Awareness of cervical cancer risk factors and symptoms and lay beliefs amongst women recently diagnosed with cervical cancer in South Africa and Zimbabwe

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Part 0: PREAMBLE

Declaration

I, Sudarshan Govender, student number GVNSUD004, hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work not any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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Dissertation abstract

Background:

Despite South Africa (SA) and Zimbabwe having nationwide cervical cancer screening and human papillomavirus (HPV) vaccination programs, the incidence and mortality rates of cervical cancer remain high in these countries. We explored awareness of cervical cancer symptoms and risk factors as well as lay beliefs amongst women recently diagnosed with cervical cancer from SA and Zimbabwe.

Methods:

This is a secondary analysis of data from a descriptive cross-sectional study of women recently diagnosed with cervical cancer in SA and Zimbabwe. Between September 2022 and November 2023 women from selected health care facilities who were either recently diagnosed with cervical cancer or were within four weeks of being told their treatment plan were invited to participate in the study. Data were collected by interviewers using a locally validated questionnaire. Unprompted, open-ended questions were used to assess participant awareness of cervical cancer symptoms and risk factors. In analysis, we described awareness of cervical cancer symptoms and risk factors (zero versus ≥1 known) and reported lay beliefs. Logistic regression was used to examine associations between sociodemographic variables and awareness stratified by country.

Results:

Among 506 women enrolled (56.1% from SA; 43.9% from Zimbabwe), 54.3% (274) were able to recall ≥1 correct symptom of cervical cancer. This proportion was higher among women from Zimbabwe (73.4%) than SA (26.6%). Only 18.8% (95) of women were able to recall ≥1 correct risk factor for cervical cancer (73.7% from Zimbabwe versus 26.3% from SA). Overall, important risk factors including HPV infection, HIV and not going for screening were known by very few women (0.8%, 3.4% and 1.4% respectively). There were no statistically significant sociodemographic predictors of symptom awareness in Zimbabwe. In SA, women who completed secondary education, lived in a peri-urban setting or who knew a family member or friend with cancer were significantly more likely to know ≥1 cervical cancer symptom compared to those with less than secondary school (aOR 2.84 95% CI 1.33-6.12), those who lived in a rural setting (aOR 4.99 95% CI 1.36-18.81) or those who did not know anyone with cancer (aOR 2.61 95% CI 1.38-4.98). For risk factor awareness, among South African women,

those who completed secondary school were significantly more likely to know ≥1 cervical cancer risk factor compared to those with less than secondary school (aOR 2.86 95% CI 1.05-7.69). Among Zimbabwean women, those in the second highest wealth index or who were known to be living with HIV were significantly more likely to know ≥1 cervical cancer risk factor compared to those in the poorest wealth index (aOR 5.69 95% CI 1.21-29.24) or those who were not living with HIV (aOR 2.14 95% CI 1.04-4.50). Overall, 90 (17.9%) women mentioned at least one lay belief about risk factors for cervical cancer. The most commonly reported risk lay belief was inserting herbs, creams, or objects into the vagina (8.7%).

Conclusion:
The awareness of cervical cancer symptoms and risk factors amongst women with cervical cancer was low, particularly in SA. There is an urgent need for interventions to improve knowledge around cervical cancer, as low levels of awareness can impact timely cancer diagnosis and limit the uptake of cervical cancer prevention programs.

List of abbreviations

AIDS	Acquired immunodeficiency syndrome
ARV	Antiretroviral
ASIR	Age standardised incidence rate
ASMR	Age standardised mortality rate
AWACAN	African Women Awareness of CANcer
HDI	Human developmental index
HIC	High-income countries
HIV	Human Immunodeficiency virus
HPV	Human papillomavirus
LIC	Low-income countries
LIMC	Low-and-Middle income countries
NCSP	National Cervical Screening Program
PCA	Principal component analysis
SA	South Africa
SSA	Sub-Saharan Africa
WHO	World Health Organisation

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Introduction

Background

With 604 000 incident cases and 342 000 related deaths globally in 2020, cervical cancer was the fourth most diagnosed cancer and fourth leading cause of cancer death in women [1]. Trends of cervical cancer over time highlight the growing public health problem that cervical cancer poses, especially in countries in Africa, which have some of the highest Age Standardized Incidence Rates (ASIR) and Age Standardized Mortality Rates (ASMR) globally [2, 3]. Sub-Saharan Africa (SSA) is the only region that has experienced an increase in both ASIR and ASMR since 1990 [4]. Despite both South Africa (SA) and Zimbabwe having nationwide cervical cancer screening and human papillomavirus (HPV) vaccination programs, the rates of cervical cancer remain high in these countries [5, 6, 7].

The aim of this study is to determine the level of awareness of cervical cancer risk factors and symptoms and lay beliefs of cervical cancer amongst women recently diagnosed with cervical cancer in SA and Zimbabwe. To the best of our knowledge, this is the first study in SSA assessing unprompted awareness of cervical cancer risk factors and symptoms amongst women with cervical cancer, using a locally validated questionnaire. This study can potentially provide valuable information that can be used when designing health promotion and health education interventions.

Literature review

Search strategy

The literature review consists of two narrative reviews. The first narrative review, titled “A global overview of cervical cancer”, forms the first part of the literature review, and outlines the burden of cervical cancer globally, as well as provides insight into the global distribution of cervical cancer and trends over time. The most recent literature on global cervical cancer burden was reviewed using the databases PubMed and Google Scholar. The second narrative review of the literature review, titled “Cervical cancer awareness”, focused on synthesizing the existing evidence on the research topic, namely awareness of cervical cancer risk factors and symptoms as well as lay beliefs about cervical cancer. The search involved the following key words and phrases: ["Cervical cancer" OR "Cervical carcinoma" OR "carcinoma of cervix"] AND ["Risk factor awareness" OR "Risk factor knowledge" OR "Risk factor understanding"

OR "Symptom awareness" OR "Symptom understanding" OR "Symptom knowledge" OR "Symptom appraisal" OR "Lay beliefs" OR "Misperceptions"].

The following databases were searched: PubMed, Google Scholar, and Africa-Wide Information. The reference lists of included articles were also reviewed to identify any additional articles that might be relevant to the research topic. There were no restrictions regarding the date of publication. While there was a focus on studies based in Africa, there were no limitations or restrictions regarding study setting when reviewing the literature.

A global overview of cervical cancer

Global burden of cervical cancer

In 2020, there were an estimated 604 000 incident cases of cervical cancer and 342 000 related deaths globally, resulting in cervical cancer being the fourth most diagnosed cancer and the fourth leading cause of cancer deaths in women [1]. The majority of both incident cases (>58%) and related deaths (58%) were estimated to have occurred in Asia, with Africa contributing approximately one-fifth of all incident cases (117 000) and deaths (77 000) globally [8, 9]. Overall, Low- and Middle-Income countries (LMICs) accounted for an estimated 80% of all incident cases, and 90% of deaths due to cervical cancer, highlighting both the uneven global distribution of the disease, and that cervical cancer is a disease of poverty and inequality [2, 10].

In 2020, the global ASIR for cervical cancer was 13.3 cases per 100 000 women-years and the ASMR was 7.2 deaths per 100 000 women-years [8]. However, there is significant variation in these rates globally, both between regions and within regions [8]. The lowest ASIRs (<7.5 per 100 000 women-years) were found in countries in western Asia, northern America, and western Europe while the highest ASIRs (>50 per 100 000 women-years) were all found in countries from the eastern, southern, and western regions of Africa, such as Malawi, Zimbabwe, Uganda, Guinea, and Lesotho to list a few [8, 10, 11]. Several studies have found an association between a country's Human Developmental Index (HDI) and the country's cervical cancer ASIR and ASMR, specifically, that a lower HDI is associated with higher rates of cervical cancer incidence and mortality [3]. Interestingly, the ASMR appears to be more strongly correlated with HDI compared to the ASIR. The mortality rates in low HDI countries were found to be six times higher compared to the mortality rates in countries with a very high HDI (19.8 deaths per 100 000 women years in low HDI countries vs 3.1 in very high HDI countries), while the

ASIR was found to be three times higher in countries with a low HDI compared to countries with a very high HDI (27.2 cases per 100 000 women-years in low HDI countries vs 9.1 in very high HDI countries) [8].

Trends of cervical cancer over time

Analyzing the trends of cervical cancer over time is important, as it not only highlights the major public health problem of cervical cancer, but also helps determine which regions are experiencing an increasing burden of the disease and need urgent intervention [11]. Globally, trends in the absolute number of cervical cancer cases have increased over time, from 335 640 in 1990 to 604 127 in 2020, representing an 80% increase in incident cases since 1990. In terms of mortality, there was an 85.2% increase in the number of deaths caused by cervical cancer between 1990 (184 530 deaths) and 2020 (341 831 deaths) [1, 4].

However, considering growth and aging of the global population, it is more useful and accurate to compare standardized rates, such as ASIR and ASMR, over time [10, 11]. Importantly, the global ASIR decreased over time, from 16.2 per 100 000 women years in 2002, to 13.3 per 100 000 women years in 2020 [10]. The global ASMR also showed a declining trend from 1990 (8.48 per 100 000) to 2019 (6.51 per 100 000) [4]. However, despite the worldwide downward trends in cervical cancer rates, some regions alarmingly experienced increasing ASIR and ASMR over time. In terms of ASIRs, two regions showed increasing trends between 1990 and 2019, namely East Asia, and Southern sub-Saharan Africa (SSA), and when looking at ASMRs, the only region which showed an increasing trend over this same two-decade period (1990-2019) was Southern SSA [4]. The increasing trend of cervical cancer ASIRs and ASMRs in Southern SSA over time, coupled with the fact that this region already has the highest ASIR (43.1 per 100 000 women years) and one of the highest ASMR (20.0 per 100 000 women years) in the world, indicates the significant burden and impact that cervical cancer is having, and will continue to have, on the individuals in this region [2, 3].

Explanations of global distribution and trends over time

Over the past few decades, most regions have experienced decreasing incidence and mortality rates of cervical cancer as a result of the human papillomavirus (HPV) vaccine (primary prevention) and increasing coverage of cervical cancer screening (secondary prevention) [1, 3]. However, these prevention strategies have not been implemented equitably, which explains

both the substantial geographical disparities in the global burden of cervical cancer as well as the association between HDI and cervical cancer rates [1, 10]. High income countries (HICs), with a higher HDI, have the resources and finances to implement and maintain effective, well-organized, population-based primary and secondary prevention programs, and this has resulted in a steady decline in the cervical cancer ASIRs and ASMRs in these countries over time [1, 8]. For example, the most significant decreases in ASIRs since 1990 have occurred in the Maldives, Taiwan, and Singapore, all of which have implemented effective HPV vaccine and cervical cancer screening programs, financed by significant government expenditure [4]. Australia, which has one of the lowest cervical cancer ASIRs and ASMRs in the world, first introduced their National Cervical Screening Program (NCSP) in 1991 and, in 2007, became the first country in the world to initiate a nationwide publicly funded HPV vaccination program. Since 1991, the ASIR of cervical cancer in Australia has decreased by approximately 50%, from 13.5 per 100 000 women, to 6.0 per 100 000 women in 2018 [11, 12]. With a national cervical cancer screening program initiated in the 1960s, Finland has one of the longest running organized cervical cancer screening services in the world, and the effectiveness of this program is reflected in the extremely low ASIR of 4.7 per 100 000 women and an even lower ASMR of 0.9 per 100 000 women in the country [13, 9].

Conversely, LMICs, which account for the majority of cervical cancer cases and deaths globally, are experiencing high rates of cervical cancer incidence and mortality, as a result of a failure to implement and maintain sustainable prevention programs on a national scale [14]. Less than 30% of LMICs have implemented national HPV vaccine programs, while more than 80% of HICs do have national HPV vaccine programs [1]. Additionally, a global analysis of 57 countries found that 63% of females from HICs have been screened for cervical cancer, compared to only 19% of females in low-income countries (LICs) [3].

Focusing on Africa, only 20% of African countries, including SA and Zimbabwe, reported having a national program for cervical cancer screening in 2019, however, in the majority of these countries, the screening coverage was less than 10% [15]. In 2020, Southern Africa had the highest estimated cervical cancer screening coverage at 51%, with SA the country with the highest coverage at 56% [16]. Only 45% of SSA countries had implemented national HPV vaccine programs by 2021, and alarmingly, only an estimated 20% of girls have been fully vaccinated against HPV in SSA [15, 16]. Factors that have contributed towards inadequate prevention programs in African countries include, but are not limited to, limited health budgets

with multiple competing priorities, weak health systems, a lack of cervical cancer knowledge and low prioritization of cervical cancer [15, 16]. Additionally, the distribution of cervical cancer screening services is inequitable in SSA, with screening services usually only being offered in secondary and tertiary healthcare facilities, which are located in urban areas [15]. This means that the majority of women who live in rural areas are not able to access and benefit from these screening facilities [15].

Another crucial factor contributing to the high burden of cervical cancer in SSA is the high prevalence of the human immunodeficiency virus (HIV) in this region. An estimated 21% of cervical cancer in Africa is attributable to HIV infection, and for women living with HIV, there is a 6-fold higher risk of developing cervical cancer compared to women without HIV [10, 16]. This emphasizes the need to incorporate and integrate cervical cancer prevention strategies into other public health programs, such as HIV prevention strategies, to reduce the high burden of cervical cancer in Africa [14].

The need for effective interventions

Without any further interventions, the annual global cervical cancer deaths are estimated to rise to 443 000 in 2030, and 90% of these deaths are expected to occur in SSA [16]. The impact of cervical cancer is significant and has far reaching negative social consequences. In low resource settings, it is estimated that, for every 100 women who die from cervical cancer, 210 children become maternal orphans, and 14 children die prematurely, before the age of 10 [8]. Realizing the extent of the cervical cancer public health crisis, the World Health Organization (WHO) launched the global Cervical Cancer Elimination Initiative in 2020, with the aim of reducing the incidence of cervical cancer to <4 cases per 100 000 women-years in every country by 2030 [8, 16]. The proposed strategy included a combination of HPV vaccination, cervical cancer screening and effective pre-cancer and invasive cancer treatment. Predictive models have indicated this strategy could result in the prevention of more than 74 million cases and more than 62 million deaths over the next century [1, 16]. However, while this goal is only expected to be achieved by 2059 in very high HDI countries, low HDI countries, which have the highest burden of cervical cancer, might only achieve this goal of <4 cases per 100 000 women-years at the end of the 21st century [1]. This means that over the next few decades, many women from LMICs will develop and die as a result of cervical cancer. Additionally, the countries that have only recently implemented HPV vaccination programs, will only see the

impact of this intervention in future generations, meaning additional approaches and interventions will be required in order to reduce the impact of cervical cancer on women currently at risk.

In Africa, cervical cancer prevention programs are not readily available in the majority of countries, with an estimated 80% of countries not having a national cervical cancer screening program, and only 45% of SSA countries having a HPV vaccination program [15]. However, as mentioned previously, many of the African countries which do have these services available have poor uptake and coverage by the public [1, 15]. This emphasizes that additional approaches and interventions need to be implemented in both countries with and without effective cervical cancer prevention strategies in order to reduce the burden of cervical cancer in Africa. One approach to consider is to increase public awareness around cervical cancer risk factors and symptoms. Not only can this potentially improve individuals help-seeking behavior, but improved awareness can also address any misperceptions and lay beliefs related to cervical cancer.

Cervical cancer awareness

Awareness of cervical cancer in Africa

Valdespinoa and Valdespinoa suggested that the combination of low levels of awareness and a lack of effective cancer screening programs are the reasons for the high incidence of cervical cancer in LMICs [17]. Other studies have also suggested that, in addition to low levels of awareness and a lack of effective screening programs, competing health priorities, such as HIV, and inadequate focus on women's health, are also major contributing factors to the high incidence rates of cervical cancer in Africa [18, 19]. Improving the awareness of cervical cancer in LMICs is therefore paramount in reducing the significant cervical cancer burden in these countries.

Several studies conducted among women and communities in SSA have found that the knowledge of cervical cancer is generally poor [20]. In a study amongst women in the Bosore community, from the Ashanti Region of Ghana, only 55.5% of participants had heard of cervical cancer, while in a study on female university students from SA, less than half (42.9%) of the participants had heard of cervical cancer [21, 22]. However, just having heard of cervical cancer before does not translate into adequate knowledge and understanding of the disease. In

a study conducted in Nigeria, despite 78.5% of women knowing of cervical cancer, alarmingly 89.9% were not aware of the HPV vaccine and only 31.7% had knowledge on the purpose of a Pap smear [23]. Similarly, the majority of women (78.7%) in a study in Ethiopia had heard about cervical cancer, however, the knowledge of cervical cancer risk factors, symptoms and prevention was far lower [18]. Interestingly, of the four studies mentioned above, conducted in Ghana, SA, Nigeria, and Ethiopia, none used a locally validated questionnaire.

Cervical cancer risk factor awareness

In terms of cervical cancer risk factor knowledge in Africa, several studies found low levels of knowledge in most SSA countries, including Cameroon, Kenya, Nigeria, and Zimbabwe [24]. In a community-based study that used an unvalidated questionnaire to assess cervical cancer awareness amongst women in Northwest Ethiopia, 47.5% of women did not know whether or not cervical cancer had any risk factors, while 18.8% of women believed cervical cancer does have risk factors but were not able to name any of these risk factors [18]. A study in Nigeria, which used a structured, unvalidated questionnaire amongst women attending antenatal and gynaecological outpatient clinics, found only 15.6% of women had good knowledge of risk factors. In this study, good knowledge of cervical cancer risk factors was defined as being able to correctly identify more than six out of the twelve risk factors of cervical cancer provided [23]. When determining the knowledge of cervical cancer among female university students in SA, researchers found that, of the 42.9% of participants that had heard of cervical cancer, 15.6% did not know any risk factors for cervical cancer, while a separate study in Zimbabwe found that only 1.3% of female university students were knowledgeable about cervical cancer risk factors [22, 25].

Interestingly, some studies in Africa found very high levels of cervical cancer risk factor awareness. For example, in a population-based cross-sectional study in Uganda, which used an unvalidated questionnaire, cervical cancer risk factors were recognized by the majority of participants, with the two most recognized risk factors being multiple male sexual partners (88.3%) and a sexually transmitted virus (82%) [24]. However, studies, such as the latter study, which tests recognition of risk factors, provide cues or limited response options, and are prone to participants guessing, potentially resulting in higher awareness scores [26]. This point is highlighted by Moodley et al, where, in a community-based cross-sectional survey, using a locally validated questionnaire, unprompted recall, followed by prompted recognition of cervical cancer risk factors was tested amongst women from SA and Uganda. When asked to

name any risk factors of cervical cancer, only 38.1% of women were able to recall at least one risk factor, however, when subsequently asked to identify cervical cancer risk factors from an evidence-based list of risk factors and lay beliefs, 99.1% of women correctly recognized at least one risk factor [26]. Similarly, a study amongst women in Libya, found that recall of cervical cancer risk factors was far lower compared to risk factor recognition [17]. This suggests that testing recall of cervical cancer risk factors is a more accurate reflection of participants level of cervical cancer risk factor knowledge.

Of concern was the poor knowledge of HPV infection and lack of cervical cancer screening as risk factors for cervical cancer in Africa. Less than 1% of participants in the previously mentioned study across SA and Uganda mentioned either risk factor [26]. While in Libya, only 2.2% and 1.2% of participants respectively identified HPV infection and not going for regular Pap smears as risk factors for cervical cancer [17]. Low levels of knowledge of HPV infection were also reported in Zimbabwe [5]. Studies conducted in Ethiopia and Kenya have also found a lack of awareness of screening as a risk factor for cervical cancer [26, 27, 28]. Despite the availability of prevention strategies in some African countries, low levels of knowledge and awareness around the role of HPV infection and the importance of cervical cancer screening can contribute to low participation in intervention programs, such as HPV vaccination and cervical cancer screening [29]. This suggests that introducing and implementing intervention programs alone is not enough, and governments also need to address and improve the low levels of awareness and knowledge around cervical cancer, to ensure high uptake and utilization of prevention programs [29].

Cervical cancer symptom awareness

Evidence suggests that improved awareness of cervical cancer symptoms can improve help-seeking behaviors, which can result in an earlier presentation to health care facilities and an earlier stage of diagnosis [24, 26, 30, 31]. An educational intervention in India, which increased the level of awareness of symptoms of cervical cancer in the intervention community to 76% compared to 25% in the control community, found a 13% increase (38% to 51%) in the proportion of cervical cancer patients from the intervention community that were diagnosed with cervical cancer at an earlier stage (stage I and II) [24]. Similarly to that of cervical cancer risk factor awareness, several studies have found low levels of awareness of cervical cancer symptoms across Africa. In a study among women attending antenatal and gynaecological outpatient clinics in Nigeria, only 40% of participants had good knowledge of cervical cancer

symptoms, which was defined as being able to identify three or more symptoms of cervical cancer, while a study among females in the Ashanti region of Ghana found that the majority of participants had no knowledge of the common signs and symptoms of cervical cancer, such as intermenstrual bleeding, persistent, foul smelling vaginal discharge, and post-menopausal bleeding [21, 23]. Both these studies used questionnaires that were not validated in the local context.

Similar to risk factor recall compared to recognition, studies that assessed the knowledge of cervical cancer symptoms using recall and recognition, found recognition of symptoms to be far higher [17, 26]. While 97.9% of women in a study in SA and Uganda were able to correctly recognize at least one symptom of cervical cancer, only 57.7% of women were able to correctly recall at least one symptom of cervical cancer [26]. The most commonly recalled symptoms in this study were intermenstrual bleeding (27.6%), lower abdominal/pelvic pain (24.1%) and smelly vaginal discharge (21.2%). This again highlights the fact that recall is a more accurate reflection of a participant's knowledge and awareness. As mentioned earlier, improving awareness around cervical cancer symptoms has the potential to improve help-seeking behavior, and with an estimated 65-85% of cervical cancer patients in SSA diagnosed at an advanced stage of disease, the need for improved awareness of cervical cancer symptoms is essential [24, 26, 30, 31, 32].

Cervical cancer lay beliefs

There are limited studies specifically focusing on cervical cancer lay beliefs in SSA [33]. In a qualitative study in Northern Uganda, respondents from all women focus group discussions correctly reported symptoms of cervical cancer, such as heavy vaginal bleeding, smelly vaginal discharge and lower abdominal pain [34]. However, despite good knowledge of the symptoms of cervical cancer, many of the focus groups suggested causes of cervical cancer that were misconceptions. For example, more than three quarters of the focus groups believed cervical cancer was a result of the civil war, blaming the fumes from bombs, and food that was distributed at the time [34]. Another lay belief is that cervical cancer is hereditary, and this is particularly harmful, as it has the potential to delay or prevent help-seeking behavior, as women might think there is nothing that can be done to change one's genetics [34]. Additionally, lay beliefs can potentially negatively impact other disease prevention programs and public health interventions. For example, in the same qualitative study from Northern Uganda, prolonged condom use was identified as a cause of cervical cancer [34]. This lay belief can increase non-

condom use which can increase the risk of sexually transmitted diseases despite condom use having been shown to be effective in controlling HIV in Uganda [34]. Other studies in Africa have reported the lay belief that inserting creams and objects into the vagina is a cause of cervical cancer [26].

Understanding lay beliefs around cervical cancer is necessary, especially when designing and implementing cervical cancer prevention interventions. It is essential that, in addition to improving awareness and knowledge around cervical cancer, health promotion programs and interventions also address and correct lay beliefs [26]. Framing health interventions around the beliefs of the individuals and communities who are going to utilize the intervention, increases the likelihood that the intervention will be accepted by the community, thereby increasing its uptake [33].

Outline of the parent study

The parent study was conducted by researchers from the AWACAN-ED (African aWAreness of CANcer and Early Diagnosis) program, which is a NIHR-funded Global Health Research Group focusing on improving early diagnosis of cancer in Southern Africa.

The three aims of the parent study were as follows:
Aim 1: To assess the current time intervals from breast, cervical and colorectal cancer symptom awareness to referral and diagnosis, as well as the factors influencing these intervals among adults in SA and Zimbabwe.
Aim 2: To develop two e-tools that promote more timely presentation and referral for breast, cervical and colorectal cancer.
Aim 3: To evaluate the e-tools across the local settings in Zimbabwe and SA.

In the parent study, data were collected by trained researchers using hand-held tablets customized with a structured, validated questionnaire with questions related to socio-demographic information, medical history as well as clinical presentation and journey to care. This current study will be a secondary analysis, using only the data collected from participants in the parent study who had cervical cancer. The secondary analysis data will include socio-demographic information, clinical data and knowledge of cervical cancer risk factors, symptoms, and lay beliefs.

Study aims

To determine the level of awareness of cervical cancer risk factors and symptoms, as well as lay beliefs of cervical cancer, among women recently diagnosed with cervical cancer in SA and Zimbabwe.

Objectives

1. To describe the awareness of cervical cancer risk factors, symptoms and lay beliefs amongst women recently diagnosed with cervical cancer in SA and Zimbabwe.
2. To determine the socio-demographic factors associated with the awareness of cervical cancer risk factors and symptoms amongst women recently diagnosed with cervical cancer in SA and Zimbabwe.
3. To compare the awareness of cervical cancer risk factors, symptoms, and lay beliefs and factors associated with cervical cancer awareness between women recently diagnosed with cervical cancer in SA and women recently diagnosed with cervical cancer in Zimbabwe.

Methodology

Study design

The parent study was a cross sectional study involving a structured, validated questionnaire with open-ended questions used to determine unprompted awareness of cervical cancer risk factors, symptoms and lay beliefs amongst women recently diagnosed with cervical cancer in SA and Zimbabwe. The questionnaire, which was developed in a study titled "Improving timely diagnosis for breast and cervical cancer in Sub-Saharan Africa", can be used to measure overall awareness of cervical cancer and breast cancer in the context of SSA. The development and validation of this questionnaire have been described in detail elsewhere [35]. Appendix A outlines the cervical cancer component of the questionnaire used in the parent study to determine awareness of cervical cancer risk factors and symptoms amongst participants.

Research setting

The parent study was conducted in SA and Zimbabwe.

South Africa:

SA, an upper middle-income country with an estimated population of 60,5 million, has a three-tiered public health system consisting of primary, secondary, and tertiary level facilities [7, 26, 36]. All patients who use the public health system enter at the primary level, either at a clinic or district hospital, and can get referred up the system for further investigation, management, and treatment. Patients suspected of having cervical cancer will usually be investigated and treated at either secondary or tertiary level facilities, depending on the severity of the disease as well as on the availability of resources, equipment, and skilled personnel. Participants in the parent study were selected from two of the nine provinces of SA, namely the Western Cape and the Eastern Cape. The Western Cape, with a population of approximately 6.9 million, is one of the wealthier provinces in the country, while the Eastern Cape, which has a population of approximately 6,5 million, is one of the poorer provinces [26, 37]. In the Western Cape, participants were selected from one of the three tertiary hospitals in the province, namely Groote Schuur Hospital (GSH). In the Eastern Cape, participants were selected from one of four tertiary level hospitals in the province, namely Nelson Mandela Academic Hospital (NMAH).

Zimbabwe:

Zimbabwe is a LMIC bordering SA, with a total population of 15.1 million, of which 52.0% are female, and 61,4% live in rural areas [38, 39, 40]. The country is divided into ten provinces, and, similarly to SA, has a three-tiered referral based public healthcare system. Patients enter the healthcare system at the primary level of care and depending on the severity of the disease or the need for further management and investigation, are referred up the system to secondary and tertiary levels of care. Participants in the parent study were selected from two of the ten provinces, namely Harare Province and Bulawayo Province. Harare Province is the most densely populated province in Zimbabwe, with a total population of 2,4 million people, accounting for 16.0% of the total population of Zimbabwe. Bulawayo Province is the least populated province in Zimbabwe, with a total population of 665 940, accounting for only 4,4% of the total population of Zimbabwe. However, Bulawayo Province is the second most densely populated province in Zimbabwe, behind Harare Province [40]. In both Harare Province and Bulawayo Province, there are no secondary hospitals, and patients with suspected cancer symptoms are referred straight to tertiary level facilities. There are three tertiary hospitals in Harare Province, namely Parirenyatwa Group of Hospitals, Sally Mugabe Central Hospital and Chitungwiza Central Hospital. In Bulawayo Province, there are two tertiary hospitals, namely

Mpilo Central Hospital and United Bulawayo Hospitals. Participants were selected from all tertiary hospitals in Harare Province and Bulawayo Province.

Study population

In the parent study, participants were patients who were recently diagnosed with cervical cancer within the preceding month and/or were within four weeks of being told of their treatment plan and awaiting treatment to start. Participants were from the Western Cape and Eastern Cape province of SA and the Harare Province and Bulawayo Province of Zimbabwe.

The inclusion criteria for participation in the parent study was as follows:

- Adults aged 18 years and older
- Recently diagnosed (in the preceding month) with cervical cancer and/or being within four weeks of being told of their treatment plan at the tertiary hospital and still awaiting treatment to start.

The exclusion criteria for participation in the parent study was as follows:

- Individuals with a previous history of cancer (these individuals would have presumably already received health education and information on cancer from health care workers, which might influence their awareness about cervical cancer)
- Individuals who were unwilling or unable to provide consent

Recruitment

Investigators in the parent study aimed to recruit consecutive consenting patients who met the inclusion criteria over a 12-month period. At each site, the clinical team would identify eligible patients and refer them to the field research team where a researcher would explain the aim of the study and obtain consent from patients who were willing to participate in the study. Approximately 500 participants with cervical cancer have been recruited into the parent study.

Data collection and key measures

In the parent study, data were collected by trained researchers using hand-held tablets customized with a structured, validated questionnaire that was used to determine cervical cancer awareness. The questionnaire collected socio-demographic information, past medical history and knowledge of cervical cancer risk factors, symptoms, and lay beliefs. More specifically, the following information was collected:

- Socio-demographic information: age, country and province residing in, relationship status, highest level of education, living context, employment status, and questions related to living environment and household such as type of dwelling, source of drinking water and access to assets, such as a fridge, car, and cellphone.
- Past medical history: previously diagnosed Tuberculosis, Hypertension, Diabetes, HIV/AIDs, and Covid-19, as well as history of cervical cancer screening
- Awareness of cervical cancer: unprompted awareness of cervical cancer risk factors and symptoms was determined by two open-ended questions, which read "Please would you name as many symptoms or signs of cervical cancer/cancer of the womb as you can think of?" and "Please could you name as many things as you can think of that could increase any person's chances of getting cervical cancer?"

Outcome variables

The three outcome variables in this study are "cervical cancer symptom awareness", "cervical cancer risk factor awareness" and "cervical cancer lay beliefs", all of which were assessed in the parent study using unprompted, open-ended questions.

Explanatory variables

Table 1: Explanatory variables with possible coding for analysis

Variable	Collected as	Possible Codes/collapse
Age	Date of Birth (continuous)	Categorize: <30 vs >30 or 18-34; 35-44; 45-54; >55
Relationship status	Married Living together Single Separated Divorced Widow	Collapse into: Married or living together Single Separated, divorced or widow
Level of Education	No schooling Primary incomplete Primary complete Secondary incomplete Secondary complete More than secondary	Collapse into: No schooling Primary incomplete Primary complete (with secondary incomplete) Secondary complete or more
Living context	Urban formal Urban informal Rural village Rural farm Peri-urban formal Peri-urban informal	Collapse into: Urban (formal or informal) Rural (village or farm) Peri-urban (formal or informal)

Employment status	Employed full time Employed part-time Self-employed Unemployed Housewife Pensioner Student	Collapse into: Employed Unemployed
Wealth asset index	Calculated using principal component analysis (PCA), based on the ownership of and access to various assets such as fridge, car etc.	Categorize: Poorest Poor Middle Richer Richest
Past medical history		
Any family or close friend that has or had cancer	Yes No	Categorize Yes No
Previous medical diagnosis (chronic conditions)	Categorical [HPT, DM, TB, Heart problems, HIV/AIDs, Covid-19]	Categorize: Yes No
Previous cervical cancer screening	Yes No	Categories Yes No Not sure
[if yes] type of last screening test	Cytology (conventional or liquid based) Visual inspection methods HPV test HPV and visual inspection or cytology Not sure	Categories Cytology (conventional or liquid based) Visual inspection methods HPV test HPV and visual inspection or cytology Not sure
[if yes] when was last test	Categories <1 year ago 1-5 years ago 6-10 years ago >10 years ago Not sure	Categories <1 year ago 1-5 years ago 6-10 years ago >10 years ago Not sure

The final collapsing of each variable into categories will depend on the distribution of the variable.

Data management and analysis

Wealth asset index

Principal component analysis (PCA) will be used to construct a wealth asset index for the total sample using the following asset variables collected in the parent study: material of wall, material of roof, water source, energy source, toilet facilities, and access to assets such as a

telephone, cellphone, fridge, internet connect, computer and a car. The wealth asset index variable will be divided into quintiles.

Coding variables

Deductive reasoning will be used to code the open-ended responses from participants and the coding process will involve several steps. The first step will be reviewing all responses to get a sense of the variation of participant responses. The next step will be grouping similar responses together, using keywords and key phrases. For example, responses such as "persistent smelling discharge", "continuous discharge" and "vaginal discharge" can all be grouped together under the symptom "vaginal discharge". Similarly, lay beliefs will also be grouped together according to common ideas or themes using the same process. The final step of measuring the symptom and risk factor outcome variables will involve scoring participants on each correct symptom and risk factor for cervical cancer identified. Appendix B outlines the list of evidence-based cervical cancer symptoms and risk factors from a previous study conducted by researchers from the AWACAN-ED programme, that will be used as the reference for cervical cancer risk factors and symptoms [35]. Participants will score one point for each correct symptom and risk factor identified and points will be aggregated to give each participant two separate scores for risk factor awareness and symptom awareness. Lay beliefs will be identified as responses that do not fit into any of the evidence-based risk factors and symptoms from the reference list. Depending on the distribution of the awareness scores, risk factor and symptom level of awareness will be dichotomized into either high and low levels of awareness using the median value, or simply categorized into participants who correctly identified zero or at least one correct risk factor and symptom of cervical cancer.

Descriptive statistics

Descriptive statistics will be used to characterize survey responses. Continuous variables, such as age, will be expressed as mean (with Standard deviation) or median (with interquartile range) depending on the distribution. Categorical data will be expressed as frequencies and percentages.

Regression analysis

A multivariable logistic regression analysis will be performed for symptom awareness and risk factor awareness separately for each country to determine which factors are associated with increased awareness of cervical cancer.

Ethical considerations

This study is a secondary analysis of data collected from the parent study titled NIHR Global Research Group on Advancing Early Diagnosis of Cancer in Southern Africa: AWACAN-ED. The parent study received ethical clearance from all relevant committees from both SA and Zimbabwe prior to commencement of the study. From SA, ethical clearance was obtained from the University of Cape Town Faculty of Health Science Research Committee, as well as the Western Cape Research Committee, Eastern Cape Research Committee and Cape Town Department of Health. From Zimbabwe, ethical clearance was obtained from the Joint Research Ethics Committee of the University of Zimbabwe, Faculty of Medicine and Health Sciences and Parirenyatwa Group of Hospitals (JREC), the ethics committees of Mpilo Central Hospital, United Bulawayo Hospitals and Sally Mugabe Central Hospital, Medical Research Council of Zimbabwe, and the Research Council of Zimbabwe (RCZ).

Informed consent

This proposed study is a secondary analysis and will involve no interaction or contact with participants from the parent study. We request a waiver of consent for this study. In the parent study, participants were required to sign an informed consent sheet prior to enrolment in the study. This process of informed consent involved a trained research assistant outlining the purpose of the study and indicating that the study is entirely voluntary and that participants can withdraw at any point in the study. Participants were informed that declining to participate or dropping out of the study would not affect the care or treatment that they received at the healthcare facility. The informed consent sheet was translated into various languages to ensure that participants would be able to understand the content. In SA, the informed consent sheet was translated into Xhosa and Afrikaans, and in Zimbabwe, it was translated into Ndebele and Shona. Lastly, participants were encouraged, by the research assistant present, to ask any questions they had, to ensure they understood all aspects of the study.

Privacy and confidentiality

All data released for this secondary analysis will not contain any identifying information. All personal identifiers will be removed in the parent data, and participants were assigned unique numeric identifiers. The secondary data used in this study will be stored on a password protected laptop, and only investigators in this study will have access to the data. Any future

publications, presentations or dissemination of results will not contain any information that can be used to identify participants in the parent study. Privacy and confidentiality will be maintained throughout the study, from data collection to results analysis and dissemination.

In the parent study, all researchers and field staff were trained in the ethical conduct of research which included maintaining privacy and confidentiality. Information from the cross-sectional survey was collected on password-protected, hand-held tablets enabled with RedCap (Research Electronic Data Capture). The data captured on the tablets were kept in a secure database, and any survey data that was temporarily stored offline was transferred onto the database as soon as possible, and the offline version immediately deleted. Only study investigators will have access to the secure database containing the survey data.

Risks

As this study is a secondary analysis of anonymized data that was collected in the parent study there are no risks or potential for harm to participants. In the parent study, researchers aimed to minimize the risk of harm to participants. The researchers in the parent study anticipated that there might be a low possibility of unintended harm as participants might experience varying degrees of psychological distress due to the recent cancer diagnosis, which could be augmented during the interview. To mitigate this risk as much as possible, social support services were made readily available, and research staff were well-trained prior to the study commencing. Other anticipated harms in the parent study were the time cost involved in participating in the study, including the interviews and survey. A reimbursement of R150/USD10 per participant was provided to each participant at the end of the interview, to thank them for their time. The risk of breaches in privacy and confidentiality in both the parent study and this study will be minimized by maintaining participants anonymity, using secure, password protected databases, and only allowing study investigators to access the data.

Benefits

There are no direct benefits to study participants in this study. On a population level, the findings from this study can be used to inform public health policies and interventions that aim to reduce the burden of cervical cancer in both SA and Zimbabwe. The information gained from this study will provide valuable insight into the beliefs and understanding of cervical cancer from a patients' perspective, as well as factors associated with cervical cancer

awareness, all of which is valuable information that can be used and incorporated into future health interventions aimed at reducing the burden of cervical cancer in SSA.

Budget

This study does not require a budget, as it is a secondary analysis of data.

Time frame

The study is expected to take 6 months as outlined below.

Component	Date
Write up and Completion of Protocol	August - October 2023
Protocol submission: Ethics	November 2023
Data analysis	November – December 2023
Manuscript write up	December - January 2024
Final thesis preparation	January 2024
Submission of dissertation	February 2024

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Part B: MANUSCRIPT

Awareness of cervical cancer risk factors and symptoms and lay beliefs amongst women recently diagnosed with cervical cancer in South Africa and Zimbabwe

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This article meets the requirements set out in the instructions for the Authors for the ecancermedicalscience journal excluding the sections of list of abbreviations, conflicts of interest, financial declaration, and acknowledgement statement. In keeping with instructions for this dissertation supplementary tables and figures for this article can be found in appendix G. As per the MPH dissertation guidelines, co-authors are not listed on the journal manuscript, but their contributions are noted in the acknowledgements section of this dissertation. The ecancermedicalscience Instructions for Authors are included in Appendix H of the dissertation.

Abstract

Background

Rates of cervical cancer remain high in sub-Saharan Africa (SSA). We explored awareness of cervical cancer risk factors and symptoms, as well as lay beliefs amongst women recently diagnosed with cervical cancer from South Africa (SA) and Zimbabwe.

Methods

Between September 2022 and November 2023, women from selected hospitals who were recently diagnosed with cervical cancer were enrolled. A locally validated questionnaire with unprompted, open-ended questions was used to assess awareness of cervical cancer symptoms and risk factors (coded as zero vs ≥1 known in analysis). Logistic regression was used to examine associations between socio-demographic variables and awareness, stratified by country, and the reported lay beliefs were described.

Results

Among 506 women (284 from SA, 222 from Zimbabwe), 54.3% (274) were able to recall ≥1 symptom and 18.8% (95) were able to recall ≥1 risk factor of cervical cancer. In SA, factors associated with symptom awareness included completed secondary education, living in a peri-urban area, and knowing a family or friend with cancer; only completed secondary education was associated with improved risk factor awareness. In Zimbabwe, those in the second highest wealth index or who were living with HIV were significantly more likely to know ≥1 cervical cancer risk factor. 90 (17.9%) women, the majority of whom were from Zimbabwe (86.7%), mentioned at least one lay belief about risk factors for cervical cancer. The most commonly reported risk lay belief, namely inserting herbs, creams, or objects into the vagina (8.7%), was only reported by women from Zimbabwe.

Conclusion

The awareness of cervical cancer symptoms and risk factors amongst women with cervical cancer was low, particularly in SA. There is an urgent need to improve knowledge around cervical cancer, as low levels of awareness can impact timely cancer diagnosis and limit the uptake of cervical cancer prevention programs.

Introduction

In 2020, there were an estimated 604 000 incident cases of cervical cancer and 342 000 related deaths globally, resulting in cervical cancer being the fourth most diagnosed cancer and the fourth leading cause of cancer death in women [1]. Low- and Middle-Income Countries (LMICs) accounted for an estimated 80% of all incident cases, and 90% of deaths, highlighting both the uneven global distribution of cervical cancer, and that cervical cancer is a disease of poverty and inequality [2, 3]. Despite a decrease in the global age standardized incidence rate (ASIR) and age standardized mortality rate (ASMR) between 1990 and 2019, Southern sub-Saharan Africa (SSA) was the only region globally in which both the ASIR and ASMR increased over the same two-decade period (1990-2019) [4]. The increasing trend of cervical cancer ASIR and ASMR in Southern SSA over time, coupled with the fact that this region already has the highest ASIR (43.1 per 100 000 women years), and one of the highest ASMRs (20.0 per 100 000 women years) in the world, indicates the significant burden and impact that cervical cancer is having, and will continue to have, in this region [2, 5].

Cervical cancer is a nearly preventable disease with highly effective primary and secondary prevention strategies, such as the Human papillomavirus (HPV) vaccine and cervical cancer screening [1]. However, these prevention strategies have not been equitably implemented worldwide [1]. In Africa, an estimated 80% of countries do not have a national cervical cancer screening program, and only 45% of SSA countries have an HPV vaccination program [6]. However, many of the African countries with cervical cancer prevention services have poor population coverage and public uptake [1, 6, 7]. Despite both South Africa (SA) and Zimbabwe having nationwide cervical cancer screening and HPV vaccination programs, the rates of cervical cancer remain extremely high in both countries [8, 9, 10]. In 2018, the ASIR for cervical cancer in SA (43.5 per 100 000 women) was three times that of the global average (13.1 per 100 000), while Zimbabwe has the highest burden of cervical cancer in Southern Africa, with an ASIR (62 per 100 000 women) that is almost five times the global average [11, 12]. Low cervical cancer screening coverage has been reported in SA and Zimbabwe, and a lack of awareness of cervical cancer screening is believed to play a major role in the low uptake of cervical cancer screening by the public [13, 14].

Low levels of public awareness have also been shown to contribute to the high incidence of cervical cancer in LMICs [15]. Several studies conducted among women and communities in SSA have found that the knowledge of cervical cancer symptoms and risk factors is generally

poor [16, 17, 18, 19]. However, many of these studies used questionnaires that were not validated in the local context [17, 18, 19]. Evidence suggests that awareness of cervical cancer symptoms can improve help-seeking behaviors, resulting in earlier presentation to health care facilities and, possibly, diagnosis at an earlier and more treatable stage of disease [19, 20]. With an estimated 65-85% of cervical cancer patients in SSA being diagnosed at an advanced stage of disease, the need for improved awareness around symptoms of cervical cancer is crucial [21]. Improving awareness of certain risk factors, such as HPV infection and the importance of cervical cancer screening is also essential [22]. In a study across SA and Uganda, less than 1% of participants mentioned either HPV infection or a lack of cervical cancer screening as risk factors for cervical cancer, with similar findings reported in a study in Libya [15, 20].

Many of the studies conducted in SSA assessing cervical cancer awareness have been conducted at a community or population level. Comparatively, little is known about the level of cervical cancer awareness amongst women diagnosed with cervical cancer in SSA. Additionally, this study will be testing unprompted recall of cervical cancer symptoms and risk factors which has been shown to provide a more accurate representation of participants level of cervical cancer symptom and risk factor knowledge compared to when recognition is tested. Studies which test symptom and risk factor recognition are prone to guessing, as they provide cues or limited response options, potentially resulting in higher awareness scores [15, 20]. The aim of this study was to determine the level of awareness of unprompted cervical cancer risk factors and symptoms and describe lay beliefs of cervical cancer amongst women recently diagnosed with cervical cancer in SA and Zimbabwe, using a locally validated questionnaire.

Methods

Study design

This is a secondary analysis of data from a descriptive cross-sectional study of women recently diagnosed with cervical cancer in SA and Zimbabwe. The analysis used participant responses to socio-demographic questions and questions related to cervical cancer symptom and risk factor awareness from the parent study.

Study setting

The study was conducted in SA and Zimbabwe, two Southern African countries.

South Africa:

SA, an upper middle-income country with a population of approximately 60.5 million, has a 3-tiered referral based public health care system [23, 24]. Participants from SA were selected from two of the nine provinces, namely the Western Cape, one of the wealthier provinces, and the Eastern Cape, one of the poorer provinces, in the country [20]. Participants were selected from one tertiary level hospital in each province.

Zimbabwe:

Zimbabwe is an LMIC, with a population of 15.1 million, 61.4% of which live in rural areas [25, 26]. Zimbabwe also has a 3-tiered referral based public health care system like SA. Participants from Zimbabwe were selected from two of the country's ten provinces, namely Harare Province, the most populated province, and Bulawayo Province, the least populated province in the country [27]. Both Harare Province and Bulawayo Province have no secondary level health care facilities, and all patients with suspected cancer symptoms are referred to tertiary level facilities. Participants were selected from all tertiary level facilities in each province.

Study population

Between September 2022 and November 2023, all women recently diagnosed with cervical cancer at these tertiary level health care facilities, and who met the inclusion criteria, were invited to participate in the study. At each site, a clinical team identified eligible patients, referring them to the field research team, who explained the study aim, and obtained consent for individuals willing to participate. The inclusion criteria were: being 18 years or older and being diagnosed with cervical cancer in the preceding month and/or being within four weeks of receiving a treatment plan at a tertiary level facility. Individuals with a previous history of cancer and those unwilling or unable to provide consent were excluded from the study.

Data collection measures

In the parent study, data were collected by trained researchers using hand-held tablets customized with a structured, validated questionnaire. The questionnaire collected information on socio-demographic and clinical data, and knowledge of cervical cancer risk factors, symptoms, and lay beliefs.

Measures of socio-demographic and clinical data: The following socio-demographic information from participants in the parent study were utilized: age, relationship status, highest level of education, place of residence, living context, employment status and information on ownership and access to various assets. Living context was based off where participants reported they lived. In the parent study, peri-urban settings were defined as areas outside of urban zones, characterized by farming and industrial land. Principal component analysis (PCA) was used to construct a wealth asset index for the total sample using the following 11 asset variables collected in the parent study: material of wall, material of roof, water source, energy source, toilet facilities, and access to assets such as a telephone, cellphone, fridge, internet connection, computer, and a car.

Information on participant's reported medical history was also obtained, including previously diagnosed hypertension, diabetes, HIV/AIDs and tuberculosis, as well as details of cervical cancer screening and knowing anyone (family or friends) with cancer.

Table S1 outlines how the above variables were collapsed into the various categories used throughout the analysis.

Measures of cervical cancer awareness: Cervical cancer risk factor and symptom awareness was assessed using an open/unprompted question. For symptom awareness, participants were asked, "Please would you name as many symptoms or signs of cervical cancer/cancer of the mouth of the womb as you can think of?". For risk factor awareness, participants were asked, "Please could you name as many things as you can think of that could increase any person's chances of getting cervical cancer?".

For cervical cancer awareness measures, deductive reasoning was used to group and code the open-ended responses. Each participant was then scored on each correct symptom and risk factor identified by comparing their responses to a list of evidence-based cervical cancer symptoms and risk factors taken from the African Women Awareness of CANcer (AWACAN) questionnaire (Table S2) [28]. The development and validation of the AWACAN questionnaire, as well as the list of evidence-based cervical cancer risk factors and symptoms used in this study, is described elsewhere [28]. Participants scored one point for each correct symptom and risk factor identified, and points were aggregated to give each participant two separate scores, one for risk factor awareness and one for symptom awareness. Drawing on the approach used in a study conducted in a similar setting, risk factor and symptom awareness was dichotomized

into participants who correctly identified 0 or at least 1 risk factor and symptom of cervical cancer [20].

Lay beliefs were identified as responses that did not fit into any of the evidence-based cervical cancer symptoms and risk factors from the reference list.

Statistical analysis

Data were analyzed using R Studio Version 2023.06.2+561. Descriptive statistics were used to characterize socio-demographic information. Continuous variables, such as age, were expressed as median (with interquartile range) and categorical data were expressed as frequencies and percentages. Symptom and risk factor awareness was stratified by country. Due to the differences in socio-demographic factors between SA and Zimbabwe, bivariate and multivariable logistic regression analysis was performed by country. Separate multivariable logistic regression analysis was performed for risk factor awareness and symptom awareness for each country. Model results were reported as adjusted odds ratios (aOR) with 95% confidence intervals (CI). The initial multivariable models were built using the *a priori method* of variable selection, in which variables were selected based on the literature [19, 20, 29, 30, 31, 32]. The same variables were included in the multivariable models for each country. The initial variables included in the multivariable logistic regression analysis were age, relationship status, level of education, employment status, wealth asset index, living context, known family or friend with cancer, known with HIV and previous cervical cancer screening.

Ethical considerations

Ethics approval for this secondary analysis study was obtained from the University of Cape Town, Faculty of Health Sciences Human Research Ethics Committee (HREC 921/2023). The parent study, titled NIHR Global Research Group on Advancing Early Diagnosis of Cancer in Southern Africa: AWACAN-ED, received ethical clearance from all relevant committees from both SA and Zimbabwe prior to commencement of the study. Informed consent was obtained from all participants who met the inclusion criteria and were willing to participate in the parent study.

Results

Participant profile

Overall, 506 women with cervical cancer participated in this study, 284 (56.1%) from SA and 222 (43.9%) from Zimbabwe (Table 1). The median age was similar in both countries (49.8 [95% CI 41.3-59.1] in SA and 51.1 [95% CI 44.8-61.7] in Zimbabwe, respectively). In both countries, there was a similar proportion of women who were employed (24.6% in SA and 30.6% in Zimbabwe). A higher proportion of women were either separated, divorced, or widowed in Zimbabwe compared to SA (49.8 % versus 29.2%), while the proportion of single women was far higher in SA (36.6% vs 6.3%). The proportion of women in Zimbabwe who completed secondary school was almost double that of SA (32.4% vs 17.3% respectively). Compared to SA, Zimbabwe had a higher proportion of both women living in urban areas (50.0% vs 38.7%) and women who fell into the poorest wealth index quintile (38.2% vs 11.7%). The proportion of women who reported previously screening for cervical cancer was higher in SA than Zimbabwe (92.6% vs 79.6%). Of the 262 South African women who reported having been previously screened for cervical cancer, 94.3% (n = 247) were screened within the last year, and 68.7% (n = 180) received a cytology screening test. Of the 176 Zimbabwean women who reported having been previously screened for cervical cancer, 75.0% (n = 132) were screened in the last year, and almost all Zimbabwean women who were screened received the visual inspection method of screening (96.6%).

Table 1: Overall participant profile, and stratified by country

Characteristics	Overall, N = 506 n (%)	South Africa, N = 284 n (%)	Zimbabwe, N = 222 n (%)
Age, (years)			
18– 34	28 (5.5)	20 (7.1)	8 (3.60)
35– 44	129 (25.5)	78 (27.6)	51 (23.0)
45– 54	163 (32.3)	86 (30.4)	77 (34.7)
>55	185 (36.6)	99 (35.0)	86 (38.7)
Median (IQR)	50.4 (43.2 – 60.2)	49.8 (41.3 – 59.1)	51.1 (44.8 – 61.7)
Province residing in			
Western Cape	123 (24.4)	123 (43.3)	
Eastern Cape	161 (31.9)	161 (56.7)	
Harare	69 (13.7)		69 (31.2)
Bulawayo	30 (5.9)		30 (13.6)
Matebeleland North	16 (3.2)		16 (7.2)
Matebeleland South	20 (4.0)		20 (9.0)
Mashonaland East	11 (2.2)		11 (5.0)
Mashonaland Central	15 (3.0)		15 (6.8)

Mashonaland West	8 (1.6)		8 (3.6)
Manicaland	23 (4.6)		23 (10.4)
Masvingo	11 (2.2)		11 (5.0)
Midlands	18 (3.6)		18 (8.1)
Relationship status			
Married/living with a partner	194 (38.4)	97 (34.2)	97 (43.9)
Single	118 (23.4)	104 (36.6)	14 (6.3)
Separated/divorced/widowed	193 (38.2)	83 (29.2)	110 (49.8)
Education			
Less than secondary school	385 (76.1)	235 (82.7)	150 (67.6)
Secondary school completed	121 (23.9)	49 (17.3)	72 (32.4)
Employment			
Employed	138 (27.3)	70 (24.6)	68 (30.6)
Unemployed	368 (72.7)	214 (75.4)	154 (69.4)
Wealth index			
1st quintile (poorest)	117 (23.3)	33 (11.7)	84 (38.2)
2nd quintile	88 (17.5)	60 (21.3)	28 (12.7)
3rd quintile (middle)	101 (20.1)	76 (27.0)	25 (11.4)
4th quintile	119 (23.7)	66 (23.4)	53 (24.1)
5th quintile (richest)	77 (15.3)	47 (16.7)	30 (13.6)
Living context			
Rural	243 (48.0)	145 (51.1)	98 (44.1)
Urban	221 (43.7)	110 (38.7)	111 (50.0)
Peri-urban	42 (8.3)	29 (10.2)	13 (5.9)
Known family member or friend with cancer			
No	334 (66.1)	185 (65.4)	149 (67.1)
Yes	171 (33.9)	98 (34.6)	73 (32.9)
Known HIV			
No	230 (45.5)	135 (47.7)	95 (42.8)
Yes	275 (54.5)	148 (52.3)	127 (57.2)
Any chronic disease*			
No	112 (22.3)	65 (23.2)	47 (21.2)
Yes	390 (77.7)	215 (76.8)	175 (78.8)
Known previous cervical cancer screening			
No	66 (13.1)	21 (7.4)	45 (20.4)
Yes	438 (86.9)	262 (92.6)	176 (79.6)
Last screened for cervical cancer			
< 1 year ago	379 (86.5)	247 (94.3)	132 (75.0)
1-5 years ago	47 (10.7)	14 (5.3)	33 (18.8)
> 6 years ago	12 (2.7)	1 (0.4)	11 (6.2)
Type of last cervical cancer screening test			
Cytology	181 (41.3)	180 (68.7)	1 (0.6)
Visual inspection	185 (42.2)	15 (5.7)	170 (96.6)
HPV test	39 (8.9)	38 (14.5)	1 (0.6)
Combination	9 (2.1)	5 (1.9)	4 (2.3)
Not sure of test	24 (5.5)	24 (9.2)	0 (0.0)

IQR – Interquartile range
*Chronic disease include hypertension, diabetes, HIV, cardiac disease

Symptom awareness

Overall, 274 (54.3%) women, the majority of whom were from Zimbabwe (73.4%), were able to recall at least one symptom of cervical cancer (Table S3). The most commonly recalled symptoms in the overall sample were generalized vaginal bleeding (29.7%), lower abdominal or pelvic pain (18.6%) and generalized vaginal discharge (14.1%) (Table S4 & Figure S1). Overall, a higher proportion of women who were able to recall at least one symptom completed secondary school (33.6% vs 12.6%) and lived in an urban area (51.1% vs 34.6%) compared to women who were unable to recall any symptoms of cervical cancer (Table S3). However, amongst women who knew at least one symptom from SA, the proportion who completed secondary school (34.2%) was similar to the proportion of women who recalled at least one symptom from Zimbabwe and completed secondary school (33.3%) (Table 2). A higher proportion of women with no symptom awareness had previously been screened for cervical cancer (91.3% vs 83.2%) compared to women who were able to recall at least one symptom of cervical cancer (Table S3).

Table 2: Cervical cancer symptom awareness stratified by country

	South Africa		Zimbabwe	
Characteristic	Symptom awareness score: Zero N = 210 n (%)	Symptom awareness score: ≥ one N = 73 n (%)	Symptom awareness score: Zero N = 21 n (%)	Symptom awareness score: ≥ one N = 201 n (%)
Age, (years)				
18-34	12 (5.7)	8 (11.0)	1 (4.8)	7 (3.5)
35-44	52 (24.9)	26 (35.6)	7 (33.3)	44 (21.9)
45-54	66 (31.6)	20 (27.4)	5 (23.8)	72 (35.8)
>55	79 (37.8)	19 (26.0)	8 (38.1)	78 (38.8)
Median (IQR)	51.0 (43.8-60.1)	46.3 (39.2-56.4)	50.1 (42.6-63.0)	51.1 (44.9-61.7)
Relationship				
Married/living with partner	66 (31.4)	30 (41.1)	11 (52.4)	86 (43.0)
Single	75 (35.7)	29 (39.7)	1 (4.8)	13 (6.5)
Separated/divorced/widowed	69 (32.9)	14 (19.2)	9 (42.9)	101 (50.5)
Education				
Less than secondary school	186 (88.6)	48 (65.8)	16 (76.2)	134 (66.7)
Secondary school completed	24 (11.4)	25 (34.2)	5 (23.8)	67 (33.3)
Employment				
Unemployed	159 (75.7)	54 (74.0)	14 (66.7)	140 (69.7)
Employed	51 (24.3)	19 (26.0)	7 (33.3)	61 (30.3)
Wealth index				
1st quintile (poorest)	28 (13.4)	5 (6.8)	6 (28.6)	78 (39.2)
2nd	52 (24.9)	8 (11.0)	4 (19.0)	24 (12.1)

3rd (middle)	62 (29.7)	14 (19.2)	1 (4.8)	24 (12.1)
4th	41 (19.6)	25 (34.2)	6 (28.6)	47 (23.6)
5th (richest)	26 (12.4)	21 (28.8)	4 (19.0)	26 (13.1)
Living context				
Rural	127 (60.5)	18 (24.7)	9 (42.9)	89 (44.3)
Urban	69 (32.9)	40 (54.8)	11 (52.4)	100 (49.8)
Peri-urban	14 (6.7)	15 (20.5)	1 (4.8)	12 (6.0)
Known family member or friend with cancer				
No	152 (72.4)	33 (45.2)	17 (81.0)	132 (65.7)
Yes	58 (27.6)	40 (54.8)	4 (19.0)	69 (34.3)
Known HIV				
No	96 (45.7)	39 (53.4)	8 (38.1)	87 (43.3)
Yes	114 (54.3)	34 (46.6)	13 (61.9)	114 (56.7)
Any chronic disease*				
No	43 (20.8)	22 (30.1)	4 (19.0)	43 (21.4)
Yes	164 (79.2)	51 (69.9)	17 (81.0)	158 (78.6)
Known previous cervical cancer screening				
No	15 (7.1)	6 (8.2)	5 (23.8)	40 (20.0)
Yes	195 (92.9)	67 (91.8)	16 (76.2)	160 (80.0)
Risk factor awareness				
No	204 (97.1)	54 (74.0)	18 (85.7)	133 (66.5)
Yes	6 (2.9)	19 (26.0)	3 (14.3)	67 (33.5)

IQR – Interquartile range
*Chronic diseases include hypertension, diabetes, HIV, cardiac disease

Among South African women, level of education, wealth index, living context and knowing a family member or friend with cancer were all associated with symptom awareness in bivariate analysis (Table 3). In a multivariable logistic regression including these covariates, level of education, living context and knowing a family member or friend with cancer were the only factors that remained significantly associated with symptom awareness. Women who completed secondary education, lived in a peri-urban setting or who knew a family member or friend with cancer were statistically significantly more likely to know at least one cervical cancer symptom compared to those with less than secondary school (aOR 2.84 95% CI 1.33-6.12), those who lived in a rural setting (aOR 4.99 95% CI 1.36-18.81) or those who did not know anyone with cancer (aOR 2.61 95% CI 1.38-4.98). Among women in Zimbabwe, there were no factors on bivariate or multivariable analysis that were associated with cervical cancer symptom awareness (Table 3 & S5).

Table 3: Predictors of cervical cancer symptom awareness in each country

	South Africa		Zimbabwe	
Characteristics	Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)
Age				
18-34	Ref	Ref	Ref	Ref
35-44	0.75 (0.28; 2.12)	0.74 (0.23; 2.51)	0.90 (0.04; 6.27)	0.50 (0.02; 4.34)
45-54	0.45 (0.16; 1.30)	0.49 (0.15; 1.68)	2.06 (0.10; 15.42)	1.66 (0.07; 16.68)
>55	0.36 (0.13; 1.03)	0.44 (0.12; 1.59)	1.39 (0.07; 9.38)	1.08 (0.05; 10.28)
Relationship				
Married/living with partner	Ref	Ref	Ref	Ref
Single	0.85 (0.46; 1.56)	0.72 (0.34; 1.50)	1.66 (0.29; 31.65)	0.80 (0.11; 16.65)
Separated/divorced/widowed	0.45 (0.21; 0.90)	0.55 (0.23; 1.27)	1.44 (0.57; 3.72)	1.22 (0.41; 3.65)
Education				
Less than secondary school	Ref	Ref	Ref	Ref
Secondary school completed	**4.04 (2.12; 7.73)**	**2.84 (1.33; 6.12)**	1.60 (0.60; 5.06)	2.60 (0.77; 10.21)
Employment				
Unemployed	Ref	Ref	Ref	Ref
Employed	1.10 (0.59; 2.00)	0.82 (0.38; 1.70)	0.87 (0.34; 2.40)	0.63 (0.20; 2.03)
Wealth index				
1st quintile (poorest)	Ref	Ref	Ref	Ref
2nd quintile	0.86 (0.26; 3.08)	0.85 (0.24; 3.31)	0.46 (0.12; 1.93)	0.36 (0.07; 2.07)
3rd quintile (middle)	1.26 (0.44; 4.22)	0.59 (0.17; 2.24)	1.85 (0.29; 35.78)	1.08 (0.10; 27.93)
4th quintile	**3.41 (1.24; 11.07)**	0.99 (0.22; 4.75)	0.60 (0.18; 2.03)	0.31 (0.04; 2.75)
5th quintile (richest)	**4.52 (1.58; 15.14)**	0.87 (0.18; 4.42)	0.50 (0.13; 2.08)	0.19 (0.02; 1.74)
Living context				
Rural	Ref	Ref	Ref	Ref
Urban	**4.09 (2.21; 7.82)**	2.51 (0.83; 7.63)	0.92 (0.36; 2.32)	2.07 (0.32; 13.03)
Peri-urban	**7.56 (3.15; 18.54)**	**4.99 (1.36; 18.81)**	1.21 (0.20; 23.37)	1.77 (0.18; 43.65)
Known family member or friend with cancer				
No	Ref	Ref	Ref	Ref
Yes	**3.18 (1.84; 5.54)**	**2.61 (1.38; 4.98)**	2.22 (0.79; 7.95)	2.75 (0.89; 10.86)
Known HIV				
No	Ref	Ref	Ref	Ref
Yes	0.73 (0.43; 1.25)	0.93 (0.44; 1.97)	0.81 (0.31; 2.00)	0.92 (0.29; 2.75)
Known previous cervical cancer screening				
No	Ref	Ref	Ref	Ref
Yes	0.86 (0.33; 2.49)	0.62 (0.20; 2.14)	1.25 (0.39; 3.41)	1.47 (0.41; 4.76)

OR – odds ratio
CI – confidence interval

Risk factor awareness

Overall, 95 (18.8%) women, the majority of whom were from Zimbabwe (73.7%), were able to name at least one correct risk factor for cervical cancer (Table S3). The most commonly recalled risk factors in the overall sample were having many sexual partners (6.2%), having unprotected sex (3.8%), and HIV/AIDs (3.4%) (Table S4 & Figure S2). Overall, a higher

proportion of women who were able to name at least one cervical cancer risk factor were married or living with a partner (50.5% vs 35.3%) and had completed secondary school (43.2% vs 19.6%) compared to women who had no cervical cancer risk factor awareness (Table S3). However, among South African women who knew one or more correct risk factor, the proportion who completed secondary school (44.0%), was similar to the proportion of Zimbabwean women who knew one or more correct risk factor and completed secondary school (42.9%) (Table 4). The majority of women with no cervical cancer risk factor awareness were unemployed (76.5%), compared to 56.8% of women who had cervical cancer risk factor awareness (Table S3). The proportion of women who had previously been screened for cervical cancer were similar in both groups.

Table 4: Cervical cancer risk factor awareness stratified by country

	South Africa		Zimbabwe	
Characteristics	Risk factor awareness score: Zero N = 258 n (%)	Risk factor awareness score: ≥ one N = 25 n (%)	Risk factor awareness score: Zero N = 151 n (%)	Risk factor awareness score: ≥ one N = 70 n (%)
Age, (years)				
18-34	18 (7.0)	2 (8.0)	6 (4.0)	2 (2.9)
35-44	68 (26.5)	10 (40.0)	30 (19.9)	21 (30.0)
45-54	78 (30.4)	8 (32.0)	48 (31.8)	29 (41.4)
>55	93 (36.2)	5 (20.0)	67 (44.4)	18 (25.7)
Median (IQR)	49.9 (42.1-59.8)	45.3 (39.6-51.8)	53.4 (45.7-63.0)	48.1 (41.6-56.9)
Relationship status				
Married/living with a partner	84 (32.6)	12 (48.0)	60 (40.0)	36 (51.4)
Single	96 (37.2)	8 (32.0)	8 (5.3)	6 (8.6)
Separated/divorced/widowed	78 (30.2)	5 (20.0)	82 (54.7)	28 (40.0)
Education				
Less than secondary school	220 (85.3)	14 (56.0)	109 (72.2)	40 (57.1)
Secondary school completed	38 (14.7)	11 (44.0)	42 (27.8)	30 (42.9)
Employment				
Unemployed	197 (76.4)	16 (64.0)	116 (76.8)	38 (54.3)
Employed	61 (23.6)	9 (36.0)	35 (23.2)	32 (45.7)
Wealth index				
1st quintile (poorest)	32 (12.5)	1 (4.0)	66 (44.3)	18 (25.7)
2nd	58 (22.6)	2 (8.0)	18 (12.1)	9 (12.9)
3rd (middle)	70 (27.2)	6 (24.0)	17 (11.4)	8 (11.4)
4th	60 (23.3)	6 (24.0)	31 (20.8)	22 (31.4)
5th (richest)	37 (14.4)	10 (40.0)	17 (11.4)	13 (18.6)
Living context				
Rural	139 (53.9)	6 (24.0)	72 (47.7)	25 (35.7)
Urban	96 (37.2)	13 (52.0)	71 (47.0)	40 (57.1)
Peri-urban	23 (8.9)	6 (24.0)	8 (5.3)	5 (7.1)

Known family member or friend with cancer				
No	170 (65.9)	15 (60.0)	106 (70.2)	42 (60.0)
Yes	88 (34.1)	10 (40.0)	45 (29.8)	28 (40.0)
Known HIV				
No	119 (46.1)	16 (64.0)	76 (50.3)	18 (25.7)
Yes	139 (53.9)	9 (36.0)	75 (49.7)	52 (74.3)
Any chronic disease*				
No	50 (19.6)	15 (60.0)	37 (24.5)	10 (14.3)
Yes	205 (80.4)	10 (40.0)	114 (75.5)	60 (85.7)
Known previous cervical cancer screening				
No	19 (7.4)	2 (8.0)	37 (24.5)	8 (11.6)
Yes	239 (92.6)	23 (92.0)	114 (75.5)	61 (88.4)
Symptom awareness				
No	204 (79.1)	6 (24.0)	18 (11.9)	3 (4.3)
Yes	54 (20.9)	19 (76.0)	133 (88.1)	67 (95.7)

IQR – Interquartile range
*Chronic diseases include hypertension, diabetes, HIV, cardiac disease

Among women in SA, level of education, living context and wealth index were all associated with cervical cancer risk factor awareness in bivariate analysis (Table 5). However, in a multivariable logistic regression including these variables, level of education was the only factor that remained significantly associated with risk factor awareness (Table 5). Among South African women, those who completed secondary school were statistically significantly more likely to know at least one cervical cancer risk factor compared to those with less than secondary school education [aOR 2.86 95% CI 1.05-7.69). Among women in Zimbabwe, level of education, employment status, wealth index, known with HIV and previously screening for cervical cancer were associated with cervical cancer risk factor awareness in bivariate analysis (Table 5). Only wealth index and known with HIV remained significantly associated in the multivariable model. Women who fell into the second highest wealth index or who were known to be living with HIV were statistically significantly more likely to know at least one cervical cancer risk factor compared to those in the poorest wealth index (aOR 5.69 95% CI 1.21-29.24) or those who were not living with HIV (aOR 2.14 95% CI 1.04-4.50) (Table 5).

Table 5: Predictors of cervical cancer risk factor awareness in each country

	South Africa		**Zimbabwe**	
Characteristic	Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)
Age, (years)				
18-34	Ref	Ref	Ref	Ref
35-44	1.32 (0.31; 9.11)	2.02 (0.38; 16.43)	2.10 (0.43; 15.30)	2.20 (0.36; 19.78)
45-54	0.92 (0.21; 6.46)	1.48 (0.27; 12.37)	1.81 (0.39; 12.93)	2.39 (0.40; 21.15)

>55	0.48 (0.10; 3.56)	0.75 (0.11; 6.96)	0.81 (0.17; 5.82)	1.68 (0.27; 15.56)
Relationship				
Married/living with partner	Ref	Ref	Ref	Ref
Single	0.58 (0.22; 1.48)	0.70 (0.23; 2.03)	1.25 (0.38; 3.88)	0.82 (0.20; 3.15)
Separated/divorced/widowed	0.45 (0.14; 1.27)	0.92 (0.24; 3.27)	0.57 (0.31; 1.03)	0.60 (0.30; 1.20)
Education				
Less than secondary school	Ref	Ref	Ref	Ref
Secondary school completed	**4.55 (1.89; 10.76)**	**2.86 (1.05; 7.69)**	**1.95 (1.07; 3.52)**	1.44 (0.66; 3.10)
Employment				
Unemployed	Ref	Ref	Ref	Ref
Employed	1.82 (0.74; 4.24)	1.15 (0.40; 3.13)	**2.79 (1.53; 5.13)**	1.72 (0.81; 3.65)
Wealth asset index				
1st quintile (poorest)	Ref	Ref	Ref	Ref
2nd quintile	1.10 (0.10; 24.29)	0.96 (0.08; 22.29)	1.83 (0.69; 4.72)	3.22 (0.87; 12.33)
3rd quintile (middle)	2.74 (0.44; 52.93)	1.73 (0.24; 35.63)	1.73 (0.62; 4.57)	3.29 (0.64; 17.58)
4th quintile	3.20 (0.52; 61.83)	1.10 (0.11; 27.39)	**2.60 (1.23; 5.60)**	**5.69 (1.21; 29.24)**
5th quintile (richest)	**8.65 (1.53; 163.07)**	1.84 (0.17; 46.25)	**2.80 (1.15; 6.88)**	4.95 (0.99; 27.50)
Living context				
Rural	Ref	Ref	Ref	Ref
Urban	**3.14 (1.20; 9.20)**	2.22 (0.43; 10.88)	1.62 (0.90; 2.97)	0.29 (0.07; 1.15)
Peri-urban	**6.04 (1.75; 20.94)**	3.75 (0.65; 20.91)	1.80 (0.50; 5.92)	0.46 (0.08; 2.32)
Known family member or friend with cancer				
No	Ref	Ref	Ref	Ref
Yes	1.29 (0.54; 2.96)	0.81 (0.30; 2.12)	1.57 (0.87; 2.84)	1.53 (0.78; 2.99)
Known HIV				
No	Ref	Ref	Ref	Ref
Yes	0.48 (0.20; 1.11)	0.49 (0.16; 1.43)	**2.93 (1.59; 5.57)**	**2.14 (1.04; 4.50)**
Known previous cervical cancer screening				
No	Ref	Ref	Ref	Ref
Yes	0.91 (0.24; 5.96)	0.53 (0.12; 3.86)	**2.47 (1.13; 6.02)**	1.70 (0.69; 4.56)

OR – odds ratio
CI – confidence interval

Lay beliefs

Overall, 90 (17.9%) women mentioned at least one lay belief about risk factors for cervical cancer (Table S4). The majority of risk lay beliefs were reported by women from Zimbabwe (Figure 1). The most commonly reported risk lay belief, inserting herbs, creams, or objects into the vagina (8.7%), was only reported by women from Zimbabwe (Figure 1 & Table S4).

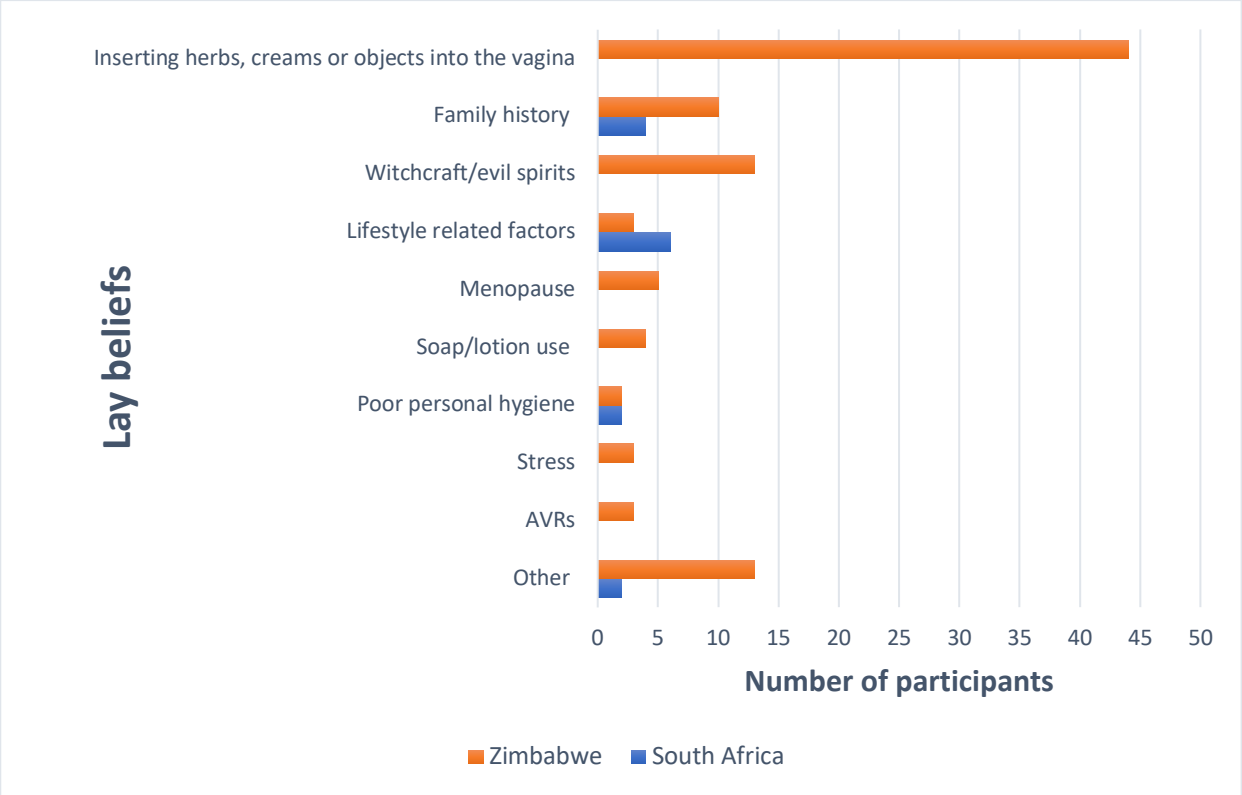

Figure 1: Bar graph showing cervical cancer risk lay beliefs, stratified by country

Discussion

To the best of our knowledge, this is the first study conducted in Southern Africa that aimed to determine the levels of awareness of cervical cancer symptoms and risk factors amongst women recently diagnosed with cervical cancer, using a locally validated questionnaire. We expected women diagnosed with cervical cancer to have higher levels of awareness around cervical cancer, however, concerningly, we found low levels of awareness. Overall, cervical cancer symptom and risk factor awareness was low, with only half the women (54.3%) being able to recall one or more correct symptom, and less than one fifth (18.8%) being able to recall one or more risk factor. Among South African women, level of education, living context and knowing a family member or friend with cancer were associated with symptom awareness, while only level of education was associated with risk factor awareness. Among Zimbabwean women, wealth index and known with HIV was associated with risk factor awareness.

The finding of low cervical cancer symptom awareness in our study was consistent with findings from other studies conducted across Africa [15, 17, 18, 20]. However, a major

difference between our study and many other studies conducted across Africa was the study population. Our study was conducted amongst women diagnosed with cervical cancer, while many other studies were conducted at a community level. One would expect the level of cervical cancer awareness to be higher in women diagnosed with cervical cancer, as, firstly, diagnosed women are likely to have experienced symptoms of cervical cancer and increasing symptom awareness, and secondly, diagnosed women likely had multiple visits to health care facilities and engaged with health care professionals, providing opportunities to receive health education and information. In this study we found that women with cervical cancer had similar low levels of awareness to that reported among women without cervical cancer [20], suggesting that women were not receiving adequate counselling, health education and information of their suspected disease by health care professionals while engaging with health care facilities. In a South African and Ugandan study, only 57.7% of women were able to recall one correct symptom of cervical cancer, while a study in Libya found that 63.3% of women were not able to recall any signs or symptoms of cervical cancer [15, 20]. Both studies were population-based, and used a validated questionnaire, assessing symptom awareness with open-ended questions. Interestingly, other studies conducted in Africa have found high levels of symptom awareness for cervical cancer. For example, a population-based study set in Northern Uganda, conducted amongst men and women without cervical cancer, found that most participants recognized cervical cancer symptoms [19]. However, the latter study tested recognition of symptoms by providing cues or limited response options, and is therefore prone to participants guessing, potentially resulting in higher recognition scores [20].

Similar to our SA findings, the association between higher levels of education and greater cervical cancer knowledge was also reported in studies conducted in Ethiopia and Cameroon [29]. This finding emphasizes that education and health literacy is essential in improving the level of cervical cancer symptom and risk factor awareness among women. However, the 2022 global education monitoring report highlighted the gender inequality in the access to and completion of education, with one in four women from SSA unable to read and write. There is therefore an urgent need for a multi-sectoral approach, which includes improving access to education for women, to address the low levels of cervical cancer awareness in SSA countries [17, 18, 20, 33].

Our study highlighted that women from SA, living in rural settings, had lower awareness of cervical cancer symptoms. SA is a country with extreme inequity, evidenced by the Gini co-

efficient of 0.6, and a large population of individuals living in rural areas [20, 34, 35]. Women living in rural areas are likely to have less access to evidence-based cervical cancer information as well as screening facilities compared to women in urban settings [6, 20]. There is therefore an urgent need to implement cervical cancer education and awareness interventions in rural communities as well as in primary health care facilities, which are the entry point into the South African healthcare system. Symptom awareness is a crucial first step in the pathway to cancer care for every patient. Thus, improving cervical cancer symptom awareness can increase the likelihood of patients seeking care, leading to a more timely diagnosis, with improved outcomes [20, 33].

An interesting finding in our study was that, in SA, women who knew a family member or friend with cancer had improved symptom awareness compared to women who did not know anyone with cancer. This finding suggests that women diagnosed with cervical cancer can act as agents of knowledge transmission within their communities. It is important to ensure that women diagnosed with cervical cancer are adequately informed about cervical cancer and its risk factors and symptoms, as they can then relay this information to other individuals within their community, thereby increasing the levels of awareness around cervical cancer in these communities.

There is previous evidence of low levels of knowledge of cervical cancer risk factors in most SSA countries, including Kenya, Zimbabwe, Cameroon, and Nigeria [19]. A study in Nigeria, which used a structured, unvalidated questionnaire amongst women attending antenatal and gynaecological outpatient clinics, found only 15.6% of women had good knowledge of cervical cancer risk factors. However, in this study, good knowledge of risk factors was defined as being able to correctly identify more than 6 out of the 12 risk factors of cervical cancer provided [18]. A study in SA conducted among female university students, found that, of the 42.9% of participants that had heard of cervical cancer, 15.6% did not know any risk factors for cervical cancer, while a separate study in Zimbabwe found that only 1.3% of female university students were knowledgeable about cervical cancer risk factors [36, 37].

HPV vaccination and cervical cancer screening are key interventions, and in countries with effective, long-standing cervical cancer prevention programs, the rates of cervical cancer are very low [4, 38, 39, 40, 41]. In LMICs, a lack of knowledge around cervical cancer, and in particular, the association between HPV and cervical cancer, is a major barrier to the uptake of

cervical cancer prevention interventions [42, 43]. Alarmingly, in our study, very few women mentioned HPV infection or not going for screening as a cervical cancer risk factor (0.8% and 1.4% respectively). Similarly low levels of awareness for these two risk factors were found in a community-based study among women conducted in SA and Uganda, which also used a validated questionnaire and tested unprompted (recall) risk factor awareness [20]. Studies conducted in Ethiopia and Kenya have also found a lack of awareness of screening as a risk factor for cervical cancer [20, 44, 45].

Both SA and Zimbabwe have nationwide cervical cancer screening and HPV vaccination programs, however, the rates of cervical cancer remain high in both these countries [8, 9, 10]. Nationwide HPV vaccination programs have recently been introduced into both countries (2014 in SA and 2018 in Zimbabwe) [46, 47]. However, SA is already experiencing a decline in the rate of young girls getting vaccinated [46]. Low levels of knowledge and awareness around the role of HPV infection can potentially contribute to decreasing participation in intervention programs, such as HPV vaccination [22]. Therefore, introducing and implementing intervention programs alone is not enough, and governments also need to address and improve the low levels of awareness and knowledge around cervical cancer, to ensure high uptake and utilization of prevention programs [22].

A crucial factor contributing to the high burden of cervical cancer in SSA is the high prevalence of HIV in this region [3,7]. Both SA and Zimbabwe have high HIV burdens, with SA accounting for approximately 20% of all people living with HIV globally [48, 49]. In SA, 53% of all cervical cancer cases are attributable to HIV [50]. One would expect symptom and risk factor awareness to be higher amongst women living with HIV considering the frequent visits to health care facilities, providing opportunities for health education. However, our study found that this was not the case, as living with HIV was not associated with cervical cancer symptom awareness in both countries and was only significantly associated with risk factor awareness amongst Zimbabwean women. Considering that women living with HIV are believed to be at a 6-times higher risk of developing cervical cancer compared to women without HIV, it is essential to incorporate health education and promotion of cervical cancer awareness at every health encounter, particularly for women living with HIV [3, 7].

The most commonly reported lay belief in our study, inserting herbs, creams, or objects into the vagina as a cause of cervical cancer (8,73%), has also been reported in other studies in

Africa [20]. It is important to understand and identify lay beliefs, as they can potentially negatively impact other disease prevention and public health interventions. For example, a few women (<1%) in our study mentioned antiretroviral (ARVs) drugs as a cause of cervical cancer. This lay belief can increase non-adherence to ARVs, despite the fact that ARVs have been proven to be effective in managing HIV. Additionally, women who have a lay belief, such as inserting herbs, creams or objects into the vagina is a cervical cancer risk factor, might believe that if they do not engage in this behaviour, they might not be at risk of developing cervical cancer.

Understanding lay beliefs around cervical cancer is necessary, especially when designing and implementing healthcare interventions. It is essential that, in addition to improving awareness and knowledge around cervical cancer, health promotion programs and interventions also address and correct lay beliefs [20]. Framing health interventions around the beliefs of the individuals and communities who are going to utilize the intervention, increases the likelihood that the intervention will be accepted by the community, thereby increasing the uptake and effectiveness of the intervention [51].

Limitations and strengths

A major strength of our study was that cervical cancer symptom and risk factor awareness was measured using a questionnaire that was locally validated. Additionally, our study tested unprompted recall of symptoms and risk factors, which has been shown to be a more accurate representation of knowledge and awareness compared to recognition of symptoms and risk factors [15, 20].

A limitation of our study was that, due to the low levels of awareness in our study, both symptom and risk factor awareness was defined as being able to mention at least one correct symptom or risk factor for cervical cancer. This meant that even women who were only able to recall one symptom or risk factor were still classified as having risk factor or symptom awareness. However, a higher cut off value to define awareness, would have been a more accurate representation of participant awareness of cervical cancer risk factors or symptoms. Another potential limitation in our study was enrolling women who were recently diagnosed with cervical cancer. A diagnosis of cancer can cause significant psychological distress, and although attempts were made to ensure that no participant was interviewed while showing signs of distress, the psychological effect of a cancer diagnosis could have resulted in limited participant engagement and responses during the interview. Additionally, due to the fact that

this study only included women who were already diagnosed with cervical cancer, the findings are not generalizable to an undiagnosed population where the level of awareness of cervical cancer symptoms and risk factors would be important to examine in future studies. Interestingly, high levels of cervical cancer screening were reported in this study, however, this is likely due to the health system structures and policy guidelines of both South Africa and Zimbabwe. This study recruited women who were diagnosed with cervical cancer at a tertiary level facility, therefore, women would have received a screening test in order to be referred up the healthcare system. Lastly, as both the South African and Zimbabwean health care system is referral based, it is likely that most women engaged with healthcare services multiple times before being diagnosed with cervical cancer and receiving care at tertiary level healthcare facilities. This means that the level of cervical cancer symptom and risk factor awareness is likely even lower than reported, as women might have been informed about cervical cancer while engaging with health care services.

Conclusion

This study highlights the low levels of cervical cancer symptom and risk factor awareness in two Southern African countries among women recently diagnosed with cervical cancer and emphasizes the dire need to implement and initiate health interventions in SA and Zimbabwe that address and improve the low levels of awareness around cervical cancer symptoms and risk factors. Improved symptom awareness can lead to earlier help-seeking behaviour resulting in earlier presentation to health care facilities, and potentially an earlier stage of disease diagnosis. Meanwhile, improved risk factor awareness, in particular HPV infection and screening, can prevent the onset of cervical cancer in women.

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Part C: APPENDICES

Appendix A: AWACAN Cervical Cancer Questionnaire

NIHR Global Research Group on Advancing Early Diagnosis of Cancer in Southern Africa: AWACAN-ED

Appendix 3

CERVICAL SYMPTOMS CROSS-SECTIONAL SURVEY

FACILITY CODE ☐☐

INTERVIEWER CODE ☐☐

MEDICAL RECORD NUMBER ☐☐☐☐☐☐☐

Enter directly from participant's medical records

DATE OF INTERVIEW ☐☐/☐☐/☐☐☐☐

(DD/MM/YYYY)

ELIGIBILITY CHECK

1. **Is the participant 18 years of age or older?**
   1 = Yes
   2 = No → Stop

2. **Has the participant been diagnosed with any cancer previously (i.e. before this current diagnosis)?**
   1 = Yes → Stop
   2 = No → Proceed with questionnaire

CERVICAL SYMPTOMS CROSS-SECTIONAL SURVEY

SECTION 1: SOCIO-DEMOGRAPHIC QUESTIONS

READ: "Thank you for agreeing to talk with me. To start, I am going to ask you some questions about yourself.

No.	Questions and filters	Response
101.	Where do you live now?	Province _____; Country _____
102.	What sex were you assigned at birth?	Female
		Male
102b.	What gender do you identify as now? RECORD AS RESPONDED: USE PARTICIPANT'S OWN WORD	_____
103.	What is your date of birth? ***Interviewer note:*** *If year is known and day or month of birth is unknown/uncertain, enter as the first day of the month or first month of the year (January, respectively. For instance, for someone born in 2000 who is unsure of their birth date and month, enter date of birth as the 1st of January 2000.*	_____ (DDMMYYYY)
104.	What is your current relationship status? **READ OUT ALL OPTIONS AND ENTER ONLY ONE RESPONSE**	Married
		Living together with a partner
		Single
		Separated/Divorced
		Widowed
105.	What is your highest level of education? *Interviewer's note: use school grade and standard guide to assist you* **ENTER ONLY ONE RESPONSE**	No schooling
		Primary incomplete
		Primary complete
		Secondary incomplete
		Secondary complete
		More than secondary
106.	What is the main language spoken at your home? **ENTER ONLY ONE RESPONSE**	English
		Afrikaans
		isiXhosa
		Ndebele
		Shona
		Other (please specify)……

107.	Where do you live now? **READ OUT ALL OPTIONS AND ENTER ONLY ONE RESPONSE**	Rural; village
		Rural; farm
		Urban; formal *For Zimbabwe, if Urban formal; ask if it is any of:* *High density* *Medium* *Low density*
		Urban; informal
		Peri-urban; formal
		Peri-urban; informal
108.	What is your current employment status? **READ OPTIONS AND CIRCLE/ENTER ONE OPTION**	Employed Full Time
		Self-employed (formal sector)
		Part-time/Contract/ Temporary
		Casual
		Self-employed (Informal sector)
		Unemployed
		Housewife
		Pensioner
		Student/ Learner/ Child

I would now like to ask you some questions about your living environment and household

109.	**How many people (including you) live in the same household where you live?** (*When I talk about your household, I include all the people (particularly people who are related by blood, marriage - including common law and traditional marriage - or adoption) who live in your house for at least 2 weeks of every month and who share the same food with you*)	☐☐ people
110.	Do you belong to a medical aid scheme (i.e., in SA or Zimbabwe) or any health insurance scheme or programme in your country?	Yes No
110b	If Yes, how much does your household pay for health insurance premiums (including medical aid schemes) **in a month**? **Interviewer note:** For Zimbabwe enter amount in US Dollar (where necessary use the current official exchange rates to convert from Zimbabwean Dollar to US Dollar). For South Africa, enter amount in Rand. **Enter '9999' if unknown/unsure.**	Amount: _ _ _ _

111	***Which type of dwelling does your household occupy?*** ***READ OPTIONS AND CIRCLE/ENTER ONE OPTION***	
	Formal	House or formal structure on a separate stand
		Flat in a block of flats
		Own/cluster/semi-detached house (simplex/duplex or triplex)
		Unit in retirement village
		Room/flatlet in main dwelling
		House/flat/room, in backyard
	Informal	Informal dwelling/shack, NOT in backyard
		Informal dwelling/shack, IN the backyard of a formal house
	Traditional	Traditional dwelling/hut/structure made of traditional materials
	Homeless	Homeless/on the street
112	What is the main material of the house's walls? **READ OPTIONS AND CIRCLE/ENTER ONE OPTION**	1 = Brick & Plaster/finished
		2 = Bare brick/cement block
		3 = Mud and cement mixture
		4 = Mud
		5 = Corrugated iron/zinc
		6 = Wood
		7 = Asbestos
		8 = Plastic/cardboard
		9 = Other (specify)
113	What is the main material of the house's roof? **READ OPTIONs AND CIRCLE/ENTER ONE OPTION**	1 = Tiles
		2 = Corrugated iron/zinc
		3 = Thatching
		4 = Asbestos
		5 = Plastic/cardboard
		6 = Other (specify)
114	How many rooms, including kitchens, does your home have? **[EXCLUDE BATHROOMS, SHEDS, GARAGES, STABLES, TOILETS ETC. UNLESS PERSONS ARE LIVING IN THEM]**	☐☐
115	What is the main source of drinking water for members of your household? **READ OPTIONS AND CIRCLE/ENTER ONE OPTION**	1 = Piped water in dwelling
		2 = Piped water in yard
		3 = Public tap
		4 = Rain-water tank
		5 = Water carrier/tanker
		6 = Borehole/well
		7 = Dam/river/stream/spring
		8 = Other (specify)
116	What type of toilet facility does your household have? **READ OPTIONS AND CIRCLE/ENTER ONE OPTION**	1 = Flush toilet (connected to sewerage)
		2 = Flush toilet (septic tank)
		3 = Chemical toilet (not connected to a sewage system but has a compartment in which waste is treated with chemicals for temporary storage)
		4 = Pit/blair latrine
		5 = Bucket toilet
		6 = No facility/bush/field

117	What is the main source of energy for cooking in your household? **READ OPTIONS AND CIRCLE/ENTER ONE OPTION**	1 = Electricity		
		2 = Solar energy		
		3 = Gas		
		4 = Paraffin		
		5 = Wood		
		6 = Coal		
		7 = Animal dung		
		8 = Other (specify)		
118	I am going to read out a list of things that are found in some households and I would like you to tell me whether you have them (currently working) in your household or not. **TICK A RESPONSE FOR EACH.**	Yes	No	NS
	1. Ordinary (e.g., Telkom/Telephone) telephone (i.e., landline)			
	2. Cell phone			
	3. Personal computer at home			
	4. An internet connection			
	5. Fridge			
	6. Car / truck / bakkie			
	7. If yes, how old is the newest car / truck / bakkie in your household since the date of manufacture **[SPECIFY AGE IN YEARS]**			
119	How many people in this household currently receive the following grants or other kinds of income from government? **[CODE '0' IF NO-ONE IS RECEIVING THAT TYPE]**	No. of people in household receiving…		
	Unemployment Insurance (UIF)			
	Worker's Compensation			
	Any of the following grants: State Old Age Pension, Disability Grant, Child Support Grant, Foster Care Grant, Care Dependency or War Veteran's Grant			
	Other (specify)			

SECTION 2: MEDICAL HISTORY:

No.	Questions and filters	Response			
201	Does anyone in your family or close friends have any cancer now or in the past? (This could be your parent/sibling/child/ parent's sibling/grandparent)		Yes	No	NS
202	Have you ever been told by a doctor, nurse or health care professional that you have […] **GO THROUGH ALL THE OPTIONS AND TICK A RESPONSE FOR EACH.**		Yes	No	NS
		a. Tuberculosis (TB			
		b. Hypertension/High Blood Pressure/			
		c. Diabetes/High blood sugar/			
		d. Heart problems/cardiac disease			
		e. HIV/AIDS			

		f. COVID-19			

NS = not sure

203. Have you ever undergone/had cervical cancer screening?	Yes
	No
	Don't know/Not sure
204. If YES was your last screening test a … **READ OPTIONS AND CIRCLE/ENTER ONE OPTION**	Cytology (conventional or liquid based)
	Visual inspection methods (VIA/VIAC/VILI)
	HPV test
	HPV test and cytology or visual inspection methods
	Not sure what test
205. If yes when was your last screening test	Less than a year ago
	1 – 5 years ago
	6 – 10 years ago
	>10 years ago
	Don't know/Not sure

SECTION 3: SYMPTOM AND RISK FACTOR AWARENESS

READ: The following is an open question seeking to find out how many symptoms or signs of cervical cancer/cancer of the mouth of the womb people know.

301. READ: "Please would you name as many symptoms or signs of cervical cancer/cancer of the mouth of the womb as you can think of?"

TYPE IN (IN ENGLISH) ALL THE SYMPTOMS OR SIGNS THE WOMAN GIVES IN THE BLANK SPACE PROVIDED. TYPE IT EXACTLY AS THEY SAY IT.

302. READ: " Please could you name as many things as you can think of that could increase **any** person's chances of getting cervical cancer?"
TYPE IN (IN ENGLISH) ALL THE RISK FACTORS THE WOMAN GIVES IN THE BLANK SPACE PROVIDED. TYPE IT EXACTLY AS THEY SAY IT.

Appendix B: Evidence-based list of cervical cancer risk factors and symptoms

Table 2: list of evidence based cervical cancer risk factors and symptoms

Risk factors
Getting a sexually transmitted infection called the Human Papillomavirus
HIV/AIDS
Being infected with other sexually transmitted diseases (other than HIV or HPV)
Using birth control pills/family planning for more than 5 years
Having unprotected sex
Smoking any cigarettes at all
Having a sexual partner who is not circumcised
Having sex at a young age
Giving birth to 3 or more children
Having many sexual partners
Not going for regular screening/testing for cervical cancer
Symptoms
Vaginal bleeding between menstrual periods
Persistent lower back pain
A persistent smelly vaginal discharge
Discomfort or pain during sex
Menstrual periods that are longer or heavier than usual
Persistent diarrhoea
Vaginal bleeding after menopause
Persistent lower abdominal/pelvic pain
Vaginal bleeding during or after sex
Blood in urine or stools
Unexplained weight loss

Appendix C: Ethics approval from relevant SA ethics committees

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room G50- Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492
Email: hrec-enquiries@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

19 October 2021

HREC REF: 664/2021

Prof J Moodley
School of Public Health & Family Medicine
& Cancer Research Initiative
FHS
Email: Jennifer.moodley@uct.ac.za

Dear Prof Moodley

PROJECT TITLE: NIHR GLOBAL RESEARCH GROUP ON ADVANCING EARLY DIAGNOSIS OF CANCER IN SOUTHERN AFRICA: AWACAN-ED

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

This approval is subject to strict adherence to the HREC recommendations regarding research involving human participants during COVID -19, dated 17 March 2020; 06 July 2020 & 01 July 2021.

Approval is granted for one year until the 30 October 2022.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

Please quote the HREC REF 664/2021 in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FACULTY OF HEALTH SCIENCES HUMAN RESEARCH ETHICS COMMITTEE
Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938

HREC/REF 664/2021sa

UNIVERSITY OF CAPE TOWN

FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

FHS016: Annual Progress Report / Renewal

HREC office use only (FWA00001637; IRB00001938) This serves as notification of annual approval, including any documentation described below.			
☑ Approved	Annual progress report	Approved until/next renewal date	30.10.2024
☐ Not approved	See attached comments		
Signature Chairperson of the HREC/ Designee		Date Signed	17/10/2023

Note: Please email this form and supporting documents (if applicable) in a combined pdf-file to hrec-enquiries@uct.ac.za.
Please clarify your plan for research-related activities during COVID-19 lockdown.
Please use the latest form found on our website:
http://www.health.uct.ac.za/fhs/research/humanethics/forms

HUMAN RESEARCH ETHICS COMMITTEE
17 OCT 2023
HEALTH SCIENCES FACULTY
UNIVERSITY OF CAPE TOWN

Comments to PI from the HREC

Principal Investigator to complete the following:

1. Protocol information

Date (when submitting this form)	16th October 2023		
HREC REF Number	664/2021	Current Ethics Approval was granted until	30/10/2023
Protocol title	Advancing Early Diagnosis of Cancer in Southern Africa - the African aWAreness of CANcer and Early Diagnosis (AWACAN-ED) project		
Protocol number (if applicable)			
Are there any sub-studies linked to this study?	☐ Yes	✓ No	
If yes, could you please provide the HREC Reference number for all sub-studies? **Note:** A separate FHS016 must be submitted for each sub-study.			
Principal Investigator	Professor Jennifer Moodley		

(Note: Please complete the Closure form (FHS010) if the study is completed within the approval period)

Province of the
EASTERN CAPE
HEALTH

Enquiries: Yvonne Gixela Tel no: 079 074 0859

Email: Yvonne.Gixela@echealth.gov.za / ygixela@gmail.com

Date: 10 November 2021

Advancing Early Diagnosis of Cancer in Southern Africa - the African awareness of Cancer and Early Diagnosis (AWACAN-ED) project (EC_202111_007)

Dear Prof J. Moodley

The department would like to inform you that your application for the abovementioned research topic has been approved based on the following conditions:

1. During your study, you will follow the submitted protocol with ethical approval and can only deviate from it after having a written approval from the Department of Health in writing.

2. You are advised to ensure, observe and respect the rights and culture of your research participants and maintain confidentiality of their identities and shall remove or not collect any information which can be used to link the participants.

3. The Department of Health expects you to provide a progress update on your study every 3 months (from date you received this letter) in writing.

4. At the end of your study, you will be expected to send a full written report with your findings and implementable recommendations to the Eastern Cape Health Research Committee secretariat. You may also be invited to the department to come and present your research findings with your implementable recommendations.

5. Your results on the Eastern Cape will not be presented anywhere unless you have shared them with the Department of Health as indicated above.

Your compliance in this regard will be highly appreciated.

SECRETARIAT: EASTERN CAPE HEALTH RESEARCH COMMITTE

2030 NDP

TOGETHER, MOVING THE HEALTH SYSTEM FORWARD

Appendix D: Ethics approval from relevant Zimbabwe ethics committees

Telephone: 08644072773/791193
E-mail: mrcz@mrcz.org.zw
Website: http://www.mrcz.org.zw

Medical Research Council of Zimbabwe
No. 20 Cambridge Road
Avondale
Harare
Zimbabwe

CONTINUING APPROVAL

MRCZ/A/2831

26 January, 2023

Prof Z. M. Chirenje
UZ-CTRC
15 Philips Avenue
Belgravia
Harare

RE: - Advancing Early Diagnosis of Cancer in Southern Africa: AWACAN-ED Version 03 dated 12 August 2022

Thank you for the application for review of research activity that you submitted to the Medical Research Council of Zimbabwe (MRCZ). Please be advised that the Medical Research Council of Zimbabwe has **reviewed** and **approved** your application to conduct the above titled study.

This approval is based on the review and approval of the following documents that were submitted to MRCZ for review:

1. MRCZ Annual Renewal Form 102
2. Progress Report

- **APPROVAL NUMBER** : **MRCZ/A/2831**

This number should be used on all correspondence, consent forms and documents as appropriate.

- **TYPE OF MEETING** : **Expedited**
- **APPROVAL DATE** : **27 January, 2023**
- **EXPIRATION DATE** : **26 January , 2024**

After this date, this project may only commence upon renewal. For purposes of renewal, a progress report on a standard form obtainable from the MRCZ Offices should be submitted three months before the expiration date for continuing review.

- **SERIOUS ADVERSE EVENT REPORTING**: All serious problems having to do with subject safety must be reported to the Institutional Ethical Review Committee (IERC) as well as the MRCZ within 3 working days using standard forms obtainable from the MRCZ Offices or website.
- **MODIFICATIONS**: Prior MRCZ and IERC approval using standard forms obtainable from the MRCZ Offices is required before implementing any changes in the Protocol (including changes in the consent documents).
- **TERMINATION OF STUDY**: On termination of a study, a report has to be submitted to the MRCZ using standard forms obtainable from the MRCZ Offices or website.
- **QUESTIONS**: Please contact the MRCZ on Telephone No. (0242) 791193/08644073772 or by e-mail on mrcz@mrcz.org.zw

Other

- Please be reminded to send in copies of your research results for our records as well as for Health Research Database.
- You're also encouraged to submit electronic copies of your publications in peer-reviewed journals that may emanate from this study.
- **In addition to this approval, all clinical trials involving drugs, devices and biologics (including other studies focusing on registered drugs) require approval of Medicines Control Authority of Zimbabwe (MCAZ) before commencement.**

Yours Faithfully

MRCZ SECRETARIAT
FOR CHAIRPERSON
MEDICAL RESEARCH COUNCIL OF ZIMBABWE

MEDICAL RESEARCH COUNCIL OF ZIMBABWE
APPROVED
27 JAN 2023
20 CAMBRIDGE ROAD
AVONDALE, HARARE

PROMOTING THE ETHICAL CONDUCT OF HEALTH RESEARCH

UNIVERSITY OF ZIMBABWE
Faculty of Medicine
& Health Sciences

Joint Research Ethics Committee
For The University of Zimbabwe,
Faculty of Medicine and Health Sciences(FMHS) &
Parirenyatwa Group of Hospitals(PGH)

JREC Office No.4, 5th Floor, Faculty of Medicine and Health Sciences Building
Telephone: +263 242 708140/791631 Extns 2241/2242
Email: jrec.office@gmail.com - website: www.jrec.uz.ac.zw

Parirenyatwa
Group of Hospitals

RENEWAL LETTER

Date: 01 November 2022 **JREC Ref**: 363/21

Names of Researcher: Dr Bothwell T Guzha

Address: **UZ-CTRC**

RE: ADVANCING EARLY DIAGNOSIS OF CANCER IN SOUTHERN AFRICA AWACAN-ED

Thank you for your application for renewal of the authority to carry on your research project. The Joint Research Ethics Committee has granted you renewal to continue conducting the above named study.

- **APPROVAL NUMBER:** JREC/363/21 **(Renewal)**
- **APPROVAL DATE:** 22 November 2023
- **EXPIRY DATE**: 21 November 2024

After the expiry date the study may only continue upon further renewal. Renewal must be processed before the expiry date and the following documents (where applicable) must be submitted:-

a. A Completed Renewal Form (obtained from the JREC Office)
b. A Progress Report
c. Summary of adverse events
d. A DSMB Report

Appendix E: University of Cape Town Ethics approval for this study

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room 45 E-52-E-Floor- Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492
Email: hrec-submissions@uct.ac.za
Website: www.health.uct.ac.za/home/human-research-ethics

22 November 2023

HREC REF 921/2023

Dr T Phillips
Epidemiology and Biostatistics
Division of Epidemiology and Biostatistics
Email: tammy.phillips@uct.ac.za
Student: GVNSUD004@myuct.ac.za

Dear Dr Phillips

PROJECT TITLE: AWARENESS OF CERVICAL CANCER RISK FACTORS AND SYMPTOMS AND LAY BELIEFS AMONGST WOMEN RECENTLY DIAGNOSED WITH CERVICAL CANCER IN SOUTH AFRICA AND ZIMBABWE (MASTER OF PUBLIC HEALTH, SPECIALISING IN EPIDEMIOLOGY AND BIOSTATISTICS: DR SUDARSHAN GOVENDER) (SUB-STUDY: 664/2021)

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30 November 2024.

Please submit a progress form, using the standardised Annual Report Form (FHS016) or FHS017 if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

The HREC acknowledges that the following student Dr Sudarshan Govender is also involved in this study.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

Please quote HREC REF 921/2023 in all your correspondence.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FACULTY OF HEALTH SCIENCES HUMAN RESEARCH ETHICS COMMITTEE

HREC/ref 921/2023

Appendix F: Informed consent form used in the parent study

Participant study ID. number _____

Information and informed consent: AWACAN-ED PROJECT

Evaluating referral and diagnostic pathways and associated factors for people with symptoms of breast, cervical and colorectal disease: Cross-sectional survey

Research Team

South Africa

Principal Investigator (PI): Prof Jennifer Moodley (University of Cape Town)

Co-investigators: Prof John Ataguba (University of Cape Town); Dr Tasleem Ras (University of Cape Town)

Zimbabwe

Co-investigator: Prof Mike Chirenje (University of Zimbabwe)

United Kingdom

Principal Investigator (PI): Prof Fiona Walter (Queen Mary University of London)

Co-investigator: Dr Suzanne Scott (Queen Mary University of London)

Information

Introduction

Please let me introduce myself, my name is ……(name of interviewer) and I work at the University of Cape Town/ University of Zimbabwe. I am part of a research team from the Universities of Cape Town, University of Zimbabwe and Queen Mary University of London and we are talking to women and men from South Africa and Zimbabwe to understand their views on breast, cervical (also known as mouth of the womb) and colorectal symptoms.

This study will help us understand people's experience of the journey from awareness of symptoms to diagnosis. This information will be useful in designing future interventions to improve patient management.

I would like to invite you to take part in the study. If there is anything that you do not understand at any time, I will be happy to explain. Please note, your participation in this study is entirely voluntary and you are free to stop participating at any time.

If you decide to take part in this study:

- I will ask you to sign a consent form
- Interview you for about 45 minutes
- With your permission review you your clinical records
- The information collected will be stored in a secure database
- Your name will not be recorded for this study
- You can choose to skip any questions you do not want to answer

If you decide <u>not</u> to take part in this research project:

- If you decide to stop at any time or to not answer any questions or decide not to participate, the quality of the medical care you receive now, or in the future, will not be affected in any way

Let me explain the benefits of participating in this study

Your participation in this study will help us understand people's experience of the journey from awareness of symptoms to diagnosis and treatment. Your participation will not directly benefit you now, however it will assist us in designing interventions to improve patient management and could benefit other women and men in the future.

Let me explain possible risks of participating in this study

There are no direct risks involved in participating in this study. There is a slight risk that you may share some personal or private information by chance or that you may feel

uncomfortable about talking about certain things. However, we do not wish this to happen, and you may decide to not answer any question or not take part in a part of the interview if you feel the question(s) are personal or if talking about them makes you uncomfortable.

Confidentiality

The information that we collect from this research project will be kept confidential. We will not record your name for this study, instead we will assign you a study number. Your name will not be used in any of the results from this study.

Right to refuse or withdraw

You do not have to take part in this study if you do not wish to do so, and not taking part will not affect your treatment at the health facility in any way. You will still have all the benefits that you would otherwise have at this and any health facility. You may stop taking part in the interview at any time that you wish without losing any of your rights as a patient.

Additional information

If you have any questions or if anything we discussed is unclear, please let me know and I will be happy to explain now or at any time during the study.

COVID-19 considerations

We are still in the COVID-19 pandemic. I want to let you know that I have had training on infection prevention and control best practices. I will wear a face mask at all times, have used hand sanitizer, and I will be adhering to physical distancing measures. You would have had your hands sanitized before entering this health facility. If you wish I will re-sanitize your hands and I ask that you please keep your face mask on throughout the interview.

If you need more information about his study, you may contact:

South Africa
Professor Jennifer Moodley
University of Cape Town
Tel: +27 21 650 5489
Email jennifer.moodley@uct.ac.za

Zimbabwe
Dr Bothwell Guzha
University of Zimbabwe
Tel: +263772287143
Email: bothwellguzha@gmail.com

If you have any questions regarding your rights as a study participant, please contact:

South Africa

Professor M Blockman
Chairperson, Human Research Ethics Committee
University of Cape Town
Tel: +27 21 406 6338

Zimbabwe

Sr Ruzario
Medical Research Council of Zimbabwe
Corner Josiah Tongogara and Mazowe Street
Harare
Telephone: +263 24 2791792, +263 242791193
Cellphone: +263 784 956 128

Ethics approval

This research project has been granted ethical approval/clearance by the following research ethics governing bodies:

South Africa: University of Cape Town Health Research Ethics Committee (HREC) , Eastern Cape Provincial Research Ethics Committee (REC) and Walter Sisulu University REC. The research will be conducted according to the ethical guidelines and principles of the International Declaration of Helsinki (2013) and the South African Guidelines for Good Clinical Practice (2021).

Zimbabwe: Joint Research Ethics Committee of the University of Zimbabwe, Faculty of Medicine and Health Sciences and Parirenyatwa Group of Hospitals (JREC), ethics committees of Sally Mugabe and Mpilo Central Hospitals, Medical Research Council of Zimbabwe and the Research Council of Zimbabwe. The research will be conducted according to the ethical guidelines and principles of the International Declaration of Helsinki (2013).

Appendix G: Supplementary tables and figures

Table S1: Outline of how variables were collapsed

Variable	Collapsed categories	Initial categories
Age	18-34	Continuous
	35-44	
	45-54	
	>55	
Relationship status	Married or living with partner	Married
		Living with partner
	Single	Single
	Separated/divorced/widowed	Separated/divorced
		Widowed
Education	Less than secondary school	No schooling
		Primary school incomplete
		Primary school complete
		Secondary school incomplete
	Secondary school completed	Secondary school complete
		More than secondary school
Employment status	Employed	Full-time
		Part-time
		Self-employed (informal)
		Self-employed (formal)
		Casual
	Unemployed	Unemployed
		Housewife
		Pensioner
		Student/child
Living context	Rural	Rural village
		Rural farm
	Urban	Urban formal
		Urban informal
	Peri-urban	Peri-urban formal
		Peri-urban informal
Known family member or friend with cancer	Yes	Yes
	No	No
		Not sure
Known chronic diseases	Yes	Hypertension, Diabetes, Cardiac disease, HIV individually collected with Yes/No/Not sure categories
	No	
Previous cervical cancer screening	Yes	Yes
	No	No
		Not sure

Table S2: Evidence-based list of cervical cancer risk factors and symptoms [28]

Symptoms
Vaginal bleeding between menstrual periods
Persistent lower back pain
Persistent smelly vaginal discharge
Discomfort or pain during sex
Menstrual periods that are linger or heavier than usual
Vaginal bleeding after menopause
Persistent lower abdominal/pelvic pain
Vaginal bleeding during or after sex
Blood in urine or stools
Unexplained weight loss
Persistent diarrhea
Risk factors
Getting a sexually transmitted infection called the Human Papillomavirus (HPV)
HIV/AIDs
Being infected with other sexually transmitted diseases (other than HIV or HPV)
Using birth control pills/family planning for more than 5 years
Having unprotected sex
Smoking any cigarettes at all
Having a sexual partner who is not circumcised
Having sex at a young age
Giving birth to three or more children
Having many sexual partners
Not going for regular screening/testing for cervical cancer

Table S3: Cervical cancer symptom and risk factor awareness in the overall sample

	Symptom awareness		**Risk factor awareness**	
Characteristic	Symptom awareness score: Zero N = 231 n (%)	Symptom awareness score: ≥ one N = 274 n (%)	Risk factor awareness score: Zero N = 409 n (%)	Risk factor awareness score: ≥ one N = 95 n (%)
Age, (years)				
18-34	13 (5.7)	15 (5.5)	24 (5.9)	4 (4.2)
35-44	59 (25.7)	70 (25.5)	98 (24.0)	31 (32.6)
45-54	71 (30.9)	92 (33.6)	126 (30.9)	37 (38.9)
>55	87 (37.8)	97 (35.4)	160 (39.2)	23 (24.2)
Median (IQR)	50.7 (43.5-60.2)	50.3 (42.7-59.9)	51.2 (44.0-61.3)	47.4 (40.5-54.0)
Country				
South Africa	210 (90.9)	73 (26.6)	258 (63.1)	25 (26.3)
Zimbabwe	21 (9.1)	201 (73.4)	151 (36.9)	70 (73.7)
Relationship				
Married/living with partner	77 (33.3)	116 (42.5)	144 (35.3)	48 (50.5)

Single	76 (32.9)	42 (15.4)	104 (25.5)	14 (14.7)
Separated/divorced/widowed	78 (33.8)	115 (42.1)	160 (39.2)	33 (34.7)
Education				
Less than secondary school	202 (87.4)	182 (66.4)	329 (80.4)	54 (56.8)
Secondary school complete	29 (12.6)	92 (33.6)	80 (19.6)	41 (43.2)
Employment status				
Unemployed	173 (74.9)	194 (70.8)	313 (76.5)	54 (56.8)
Employed	58 (25.1)	80 (29.2)	96 (23.5)	41 (43.2)
Living context				
Rural	136 (58.9)	107 (39.1)	211 (51.6)	31 (32.6)
Urban	80 (34.6)	140 (51.1)	167 (40.8)	53 (55.8)
Peri-urban	15 (6.5)	27 (9.9)	31 (7.6)	11 (11.6)
Wealth index				
1st quintile (poorest)	34 (14.8)	83 (30.5)	98 (24.1)	19 (20.0)
2nd quintile	56 (24.3)	32 (11.8)	76 (18.7)	11 (11.6)
3rd quintile (middle)	63 (27.4)	38 (14.0)	87 (21.4)	14 (14.7)
4th quintile	47 (20.4)	72 (26.5)	91 (22.4)	28 (29.5)
5th quintile (richest)	30 (13.0)	47 (17.3)	54 (13.3)	23 (24.2)
Known family member or friend with cancer				
No	169 (73.2)	165 (60.2)	276 (67.5)	57 (60.0)
Yes	62 (26.8)	109 (39.8)	133 (32.5)	38 (40.0)
Known hypertension				
No	148 (64.3)	176 (64.2)	255 (62.5)	69 (72.6)
Yes	82 (35.7)	98 (35.8)	153 (37.5)	26 (27.4)
Known diabetes				
No	208 (90.8)	259 (94.5)	374 (91.9)	92 (96.8)
Yes	21 (9.2)	15 (5.5)	33 (8.1)	3 (3.2)
Known cardiac disease				
No	219 (94.8)	265 (96.7)	390 (95.4)	93 (97.9)
Yes	12 (5.2)	9 (3.3)	19 (4.6)	2 (2.1)
Known HIV				
No	104 (45.0)	126 (46.0)	195 (47.7)	34 (35.8)
Yes	127 (55.0)	148 (54.0)	214 (52.3)	61 (64.2)
Any chronic disease*				
No	47 (20.6)	65 (23.7)	87 (21.4)	25 (26.3)
Yes	181 (79.4)	209 (76.3)	319 (78.6)	70 (73.7)
Known previous cervical cancer screening				
No	20 (8.7)	46 (16.8)	56 (13.7)	10 (10.6)
Yes	211 (91.3)	227 (83.2)	353 (86.3)	84 (89.4)
Risk factor awareness				
No	222 (96.1)	187 (68.5)		
Yes	9 (3.9)	86 (31.5)		
Symptom awareness				
No			222 (54.3)	9 (9.5)
Yes			187 (45.7)	86 (90.5)

IQR - interquartile range
*Chronic disease include: Hypertension, diabetes, HIV, cardiac disease

Table S4: Cervical cancer symptoms, risk factors and lay beliefs mentioned by women in this study

	Overall N = 506 n (%)	South Africa N = 284 n (%)	Zimbabwe N = 222 n (%)
Symptoms			
Intermenstrual bleeding	21 (4.16)	2 (0.71)	19 (8.56)
Lower back pain	41 (8.1)	3 (1.1)	38 (17.1)
Smelly vaginal discharge	60 (11.9)	11 (3.9)	49 (22.1)
Generalized vaginal discharge	71 (14.1)	14 (4.9)	57 (25.7)
Discomfort/pain during sex	9 (1.8)	2 (0.7)	7 (3.2)
Longer or heavier menstrual periods	6 (1.2)	3 (1.1)	3 (1.4)
Post-menopausal bleeding	34 (6.7)	2 (0.7)	32 (14.4)
Lower abdominal/pelvic pain	94 (18.6)	25 (8.8)	69 (31.1)
Vaginal bleeding during or after sex	13 (2.6)	6 (2.1)	7 (3.2)
Unexplained weight loss	6 (1.2)	2 (0.7)	4 (1.8)
Blood in urine or stool	1 (0.2)	0 (0.0)	1 (0.5)
Generalized vaginal bleeding	150 (29.7)	47 (16.6)	103 (46.4)
Vaginal pain	6 (1.2)	5 (1.8)	1 (0.5)
Risk factors			
HPV infection	4 (0.8)	2 (0.7)	2 (0.9)
HIV/AIDs	17 (3.4)	1 (0.4)	16 (7.2)
Sexually transmitted diseases	11 (2.2)	1 (0.4)	10 (4.5)
Birth control longer than 5 years	3 (0.6)	2 (0.7)	1 (0.5)
Unprotected sex	19 (3.8)	5 (1.8)	14 (6.3)
Smoking cigarettes	13 (2.6)	13 (4.6)	0 (0.0)
Sexual onset at a young age	3 (0.6)	1 (0.4)	2 (0.9)
Many sexual partners	31 (6.2)	4 (1.4)	27 (12.2)
Not going for regular screening	7 (1.4)	5 (1.8)	2 (0.9)
Sexual partner with many partners	11 (2.2)	0 (0.0)	11 (5.0)
Lay beliefs			
Family history	14 (2.78)	4 (1.4)	10 (4.5)
Menopause	5 (1.0)	0 (0.0)	5 (2.3)
ARVs	3 (0.6)	0 (0.0)	3 (1.4)
Stress	3 (0.6)	0 (0.0)	3 (1.4)
Inserting herbs, creams, or objects into vagina	44 (8.7)	0 (0.0)	44 (19.9)
Poor personal hygiene	4 (0.8)	2 (0.7)	2 (0.9)
Witchcraft/bewitched/evil spirits	13 (2.6)	0 (0.0)	13 (5.9)
Lifestyle related	9 (1.8)	6 (2.1)	3 (1.4)
Soap/lotion	4 (0.8)	0 (0.0)	4 (1.8)
Other	15 (3.0)	2 (0.7)	13 (5.9)
At least one risk lay belief	90 (17.9)	12 (4.2)	78 (35.3)

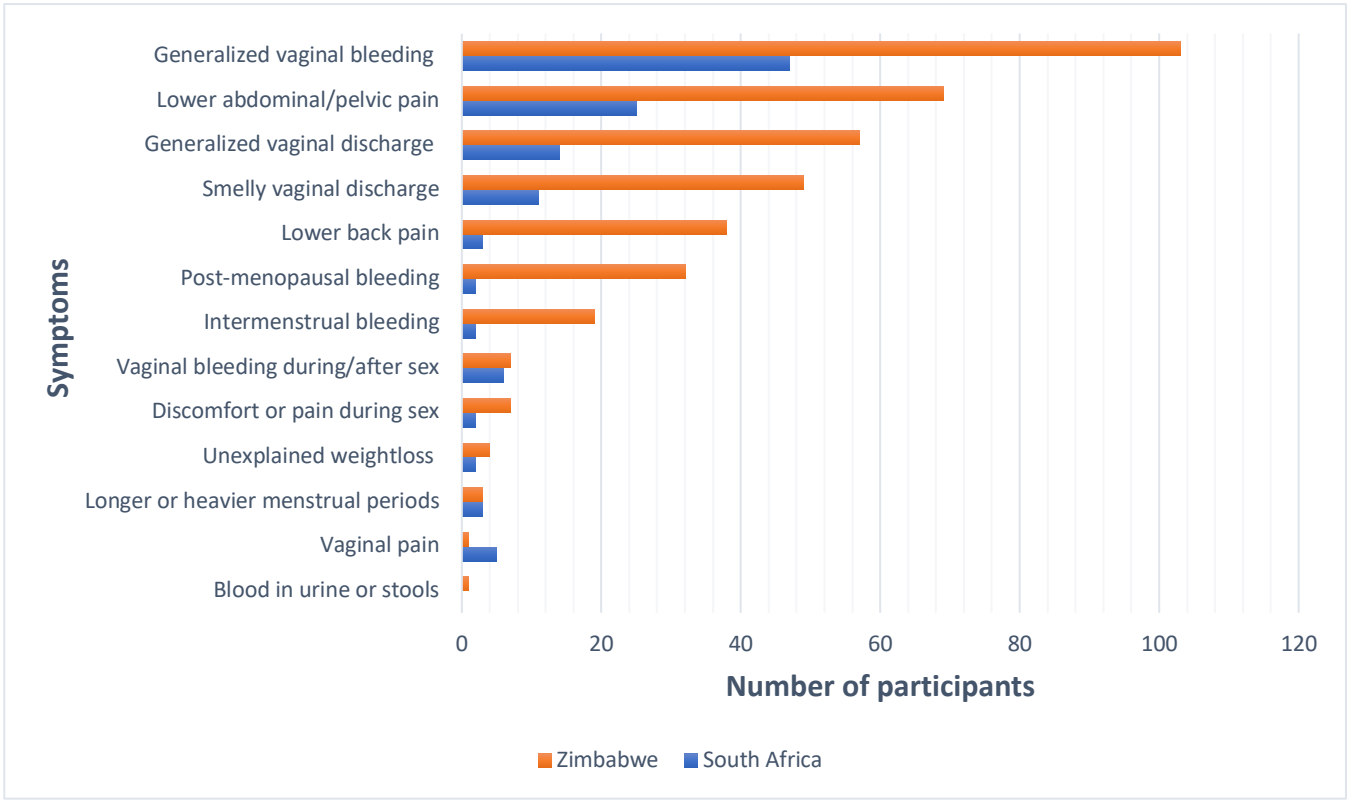

Figure S1: Bar chart showing cervical cancer symptom awareness stratified by country

Table S5: Univariate regression analysis of symptom awareness for each country

	South Africa	Zimbabwe
Characteristics	Crude OR (95% CI)	Crude OR (95% CI)
Age, (years)		
18-34	Ref	Ref
35-44	0.75 (0.28; 2.12)	0.90 (0.04; 6.27)
45-54	0.45 (0.16; 1.30)	2.06 (0.10; 15.42)
>55	0.36 (0.13; 1.03)	1.39 (0.07; 9.38)
Relationship		
Married/living with partner	Ref	Ref
Single	0.85 (0.46; 1.56)	1.66 (0.29; 31.65)
Separated/divorced/widowed	0.45 (0.21; 0.90)	1.44 (0.57; 3.72)
Education		
Less than secondary school	Ref	Ref
Secondary school complete	**4.04 (2.12; 7.73)**	1.60 (0.60; 5.06)
Employment		
Unemployed	Ref	Ref
Employed	1.10 (0.59; 2.00)	0.87 (0.34; 2.40)
Wealth index		
1st quintile (poorest)	Ref	Ref
2nd quintile	0.86 (0.26; 3.08)	0.46 (0.12; 1.93)
3rd quintile (middle)	1.26 (0.44; 4.22)	1.85 (0.29; 35.78)
4th quintile	**3.41 (1.24; 11.07)**	0.60 (0.18; 2.03)
5th quintile	**4.52 (1.58; 15.14)**	0.50 (0.13; 2.08)

Living context		
Rural	Ref	Ref
Urban	**4.09 (2.21; 7.82)**	0.92 (0.36; 2.32)
Peri-urban	**7.56 (3.15; 18.54)**	1.21 (0.20; 23.37)
Known family member or friend with cancer		
No	Ref	Ref
Yes	**3.18 (1.84; 5.54)**	2.22 (0.79; 7.95)
Known previous TB		
No	Ref	Ref
Yes	0.96 (0.53; 1.69)	1.54 (0.41; 9.98)
Known hypertension		
No	Ref	Ref
Yes	1.08 (0.61; 1.87)	0.51 (0.20; 1.26)
Known diabetes		
No	Ref	Ref
Yes	1.32 (0.55; 2.97)	0.62 (0.10; 11.93)
Known cardiac disease		
No	Ref	Ref
Yes	1.21 (0.37; 3.40)	Too wide
Known HIV		
No	Ref	Ref
Yes	0.73 (0.43; 1.25)	0.81 (0.31; 2.00)
Any chronic disease*		
No	Ref	Ref
Yes	0.61 (0.33; 1.12)	0.86 (0.24; 2.48)
Known previous screening cervical cancer		
No	Ref	Ref
Yes	0.86 (0.33; 2.49)	1.25 (0.39; 3.41)

OR – Odds ratio

CI – confidence interval

*Chronic disease include: Hypertension, diabetes, HIV, cardiac disease

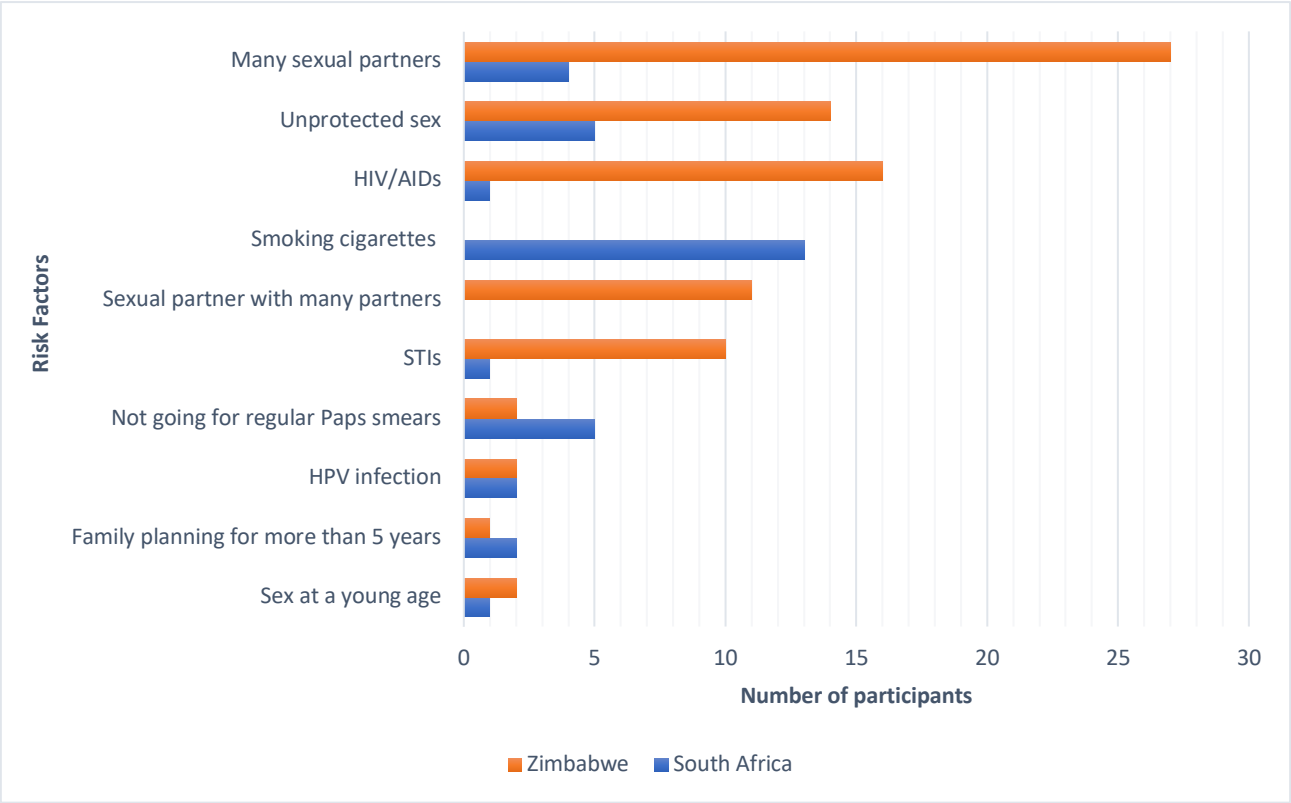

Figure S2: Bar chart showing cervical cancer risk factor awareness stratified by country

Table S6: Univariate regression analysis of risk factor awareness in each country

	South Africa Crude OR (95% CI)	Zimbabwe Crude OR (95% CI)
Characteristic		
Age, (years)		
18-34	Ref	Ref
35-44	1.32 (0.31; 9.11)	2.10 (0.43; 15.30)
45-54	0.92 (0.21; 6.46)	1.81 (0.39; 12.93)
>55	0.48 (0.10; 3.56)	0.81 (0.17; 5.82)
Relationship		
Married/living with partner	Ref	Ref
Single	0.58 (0.22; 1.48)	1.25 (0.38; 3.88)
Separated/divorced/widowed	0.45 (0.14; 1.27)	0.57 (0.31; 1.03)
Education		
Less than secondary school	Ref	Ref
Secondary school completed	**4.55 (1.89; 10.76)**	**1.95 (1.07; 3.52)**
Employment		
Unemployed	Ref	Ref
Employed	1.82 (0.74; 4.24)	**2.79 (1.53; 5.13)**
Wealth index		
1st quintile (poorest)	Ref	Ref
2nd quintile	1.10 (0.10; 24.29)	1.83 (0.69; 4.72)
3rd quintile (middle)	2.74 (0.44; 52.93)	1.73 (0.62; 4.57)

4th quintile	3.20 (0.52; 61.83)	**2.60 (1.23; 5.60)**
5th quintile (richest)	**8.65 (1.53; 163.07)**	**2.80 (1.15; 6.88)**
Living context		
Rural	Ref	Ref
Urban	**3.14 (1.20; 9.20)**	1.62 (0.90; 2.97)
Peri-urban	**6.04 (1.75; 20.94)**	1.80 (0.50; 5.92)
Known family member or friend with cancer		
No	Ref	Ref
Yes	1.29 (0.54; 2.96)	1.57 (0.87; 2.84)
Known previous TB		
No	Ref	Ref
Yes	0.53 (0.17; 1.37)	1.53 (0.68; 3.35)
Known hypertension		
No	Ref	Ref
Yes	0.34 (0.10; 0.91)	0.70 (0.38; 1.26)
Known diabetes		
No	Ref	Ref
Yes	0.34 (0.02; 1.71)	0.86 (0.12; 4.10)
Known HIV		
No	Ref	Ref
Yes	0.48 (0.20; 1.11)	**2.93 (1.59; 5.57)**
Any chronic disease*		
No	Ref	Ref
Yes	0.16 (0.07; 0.38)	1.95 (0.94; 4.38)
Known previous cervical cancer screening		
No	Ref	Ref
Yes	0.91 (0.24; 5.96)	**2.47 (1.13; 6.02)**

OR – Odds ratio
CI – confidence interval
*Chronic disease include: Hypertension, diabetes, HIV, cardiac disease

Appendix H: Author Guidelines for submission to ecancermedicalscience journal

Article Information

Article Types

PLEASE NOTE, ECANCER NO LONGER CONSIDERS CASE REPORTS OR CONFERENCE REPORTS

Upon submission, authors will be asked to identify the type of article. *e*cancermedicalscience accepts the following:

- **Research Papers -** Research articles have no page or word limit and may be in the areas of laboratory science, epidemiology, translational medicine, clinical trial reports (with positive or negative results) or nursing research. The methods section needs to prove that experiments carried out were appropriate to test the hypothesis. The conclusions must reflect whether or not the hypothesis is correct.
- **Policy Papers -***e*cancermedicalscience is keen to attract Policy papers from individuals, learned societies, charities, advocacy groups or government agencies. They should be looked on as 'Green Papers' which, with the benefit of wide consultation through the journal, may develop into 'White Papers'.
- **Short Communication -** A short communication is a concise but independent report representing a significant contribution to cancer understanding. To be considered for publication a short communication should present results which are of exceptional interest and are particularly topical and relevant. It should be no more than 4,000 words, however there is no restriction on figures, tables or video content. Short communications may include descriptions of training, of research tools, of novel techniques or presentations of preliminary results such as conference posters. *e*cancermedicalscience will respect conference embargoes.
- **Review Article -** While the majority of our review articles will be commissioned, *e*cancermedicalscience is willing to consider unsolicited reviews in “niche" areas, and will be subject to full peer review. ecancermedicalscience is willing to consider mini-reviews of 4-5 pages in length, or full reviews, which can be up to 20 pages in length. Review articles should cover recent advances and, where appropriate, discuss up-to-date techniques.
- **Clinical Study** - This is a study of a new medical treatment or medicine using human volunteers. ecancermedicalscience supports the guidelines set forth by the International Committee on Medical Journal editors (http://www.icmje.org/index.html) and encourages clinical trials to be registered prior to submission in a suitable publicly accessible registry.
- **Editorials** - Editorials are predominately commissioned by the *e*cancer staff. They should be around 1,000 words and should contain references where appropriate. An abstract and conclusion section must also be

added. Like the other articles published by *e*cancer, editorials will be subject to peer review.

- **Errata** - Should an author discover an error in their previously published ecancer article, they should submit an erratum as soon as possible. This should contain the article title, authors and affiliations and the nature of the error. It should be submitted as normal and the Editor will deem its suitability for publication. Any questions should be directed to the Journal team.

Article Formats
The main manuscript should be submitted as a Microsoft Word document.

*e*cancermedicalscience encourages the submission of movie clips with or without audio facility, to illustrate complicated surgery or new technologies. We especially welcome case studies that are animation and video based.

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Layout of Manuscript

Article Classifications Upon submission authors will be asked to assign appropriate article classifications for their article, a list of which can be found at the bottom of every page on the *e*cancer site. Please tick all that apply.

Manuscript Sections

Where appropriate, articles should be broken down into the below sections. Please note that all articles should include a title page, abstract, keywords, conclusions and references.

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- **Title page**
- **Abstract**
- **Keywords**
- Background/Introduction
- Methods
- Results
- Discussion
- **Conclusions**
- List of abbreviations used (if any)
- Conflicts of interest
- Acknowledgments
- **References**
- Figure legends (if any)

- Tables and captions (if any)

Please note that sections in **bold** are required for all submissions, regardless of the type of manuscript. More information on the requirements for each section of your manuscript is provided below.

Title page
The full names and institutional addresses for all authors must be included on the title page. ORCID ids should also be included (if known). The corresponding author should also be indicated and the email address for this person should be provided.

All authors should have given final approval of the version to be published. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content.

All contributors who do not meet the criteria for authorship should be listed in an acknowledgements section. Further information about authorship criteria can be found on the International Committee of Medical Journal Editors website. Further information on our authorship policies can be found here.

Abstract
Abstracts should be a maximum of 300 words. Please note that all articles should include an abstract.

The abstract should clearly and concisely convey the conceptual advance and significance of the work to a broad readership. In particular, the abstract should contain a brief background of the question, a description of the results without extensive experimental detail, and a summary of the significance of the findings. Ideally the abstract will be one or two paragraphs and not broken down into sections.

Our electronic submission system will ask you to copy and paste this section at the "Submit Abstract" stage.

Keywords

Appropriate keywords should be provided for all submissions to *e*cancermedicalscience. The keywords should comply with the MeSH terms (http://www.nlm.nih.gov/mesh/). If you need help selecting the keywords, this service http://ii.nlm.nih.gov/Interactive/MeSHonDemand.shtml provides MeSH keywords for your text.

Background/Introduction
The background section should be written from the standpoint of researchers without specialist knowledge in that area and must clearly state the background to the research and its aims. Reports of clinical research should, where appropriate, include a summary of a search of the literature to indicate why this study was necessary and what it aimed to contribute to the field. The section should end with a very brief statement of what is being reported in the article.

Methods
This should include the design of the study, the setting, the type of participants or materials involved, a clear description of all interventions and comparisons, and the type of analysis used, including a power calculation if appropriate.

Results and Discussion
The results and discussion may be combined into a single section or presented separately. Results of statistical analysis should include, where appropriate, relative and absolute risks or risk reductions, and confidence intervals.

Please note: at any time up to five years after publication of research in the journal, authors may be asked to provide the raw data.

Conclusions
This should state clearly the main conclusions of the research and give a clear explanation of their importance and relevance. Summary illustrations may be included.

List of abbreviations
If abbreviations are used in the text they should either be defined in the text where first used, or a list should be provided.

Conflicts of interest
A conflict of interest exists when your interpretation of data or presentation of information may be influenced by your personal or financial relationship with other people or organisations. Authors should disclose any competing interests, (financial or otherwise) that may cause them embarrassment were they to become public after the publication of the manuscript.

Authors are required to declare all conflicts of interests, which will be listed at the end of published articles. Where an author declares no conflict of interest, the listing will read: "The author(s) declare that they have no conflict of interest."

When completing your declaration, please consider the following questions:

Financial conflict of interest
Please declare relationships with any organisation that might gain or lose financially from publication of the paper including:

- Research support or employment (including salaries, equipment, supplies, reimbursement for attending symposia, and other expenses) during the past two years, currently or pending.
- Any stocks or shares; and other interests, such as consultation fees or other remuneration.
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Non-financial conflict of interest
Are there any non-financial competing interests (political, personal, religious,

ideological, academic, intellectual, commercial or any other) to declare in relation to this manuscript? If so, please specify.

If you are unsure as to whether you, or one your co-authors, has a competing interest please state the conflict and the editorial team can review it.

Disclosure of results at a meeting
Presentation of data at a scientific meeting, as a poster, abstract, orally, on a CD, or as an abstract on the web, has no conflict with submission to *e*cancermedicalscience. However, divulging results in other circumstances (eg, investors' meetings) is discouraged and may jeopardise consideration of the manuscript.

Institutional review
Submission of a manuscript to ecancermedicalscience implies that all authors have read and agreed to its content - and that any experimental research that is reported in the manuscript has been performed with the approval of an appropriate ethics committee. Research carried out on humans must be in compliance with the Helsinki Declaration.

Any experimental research on animals must follow internationally recognised guidelines. Papers disregarding the welfare of experimental animals will be rejected. A statement to this effect must appear in the Methods section of the manuscript, including the name of the body which gave approval, with a reference number where appropriate. Informed consent must also be documented. Manuscripts may be rejected if the editorial office considers that the research has not been carried out within an ethical framework, e.g. if the severity of the experimental procedure is not justified by the value of the knowledge gained.

Authors may find the National Centre for the Replacement Refinement and Reduction of Animals in Research (NC3Rs) latest report “Animal Research: Reporting of In Vivo Experiments” or the United Kingdom's Co-ordinating Committee on Cancer Research (UKCCCR) 'Guidelines for the welfare and use of animals in cancer research' helpful, published in the British Journal of Cancer (2010) 102 1555-1557.

Acknowledgements
Please acknowledge anyone who contributed substantially towards the study but who does not meet the criteria for authorship. Please also include source(s) of funding. Authors must describe the role of the funding body, if any, in study design; in the collection, analysis, and interpretation of data; in the writing of the manuscript; and in the decision to submit the manuscript for publication.

The role of a medical writer must be included in the acknowledgements section, including their source(s) of funding.

References
All references should be from scientific and indexed sources.

All references must be numbered consecutively, in square brackets, in the order in which they are cited in the text. Reference citations should not appear in titles or headings.

Only articles and abstracts that have been published or are in press may be cited; unpublished work and personal communications do not need to be included in the reference list, but may be included in the text. Obtaining permission to quote personal communications and unpublished data from the cited author(s) is the responsibility of the author. Journal abbreviations follow Index Medicus/MEDLINE http://www2.bg.am.poznan.pl/czasopisma/medicus.php?lang=eng. Citations in the reference list should contain all named authors, regardless of how many there are.

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*e*cancermedicalscience Reference Style

*e*cancermedicalscience uses the Vancouver reference format.

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- Figure number (in sequence, using Arabic numerals— i.e. Figure 1, 2, 3 etc)
- short title of figure (maximum 15 words)

In order to keep the size of the final manuscript file manageable, authors may use lower resolution images within the text. However, high resolution images (minimum 300dpi) should also be provided as separate files. These may be uploaded when you are requested to 'upload images'. Each figure should include a single illustration. Colour figures are accepted. File size should not exceed 5MB.

Please note that it is the responsibility of the author(s) to obtain permission from the copyright holder to reproduce figures or tables that have previously been published elsewhere.

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All tables must be cell-based, similar to that produced in a spreadsheet. Acceptable program file types are .doc, .csv and .xls (not .pdf).

Tables should have a caption that summarizes what is shown, maximum 15 words.

Larger datasets can be uploaded separately as additional files. Additional files will not be displayed in the final published PDF of the article, but will appear as supplementary data alongside the article.

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Image conversion tools
There are many software packages, capable of converting to and from different graphics formats, including PNG.

Good general tools for image conversion include PaintShop Pro, Photoshop or Paint for Windows, and ImageMagick, which is available on Macintosh, Windows and UNIX platforms.

e illustration
Photographs should be provided with a scale bar if appropriate. If photographs of patients' body parts, X-rays or scans are given as part of the manuscript, written and signed consent of the patient should be collected using the patient consent form. Please fill in this form and submit it when it is requested during the article submission process.

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*e*cancermedicalscience encourages the submission of movie clips with or without audio facility, to illustrate complicated surgery or new technologies. We especially welcome case studies that are animation and video based.

The journal also accepts self-filmed author interviews - these will be assessed for editorial suitability and quality before acceptance.

If you wish to submit video or animation files, please contact us at editor@ecancer.org for more information

*e*cancermedicalscience accepts video and motion graphics in the following formats:

- .mpeg
- .mp4
- .flv
- .mov
- .avi

- .wmv
- .fla
- .swf

And many more.

Ideally videos should be unprocessed and in their largest, most original format. Video motion clips should be submitted with a title of a maximum of 15 words that summarizes the whole clip. They can be submitted by post or FTP.

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  We encourage authors to deposit copies of their plasmids as DNA or bacterial stocks with Addgene, a non-profit repository, or PlasmID, the Plasmid Information Database at Harvard.
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- **Structures**
  Protein structures can be deposited with one of the members of the Worldwide Protein Data Bank. Nucleic Acids structures can be deposited with the Nucleic Acid Database at Rutgers. Crystal structures of organic compounds can be deposited with the Cambridge Crystallographic Data Centre.

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