

Leveraging implementation science for secondary prevention of cervical cancer in South Africa

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<https://doi.org/10.61473/001c.120636>

South African Health Review

Vol. 26, 2023

Aim

Cervical cancer is the second most common cancer and the top cause of cancer deaths amongst women in South Africa. Evidence-based interventions for secondary prevention of cervical cancer (cervical screening followed by treatment of identified pre-cancerous lesions) are available in South Africa's health system, yet cervical cancer incidence remains high. This paper argues that this is partly due to implementation failure, i.e., deploying a good intervention ineffectively. Interventions found efficacious in controlled research settings may not achieve desired health outcomes when deployed in the real world due to implementation failure.

Methods

The field of implementation science offers frameworks for enhancing effective implementation. These frameworks guide the identification of implementation barriers and selection of context-relevant strategies for addressing them. This paper applies implementation science frameworks to secondary prevention in South Africa and promotes using such frameworks in cervical cancer prevention programming.

Findings

The problem of secondary prevention of cervical cancer in South Africa is contextualised. The paper conceptualises effective implementation as the attainment of implementation outcomes including acceptability, adoption, appropriateness, feasibility, fidelity, implementation cost, reach, and sustainability of evidence-based interventions. Drawing from the South African literature, examples of ineffective and failed implementation of secondary prevention interventions are presented including: low acceptability of screening by users and providers, sub-optimal adoption of screening provision by providers, low feasibility of hospital-centred pre-cancer treatment provision, low implementation fidelity, and limited reach of screening and pre-cancer treatment. Finally, using two examples, the paper provides practical guidance on how implementation science frameworks could be leveraged in South Africa to mitigate implementation failure.

Conclusions

Greater application of and capacity building in implementation science are recommended to contribute towards strengthening cervical cancer secondary prevention in South Africa.

Introduction

Background

Cervical cancer is a preventable public health problem affecting women in the prime of their lives, causing premature deaths and detrimental effects on their families and communities. Globally, in 2022, it was the fourth most common cancer (661 021 new cases; 6.8% of female

cancers) and the fourth top cause of cancer deaths in women (348 189 deaths; 7.1 deaths per 100 000 women; 8.1% of female cancer deaths).¹ In terms of age-standardised incidence (ASIR), eastern and southern Africa had the highest rates at 40.4 and 34.9 per 100 000 women, respectively, compared to less than 10 per 100 000 women in most of Europe.¹ The global ASIR in 2022 was 14.1 per 100 000 women.¹ In South Africa (SA), cervical cancer is the second most common cancer and

the top cause of cancer deaths among women.² In 2022, SA reported 7499 new cases of cervical cancer with an ASIR of 23 per 100 000 women (26.1 and 18.9 per 100 000 in black and white women, respectively).²

Cervical cancer is caused by persistent human papillomavirus (HPV) cervical infection, particularly by high-risk subtypes 16 and 18.³ Most persistent high-risk HPV infections progress to high-grade squamous intraepithelial lesions (HSIL), a significant proportion of which progress to invasive cancer over years. Women living with HIV (WLHIV) have a higher risk of cervical cancer development and progression than HIV negative women globally⁴ and in SA.⁵

Effective tools for reducing cervical cancer are available, including: a) primary prevention - HPV vaccines protect against high-risk HPV sub-types⁶ b) secondary prevention - screening to detect HSIL (pre-cancer) followed by pre-cancer treatment⁷; and c) tertiary prevention - early diagnosis and treatment of invasive cervical cancer.

Secondary prevention evidence-based interventions (EBIs) recommended by the World Health Organization (WHO) include⁸:

- *Cervical screening EBIs*: cytology - Pap smear and liquid-based cytology (LBC), HPV testing, and visual inspection with acetic acid (VIA). HPV DNA testing is the WHO's preferred primary screening method in low-resource settings as it is cost-effective and feasible in low- and middle-income countries (LMICs).⁹ For WLHIV, the WHO recommends HPV DNA testing and triage with a second screening test for positive HPV DNA tests.⁸
- *Pre-cancer treatment EBIs*: a) excision methods - cold knife conisation and large loop excision of the transformation zone (LLETZ); and b) ablative methods - cryotherapy and thermal ablation - all with proven effectiveness and feasibility in LMICs.¹⁰

In 2020, the WHO launched a global strategy to accelerate the elimination of cervical cancer as a public health problem.¹¹ Regarding secondary prevention, the strategy aims to screen 70% of women and treat 90% of women with pre-cancer by 2030.¹¹ These are ambitious targets, as in 2019, fewer than 40% of low-income nations had a national screening programme, compared to 80% in high-income countries (HICs),¹² and 84% of women aged 30-49 in HICs had been screened compared to only 11% in low-income countries.¹³

The cervical cancer secondary prevention challenge in South Africa

South Africa endorsed the WHO elimination strategy, but a high coverage of available secondary prevention EBIs remains elusive despite an enabling policy.

The 2000 National Guideline on Cervical Cancer Screening provided for every woman to receive three free Pap smears in the public sector every ten years, starting at the age of 30.¹⁴ The 2017 National Department of Health Cervical Cancer Prevention and Control Policy introduced three-yearly screening for HIV positive

women, starting from HIV diagnosis.¹⁵ Women typically screen at primary care clinics and, as per the 2017 policy, those found with HSIL must receive pre-cancer treatment using ablative or excisional methods.¹⁵

The 2000 policy aimed to screen 70% of women 30 years or older by 2010.¹⁴ The 2017 policy aimed to increase, by 2030, the proportion of 30-55-year-old women who are screened at least once and the proportion of women with HSIL who are treated for pre-cancer (no coverage goal specified).¹⁵

The promise of secondary prevention is unrealised as cervical cancer ASIR remains persistently high.¹⁶

- The national screening coverage reached 65% in 2019 but was revised to 47% to account for three-yearly screening of WLHIV.¹⁷
- The pre-cancer treatment coverage is also sub-optimal; a recent analysis shows only 16% of women with HSIL receive pre-cancer treatment.¹⁸

The HIV burden partly accounts for this sub-optimal performance.⁵ Health system challenges also contribute, i.e., historical health system fragmentation,¹⁹ inadequate stewardship,²⁰ and insufficient investment in health system inputs (funding, human and material resources, equipment),²¹ and management capacity.²²

Implementation failure (deploying a good intervention badly or ineffectively)²³ also contributes. Having an EBI is only the first step; the EBIs must be implemented effectively to improve health.²⁴ Implementation refers to deploying an intervention that was efficacious in controlled research settings in real-world service delivery settings. In SA, where making EBIs available is prioritised over implementing them,²⁵ implementation must be considered.

As SA decision-makers plan towards cervical cancer elimination, this is an opportune time to consider how to implement secondary prevention EBIs effectively in the SA context. This paper proposes implementation science (IS) to add to the existing toolkit for cervical cancer prevention in SA. Implementation science is:

the scientific study of methods to promote the systematic uptake of research findings and other evidence-based practices into routine practice, and, hence, to improve the quality and effectiveness of health services.^{26(p3)}

It is a multi-disciplinary field increasingly used in HICs, but less so in sub-Saharan Africa (SSA). Calls to leverage IS for cancer prevention have been made²⁷ and are applicable to policy makers, programme managers, health workers, researchers, and health research funders, amongst others. This paper presents findings on secondary prevention implementation failure in SA and discusses how IS could be leveraged to mitigate this. The focus is cervical cytology and LLETZ because these EBIs are currently implemented in the SA public sector.

Table 1. Implementation outcomes used to describe implementation failure

Implementation outcomes ²⁸	Operational definitions used
Acceptability	Health providers' / women's perception that cytology / LLETZ is agreeable.
Adoption	Individual provider or user's decision or action to try / use cytology / LLETZ.
Appropriateness	Perceived fit of cytology / LLETZ for SA context or secondary prevention.
Feasibility	Actual fit – whether cytology / LLETZ deployment is practicable for SA setting.
Fidelity	The extent to which cytology / LLETZ is used as intended by the programme (adherence to programme design or quality of delivery).
Cost	The incremental or implementation cost of deploying cytology / LLETZ.
Penetration or reach	Proportion of eligible women reached by cervical cytology or LLETZ.
Sustainability	The degree to which cytology / LLETZ is maintained in ongoing operations.

Box 1. IS frameworks and models commonly used to enhance implementation of EBIs

EPIS phases of implementation³⁰ • Exploration: Determine health need. Select and decide to adopt the best EBI(s) for the need. • Preparation: Identify potential implementation barriers, formulate strategies to address them. • Implementation: Deploy EBI and strategies to enable fidelity, reach. • Sustainment: Ensure continued use of EBI, address hindering factors.	CFIR for exploring determinants of implementation effectiveness³² Comprises 39 constructs grouped in five domains: • Innovation characteristics: e.g., EBI complexity, adaptability. • Individual characteristics: e.g., provider self-efficacy, beliefs. • Inner context (within organisation): e.g., resources, leadership. • Outer context: e.g., community resources, external policy. • Implementation process: mechanisms to support process.
ERIC: strategies for addressing implementation determinants³⁷ Consists of 73 consensus strategies categorised as follows based on the kind of barriers to be addressed: • Use evaluative and iterative strategies. • Provide interactive assistance. • Adapt and tailor to context. • Develop stakeholder interrelationships. • Train and educate stakeholders. • Support clinicians. • Engage consumers. • Utilise financial strategies. • Change infrastructure.	RE-AIM for evaluating implementation effectiveness³⁸ Considers five factors: • Reach: % of target group participating in EBI. • Efficacy: % individuals implementing as per guidelines. • Adoption: % organisations adopting the EBI. • Implementation: % organisations implementing as per guidelines. • Maintenance: Extent to which EBI implementation is sustained over time.

gies for the same EBI.³⁶ The ERIC compilation (Box 1) provides a list of evidence-based strategies.³⁷ Though based largely on HIC experiences, it is a useful resource for implementers.

Frameworks for evaluating implementation effectiveness

Evaluation frameworks assess whether an implementation strategy has improved implementation effectiveness.²⁹ For example, the RE-AIM framework (Box 1),³⁸ has been used to evaluate HPV DNA self-collection in African settings.³⁹ EPIS, CFIR, and Proctor's IO frameworks are also useful for evaluating implementation effectiveness.²⁹

Findings

Secondary prevention implementation failure in SA

The SA literature revealed indicators of implementation failure regarding acceptability, adoption, feasibility, fidelity, and reach (Table 2).

Acceptability

- Low user and provider acceptance of screening was reported during early (2-3 years after 2000 pol-

Table 2. Indications of secondary prevention implementation failure in SA

Implementation outcome	Examples of implementation failure
Acceptability ⁴⁰⁻⁴⁵	• Providers: unwilling, disagreed with policy, felt that screening deterred them from 'pushing queues'. • Users: did not accept long wait time, unsupportive provider interactions, perceived link to HIV test, uncomfortable pelvic exam, male providers.
Adoption by providers ^{40,46}	• Too few providers started providing screening soon after the policy, with little change several years later.
Feasibility ⁴⁷	• Hospital-based LLETZ services not a good fit for the SA context.
Fidelity ^{44,48-53}	• Sub-optimal smear adequacy rates across SA (poor quality of delivery). • Performing fewer than the required screens. • Poor adherence (fidelity) to guidelines on timing and frequency of screening WLHIV and women in the general population.
Reach ^{18,54-56}	• Too few eligible women reached with cervical cytology and with LLETZ.

icy),⁴⁰ ongoing,⁴¹⁻⁴⁴ and late⁴⁵ phases of implementation.

- Providers' non-acceptance of the 10-yearly screening policy hampered their adoption of screening.⁴⁰

Adoption

Few providers performed screening in the early (35% in three districts)⁴⁰ and on-going (28% at E. Cape hospital)⁴⁶ phases of implementation.

Feasibility

- LLETZ provision was largely centralised at tertiary hospitals, performed by specialist doctors⁴⁷ (a scarce resource in SA), resulting in long wait times between screening and LLETZ services.¹⁸
- The complex service provision and referral model required five separate health facility visits between screening and LLETZ, resulting in high attrition.^{18,47}

Fidelity

- Lower Pap smear adequacy rates than the required quality of delivery (programme target 70% or higher)^{48,49} occurred. One study found a median of 47% across all SA districts, and all but six districts were below 70% (lowest 29%).⁴⁸
- In a KZN municipality, 72% of health providers performed screens but at less than the number required by programme guidelines (despite available resources).⁵⁰
- Low provider adherence (fidelity) to screening guidelines. According to guidelines, all WLHIV should be screened three-yearly starting from HIV diagnosis, and women in the general population should be screened when asymptomatic from age 30 years or older. However, studies showed that:
 - Only 33% WLHIV were screened at diagnosis (65% screened > 48 weeks after starting

ART)⁵¹; 35% attending an ART clinic were ever screened,⁵² and 45% attending a hospital HIV clinic were screened three-yearly.⁵³

- Some health providers screened women in the general population who were under 30 years old⁴⁰ or symptomatic.⁴⁴

Reach

- Too few eligible women at population (25-52%)^{54,55} and facility level (42%)⁵⁶ were reached with screening by 2012.
- A laboratory data-linkage analysis found only 16% of women needing LLETZ had received it two years after their HSIL result.¹⁸

Applying IS frameworks to mitigate secondary prevention implementation failures in SA

Two examples from the above findings are used to simulate how IS frameworks could be applied to mitigate secondary prevention implementation failure.

Example 1: Enhancing acceptability of cervical cytology

[Box 2](#) proposes how IS frameworks could be used to mitigate the low acceptability of screening described above.

Example 2: Enhancing feasibility of LLETZ

The previous section reported low LLETZ feasibility and reach (implementation failure) due to hospital-based provision (the barrier). Changing the service site (decentralising LLETZ provision to district level) is a proven strategy for overcoming this implementation failure in the SA context.⁵⁷ [Box 3](#) proposes how IS frameworks could be leveraged to improve LLETZ feasibility and reach through the decentralisation strategy.

Box 2. How to leverage IS frameworks in practice: cervical cytology example

Using IS frameworks to mitigate low acceptability of cervical cytology

Use EPIS framework to guide implementation (cervical cytology is already in implementation phase).

During the implementation phase

- Understand the determinants of acceptability.
 - Use a determinants framework (e.g., CFIR)³² to identify barriers of acceptability, based on stakeholder insights, existing health information or formal research.
 - Time and resources permitting, do this across sub-districts/districts, rural/urban, and population groups (e.g., WLHIV and HIV negative).
- Identify implementation strategies for addressing barriers.
 - Use the ERIC³⁷ compilation to select strategies that fit the context and stakeholders.
 - Align strategies to barriers (e.g., if barrier is long distance to facilities, the strategy may be 'change the service site', e.g., introduce community-based screening sites).
- Deploy the identified strategies and evaluate for improvements in acceptability (measure acceptability before and after the strategy to assess for change).

Box 3. How to leverage IS frameworks in practice: LLETZ example

Using IS frameworks to plan, execute and evaluate implementation of decentralised LLETZ

Use the EPIS framework to guide decentralised LLETZ implementation.

During the preparatory phase

- With stakeholders, define what the decentralisation strategy entails – what will be done (e.g., training LLETZ providers at district level, supportive supervision, referral criteria, etc.), and where (districts, sub-districts), to enhance feasibility and reach.
- Include the strategy and planned IOs in programme operational plans.

During the implementation phase

- Deploy LLETZ through the decentralisation strategy. Deploy in selected sites initially.
- Assess implementation outcome indicators (reach, feasibility) during programme monitoring.
- Evaluate if implementation is effective.
 - Use an evaluation framework to compare implementation outcomes (feasibility, reach) between sites with and without the decentralisation strategy.
 - Could also evaluate whether sites with decentralisation strategy improve HSIL cure rates, and cancer aversion rates more than sites without the strategy.

Discussion

This paper describes implementation failure when deploying cervical cytology and LLETZ in the SA health system and proposes how implementation science may be leveraged to mitigate such failure (i.e., low implementation fidelity, acceptability and adoption of cervical cytology by users and providers, and low feasibility and reach of LLETZ). Since IOs are preconditions for improved health outcomes, these failures must be addressed if population coverage of screening and pre-cancer treatment, as well as cancer aversion rates are to improve.

Understanding the factors contributing to implementation failure is a key step towards improvements. Published literature offers insights into implementation barriers contributing to the identified failures above. For instance, women's low knowledge of cervical cancer symptoms and risks, fear of testing or having an HIV test performed at the same time, and negative experiences and perceptions regarding services may limit acceptability and uptake of screening^{42,43,58} and pre-cancer treatment.⁴² Receiving little information from health workers on how to navigate referral to LLETZ clinics, and long wait

time between screening and treatment⁴² are further barriers.

System factors hampering adoption, fidelity and sustainability (of screening include low provider knowledge (of screening and guidelines), skills, and willingness to screen,^{40,59} as well as inadequate material resources, infrastructure, and supervisory support.⁶⁰ Sociocultural issues such as gender norms, patriarchy, and stigma also impede acceptability of screening and pre-cancer treatment.⁴² The low cytology specimen adequacy rates (low implementation fidelity) reported in this paper were likely due to EBI (Pap smear) characteristics; LBC provides higher yields.⁸

Different approaches may be used to address implementation barriers. An IS approach entails applying context-relevant implementation strategies to overcome the barriers hindering adoption, acceptability, feasibility, fidelity, and reach.^{29,61} Considering adoption, a recent review reported that effective strategies for increasing screening uptake (adoption) by women in SSA include educational (e.g., using local religious leaders' wives to provide peer education), incentive-based (e.g., e-voucher for transport to screening facility), and service delivery

change strategies (e.g., outreach workers distributing and collecting home HPV self-sampling test kits, phone call reminders about missed appointments, and community-based screening).⁶¹ In SA, service integration offering screening with HPV vaccination improved screening uptake by mothers of vaccine recipient girls.⁶²

IS frameworks can be used to assess implementation effectiveness of existing secondary prevention EBIs, and guide on how to deploy into the SA public sector new secondary prevention EBIs (e.g., HPV DNA testing or thermal ablation). While these latter EBIs have been implemented successfully in other settings, they may not be similarly implementable in SA.²⁴ IS-guided pilot studies are needed prior to deploying these EBIs in the SA health system to avoid implementation failures. A determinant framework such as CFIR could guide an exploration of factors potentially hindering implementation of these EBIs, e.g.: barriers relating to the context (HIV and HPV prevalence, health system capacity); HPV test characteristics (assay complexity and performance); implementation process (requirements for point-of-care testing and additional triage testing), and individual characteristics (e.g., skill needs of those delivering the intervention, including laboratory personnel⁸).

Greater use of IS in the SA health system for both research and practice would contribute to generating generalisable evidence about which implementation strategies work best in which circumstances and why.³⁰ In SA, research on implementation outcomes is available for cytology and LLETZ and is becoming available for HPV testing (e.g., on women's acceptance of HPV self-sampling).⁶³ More IS studies are needed to: a) understand secondary prevention implementation determinants in different settings; b) identify suitable strategies for addressing these determinants, and c) test whether and which strategies successfully overcome identified determinants. Conducting studies in different settings (across districts, provinces, rural/urban settings), and groups (e.g., WLHIV, marginalised women) will enable adaptation of implementation to fit respective groups. For instance, research showing that SA rural women were significantly less likely to uptake Pap smear screening⁵⁵ suggests that strategies for increasing uptake may require tailoring to rural vs urban settings.

At a global level, initiatives to enhance IS use are emerging. International funding is available for implementation research (e.g., National Institutes of Health, Fogarty International Centre, National Cancer Institute, UK Research and Innovation, and Global Alliance for Chronic Diseases) and IS training opportunities (e.g., WHO's special programme in research and training in tropical diseases (TDR), a free massive open online course). Recently, a WHO panel of global experts formulated priority implementation research questions towards cervical cancer elimination which countries are encouraged to explore.⁶⁴ Government and other actors could leverage these opportunities for cervical cancer prevention in SA.

Recommendations

Suggestions that SA health authorities at all levels could consider include:

- Addressing implementation failures identified in this paper. Suggestions for how IS frameworks could be used to mitigate implementation failures have been elaborated on above. Involving relevant stakeholders (service users, communities, health workers and other implementers, and health managers, amongst others) is essential to ensure context-relevant solutions.
- Engaging local stakeholders and IS experts to foster the integration of IS concepts into cervical cancer prevention programme plans.
- Creating IS training opportunities for practitioners (providers, district health facility and programme managers, middle- and senior-level managers, and policy makers). Training could be on-the-job in partnership with existing IS course providers, including higher education institutions.
- Considering the IS research questions proposed by the WHO-convened expert panel, commission further implementation research to inform the unfolding comprehensive cervical cancer elimination strategy.

Conclusion

While evidence-based interventions for screening and pre-cancer treatment (secondary prevention) exist, their effective implementation in real world practice settings in South Africa remains a challenge. Greater application of, and capacity building in, implementation science are recommended to enhance implementation effectiveness and contribute towards improving cervical cancer secondary prevention in South Africa.

Published: October 01, 2024 CAT.

Abbreviations

Abbreviation	Description
ART	antiretroviral therapy
ASIR	age-standardised incidence rate
CFIR	consolidated framework for implementation research
EBIs	evidence-based interventions
EPIS	exploration, preparatory, implementation and sustainment
ERIC	expert recommendations for implementing change
HIC	high-income country
HPV	human papilloma virus
HSIL	high-grade squamous intraepithelial lesions
IOs	implementation outcomes
IS	implementation science
LBC	liquid-based cytology
LLETZ	large loop excision of the transformation zone
LMIC	low- and middle-income country
SA	South Africa
SSA	sub-Saharan Africa
VIA	visual inspection with acetic acid
WHO	World Health Organization
WLHIV	women living with HIV



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