Trends in cervical cancer screening and treatment coverage in sub-Saharan Africa: A systematic analysis of population-based surveys

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Abstract

Background: Cervical cancer (CC) is one of the leading causes of cancer death in sub-Saharan Africa (SSA) among women. Scale-up of prevention programs in high-income countries have contributed to large reductions in CC incidence. However, many countries continue to see rising cases. In SSA, HIV epidemics exacerbate this situation as women living with HIV (WLHIV) are 6 times more likely to develop CC. In 2020, the World Health Organization announced its global strategy for CC elimination as a public health threat. Targets for elimination include having 90% of girls vaccinated against human Papillomavirus (HPV) –the necessary cause of CC–, 70% of all women screened with a high-performance test once by age 35 and again by age 45, and 90% of women with pre-cancer treated and invasive cancer managed by 2030.

Objectives: My thesis aims to improve our understanding of the trends and coverage of CC screening and treatment uptake in SSA. Specifically, I aim to 1) estimate country-level time trends in CC screening, 2) examine coverage of screening by HIV status (3) and measure gaps in achieving the 70% screening and 90% treatment targets.

Methods I collected data from all available nationally representative surveys from SSA with information on CC screening or treatment (2000-2020). Time trends for lifetime and past three years screening among women 25-49 were jointly estimated using a Bayesian multilevel binomial logistic regression model (levels: survey, country, region, SSA) which controlled for the effect of age (5-year age groups) and HIV. For surveys without data on HIV status, I applied standardization based on the UNAIDS HIV prevalence estimates. Post-stratification and imputations for countries without survey information was done to obtain aggregate region- and SSA-level estimates. To measure gaps in the WHO screening goal, I used life-table methods to estimate the proportion of women screened twice by age 45 in 2020. Finally, treatment coverage was estimated using a Bayesian meta-analysis approach.

Results: I pooled 52 surveys across 28 countries (151,338 respondents). In the two regions of Western/Central and Eastern Africa, the proportion of women ever screened remained stable from 2000-2020. In these regions, WLHIV had greater odds of being screened compared to women without HIV. In Southern Africa however, screening coverages had been increasing and WLHIV had equal odds of being screened. Overall, it was estimated that in 2020, 14% (95% Credible intervals [95%CrI]: 11-21%) of women 30-49 years in SSA have been screened in their lifetime for cervical cancer with 12% (95%CrI: 10-18%)

of women having been screened at least twice by the age of 45. On average re-screening rates were found to be 20 times greater than first-time screening rates. Finally, average treatment coverage among the countries with available information was estimated to be 84% (95%CrI: 70-95%).

Discussion: Trends in screening coverages are likely reflective of the presence or lack thereof of effective screening initiatives. Overall, the proportion of women screened twice by age 45 is well below the WHO elimination targets. Additionally, treatment coverage for countries with available data is below the 90% target, however screening currently constitutes the principal bottleneck. Although many countries are beginning to implement HPV vaccination programs in SSA, screening remains highly important for the many cohorts of women who have already been infected with HPV or cannot access a vaccine. As such, improving screening coverage is imperative for the reduction of CC incidence and mortality. Limitations of this analysis include that only 50% of countries have survey data from more than one year to infer time trends. However, strengths include the large number of surveys and countries analyzed.

Conclusion: Overall trends in screening coverage have been stagnant over the past two decades in SSA with significant increases only seen in the Southern Africa region. Although, WLHIV have greater or equal odds of being screened compared to women without HIV, overall screening remains low. Action is needed to increase CC screening and treatment programs to eliminate this preventable disease.

Résumé

Contexte : Le cancer du col de l'utérus (CC) est la principale cause de décès par cancer en Afrique sub-Saharienne (ASS). La mise à l'échelle de programmes de prévention et de traitement dans les pays à revenu élevé a contribué à réduire considérablement l'incidence du CC, mais de nombreux pays continuent de voir le nombre de cas augmenter. En ASS, ces problèmes sont aggravés par l'épidémie de VIH : les femmes vivant avec le VIH (FVVIH) sont six fois plus susceptibles de développer un CC. En 2020, l'Organisation mondiale de la santé (OMS) a annoncé sa stratégie mondiale pour l'élimination du CC comme menace à la santé publique. Les cibles pour atteindre l'élimination incluent la vaccination de 90% des filles contre le virus du Papillome humain (VPH) –la cause du CC–, le dépistage de 70 % des femmes à l'aide d'un test performant une première fois à 35 ans et une seconde fois à 45 ans, et que 90 % des femmes ayant un résultat positif ou anormal soient traitées d'ici 2030.

Objectifs : Ma thèse vise à améliorer notre compréhension des tendances de la couverture du dépistage du CC et de l'adoption du traitement en ASS. Plus précisément, mes objectifs sont 1) d'estimer les tendances temporelles du dépistage du CC dans la population générale et chez les FVVIH, 2) d'examiner les patrons de redépistage afin de calculer la proportion de femmes de 45 ans ayant été dépistée au moins deux fois en 2020, et 3) de mesurer la proportion des femmes traitées pour le CC suite à un dépistage positif.

Méthodes : J'ai colligé toutes les enquêtes populationnelles d'ASS, représentatives au niveau nationale, avec des informations sur le dépistage ou le traitement de la CC (2000-2020). Les tendances temporelles du dépistage à vie et au cours des 3 dernières années chez les femmes de 25 à 49 ans ont été estimées conjointement à l'aide d'un modèle bayésien de régression logistique binomiale multi-niveaux (niveaux : enquête, pays, région, ASS) qui contrôlait pour l'effet de l'âge (groupes d'âge de 5 ans) et du statut VIH. Pour les enquêtes sans données sur le statut VIH, j'ai adopté une approche de standardisation en se basant les estimations de prévalence du VIH de l'ONUSIDA. Une post-stratification et des imputations pour les pays sans information d'enquête ont été effectuées pour obtenir des estimations agrégées au niveau de la région et du continent. Pour mesurer les écarts par rapport à l'objectif de dépistage de l'OMS, j'ai utilisé les méthodes des tables de survie pour estimer la proportion de femmes ayant subi au moins deux dépistages entre 30 et 45 ans. Pour ce faire, j'ai estimé le rapport entre les taux de redépistage et les taux de dépistage initial en exploitant des données transversales ventilées par âge. Enfin, le

recours au traitement du CC chez les femmes avec un dépistage positif a été estimé à l'aide d'une approche de méta-analyse bayésienne.

Résultats : J'ai regroupé 52 enquêtes, réalisées dans 28 pays (151,338 répondants). Dans les régions de l'Afrique centrale/occidentale et orientale, les proportions de femmes ayant déjà subi un dépistage pour le CC sont restées relativement stables entre 2000 et 2020. Dans ces régions, les FVVIH avaient plus de chances d'être dépistées que les femmes séronégatives. En Afrique australe, cependant, la couverture du dépistage a augmenté et il n'existe que peu de différence de dépistage entre les FVVIH et celle séronégatives. Pour l'ensemble de l'ASS, il a été estimé qu'en 2020, 14 % (intervalles de crédibilité à 95 % [ICr à 95 %] : 11-21 %) des femmes de 30 à 49 ans en ASS ont été dépistées au cours de leur vie pour le cancer du col de l'utérus, dont 12% (95% intervalle de crédibilité [ICr]: 10-18%) des femmes de 45 ans auront été dépistées au moins deux fois. En moyenne, les taux de redépistage étaient 20 fois plus élevés que les taux de dépistage initial. Enfin, dans les pays disposant d'enquêtes la proportion de femmes rapportant un dépistage positif ayant été traitée est de 84% (95%ICr : 70-95%).

Discussion : L'absence de progrès significatifs au cours de 20 dernières années reflète l'absence d'initiatives de dépistage efficaces. Globalement, la proportion de femmes de 45 ans dépistées au moins deux fois en 2020 est bien inférieure aux objectifs d'élimination de l'OMS. De plus, l'adoption du traitement dans les pays pour lesquels des données sont disponibles est inférieure à l'objectif de 90 %, mais le dépistage constitue actuellement le principal goulot d'étranglement. Bien que de nombreux pays commencent à mettre en œuvre des programmes de vaccination contre le VPH en ASS, le dépistage reste très important pour les grandes cohortes de femmes qui ont déjà été infectées par le VPH ou qui n'ont pas accès à un vaccin. En tant que tel, l'amélioration de la couverture du dépistage est impérative pour la réduction de l'incidence et de la mortalité des CC. Les limites de cette analyse incluent le fait que seuls 50 % des pays disposent de données d'enquête sur plus d'une année pour déduire les tendances temporelles. Cependant, les points forts incluent le grand nombre d'enquêtes et de pays analysés.

Conclusion : La couverture du dépistage du CC est demeurée stagnante au cours des deux dernières décennies pour l'ASS, et n'a augmenté qu'en Afrique australe. Bien que les FVVIH aient des chances supérieures ou égales d'être dépistées par rapport aux femmes séronégatives, globalement le dépistage du CC reste faible. Des actions sont nécessaires pour améliorer le dépistage du CC et les programmes de traitement afin d'éliminer cette maladie.

Preface

This thesis evaluates the prevalence of cervical cancer screening and treatment coverage using population-based surveys in sub-Saharan Africa for both women living with HIV and the general population. Throughout this thesis, I use the term *women* to refer to individuals with a uterus who are susceptible to the development of cervical cancer. This report begins with an introduction to provide contextual information regarding the current global state of cervical cancer, cervical cancer in sub-Saharan Africa, and the recent proposed strategy for the elimination of cervical cancer as a public health threat. Chapter 1 reviews the literature regarding cervical cancer, including its epidemiology, national history, and methods employed for its prevention. Chapter 2 presents the objectives. Chapter 3 describes the methodology employed. Chapter 4 consists of a manuscript that summarizes the importance of this work, the methodology, results, and a discussion of their relevance, limitations, and strengths . Finally, Chapter 5 situates these results within the broader context of cervical cancer prevention efforts and Chapter 6 provides concluding remarks to this work.

This thesis was prepared in the style of a Manuscript-Based Thesis. Results are given in the following manuscript:

> **Lily Yang**, Marie-Claude Boily, Minttu Rönn, Dorcas Obiri-Yeboah, Imran Morhason-Bello, Nicolas Meda, Olga Lompo, Philippe Mayaud, Michael Pickles, Marc Brisson, Caroline Hodgins, Sinead Delany-Moretlwe, Mathieu Maheu-Giroux. Regional and national-level trends in cervical cancer screening coverage in high HIV prevalence settings: a systematic analysis of population-based surveys in sub-Saharan Africa (2000-2020).
>
> Some of the results will also be presented at the following conference:
>
> **L Yang**, MC Boily, M Rönn, S Delany-Moretlwe, D Obiri-Yeboah, I Morhason-Bello, N Meda, T Gauthier, P Mayaud, M Pickles, M Brisson, M Maheu-Giroux. Cervical cancer screening among women living with HIV: a systematic analysis of population-based surveys in sub-Saharan Africa. Poster presentation. *The 24th International AIDS Conference.* July 2022.

Contribution of Authors

LY and MM-G conceptualized the project. LY conducted the literature review, search for surveys and harmonized survey data. LY and MM-G conceived the model for analysis and MB, MMR, and MP contributed to the development of the methodology for the second objective regarding re-screening estimates. All authors provided inputs on the methodology and statistical analyses. LY oversaw data management, coded the statistical models, performed model checks, and wrote the manuscript. All authors contributed to interpretation of the results and reviewed the manuscript.

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List of Abbreviations/Acronyms

AIDS	Acquired Immunodeficiency Syndrome
ASIR	Age-Standardized Incidence Rate
ASMR	Age-Standardized Mortality Rate
CC	Cervical Cancer
CI	Confidence Interval
CIN	Cervical Intraepithelial Neoplasia
CrI	Credible Interval
DHS	Demographic Health Surveys
FIGO	International Federation of Gynecology and Obstetrics
GAVI	Global Alliance for Vaccines and Immunization
HIV	Human Immunodeficiency Virus
HPV	Human Papillomavirus
HSIL	High-grade Squamous Intraepithelial Lesion
KAIS	Kenya Aids Indicator Survey
LBC	Liquid Based Cytology
LEEP	Loop Electrosurgical Excision Procedure
LLETZ	Large Loop Excision of Transformation Zone
LSIL	Low-grade Squamous Intraepithelial Lesion
OR	Odds Ratio
PHIA	Population-based HIV Impact Assessment
PSU	Primary Sampling Unit
SABSSM	South Africa National HIV Prevalence, Incidence, Behavior and Communication Survey
SAGE	Study on Global AGEing and Adult Health
SDG	Sustainable Development Goals
SSA	Sub-Saharan Africa
STEPS	STEPwise Approach to NCD Risk Factor Surveillance
UNAIDS	The Joint United Nations Programme on HIV/AIDS
VIA	Visual Inspection with Acetic Acid
VILI	Visual Inspection with Lugol's Iodine
WHS	World Health Surveys
WHO	World Health Organization
WLHIV	Women living with HIV

Introduction

Cervical cancer is the fourth most common cancer and cause of cancer death among women despite its highly preventable nature (1). This disease is caused by the sexually transmitted human Papillomavirus (HPV) and has a long pre-cancerous phase which creates ample opportunity for detection prior to the development of invasive cancer (2). As a result, early primary and secondary prevention techniques through HPV vaccinations and screening have allowed for large reductions in cervical cancer incidence in many high-income countries (3-5). In contrast, many low- and middle-income countries continue to see rising incidence and mortality, with sub-Saharan Africa having the highest burden of disease (1, 6).

In sub-Saharan Africa, the effects of cervical cancer (CC) are exacerbated by the high burden of HIV epidemics. Women living with HIV (WLHIV) have a higher risk of acquiring HPV infection and are 6 times more likely to develop CC (7). In the region, it is estimated that 1 in 5 cases of cancer can be attributable to HIV (8). Public health efforts should ensure that this population has adequate access to vaccinations, screening, and treatment.

In 2020, the World Health Organization (WHO) announced its global strategy for the elimination of cervical cancer alongside updated recommendations for primary and secondary prevention approaches for both the general population and WLHIV (9, 10). Included in these goals are targets for vaccinations, screening, and treatment coverage. To effectively reach these goals it is necessary to understand historical progress and to benchmark and monitor program indicators. Currently, however, information regarding CC screening coverage, as well as the subsequent cascade of care (e.g., re-screening and treatment) is limited.

Objectives

This thesis aims to address knowledge gaps regarding current progress towards the WHO CC elimination goals in sub-Saharan Africa. Using nationally representative population-based surveys, this thesis explores trends in screening coverage, for both the general population and WLHIV, and furthers our understanding of the CC screening care and treatment cascade, including rates of re-screening and treatment coverage.

Chapter 1

Literature Review

In this first chapter, I will provide a brief overview of cervical cancer (CC), its natural history, and its epidemiology, with a focus on women living with HIV (WLHIV). Then, I will present the history and methods developed for the primary and secondary prevention of the disease, and the strategies implemented in low-resource settings to promote uptake. Finally, I will discuss the World Health Organization (WHO) elimination goals put forward in 2020 and explore the methods and data used to track progress towards these goals.

1.1 Epidemiology and natural history of cervical cancer

1.1.1 Burden and epidemiology of cervical cancer

Globally, CC is the fourth most common cancer and cause of cancer death among women with an estimated 604,000 new cases and 342,000 deaths attributed to the disease in 2020 (1, 11). The disease is characterized by the severe and abnormal growth of cells in the cervix and is caused by infection with the sexually transmitted human Papillomavirus (HPV) in virtually all cases (2, 12). Despite its high burden, CC is entirely avoidable: preventable through vaccination and screening, and curable through early detection and treatment. Furthermore, it often develops during a women's most economically productive years and as such have significant economic and social implications on a women's family and community (13).

It is expected that without any intervention, there will be 45 million more cases in the next 50 years with 30 million cases and 15 million deaths occurring in low-and middle-income countries (LMICs) (14). The average global age-standardized incidence rate (ASIR) of CC has been estimated to be 13.1 per 100 000 women-years and the age-standardized CC mortality rate (ASMR) to be 6.9 per 100 000 women-years (1). Overall, both rates have followed declining trends over the past two decades owing to the implementation of successful prevention and early treatment strategies primarily in high-income countries (1, 15).

In contrast to high-income countries, sub-Saharan Africa has witnessed an increase in CC incidence over the past 25 years where CC is the second most common cancer and the leading cause of cancer death among women (16, 17). Approximately 80% of all CC cases can be found in LMICs including countries in sub-Saharan Africa where the ASIR is 2-3 times greater than the global average and ranges from 26.8 per 100 000 women-years in Central Africa to 43.1 per 100 000 women-years in Southern Africa (1). Mortality is also much greater in sub-Saharan Africa in comparison to high-income countries, ranging from 20 per 100 000 women-years in Southern Africa to 30 per 100 000 women-years in Eastern Africa which is 3 to 4 times greater than the global average (1). Furthermore, it is estimated that the 3- and 5-year survival of CC in 11 countries of sub-Saharan Africa are 45% and 33%, respectively (18). In comparison, the 3-year survival rate in the United States was estimated at 74% (18).

1.1.2 Natural history of cervical cancer

Nearly all CCs can be attributed to HPV with HPV16 and HPV18 responsible for over 70% of all cases (19, 20). HPV types can be sub-divided into two categories: 1) high-risk HPV types (e.g., HPVs 16 and 18) which are considered oncogenic strains most commonly associated with cancer and 2) low-risk HPV types (e.g., HPVs 6 and 11) which are non-carcinogenic and only cause benign disease (e.g. genital warts) (21). Although most HPV infections will resolve themselves within a few years, a proportion of infections will persist, increasing the risk for cervical lesions and subsequent development of CC (22, 23). Most lesions are characterized by neoplastic growth of cervical cells on the surface of an area known as the transformation zone. Once this growth crosses the surface of the cervix and invasion of the basement membrane occurs, is it considered cancer (24). CC can be divided into two primary types, cervical squamous cell carcinoma, the most common type of the disease, and cervical adenocarcinoma which is estimated to make up 7-29% of all CCs (25).

Most cervical lesions are categorized as either low-grade or high-grade squamous intraepithelial lesions (LSIL or HSIL) and are also commonly classified into one of three levels of cervical intraepithelial neoplasia (CIN) (24, 26). The first level, CIN-1, is equivalent to LSIL and is characterized by lesions that are only present within one-thirds of the cervical epithelium. Such lesions are considered low-risk and will regress in most cases (27). Persistence of CIN-1 may lead to CIN-2 and CIN-3, which are HSIL and are defined as

lesions which cover at least two-thirds of the epithelium. Although ambiguities exist regarding the severity of CIN-2, these lesions are generally considered to be pre-cancerous and require treatment (28-30). Finally, persistence of CIN-2/3 may lead to the development of squamous cell carcinoma. Once it becomes invasive disease, CC is classified into four stages often based on level of invasion and loco-regional and distant spread, as defined by the *2009 International Federation of Gynecology and Obstetrics* (FIGO) guidelines (31). This staging then helps to determine prognosis and treatment plans (31).

Although data is limited, the development of pre-cancerous lesions generally occurs within 7-10 years after initial HPV infection. Once pre-cancerous lesions appear, it can take more than 10 years for CC to develop (32). A unique retrospective cohort study using data from 1229 New Zealand women, who were withheld treatment in an unethical clinical study in the 1960s, found that 31-50% of women who had CIN-3 developed CC within 30 years (33).

1.1.3 Cervical cancer among WLHIV

CC is classified as an Acquired Immunodeficiency Syndrome (AIDS) -defining illness and WLHIV are at a significantly increased risk for HPV persistence and the subsequent development of cancer. Globally, close to 5% of all CCs can be attributed to HIV (7). In sub-Saharan Africa, however, this proportion rises to 20% of all CCs due to an HPV/HIV syndemic (synergistic epidemic) (7). Overall, 85% of all WLHIV with CC reside in sub-Saharan Africa (7).

Studies have shown that both the incidence and persistence of HPV infection is greater in WLHIV, and these women are 6 times more likely to develop CC in comparison to the general population (7, 34-36). Both direct biological interactions, as well as indirect immunosuppressive effects of HPV/HIV co-infection, have been theorized to contribute to this association. A small number of studies have suggested that interactions between the HPV and HIV virus can trigger the upregulation of the HPV oncogenes E6 and E7 (37, 38).

As HIV primarily targets CD4+ immune cells, many studies have been conducted to examine the immunosuppressive of effects of HIV on CC progression; more specifically, the relationship between CD4+ cell counts, antiretroviral therapy (ART) and the progression of

cervical disease (12, 39). Currently, weak evidence points to correlations between decreased CD4+ cell counts, and increased incidence of HPV infection and progression of pre-cancerous cervical disease (34, 40-42). However, when looking at the relationship between CD4+ cell counts and progression to invasive CC, the evidence becomes much less clear (41). Similarly, evidence regarding ART and CC incidence have also yielded mixed results. ART is used to treat individuals living with HIV and allows for a rebounding of CD4+ cell counts, thus, partially mitigating the immunosuppressive effects of HIV infection (43). Some studies have suggested ART is protective against the development of CC whereas other studies have shown no effect (42, 44, 45). Overall, however, the current pool of evidence points to the likely protection of ART against the development of CC in WLHIV (46). Despite this, ART alone is likely not sufficient to bring CC incidence among WLHIV to the levels of the general population. A meta-analysis of 11 studies found that CC, unlike other AIDS-defining cancers such as Kaposi's sarcoma and Non-Hodgkin's Lymphoma, has seen an increase in incidence among WLHIV since the introduction of combination ART (47). The authors postulate that this may be due to longer lifespans of WLHIV, minimal effectiveness of ART on CC development, and inadequate CC screening of WLHIV (47). As access to ART increases, and mortality in WLHIV decreases, the incidence of CC is also expected to increase in this population (48). As a result, early detection and treatment through CC screening remains essential for WLHIV both on and off ART. (48).

1.2 Cervical cancer prevention and treatment methods

HPV vaccinations and CC screening at regular intervals has been associated with significantly reduced risks of CC development (4, 49). As such, the introduction of CC screening in the early 1960s and HPV vaccinations in the 2000s, have resulted in dramatic reductions of CC incidence and mortality in high-income countries (3, 5). This following section will detail the history and development of CC prevention and treatment methods including current practices, and the most common screening methods and treatment strategies.

1.2.1 Screening methods for pre-cancerous cervical lesions and cervical cancer

Screening began with the development of the "Pap smear" otherwise known as conventional cervical cytology by Dr. George N. Papanicolaou. In the early 1900s,

Papanicolaou and Dr. Aurel A. Babes, separately identified the potential in using cells exfoliated from the cervicovaginal area to visualize cell morphology using microscopy for the detection of cervical lesions. In 1941, Papanicolaou alongside Dr. Herbert F. Trout published a landmark paper which detailed the method and demonstrated its ability to detect pre-cancerous and cancerous cervical lesions in otherwise asymptomatic individuals (50). Following this, screening programs using cytology began to be endorsed by governments, health professionals, and cancer organizations resulting in its widespread implementation in high-income countries over the next few decades (51).

Despite its ubiquitous use in high-income settings, many limitations exist to this technique. For LMICs, the resource-intensive nature of the method (i.e., requirement of specialized medical equipment and skilled technicians) makes its widespread implementation in many countries challenging (52, 53). In addition, differences in cell collection and fixation techniques between technicians makes the method difficult to standardize (53).

Liquid-based cytology (LBC) has been developed to address issues of reproducibility associated with conventional cytology. While there are various types of liquid-based systems (e.g., SurePath and ThinPrep, named as per their manufacturers' trademarks), this technique generally involves placement of cell samples in a preservative liquid after collection, followed by processing to remove cell clumping and unwanted cell types, and finally preparation of thin monolayers of cells on glass slides (53). In theory, this decreases the number of inadequate samples and improves interpretation of cytology results. Studies conducted comparing LBC to conventional cytology suggest that LBC is no more sensitive or specific than conventional cytology (53, 54). However, advantages of LBC include more consistent and adequate cervical samples that are more reliably interpreted (55-58). Furthermore, technology continues to be developed to improve upon this method. Automation of LBC systems have started to become more commonly used and machine learning technologies are currently being developed with the hopes of improving validity and reproducibility (52, 53, 59). Currently, LBCs are preferred in many high-income countries as it allows for standardization, increased efficiency, and are amenable to use with HPV testing. Despite this, these systems are cost prohibitive, which hamper their widespread adoption in LMICs (58, 60).

Visual inspection with acetic acid (VIA) is a screening approach adapted for low-resource settings (61). Rather than using microscopy, which is required for cytology, VIA allows for the identification of abnormal cells using the "naked eye". As abnormal cervical cells turn white when exposed to acetic acid, this technique involves the application of 3% to 5% acetic acid to the transformation zone of the cervix followed by the identification of the presence or lack thereof, of an aceto-whitening reaction. (61). Visual inspection with Lugol's Iodine (VILI) is a similar approach (62). These inspection methods are much less resource intensive, can be taught to nurses and midwifes, and can provide instant results allowing for same day treatment using screen-and-treat approaches (61). Studies have found that VIA, followed by treatment (if recommended), is effective in reducing population-level CC incidence and mortality (63). However, limitations of this method include the subjective nature of the technique which result in issues with validity and reliability (64). Efforts have been made to reduce subjectivity, such as the development of digital-VIA alongside smartphone technology to assist health practitioners (64, 65). Despite lower sensitivity and specificity of VIA in comparison to other methods, its effectiveness in reducing disease incidence, compatibility with same-day treatment and low-cost have resulted in its recommendation in many low-resource settings (61).

In contrast to cytology and VIA, which visualizes cytological changes, HPV DNA testing screens for present and future risk of CC through the targeted identification of levels of high-risk HPV DNA in the cervix that is likely associated with existing lesions (66). HPV DNA testing has been found to be more sensitive than other screening methods, although it is less specific because it can identify the presence of high-risk HPV in the cervix before cervical lesions develop (64, 67). Thus, with more false positives, standalone HPV DNA testing can contribute to over treatment if the presence of high-risk HPV is acted upon by a practitioner without first confirming its association with existing pre-cancerous or cancerous lesions (64, 67). Triaging approaches using a second screening modality such as VIA or cytology for women positive for high-risk HPV can potentially address this issue. Such an approach has been found to decrease the number of women treated without impacting sensitivity for women with CIN-3 (64). Although studies have also suggested HPV DNA testing alone may be more effective because of its much greater sensitivity despite the overdiagnosis and overtreatment that may ensue (61, 64, 68). Overall, a few large studies have found significant reductions in CC incidence following the implementation of HPV DNA testing (69-71). Furthermore, adaptations of this method for self-sampling helps to

address many traditional barriers to screening such as discomfort and fear as well as accessibility issues for those living far from a health clinic (62, 72).

Colposcopy is not a screening method *per se,* but it is often performed after an initial abnormal screening test (i.e., Pap test, VIA/VILI, HPV test) for diagnostic confirmation. Colposcopy refers to the use of a stereoscopic microscope –the colposcope– for magnified visualization of the cervix (73). Similarly to VIA, a 3% to 5% acetic acid solution or Lugol's iodine will often also be applied to examine cervical lesions more closely and assess the whitening density of the area. If necessary, colposcopic biopsies can also be obtained for closer histopathological analysis (73). Colposcopy is advantageous as it allows further ascertainment of ambiguous or uncertain results and can reduce over-treatment of low-grade lesions (73). Conversely, the procedure may be uncomfortable, and some studies have recommended against its use if CC is not suspected (73, 74).

HPV DNA testing is currently regarded as a high-performance screening test and is the recommended method of screening for many countries and organizations, including the WHO (10, 62, 66, 75, 76). This is due to the high sensitivity of the test as well as its cost-effectiveness in comparison to other methods (77, 78). Despite these advantages however, concerns remains about the affordability of HPV DNA testing which prevents its uptake in many low-resource settings (62, 66, 76). A study of the cost-effectiveness of various screening strategies in Burkina Faso among WLHIV found that CareHPV (a point-of-care HPV test) costs $23.87 USD in comparison to VIA which costs much less at $3.22 USD (78). Thus, despite greater cost-effectiveness of HPV testing, VIA may be more feasible for many low-resource settings that are not be able to currently afford the initial costs of HPV testing (61). Regardless of screening method however, tests that can be done during a single visit such as VIA or point-of-care HPV tests have been found to be more effective than tests which required multiple visits such as cytology (77).

1.2.2 Treatment methods for pre-cancerous cervical lesions and cervical cancer

Many strategies exist for the treatment of pre-cancerous lesions and CC (79). For pre-cancerous lesions, the two most common ablation techniques are cryotherapy and thermal ablation which involves the destruction of abnormal cells in the transformation zone using either extreme cold or heat, respectively (61, 79). Excision, on the other hand, involves the

surgical removal of the abnormal growth with common techniques including large loop excision of transformation zone (LLETZ, as known in the European literature) –otherwise known as loop electrosurgical excision procedure (LEEP) in the North American literature– or cold knife conization (CKC) (61, 79). Currently, cryotherapy is the treatment recommended by the WHO for eligible women where eligibility depends on the accessibility and size of the lesion (61, 79). If the lesion is too large or difficult to reach, LEEP is the recommended treatment. More recently, the WHO has also begun to support the use of thermal ablation as an acceptable alternative to cryotherapy, especially in countries were cryotherapy equipment may be unaffordable (61).

For women who have progressed to invasive CC, other techniques must be considered to treat the disease, including chemotherapy, radiotherapy, surgery, and immunotherapy. Women in the early stages of CC can be treated relatively easily, however those who have progressed to metastatic disease or have recurrent cancer can often only be given palliative treatment (80). Conversely however, cure is possible for women who have had treatment for pre-cancerous lesions pointing to the importance of screening and early treatment. In these women, recurrence of a precancerous lesion or progression to invasion is uncommon and when it occurs, it is often due to the initial incomplete excision of the lesion (81, 82).

To improve treatment coverage and mitigate issues that arise due to losses to follow-up in low-resource settings, screen-and-treat approaches are commonly used. Screen-and-treat involves initial testing with VIA or a point-of-care HPV test that allows for same day results (74). If an abnormal or suspect cancer result is obtained, treatment such as cryotherapy, can then be done on eligible women in the same visit (74). Screen, triage and treat approaches have also become increasingly widespread which uses a secondary screening test such as VIA or colposcopy following a positive HPV test to confirm cervical abnormalities (68, 83). Overall, screen-and-treat approaches alongside other variations such as screen, triage and treat, and screen, notify, screen-and-treat have been found to be an effective strategy which has contributed to significant success in decreasing incidence and mortality of CC (83-86). Additionally, to target WLHIV, many screen-and-treat programs have been placed within existing HIV care clinics (87, 88). A 2018 review found that this integration was feasible and acceptable to both staff and patients, however more studies need to be conducted to evaluate its effectiveness in increasing screening coverage and reducing cancer burden (88).

1.2.3 HPV vaccination

In the early 1980s, Dr. Harold zur Hausen first demonstrated the link between HPV and CC. This discovery was monumental as having an infectious agent as the cause of a cancer meant that it could be immunized against and prevented. In 2006, the first HPV vaccine, Gardasil, a quadrivalent vaccine against HPV 6/11/16 and 18, and was first approved for use after completed clinical trials (89). Soon after, Cervarix (a bivalent vaccine against HPV 16/18) and Gardasil-9 (a nonvalent vaccine against HPV 6/11/16/18/31/33/45/52/58) were approved in 2007 and 2014, respectively (90). Research into the effectiveness of these vaccines have found that they significantly reduce risk of both pre-cancer and invasive CC and are able to prevent over 95% of HPV infections specific to the HPV type of the vaccine (4, 91-93). Furthermore, high levels of HPV vaccine coverage in a population also offer herd immunity benefits (94). Despite the high efficacy of HPV vaccines in the general population, concerns exist about its efficacy in people living with HIV as some studies have shown reduced effectiveness of the vaccine in this population (95).

As of 2019, over 100 countries have established national HPV vaccination programs with most vaccination campaigns targeting adolescent girls around the age of 12 with two-doses within a 6-month period (93, 96). Currently in Canada, all three vaccine types are approved for use in females 9-45 years and males 9-26 years (97). In resource-limited settings, however, the WHO recommends the prioritization of girls 9-13 years for vaccination before sexual debut (98). Furthermore, to aid in the roll-out of HPV vaccination programs in low-resource settings many partnerships have been formed between international organizations (e.g., Global Alliance for Vaccines and Immunizations (GAVI) and Merck) and national Ministries of Health. GAVI for example, has created a demonstration projects program whereby eligible countries interested in starting HPV vaccination programs may receive monetary support (99). Altogether, these partnerships primarily help to subsidize costs and have seen high vaccine uptake and final dose coverage (100-103). Additionally, countries such as Rwanda have attributed their vaccine success to multisectoral collaboration (e.g., between the Ministry of Health and Ministry of education) and involvement of local leaders and community members (101, 104).

1.3 Global strategy for the elimination of cervical cancer

1.3.1 WHO elimination goals

The incidence and mortality of CC has been rising over the past few years in LMICs. Without intervention, it has been predicted that mortality could rise to 443,000 deaths in 2030 with the majority of deaths occurring in sub-Saharan Africa (11, 105). To address this, the WHO Director-General announced in May of 2018 a global call to action for the development of a strategy to eliminate CC as a public health threat. In August of 2020, a strategy was adopted for the acceleration of CC elimination. Specifically, the WHO has put forward the 90-70-90 goals to have, by 2030, 90% of all girls fully vaccinated against HPV by the age of 15, 70% of all women screened once by 35 and again by 45 with a high-performance test (i.e., HPV DNA testing), and finally 90% of all women with pre-cancer or cancer treated (106). Modelling studies suggested that if targets for the WHO elimination strategy are achieved, over the next 100 years, CC mortality could decrease by 99% and 62 million lives may be saved (107).

1.3.2 WHO screening and treatment guidelines

As HPV vaccination programs are being scaled-up, large cohorts of unvaccinated women still remain at risk of CC thus having effective and accessible screening programs is crucial. Alongside ambitious elimination objectives, the WHO has also released updated guidelines for CC screening and treatment in 2021. These guidelines include evidence-based recommendations for both the general population of women as well as WLHIV. For all women, HPV DNA testing is the recommend screening modality over VIA and cytology. In addition, women without HIV are recommended to have regular screenings between the ages of 30-49 and to be screened every 5 to 10 years when HPV DNA testing is available or every 3 years when using VIA or cytology. In contrast, WLHIV are recommended to be screened between 25-49 and at intervals of 3 to 5 years when using HPV DNA testing or every 3 years when using VIA or cytology. Finally, either a screen-and-treat approach or screen, triage and treat approach is recommended for the general population, whereas only the screen, triage, and treat approach is recommended for WLHIV (10).

1.3.3 Monitoring progress towards the WHO cervical cancer elimination goals

Estimates of screening and treatment coverage are currently limited. Most studies investigating screening rates leverage regional cohort studies, but these are not nationally representative. Other studies have used population-based surveys to estimate national screening proportions, however, geographical, and temporal coverage of these cross-sectional surveys are limited. Estimates that are available regarding screening coverage suggest that screening is quite low across sub-Saharan Africa with a 2017 study estimating that only 10% of women have ever been screened for CC in this region (108). A WHO report from 2020 suggested that 5% of countries had less than 10% screening coverage, 10% had 10-50% coverage, and less than 5% had 50-70% coverage (109). Most recently, a 2021 meta-analysis estimated that lifetime cervical screening coverage was 13% in sub-Saharan Africa, with 8% screening in Southern Africa and 14% screening in Eastern Africa (110). This review however, only used data from 12 countries in sub-Saharan Africa. Overall, available studies suggest that there is considerable heterogeneity between countries however overall lifetime screening coverage is well below the 70% WHO target for 2030.

Although estimates for lifetime screening are important, it is also important to ensure that women are also being screened at regular intervals. Data regarding re-screening however is quite sparse and limited to individual country, cohort, or cross-sectional studies. Available research shows a large range of values for re-screening rates. One retrospective cohort study using data from an HIV clinic in Harare, Zimbabwe between 2012 and 2018 found that 74% of WLHIV who initially tested negative were re-screened after 12 months, 78% of WLHIV who initially tested positive were treated within 6 months, and 80% of women attended a follow up appointment within 6 months (111). However, an investigation of screening coverage in Mozambique found that only 29% of all women were screened more than once (112). Altogether, rates of re-screening appear to be variable across different countries, however more data on re-screening needs to be collected to evaluate the screening cascade and measure progress towards re-screening goals.

Finally, efficient treatment programs upon detection of an abnormal screening result is essential to decreasing burden. Data on treatment coverage however is also quite varied and sparse. One review found that proportion treated ranged between 24-67% among those diagnosed with CC in Tanzania, Zimbabwe, Uganda, and Nigeria (113). However, a cohort

study in Lusaka, Zambia between 2010 and 2019 found that 76% of women who screened positive received treatment with 34% receiving cryotherapy on the day of (114). Finally, a study in Johannesburg, South Africa found that only 26% of women with a high-risk Pap test completed any sort of follow-up (e.g., colposcopic biopsy or treatment) within 18 months of screening (85). Overall, data on treatment coverage is limited in sub-Saharan Africa despite the prominence of this indicator (the third 90%) in the WHO elimination strategy.

1.4 Concluding remarks

CC is a highly preventable disease with effective, evidence-based primary and secondary prevention methods available. As the cancer is caused by an infectious agent and has a long pre-cancerous stage, adequate implementation of prevention techniques can very possibly lead to the elimination of this disease as a public health threat. To monitor progress, however, continuous appraisal of the screening and treatment cascades is necessary. In sub-Saharan Africa there are a few studies that investigate lifetime screening trends; however, these studies are limited to a few countries in the region. To date, there has yet to be a comprehensive analysis of trends in CC screening in sub-Saharan Africa and limited analysis exists regarding rates of re-screening and treatment coverage. Importantly, potential unmet screening needs among WLHIV have not been assessed in this region where 4% of women are estimated to live with HIV.

As will be described in the following chapter, this thesis aims to address these knowledge gaps and improve our understanding of progress towards the WHO elimination goals.

Chapter 2

Study Objectives

My thesis' overarching goal is to improve our understanding of CC screening and treatment gaps in sub-Saharan Africa, a region with a high CC burden that is exacerbated by the HIV syndemic. Specifically, my aims are to:

1) Characterize regional- and national-level and sub-Saharan Africa wide trends in CC screening coverage for the general population and among women living with HIV.
2) Assess the proportion of women screened at least twice by age 45 in 2020.
3) Estimate treatment coverage among women with a positive screening result suspected to have pre-cancerous lesions.

Chapter 3

Study Methodology

3.1 Data sources

To achieve my aims, I leveraged existing nationally representative population-based surveys. These surveys are advantageous as they employ complex sampling methods that yield observations that can be generalized to the whole population of a country. Data from surveys were obtained through searches of online data catalogs, Google engine searches, searches of the literature and previous experiences from members of my lab who have worked with population-based surveys. All surveys were household-based and used multi-stage cluster sampling with most employing a stratified, two- or three- stage clustering design. Surveys using stratification divided the population into strata often based on province or geotype (e.g., urban/rural). For all surveys, the first stage of sampling involved the selection of primary sampling units (PSU) from a master list of enumeration areas. For the majority of surveys, this was done using a probability proportional to size independently within each stratum. Following this, a second stage of sampling for all surveys involved the random selection from a list of households within each sampled enumeration area. Some surveys then conducted face-to-face questionnaire interviews for eligible individuals within the household. Other surveys, however, proceeded with a third stage of sampling by randomly selecting an individual household member for the completion of the questionnaire (i.e., STEPS and WHS surveys; SAGE surveys for those 18-49). Finally, due to the nonproportional allocation of samples, sampling weights were calculated to allow for regionally and nationally representative statistics. Table S1 provides links to each survey report, with full details on the sampling strategies adopted by each survey.

3.2 Study population

The WHO recommends the prioritization of screening for women aged 30-49 years old among the general population and those aged 25-49 years among WLHIV(10). To match these criteria, I restricted the primary analyses to women aged 25-49 years. For treatment coverage, we kept all women regardless of age reporting a positive screening test result suspected to be pre-cancer since the treatment recommendations are not age specific.

3.3 Outcome definitions

Our outcomes of interest were self-reported lifetime screening for CC, screening in the past three years, and self-reported treatment coverage following a positive screening result suspected to be pre-cancer. Differences in screening questions existed between surveys regarding the screening modality as some surveys would ask specifically about receiving a Pap smear whereas others would ask about CC screening in general (Table S1). Differences between the survey instruments were small however and considered comparable in this study.

3.4 Statistical analyses

All analyses for the three objectives were conducted using a Bayesian framework which allows for greater model flexibility that would have otherwise been difficult to achieve if working under a frequentist framework. Bayesian frameworks also allow for efficient propagation of uncertainty to results and at different aggregation levels. Furthermore, multilevel models were used as relevant survey data was relatively sparse and multilevel models allowed for the borrowing of strength across countries, age groups, HIV status, and time. All analyses were conducted using the R statistical software (version 4.1.3) and the *rstan* package (version 2.26.8) for Bayesian statistical inferences (115, 116).

3.4.1 Screening time trends model (Objective 1)

Lifetime CC screening and screening in the past three years were jointly modelled using a multilevel binomial logistic regression model with four nested levels: survey, country, region, and sub-Saharan Africa. Multilevel models, otherwise known as random effects models, were used here as it addressed within-survey, -country and -region clustering. Furthermore, the random effects helped to address issues of data sparseness as it allowed for partial pooling of data (i.e., borrowing strengths between units). This model included 5-year age groups (i.e., 25-29, 30-34, 35-39, 40-44, 45-49) and the women's HIV status (if available). If biomarkers of HIV status were not recorded in the survey, a standardization was done using data from The Joint United Nations Programme on HIV/AIDS (UNAIDS). As data was relatively sparse, both self-reports of lifetime screening and screening in the past three years were modelled in a joint analysis to increase geographic and temporal coverage, and thus the overall robustness of estimates. Age-specific dummy variables were included to adjust for the recall period (lifetime versus past three years). The model was fitted to survey-adjusted empirical observations for every combination of country, year, survey, 5-year age

group, recall period and HIV status, accounting for survey weights and the effective sample size (i.e., PSU and stratification) for each denominators calculated using the *survey* package (version 4.0). More specific details regarding the model will be described in Chapter 4 of this thesis.

The model specification was chosen such that age- and time-specific country-level estimates of screening coverage, stratified by HIV status and recall period (i.e., lifetime screening vs screening in the past three years) could be obtained. To aggregate at higher levels (e.g., national, regional, and sub-Saharan Africa), I used post-stratification to appropriately weight the different strata. Using post-stratification allows for differences in age structure, HIV prevalence and population sizes to be accounted for when pooling estimates by assigning each estimate a post-stratification weight and subsequently obtaining a weighted average. For the calculation of regional and sub-Saharan African estimates, imputations were done for countries without data alongside this post-stratification. As roughly 60% of countries in sub-Saharan Africa had available survey data, imputing estimates for countries without data allowed for more representative estimates while also accounting for the relevant uncertainty.

To compare modelled estimates to the empirical data and assess model fit, posterior predictive checks were conducted. This involved the comparison of each empirical observation with the model-predicted outcome to examine any systematic deviations that would indicate model inadequacies. In-sample comparisons were also performed, and I calculated the median error (i.e., the difference between the observed data and modelled data), the median absolute error (i.e., the absolute value of the difference between the observed data and modelled data) and the percentage of modelled observations below and above the 95% Credible Intervals (95%CrI) the model-predicted observations.

3.4.2 Proportion of women screened twice by the age of 45 in 2020 (Objective 2)

The proportion of women screened twice in their lifetime by the age of 45 in 2020 was estimated using life table methods, leveraging the age-, country-, and year-specific estimates obtained in the preceding objective. Preliminary results suggested that the rates of first-time screening versus re-screening were not independent. As such, I proceeded in two steps. Firstly, a rate ratio between re-screening and first-time screening was estimated. Due to a lack of survey data on the frequency of screening, this re-screening ratio was calculated

using the difference in lifetime screening between two consecutive one-year age groups and past year screening for that age group. Similarly to the time trends model, this model allowed for partial pooling of the data by assuming the re-screening rate ratios of each country fell under the same log-normal distribution. The modelled rate ratio was then used to obtain age-specific rates of re-screening and first-time screening for each country. Secondly, these rates were applied to a cohort of women aged 30 for a period of 15 years using life table methods to obtain the proportion of women who were screened at least twice by the age of 45. Women entered the life table at the age of 30 as either never screened or screened once, using previously obtained lifetime screening estimates. As such, this method assumed that women are not screened more than once before the age of 30. The uncertainty in these estimates were obtained from the posterior distributions of the parameters of interests.

3.4.3 Treatment coverage among those with a positive screening result suspected to be pre-cancer (Objective 3)

Treatment coverage was pooled across surveys using a Bayesian meta-analysis approach. Specifically, I used a multi-level binomial logistic regression model. As there were very few observations that reported treatment coverage, this model was not stratified by age or HIV status. However, a random intercept for country was used in this model to account for within-country clustering and allow for partial pooling of the data.

Chapter 4

Study Results (Manuscript 1)

This manuscript addresses all three objectives of my thesis and describes the analysis and results for screening coverage time trends, screening twice by the age of 45 years and treatment coverage for the general population of women and WLHIV in sub-Saharan Africa. This study uses data from population-based surveys.

Lily Yang, Marie-Claude Boily, Minttu Rönn, Dorcas Obiri-Yeboah, Imran Morhason-Bello, Nicolas Meda, Olga Lompo, Philippe Mayaud, Michael Pickles, Marc Brisson, Caroline Hodgins, Sinead Delany-Moretlwe, Mathieu Maheu-Giroux. Regional and national-level trends in cervical cancer screening coverage in high HIV prevalence settings: a systematic analysis of population-based surveys in sub-Saharan Africa (2000-2020).

Regional and country-level trends in cervical cancer screening coverage in high HIV prevalence settings: a systematic analysis of population-based surveys in sub-Saharan Africa (2000-2020)

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Abstract

Background: Sub-Saharan Africa (SSA) has the highest cervical cancer (CC) burden globally which is worsened by its HIV epidemics. In 2020, the World Health Organization introduced a CC elimination strategy with goals for vaccination, screening, and treatment. To benchmark progress, we examined temporal trends in screening coverage, monitored re-screening by age 45, and assessed treatment coverage in SSA.

Methods: Data was collected from population-based surveys to estimate lifetime and past three-year screening by age, year, country, and HIV serostatus using a Bayesian multilevel model. Post-stratification and imputations were done to obtain aggregate national, regional, and SSA-level estimates. To measure re-screening by age 45, a life table model was utilized. Finally, self-reported treatment coverage for women suspected to have pre-cancerous lesions was pooled across surveys using a Bayesian meta-analysis.

Findings: 52 surveys from 28 countries (2000-2020) informed our analysis. In Eastern and Western/Central Africa, regional screening coverages remained constant from 2000-2020 and women living with HIV (WLHIV) had greater odds of being screened compared to women without HIV. In Southern Africa, however, screening coverages increased and WLHIV had equal odds of screening. In comparison to first-time screening, rescreening rates were high, and it was estimated that 12% (95%Credible Interval[CrI]: 10-18%) of women had been screened twice or more by age 45 in 2020. Finally, treatment coverage among four countries with data was 84% (95%CrI: 70-95%).

Interpretation: Overall, CC screening coverage remains sub-optimal. Action is needed to increase screening coverage if CC elimination is to be achieved.

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Introduction

With approximately 604,000 new cases and 342,000 deaths reported in 2020, cervical cancer (CC) is the fourth most common cancer in women globally and one of the leading causes of cancer death in women in sub-Saharan Africa[1]. Low- and middle-income countries are disproportionately affected by the disease as they account for over 80% of the global CC burden, with sub-Saharan Africa having the highest age-standardized incidence and mortality rates in 2018[2]. This high burden can be partially attributed to the existence of a syndemic (synergistic epidemic) between HIV and human papillomaviruses (HPV). HPV is the necessary cause of most cervical cancers[3] and the risk of CC development is six-fold higher in women living with HIV (WLHIV) in comparison to those without HIV[4].

Prevention and early treatment programs are highly effective measures that can reduce CC burden. Roll-out of national screening programs starting in the 1950s alongside effective HPV vaccinations beginning in the 2000s have resulted in dramatic reductions of disease incidence in high-income countries[5,6]. Countries in sub-Saharan Africa, however, face a range of challenges in implementing population-wide screening programs, including financial and logistical constraints[7]. This lack of access to critical prevention methods exacerbates CC burden. Globally, it is estimated that, without further interventions, annual CC deaths will rise to 443,000 in 2030 with 90% of the mortality occurring in sub-Saharan Africa[8].

In 2020, the World Health Organization (WHO) adopted a global strategy for the elimination of CC as a public health threat by 2030. This strategy included "90-70-90" targets which called for 90% of all girls to be vaccinated against HPV by the age of 15, 70% of all women screened with a high-performance test once by age 35 and again by 45, and 90% of all invasive cancer cases managed and pre-cancers treated by 2030[9]. Alongside this strategy, the WHO also released new screening and treatment recommendations. These recommendations indicated that screening should be prioritized for women 30-49 years among the general population and 25-49 years among WLHIV[10]. When high-performance tests (i.e. HPV DNA tests) are unavailable, which is the case for many countries, screening is recommended every three years with visual inspection with acetic acid (VIA) or cytology[10]. Despite the importance of screening frequency in the WHO recommendations, little data exists on re-screening frequency in sub-Saharan Africa.

Understanding trends in screening coverage, especially among WLHIV, and their re-screening pattern are crucial to benchmark and evaluate progress towards CC elimination. Leveraging data from population-based surveys conducted in sub-Saharan Africa, our overall aim was to

inform and strengthen CC elimination strategies by 1) examining overall, regional, and national trends in CC screening coverage (lifetime and past three-year) by HIV status, 2) estimating the proportion of women screened twice between before age 45, and 3) investigating CC treatment coverage among those with pre-cancerous lesions.

Methods

Data sources

We performed searches for nationally representative population-based surveys with data on CC screening or treatment. Specifically, we searched data catalogs (i.e., the *Global Health Data Exchange*, the *WHO Multi-Country Studies Data Archive*, and the *WHO NCD Microdata Repository*) and conducted Google engine and literature searches. Building from previous HIV testing and CC screening reviews[11,12], we also systematically reviewed the following surveys: *Demographic and Health Surveys* (DHS), *Population-Based HIV Impact Assessment* (PHIA), *Study on Global AGEing and Adult Health* (SAGE), *STEPwise Approach to NCD Risk Factor Surveillance* (STEPS), *World Health Surveys* (WHS), *Kenya AIDS Indicator Survey* (KAIS), and the *South Africa National HIV Prevalence, Incidence, Behavior and Communication Survey* (SABSSM). This study followed the *Guidelines for Accurate and Transparent Health Estimates Reporting* (GATHER) (Supplementary materials Table S6)[13].

Data pre-processing

Data on CC screening (i.e., lifetime screening, screening in the past three years, and screening in the past year) and treatment outcomes were extracted from survey data. Survey outcomes were summarized by country, year, five-year age groups, and HIV serostatus, if available. Treatment outcomes were summarized by country. Due to potential clustering within primary sampling units, a design effect was calculated using the individual-level data to estimate the surveys' effective sample size. In the few instances where individual-level data was unavailable, we abstracted the most granular estimates available from survey reports and used the survey-adjusted confidence intervals to estimate the effective sample size.

A conceptual overview of the methods used for estimates of the trends in CC screening coverage is presented in Figure 1.

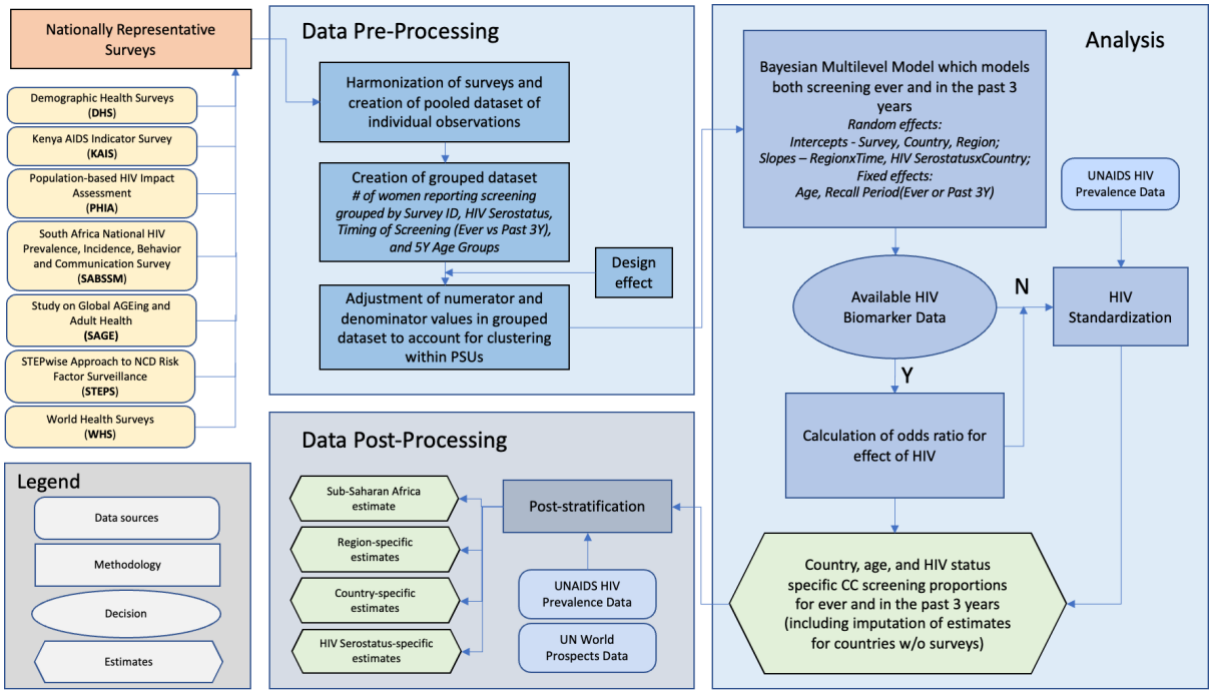

Figure 1. Conceptual framework outlining data inputs, data pre-processing, statistical analyses, and data post-processing to estimate lifetime and past three-year cervical cancer screening time trends by age, country, and HIV serostatus. CC=cervical cancer; PSU=primary sampling units; UNAIDS=Joint United Nations Programme for HIV/AIDS; UN=United Nations.

Regional and national estimates of cervical cancer screening coverage time trends

Statistical analyses for the estimation of trends in screening coverage

CC screening coverage for lifetime screening and screening in the past three years for women 25-49 years was modeled using a flexible Bayesian multilevel binomial logistic regression model. To increase the number of included surveys, self-reports of lifetime and past three-year screening were modelled jointly. The model structure, which was based on similar meta-regression models of health indicators[14,15] had four nested levels: survey, country, region, and sub-Saharan Africa. This hierarchical structure allowed us to borrow statistical strength across observations. The model also accounted for age (by five-year age groups), calendar year (continuous), recall period (lifetime versus past three-year), and HIV serostatus (see Text S1 for model equations). Here, we defined regions based on the 2015 *Global Burden of Disease* classification (apart from Mauritius coded as an Eastern African country). Given the few surveys available in Western and Central Africa, these two regions were combined into one (i.e., Western/Central Africa).

Information regarding HIV serostatus was not collected in most surveys. To include surveys with and without information on HIV serostatus, we adopted a standardization approach[15]. To perform this, we included random slopes (nested levels: country, region, overall) to estimate

odds ratios for screening coverage among WLHIV compared to women without HIV. For observations without information on HIV serostatus, we assumed the overall screening coverage was a weighted average of screening among WLHIV and those without HIV using UNAIDS HIV prevalence estimates[19] (Text S1).

Model performance was assessed through posterior predictive checks and in-sample comparisons. Alternative model specifications, with different nested structures of random effects and addition of covariates such as existence of national screening programs and gross national incomes were also considered (Text S1). The "*rstan*" package[16] was used to fit models and the R statistical software[17] employed for all analyses.

Post-processing of modeled estimates of screening coverage

Our fitted model provided lifetime and past three-year screening coverage estimates by country, year, five-year age groups, and HIV serostatus. To estimate screening coverage for broader age groups (i.e., the general population of women 30-49 years and WLHIV 25-49 years), combined HIV serostatus, and higher levels of aggregation (i.e., country, region, and sub-Saharan Africa), we pooled strata-specific estimates using post-stratification. Specifically, for each country and year, we took into consideration the underlying age distribution of the population and its HIV prevalence using the *UN World Population Prospects* (2019 revision)[18] and the UNAIDS HIV prevalence estimates[19], respectively. For countries without any surveys, screening coverages were imputed based on regional averages obtained from the model and we considered the additional uncertainty by sampling through the posterior distribution of country-level intercepts (Text S1). We provided estimates for each region and sub-Saharan Africa overall using all data available, however, country-level estimates were only presented for countries with at least two surveys.

WHO recommendations for re-screening frequency

Available population-based surveys did not have direct re-screening information. It therefore was not possible to empirically estimate the WHO goal of screening twice by age 45. To address this issue, we used life table methods[12,20] (Text S2; Figure S6).

Our preliminary analyses suggested that first-time screening and re-screening were independent. As such, we first estimated a rate ratio between the rate of re-screening and first-time screening for each region (due to limited data, Western, Central, and Eastern Africa were estimated as one region). Estimating these rate ratios ideally requires longitudinal follow-up data. As this was unavailable, we compared increases in lifetime screening between successive

one-year age groups with the fraction of women reporting screening in the past year. We related the two values to obtain rate ratios for re-screening using a Bayesian multilevel model (see Text S2 for model equations). Simulations suggested that the rate ratio can be correctly estimated if there are no strong cohort or period effects. If screening rates changed through time, simulations suggested that biases could be minimized by restricting analyses to younger women (i.e., 18-29 years old; Text S2).

Using our estimated regional rate ratios alongside previously calculated age-, country- and time- specific estimates of past three-year screening coverage, we were then able to obtain age-, country-, and time-specific re-screening and first-time screening rates that were then applied to our life table methods (Text S2). Specifically, we subjected a cohort of women aged 30 in 2005 to these calculated screening rates and estimated the proportion that would have been screened twice when aged 45 in 2020. To check the robustness of these estimates, lifetime screening estimates taken from the life tables were compared to those obtained from the time trends model described above (Text S2).

Estimating cervical cancer treatment coverage

Survey-level treatment coverage was estimated for women reporting an abnormal screening result that was not suspected to be cancer. That is, women who have been screened and are suspected to have pre-cancerous lesions. Treatment coverage was meta-analyzed using a Bayesian logistic regression model with random effects for country (Text S3).

Ethics

Informed consent was obtained for participants in each survey and the specific consent procedures are described in the individual survey reports (Table S1). Ethics approval for secondary data analyses was obtained by the Institutional Review Board of McGill University (A03-M19-20A).

Role of the funding source

Funders of this study had no role in the study design, data curation, analysis, interpretation, or writing of the report.

Results

Survey characteristics

A total of 52 population-based surveys from 28 sub-Saharan African countries conducted between 2000 and 2020 were used for our inferences (Figure 2). Individual-level data was available for 49/52 of these surveys. Tabulations from reports were used for the remaining three surveys: Burkina Faso STEPS 2013, Mozambique STEPS 2015, and Zimbabwe PHIA 2020 (only WLHIV). Among these 52 surveys, only 4 had information regarding treatment coverage. Information on both lifetime and past three-year screening was available from 15/52 surveys, 19/52 surveys had data on lifetime screening only, and 18/52 surveys on screening in the past three years only (Figure 2). A total of 14 countries had 2 or more surveys and 16 surveys had information on HIV serostatus. Additionally, 14/52 surveys had information regarding screening in the past year. In total 151,338 women aged 25-49 years were included in the screening analysis and 113 women (without age restriction) were included in the CC treatment analysis. The full list of survey questions can be found in the supplementary materials (Table S1).

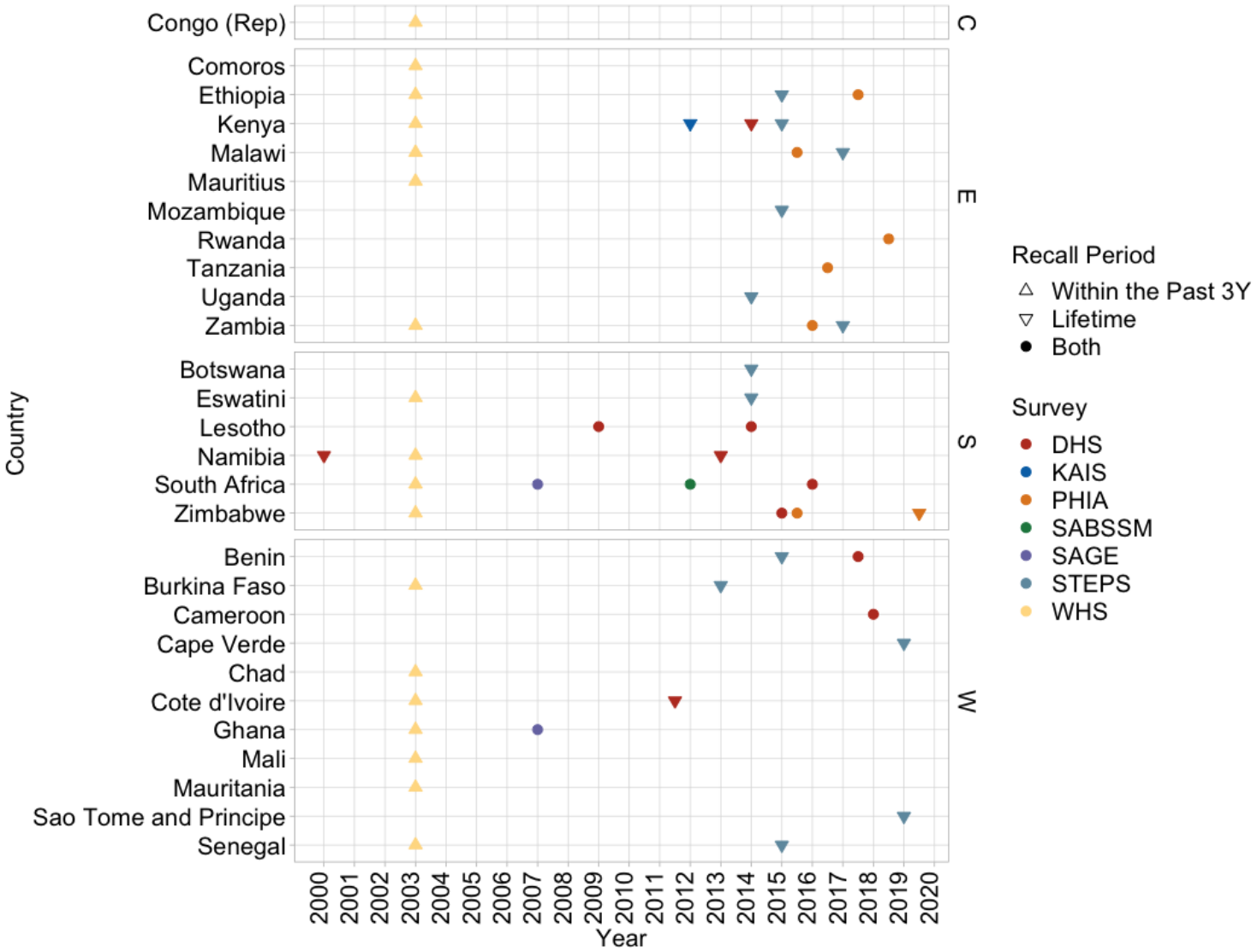

Figure 2. Survey data availability plots. Available surveys with information on cervical cancer screening by survey type, recall period, and region (C = Central Africa, E = Eastern Africa, S = Southern Africa, W = Western Africa). Colors represent survey type and shape represents recall period. (DHS = Demographic and Health Surveys; KAIS = Kenya AIDS Indicator Survey; PHIA = Population-based HIV Impact Assessment; SABSSM = South Africa National HIV Prevalence, Incidence, Behavior and Communication Survey; SAGE = Study on Global AGEing and Adult Health; STEP = STEPwise Approach to NCD Risk Factor Surveillance; WHS = World Health Surveys.)

Regional and national estimates of cervical cancer screening coverage trends

Overall, our results suggested that lifetime CC screening among women aged 30-49 years remained constant over the 2000-2020 period in sub-Saharan Africa (Figure 3): starting from 14% (95%CrI: 8-25%) in 2000 to 14% (95%CrI: 11-21%) in 2020 (Table 1). Over these two decades, only Southern Africa was estimated to have increased its screening coverage. In Eastern and Western/Central Africa, coverages appeared to be slightly increasing and slightly decreasing, respectively, with large uncertainties (Figure 3).

In 2020, Southern Africa had the highest estimated screening coverage, with 51% (95%CrI: 40-62%) of women estimated to have been screened in their lifetime (Table 1). This was much lower in Eastern and Western/Central Africa regions with 13% (95%CrI: 9-19%) and 6% (95%CrI: 2-21%), respectively (Table 1). There were important country-level variations: Benin had the lowest screening coverage in 2020, with 1% (95%CrI: 0-2%) of women 30-49 ever screened, whereas South Africa had the highest coverage at 56% (95%CrI: 43-69%) (Figure 4; Table 1). Overall, most women who have ever been screened in 2020 (14%; 95%CrI: 11-21%) reported that their last screening occurred in the past three years (10%; 95%CrI: 8-15%) (Table S2). Finally, model validation through posterior predictive checks and in-sample comparisons suggested good model fit to the data (Figure S3; Table S3).

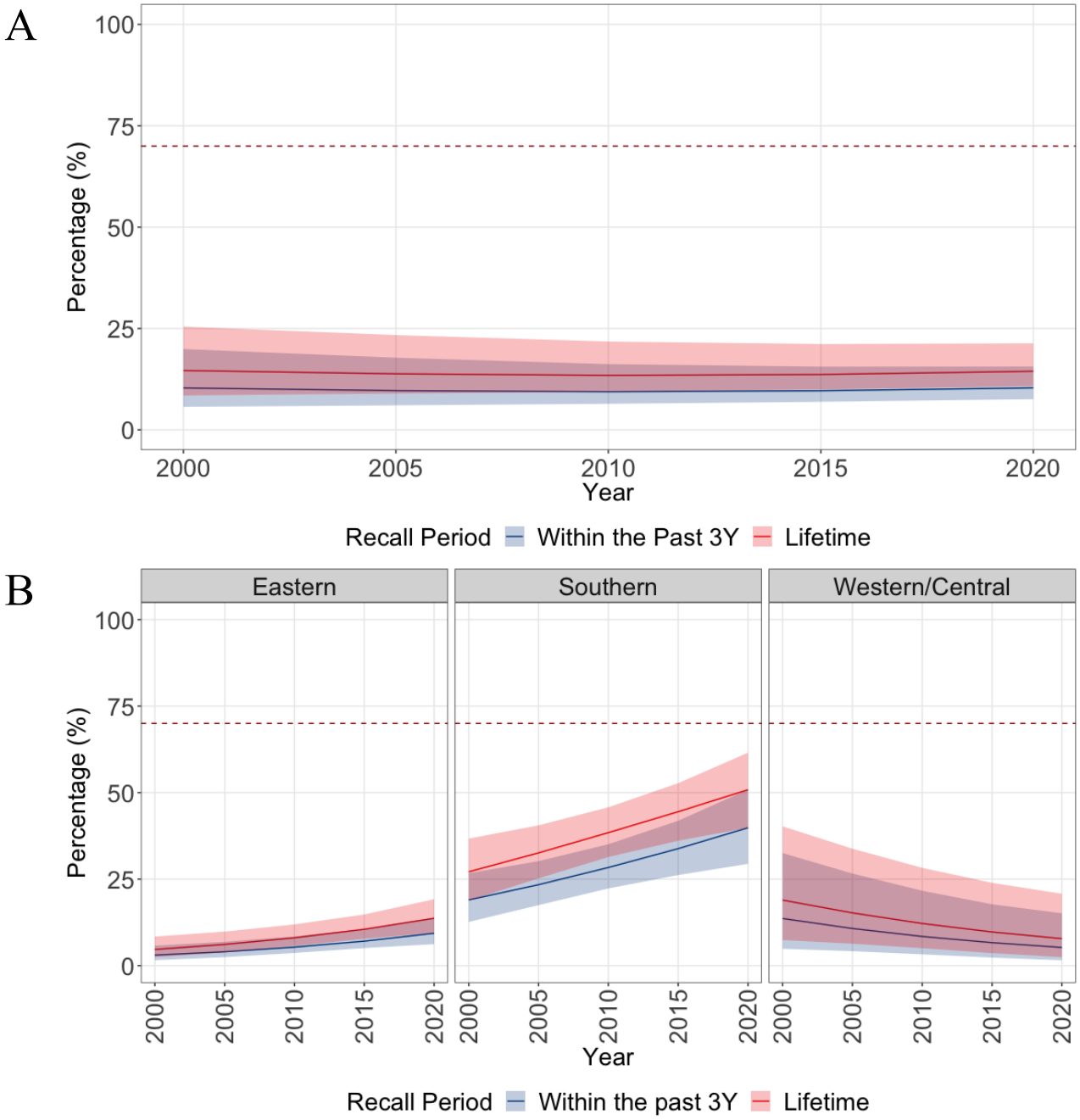

Figure 3. Overall and regional-level trends in lifetime and past three years cervical cancer screening coverage among women aged 30-49 years between 2000-2020. A) Overall time trends for proportion of women screened. B) Time trends for proportion of women screened by region. The red trendline represents lifetime screening trends. The blue trendline represents screening trends for screening in the past 3 years. The dotted red line represents the 70% screening goal set by the World Health Organization.

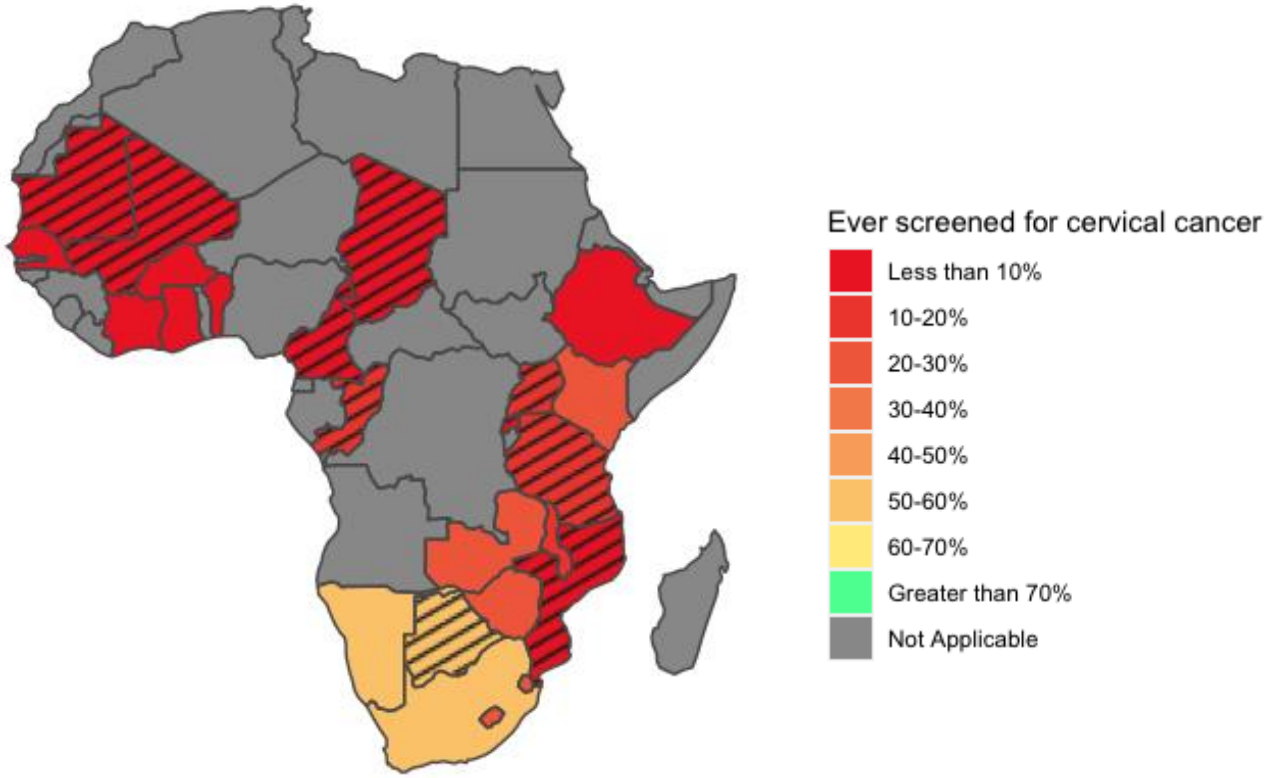

Figure 4. Map of the percentage of women aged 30-49 years reporting having been screened in their lifetime for cervical cancer in 2020. Hatched areas represent countries for which estimates are extrapolated from 1 survey. Countries without hatching have data from 2 or more surveys and grey-colored countries do not have any survey data.

Table 1. Overall, regional, and national-level estimates for the proportion of women aged 30-49 years old screened for cervical cancer in their lifetime and in the past three years in 2020. National-level estimates are presented only for countries with 2 or more surveys. Results broken down by five-year age groups can be found in Table S2.

	Proportion of women 30-49 years old screened for cervical cancer, median (95%CrI)	
Regions and countries	**Lifetime**	**Past three years**
Overall*	14% (11-21%)	10% (8-16%)
Western/Central Africa*	6% (2-21%)	4% (2-15%)
Benin	1% (0-2%)	0% (0-1%)
Burkina Faso	4% (2-11%)	3% (1-7%)
Côte d'Ivoire	2% (1-6%)	1% (1-4%)
Ghana	3% (1-7%)	2% (1-5%)
Senegal	8% (4-18%)	5% (3-12%)
Eastern Africa*	13% (9-19%)	9% (6-14%)
Ethiopia	6% (3-9%)	4% (2-6%)
Kenya	21% (14-30%)	14% (9-21%)
Malawi	17% (11-25%)	12% (7-18%)
Zambia	23% (15-32%)	16% (10-23%)
Southern Africa*	51% (40-62%)	40% (29-51%)
Eswatini	25% (15-40%)	17% (10-29%)
Lesotho	20% (13-32%)	14% (8-23%)
Namibia	50% (34-66%)	39% (24-55%)
South Africa	56% (43-68%)	44% (32-58%)
Zimbabwe	30% (22-40%)	21% (15-30%)

CrI=95% credible intervals.
*The overall and region-specific estimates consider the uncertainty and the population sizes of countries without surveys.

Coverage of cervical cancer screening by HIV serostatus

WLHIV were found to have equal or greater odds of being screened (Table 2). In countries outside of Southern Africa, the adjusted odds ratio of women reporting screening among WLHIV varied between 1.7 in Kenya (95%CrI: 1.1-2.4) to 2.7 in the Tanzania (95%CrI: 2.2-3.3). In almost all countries in Southern Africa, except Zimbabwe (OR=1.3; 95%CrI: 1.2-1.4), the ORs were close to the null.

Overall, 30% (95%CrI: 24-37%) of WLHIV aged 25-49 years had ever been screened for CC in 2020, compared to 11% (95%CrI: 8-18%) of women without HIV. This large difference is attributable to the higher prevalence of HIV in Southern Africa where screening coverage is also higher. Among women 25-49 years in Eastern Africa 19% (95%CrI: 14-25%) of WLHIV had ever been screened in 2020, compared to 11% (95%CrI: 8-17%) among women without HIV. In Western/Central Africa, 12% (95%CrI: 5-30%) of WLHIV compared to 6% (95%CrI: 2-19%) of women without HIV had ever been screened. In Southern Africa, screening coverage for both groups were similar with 49% (95%CrI: 35-61%) of WLHIV having ever been screened compared to 47% (95%CrI: 37-57%) of women without HIV (Table 2).

Table 2. Country-level odds ratios of the impact of HIV serostatus on cervical cancer screening and regional and country-level estimates of lifetime cervical cancer screening among women aged 25-49 living with and without HIV in 2020.

		Ever screened in 2020 (95%CrI)	
Country	**OR** (95%CrI)**	**Women living with HIV**	**Women not living with HIV**
Overall*	1.6 (0.3-12.8)	30% (24-37%)	11% (8-18%)
Western/Central Africa*	2.1 (1.1-4.1)	12% (5-30%)	6% (2-19%)
Cameroon	1.9 (1.2-3.2)	10% (4-20%)	5% (2-9%)
Côte d'Ivoire	2.3 (1.1-5.3)	5% (2-12%)	2% (1-5%)
Eastern Africa*	2.0 (1.6-2.6)	19% (14-25%)	11% (8-17%)
Ethiopia	2.2 (1.7-3.1)	10% (6-17%)	5% (3-8%)
Kenya	1.7 (1.1-2.4)	27% (16-39%)	19% (12-27%)
Malawi	1.7 (1.4-2.0)	21% (13-31%)	14% (9-21%)
Rwanda	2.1 (1.5-3.0)	8% (4-16%)	4% (2-8%)
Tanzania	2.7 (2.2-3.4)	19% (10-33%)	8% (4-15%)
Zambia	1.9 (1.6-2.2)	29% (18-41%)	18% (11-27%)
Southern Africa*	1.1 (0.8-1.5)	49% (35-61%)	47% (37-57%)
Lesotho	1.0 (0.8-1.3)	19% (11-32%)	18% (11-29%)
Namibia	0.9 (0.7-1.2)	46% (28-63%)	47% (31-63%)
South Africa	0.9 (0.8-1.0)	53% (38-67%)	53% (41-65%)
Zimbabwe	1.3 (1.2-1.4)	32% (22-44%)	26% (19-35%)

CrI=95% credible intervals; OR=odds ratio.
*The overall and region-specific estimates consider the uncertainty and the population sizes of countries without surveys.
**The odds ratios are adjusted for age, time, and the type of recall period for screening (lifetime versus past three years).

Proportion of women aged 45 years of age screened at least twice

Using 14 surveys across 11 countries with information on both lifetime and past-year screening coverage, we estimated that the rate ratio of re-screening versus first-time screening was largely above one in all instances. For Western/Central/Eastern Africa we estimated the rate ratio to be 34.1 (95%CrI: 16.8, 60) and for Southern Africa we estimated the rate ratio to be 21.2 (95%CrI: 4.7, 64.9).

Among women aged 45 in 2020 in sub-Saharan Africa who have ever been screened, we estimated that 73% (95%CrI: 61-80%) of them have been screened at least twice. This corresponds to 12% (95%CrI: 9-18%) of women aged 45 having been screened twice in 2020 (Figure 5). Here again, there is significant between-country variation, and estimates are associated with large uncertainties. Validity checks for these estimates suggest that pooled estimates for screening twice are robust. However, the proportion of women screened twice in Southern Africa could be slightly underestimated (Text S2). Altogether, the results suggest that women who have been screened once are likely to be screened a second time. Given the high proportion of women who have never been screened, none of the countries were close to reaching the target of 70% of women screened for CC twice by the age of 45 in 2020.

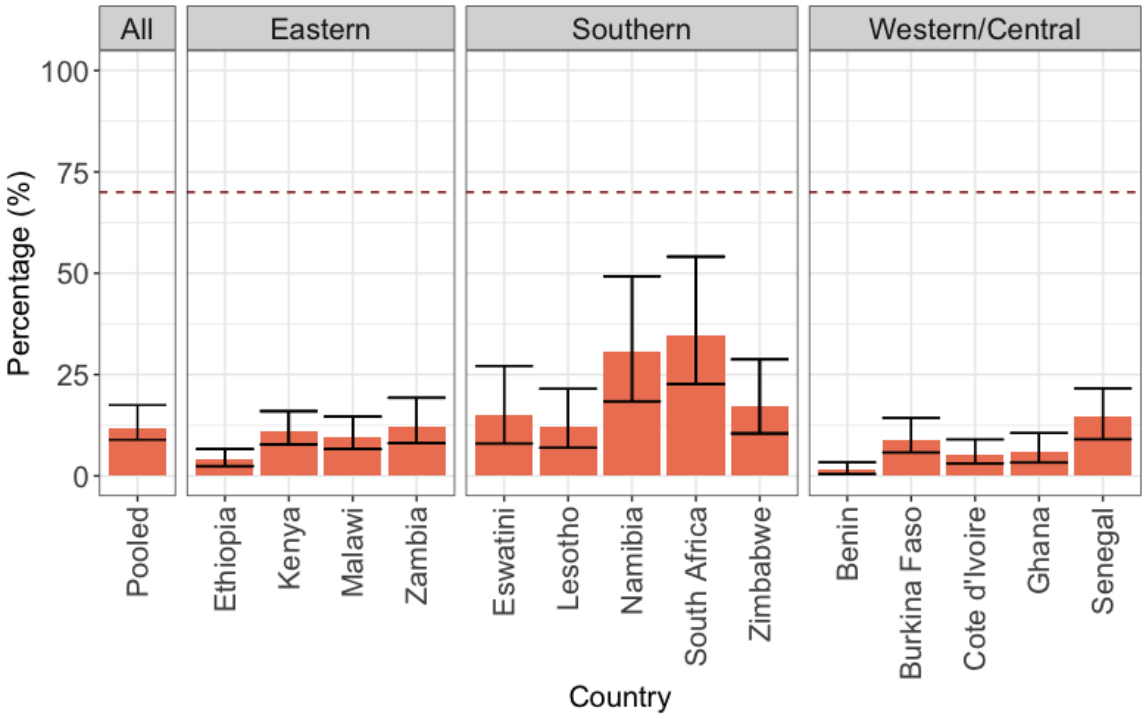

Figure 5. Estimates of women aged 45 years in 2020 who have been screened twice for cervical cancer in 2020. The pooled estimate is for the whole sub-Saharan region. The dotted red line represents the 70% screening goal set by the World Health Organization.

Coverage of cervical cancer treatment among women with a positive screen result for pre-cancerous lesions

Four countries had information on treatment coverage among women who had received an abnormal screening result that was suspected to be pre-cancer. Overall, the proportion of women who underwent treatment across the four countries was 84% (95%CrI: 70-95%). Despite wide uncertainties, treatment coverage was lowest in Malawi (77%; 95%CrI: 60-88%), followed by Cape Verde (82%; 95%CrI: 55-94%), Tanzania (90%; 95%CrI: 66-98%), and Zambia (90%; 95%CrI: 65-98%) (Figure 6). As this analysis was limited to women who had been screened and had received their screening result, the true number of women with pre-cancerous lesions who are treated is likely to be lower.

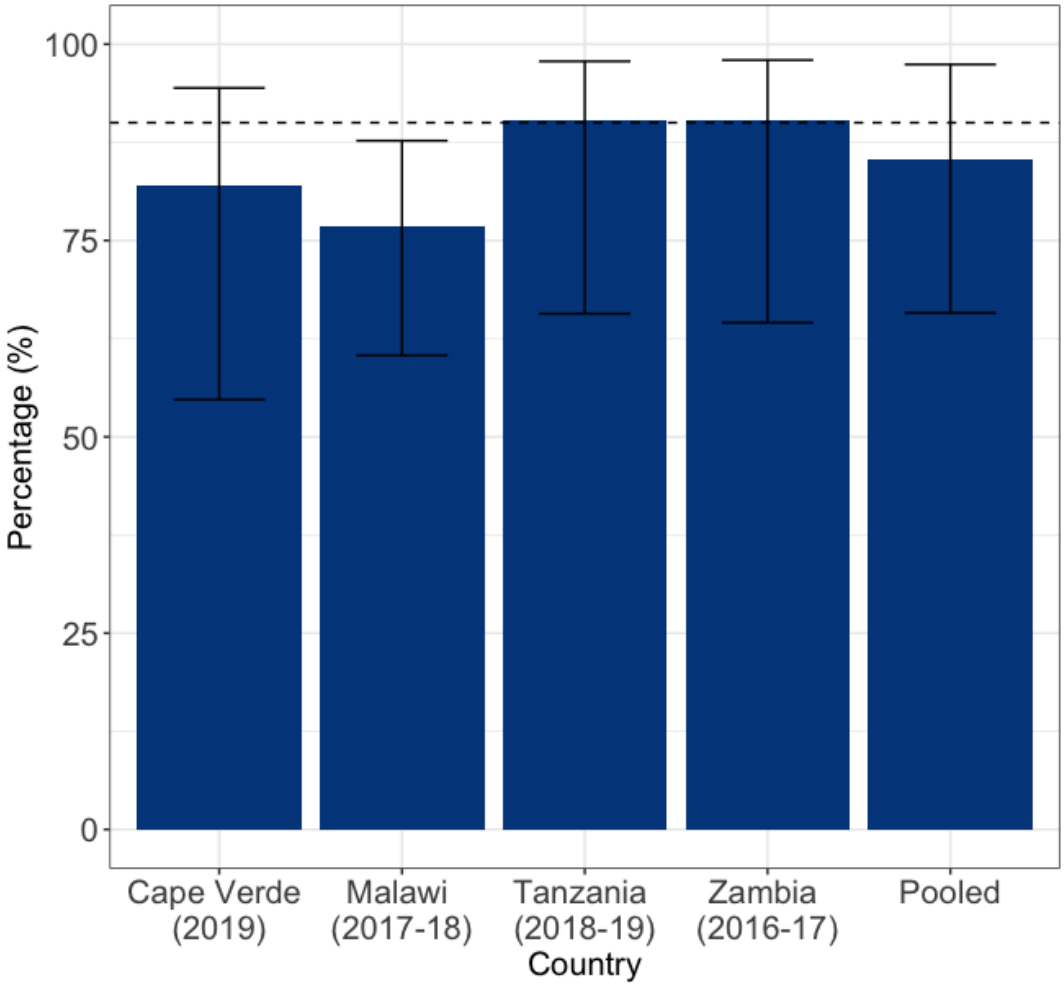

Figure 6. Reported treatment coverage among women with an abnormal or positive screening result. Country-level estimates are taken directly from the survey data. Pooled estimates are obtained from the model. The dotted blue line represents the 90% treatment goal set by the World Health Organization.

Discussion

Using data from 52 population-based surveys from 28 countries in sub-Saharan Africa, we estimated that 14% of women aged 30-49 had ever been screened in 2020 and that, despite regional variations, overall screening coverage remained stagnant over the last two decades with only Southern Africa witnessing increases. WLHIV were more likely to be screened in their lifetime than women without HIV in all regions, except in Southern Africa. Additionally, we found that women who had been screened once were more likely to be re-screened, and estimated that in 2020, 12% of women aged 45 had been screened at least twice: well below WHO's 70% target. Finally, among the four countries with available data, 84% of women tested to have pre-cancerous lesions reported undergoing treatment. Although this value is approaching the WHO's 90% recommendation, low screening coverages suggest that many women with pre-cancerous lesions have likely not been screened and thus have not received treatment.

To eliminate CC, it is essential for countries to develop adequate national primary (e.g., HPV vaccinations) and secondary (e.g., CC screening) prevention programs. Although HPV vaccination programs are becoming more prevalent[21], vaccinations are not prophylactic and will not cure women already infected with HPV. As such, quality screening programs remain imperative to prevent CC in the decades to come for large cohorts of women who have not been vaccinated prior to sexual debut[22]. Our findings suggest that screening coverage has remained largely stagnant over the last two decades in most regions of sub-Saharan Africa. Efforts are needed to strengthen and rapidly scale-up screening programs if the 2030 WHO targets are to be met.

Many barriers currently exist to achieving higher screening coverages in several sub-Saharan African countries. These include, but are not limited to, various financial, social, and structural constraints such as lack of CC knowledge, competing interests and absence of political will to invest in CC screening programs, among others[7]. Integration of CC screening with existing health services has been a strategy utilized to address some of these barriers, notably integration with HIV care clinics[7,23]. Although the impact of service integration is still being evaluated, this approach could partially explain why we found WLHIV in some regions had higher screening coverages compared to women without HIV. It is also important to note that the COVID-19 pandemic has likely exacerbated many barriers to CC screening. Disruptions to health services, changes in health-seeking behaviour[24,25] as well as indirect

economic effects[26] have likely resulted in reduced access and demand for CC screening and treatment services in the short and long-term.

The COVID-19 pandemic has likely also widened inequities in screening and treatment coverage. Empirical studies have found that disparities in screening coverage exist along various social determinants of health such as education and geography[11]. Our findings similarly suggest that only a small subset of the population may be screened and re-screened as we found that re-screening rates were many folds that of first-time screening. Although research regarding re-screening is limited these findings are aligned with a 1993 study conducted in South Africa which found that certain rural workers were being over-screened whilst others were excluded altogether[27].

In general, more data should be collected with regards to the screening care cascade (i.e., re-screening and treatment). Information on re-screening in the literature is sparse and data on screening frequency is not collected in most population-based surveys. Our study estimated that overall, 73% of women who have been screened once have been screened a second time, however important country-level variations likely exists. One study from Mozambique[28] found that only 29% of women 30-55 years had ever been screened more than once. On the other hand, a cohort study[29] in Harare, Zimbabwe found that over 70% of WLHIV were re-screened. Given the limitations of our methods to estimate re-screening rate ratios, more information needs to be collected with regards to screening frequency to obtain more robust and granular estimates of re-screening patterns. Similarly, only 4 countries had surveys with information related to treatment. To monitor progress towards the CC elimination goals, survey instruments should capture the entire CC screening care cascade.

Our results need to be interpreted considering this study's limitations. First, survey data on CC screening was relatively sparse. Only 14 countries had surveys from multiple years, and only 12 countries had information regarding HIV serostatus. We addressed this by using a multilevel statistical approach which allowed us to borrow strength across countries and to propagate the uncertainty to the model results. Secondly, our estimates of re-screening ratios were modeled from cross-sectional data, assuming no cohort or period effects. This assumption was likely violated for Southern Africa, even if we limited bias by focusing on the younger age groups. Nevertheless, the strong patterns observed suggest high rates of re-screening. Finally, different survey questionnaires asked slightly different questions. For example, some surveys asked specifically about Pap smears, while other asked about CC screening in general. Although there

is limited information regarding primary screening modalities prior to 2015, to the best of our knowledge, when information was available, the primary method of screening within a country matched the screening method asked about in the survey[30].

Strengths of this investigation include the incorporation of population-based survey data from the greatest number of countries and sources in sub-Saharan Africa to date. Second, model validation suggested that we accurately reproduced empirical observations with appropriate propagation of uncertainty to model results. Third, by quantifying re-screening patterns, we provided valuable information on indicators to benchmark WHO elimination targets for CC screening that are currently limited. Finally, this study unequivocally established that screening coverage in 2020 is low and that there are important disparities between countries and regions.

In conclusion, screening and treatment coverages for CC are currently below the WHO elimination goals. To reach these goals by 2030 and eliminate this highly preventable disease, screening and treatment programs need to be scaled-up alongside HPV vaccination programs. Use of effective roll-out strategies which educate and engage communities will be beneficial to improving screening and treatment coverage. Finally, to be able to effectively track progress towards these goals future studies and surveys should prioritize greater data collection along the CC screening and treatment cascade.

Contributors

LY contributed to project conceptualization, data extraction and curation, investigation, formal analysis, methodology, validation, visualization and writing the original draft. MB, MMR, and MP contributed to the methodology of the second objective regarding re-screening estimates, visualization, result interpretations, and editing and reviewing the manuscript. DO-Y, IM-B, NM, OL, PM, CH, and SD-M provided inputs on the methodology and analysis, interpretation of the results, visualization, and edited and reviewed the manuscript. MM-G contributed to project conceptualization, investigation formal analysis, methodology, supervision, validation, visualization, and the reviewing and editing of the manuscript. LY and MM-G both directly had access to and verified the data.

Data Sharing

How to access and request sources of data for this analysis can be found in Table S1 in the supplementary materials. A cleaned dataset alongside code used for the project can be found here: https://github.com/pop-health-mod/cc-screening

Declaration of interests

MM-G reports an investigator-sponsored research grant from Gilead Sciences Inc., and contractual arrangements from the *Institut national de santé publique du Québec* (INSPQ), the *Institut d'excellence en santé et services sociaux* (INESSS), the *World Health Organization*, and the *Joint United Nations Programme on HIV/AIDS* (UNAIDS), all outside of the submitted work.

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Supplementary Materials

Table of Contents

Table S1: Survey Questions

Country	Survey	Year	Sample Size of women 25-49	Ever tested for cervical cancer	Timing of last cervical cancer test	Treatment as a result of last cervical cancer test	Survey Report	Source
Central Africa								
Republic of the Congo	WHS	2003	637	Asked to those who've ever had a pelvic exam within the past three years: The last time you had the pelvic examination, did you have a Pap smear test?(By Pap smear test, I mean did a doctor or nurse use a swab or stick to wipe from inside your vagina, take a sample and send it to a laboratory?)	N/A	N/A	https://www.who.int/healthinfo/survey/whscog-congo.pdf	https://apps.who.int/healthinfo/systems/surveydata/index.php/catalog/103
Eastern Africa								
Comoros	WHS	2003	433	Asked to those who've ever had a pelvic exam within the past three years: The last time you had the pelvic examination, did you have a Pap smear test?(By Pap smear test, I mean did a doctor or nurse use a swab or stick to wipe from inside your vagina, take a sample and send it to a laboratory?)	N/A	N/A	https://www.who.int/healthinfo/survey/whscom-comoros.pdf	https://apps.who.int/healthinfo/systems/surveydata/index.php/catalog/113
Ethiopia	WHS	2003	1321	Asked to those who've ever had a pelvic exam within the past three years: The last time you had the pelvic examination, did you have a Pap smear test?(By Pap smear test, I mean did a doctor or nurse use a swab or stick to wipe from inside your vagina, take a sample and send it to a laboratory?)	N/A	N/A	https://www.who.int/healthinfo/survey/whseth-ethiopia.pdf	https://apps.who.int/healthinfo/systems/surveydata/index.php/catalog/37
Ethiopia	STEPS	2015	3276	Have you ever had a screening test for cervical cancer, using any of these methods described above (i.e., VIA, Pap smear or HPV test)?	N/A	N/A	https://extranet.who.int/ncdsmicrodata/index.php/catalog/794/download/5522	https://extranet.who.int/ncdsmicrodata/index.php/catalog/794
Ethiopia	PHIA	2017-18	11683	Have you ever been tested for cervical cancer?	What month and year was your last test for cervical cancer?	N/A	https://phia.icap.columbia.edu/wp-content/uploads/2020/11/EPHIA_Report_280820_Web.pdf	https://phia-data.icap.columbia.edu/files
Kenya	WHS	2003	1373	Asked to those who've ever had a pelvic exam within the past three years: The last time you had the pelvic examination, did you have a Pap smear test?(By Pap smear test, I mean did a doctor or nurse use a swab or stick to wipe from inside your vagina, take a sample and send it to a laboratory?)	N/A	N/A	https://www.who.int/healthinfo/survey/whsken-kenya.pdf	https://apps.who.int/healthinfo/systems/surveydata/index.php/catalog/80
Kenya	KAIS	2012	4255	Have you ever been screened by a doctor or other health professional for cervical cancer?	N/A	N/A	https://nacc.or.ke/wp-content/uploads/2015/10/KAIS-2012.pdf	http://catalog.ihsn.org/catalog/6697/study-description

Kenya	DHS	2014	9338	Asked to those who've heard of CC: Have you ever had a test or exam to see if you had cervical cancer?	N/A	N/A	https://dhsprogram.com/pubs/pdf/FR308/FR308.pdf	https://dhsprogram.com/methodology/survey/survey-display-451.cfm
Kenya	STEPS	2015	1616	Have you ever had a screening test for cervical cancer, using any of these methods described above (i.e., VIA, Pap smear or HPV test)?	N/A	N/A	https://extranet.who.int/ncdsmicrodata/index.php/catalog/247/download/2092	https://extranet.who.int/ncdsmicrodata/index.php/catalog/247
Malawi	WHS	2003	1366	Asked to those who've ever had a pelvic exam within the past three years: The last time you had the pelvic examination, did you have a Pap smear test?(By Pap smear test, I mean did a doctor or nurse use a swab or stick to wipe from inside your vagina, take a sample and send it to a laboratory?)	N/A	N/A	https://www.who.int/healthinfo/survey/whsmwi-malawi.pdf	https://apps.who.int/healthinfo/systems/surveydata/index.php/catalog/85
Malawi	STEPS	2017	1561	Have you ever had a screening test for cervical cancer, using any of these methods described above (i.e., VIA, Pap smear or HPV test)?	N/A	N/A	https://extranet.who.int/ncdsmicrodata/index.php/catalog/629/download/5770	https://extranet.who.int/ncdsmicrodata/index.php/catalog/629
Malawi	PHIA	2015-16	11991	Have you ever been tested for cervical cancer?	What month and year was your last test for cervical cancer?	Did you receive treatment after your last test for cervical cancer? Did you receive treatment on the same day or on a different day?	https://phia.icap.columbia.edu/wp-content/uploads/2020/02/MPHIA-Final-Report_web.pdf	https://phia-data.icap.columbia.edu/files
Mauritius	WHS	2003	1150	Asked to those who've ever had a pelvic exam within the past three years: The last time you had the pelvic examination, did you have a Pap smear test?(By Pap smear test, I mean did a doctor or nurse use a swab or stick to wipe from inside your vagina, take a sample and send it to a laboratory?)	N/A	N/A	https://www.who.int/healthinfo/survey/whsmus-mauritius.pdf	https://apps.who.int/healthinfo/systems/surveydata/index.php/catalog/90
Mozambique[a]	STEPS	2015	697	Asked to those who've ever had a pelvic exam within the past three years: The last time you had the pelvic examination, did you have a Pap smear test?(By Pap smear test, I mean did a doctor or nurse use a swab or stick to wipe from inside your vagina, take a sample and send it to a laboratory?)	N/A	N/A	https://cdn.who.int/media/docs/default-source/ncds/ncd-surveillance/data-reporting/mozambique/relatorio_final_steps_2015_mozambique.pdf?sfvrsn=1907f08a_1&download=true	https://oce-ovid-com.proxy3.library.mcgill.ca/article/00008469-201907000-00013/PDF
Rwanda	PHIA	2018-19	17077	Have you ever been tested for cervical cancer?	What month and year was your last test for cervical cancer?	N/A	https://phia.icap.columbia.edu/wp-content/uploads/2020/11/RPHIA-Final-Report_Web.pdf	https://phia-data.icap.columbia.edu/files

Uganda	STEPS	2014	1387	Have you ever had a screening test for cervical cancer, using any of these methods described above (i.e., VIA, Pap smear or HPV test)?	N/A	N/A	https://extranet.who.int/ncdsmicrodata/index.php/catalog/633/download/4536	https://extranet.who.int/ncdsmicrodata/index.php/catalog/633
United Republic of Tanzania	PHIA	2016-17	18313	Have you ever been tested for cervical cancer?	What month and year was your last test for cervical cancer?	Did you receive treatment after your last test for cervical cancer? Did you receive treatment on the same day or on a different day?	https://phia.icap.columbia.edu/wp-content/uploads/2020/02/FINAL_THIS-2016-2017_Final-Report__06.21.19_for-web_TS.pdf	https://phia-data.icap.columbia.edu/files
Zambia	WHS	2003	1060	Asked to those who've ever had a pelvic exam within the past three years: The last time you had the pelvic examination, did you have a Pap smear test?(By Pap smear test, I mean did a doctor or nurse use a swab or stick to wipe from inside your vagina, take a sample and send it to a laboratory?)	N/A	N/A	https://www.who.int/healthinfo/survey/whszmb-zambia.pdf	https://apps.who.int/healthinfo/systems/surveydata/index.php/catalog/105
Zambia	PHIA	2016	12615	Have you ever been tested for cervical cancer?	What month and year was your last test for cervical cancer?	Did you receive treatment after your last test for cervical cancer? Did you receive treatment on the same day or on a different day?	https://phia.icap.columbia.edu/wp-content/uploads/2020/02/ZAMPHIA-Final-Report__2.22.19.pdf	https://phia-data.icap.columbia.edu/files
Zambia	STEPS	2017	1398	Have you ever had a screening test for cervical cancer, using any of these methods described above (i.e., VIA, Pap smear or HPV test)?	N/A	N/A	https://extranet.who.int/ncdsmicrodata/index.php/catalog/620/download/4457	https://extranet.who.int/ncdsmicrodata/index.php/catalog/620
Southern Africa								
Botswana	STEPS	2014	1507	Have you ever had a screening test for cervical cancer, using any of these methods described above (i.e., VIA, Pap smear or HPV test)?	N/A	N/A	https://extranet.who.int/ncdsmicrodata/index.php/catalog/318/download/2484	https://extranet.who.int/ncdsmicrodata/index.php/catalog/318
Eswatini	WHS	2003	599	Asked to those who've ever had a pelvic exam within the past three years: The last time you had the pelvic examination, did you have a Pap smear test?(By Pap smear test, I mean did a doctor or nurse use a swab or stick to wipe from inside your vagina, take a sample and send it to a laboratory?)	N/A	N/A	https://www.who.int/healthinfo/survey/whsswz-swaziland.pdf	https://apps.who.int/healthinfo/systems/surveydata/index.php/catalog/70
Eswatini	STEPS	2014	1104	Have you ever had a screening test for cervical cancer, using any of these methods described above (i.e., VIA, Pap smear or HPV test)?	N/A	N/A	https://extranet.who.int/ncdsmicrodata/index.php/catalog/688/download/4938	https://extranet.who.int/ncdsmicrodata/index.php/catalog/688

Lesotho	DHS	2009	8452	Asked to those who've heard of a Pap smear: Have you ever had such an exam in your lifetime?	How long ago was the last exam performed?	N/A	https://dhsprogram.com/pubs/pdf/FR241/FR241.pdf	https://dhsprogram.com/methodology/survey/survey-display-317.cfm
Lesotho	DHS	2014	7558	Asked to those who've heard of a Pap smear: Have you ever had such an exam in your lifetime?	How long ago was the last exam performed?	N/A	https://dhsprogram.com/pubs/pdf/FR309/FR309.pdf	https://dhsprogram.com/methodology/survey/survey-display-462.cfm
Namibia	DHS	2000	3977	Est-ce qu'un médecin ou un autre professionnel de santé vous a déjà fait un test de détection du cancer du col de l'utérus ?	N/A	N/A	https://dhsprogram.com/pubs/pdf/FR141/FR141.pdf	https://dhsprogram.com/methodology/survey/survey-display-205.cfm
Namibia	WHS	2003	1261	Asked to those who've ever had a pelvic exam within the past three years: The last time you had the pelvic examination, did you have a Pap smear test?(By Pap smear test, I mean did a doctor or nurse use a swab or stick to wipe from inside your vagina, take a sample and send it to a laboratory?)	N/A	N/A	https://www.who.int/healthinfo/survey/whsnam-namibia.pdf	https://apps.who.int/healthinfo/systems/surveydata/index.php/catalog/94
Namibia	DHS	2013	5548	Have you ever had a test or exam to see if you have cervical cancer?	N/A	N/A	https://dhsprogram.com/pubs/pdf/FR298/FR298.pdf	https://dhsprogram.com/methodology/survey/survey-display-363.cfm
South Africa	WHS	2003	653	Asked to those who've ever had a pelvic exam within the past three years: The last time you had the pelvic examination, did you have a Pap smear test?(By Pap smear test, I mean did a doctor or nurse use a swab or stick to wipe from inside your vagina, take a sample and send it to a laboratory?)	N/A	N/A	https://www.who.int/healthinfo/survey/whszaf-southafrica.pdf	https://apps.who.int/healthinfo/systems/surveydata/index.php/catalog/71
South Africa	SAGE	2007	352	Asked to those who ever had a pelvic exam: The last time you had the pelvic examination, did you have a Pap smear test?(By Pap smear test, I mean did a doctor or nurse use a swab or stick to wipe from inside your vagina, take a sample and send it to a laboratory?)	N/A	N/A	https://www.spirometry.com/wp-content/uploads/2020/02/South-Africa-WEB.pdf	https://apps.who.int/healthinfo/systems/surveydata/index.php/catalog/5
South Africa	SABSSM	2012	12821	Have you ever had a test for a Pap smear? (By Pap smear test, I mean did a doctor or nurse use a swab or stick to wipe from inside your vagina, take a sample and send it to the laboratory).	When was the last time you had this test?	N/A	http://www.hsrc.ac.za/uploads/pageContent/4565/SABSSM%20IV%20LEO%20final.pdf	http://curation.hsrc.ac.za/index.php?module=pagesetter&type=user&func=hsrcdataset&ppnumber=PFAJLA&datasetno=30

South Africa	DHS	2016	5546	Have you ever had a Pap smear? PROBE: When visiting a doctor or nurse, have you ever been asked to lie on your back with your legs apart so they could use a stick to take a sample from your vagina? The sample would have been sent to a laboratory for testing.	How many years ago was your last Pap smear?	N/A	https://dhsprogram.com/pubs/pdf/FR337/FR337.pdf	https://dhsprogram.com/methodology/survey/survey-display-390.cfm
Zimbabwe	WHS	2003	1337	Asked to those who've ever had a pelvic exam within the past three years: The last time you had the pelvic examination, did you have a Pap smear test?(By Pap smear test, I mean did a doctor or nurse use a swab or stick to wipe from inside your vagina, take a sample and send it to a laboratory?)	N/A	N/A	https://www.who.int/healthinfo/survey/whszwe-zimbabwe.pdf	https://apps.who.int/healthinfo/systems/surveydata/index.php/catalog/69
Zimbabwe	DHS	2015	11955	Have you ever been screened for cervical cancer?	When were you last screened for cervical cancer?	N/A	https://dhsprogram.com/pubs/pdf/FR322/FR322.pdf	https://dhsprogram.com/methodology/survey/survey-display-475.cfm
Zimbabwe[a, b]	PHIA	2020	1439	Have you ever been tested for cervical cancer?	What month and year was your last test for cervical cancer?	Did you receive treatment after your last test for cervical cancer? Did you receive treatment on the same day or on a different day?	https://phia.icap.columbia.edu/wp-content/uploads/2021/11/171121_ZIMPHIA2020_V13_18MB.pdf	https://phia.icap.columbia.edu/zimbabwe2020-final-report/
Zimbabwe	PHIA	2015-16	26730	Have you ever been tested for cervical cancer?	What month and year was your last test for cervical cancer?	N/A	https://phia.icap.columbia.edu/wp-content/uploads/2020/02/ZIMPHIA-Final-Report_integrated_Web-1.pdf	https://phia-data.icap.columbia.edu/files
Western Africa								
Benin	STEPS	2015	1739	Have you ever had a screening test for cervical cancer, using any of these methods described above (i.e., VIA, Pap smear or HPV test)?	N/A	N/A	https://extranet.who.int/ncdsmicrodata/index.php/catalog/107/download/1044	https://extranet.who.int/ncdsmicrodata/index.php/catalog/107
Benin	DHS	2017-18	9318	Est-ce qu'un médecin ou du personnel de santé vous a déjà fait un test de détection du cancer du col de l'utérus ?	Quand a eu lieu votre dernier test pour le cancer de l'utérus ?	Avez-vous suivi un traitement pour le col de l'utérus ou avez-vous fait des visites de suivi à cause des résultats du test ?[c]	https://dhsprogram.com/pubs/pdf/FR350/FR350.pdf	https://dhsprogram.com/methodology/survey/survey-display-491.cfm
Burkina Faso	WHS	2003	1305	Asked to those who've ever had a pelvic exam within the past three years: The last time you had the pelvic examination, did you have a Pap smear test?(By Pap smear test, I mean did a doctor or nurse use a swab or stick to wipe from inside your vagina, take a sample and send it to a laboratory?)	N/A	N/A	https://www.who.int/healthinfo/survey/whsbfa-burkinafaso.pdf	https://apps.who.int/healthinfo/systems/surveydata/index.php/catalog/20

Burkina Faso[a]	STEPS	2013	528	Have you ever had a screening test for cervical cancer, using any of these methods described above (i.e., VIA, Pap smear or HPV test)?	N/A	N/A	https://extranet.who.int/ncdsmicrodata/index.php/catalog/318/download/2484	https://www.who.int/publications/m/item/2013-steps-country-report-burkina-faso
Cameroon	DHS	2018	15400	Est-ce qu'un médecin ou un autre professionnel de santé vous a déjà fait un test de détection du cancer du col de l'utérus ?	N/A	N/A	https://dhsprogram.com/pubs/pdf/FR360/FR360.pdf	https://dhsprogram.com/methodology/survey/survey-display-511.cfm
Cape Verde	STEPS	2019	1431	Have you ever had a screening test for cervical cancer, using any of these methods described above (i.e., VIA, Pap smear or HPV test)?	N/A	Did you receive any treatment to your cervix because of your test result?	N/A	Requested through internal communications
Chad	WHS	2003	1115	Asked to those who've ever had a pelvic exam within the past three years: The last time you had the pelvic examination, did you have a Pap smear test?(By Pap smear test, I mean did a doctor or nurse use a swab or stick to wipe from inside your vagina, take a sample and send it to a laboratory?)	N/A	N/A	https://www.who.int/healthinfo/survey/whstcd-chad.pdf	https://apps.who.int/healthinfo/systems/surveydata/index.php/catalog/77
Cote d'Ivoire	WHS	2003	682	Asked to those who've ever had a pelvic exam within the past three years: The last time you had the pelvic examination, did you have a Pap smear test?(By Pap smear test, I mean did a doctor or nurse use a swab or stick to wipe from inside your vagina, take a sample and send it to a laboratory?)	N/A	N/A	https://www.who.int/healthinfo/survey/whsciv-cotedivoire.pdf	https://apps.who.int/healthinfo/systems/surveydata/index.php/catalog/93
Cote d'Ivoire	DHS	2011-12	6063	Avez-vous déjà fait un test du col de l'utérus ?	N/A	N/A	https://dhsprogram.com/pubs/pdf/FR272/FR272.pdf	https://dhsprogram.com/methodology/survey/survey-display-311.cfm
Ghana	WHS	2003	1146	Asked to those who've ever had a pelvic exam within the past three years: The last time you had the pelvic examination, did you have a Pap smear test?(By Pap smear test, I mean did a doctor or nurse use a swab or stick to wipe from inside your vagina, take a sample and send it to a laboratory?)	N/A	N/A	https://www.who.int/healthinfo/survey/whsgha-ghana.pdf	https://apps.who.int/healthinfo/systems/surveydata/index.php/catalog/96
Ghana	SAGE	2007	628	Asked to those who ever had a pelvic exam: The last time you had the pelvic examination, did you have a Pap smear test?(By Pap smear test, I mean did a doctor or nurse use a swab or stick to wipe from inside your vagina, take a sample and send it to a laboratory?)	When was the last time you had a pelvic examination, if ever? (By pelvic examination, I mean when a doctor or nurse examined your vagina and uterus?)	N/A	https://apps.who.int/healthinfo/systems/surveydata/index.php/catalog/6/download/1940	https://apps.who.int/healthinfo/systems/surveydata/index.php/catalog/6

Mali	WHS	2003	724	Asked to those who've ever had a pelvic exam within the past three years: The last time you had the pelvic examination, did you have a Pap smear test?(By Pap smear test, I mean did a doctor or nurse use a swab or stick to wipe from inside your vagina, take a sample and send it to a laboratory?)	N/A	N/A	https://www.who.int/healthinfo/survey/whsmli-mali.pdf	https://apps.who.int/healthinfo/systems/surveydata/index.php/catalog/79
Mauritania	WHS	2003	1064	Asked to those who've ever had a pelvic exam within the past three years: The last time you had the pelvic examination, did you have a Pap smear test?(By Pap smear test, I mean did a doctor or nurse use a swab or stick to wipe from inside your vagina, take a sample and send it to a laboratory?)	N/A	N/A	https://www.who.int/healthinfo/survey/whsmrt-mauritania.pdf	https://apps.who.int/healthinfo/systems/surveydata/index.php/catalog/98
Sao Tome and Principe	STEPS	2019	878	Have you ever had a screening test for cervical cancer, using any of these methods described above (i.e., VIA, Pap smear or HPV test)?	N/A	N/A	N/A	Requested through internal communications
Senegal	WHS	2003	620	Asked to those who've ever had a pelvic exam within the past three years: The last time you had the pelvic examination, did you have a Pap smear test?(By Pap smear test, I mean did a doctor or nurse use a swab or stick to wipe from inside your vagina, take a sample and send it to a laboratory?)	N/A	N/A	https://www.who.int/healthinfo/survey/whssen-senegal.pdf	https://apps.who.int/healthinfo/systems/surveydata/index.php/catalog/87
Senegal	STEPS	2014	1976	Have you ever had a screening test for cervical cancer, using any of these methods described above (i.e., VIA, Pap smear or HPV test)?	N/A	N/A	https://www.ansd.sn/ressources/publications/DV-STEPS-1-06-2016%20-%20MF-fin_ANSD%20vf.pdf	https://demostaf.web.ined.fr/index.php/catalog/114/study-description

[a] microdata unavailable only use of survey tabulations
[b] only information regarding WLHIV is available
[c] only 3 respondents answered these questions thus data from this question was not used

Text S1: Description of the methods and additional results for regional and national estimates of cervical cancer screening coverage time trends

S1.1 Screening Time Trends Model Equations

This section describes the model equations used to estimate the time trends in screening coverage for cervical cancer (CC).

When HIV serostatus data was available, the model took the following form:

$$Y_i \sim Binomial(N_i, p_i)$$

$$logit(p_i) = \alpha + \mu_{s[i]} + \upsilon_{c[i]} + \omega_{r[i]} + \delta_{r[i]} \times T_i + \sum_a (\beta_{a[i]} \times A_i) + \sum_a (\kappa_{a[i]} \times L_i) + \gamma_{c[i]} \times H_i$$

Where Y_i was the survey-adjusted number of women reporting CC screening for observation i, N_i was the effective sample size for that observation and p_i was the estimate of screening which was modelled on the logistic scale. CC screening coverage was modeled hierarchically with α as the global intercept, $\mu_{s[i]}$ as the survey-level intercepts, $\upsilon_{c[i]}$ as the country-level intercepts, and $\omega_{r[i]}$ as the region-level intercepts. We considered potential regional time trends through random slope coefficients $\delta_{r[i]}$ (i.e., linear trends on the logistic scale) and T_i as the centered calendar time in years. Age was modeled as a vector of fixed effects $\beta_{a[i]}$ using five categories (25-29, 30-34, 35-39, 40-44, and 45-49 years) that corresponded to the age group of the observation using indicator variable A_i. As the model included CC screening outcomes for both lifetime and past three years, we used age-specific indicators $\kappa_{a[i]}$ (as fixed effects) to "*cross-walk*" between the two recall periods[14], with L_i being a dummy variable indicating if the outcome for observation *i* corresponded to the three-year recall period. Finally, any potential effect of living with HIV on CC screening coverage was considered using country-level ($\gamma_{c[i]}$) random slope coefficients with H_i being an indicator of HIV status. This country-level random effect for HIV was nested within an overall and region-level effect ($\gamma_{c[i]} = \rho_{h[i]} + \rho_{r[i]} + \rho_{c[i]}$)

When HIV serostatus was not available, standardization was done which took the following form:

$$p_i = \widehat{HIV}_{c[i]} \times logit^{-1}\left(\alpha + \mu_{s[i]} + \upsilon_{c[i]} + \rho_{r[i]} + \delta_{r[i]} \times T_i + \sum_a (\beta_{a[i]} \times A_i) + \sum_a (\kappa_{a[i]} \times L_i) + \gamma_{r[i]}\right) +$$

$$(1\text{-}\widehat{HIV}_{c[i]}) \times logit^{-1}\left(\alpha + \mu_{s[i]} + \upsilon_{c[i]} + \rho_{r[i]} + \delta_{r[i]} \times T_i + \sum_a (\beta_{a[i]} \times A_i) + \sum_a (\kappa_{a[i]} \times L_i)\right)$$

Where $\widehat{HIV}_{c[i]}$ represents the country and year-specific HIV prevalence among women 25-49 years obtained from UNAIDS. As HIV prevalence estimates for women 25-49 years were not publicly available, it was estimated using the UNAIDS estimates for women 15-24 years and 15-49 years alongside the *UN World Population Prospects* (2019 revision) using the following formula where N represents the population of women at each age group (i.e., 15-24, 15-49 or 25-49).

$$\widehat{HIV}_{c,25-49} = (\widehat{HIV}_{c,15-49} * N_{15-49} - \widehat{HIV}_{c,15-24} * N_{15-24})/N_{25-49}$$

The model specification was completed using weakly informative prior distributions (see below). Posterior distributions of the parameters of interest were obtained using Hamiltonian Monte Carlo simulations. Specifically, inferences were based on 6 chains of 3000 iterations including 1000 iterations used for warm up. Convergence was examined using trace plots and by ensuring that the potential scale reduction factor for all parameters and hyperparameters remained close to one[1].

S1.2 Model Priors

Priors for the global, regional, country, and survey-level intercepts

The Bayesian model specification presented in the manuscript was completed using the following prior distributions.

$$\alpha \sim \mathcal{N}(0,\ 5)$$
$$\omega_r \sim \mathcal{N}(0,\ \sigma_r) \quad and \quad \sigma_r \sim \mathcal{HC}(0,3)$$
$$\upsilon_c \sim \mathcal{N}(0,\ \sigma_c) \quad and \quad \sigma_c \sim \mathcal{HC}(0,3)$$
$$\mu_s \sim \mathcal{N}(0,\ \sigma_s) \quad and \quad \sigma_s \sim \mathcal{HC}(0,3)$$

Where α represents the global intercept, ω_r represents region-level random intercepts, υ_c represents country-level, and μ_s is the survey-level random intercept. Each random intercept follows a normal distribution with mean 0 and has its own standard deviation (i.e., σ_r, σ_s, and σ_s). These standard deviations are given weakly informative half-Cauchy ($\mathcal{HC}$) priors.

Priors for the region-level random slope for time

$$\eta_t \sim N(0, 10)$$
$$\delta_r \sim \mathcal{N}(\eta_t,\ \sigma_t) \quad and \quad \sigma_t \sim \mathcal{HC}(0, 3)$$

Where η_t is the overall time trend (i.e., the log-odds ratio for time) and δ_r is the region-level time trend. The degree of pooling between the different regions' trends is determined by the standard deviation σ_t which is given a half-Cauchy prior.

Priors of the fixed effects for age and recall period

$$\beta_a \sim \mathcal{N}(0,\ 5)$$
$$\kappa_a \sim \mathcal{N}(0,\ 5)$$

Where β_a represents the fixed effect for each 5-year age group *a* and κ_a is the vector of fixed effects for the recall period (i.e., lifetime versus past three years) for each 5-year age group *a*.

Priors of the overall, region- and country-level random slopes for HIV

$$\rho_h \sim N(0, 10)$$
$$\rho_r \sim \mathcal{N}(0,\ \pi_r) \quad and \quad \pi_r \sim \mathcal{HC}(0, 3)$$
$$\rho_c \sim \mathcal{N}(0,\ \pi_c) \quad and \quad \pi_c \sim \mathcal{HC}(0, 3)$$

Where ρ_h is the overall pooled log-odds ratio for the effect of HIV on cervical cancer (CC) screening, ρ_r contains the region-level random slopes, and ρ_c the country-level random slopes for HIV. The standard deviations for the region-level (π_r) and the country-level (π_c) random slopes are given half-Cauchy priors.

Imputations and post-stratification

The Bayesian multilevel model provides estimates of the many parameters for the global, regional, and country-level intercepts. When combined with the regional random slopes for time, the fixed effects for age, the recall period, and HIV status, we can estimate screening

coverage ($\hat{p}_{c,a,t,r,h}$) for all relevant strata for country (c), age (a), time (t), recall (r), and HIV status (h) using the equation below

$$logit(\hat{p}_{c,a,t,r,h}) = \hat{\alpha} + \hat{\rho}_{r[c]} + \hat{\mu}_c + \hat{\delta}_{r[c]} \times T_t + \sum_a (\hat{\beta}_a \times A_a) + \sum_a (\hat{\kappa}_a \times L_a) + \hat{\gamma}_c \times H_h$$

In instances where we needed to predict a country without any survey data, we imputed their coverage based on the regional coverage and added the country-level uncertainty by sampling from the distribution of country-level intercepts (i.e., $\upsilon_c \sim \mathcal{N}(0,\ \sigma_c)$). Similarly, if a country did not have HIV information, coverage among WLHIV was estimated from the region-level random slope and the country-level uncertainty sampled from the distribution of the country-level random slopes.

The overall aggregate value for proportion of women screened was obtained by summing the proportion of women screened per age group and HIV status for each draw from the posterior multiplied by a weighted value for the specific age group, HIV status and country using the UN world prospects data and UNAIDS HIV prevalence estimates. This value is then divided by the overall sum to obtain our aggregate estimate.

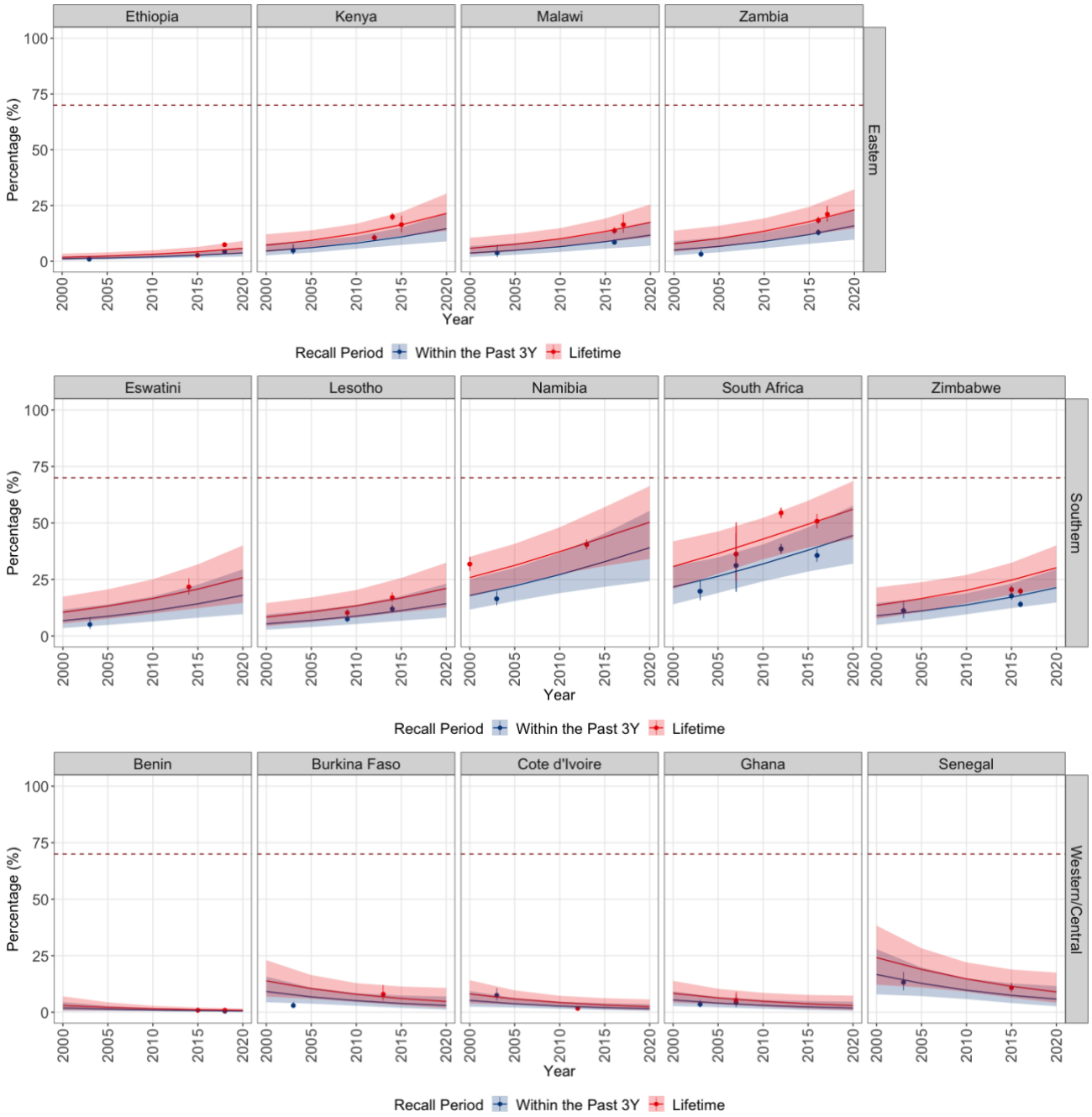


Figure S1. Country-level trends in lifetime and past three years cervical cancer screening coverage among women aged 30-49 years between 2000-2020. The red trendline represents screening trends for lifetime screening. The blue trendline represents screening trends for screening in the past three years. Points represent the empirical survey estimates of women reports of having been screened for cervical cancer. The dotted red line represents the 70% screening goal set by the World Health Organization.

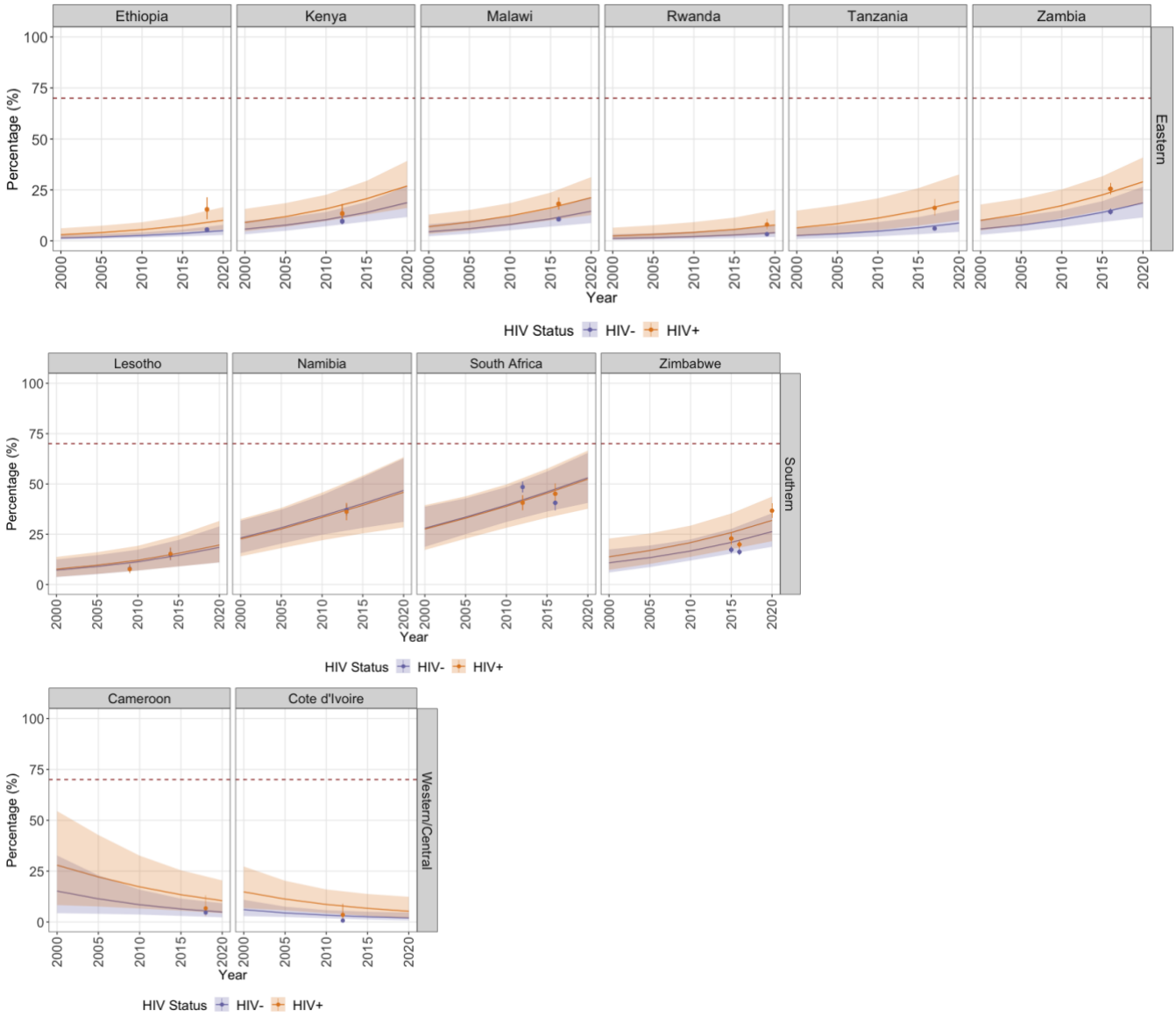


Figure S2. Country-level trends of lifetime cervical cancer screening stratified by HIV status for women aged 25-49 years between 2000-2020. The purple trendline represents screening trends for women living with HIV. The orange trendline represents screening trends for women without HIV. Points represent weighted screening proportions directly from survey data stratified by HIV status. The dotted red line represents the 70% screening goal set by the World Health Organization.

Table S2. Regional and country-level estimates of the percentage of women screened for cervical cancer in their lifetime and in the past three years in 2020 for countries with 2 or more surveys by 5-year age groups between 30-49.

	Lifetime screening (95%CrI)			
	30-34 years	**35-39 years**	**40-44 years**	**45-49 years**
Overall	12% (9-19%)	14% (11-21%)	15% (12-23%)	15% (12-24%)
Western/Central Africa	5% (2-18%)	6% (2-21%)	7% (3-23%)	7% (3-23%)
Benin	1% (0-1%)	1% (0-2%)	1% (0-2%)	1% (0-2%)
Burkina Faso	3% (2-9%)	4% (2-11%)	5% (2-12%)	5% (2-12%)
Côte d'Ivoire	2% (1-5%)	2% (1-6%)	2% (1-6%)	2% (1-6%)
Ghana	2% (1-6%)	2% (1-7%)	3% (1-8%)	3% (1-8%)
Senegal	7% (3-15%)	8% (4-17%)	9% (5-20%)	9% (5-20%)
Eastern Africa	11% (8-17%)	13% (9-19%)	15% (11-21%)	15% (11-21%)
Ethiopia	5% (3-8%)	6% (3-9%)	6% (4-10%)	6% (4-10%)
Kenya	18% (11-26%)	21% (14-31%)	24% (15-34%)	24% (15-34%)
Malawi	15% (9-22%)	17% (11-26%)	20% (12-28%)	20% (12-28%)
Zambia	20% (12-28%)	23% (15-32%)	26% (17-36%)	26% (17-36%)
Southern Africa	46% (35-57%)	51% (40-62%)	54% (43-65%)	55% (44-66%)
Eswatini	22% (12-35%)	25% (15-40%)	28% (17-44%)	28% (16-43%)
Lesotho	17% (11-28%)	21% (13-33%)	23% (14-36%)	23% (14-36%)
Namibia	45% (30-62%)	51% (34-67%)	54% (37-70%)	54% (38-70%)
South Africa	51% (38-64%)	56% (43-69%)	60% (47-72%)	60% (47-72%)
Zimbabwe	26% (19-36%)	30% (22-40%)	33% (24-44%)	33% (24-44%)
	Screening in the past three years (95%CrI)			
	30-34 years	**35-39 years**	**40-44 years**	**45-49 years**
Overall	9% (7-14%)	10% (8-16%)	11% (8-17%)	10% (7-16%)
Western/Central Africa	4% (1-14%)	4% (2-15%)	5% (2-16%)	4% (2-15%)
Benin	0% (0-1%)	1% (0-1%)	1% (0-1%)	0% (0-1%)
Burkina Faso	2% (1-6%)	3% (1-7%)	3% (1-8%)	3% (1-7%)
Côte d'Ivoire	1% (1-3%)	1% (1-4%)	1% (1-4%)	1% (1-4%)
Ghana	1% (1-4%)	2% (1-5%)	2% (1-5%)	2% (1-5%)
Senegal	5% (2-11%)	5% (3-12%)	6% (3-13%)	5% (3-11%)
Eastern Africa	8% (6-13%)	9% (6-14%)	10% (7-15%)	9% (6-14%)
Ethiopia	3% (2-5%)	4% (2-6%)	4% (2-6%)	4% (2-6%)
Kenya	13% (8-20%)	15% (9-22%)	16% (10-23%)	14% (9-21%)
Malawi	11% (6-17%)	12% (7-18%)	13% (8-19%)	11% (7-18%)
Zambia	15% (9-22%)	16% (10-24%)	17% (11-25%)	15% (10-23%)
Southern Africa	37% (27-49%)	40% (30-52%)	42% (31-53%)	40% (29-51%)
Eswatini	16% (9-28%)	18% (10-30%)	19% (10-32%)	17% (9-29%)
Lesotho	13% (8-22%)	14% (8-24%)	15% (9-25%)	14% (8-23%)
Namibia	37% (23-53%)	40% (25-56%)	41% (26-58%)	38% (24-55%)
South Africa	42% (30-56%)	45% (33-59%)	47% (34-60%)	44% (31-57%)
Zimbabwe	20% (14-28%)	22% (15-30%)	23% (16-32%)	21% (14-29%)

Model validation for regional and national estimates of cervical cancer screening coverage

Several candidate models were evaluated prior to selection of the final model. These candidate models included a) different nested structures for the random effects, b) addition of time-varying fixed effects indicating whether a national screening program was implemented, and c) using Gross National Income (GNI) per capita as a time-varying fixed effect. Ultimately, the model without an effect for national screening programs was preferred due to the limited amount of high-quality data regarding the actual implementation of those programs and limited impact on model fit. Similarly, adding GNI per capita did not influence our results (Figure S4 and Figure S5).

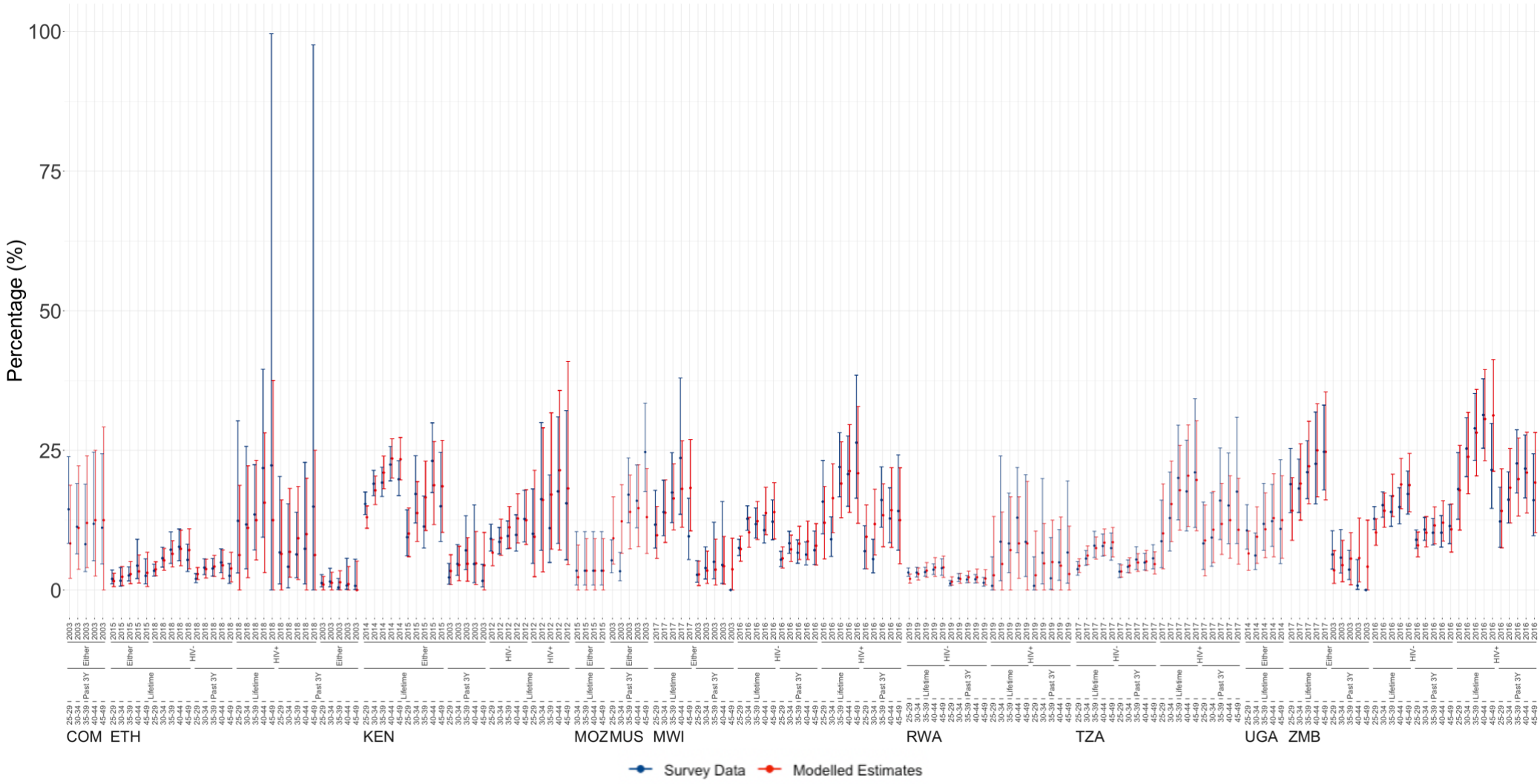
The posterior predictive checks (Figure S3), where model predictions are compared to the empirical observations, suggested that the current model fitted the data well and that differences, if any, were small and within uncertainty intervals. Finally, in-sample comparisons suggest small prediction errors with median absolute errors around 2% and reasonable coverage of credible intervals (Table S3).

Table S3: Posterior predictive checks: In-sample comparisons

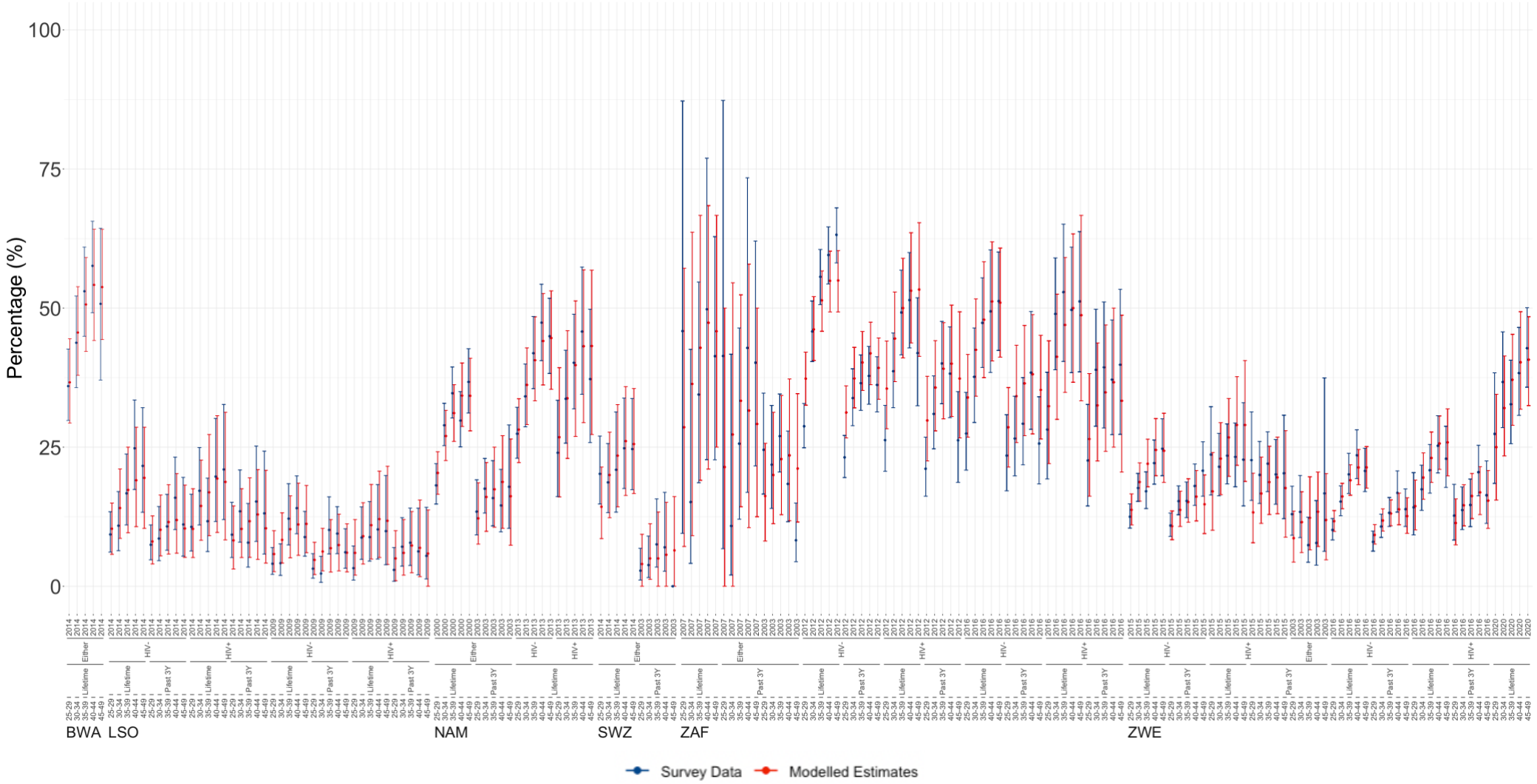
Recall period	Median error (%)	Median absolute error (%)	Below 95% CI (%)	Above 95% CI (%)
Within the past three years	0.1	2.4	6.4	3.2
Lifetime	-0.5	2.1	3.6	2.6
Overall	-0.3	2.2	4.9	2.9

Error represents median value for observed data – modelled data
Absolute error represents the median value for | observed data – modelled |
Above and below 95%CrI represents the number of data points modelled data points above and below the 95% CI of the observed data, respectively

A


Percentage (%)
100
75
50
25
0
Either
HIV-
HIV+
Lifetime
Past 3Y
COM
ETH
KEN
MOZ
MUS
MWI
RWA
TZA
UGA
ZMB
Survey Data
Modelled Estimates

B


Percentage (%)
100
75
50
25
0
BWA
LSO
NAM
SWZ
ZAF
ZWE
Survey Data
Modelled Estimates

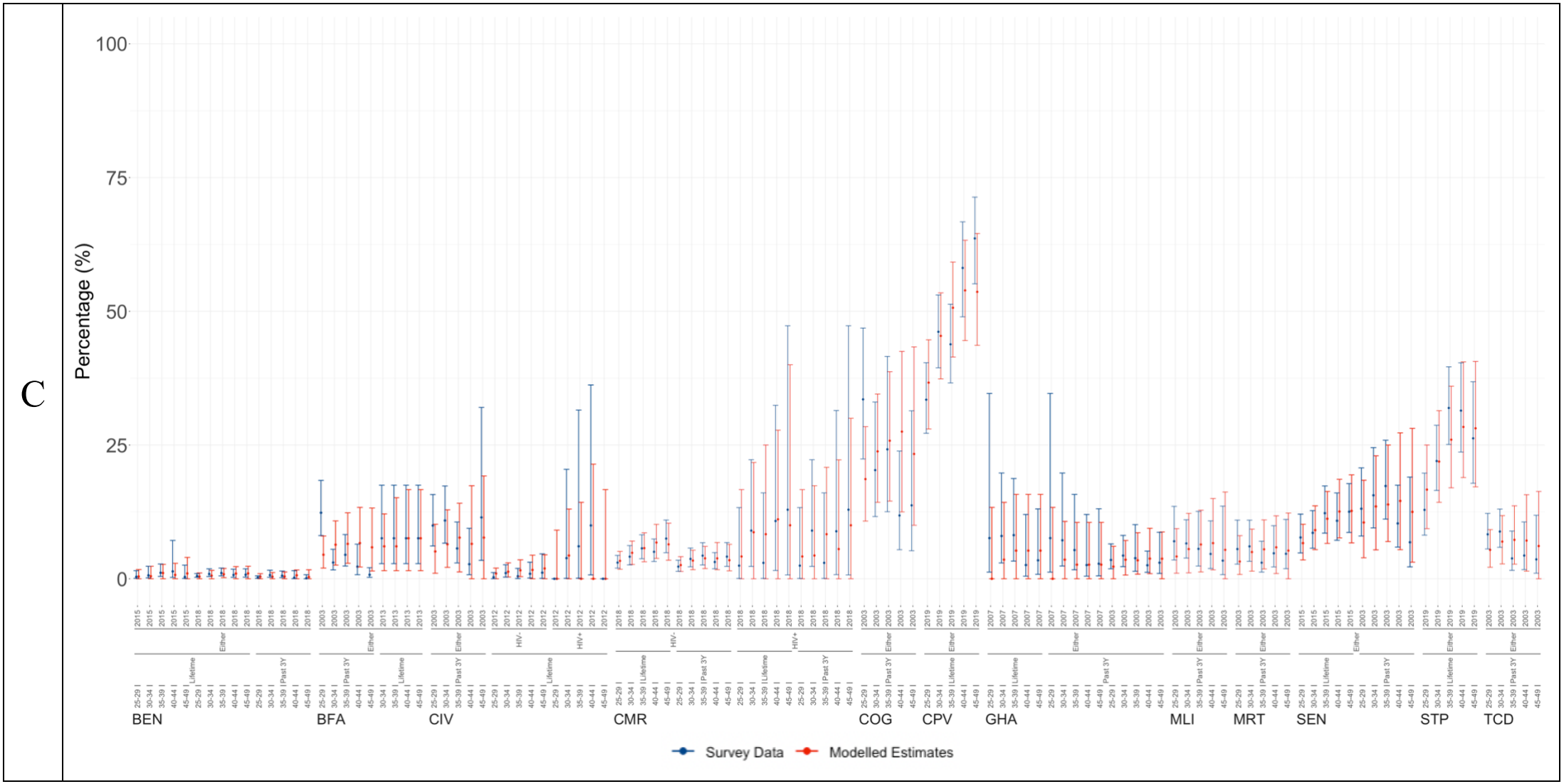


Figure S3. Posterior predictive checks comparing modelled estimates (red) to each empirical data point (blue) for the three regions. A) Eastern Africa region B) Southern Africa region C) Western/Central Africa region.

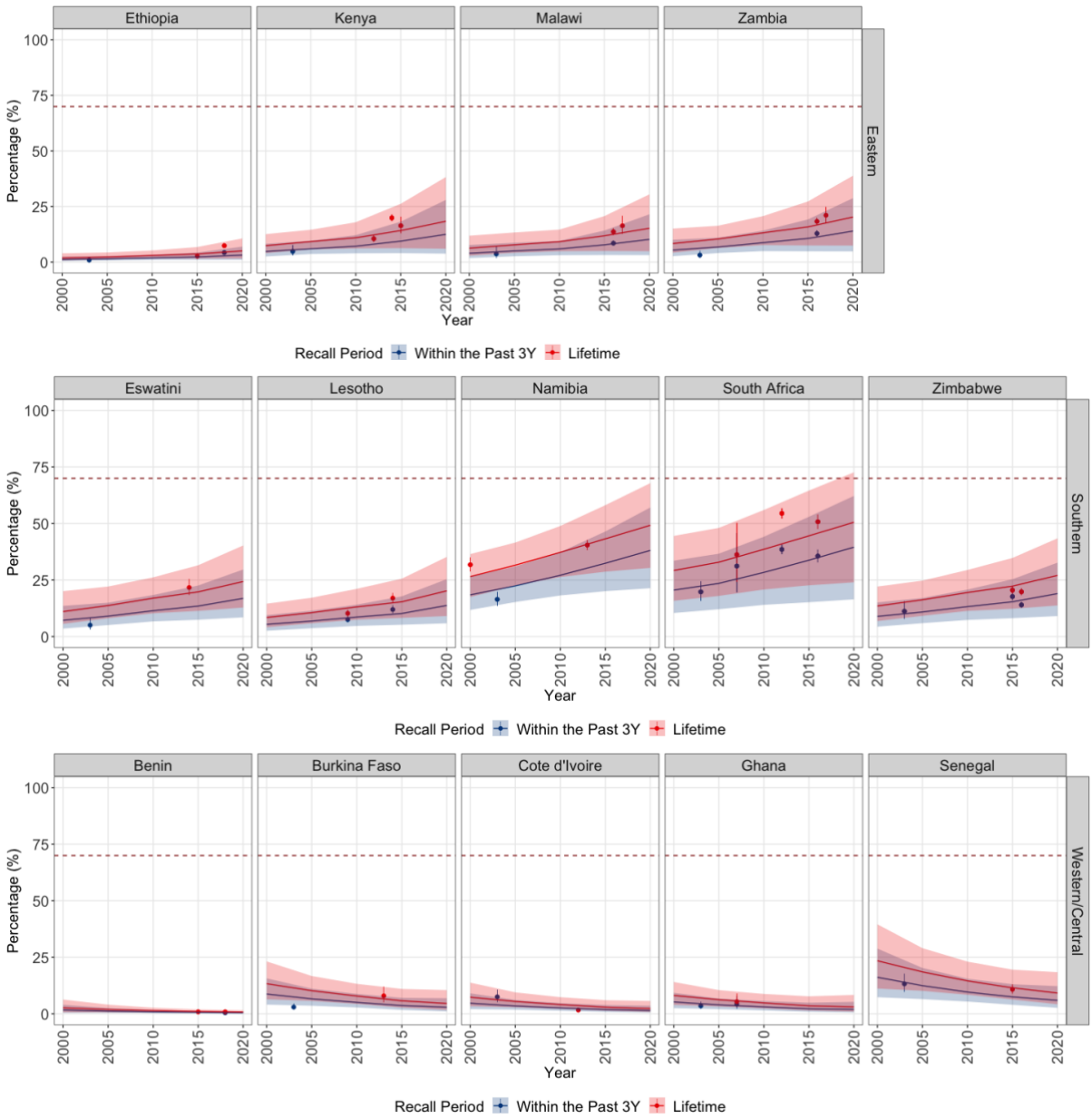


Figure S4. Country-level screening time trends with a fixed effect for national screening program.

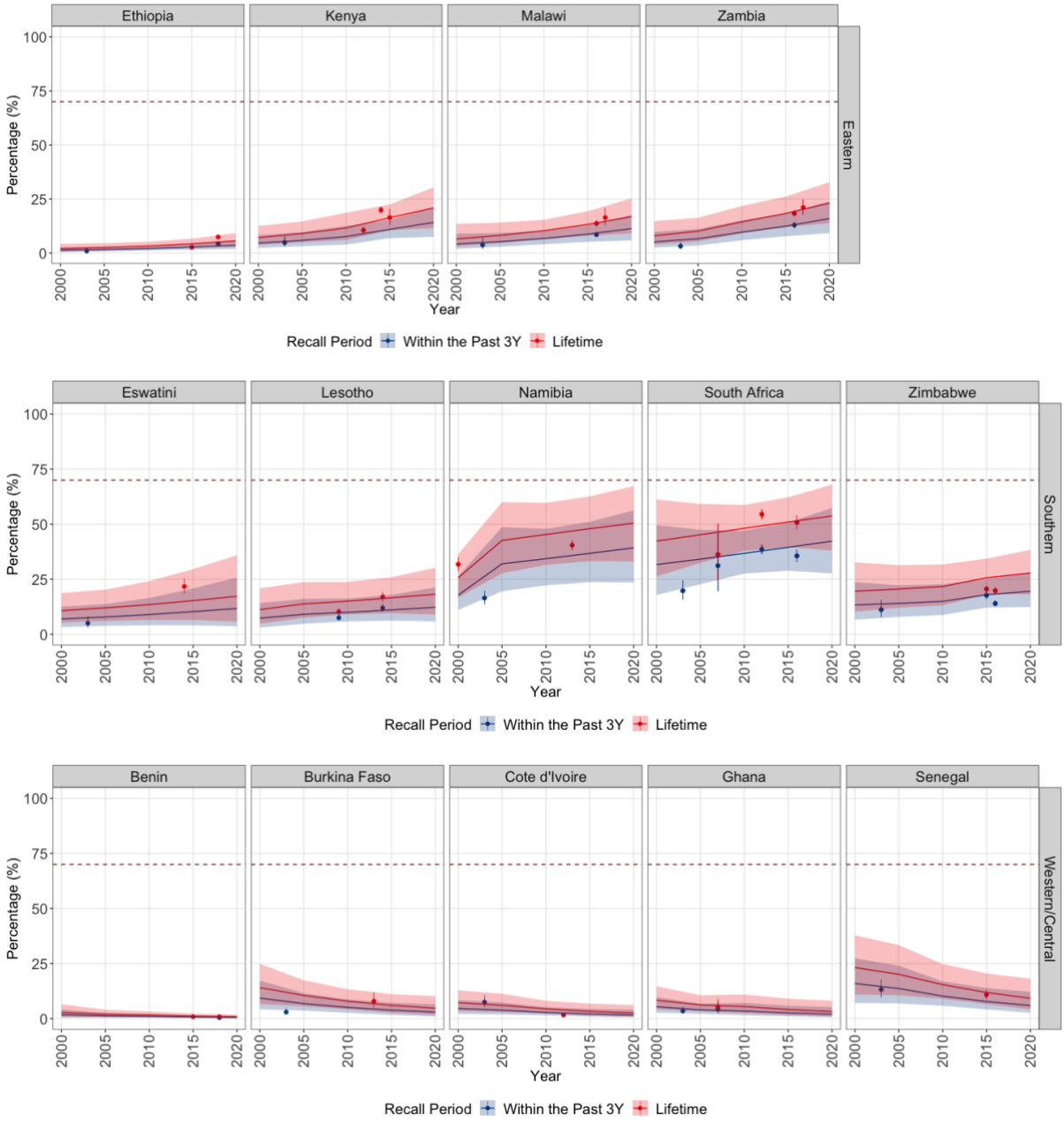


Figure S5: Country-level screening time trends with a fixed effect for Gross National Income

Text S2: Description of the methods and additional results for the WHO recommendations for frequency of re-screening

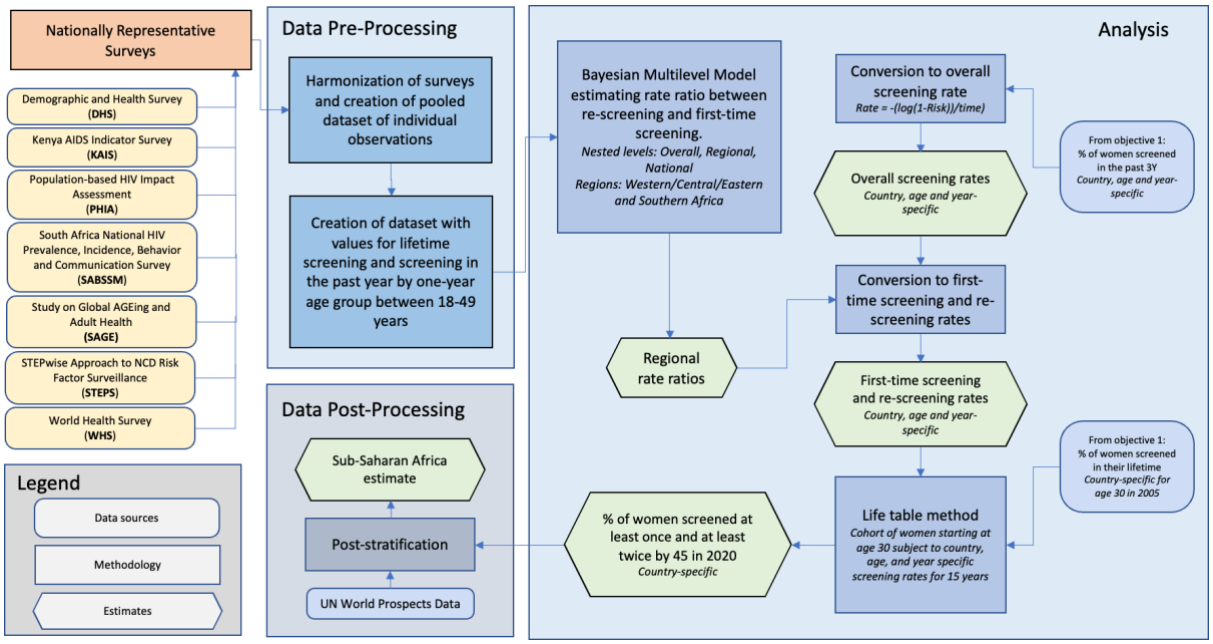


Figure S6. Conceptual framework to estimate re-screening rates and screening twice in a lifetime by age 45 outlining data inputs, data pre-processing, statistical analyses, and data post processing. UN=United Nations.

Life table method to estimate the number of times women have been screened

Age- and country-specific estimates of screening rates were obtained for every calendar year from 2005-2020 from the Bayesian multilevel model from the first objective. Specifically, we used estimates of the proportion screened in the past three years for each country, year, and five-year age group and converted that to an annual screening rate. This conversion assumed that screening rates were exponentially distributed (i.e., *rate = -(log(1-risk))/time*) and that it was an overall rate (i.e., includes first-time screen and repeated screens). This overall rate was then converted into re-screening and first-time screening rates using a modelled rate ratio between the rate of re-screening and first-time screening. Using life table methods, we then subjected a cohort of women aged 30 years to the age-, country-, and year-specific rates of first-time screening and re-screening (similar to calculations of life expectancy). The model was initialized in 2005 with women entering the life table as either never screened or screened once by the age of 30. The number of women who entered each category was informed by the Bayesian multilevel model from the first objective, specifically the proportion of women who had ever been screened between the ages of 25-29 years. At each time step (Δt = 0.1 year), never screened women could receive their first CC screen at an age and country-specific first-time screening rate. Those that had already been screened can be re-screened again, albeit at a different rate. This re-screening rate was informed by our analyses of the re-screening rate ratio (next section). At the end of each calendar year, the

cohort of women was aged, and age-specific rate of first-time screening and re-screening updated. We do not consider mortality as we assumed that, besides CC mortality, background mortality rates should not differ as a function of screening status. We proceeded as such for the next 15 years when this cohort of women would have reached the age of 45 years. Uncertainty was considered by using draws from the posterior distributions of the estimates (i.e., screening rates and re-screening ratios) to obtain the proportion of women screened twice by the aged of 45. The life table can be modelled using the following difference equations:

$$S^0_{a,t} = S^0_{a,t-1} - \Delta t(\lambda_{a,t} \times S^0_{a,t-1})$$
$$S^1_{a,t} = S^1_{a,t-1} + \Delta t(\lambda_{a,t} \times S^0_{a,t-1} - \phi \times \lambda_{a,t} \times S^1_{a,t-1})$$
$$S^2_{a,t} = S^2_{a,t-1} + \Delta t(\phi \times \lambda_{a,t} \times S^1_{a,t-1})$$

Where $S^0_{a,t}$ represents the number of women age *a* never screened at time *t*, $S^1_{a,t}$ represents the number of women age *a* screened once at time *t*, and $S^2_{a,t}$ represents the number of women age *a* screened twice or more at time *t*. Here, λ_a represents the first-time screening rate for women at age *a* (one of three 5-year age groups between 30-45 years). Finally, ϕ is the rate ratio between the rate of re-screening and first-time screening.

Estimation of the re-screening rate ratio

To obtain rates of first-time screening and re-screening, a Bayesian model was employed to estimate a re-screening rate ratio. This rate ratio was estimated from cross-sectional survey data where we abstracted information on lifetime and past year screening coverage for one-year age groups. The data is thus composed of the proportion of women reporting having ever been screened and the proportion screened in the last year for each survey and for each one-year age group. From this data, we estimated two key parameters: i) the age-specific rate of first screening and ii) the rate ratio for re-screening. The equations for this model are the following:

$$p^{ever}_{s,a} = P^{ever}_{s,a-1} + \lambda_{s,a} \times P^{never}_{s,a-1}$$
$$p^{past}_{s,a} = \left(\left(\lambda_{s,a} \times P^{never}_{s,a-1}\right) + \phi_s \times \lambda_{s,a} \times P^{ever}_{s,a-1}\right) \times \tau$$

These equations state that the proportion of women ever screened among all women in survey *s* for age *a* ($p^{ever}_{s,a}$) is the sum of the survey estimates of the proportion of women ever screened in the previous age group ($P^{ever}_{s,a-1}$), and the product of the survey- and age-specific first-time screening rate ($\lambda_{s,a}$) and the survey estimates of women who have never been screened in the previous age group ($P^{never}_{s,a-1}$). Similarly, the proportion of women screened in

the past year for survey *s* and age *a* ($p_{s,a}^{past}$) is the sum of the proportion of women who are screened for the first time ($\lambda_{s,a} \times P_{s,a-1}^{never}$) and the proportion who have been re-screened ($\phi \times \lambda_{s,a} \times P_{s,a-1}^{ever}$). Here, ϕ_s represents the survey-specific rate ratio between first-time screening and re-screening. The ϕ_s parameter was assumed to be age and time-invariant. Further, it was not possible to adjust for the age and HIV status since the denominators for WLHIV by one-year age group would have been too small to be reliable. Finally, we adjusted for potential telescoping bias using the τ parameter in sensitivity analyses. Simulations were done to validate this model and understand under which conditions it could produce unbiased estimates of the rate ratio (see next section). The model was fitted to the survey data using the following binomial likelihoods:

$$Y_{s,a}^{ever} \sim Binomial\left(N_{s,a}^{ever},\ p_{s,a}^{ever}\right)$$
$$Y_{s,a}^{past} \sim Binomial\left(N_{s,a}^{past},\ p_{s,a}^{past}\right)$$

Where $Y_{s,a}^{ever}$ is the survey-adjusted number of women reporting have ever been screened for CC in survey s and age group a, $N_{s,a}^{ever}$ is the survey denominator, $Y_{s,a}^{past}$ is the survey-adjusted number of women reporting have been screened in the past year, and $N_{s,a}^{past}$ is the denominator.

Priors used for this model were weakly informative.

$$\log\left(\lambda_{s,a}\right) \sim N(\log\,(0.005),\ 5)$$
$$\log(\phi_s) \sim N\left(\log\,(\phi_{r[s]}),\ \vartheta_{r[s]}\right)$$
$$\log\left(\phi_{r[s]}\right) \sim N(\log\,(\phi_o),\ \vartheta_o)$$
$$\log(\phi_o) \sim N(0,\ 5) \quad \text{and} \quad \vartheta_o \sim HC(0,\ 5)$$
$$\vartheta_{r[s]} \sim HC(0,\ 5)$$

Where $\lambda_{s,a}$ represents the survey and age specific rates of first-time screening. ϕ_s represents the survey-specific rate ratio between re-screening and first-time screening, ϕ_r represents the region-specific rate ratio (i.e., Western/Central/Eastern Africa or Southern Africa), and ϕ_o represents the overall rate ratio for sub-Saharan Africa. Western, Central, and Eastern Africa were modelled together as there was limited data on screening in the past year from surveys in Western/Central Africa. The survey-specific rate ratios are assumed to be distributed across a normal distribution with the mean as the overall region-specific rate ratio, and a region-specific standard deviation (ϑ_r). Similarly, the region-specific rate ratios are distributed across a normal distribution with the mean as the overall rate ratio for sub-Saharan Africa, and standard deviation ϑ_o

Our results found that the survey-specific rate ratios estimated by the model were highly variable (Table S4). As a result, the region-specific rate ratios were used to calculate the age-specific first-time screening and re-screening rates to be used in the life table.

Simulations to validate the proposed approach

To validate the approach for the estimation of re-screening rate ratios using cross-sectional survey data, we investigated the impact of age, cohort effects and period effects using simulations. Simulations were done to mimic the levels of lifetime screening found from the first objective and was done using two simulated regions with three countries each. Estimates for the rate ratio for the two regions were jointly modelled. First simulations were performed using screening rates that varied with age but were assumed stable throughout time (i.e., no cohort effects). The model predicted the "true" simulated estimates well under these conditions (Figure S8). Simulations were then performed using screening rates that differed with age and changed with time (i.e., cohort effects). These simulations found that the model only reproduced the "true" simulated results when the cohort effects were weak. When screening rates increased significantly throughout time however, the model would overestimate the rate ratios (ϕ_s) and these cohort effects would bias our results (Figure S8). However, these biases could be minimized when restricting the analyses to younger age groups (Figure S8). Finally, simulations were performed using screening rates that remained constant through time apart from a three-year period where screening was elevated proportionately for all age groups (e.g., period effects). In the presence of a weak period effect, our model was able to predict the true estimates relatively well. However, stronger period effects led to greater underestimation of the rate ratios (Figure S8).

Previous analyses of the time trends of screening coverage suggest that cohort effects could be absent or small in countries within Western/Central and Eastern Africa as screening coverage was found to be relatively stagnant over time. However, this was not the case for Southern Africa, as such we only used data from women 18-29 years in this region. In contrast, we used all data from women aged 18-49 years in Western/Central/Eastern Africa. Age groups start at age 18 as that is the age in which all available surveys have data. Additionally, this analysis assumes that period effects are minimal and that screening services were available in sub-Saharan Africa for at least 30 years prior to 2020.

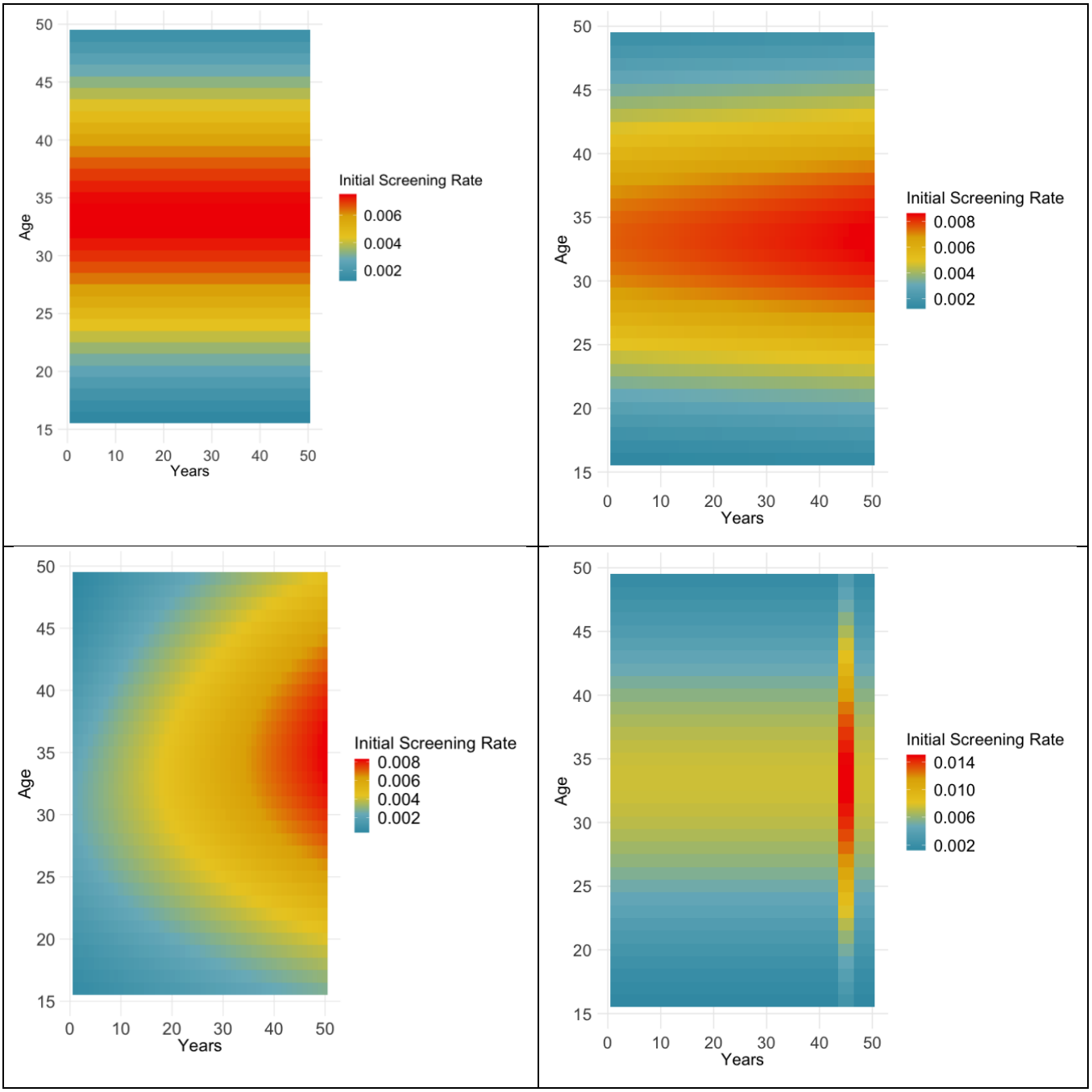
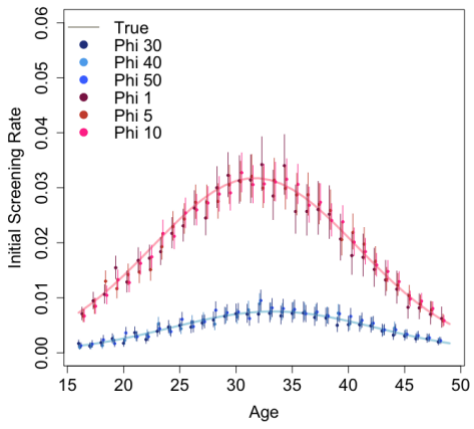
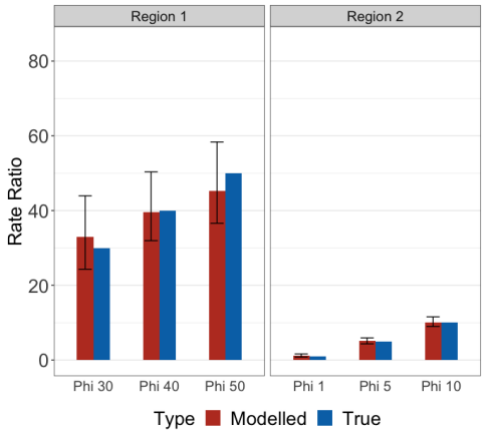
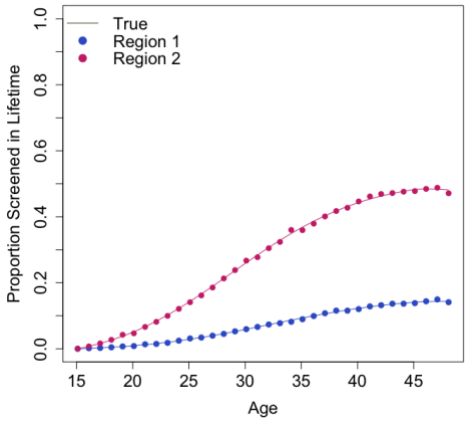
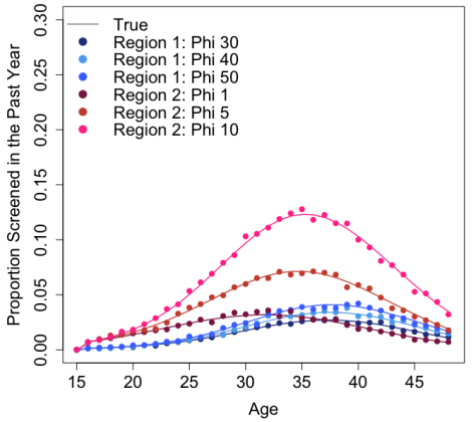
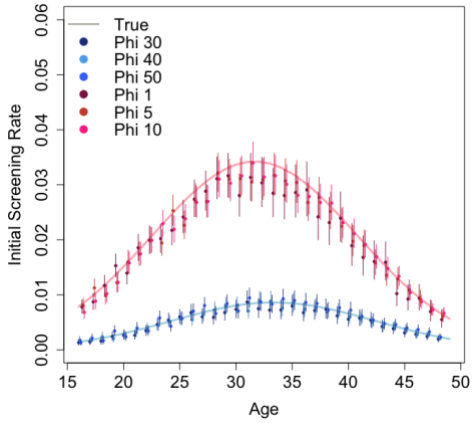
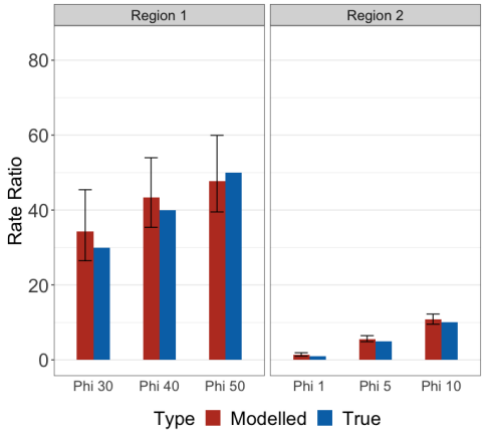
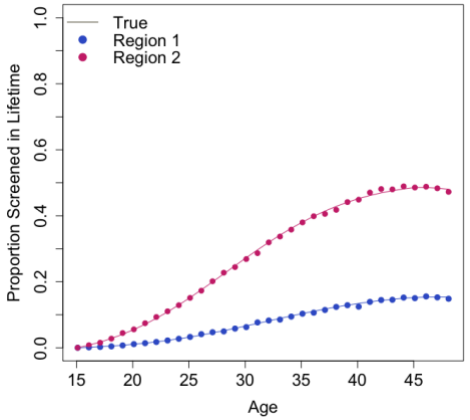
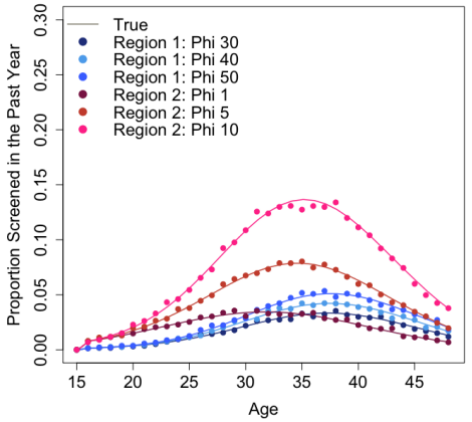
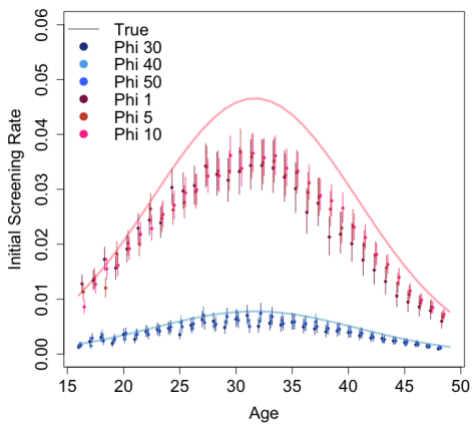
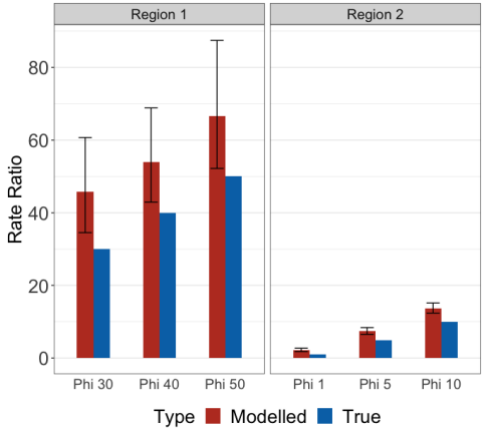


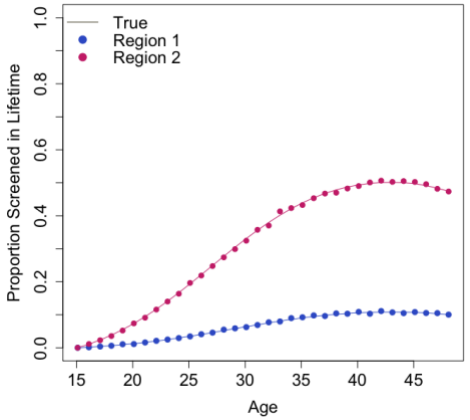
Figure S7. Heat map of simulated first-time screening rates across 50 years for women 15-49. The top-left panel represents screening rates that remain constant through time but that increases with age up until age 35 (i.e., no cohort effects). The top-right panel represent screening rates that are slowly changing through time but increases with age (i.e., weak cohort effects). The bottom-left panel represents screening rates that are changing over time and age (i.e., strong cohort effects). The bottom-right panel represents screening rates that are constant over time but except for a 3-year period where screening is 2-fold greater for all age groups (i.e., strong period effects).

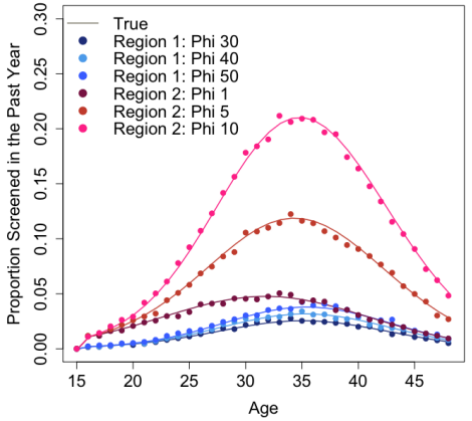
	First-time Screening Rate (λ)	Rate Ratio (ϕ)	Lifetime Screening	Screening in the Past Year
A				
B				

C

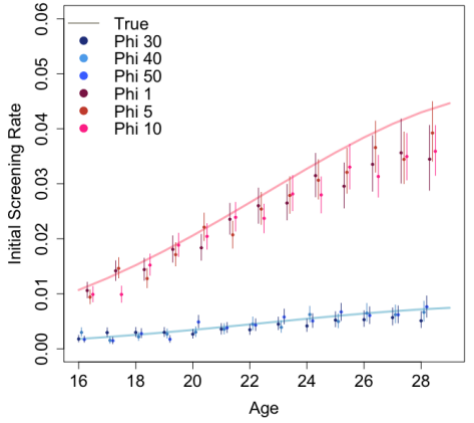

True
Phi 30
Phi 40
Phi 50
Phi 1
Phi 5
Phi 10
Initial Screening Rate
Age

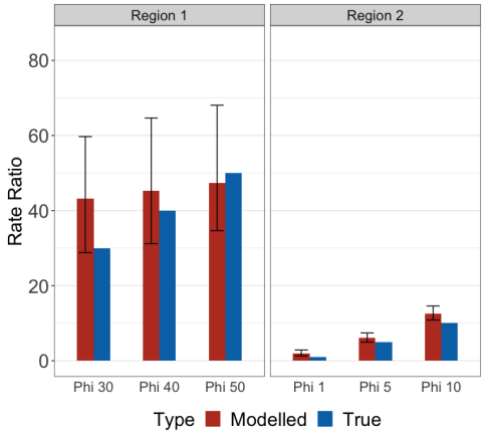

Region 1
Region 2
Rate Ratio
Phi 30
Phi 40
Phi 50
Phi 1
Phi 5
Phi 10
Type Modelled True

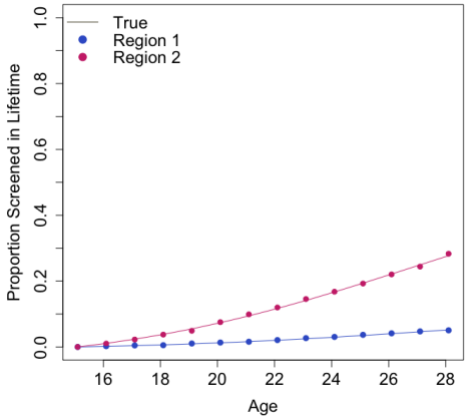

True
Region 1
Region 2
Proportion Screened in Lifetime
Age

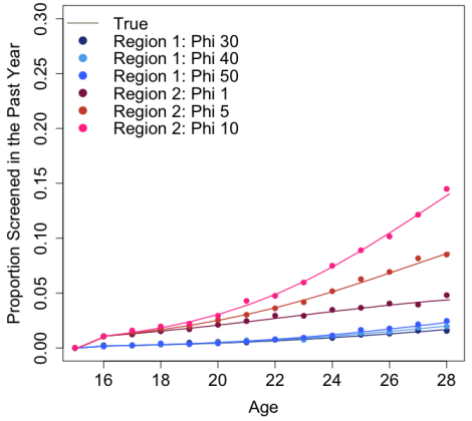

True
Region 1: Phi 30
Region 1: Phi 40
Region 1: Phi 50
Region 2: Phi 1
Region 2: Phi 5
Region 2: Phi 10
Proportion Screened in the Past Year
Age

D

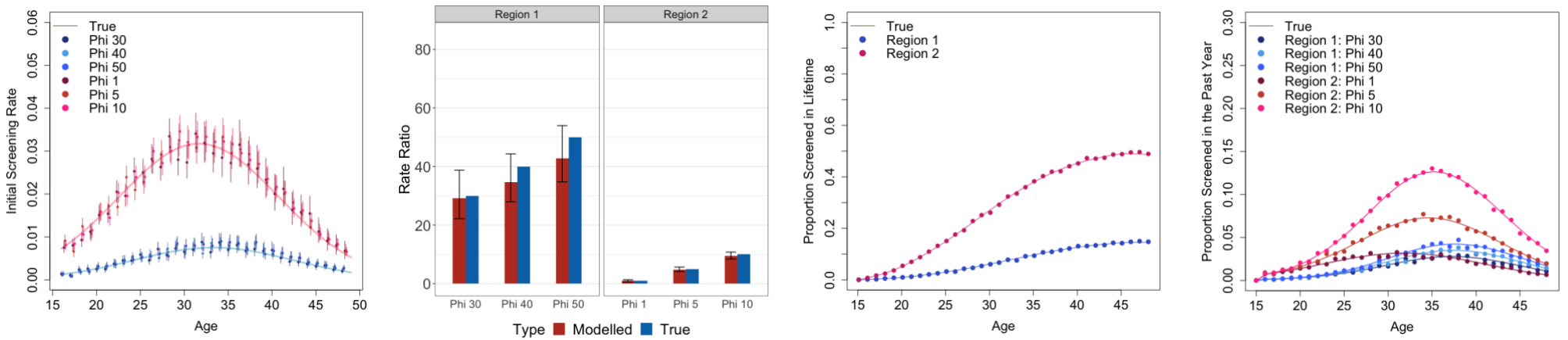

True
Phi 30
Phi 40
Phi 50
Phi 1
Phi 5
Phi 10
Initial Screening Rate
Age


Region 1
Region 2
Rate Ratio
Phi 30
Phi 40
Phi 50
Phi 1
Phi 5
Phi 10
Type Modelled True


True
Region 1
Region 2
Proportion Screened in Lifetime
Age


True
Region 1: Phi 30
Region 1: Phi 40
Region 1: Phi 50
Region 2: Phi 1
Region 2: Phi 5
Region 2: Phi 10
Proportion Screened in the Past Year
Age

E



F

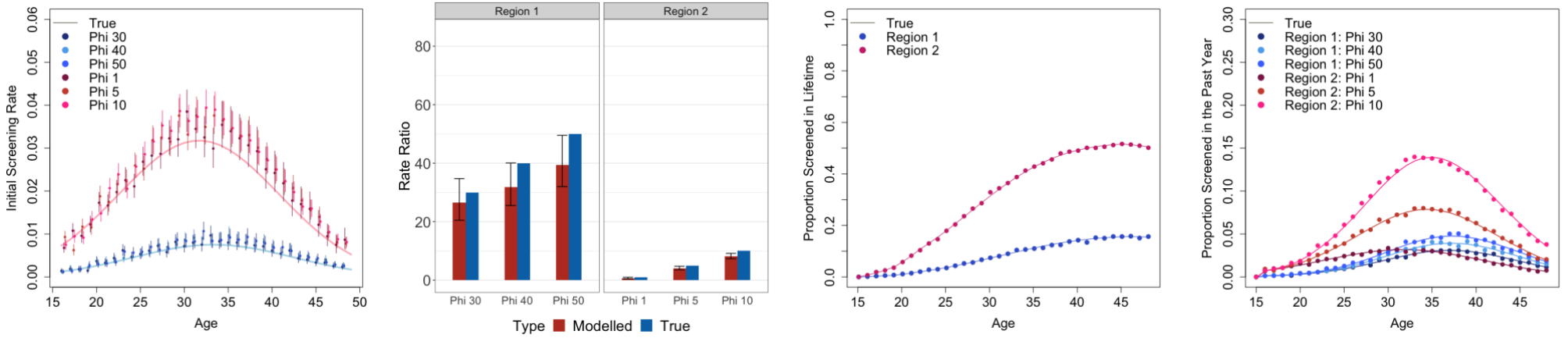


Figure S8. Re-screening model simulations comparison of simulated first-time screening rate and rate ratio estimates to modelled estimates. 6 re-screening rate ratios (i.e., 1, 5, 10, 30, 40, 50) belonging to two simulated region and a sample size of 10000 are estimated. Simulations were done to approximately replicate lifetime and past year screening proportions in Western/Central/Eastern Africa (Region 1) and Southern Africa (Region 2). A) When simulated age-specific first-time screening rates are unchanging for women 15-49. B) When age-specific first-time screening rates are only minimally changing over time for women 15-49. C) When there are important changes in age-specific first-time screening rates over time from for women 15-49. D) When there are important changes in age-specific first-time screening rates over time from for women 15-29. E) When age-specific first-time screening rates are unchanging except for a 3-year period where screening rates are increased 1.2-fold for women 15-49. F) When age-specific first-time screening rates are unchanging except for a 3-year period where screening rates are increased 2-fold for women 15-49.

Results for the estimates of re-screening rate ratio

Survey-specific re-screening rate ratios (ϕ_s) were obtained from countries with available survey data (Table S4), as well as region-specific rate ratios, and an overall rate ratio.

Estimates for the rate ratio parameters were characterized by wide uncertainties. However, all re-screening ratios were large and ranged from 8.3 (95%CrI: 3.9-20.8) in South Africa to 47.1 (18.5, 212.5) in Zimbabwe (Table S4). We also report on a sensitivity analysis that adjust for potential telescoping bias. Specifically, we assumed that women would report all screened occurring in the past 18 months as being performed in the last year. Qualitatively, the results for the rate ratio point to high re-screening rates in most countries (Table S4).

Table S4. Estimates of the rate ratio for rate of re-screening for cervical cancer as compared to rate of first-time screening with and without adjustment for telescoping bias.

	Rate Ratios (95%CrI)	
Country	**Recall period of one year (no bias)**	**Recall period of 18 months (telescoping bias)**
Overall	22.8 (0, 610)	10.7 (0, 476.4)
Western/Central/Eastern Africa	34.1 (16.8, 60)	17.4 (6.8, 36)
Benin DHS 2018	32.6 (6, 75)	16.5 (2.1, 47.3)
Cape Verde STEPS 2019	32.4 (5.7, 77.3)	16.5 (2, 50)
Ethiopia PHIA 2018	39.7 (20.2, 96.2)	20.8 (8.3, 60.1)
Ghana SAGE 2007	31.2 (4.7, 69.8)	16 (2, 46.2)
Malawi PHIA 2016	36.5 (18.6, 71.4)	19.1 (7.9, 47.8)
Rwanda PHIA 2019	35.1 (13.5, 83)	17.1 (2.8, 45.1)
Tanzania PHIA 2017	39.0 (19.9, 89.3)	20.5 (8, 57.6)
Zambia PHIA 2016	33.4 (16.3, 68.5)	18 (8.2, 41.5)
Southern Africa	21.2 (4.7, 64.9)	8.8 (0.5, 35.4)
Lesotho DHS 2009	17.4 (0.8, 79.8)	6.2 (0, 41.7)
Lesotho DHS 2014	27.1 (5, 136.8)	10.7 (0.1, 100)
South Africa SABSSM 2012	8.3 (3.9, 20.8)	3.9 (1.3, 11.7)
South Africa SAGE 2007	9.6 (0.5, 84.7)	3.6 (0, 31.3)
Zimbabwe DHS 2015	29.2 (11.6, 99.6)	12.2 (2.7, 50.4)
Zimbabwe PHIA 2016	47.1 (18.5, 212.5)	24.8 (6.5, 114)

(DHS = *Demographic and Health Survey*; PHIA = *Population-based HIV Impact Assessment*; SABSMM = *South Africa National HIV Prevalence, Incidence, Behavior and Communication Survey*; SAGE = *Study on Global AGEing and Adult Health*; STEP = *STEPwise Approach to NCD Risk Factor Surveillance*.)
For this analysis, the Western/Central and Eastern Africa regions were combined (hence the same rate ratio)

Robustness check for the life table methods

To investigate the robustness of our approach for the estimation of the proportion of women screened twice, we compared the estimates of lifetime screening by age 45 years in 2020 from the life table to those of lifetime screening among women aged 40-44 years old obtained from the model from objective 1 (see Text S1). Because the age groups differ slightly, as well as the underlying modeling assumptions, we do not expect estimates to be exactly the same. However, they should be relatively similar. Overall, our results suggest that the pooled estimates of lifetime screening from both methods are concordant (Figure S9). Country-level estimates with countries with 2 or more surveys are also presented here. Greater discrepancies exist for the country-level estimates, and they are also characterized by wide uncertainties.

Additionally, sensitivity analyses using various rate ratio values was done (Figure S10). Although country-level estimates varied greatly with different rate ratio values, pooled estimates for screening twice in a lifetime did not vary greatly. Altogether, these results suggest that estimates of lifetime testing are generally robust for the pooled estimates.

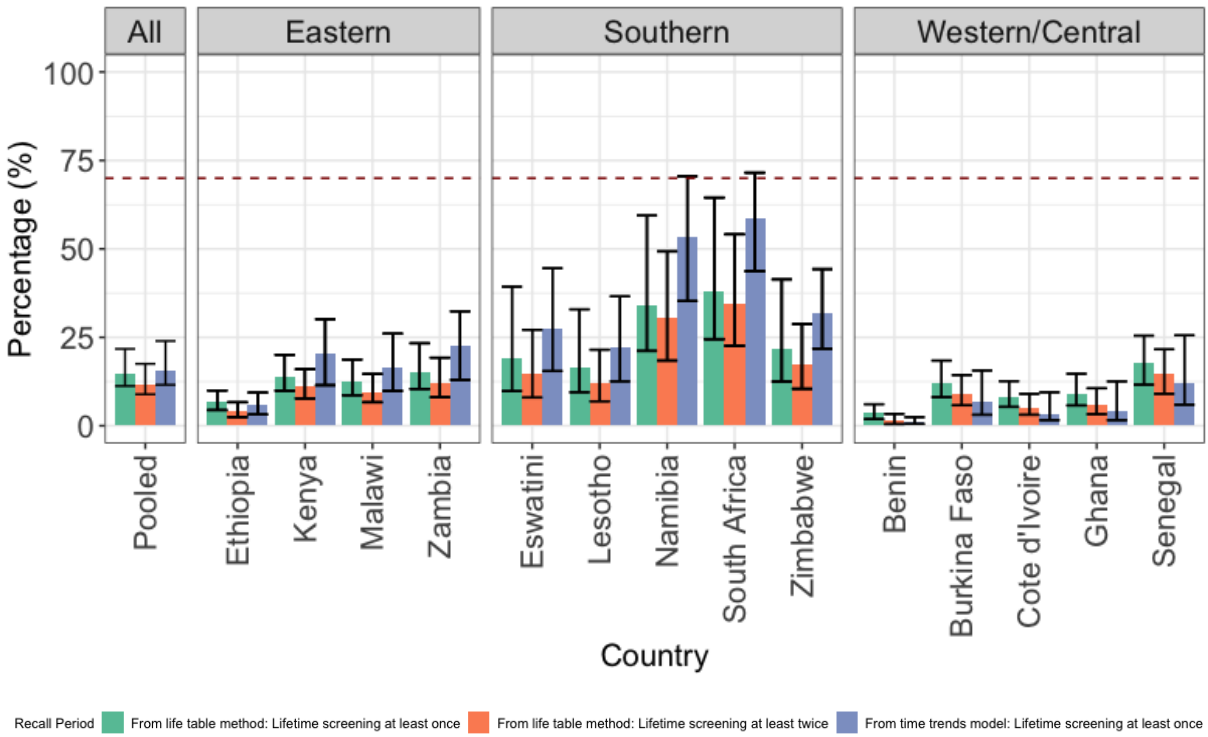
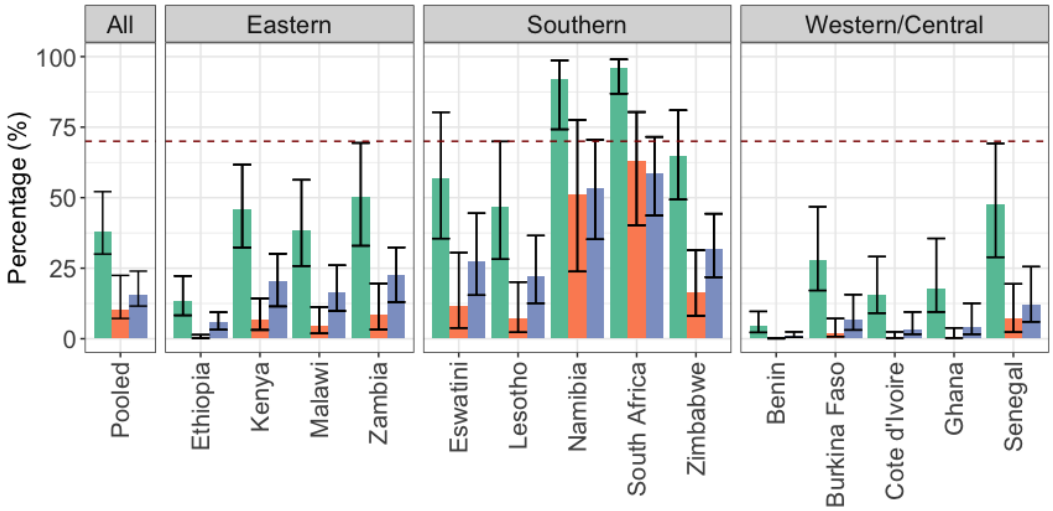
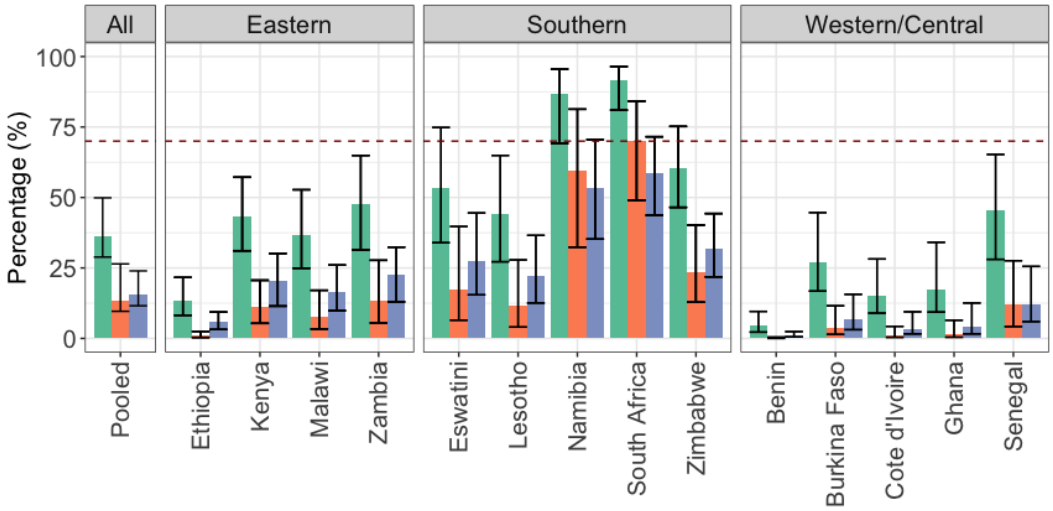
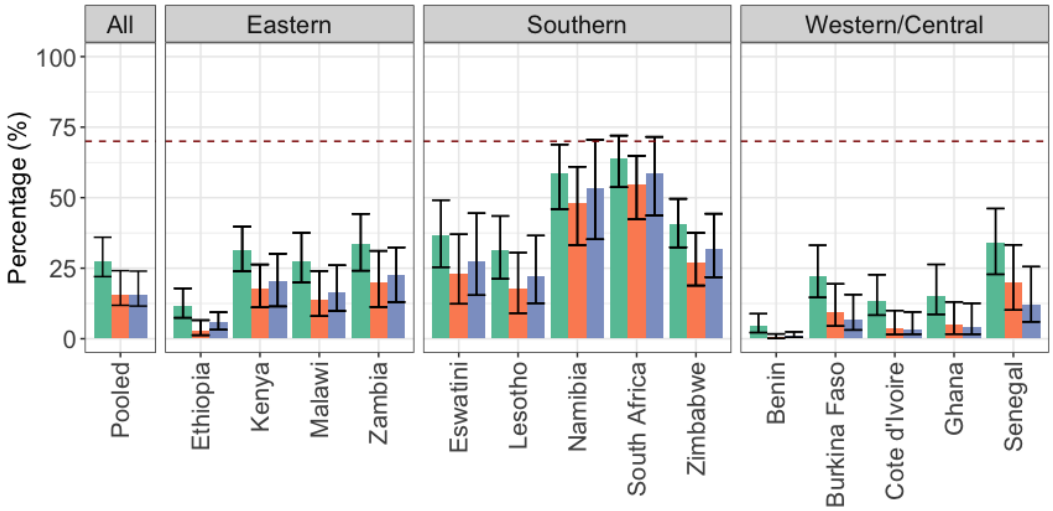


Figure S9. Robustness check of estimates for screening twice by the age of 45 years. This allows for comparison of lifetime screening estimates from the life table method (green bar) to the lifetime screening estimates from the time-trends model (purple bar). Orange bars represent estimates for screening twice. This is done to investigate the robustness of the life table method as the green bars and the purple bars should give comparable estimates.

	Rate Ratio (ϕ)	Estimates from Life Table
A	0.5	
B	1	
C	5	

D 10

E 30

F 50

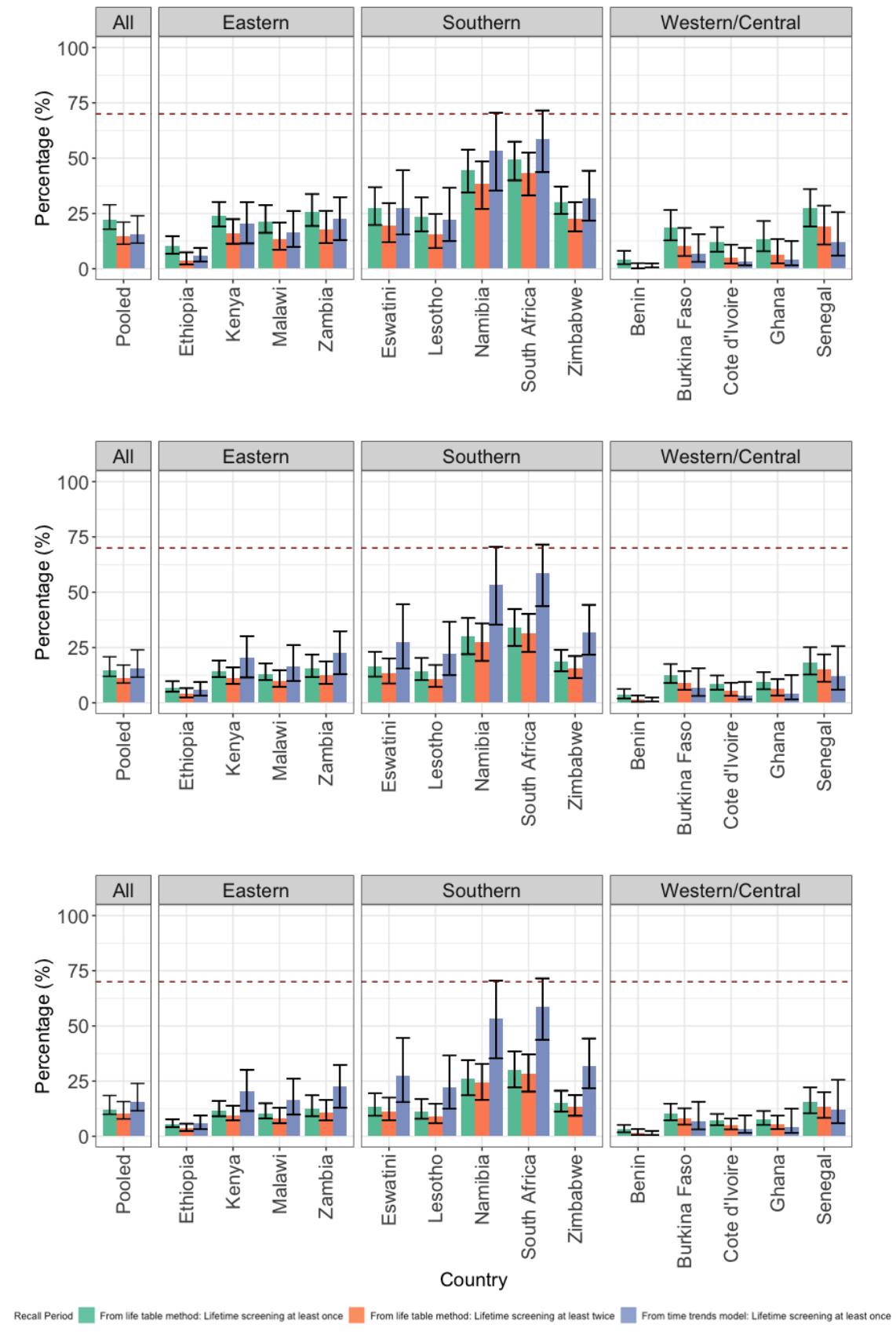


Figure S10. Life table methods sensitivity analysis using various rate ratio values. One rate ratio value was used to obtain age- and country-specific first-time screening and re-screening rates that were then applied to the life table methods.

Text S3. Description of the methods for cervical cancer treatment coverage

Surveys with information on CC treatment coverage were used to estimate the proportion of women treated after receiving a screening result that suggested the presence of a pre-cancerous lesion. These surveys were pooled using a Bayesian meta-analysis approach as described below:

$$Y_i \sim Binomial(N_i,\ p_i)$$
$$logit(p_i) = \alpha + v_{c[i]}$$

Where Y_i is the outcome for women's report i of treatment coverage and p_i the predicted probability of treatment coverage. This probability is modeled on the logit scale as the sum of an overall intercept (α), and a country-specific random intercept ($v_{c[i]}$). The model specification is completed using the following priors.

$$\alpha \sim \mathcal{N}(0,\ 10)$$
$$v_c \sim \mathcal{N}(0,\ \sigma_c) \quad and \quad \sigma_c \sim \mathcal{HC}(0, 3)$$

The overall intercept is given a non-informative prior and the country-level intercept are assumed to follow a normal distribution. The degree of pooling between country is governed by the standard deviation parameters (σ_c) with a half-Cauchy prior.

Table S5: Summary of Major Model Assumptions and Justifications

Objective	Model Assumption	Justification
All	No information or sampling biases.	Despite potential limitations due to the self-reported nature of screening coverage, population-based surveys are representative and have comparable methodology that allow us to track coverage across countries and over time.
	Countries with surveys that ask about a specific screening modality (i.e., Pap smears) have that modality as the primary method of screening.	Data is limited regarding primary screening modalities in many countries partially due to a lack of screening programs in these countries in the early 2000s. Despite this, when data is available the primary screening modalities match those asked in the surveys.
1	Lifetime and past three years screening coverages are proportional, conditional on age, on the logistic scale through time.	Lifetime screening and screening in the past three years were jointly modelled under this assumption as only 33 surveys had information regarding lifetime screening and 34 on screening in the past three years. Lifetime and past three years screening were modelled jointly to improve statistical power. Posterior predictive checks as seen in Figure S3 suggest good fit to the model.
	Time trends in screening coverage are linear on the logistic scale and vary by regions.	Only half the countries with survey data had two or more surveys to inform trends. Imposing linear trends at the regional level was required because of this data paucity. Here too, posterior predictive checks suggest good fit to the model.
	The odds ratio for the effect of HIV on screening coverage is time and age-invariant.	In several countries, HIV prevalence is relatively low, and we would not have had the required statistical power to model this heterogeneity.
2	The rate ratio between re-screening and first-time screening is time and age-invariant	This assumption was required as our proposed methodology to estimate rate ratio is not able to detect such variations.

Table S6: Gather Checklist

Item #	Checklist item	Reported in section
Objectives and funding		
1	Define the indicator(s), populations (including age, sex, and geographic entities), and time period(s) for which estimates were made.	Methods: Data Sources; Results: Survey Characteristics
2	List the funding sources for the work.	Funding
Data Inputs		
For all data inputs from multiple sources that are synthesized as part of the study:		
3	Describe how the data were identified and how the data were accessed.	Methods: Data Sources
4	Specify the inclusion and exclusion criteria. Identify all ad-hoc exclusions.	Methods: Data Sources
5	Provide information on all included data sources and their main characteristics. For each data source used, report reference information or contact name/institution, population represented, data collection method, year(s) of data collection, sex and age range, diagnostic criteria or measurement method, and sample size, as relevant.	Table S1
6	Identify and describe any categories of input data that have potentially important biases (e.g., based on characteristics listed in item 5).	NA
For data inputs that contribute to the analysis but were not synthesized as part of the study:		
7	Describe and give sources for any other data inputs.	Table S1
For all data inputs:		
8	Provide all data inputs in a file format from which data can be efficiently extracted (e.g., a spreadsheet rather than a PDF), including all relevant meta-data listed in item 5. For any data inputs that cannot be shared because of ethical or legal reasons, such as third-party ownership, provide a contact name or the name of the institution that retains the right to the data.	Table S1
Data analysis		
9	Provide a conceptual overview of the data analysis method. A diagram may be helpful.	Methods: Data pre-processing
10	Provide a detailed description of all steps of the analysis, including mathematical formulae. This description should cover, as relevant, data cleaning, data pre-processing, data adjustments and weighting of data sources, and mathematical or statistical model(s).	Methods; Supplementary Materials
11	Describe how candidate models were evaluated and how the final model(s) were selected.	Methods; Supplementary Materials
12	Provide the results of an evaluation of model performance, if done, as well as the results of any relevant sensitivity analysis.	Supplementary Materials
13	Describe methods for calculating uncertainty of the estimates. State which sources of uncertainty were, and were not, accounted for in the uncertainty analysis.	Methods; Supplementary Materials
14	State how analytic or statistical source code used to generate estimates can be accessed.	https://github.com/pop-health-mod/cc-screening
Results and Discussion		
15	Provide published estimates in a file format from which data can be efficiently extracted.	https://github.com/pop-health-mod/cc-screening
16	Report a quantitative measure of the uncertainty of the estimates (e.g., uncertainty intervals).	Results
17	Interpret results in light of existing evidence. If updating a previous set of estimates, describe the reasons for changes in estimates.	Discussion
18	Discuss limitations of the estimates. Include a discussion of any modelling assumptions or data limitations that affect interpretation of the estimates.	Discussion

Chapter 5

Discussion

5.1 Main Findings

In 2015, all members states of the United Nations adopted the *2030 Agenda for Sustainable Development*. Within this agenda were 17 *Sustainable Development Goals* (SDGs) with the purpose of improving the well-being of every human and emphasizing the principle of "*leaving no one behind*". Situated within these goals included targets to reduce mortality from non-communicable diseases (NCDs), achieve universal health care, and reduce gender inequalities. Cervical cancer (CC) is a devastating yet highly preventable disease that affects women in their economic prime. As such, eliminating CC is an important step to reaching these goals and bettering the physical, economic, and social well-being of every woman (117). Highly aligned with the SDGs is the WHO global CC elimination strategy which include the three main pillars of increasing coverage for i) HPV vaccinations, ii) screening, and iii) treatment/management (9). My thesis' results provide useful information that benchmark these elimination indicators for regional- and country-level CC screening coverage and treatment.

Overall, my findings suggest that 14% of women aged 30-49 years old in sub-Saharan Africa have ever been screened for CC in 2020 and that, overall, screening coverage did not change from 2000 to 2020. Although WLHIV have higher screening coverages than women without HIV, screening remains well below target in this priority population. Additionally, I estimated that 84% of women reporting a positive screening result for pre-cancerous lesions also reported being treated. However, the percentage of all women with pre-cancerous lesions receiving treatment is likely much lower due to low screening rates. Distinct country- and region-level variations exist in screening coverage. Some countries in the Southern Africa region (e.g., South Africa and Namibia) have much higher rates of screening than those found in Western/Central Africa and Eastern Africa regions. Nevertheless, I estimate that no countries in 2020 had achieved the goal of 70% of women having been screened twice or more by the age of 45 years.

Across sub-Saharan Africa many barriers to screening and treatment coverage persist which hinders progress toward the WHO CC elimination goals. On the demand side, competing interests, low perception of risk, stigma, fear, and transport costs especially for

women in rural areas have all been shown to contribute to decreased uptake of screening (61, 104, 113, 118). On the supply side, high costs of screening and treatment tools, lack of skilled technicians and the quality of health infrastructure prevent the adequate provision of many of these programs (61, 104, 113, 118). Furthermore, these barriers to screening are exacerbated for certain groups of women who are often the most affected by the impacts of CC, including those living in rural areas or of lower socioeconomic status. Several studies have recorded pro-rich inequalities in CC screening coverage. Although my thesis did not directly address inequalities in CC screening, I found that rates of re-screening were much higher than rates of first-time screening. This finding, alongside low overall screening coverages, suggests that screening efforts may concentrated to certain groups of women.

My estimates of screening coverage were projected up to 2020, prior to the COVID-19 pandemic. Disruptions of health services associated with the pandemic may have exacerbated the barriers described above, and paused or reduced access to CC screening and treatment services (119, 120). Scarce healthcare resources including availability of trained healthcare workers have likely been reallocated to the COVID-19 response and individuals may have avoided seeking screening services with the fear of contracting the disease (119, 120). Similarly, economic effects of COVID-19 may have further impacted individual capacity to cover out-of-pocket health expenses (e.g., travel costs to a health facility) (121). These may have longer term effects that extend past the initial acute phase of the COVID-19 pandemic. At this time, however, these effects are difficult to accurately measure and their longer-term impacts on the WHO CC elimination targets are uncertain.

To reach the WHO elimination goals, action needs to be taken to reduce barriers and address the additional effects of COVID-19 on screening and treatment coverage. Notably, these efforts must ensure equitable access and uptake of services and address the unique challenges faced by each community (122). Methodological frameworks such as INSPIRE (*Integrative Systems Praxis for Implementation Research*) have been developed to provide holistic systems thinking approach and allow for a context-adapted implementation of CC prevention services (123). Furthermore, community engagement is essential for effective service implementation (124). Approaches such as community-led monitoring allow for the inclusion of marginalized voices and may be highly beneficial to ensuring an effective implementation and scale-up of screening and treatment services (125). Community-led monitoring is an accountability tool which involves evaluation of services by a community organization, the development of recommendations for improvement and advocacy strategies,

and finally the monitoring of changes (125, 126). Current community-led monitoring efforts for HIV service delivery through initiatives such as the Ritshidze project in South Africa are showing great success (125, 127). Altogether to enact effective CC prevention initiatives and to truly uphold the SDG principle of "leaving no one behind", communities need to be at the center of the conversation and supported through greater investments in NCD prevention.

5.2 Strengths and Limitations

Certain limitations needs to be considered while interpreting my results. First, this analysis relied on self-reported survey data which can be affected by information bias. In particular, social desirability bias and telescoping bias may affect data regarding recency of screening. Women, especially those of a lower socioeconomic status have been found to overestimate recency of testing services (128-130). Despite this, results for lifetime CC screening are likely robust if the information biases for screening in the past three years are constant across time and countries. In addition, for the analyses of re-screening rates, I conducted sensitivity analyses adjusting for potential telescoping biases and found no major qualitative differences in comparison to when this adjustment was not made. Other biases that may arise from survey data are non-response and sampling bias. However, the effects of this are likely to be minimal as response rates for all surveys are high and these surveys employ complex sampling designs and provide survey weights to maximize the representativeness of their sample (Table S1).

Second, differences in the data collected by the surveys also resulted in several challenges. For instance, some surveys referred to a specific screening modality (i.e., Pap smears) whereas others only asked about CC screening in general. This model worked under the assumption that if a survey asked about a Pap smear it was likely the primary screening modality of the region. In other words, asking about lifetime screening with a Pap smear would be equivalent to asking about lifetime screening in general. Data regarding available screening modalities in sub-Saharan African is sparse, however when information was available, the primary screening modality matched the modality asked in the survey (131).

Third, data was only available for a little over half of the countries in sub-Saharan Africa (28/47), covering close to 60% of the region's female population. Countries without survey data were imputed to obtain regional CC screening estimates. With the imputations I accounted for their age distribution and HIV prevalence when aggregating results –including the increased uncertainty in these estimates. In addition, only half the countries with data had

two or more surveys to inform temporal trends. This limited my ability to investigate trends that deviated from linearity (logit-scale). The projected estimates of CC screening coverage to 2020 also rely on these assumptions of strong linear trends. However, the projections to 2020 should be reasonably accurate since several recent surveys were available and the extrapolation is limited to a few years in most cases. Furthermore, I only presented estimates of screening coverage for countries with at least two surveys. Similarly, there was also limited data on the screening care cascade (i.e., re-screening and treatment). The proportion of women screened twice by the age of 45 years in 2020 was estimated using indirect methods which my simulations suggested could suffer from biases in the presence of strong cohort and period effects. Despite this, the analysis provides strong qualitative evidence of high re-screening rates and my finding of stable trends in CC screening suggest that there are no strong cohort or period effects in most countries. Finally, data on treatment coverage is also limited and the current reported pooled estimate is an average of the only 4 countries with available data. This limited treatment data prevents estimates of regional- and continent-level treatment coverage.

Despite these limitations, several strengths provide credence to my estimates. This study is the first to systematically examine and analyze nationally representative surveys of CC screening coverage to provide estimates of temporal trends across two decades. I developed a flexible Bayesian modeling framework that consider some of the most salient data issues and provided the first regional estimates of screening coverage by HIV status. Finally, I developed a methodology to benchmark and monitor the WHO CC elimination goal for testing frequency.

5.3 Future monitoring of cervical cancer elimination targets

This thesis provides estimates for the current progress towards the WHO CC elimination goals given available data from population-based surveys. Several knowledge gaps remains and estimates regarding re-screening and treatment are associated with wide uncertainties. Overall, few surveys collected information on the CC screening cascade which constitutes missed opportunities to monitor these important indicators. Without this data, it is not possible to track the WHO elimination targets and hold countries and international institutions accountable. Such information is vital to reach both the SDGs and WHO elimination goals. The modeling framework presented in my thesis can be used to update these estimates as new data becomes available.

Chapter 6

Conclusion

To the best of my knowledge, this analysis provides the most comprehensive estimates of the current progress towards the WHO cervical cancer screening and treatment goals in sub-Saharan Africa. Although, screening coverage has been found to increase in Southern Africa, there have been minimal changes in Western/Central and Eastern Africa from 2000 to 2020. Additionally, screening coverage is slightly higher for WLHIV –while remaining well below targets– in comparison to women without with HIV in both Western/Central and Eastern Africa but similar in Southern Africa. Although country-level heterogeneities exist, overall screening remains low across sub-Saharan Africa. Despite this, rates of re-screening are high suggesting an inequitable coverage of screening. Finally, treatment coverages for the four countries among women who tested positive for pre-cancerous lesions approach the 90% goal. Low screening rates, however, suggest that the true percentage of all women with pre-cancerous lesions who are treated is likely below the WHO elimination goal.

These low coverages suggest that, if CC is to be eliminated, substantial actions are required to improve equitable screening coverage and address barriers to access and service provision. Despite current HPV vaccines programs among young girls, large cohorts of older women are unprotected and as such, secondary prevention of CC will remain key in the next decades. To achieve the goal of CC elimination, interventions need to be community-centered, funding for these programs needs to be scaled-up, and improved data collection needs to adequately monitor progress –or lack thereof– towards the WHO elimination goals.

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Appendix

List of R Packages Used

Data analysis

Hadley Wickham, Romain François, Lionel Henry and Kirill Müller (2021). **dplyr**: A Grammar of Data Manipulation. R package version 1.0.6. https://CRAN.R-project.org/package=dplyr

Hadley Wickham and Evan Miller (2021). **haven**: Import and Export 'SPSS', 'Stata' and 'SAS' Files. R package version 2.4.1. https://CRAN.R-project.org/package=haven

Hadley Wickham and Jennifer Bryan (2019). **readxl:** Read Excel Files. R package version 1.3.1. https://CRAN.R-project.org/package=readxl

Hadley Wickham (2019). **stringr**: Simple, Consistent Wrappers for Common String Operations. R package version 1.4.0. https://CRAN.R-project.org/package=stringr

Hadley Wickham (2021). **tidyr:** Tidy Messy Data. R package version 1.1.3. https://CRAN.R-project.org/package=tidyr

Helske J (2021). **_diagis**: Diagnostic Plot and Multivariate Summary Statistics of Weighted Samples from Importance Sampling_. R package version 0.2.1, https://github.com/helske/diagis

Henrik Bengtsson (2021). **matrixStats**: Functions that Apply to Rows and Columns of Matrices (and to Vectors). R package version 0.60.1. https://CRAN.R-project.org/package=matrixStats

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Data visualization

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