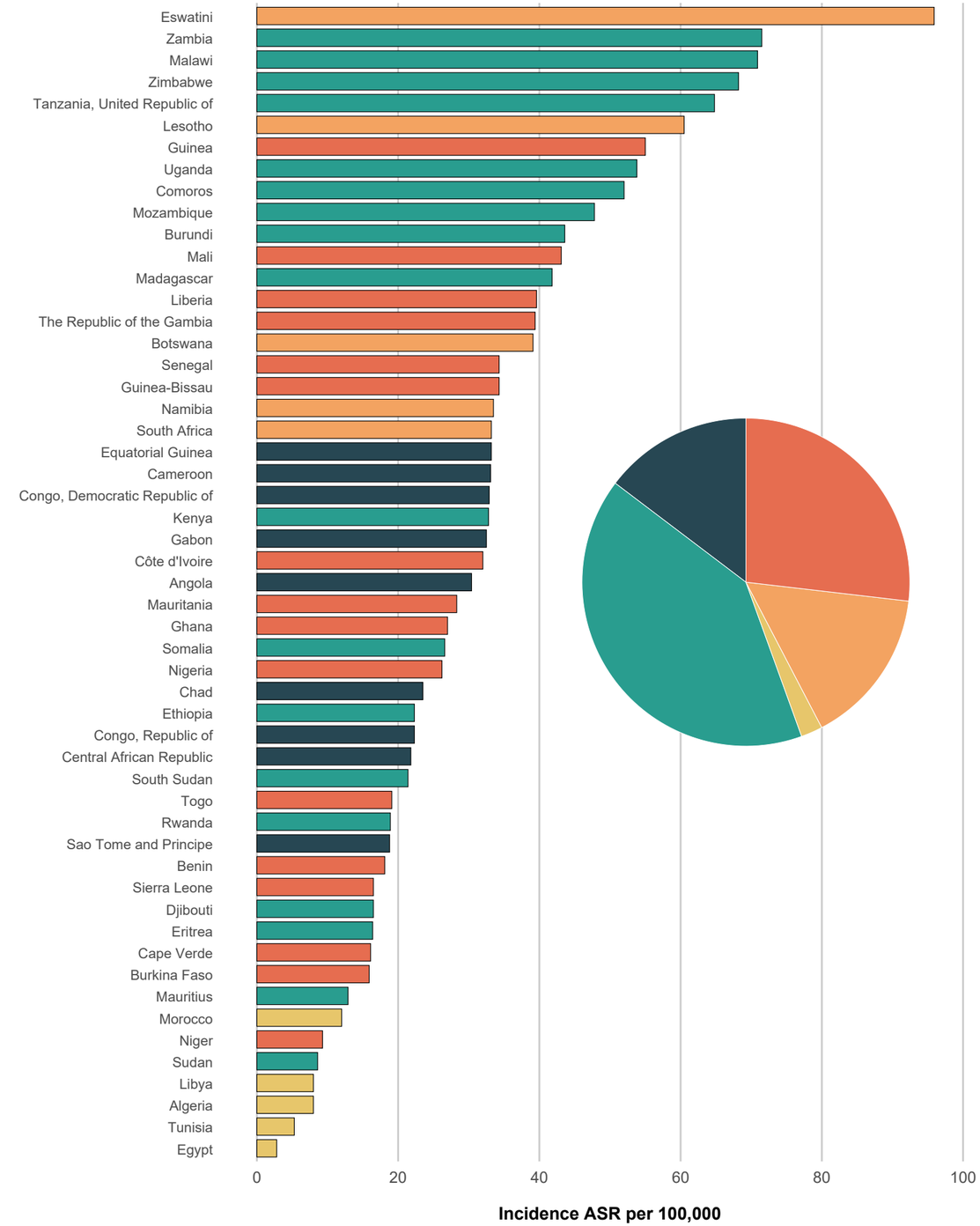
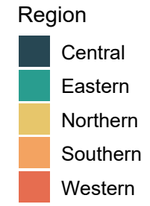
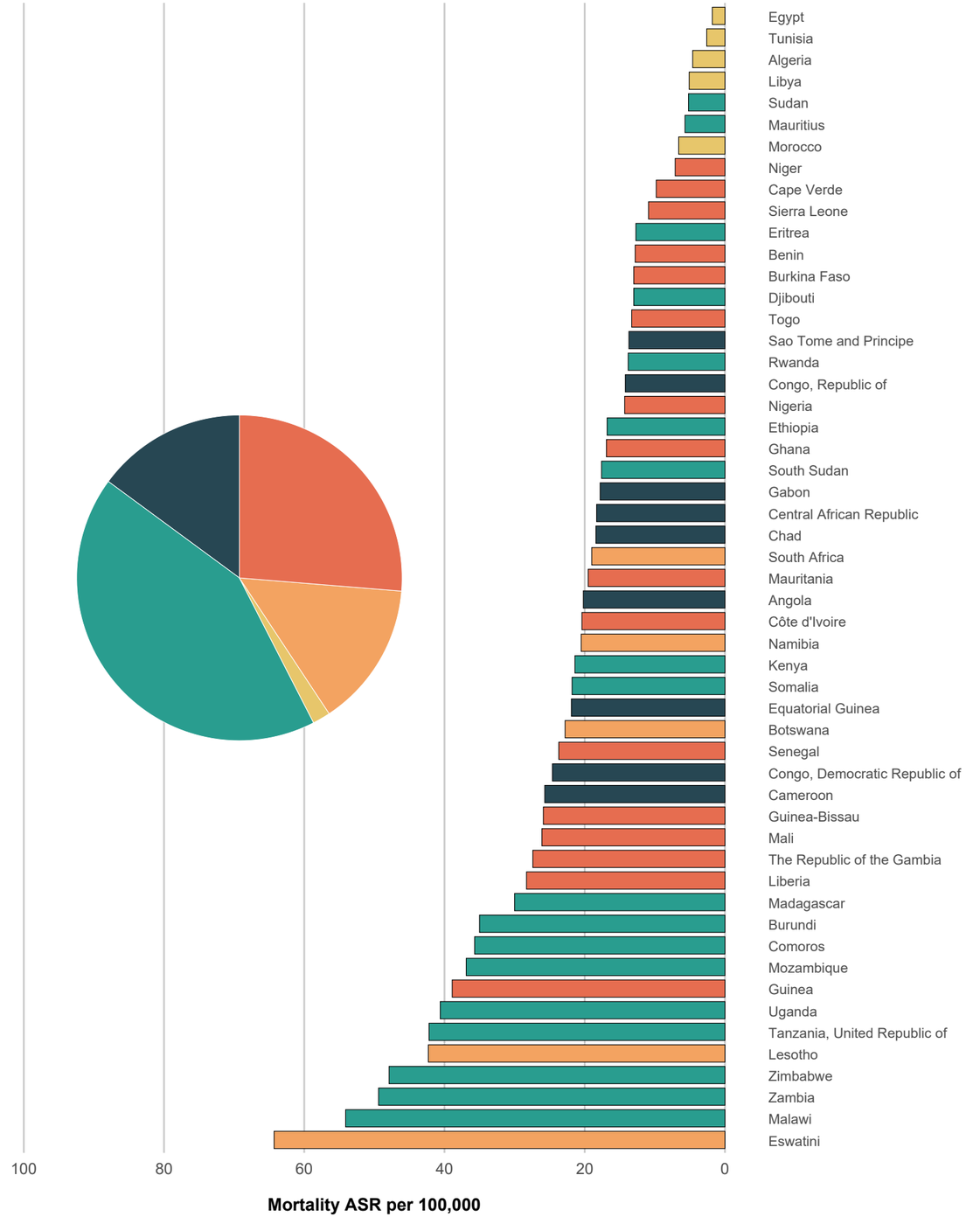

Eswatini
Zambia
Zimbabwe
Malawi
Lesotho
Tanzania, United Republic of
Uganda
Botswana
Comoros
Guinea
South Africa
Mozambique
Gabon
Madagascar
Namibia
The Republic of the Gambia
Kenya
Equatorial Guinea
Liberia
Mali
Burundi
Cameroon
Senegal
Angola
Côte d'Ivoire
Guinea-Bissau
Ghana
Congo, Democratic Republic of
Mauritania
Congo, Republic of
Nigeria
Sao Tome and Principe
Cape Verde
Ethiopia
Rwanda
Mauritius
Chad
Sierra Leone
Benin
Togo
South Sudan
Djibouti
Central African Republic
Morocco
Somalia
Eritrea
Burkina Faso
Algeria
Libya
Sudan
Tunisia
Niger
Egypt
0
50
100
150
200
250
Region
Central
Eastern
Northern
Southern
Western
Proportion (World) per 100,000


Eswatini
Zambia
Malawi
Zimbabwe
Tanzania, United Republic of
Lesotho
Guinea
Uganda
Comoros
Mozambique
Burundi
Mali
Madagascar
Liberia
The Republic of the Gambia
Botswana
Senegal
Guinea-Bissau
Namibia
South Africa
Equatorial Guinea
Cameroon
Congo, Democratic Republic of
Kenya
Gabon
Côte d'Ivoire
Angola
Mauritania
Ghana
Somalia
Nigeria
Chad
Ethiopia
Congo, Republic of
Central African Republic
South Sudan
Togo
Rwanda
Sao Tome and Principe
Benin
Sierra Leone
Djibouti
Eritrea
Cape Verde
Burkina Faso
Mauritius
Morocco
Niger
Sudan
Libya
Algeria
Tunisia
Egypt
0
20
40
60
80
100
Incidence ASR per 100,000


Region
Central
Eastern
Northern
Southern
Western


Egypt
Tunisia
Algeria
Libya
Sudan
Mauritius
Morocco
Niger
Cape Verde
Sierra Leone
Eritrea
Benin
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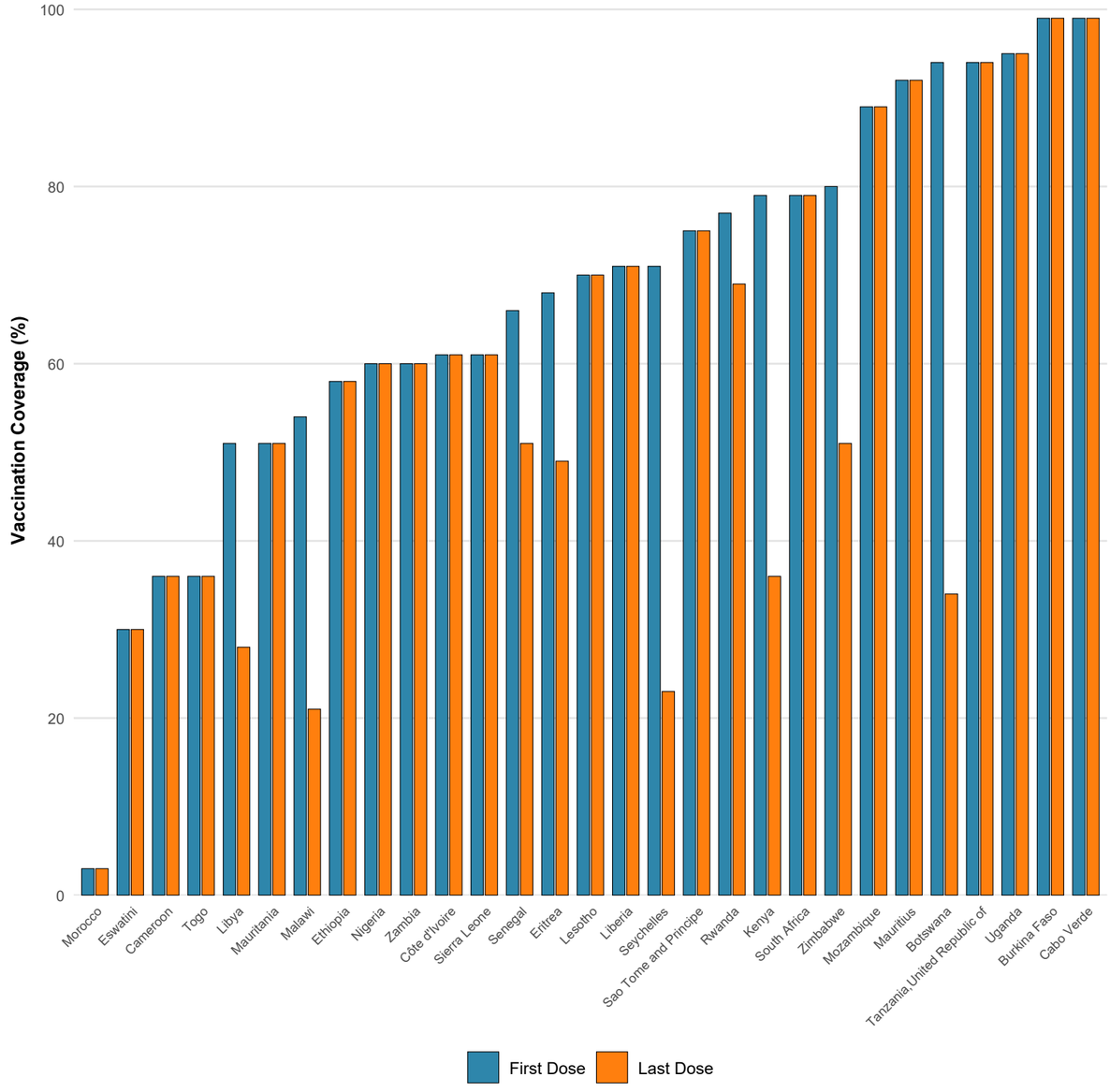
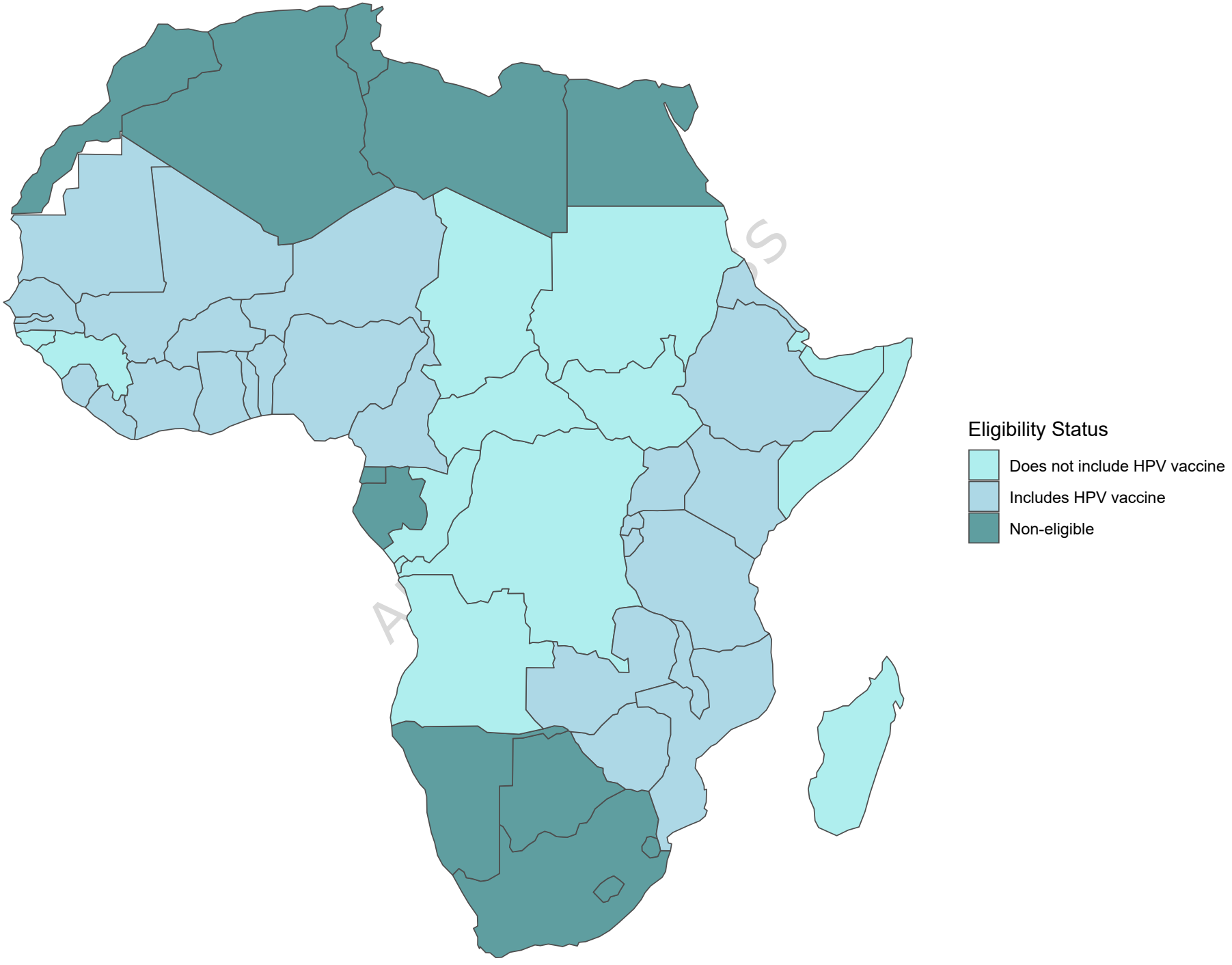
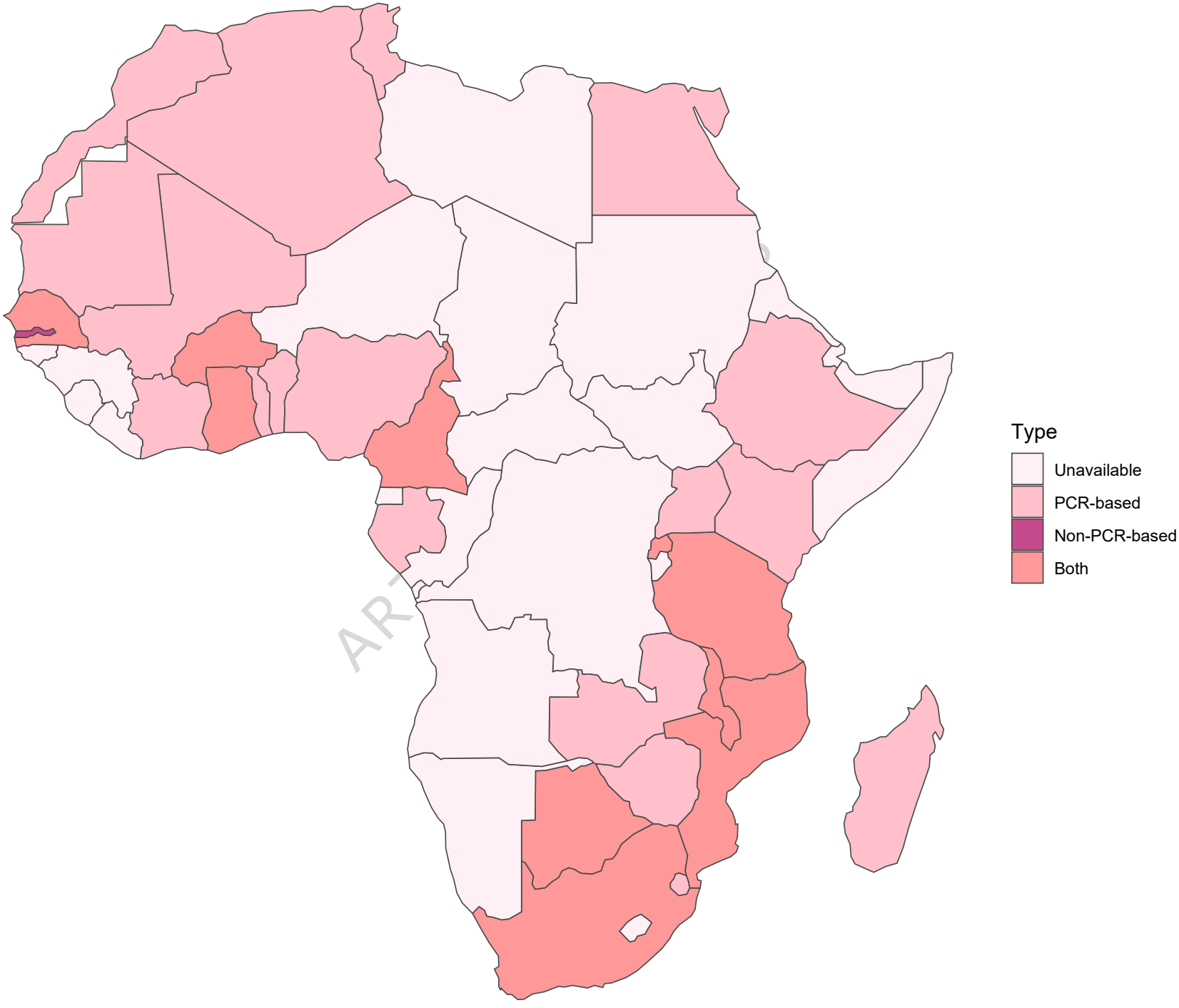
Djibouti
Togo
Sao Tome and Principe
Rwanda
Congo, Republic of
Nigeria
Ethiopia
Ghana
South Sudan
Gabon
Central African Republic
Chad
South Africa
Mauritania
Angola
Côte d'Ivoire
Namibia
Kenya
Somalia
Equatorial Guinea
Botswana
Senegal
Congo, Democratic Republic of
Cameroon
Guinea-Bissau
Mali
The Republic of the Gambia
Liberia
Madagascar
Burundi
Comoros
Mozambique
Guinea
Uganda
Tanzania, United Republic of
Lesotho
Zimbabwe
Zambia
Malawi
Eswatini
100
80
60
40
20
0
Mortality ASR per 100,000


No
Yes
Partial


Vaccination Coverage (%)
100
80
60
40
20
0
Morocco
Eswatini
Cameroon
Togo
Libya
Mauritania
Malawi
Ethiopia
Nigeria
Zambia
Côte d'Ivoire
Sierra Leone
Senegal
Eritrea
Lesotho
Liberia
Seychelles
Sao Tome and Principe
Rwanda
Kenya
South Africa
Zimbabwe
Mozambique
Mauritius
Botswana
Tanzania,United Republic of
Uganda
Burkina Faso
Cabo Verde
First Dose
Last Dose


Eligibility Status
Does not include HPV vaccine
Includes HPV vaccine
Non-eligible


Type
Unavailable
PCR-based
Non-PCR-based
Both