
Effectiveness and cost-effectiveness of population-based cervical cancer screening in LMICs: a systematic review

Kanchan Mukherjee, Deepika Singh Saraf, Vijayluxmi Bose, Ashoo Grover, Akriti Chahar, Myron Anthony Godinho, Denny John

Submitted to the Coordinating Group of:

Crime and Justice

Education

Disability

International Development

Nutrition

Social Welfare

Methods

Knowledge Translation and Implementation

Other:

Plans to co-register:

No

Yes Cochrane Other

Maybe

Date submitted: 23.08.2017

Date revision submitted:

Approval date:

Title of the review

Effectiveness and cost-effectiveness of population-based cervical cancer screening in LMICs: a systematic review

Background

Cervical cancer represents the fourth most common malignancy affecting women all over the world and is the second most common in developing countries (Catarino, 2015). Cervical cancer, although a preventable disease, has an annual world-wide burden of 530,000 new cases and 275,000 deaths. (Ferlay, 2010). In India, a comparison of incidences of cancer among all the Population Based Cancer Registries (PBCR) indicates that cervical cancer is one of the leading causes of cancer related mortality in females across the country. 88% of cervical cancer deaths around the world occur in low and middle-income countries and is expected to rise to 91.5% by 2030 (Ferlay, 2010). In India, for example, as per 2014 estimates, 122,844 women are diagnosed with cervical cancer and 67,477 die from the disease (ICO, 2014).

Screening for cervical cancer and its subsequent management ensures a decrease in mortality and disability. The current screening practices on cervical cancer include conventional cytology, HPV-DNA testing, visual inspection methods, colposcopy and polar probe (Denny, et.al., 2006.) The American Cancer Society guidelines recommends screening for cervical cancer in women age 21 to 65 years with cytology (Pap smear) every 3 years or, for women age 30 to 65 years who want to lengthen the screening interval, screening with a combination of cytology and human papillomavirus (HPV) testing every 5 years. These screening efforts covering a larger population helped the high-income countries to reduce cervical cancer mortalities. However, cytology based screening is difficult to implement in low-resource countries due to the lack of high quality cytology laboratories, competing health needs, widespread poverty, uninformed and disempowered women. (Denny et al, 2006).

The WHO guideline for cervical cancer screening recommends HPV testing for cervical cancer screening. Many countries, however have already established cytology (Pap smear) based, or visual inspection based (VIA) screening programs, and while the scientific evidence illustrates that HPV testing is more sensitive than other tests, implementing HPV test based programs in LMICs is difficult because of obstacles in implementing cytology-based screening programmes. Studies from India have showed that visual screening tests for cervical abnormalities are affordable, simple, acceptable, feasible and reasonably accurate clinical tools for early detection that can be readily used in a variety of healthcare settings in both developing and developed countries (Sankaranarayanan et al 2001, 2005, Goldie et al 2005, Legwood et al 2005). Every woman has the right to cervical screening at least once in her lifetime and the most optimal age for screening to achieve the greatest public health impact is between 30 and 40 years (Saxena, 2012). The WHO also advocated in a recent

guidance note that the lower age limit of cervical screening should not be under 30 years in low and middle-income countries (LMICs).

Population based screening interventions are designed to identify disease in a community earlier, thus enabling earlier intervention and management in order to reduce mortality and suffering from a disease. Although screening may lead to an earlier diagnosis, not all screening tests have been shown to benefit the person being screened. Over diagnosis and creating a false sense of security are some potential adverse effects of population based screening. For these reasons, a test used in a screening program, especially for a disease with low incidence, must have good sensitivity in addition to acceptable specificity.

Several developing countries including India have included population-based cervical cancer screening as part of the National Health Programs. The strategy behind such population based screening, while improving detection and further treatment, is also to increase the awareness in the community about the rising burden of cancers and other non-communicable diseases in such settings.

With this background, the proposed review focuses on collecting and collating evidence on effectiveness and cost-effectiveness of cervical cancer screening programs and methods in LMICs. The evidence from this review would attempt to lay the foundation for future HPV testing-based screening programs when affordable HPV tests become widely available.

Objectives

The review will aim to answer the following questions:

What is the current knowledge around effectiveness and cost-effectiveness of population based cervical cancer screening in LMICs?

What is the effectiveness of opportunistic cervical cancer screening in comparison with universal screening or no screening?

What are the recommendations for improving policy and practice based on the findings from the above review?

Existing reviews

In the last few years there have been a few systematic reviews conducted on effectiveness and cost effectiveness of cervical cancer screening. However, most of these studies were done in the context of providing guidelines for high-income countries (Pierson, 2013), effectiveness of cervical cancer screening methods (Fokom-Domgue, 2015), determining diagnostic accuracy of tests for detecting cervical cancer (Arbyn, 2012; Koliopoulos, 2017) or highlighted several obstacles that are responsible for the failure to implement an effective screening program in LMICs, such as supply-side factors (lack of healthcare infrastructure, trained

practitioners and laboratory supplies), demand-side factors (lack of knowledge of cervical cancer, limited access of the population to information, etc.), and political (lack of support from Ministry of Health, competing healthcare priorities, etc.). Among the cost-effectiveness studies, the reviews focused mainly on model-based studies (Mendes, 2015), or between methods of cervical screening (Nahvijou, 2014; Mezei, 2017). None of these reviews provided a comprehensive knowledge on the evidence of universal cervical cancer screening implementation and cost-effectiveness of opportunistic cervical cancer screening in comparison with universal or no screening approaches. This review will attempt to fill that gap.

Intervention

In population based cervical cancer screening all eligible women are screened for pre-cancerous lesions and cancerous lesions either by Health Workers or paramedical personnel or physicians. In resource poor settings, the first level of screening may be undertaken by the health workers at the grass root level health facility which could be a sub-centre or primary health centre. They are then referred/reviewed to physicians at Primary Health Centres. The aim is to ensure that screening for cervical cancer is provided as close to the home as possible by competently trained personnel in well-equipped facilities and ensuring privacy. The various methods currently available for cervical cancer screening include: cytology (Papanicolaou smear), visual methods (visual inspection with acetic acid (VIA) and Lugol's iodine (VILI)), and HPV DNA-based detection tests. In population based cervical cancer screening VIA or VILI are the commonly used methods by grass root level Health Workers in Low & Middle Income Countries. In VIA, while performing a vaginal speculum examination, the Health worker applies dilute (3-5% acetic acid) to the cervix. Abnormal tissue temporarily appears white which can be easily recorded by naked eye. Results of the test are available immediately and do not require laboratory support. In population based screening, screening invitation is given to all women above a certain age (differs country to country). In opportunistic screening it is given to high risk women only and is usually done at the facility level by physicians. In the absence of a screening programme, the woman goes to a health care provider/physician with her complaints when she becomes symptomatic and then referred to a specialist for further evaluation.

Eligible comparisons are opportunistic screening or no screening.

Population

Females aged 30 years and above in living in low and middle income countries (LMICs) will be included.

Outcomes

The primary outcomes are:

- a) Early diagnosis of cervical cancer/precancerous lesions.
- b) Cost to the healthcare system.
- c) QALYs gained/DALY's averted.

From the cost-effectiveness studies, the following outcome measures will be recorded from the included studies:

1. Incremental cost-effectiveness ratio (ICER).
2. Incremental cost per QALY (quality-adjusted life years).
3. Incremental cost per DALY (disability-adjusted life years).
4. Net benefits.

In addition, we will also include data on clinical effectiveness measured in terms of detection of precancerous lesions like Cervical Intraepithelial Neoplasia (CIN), and safety from the included studies.

Study designs

We will include the following study designs:

5. Randomised controlled trials, and quasi-randomised trials (for effectiveness of screening programmes).
6. Observational studies (for safety outcomes).
7. Full economic evaluations (i.e. cost-effectiveness, cost-benefit, cost-utility analysis) and partial (costs, and cost analysis).
8. Mixed methods study and Qualitative studies (for understanding barriers and enablers for uptake).

References

- Abyn M, Fisher A, Martin-Hirsch PPL, Zhao Fang-Hui, Qiao Y. (2012). Low cost versus other screening tests to detect cervical cancer or precancer in developing countries. *Cochrane Database of Systematic Reviews*; doi: 10.1002/14651858.CD010186
- Catarino R, Petignat P, Dongui G, Vassailakos P. (2015). Screening for cervical cancer screening in developing countries. *World J Clin Oncol*; 6(6): 281-290.
- Denny L, Quinn M, Sankaranarayanan R. (2006) Screening for Cervical Cancer in developing countries. *Vaccine* 24S3; S3/71–S3/77.
- Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM.(2010) Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer.*; 127:2893–2917.
- Fokom-Domgue, J., Fokom-Defo, V., Kengne, AP. (2015). Performance of alternative strategies for primary cervical cancer screening in sub-Saharan Africa: Systematic review and meta-analysis of diagnostic test accuracy studies. *BMJ*; 351;h3084

Goldie SJ, Gaffikin L, Goldhaber-Fiebert JD, Gordillo-Tobar A, Levin C, Mahe C, et al (2005). Cost-effectiveness of cervical- cancer screening in five developing countries. *N Engl J Med* ;353(20):2158–68.

ICO Information Centre on HPV and cancer (Summary Report 2014). (2014). Human Papillomavirus and Related Diseases in India.

Koliopoulos G, Nyaga VN, Santesso N, Bryant A, Martin-Hirsch PL, Mustafa RA, Schunemann H, Paraskevaidis E, Arbyn M. (2017). Cytology versus HPV testing for cervical cancer screening in general population. *Cochrane Database of Systematic Reviews*; doi: 10.1002/14651858.CD008587.pub2

Legood R, Gray AM, Mahe C, Wolstenholme J, Jayant K, Nene BM, et al (2005). Screening for cervical cancer in India: How much will it cost? A trial based analysis of the cost per case detected. *Int J Cancer*;117(6):981–7.

Mendes, D., Bains, I., Vanni, T., Jit, M. (2015). Systematic review of model-based cervical screening evaluations. *BMC Cancer*, 15:334

Mezei AK, Armstrong HL, Pedersen HN, Campos NG, Mitchell SM, Sekikubo M, Byamugisha JK, Kim JJ, Bryan S, Ogilvie GS. (2017). Cost-effectiveness of cervical cancer screening methods in low- and middle-income countries: A systematic review. *Int J Cancer*, Aug 1; 14(3):437-446

Nahvijou, A., Hadji M., Marnani AB., Tourang, F., Bayat N., Weiderpass, E., Daroudi, R., AkbariSari, A., Zendehdel, K. (2014). A systematic review of economic aspects of cervical cancer screening strategies worldwide: Discrepancy between economic analysis and policymaking. *Asian Pac J Cancer Prev*, 15(19), 8229-8237

Sankaranarayanan R, Gaffikin L, Jacob M, Sellors J, Robles S (2005). A critical assessment of screening methods for cervical neoplasia. *Int J Gynaecol Obstet* ;89(Suppl. 2):S4–S12.

Sankaranarayanan R, Budukh AM, Rajkumar R (2001). Effective screening programmes for cervical cancer in low- and middle-income developing countries. *Bull World Health Organization*;79(10):954–62.

Sankaranarayanan R, Nene BM, Dinshaw KA, Mahe C, Jayant K, Shastri SS, et al (2005). A cluster randomized controlled trial of visual, cytology and human papillomavirus screening for cancer of the cervix in rural India. *Int J Cancer*;116(4):617–23.

Saxena U, Sauvaget C, Sankaranaayanan R.(2012). Evidence-based Screening, Early Diagnosis and Treatment Strategy of Cervical Cancer in India. *Asian Pacific J Cancer Prev*, 13:1699-1703.

Pierson, L., Fitzpatrick-Lewis, D., Ciliska, D., Warren, R. (2013). Screening for cervical cancer: A systematic review and meta-analysis. *Systematic Reviews*, 2:35.

Review authors

Lead review author: The lead author is the person who develops and co-ordinates the review team, discusses and assigns roles for individual members of the review team, liaises with the editorial base and takes responsibility for the on-going updates of the review.

Name:	Kanchan Mukherjee
Title:	Professor
Affiliation:	Centre for Health Policy, Planning and Management, Tata Institute of Social Sciences
Address:	V.N. Purav Marg, Deonar
City, State, Province or County:	Mumbai, Maharashtra
Post code:	400088
Country:	India
Phone:	+919820615743, +912225525533
Email:	kanch@tiss.edu; kanchanindia74@gmail.com

Co-authors:

Name:	Deepika Saraf
Title:	Scientist-D
Affiliation:	National Institute of Cancer Prevention and Research (Indian Council of Medical Research)
Address:	I-7, Sector 39
City, State, Province or County:	Noida, Uttar Pradesh
Post code:	201301
Country:	India
Phone:	9910954455
Email:	drdeepika.aiims@gmail.com

Name:	Bhavesh Jain
Title:	Program Manager
Affiliation:	ACCESS Health International
Address:	B1-801, Green Acres, Prahlad Nagar
City, State, Province or County:	Ahmedabad, Gujarat

Post code:	380015
Country:	India
Phone:	+91-9819109819
Email:	Bhavesh_28@yahoo.com
Name:	Vijayluxmi Bose
Title:	Health Communication & Advocacy Specialist
Affiliation:	Independent Consultant
Address:	2B, Pocket 4. Mayur Vihar, Phase 1.
City, State, Province or County:	Delhi
Post code:	110091
Country:	India
Phone:	+919811415443
Email:	vijayluxmi.bose@gmail.com
Name:	Ashoo Grover
Title:	Scientist E (Medical)
Affiliation:	Indian Council of Medical Research, HQ
Address:	Ansari Nagar East
City, State, Province or County:	New Delhi
Post code:	110029
Country:	India
Phone:	9818966565
Email:	ashoogrover@gmail.com
Name:	Akriti Chahar Tomar
Title:	Consultant (Health technology Division)
Affiliation:	Healthcare Technology Division, WHO Collaborating Centre for Priority Medical Devices & Health Technology Policy
Address:	National Health Resource Centre
City, State, Province or County:	Delhi

Post code:	110067
Country:	India
Phone:	8826250728
Email:	akritichahar.hta@gmail.com
Name:	Myron Anthony Godinho
Title:	Research Associate
Affiliation:	Public Health Evidence South Asia (PHESA), Manipal University
Address:	EDU Building, Madhav Nagar, Manipal
City, State, Province or County:	Karnataka
Post code:	576104
Country:	India
Phone:	+917356844782
Email:	myrongodinho@gmail.com
Name:	Denny John
Title:	Evidence Synthesis Specialist
Affiliation:	Campbell Collaboration
Address:	2nd Floor, West Wing, Vasant Kunj Institutional Enclave, ISID Complex
City, State, Province or County:	New Delhi
Post code:	110070
Country:	India
Phone:	+91-9987021553
Email:	djohn@campbellcollaboration.org

Roles and responsibilities

- (a) Content: Kanchan Mukherjee, Deepika Saraf, Ashoo Grover, and Denny John, have experience of cervical cancer screening strategies in Indian context. Along with the above, Bhavesh Jain, and Vijayaluxmi Bose, have knowledge of public health systems and NCDs in LMICs context.
- (b) Systematic review methods: Myron Godinho and Denny John have methodological expertise
- (c) Statistical analysis: Akriti Chahar, Denny John and Ashoo Grover have statistical expertise
- (d) Economic methods: Kanchan Mukherje, Denny John, Akriti Chahar and Ashoo Grover have experience in economic evaluation methods
- (e) Information retrieval: Myron Godinho, and Denny John have information retrieval expertise.

Funding

Do you receive any financial support, and if so, from where? What are your deliverable deadlines for the review? If not, are you planning to apply for funding, and if so, from where?

No funding

Potential conflicts of interest

For example, have any of the authors been involved in the development of relevant interventions, primary research, or prior published reviews on the topic?

Denny John was involved in the monitoring and evaluation of the National Programme for Prevention and Control of Cancer, Diabetes, CVD and Stroke (NPCDCS) pilot in 2 districts in Karnataka state, India, from 2014-15.

Vijayluxmi Bose is involved in secondary data analysis of a study titled ‘Patient perception and health seeking behaviour related to occurrences of cancers in Delhi, India: a qualitative analytical summary’ with Dr. Tulika Seth from the All India Institute of Medical Sciences, New Delhi India.

Preliminary timeframe

- (f) Date you plan to submit a draft protocol: December 2017
- (g) Date you plan to submit a draft review: July 2018