Evaluating the Impact of a Population-Based Electronic Surveillance Tool for Cervical Cancer Risk Identification: A Quasi-Experimental Study

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ABSTRACT

Background: Digital tools may strengthen population-based cervical cancer screening in low-resource settings. We evaluated an Android application (Mcerv) for risk documentation and case finding in public clinics. This study aims to implement and evaluate an informatics tool for risk identification to strengthen cervical cancer screening. Methods: A quasi-experimental study was conducted in selected Sampoorna clinics in Lucknow, India. An app-based decision tool was developed to identify cervical cancer among high-risk populations. In the intervention group, the tool was implemented, and healthcare workers were trained for data collection. Outcomes assessed feasibility, usability and identification of risk factors. Results: The electronic surveillance tool was successfully developed and implemented among identified Sampoorna clinics in Uttar Pradesh. Symptoms such as worrisome vaginal discharge, abnormal bleeding, vaginal bleeding, abnormal discharge are associated with the high risk for cervical cancer. After adjusting for other variables, factors such as tobacco use, acute illnesses, cold/cough, skin infection, and body ache were associated with the cervical cancer. Conclusion: The study demonstrates the feasibility of implementing electronic surveillance tools in resource-constrained settings to aid risk analysis. Wider adoption of such informatics platforms can enable robust, real-time cervical cancer monitoring. Overall, the tool shows promise for data-driven decision making to accelerate cervical cancer prevention and control.

Keywords: Cervical cancer, evaluation, population-based study, app-based surveillance tool

1. INTRODUCTION

Cancer remains one of the leading global health challenges, responsible for approximately 9.6 million deaths in 2018[1], with projections indicating an increase in cases due to the aging population and lifestyle factors with an increasing incidence in both developing and developed countries. As per Globocon 2022, Cervical cancer is among the top four cancer with the incidence of 14.1 per 100,000 women years[2]. Cervical cancer remains a significant public health concern globally, accounting for an estimated 604,000 new cases and 342,000 deaths annually in 2020 [2]. In India, it is the second most common cancer among women, contributing to nearly 22% of the global cervical cancer burden [3]. Despite being preventable and treatable through early detection and timely interventions, many women are diagnosed at advanced stages due to inadequate screening and awareness.[4]

Persistent infection with high-risk strains of Human Papillomavirus (HPV) is the leading cause of cervical cancer, making cervical cancer screening and vaccination vital for prevention[5]. Government of India launched National Programme for Prevention and Control of Non-Communicable Diseases (NPNCD) to screen all women aged more than 30 years for

cervical cancer in India through Population based screening. Other components of NPNCD are population enumeration, assessment of risk factors, mobilizing communities for screening at Sub-Centres, Primary Health Centres, health promotion, initiation of treatment at a PHC, referral to higher centres for further treatment [6]. Additionally, the introduction of the HPV vaccine in other countries has shown promise in reducing cervical cancer incidence by preventing HPV infections[7]. However, despite the availability of vaccines, uptake remains low in many regions, especially in low- and middle-income countries (LMIC), due to a lack of awareness and cultural barrier[8].

Emerging technologies in digital health offer innovative solutions to address the challenges of cervical cancer prevention and control. Mobile applications and electronic dashboards are transforming the landscape of public health[9,10]. These tools facilitate a more systematic approach to cervical cancer screening, particularly in resource-limited settings, by integrating community-based screening programs with centralized data systems. Digital health innovations for other NCDs has also shown promise for its management[11]. The integration of a mobile application feeding system and a dashboard provides a comprehensive platform for tracking risk factors, including socio-demographic, behavioural, and clinical attributes. This approach allows for enhanced surveillance, risk stratification, and targeted interventions, addressing the barriers of conventional screening programs such as accessibility, affordability, and follow-up challenges[11,12].

Recent studies highlight the significance of early detection of risk factors like human papillomavirus (HPV) infection, smoking, multiple pregnancies, and prolonged use of oral contraceptives[13,14]. However, the real-time analysis of such data through digital tools remains underexplored in large-scale public health initiatives[15]. Furthermore, the usability and impact of these applications on improving health outcomes, especially in low- and middle-income countries, require more evidence-based documentation[16,17]. The present study explores the implementation and outcomes of a novel mobile health application for identifying and managing cervical cancer risk factors to enhance screening efficiency.

2. METHODOLOGY

The primary objective of this study is to assess the effectiveness of tool in identifying risk factors for cervical cancer through quasi experimental study.

Hypothesis
Null hypothesis
There is no significant impact of Population based electronic surveillance tool to identify risk factors for developing cervical cancer.

Alternate hypothesis
There is a significant impact of Population based electronic surveillance tool to identify risk factors for developing cervical cancer.

Study Design
The implementation strategy has been discussed in the study protocol published elsewhere[1]. A quasi-experimental research study was conducted at selected Sampoorna clinics in Lucknow, India to evaluate the application of a population-based electronic surveillance tool to identify cervical cancer risk factors.

Ethical Approval
The study received ethical approval from the University Research Ethical Committee, DIT University, on 12/5/2022 (Protocol No: UREC No. DITU/UREC/2022/04/12) and all necessary administrative approvals were obtained.

Study Phases
Phase 1: The primary outcome of Phase 1 was the development of a Population-Based (App based) Electronic Surveillance Tool for Cervical Cancer Risk Identification, which encompasses categories and variables to detect the high-risk population for cervical cancer, collecting information on personal details, demographic details, socio-economic status, family history, lifestyle, menstrual history, HPV vaccine status, past and present medical history, anthropometry measurements, clinical history, and Visual inspection of acetic acid (VIA) screening findings.

Phase 2 and Phase 3: Two Sampoorna clinics were conveniently selected in urban Lucknow, with one serving as the intervention group (District Hospital, Lucknow) and the other as the control group (Maliabhag, Sampoorna Clinic). Both these clinics were matched based on the fact that both groups should be similar in terms of population load especially females aged more than 30 years. The informatics tool was implemented in the selected intervention group clinics, where

healthcare workers were trained to use the app for real-time data collection from women aged 30 to 60. Regular mentoring and follow-up visits addressed data quality, validation, and feedback. Outcomes of Phase 3 focused on implementation issues, feasibility, and the usability of the informatics platform.

Intervention

A Mcerv smartphone based android application has been developed wherein screening for the identification of risk factors for cervical cancer was done real time in the purposively selected Sampoorna clinics in Uttar Pradesh. Mcerv application was designed to facilitate structured, secure, and real-time digital entry of cervical screening data under following heading: Personal details and demographics, Socio-economic status, Family history and lifestyle habits, Menstrual and reproductive history, HPV vaccination status, Medical history (past and current), Anthropometric measurements, Clinical symptoms and history, VIA screening findings.

The app was configured with:
- Required data fields and form validation
- Built-in logic was embedded to stratify patients into low, moderate, or high risk
- Secure cloud sync (via Firebase) or local offline save with later upload

The Mcerv app is patented under application number **202411098245** with the Indian Patent Office, Ministry of Commerce and Industry, Government of India.

Figure 1 & 2: Login page of the drafted: Population Based Electronic Surveillance Tool to Identify Risk Factors for Developing Cervical Cancer application.
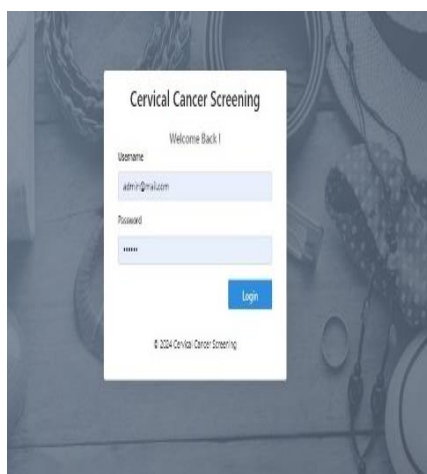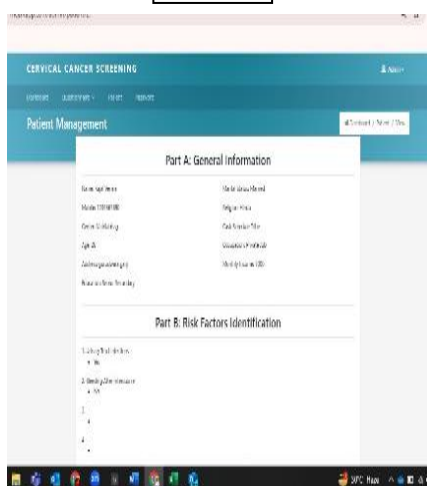

Fig: 1

Fig: 2

Figure 3, 4, 5: Dashboard screen of the Mcerv Application for identifying the risk factors.

Fig: 3

Fig: 4

Fig: 5

Control group
Paper based screening for the identification of risk factors for cervical cancer or no other digital tool should be utilized for the screening of cervical cancer.

The women aged 30 to 60 years visiting Sampoorna clinics were included in this study and with no prior diagnosis or treatment of cervical cancer were included in the study. The patient which were exclusion criteria were severely ill individuals unwilling to participate and women who didn't provide consent to participate in the study.

Sample size estimation
Sample size calculation was done based on following:

$$n = \frac{2P(1-P)[Z_{1-\alpha} + Z_{1-\beta}]^2}{(d)^2}$$

P = Previous cervical cancer detection rates (23.7 per 100,000 population) (Reference)

d = 10% (difference in early detection of cervical cancer), Power = 80% or 0.8, Alpha = 0.05

The required sample size was 221 women per group and additionally, for adjusting a dropout, the sample size was inflated by 10%, leading to a total of 250 women per group.

Study procedure
Written informed consent was taken from the participants before the data collection. The data was collected from the participants through direct interviews administering a standardized questionnaire to collect socio-demographic characteristics, personal habits, self-reported health conditions, HPV vaccination status and associated risk factors. The collected data was entered into Microsoft Excel and analysed using SPSS Statistics 26.0. A p-value ≤ 0.05 was considered statistically significant.

Data Analysis
Data was analysed using SPSS 26.0 version. Descriptive statistics summarized participant characteristics, while t-tests and chi-square tests assessed differences and associations between intervention and control groups. The descriptive statistics of socio-demographic variables, personal habits, self-reported health conditions, HPV vaccination status and associated risk factors were depicted in percentages and proportions. A chi-square test was conducted to find an association between the socio- demographic variables, personal habits and HPV vaccination with abnormal and worrisome vaginal discharge and bleeding.

Outcomes
Outcomes measured included the number of women identified at risk for cervical cancer and the number identified with associated risk factors among intervention and control group.

3. RESULTS

Socio-demographic characteristics
A total of 501 participants- intervention group (252) and the control group (249) were recruited for this study. The socio-demographic characteristics such as age (in years) and personal habits of participants are summarized in Table 1. Most participants were from the OBC (44.4%, 41.8%) and Scheduled Caste (37.7%, 28.1%) categories, with only 4.8% and 0.8% from Scheduled Tribes. Most were Hindus (98.0%, 95.2%), and a large proportion reported a monthly income of ₹15,000 or less (69%, 63.5%) in both groups.

Table 1: Socio-demographic characteristics among intervention and control group

Socio-demographic Characteristics	Intervention group (n, %)	Control group (n, %)	p value
Age (in years), mean (SD)	47.8 (8.3)	43.6 (8.4)	
≤ 45 years >45 years	101 (40.1) 151 (59.9)	150 (60.2) 99 (39.8)	< 0.001
Personal habits			
Tobacco consumption			
Yes	45 (17.9)	11 (4.4)	< 0.001

No	207 (82.1)	238 (95.6)	
Smoking			
Yes	19 (7.5)	4(1.6)	0.002
No	233 (92.5)	245(98.4)	
Gutka chewer			
Yes	37(14.7)	7(2.8)	< 0.001
No	215(85.3)	242 (97.2)	
Alcohol consumption			
Yes	7(2.8)	11(4.4)	0.324
No	245(97.2)	238(95.6)	

Table 2 summarizes that stomach-ache was significantly more common among intervention group (5.6%) as compared to the control group (0.8%) with p value < 0.05. Similarly, the intervention group reported significantly higher cases of skin infections (14.7%) as compared to the control group (2.0%). Abnormal bleeding was significantly prevalent (15.9%) among intervention group compared to the control group (6.4%).

Table 2: Self-reported Health conditions among intervention and control group

Variables	Intervention group, n (%)	Control group, n (%)	p-value
Stomach-ache			
Yes	14 (5.6)	2 (0.8)	0.002**
No	238 (94.4)	247 (99.2)	
Body ache			
Yes	105 (41.7)	63 (25.3)	< 0.001*
No	147 (58.3)	186 (74.7)	
Skin infections			
Yes	37 (14.7)	5 (2.0)	< 0.001*
No	215 (85.3)	244 (98.0)	
No	211 (83.7)	213 (85.5)	
Worrisome vaginal discharge			0.013**
Yes	30 (11.9)	14 (5.6)	
No	222 (88.1)	235 (94.4)	
Abnormal bleeding			< 0.001*
Yes	40 (15.9)	16 (6.4)	
No	212 (84.1)	233 (93.6)	

*Fisher Test is used
** Statistically significant at p value≤0.05

4. LEVEL OF RISKS

The health-related symptoms were categorized as low, moderate and high risk. The low-risk category comprised of 4 variables i.e. tobacco, smoking, gutka chewer and alcohol consumption. The moderate risk comprises of 9 variables which are fever, cough/cold, stomach-ache, headache, body ache, skin infection, diarrhoea, oral infection and Urinary Tract Infection (UTI). High risk category comprises of 5 variables: HPV vaccination, worrisome vaginal discharge, abnormal bleeding, vaginal bleeding, abnormal discharge.

Worrisome vaginal discharge, abnormal bleeding, abnormal discharge and vaginal bleeding are significantly associated with high-risk status in both groups with p value < 0.001. For sparse outcomes (e.g., VIA positivity), Fisher's exact test was used. VIA findings were not significantly associated with high-risk status in both groups.

Association between High-Risk group and sociodemographic characteristics
A logistic regression model was used to identify factors associated with high risk among the high-risk group population. Variables with p < 0.2 were included, excluding those with wide confidence intervals. Adjusted odds ratios (AOR) were calculated, controlling for group type to assess intervention effects. Significant factors associated with high risk included tobacco use, acute illness, oral infections, and diarrhoea/vomiting, while fever showed a protective effect. Other symptoms like cough/cold, body ache, skin infections, and UTIs were not significant after adjustment.

Table 3: Logistic Regression modelling among High-Risk group

Characteristics	Total	Unadjusted OR (95% CI)			Adjusted OR (95% CI)		
		OR	95% CI	p-value	AOR	95% CI	p-value
Age Groups							
≤ 45 years	251	-		0.746	1.086	(0.697, 1.693)	0.714
>45 years	250	1.066	(0.724, 1.568)				
Tobacco Consumption							
Yes	56	3.6	(2.04, 6.355)	<0.001*	3.176	(1.686, 5.981)	< 0.001*
No	445	-			-		
Acute Illness							
Yes	19	14.594	(4.183, 50.913)	<0.001*			
No	482	-					
Fever							
Yes	107	0.696	(0.424, 1.144)	0.153	0.447	(0.246, 0.812)	0.008*
No	394	-			-		
Cough/cold							
Yes	42	2.702	(1.426, 5.118)	0.002*	1.602	(0.745, 3.441)	0.228
No	459	-			-		
Body-ache							
Yes	168	1.491	(0.998, 2.227)	0.051*	1.328	(0.858, 2.057)	0.204
No	333	-			-		
Skin Infections							
Yes	42	1.961	(1.029, 3.375)	0.041*	0.805	(0.347, 1.868)	0.614
No	459	-			-		
Diarrhea/Vomiting							
Yes	31	28.160	(8.408, 94.314)	<0.001*			
No	470	-					
Oral Infections							
Yes	30	5.536	(2.522, 12.151)	<0.001*	3.968	(1.607, 9.800)	0.003*
No	471	-			-		
Urinary Tract Infections							
Yes	77	1.715	(1.034, 2.844)	0.037*	1.338	(0.755, 2.371)	0.318
No	424	-			-		

* The odds ratios are adjusted for group where intervention group is taken as reference.

5. DISCUSSION

Government of India has launched National Programme for Prevention and Control of Non-Communicable Diseases (NP-NCD) previously known as National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke (NPCDCS) in 2010 in 21 states with the focus to prevent non-communicable diseases. Under NP-NCD, identification of risk factor through population-based screening for individuals aged more than 30 years has been considered as the primary strategy for NCDs such as Diabetes, Hypertension and Cancers (Cervical, Oral and Breast), COPD, Asthma etc.

In line with this vision, this study provides valuable insights into the association of various factors, including tobacco consumption, acute illness, and oral infections, with cancer risks, leveraging digital health innovation. The present study implemented and evaluated the android-based smartphone application for the real time identification of risk factors for cervical cancer and its association with sociodemographic characteristics. Study conducted by Ryhänen AM et al reported the importance and of digital devices for the multiple intervention for patient education and Behaviour insights[12]. Evidence from previous studies also shown promising results for the utilization and implementation of smartphone application for wider range of NCDs[13,14,15].

Evidence from the previous studies reported the utilization of mobile applications shows a promising result in improving the patient education and health care workers about Ebola in Africa [16] and HIV and Hepatitis B.[17]

Through mobile application, the present study also demonstrates the statistically significant difference for more than five self-reported heath conditions such as stomach ache, body ache, skin infections, worrisome vaginal discharge, abnormal bleeding among intervention and control group which are considered as the vital risk factors for cervical cancer.

The level of risk has been categorized as high, medium and low based on the multiple parameters which could serve as a marker for knowledge about their health behaviour. Our study suggests no statistically significant difference in the identification of risks between two groups. Previous studies highlighted that multiple education interventions have significantly impacted in spreading awareness for cervical cancer among larger population[18].

Interestingly, fever was associated with lower odds of cancer risk. This finding suggest that fever may reflect as a marker of robust immune responses among study participants and further supported by the study conducted by Dunn et al. in 2002 which explored the immune surveillance in cancer (Dunn et al., 2002). Additionally, digital health platforms can further provide this protective association by analysing fever patterns in cervical cancer progression on the real time basis enhancing early diagnosis of cervical cancer.

Tobacco consumption emerged as a significant risk factor for many NCDs such as Cancer, Hypertension, COPD, Asthma etc. In our study, finding suggested that adjusted odds led to a threefold increase in cancer risk among study population. This aligns with a wealth of evidence identifying tobacco as a leading cause of cancers, particularly oral, lung, and oesophageal cancers[19].

Participants with acute illnesses were at significantly higher risk of developing cervical cancer. Additionally, oral infections demonstrated strong associations with cancer risk. This is in line with the findings of the study conducted by Balkwill & Mantovani in 2001 linked chronic infections and inflammation to oncogenesis. Guha et al. in 2007 reported the associated between persistent oral infections and head and neck cancers has been well-documented. Incorporating such data into cancer dashboards can enable real-time monitoring of infection-associated cancer risks, aiding in early detection and prevention. Ricard-Gauthier et al. in their study reported the higher feasibility and reliability of smartphone innovations for cervical cancer among Low resource settings[20].

The association between diarrhoea/vomiting and cancer risk highlights the role of gastrointestinal disturbances in identifying potential malignancies, such as colorectal or gastric cancers. Sung et al in 2021 also highlighted the role and emphasized the importance of gastrointestinal symptoms as early indicators of cancer and these findings are in line with the findings of our study.

6. CONCLUSION

The Mcerv mobile application proved to be a valuable tool for enhancing cervical cancer risk assessment, offering structured, real-time data collection and automated classification of risk levels. Compared to traditional paper-based screening, the digital approach improved the identification of important modifiable risk factors such as tobacco use, infections, and gastrointestinal symptoms. These differences were statistically significant and indicate the app's potential to support faster, more accurate screening in clinical and community settings. The ability to stratify individuals based on

risk levels can help prioritize follow-up care and strengthen the public health response. Additionally, integrating this tool with digital dashboards can provide actionable insights for health authorities, enabling them to plan focused awareness campaigns and monitor trends among high-risk groups. By facilitating timely interventions and improving data quality, such digital solutions are especially beneficial in resource-constrained environments, contributing to more effective prevention and early detection of cervical cancer. Strengths and Implications

The study's strength lies in its comprehensive statistical approach, combining univariate and multivariate analyses to identify independent risk factors. These findings can inform the development of dashboards that integrate population health data with clinical outcomes, ensuring a proactive approach to cancer prevention.

REFERENCES

[1] Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates. *CA Cancer J Clin*. 2018;68(6):394–424. doi:10.3322/caac.21492.

[2] Jokhadze N, Das A, Dizon DS. Global cancer statistics: A healthy population relies on population health. *CA Cancer J Clin*. 2024;74(3):224–6. doi:10.3322/caac.21889.

[3] Ramamoorthy T, Kulothungan V, Sathishkumar K, et al. Burden of cervical cancer in India: estimates of years of life lost, years lived with disability and disability adjusted life years at national and subnational levels using the National Cancer Registry Programme data. *Reprod Health*. 2024;21:111. doi:10.1186/s12978-024-01837-7.

[4] World Health Organization. Global strategy to accelerate the elimination of cervical cancer as a public health problem [Internet]. Geneva: WHO; 2020 [cited 2025 Jul 6]. Available from: https://www.who.int/publications/i/item/9789240014107

[5] World Health Organization. Human papillomavirus (HPV) and cervical cancer [Internet]. Geneva: WHO; 2022 [cited 2025 Jul 6]. Available from: https://www.who.int/news-room/fact-sheets/detail/human-papillomavirus-(hpv)-and-cervical-cancer

[6] Ministry of Health and Family Welfare, Government of India. National Programme for Prevention and Control of Non-Communicable Diseases (NP-NCD): Operational Guidelines [Internet]. New Delhi: MoHFW; 2023 [cited 2025 Jul 6]. Available from: https://www.mohfw.gov.in/sites/default/files/NP-NCD%20Operational%20Guidelines_0.pdf

[7] Black E, Richmond R. Prevention of cervical cancer in sub-Saharan Africa: the advantages and challenges of HPV vaccination. *Vaccines (Basel)*. 2018;6(3):61. doi:10.3390/vaccines6030061. PMID: 29933603

[8] Rossman AH, Reid HW, Pieters MM, Mizelle C, von Isenburg M, Ramanujam N, et al. Digital health strategies for cervical cancer control in low- and middle-income countries: systematic review of current implementations and gaps in research. *J Med Internet Res*. 2021;23(5):e23350. doi:10.2196/23350. PMID: 34042592

[9] Quintiliani L, Cantarelli G, Ciancio G, Imoize AL, Afolabi OO, Zennaro F. mHealth for cervical cancer prevention in low- and middle-income countries: a systematic review. *JMIR Mhealth Uhealth*. 2022;10(7):e35622. doi:10.2196/35622. PMID: 35895894

[10] Sai Bharath CNV, Gupta SK, Islam KM, Bhoi B, Sharma A, Kapoor R, et al. Electronic tool for cervical cancer risk. *Natl J Community Med*. 2024;15(5):395–9.

[11] Nassiri N, Niazi M, Bagheri M, Amini A, Doshmangir L. Use of digital health technologies in non-communicable disease management in low- and middle-income countries: a systematic review. *BMC Public Health*. 2022;22(1):57. doi:10.1186/s12889-021-12419-1. PMID: 35012549

[12] Shivashankar R, Kondal D, Ali MK, et al. Mobile health intervention in improving lifestyle behaviors among high-risk individuals for cardiovascular disease in India: A randomized controlled trial. *Glob Heart*. 2019;14(1):43–52. doi:10.1016/j.gheart.2019.01.003. PMID: 30871885

[13] Plummer M, Herrero R, Franceschi S, Meijer CJ, Snijders P, Bosch FX, et al. Smoking and cervical cancer: pooled analysis of the IARC multi-centric case–control study. *Cancer Causes Control*. 2003;14(9):805–14. doi:10.1023/B:CACO.0000003811.98261.3f. PMID: 14674738

[14] Castellsagué X. Natural history and epidemiology of HPV infection and cervical cancer. *Gynecol Oncol*. 2008;110(3 Suppl 2):S4–7. doi:10.1016/j.ygyno.2008.07.045. PMID: 18760711

[15] Whitelaw S, Mamas MA, Topol E, Van Spall HGC. Applications of digital technology in COVID-19 pandemic planning and response. *Lancet Digit Health*. 2020;2(8):e435–40. doi:10.1016/S2589-7500(20)30142-4. PMID: 32835195

[16] Labrique AB, Vasudevan L, Kochi E, Fabricant R, Mehl G. mHealth innovations as health system strengthening tools: 12 common applications and a visual framework. *Glob Health Sci Pract*. 2013;1(2):160–71. doi:10.9745/GHSP-D-13-00031. PMID: 25276529

[17] Higgins JP, Green S, editors. *Cochrane Handbook for Systematic Reviews of Interventions*. Version 5.1.0 [Internet]. Oxford: The Cochrane Collaboration; 2011 [cited 2025 Jul 6]. Available from: https://training.cochrane.org/handbook

[18] Bruni L, Albero G, Serrano B, Mena M, Collado JJ, Gómez D, et al. Human Papillomavirus and Related Diseases in India. Summary Report 2023-02-20. ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre) [Internet]. 2023 [cited 2025 Jul 6]. Available from: https://hpvcentre.net/statistics/reports/IND.pdf

[19] Dunn GP, Old LJ, Schreiber RD. The immunobiology of cancer immunoediting and the elimination, equilibrium, and escape hypothesis. *Nat Immunol*. 2002;3(11):991–8. doi:10.1038/ni1102-991. PMID: 12407405

[20] Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2021;71 (3):209–49. doi:10.3322/caac.21660. PMID: 33538338