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Innovations to Improve Cervical Cancer Screening: A Systematic Review

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Background

Cervical cancer is the fourth most common cancer among women worldwide (estimated at 604,000 new cases and 342,000 deaths in 2020 globally (WHO, 2023)) and the second most common in Bangladesh. However, when detected at the early stage, cervical cancer is treatable. Therefore, identifying accessible screening methods, tools, and innovations in screening tests, processes, and implementation is crucial for prevention. In this context, a comprehensive scenario driven by a literature review will help to identify future practices and strategies for improving cervical cancer screening.

This systematic review, registered at PROSPERO (CRD42023402296) by AdSEARCH at icddr,b, aimed to explore innovations and diverse approaches, techniques, and strategies in screening methods for the prevention and early diagnosis of cervical cancer.

Projections indicate by 2030, Globally there will be a **21.3%** increase in number of cases and **26.7%** in number of deaths over just the 12-year period from 2018 due to cervical cancer (WHO, 2019).

Methods

The search spanned from 1 January 2000 to 25 June 2023, and encompassed major databases including MEDLINE, CINAHL, Web of Science, EMBASE, Scopus, and the Cochrane Library, with inclusion criteria covering various study designs and women aged 18-64 years.

Articles were screened through a rigorous process using the 'Rayyan' application, and data extraction was done focusing on study characteristics, innovations, advantages, challenges, outcomes, and findings. Quality assessment was conducted using Joanna Briggs Institution's (JBI) critical appraisal tools, with disagreements resolved through consensus. A narrative synthesis was conducted of the included articles, illustrating the characteristics of the studies, innovation techniques or approaches, study outcomes (early diagnosis and screening coverage) and outcome measurements (diagnostic accuracy)

Given the heterogeneity of study designs and innovation approaches, conducting a meta-analysis was not feasible for this review.

Research Question

What are the innovations in screening for prevention and early diagnosis of Cervical cancer and what are their effectiveness?

Search Timeline

From 1 January 2000 to 25 June 2023

Major Databases:

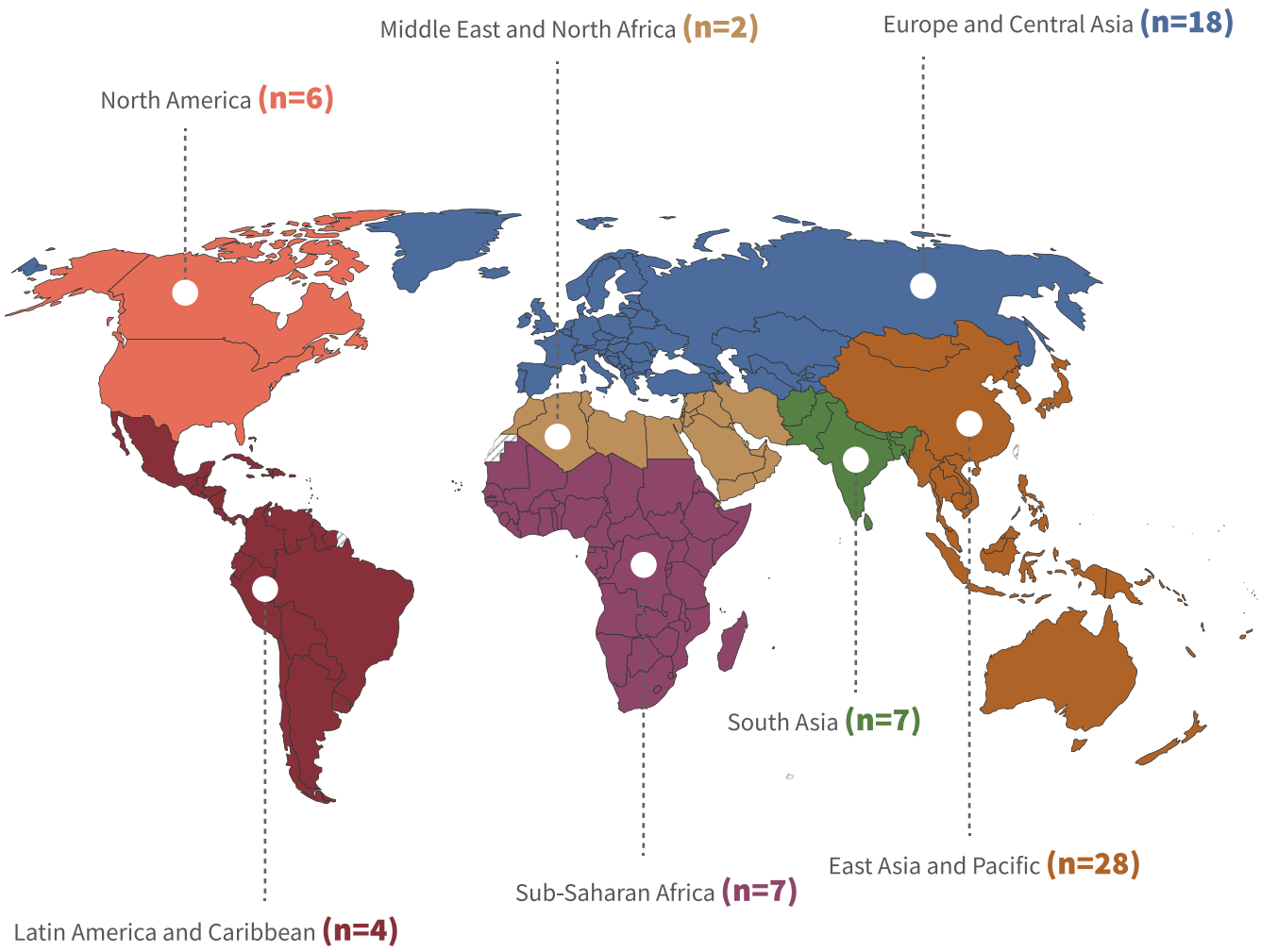
MEDLINE (through PubMed), CINAHL, Web of Science, EMBASE, Scopus, and the Cochrane Library

Eligible Criteria:

Women aged 18-64 years

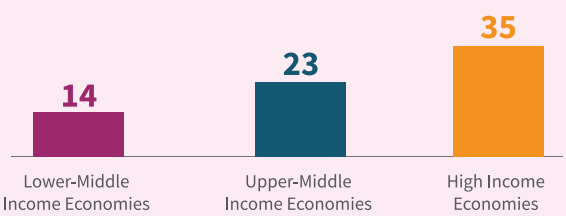
Characteristics of the Included Studies

Articles by World Bank Geographic Region

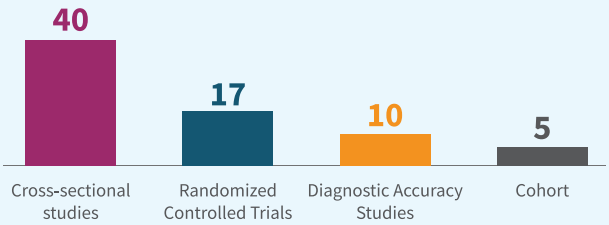


Articles by economies at all income levels

World Bank Geographic Region



Study designs



Study conducted in:

Hospitals	Clinics	Community	Labs
(n=30)	**(n=20)**	**(n=13)**	**(n=9)**

Key Findings (Based on Types of Innovations)

Medical Devices

Medical instruments or tools designed to identify or detect abnormalities in the cervix

Liquid-based cytology techniques, such as Papspin and PathTezt™, have shown high diagnostic concordance (86%) and high performance (99%) in screening. Colposcopy and visual inspection techniques, including the Swede score for pocket and Gynocular colposcopes, as well as Visual Inspection of Acetic Acid under Magnification (VIAM), have demonstrated comparable performance to standard-of-care colposcopy, exhibiting higher sensitivity (95%) and accuracy (79%). Automated screening systems like CytoProcessor™ have offered enhanced sensitivity for ASC-US+ (96%) and LSIL+ (95%) of Bethesda categories. Point of care digital cytology with AI (deep learning system) have shown improved sensitivity (96%) and specificity (85%) in identifying high-grade lesions. ThinPrep Integrated Imager screening has similar sensitivity (92%) and specificity (89%) compared to manual microscopy. Microendoscopic imaging systems, digital cervicography, and VIA-Md, have also demonstrated high sensitivity (97.6%, 72.41%, 100% respectively) and specificity (95%, 97%, 89.5% respectively) in detecting cervical intraepithelial neoplasia (CIN) lesions.

Laboratory Techniques

Advanced procedures and methodologies used to detect abnormalities in cervical cells

The CareHPV test demonstrated high sensitivity (90.0%) for detecting CIN2+ lesions, with specificities ranging from 84.2% to 82.4%. Liquid-based Cytology (LBC) showed improved detection of grade 1 lesions with a relative sensitivity of 1.68 and reduced the rate of unsatisfactory slides compared to conventional cytology. The Thin layer Advanced Cytology Assay System (TACAS) exhibited even cell distribution and low abnormal cytology incidence, with only 5% shrinkage based on nuclear diameter measurements. The NovaPrep Processor System (NPS) demonstrated improved sensitivity compared to conventional cytology and decreased the number of unsatisfactory specimens. Anyplex™II HPV28 Assay showed higher sensitivity (84.8%) and specificity (94%) compared to conventional cytology. HPV testing alone increased sensitivity but decreased Positive Predictive Value compared to conventional cytology. Biomarker detection combining serum proteins and microRNAs resulted in high accuracy, while specific mRNA biomarkers like TOP2A and CDKN2A/p16 showed varying sensitivity and specificity (96%, 71%). Novel screening techniques showed promising performance with sensitivity ranging from 84.8% to 97.9% and specificity from 74.6% to 91%. FTIR spectroscopy and LA-REIMS, demonstrated promising performance, with sensitivity values around 85% to 91% and specificity ranging from 83% to 91%. Dual stain cytology demonstrated superior performance to VIA screening, particularly in HPV infection detection, with sensitivity (94%) and specificity (69%) for HPV testing.

Combined Techniques

Integration of both a physical device for sample collection and a laboratory method for analysing samples

Among 10 studies, 2 studies reported HPV testing with conventional cytology, 5 studies reported with liquid-based cytology, 1 study with automated assisted and 2 studies compared HPV testing between conventional cytology and liquid-based cytology. Out of 10 studies, 70% of studies reported sensitivity and specificity, and 30% of studies reported sensitivity, specificity, PPV and NPV. Sensitivity and specificity of detecting CIN2+ ranged from 39% to 98% and 69% to 100% respectively and CIN3+ ranged from 73.7% to 100% and 69% to 99.9% respectively.

Strategies (self-collection devices, pocket colposcopes, referral system)

Devices designed to enable individuals to collect cervical cell samples themselves, triages and referrals

Nine studies analysed the diagnostic accuracy and acceptability of self-sampling devices, with five focusing on acceptability and four on both accuracy and acceptability. Various devices, including SelfCervix®, Evalyn Brush, and Care HPV kit, were investigated, with 56% of studies reporting comparable sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) between self-collected and clinician-collected samples.

Sensitivity for detecting CIN2+ ranged from 62.5% to 100%, with specificity ranging from 59.3% to 71.9%, PPV from 14% to 18%, and NPV from 91.7% to 100%. Acceptability varied between 36.6% and 95.8% for various devices. Additionally, self-sampling showed substantial agreement with physician sampling, with agreement percentages ranging from 82.1% to 89.1% and kappa scores from 0.519 to 0.932. Implementation of Pocket colposcope significantly improved optimal treatment rates (94.0% to 95.9%) and reduced overtreatment (from 46.8% to 4.8%) and referral rates (from 12.4% to 6.0%) when combined with VIA testing. Mobile van-equipped colposcopy and in vivo microscopy enhanced compliance with diagnostic follow-up, and the screening process received positive patient acceptance, with 99.4% of women comfortable with having an image of their cervix taken.

Way forward

- Need to emphasise a transformative approach for early detection of cervical cancer.
- Embrace innovative screening methods with high diagnostic accuracy like HPV DNA test (careHPV), AI-based image classification, and point-of-care devices (pocket colposcope).
- Lab-based innovative strategies and methods which demonstrated superior performances have the scope for population-based research.
- Prioritise methods that not only improve accuracy but also enhance accessibility and focus on patient-centric care.
- Encourage policymakers to develop guidelines, ensure standardized implementation, and invest in healthcare infrastructure for equitable access.

Scan this code to access the 72 Study Mapping

**This situational assessment is based on the data available from 1 January 2000 to 25 June 2023*

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