






# State of the Science of Scale-Up of Cancer Prevention and Early Detection Interventions in Low- and Middle-Income Countries: A Scoping Review

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## ABSTRACT

**PURPOSE** Cancer deaths in low- and middle-income countries (LMICs) will nearly double by 2040. Available evidence-based interventions (EBIs) for cancer prevention and early detection can reduce cancer-related mortality, yet there is a lack of evidence on effectively scaling these EBIs in LMIC settings.

**METHODS** We conducted a scoping review to identify published literature from six databases between 2012 and 2022 that described efforts for scaling cancer prevention and early detection EBIs in LMICs. Included studies met one of two definitions of scale-up: (1) deliberate efforts to increase the impact of effective intervention to benefit more people or (2) an intervention shown to be efficacious on a small scale expanded under real-world conditions to reach a greater proportion of eligible population. Study characteristics, including EBIs, implementation strategies, and outcomes used, were summarized using frameworks from the field of implementation science.

**RESULTS** This search yielded 3,076 abstracts, with 24 studies eligible for inclusion. Included studies focused on a number of cancer sites including cervical (67%), breast (13%), breast and cervical (13%), liver (4%), and colon (4%). Commonly reported scale-up strategies included developing stakeholder inter-relationships, training and education, and changing infrastructure. Barriers to scale-up were reported at individual, health facility, and community levels. Few studies reported applying conceptual frameworks to guide strategy selection and evaluation.

**CONCLUSION** Although there were relatively few published reports, this scoping review offers insight into the approaches used by LMICs to scale up cancer EBIs, including common strategies and barriers. More importantly, it illustrates the urgent need to fill gaps in research to guide best practices for bringing the implementation of cancer EBIs to scale in LMICs.

## ACCOMPANYING CONTENT

 Appendix

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## INTRODUCTION

Evidence suggests that cancer mortality in low- and middle-income countries (LMICs) will nearly double over the next 20 years. By 2040, cancer mortality in LMICs will account for almost 70% of the estimated 16 million global cancer deaths.<sup>1</sup> To curb the growing global burden of cancer that is largely concentrated in LMICs, the WHO has launched several initiatives, including the Global Breast Cancer Initiative,<sup>2</sup> the Global Strategy to Accelerate the Elimination of Cervical Cancer,<sup>3</sup> and the Best Buys report that recommends cost-effective approaches for cancer prevention.<sup>4,5</sup> Despite the clear evidence for cancer prevention and early detection interventions and the

investments made to date, scale-up in LMICs has been slow. To reach at-risk populations and reduce inequities in cancer outcomes between high-income countries (HICs) and LMICs, effective guidance for scaling evidence-based cancer prevention and early detection interventions is urgently needed.

Scaling evidence-based cancer prevention and early detection interventions is challenging for both HICs and LMICs. Although HICs have implemented national and regional initiatives to reduce the cancer burden, disparities in access persist.<sup>6</sup> In LMICs, there are a relatively large number of successful pilot and demonstration projects implementing evidence-based interventions (EBIs) for

cancer prevention and early detection,<sup>7-9</sup> but many have experienced barriers in scaling these interventions to regional and national levels.<sup>10,11</sup> Yet, there are examples of successful scale-up programs in LMICs to address other public health priorities although the disease complexity and continuums of care differ. For example, with appropriate funding, resources, and engagement at a national level, LMICs have demonstrated significant capacity to scale health services for HIV,<sup>12,13</sup> maternal and child health,<sup>14</sup> and malaria.<sup>15</sup>

Currently, there is little guidance for scaling-up cancer prevention and early detection EBIs in resource-constrained environments, including what strategies are most effective and at what level (ie, individual, system). To begin to fill this gap in knowledge, we conducted a scoping literature review focusing on LMICs.<sup>16,17</sup> To select relevant articles, we used two common definitions of scale-up: (1) the WHO definition of deliberate efforts to increase the impact of effective intervention to benefit more people and to foster policy and program development on a lasting basis<sup>18</sup> and (2) a definition by Milat et al,<sup>19</sup> which defines scale-up as interventions shown to be efficacious on a small scale and/or under controlled conditions to be expanded under real-world conditions to reach a greater proportion of eligible population.

This analysis was guided by principles of implementation science (IS) to provide a common language when describing scale-up study characteristics. IS offers a set of rigorous methods and a systematic approach to describe implementation strategies to overcome identified barriers and accelerate the implementation of EBIs in real-world settings, allowing for the adaptation and flexibility needed to implement contextually appropriate and sustainable EBIs.<sup>8</sup> The application of IS methods can further inform efforts to scale effective interventions to regional and national levels in LMICs. This review summarizes the current literature on scaling up EBIs in LMICs to reduce the high cancer burden and mortality in these settings.

## METHODS

### Search Strategy and Inclusion and Exclusion Criteria

A scoping review was selected to examine the emerging evidence for effective approaches to scaling evidence-based cancer prevention and early detection interventions only for cancer control.<sup>20</sup> The review was guided by the Johanna Briggs Institute and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension.<sup>21,22</sup> The search strategy was developed with the guidance from a Life Science Librarian at New York University (H.L.). Our research strategy cast a wide net to identify studies that reported on scale-up per the two definitions previously specified.<sup>18,19</sup> Published articles were identified using Medline (PubMed); Embase and Global Health (Ovid); CINAHL (EBSCO); PsycInfo (PsycNet); and Web of Science, Scopus. The search strategy is provided in Appendix [Table A1](#).

For the search strategy, all citations were saved and uploaded to Endnote (v.X9, Clarivate Analytics, 2013), where duplicates were removed on the basis of the Wichor Bramer method.<sup>21,23</sup> Studies were then uploaded to Covidence (Veritas Health Innovation, Melbourne, Australia), where deduplication filters were applied and articles were analyzed. Studies were included if they were (1) published between January 1, 2012, and December 31, 2022; (2) published in the English language; (3) met at least one of two definitions of scale-up noted above; (4) evaluated a primary (eg, human papillomavirus [HPV] vaccination) or secondary cancer prevention (eg, breast cancer early detection) intervention or program; and (5) conducted in a lower-, lower-middle-, or upper-middle-income country on the basis of the World Bank<sup>24</sup> LMIC designation. Studies were excluded if they (1) were conducted in a HIC, (2) reported scale-up of cancer treatment only (eg, scaling-up radiotherapy); or (3) were articles without primary data collection or original analysis, such as commentary/opinion articles, articles reporting monitoring and surveillance data, abstract-only studies, reviews, and unpublished work (Appendix [Table A2](#)).

### Multistage Screening Process

A multistage review process was conducted using Covidence. Stage 1: titles were independently screened by T.M.F.-K. and G.G.A. Stage 2: abstracts were independently reviewed by T.M.F.-K. and G.G.A. During this stage, some studies were tagged for manual review of references. Eligible articles found in the reference search were then added to the first stage (ie, title screening). Stage 3: studies eligible for full-text review were saved and reviewed by T.M.F.-K. and G.G.A. Discrepancies were resolved through discussion and mutual agreement. Stage 4: four authors, T.M.F.-K., A.F.R., G.G.A., and D.S., screened articles in full-text review. Stage 5: an additional manual search of the reference lists of all articles included in the full-text review (n = 34). We then evaluated eligibility of these additional articles on the basis of a review of the abstract using the same criteria described in stages 1-3.

### Data Extraction

Papers were double coded by T.M.F.-K. and G.G.A. Data extraction was conducted directly in Covidence. Open-text fields were reviewed by T.M.F.-K. and G.G.A. and summarized. An open-text field was used to determine if IS scale-up framework/theories/methods were used in the scale-up study. Most characteristics were captured categorically: level of scale-up (regional, national, or others), scale-up setting (rural, urban, periurban, or unreported), scale-up institutional-level target (hospitals, health clinics, primary health care, schools, communities, or others), and scale-up strategy target population (providers, patients, health care leadership, policymaker, or others). Studies were characterized as primary prevention (eg, vaccines) and/or secondary prevention (eg, screening, early detection). Study designs included cross-sectional, randomized controlled

trial, prospective, retrospective, cohort, qualitative, prepost, mixed methods, descriptive, evaluation, or others and were documented if qualitative data were collected (interviews, focus groups, or others). The dates that a study was implemented, the duration, the sample size, and age of the target population were captured as numerical data. The explicit mention of scale-up in the study text was recorded dichotomously as yes or no.

### Stakeholder Partnerships, Scale-Up Strategies, and Barriers

An open-text field was used to capture data on stakeholder partnerships, and then the data were categorized into seven mutually exclusive groups: (1) international partners, where at least one partner was from outside the country that was scaling the intervention; (2) national partners, where one partner operated in the country at the national level; (3) National Ministry of Health (MOH), indicating that the MOH was involved in any aspect related to scaling the intervention; (4) regional partners, where one partner operated in the country beyond the local (eg, city or village) level; (5) community partners, where those operating within the community in which the intervention was being scaled; (6) international pharmaceutical partners, indicating a pharmaceutical company outside the country scaling the intervention; and (7) academic partners, indicating a university or research center inside or outside the country.

Strategies were captured in an open-text field using the exact language from the article and subsequently categorized. The Expert Recommendations for Implementing Change (ERIC) taxonomy,<sup>25</sup> a compilation of strategies on the basis of systematic literature review and expert recommendations, guided the categorization.<sup>25</sup> Specifically, ERIC's nine domains were used, which represent an abbreviated version of the original 73 implementation strategies.<sup>26</sup> The nine domains include: evaluative and iterative strategies, provide interactive assistance, adapt and tailor to context, develop stakeholder inter-relationships, train and educate stakeholders, support clinicians, engage consumers, use financial strategies, and change infrastructure.<sup>25</sup> The approach by which strategies were implemented was recorded as a dichotomous variable: top-down (study described the national program) or bottom-up (study described the program started with pilot and then scaled regionally or nationally). Partnerships with stakeholders were common and included National Ministries and pharmaceutical and community relationships. Finally, barriers to scale-up that were mentioned in the studies were documented in an open-text field and subsequently grouped into three levels: individual, health facility, or community.

### Evaluation Frameworks

IS evaluation frameworks Reach, Effectiveness, Adoption, Implementation, and Maintenance (RE-AIM) and Proctor (eg, fidelity, acceptability, appropriateness; adherence;

feasibility; penetration; implementation cost; sustainability; and adaptability) were used to identify IS outcomes.<sup>27,28</sup> RE-AIM and Proctor outcomes were included if specifically mentioned by name in the study abstract, introduction, methods, results, and/or discussion.

## RESULTS

### Overall Study Characteristics

The study selection process yielded 24 studies (Fig 1).<sup>29-53</sup> Table 1 provides the overall summary of study characteristics, and Appendix Table A3 includes detailed characteristics. Included were six low-income countries (25%), seven lower-middle-income countries (29.2%), and nine upper-middle-income countries (38%). Two studies included more than one country: one study (4%) included a low-income and upper-middle-income country and the other (4%) included two lower-middle-income countries and an upper-middle-income country. Twelve studies (50%) were conducted in Africa; six (25%) in South Asia, East Asia, or the Pacific; and six (35%) in Latin America/Caribbean. Seven (30%) studies were published between 2013 and 2015, seven (30%) studies were published between 2016 and 2018, and 10 (40%) studies were published between 2019 and 2022. Thirteen (54%) studies explicitly used the term scale-up, and three (13%) studies intentionally incorporated an IS framework. Soi et al<sup>50</sup> used CFIR,<sup>54</sup> Arrossi et al<sup>42</sup> described using the evaluation framework RE-AIM,<sup>28</sup> and Johnson et al<sup>33</sup> specifically studied adherence from the Proctor<sup>27</sup> evaluation framework.

Eleven studies (46%) scaled the EBI to a national level, eight (33%) to a regional level (ie, region within one country), and five (8%) to a district or city level. Sixteen studies (67%) started with a pilot and then scaled-up (bottom-up). Most studies (70%, n = 17) described scaling secondary prevention EBIs (eg, cervical cancer screening), three scaled a primary prevention intervention (eg, vaccines), and four scaled both primary and secondary prevention EBIs. Sixteen (67%) scale-up programs focused on cervical cancer, three (13%) on breast cancer, and three (13%) on both breast and cervical cancers. Only one study (4%) focused on liver cancer, and one (4%) on colon cancer. The median duration of scale-up was 36 months (IQR, 24-44). Participant sample sizes varied widely from 4,015 to 105,527. Nineteen studies (79%) collected quantitative data, three (13%) collected qualitative data, and two (8%) collected both quantitative and qualitative data.

### Scale-Up Strategies

The implementation strategies used to scale up the cancer prevention and early detection programs are presented in Table 2 with illustrative examples (Appendix Table A4 lists all strategies used). All studies used one or more implementation strategies<sup>26</sup> that fit into one of ERIC's nine domains.<sup>25</sup> All 24 studies (100%) reported having

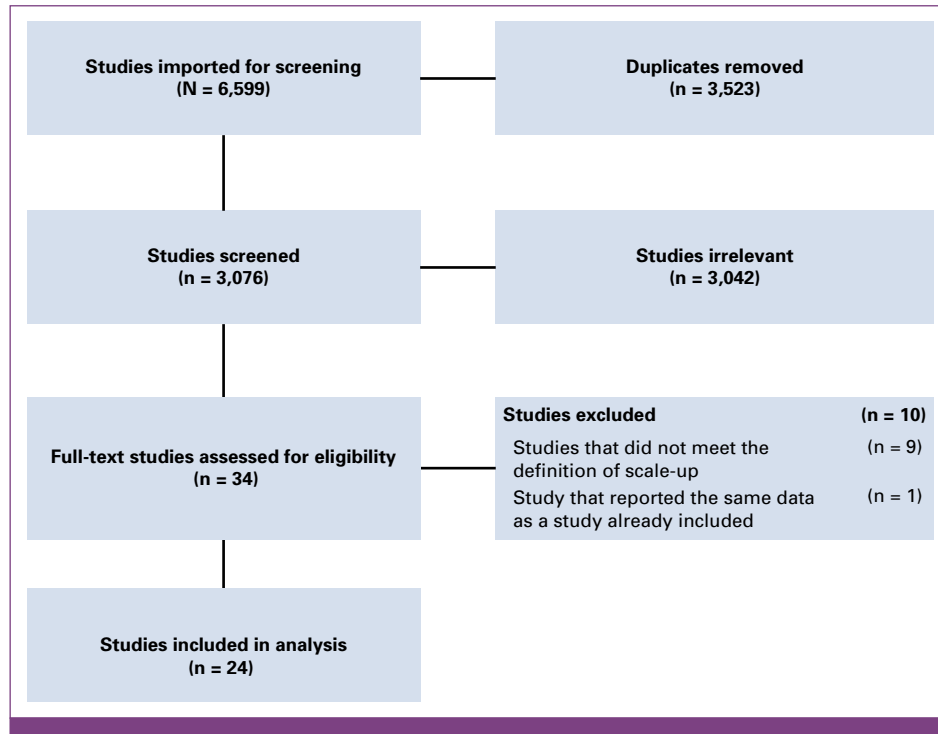


FIG 1. Flowchart of the article selection process for scoping review.

stakeholder partnerships, but only 12 (50%) of those studies identified stakeholder inter-relationships as a strategy for scale-up. Nineteen studies (79%) used the train and educate stakeholders' strategy; 16 studies (67%) used change in infrastructure; 14 studies (58%) used engaging consumers; 10 studies (42%) described using evaluative and iterative strategies; six (25%) referenced providing interactive assistance; six (25%) described using financial strategies; and three (13%) referenced adapt and tailor to context strategies. No studies specifically described strategies aimed at supporting clinicians.

Table 3 presents the types of stakeholder partnerships reported in the 24 scale-up studies. International partnerships were reported in 18 studies (75%); national partnerships were reported in 16 studies (66%); community-level partnerships were reported in 12 (50%); partnerships with the National MOH were reported in nine (38%); seven (29%) mentioned regional partnerships; international pharmaceutical partnerships were reported in four (17%); and academic partnerships were reported in five (21%). The role of the different partners in the scale-up of the cancer prevention and early detection interventions primarily included financial support, community awareness, provision of product, and access to laboratory facilities.

### Evaluation Frameworks and Outcomes

Two studies explicitly mentioned using IS evaluation frameworks: the study by Arrossi et al<sup>42</sup> used RE-AIM<sup>28</sup> and

the study by Johnson et al<sup>33</sup> specifically studied adherence.<sup>27</sup> While the remaining studies did not explicitly mention the use of an IS evaluation framework, most included one or more IS outcomes by name (n = 20). Eleven studies explicitly evaluated a RE-AIM outcome<sup>55</sup>: reach (n = 3), effectiveness (n = 2), adoption (n = 4), implementation (n = 1), and maintenance (n = 1). Twenty-two studies identified one of Proctor's eight IS outcomes<sup>27</sup> by name: fidelity (n = 3), adherence (n = 2), acceptability (n = 9), appropriateness (n = 1), feasibility (n = 10), penetration (n = 6), implementation cost (n = 2), sustainability (n = 7), and adaptability (n = 2; Table 1).

### Study-Reported Barriers

The reported barriers to scale-up are listed in Table 4. Although these were defined as scale-up studies, most barriers were reported at the individual level (n = 10). This included, for example, lack of knowledge about prevention interventions among patients and low participant compliance. Barriers at the health care center level (n = 9) included a lack of funding and infrastructure (eg, equipment, record systems) needed to support program implementation and lack of trained personnel (eg, supervisory staff, specialized staff). Community-level barriers (n = 4) included challenges in reaching eligible groups, a lack of relationships between the community and health care centers, and community beliefs and values that do not align with specific prevention approaches (eg, religious values related to vaccination).

**TABLE 1. Summary Characteristics of the 24 Included Scale-Up Studies**

Study Characteristic	No. (%)
Total	24 (100)
World bank classification	
Low-income	6 (25.0)
Lower-middle-income	7 (29.2)
Upper-middle-income	9 (37.5)
Low-income country; upper-middle-income	1 (4.2)
Lower-middle income; upper-middle-income	1 (4.2)
World regional	
Africa	12 (50.0)
South Asia/East Asia and Pacific	6 (25.0)
Latin America/Caribbean	6 (25.0)
Years published	
2013-2015	7 (29.2)
2016-2018	7 (29.2)
2019-2022	10 (41.7)
Explicitly mention scale-up	13 (54.2)
Implementation science frameworks used in the scale-up studies	3 (12.5)
CFIR	1 (4.2)
RE-AIM	1 (4.2)
Proctor	1 (4.2)
Scale to	
Regional level (ie, within one country)	8 (33.3)
National level	11 (45.8)
Other (ie, district, city)	5 (20.8)
Scale-up method	
Top-down (national program)	8 (33.3)
Bottom-up (start with pilot and then scale it up)	16 (66.7)
Evidence-based intervention	
Primary intervention	3 (12.5)
Secondary prevention intervention	17 (70.8)
Both primary and secondary	4 (16.7)
Target cancer	
Cervical	16 (66.7)
Breast	3 (12.5)
Cervical and breast	3 (12.5)
Colon	1 (4.2)
Liver	1 (4.2)
Study duration and sample size, median (IQR)	
Duration of scale-up, months	36 (24-44)
No. of participants	17,067 (4,015-105,527)
Data collected	
Qualitative	3 (12.5)
Quantitative	19 (79.2)
Qualitative and quantitative	2 (8.3)
Implementation strategies (ERIC's nine domains)	
Develop stakeholder inter-relationships	24 (100)
Train and educate stakeholders	19 (79.2)
Change infrastructure	18 (75.0)
Engage consumers	12 (50.0)

(continued in next column)

**TABLE 1. Summary Characteristics of the 24 Included Scale-Up Studies (continued)**

Study Characteristic	No. (%)
Use evaluative and iterative strategies	10 (41.7)
Provide interactive assistance	6 (25.0)
Use financial strategies	6 (25.0)
Adapt and tailor to context	3 (12.5)
Support clinicians	0 (0)
Evaluation frameworks used in the scale-up studies	22 (88)
RE-AIM outcomes—No. of total studies	7 (29.2)
Reach	3 (12.5)
Effectiveness	2 (8.3)
Adoption	4 (16.7)
Implementation	1 (4.2)
Maintenance	1 (4.2)
Proctor outcomes—No. of total studies	22 (88)
Fidelity	3 (12.5)
Adherence	2 (8.3)
Acceptability	9 (37.5)
Appropriateness	1 (4.2)
Feasibility	10 (41.7)
Penetration	6 (25.0)
Implementation cost	2 (8.3)
Sustainability	9 (25.0)
Adaptability	2 (8.3)

Abbreviations: CFIR, Consolidated Framework for Implementation Research; ERIC, Expert Recommendations for Implementing Change; RE-AIM, Reach, Effectiveness, Adoption, Implementation, and Maintenance.

## DISCUSSION

This scoping review identified only 24 studies describing approaches to scaling EBIs for cancer prevention and early detection in LMICs, highlighting a critical need for more work in this area. Among these studies, there was a disproportionate focus on cervical and breast cancers, with few describing scale-up of cancer prevention and early detection EBIs for lung and liver cancers, and none for other common cancer types (eg, colorectal). Breast cancer and cervical cancer are the two most common cancers among women and have been prioritized by key global organizations like the WHO and USAID.<sup>2,56,57</sup> These cancers also have more established EBIs, including ones that are increasingly feasible in LMIC settings. That said, the most prevalent cancer types vary by country and region, and therefore, resource allocation and policy changes that support scale-up will reflect those differences.<sup>58-60</sup> The small number of studies, albeit in English language only publications, belies the scope of the global cancer burden of disease in LMICs and the attention cancer disparities continue to receive. For example, the 2030 Agenda for Sustainability Goals provides a road map for the prevention and control of cancer and

**TABLE 2. Implementation Science Strategies Identified According to ERIC's Nine Domains**

IS Strategy	No. of Studies Using Strategy	Strategy Target	Example Strategies Cited
Train and educate stakeholders	19	Hospital/health care personnel, <sup>2,29</sup> CHW and doctors/providers, <sup>30,42,49</sup> providers, <sup>34-36,39,40,45,47,52</sup> CHW/health care workers, <sup>31,37,38,43</sup> nurses, <sup>43,48</sup> physicians and nurses, <sup>49</sup> MOH staff, <sup>31</sup> female community health workers, <sup>32</sup> patients, <sup>35,37</sup> community <sup>48</sup>	Highly skilled health care providers who delivered capacity-strengthening training to a small group of STMM volunteers who became trainers in the Philippines and proceeded to transfer those skills to local health care providers. As a result, upskilling through training becomes self-sustaining over time <sup>35</sup> ; the program used a training curriculum adapted from the WHO's IARC, and key nurses underwent additional training in cryotherapy and cervicography in Lusaka, at the Centre for Infectious Disease Research in Zambia. These key nurses then trained (using IARC-based materials) and mentored other local MOH nurses who staffed the cervical cancer screening services in their clinics <sup>43</sup>
Change infrastructure	16	Nurses <sup>33</sup> ; health system/hospitals; health centers <sup>29,32,36,40,41,45,47-49</sup> ; patients <sup>29,37,46,48,52</sup> ; CHW <sup>49</sup> ; clinics <sup>31,37</sup> ; prevention, screening, and treatment delivery systems from the community to the tertiary level <sup>36</sup> ; staff <sup>38</sup> ; data clerks <sup>46</sup> ; patients and clinicians <sup>44</sup> ; providers only <sup>52</sup>	Development of data collection tools: individual client form, client registry, and monthly summary sheet; provision of initial equipment for VIA, cryotherapy, and LEEP including parts and supplies <sup>45</sup> ; vaccination data were inserted in a specific vaccination program database, namely, SIVAC, which functions as an electronic vaccination notebook, informing when the next vaccination routine for adolescents will be held <sup>52</sup>
Engage consumers	14	Patients, <sup>34-36,38,42,43,52</sup> community/consumers/population, <sup>30,32,39,41,43-45,49</sup> patients and clinicians, <sup>44</sup> participants, <sup>38</sup> patients and consumers, <sup>52</sup> CHW <sup>43</sup>	During the visit, CHWs provided women with information about cervical cancer prevention and HPV testing and then offered them HPV self-collection, followed by a 10-minute step-by-step explanation on how to perform it using communication support material <sup>42</sup> ; Information Education Campaign was implemented by means of health talks, T-shirts, and print media to raise awareness about the necessity of screening <sup>43</sup>
Develop stakeholder inter-relationships	12	Community <sup>41</sup> ; stakeholders: teachers, health facility staff, district education managers, medical heads, and national program staff, as well as staff from research institutions and NGOs <sup>50</sup> ; hospitals, clinics, and community <sup>29</sup> ; private practitioners <sup>30</sup> ; collaboration between MOH and BUP <sup>33</sup> ; health system <sup>31</sup> ; teachers, village leaders, and CHWs <sup>34</sup> ; the governor of the province, mayors, and the provincial medical directors requesting their support and approval of the program <sup>35</sup> ; health care leadership <sup>44</sup> ; government officials and local health care providers <sup>35</sup> ; health system <sup>38</sup> ; AMPATH MUSOM collaboration <sup>43</sup>	Community-level stake holder engagement: We organized a meeting in each enumeration area with the help of the village head <sup>41</sup> ; hospitals formed collaborations with the local Women's Federation, Family Planning Commission, and the Community Board to develop outreach mechanisms that promote participant recall and periodical follow-up with high-risk individuals <sup>29</sup>
Use evaluative and iterative strategies	10	CHW, <sup>32,43</sup> staff, <sup>39,44,53</sup> health system <sup>30,32</sup> practitioners, <sup>30</sup> nurses, <sup>33</sup> NGO staff members <sup>31</sup>	SSV was to identify any gaps in the beginning of the program and find any appropriate solution <sup>30</sup> and review progress of each community health center; the CHCs were also required to submit monthly progress reports to the CDC of the district. The local CDC was responsible for the quality control of the whole process of the screening program <sup>39</sup>
Use financial strategies	6	Health system, <sup>34,42</sup> physicians, <sup>39</sup> consumers, <sup>30,39,45</sup> patients <sup>53</sup>	Increase incentives for physicians, paid with subsidies, the amount of which was associated with the quality control outcomes <sup>39</sup> ; the private practitioners provided cervical cancer screening at subsidized rates <sup>30</sup>
Provide interactive assistance	5	Nurses, <sup>33</sup> staff, <sup>38</sup> gynecologists/physicians, <sup>43</sup> staff and health care workers, <sup>38,45</sup> health system <sup>39</sup>	To balance the workloads, each designated hospital took charge of the referrals from several community health centers, which were determined according to the average travel distance of the participants to the hospital and the COL service capacity of the hospital <sup>39</sup> ; core group of local gynecologists from MUSOM underwent specialized training and continuous mentorship from visiting North American gynecologists to become skilled at colposcopy, biopsy, and LEEP, and a training and mentorship program in medical and surgical gynecologic oncology was developed <sup>43</sup>

(continued on following page)

**TABLE 2.** Implementation Science Strategies Identified According to ERIC's Nine Domains (continued)

IS Strategy	No. of Studies Using Strategy	Strategy Target	Example Strategies Cited
Adapt and tailor to context	3	Health systems from the community to the tertiary level, <sup>36</sup> patients/clinicians, <sup>44</sup> health care providers <sup>45</sup>	Adapt model by country <sup>36</sup> ; sessions were adapted to focus on the trainees' weaknesses identified through an initial assessment of baseline knowledge and skills <sup>45</sup>
Support clinicians	0		

Abbreviations: AMPATH, Academic Model Providing Access to Healthcare; BUP, Botswana-UPenn Partnership; CDC, Center for Disease Control and Prevention; CHC, community health centers; CHWs, community health workers; COL, colonoscopy; ERIC, Expert Recommendations for Implementing Change; HPV, human papillomavirus; IARC, International Agency for Research on Cancer; IS, implementation science; LEEP, loop electrical excision procedure; MOH, Ministry of Health; MUSOM, Moi University School of Medicine; NGOs, nongovernmental organizations; SSV, supportive supervision visit; STMM, short-term medical missions; VIA, visual inspection with acetic acid.

other noncommunicable diseases.<sup>61</sup> However, scaling-up evidence and the associated guidelines, tools, and policies is a complex process. Yet, only a few of the studies reported specific challenges or barriers to scale-up. Progress will require more transparency when reporting scale-up projects in terms of sharing challenges and resource needs and, similarly, a greater emphasis on developing and sharing best practices to overcome barriers to scaling cancer prevention and early detection EBIs.

Regardless of the cancer type, there are frameworks for implementing and scaling EBIs that address multilevel contextual challenges and can be adapted to different contexts.<sup>27,62</sup> For example, the WHO has defined global strategies for eliminating cervical cancer<sup>3</sup> that are applicable to other high-prevalence cancers. These include advocacy and communication, deep continuous commitment by national governments, local and national partnerships, understanding barriers, integrating screening and treatment into primary care, strengthening laboratory capacity, and ensuring that care is affordable. The articles reviewed

described using strategies such as stakeholder engagement, training, changing infrastructure, engaging consumers/patients, interactive assistance, and financing strategies. Broader system-level scale-up strategies were reported less frequently than individual-level approaches, yet achieving scale-up requires a multilevel approach. This includes the need for policies that ensure sustained government commitments to finance cancer screening and treatment at the health system level; the need to invest in developing IS training programs for researchers in LMICs, specifically as it relates to scale-up<sup>63</sup>; facilitating changes through processes such as staff retraining, mentoring, leadership development, and coaching provider incentives; monitoring and feedback; task sharing and other system changes; and at the individual level, education, communication, and shared decision making.<sup>62</sup>

There are several frameworks that offer guidance for scaling-up health interventions,<sup>17,19,62,64</sup> yet none of the studies reported using a framework for guiding the scale-up

**TABLE 3.** Types of Stakeholder Relationships Reported by Partner Level

Type of Relationship Reported by Partner Level	Income Level of Study Country				Studies
	Upper-Middle-Income (n = 9)	Lower-Middle-Income (n = 4)	Low-Income (n = 4)	Multi-Income (n = 5)	
International partners (foreign agency, NGO, foundation)	3	4	3	2	31-34,36,38,41,43-45,48
National partners (in-country organization, NGO)	2	5	2	1	30-32,35,36,41,42,47,49,53
Community partners (individuals, groups, or organizations based in the community where the intervention or program is being implemented)	4	2	3	—	29,30,34,35,39,41,45,52
National Ministry of Health	3	3	2	1	31,32,34,38,43-47
Regional partners (individuals, groups, or organizations based in the district or state near where the intervention or program is being implemented)	5	1	—	—	29,35,39,42,43,52
International pharmaceutical partners (provided product or product and access to laboratory)	1	1	2	1	34,36,38,41,52
Academic partners (universities in country or abroad)	1	2	1	1	30,33,35,36,45

NOTE. Some studies had more than one partner at each level. Multi-income refers to a study that included countries from different income levels (eg, one country was low-income, and one country was upper-middle-income).

Abbreviation: NGO, nongovernmental organization.

**TABLE 4. Identified Barriers to Scale-Up of Primary and Secondary Cancer EBIs in LMICs**

Barrier	Example
Individual	
Patients' fidelity (follow-up) to program	Poor communication about follow-up visits from providers to patients <sup>33</sup> Commuting costs and because of poor communication <sup>43</sup> Expansion of participants and program <sup>38</sup> Missed repeat cryotherapy at 1 year for those who tested VIA-positive <sup>47</sup> Embarrassment by female patients being screened by a male doctor <sup>38</sup>
Lack of information	Little knowledge about the disease HPV and the HPV vaccine <sup>52</sup> Breast cancer <sup>32</sup>
Low participant compliance	Low screening uptake or adherence <sup>32</sup> Varied compliance within specific subgroups (higher socioeconomic status of the participants in terms of education levels and employment status) <sup>39</sup>
Lack of access and resources	High costs of service and financial concerns <sup>34,45</sup> No insurance <sup>35</sup>
Health facility	
Poor infrastructure to support a program	Lack of ability to see referral through after screening for VIA, leading to program failure to treat VIA-positive eligible women <sup>47</sup> Lack of pathology-related infrastructure like lack of histopathologists <sup>43</sup> Difficulties in tracking referred patients <sup>45</sup>
Inaccurate reporting of program use	Varying performance of the screening across geographic areas not clearly reported and under-counting patients who completed follow-up treatment because of patients in urban areas that had easy access to follow-up care without having to follow the programs workflow, thereby not being observed in the data from the program reporting system <sup>39</sup>
Resource allocation and use	Lack of personnel/providers (at different levels including supervision staff, specialized personnel like gynecologists) available for the delivery of the intervention, <sup>31,38,43</sup> fatigue among existing staff <sup>43</sup> Reasons include staff turnover <sup>31</sup> Unavailability of the coordinating nurse, especially during Ramadan holidays <sup>41</sup> Few providers compared with patients in urban areas, low provider: patient ratio affected the number of patients screened and treated <sup>39</sup> Lack of supplies and equipment: stock-outs of key supplies including diagnostic kits, <sup>41,45</sup> cryotherapy machine, and gas for machine <sup>47</sup> Lack of specific equipment needed to perform screen and treatment <sup>40</sup>
Community	
Link to community	Targeting and reaching the eligible group <sup>50</sup> Lack of community health care worker ties at a blood bank compared with the community <sup>41</sup> Community transformations, because of high rates of migration out of service delivery area <sup>38</sup>
Value system/alignment with values	Linking community values the need for an HPV vaccine not in line with controversial issues such as virginity, which leads to refusal to vaccination. Identifying a need to connect with churches about health education <sup>52</sup>

Abbreviations: EBIs, evidence-based interventions; HPV, human papillomavirus; LMICs, low- and middle-income countries; VIA, visual inspection with acetic acid.

process. Barker et al<sup>17</sup> developed a framework that describes three main components of scaling-up: (1) using a clear sequence of activities needed to take interventions to scale (ie, setup, develop the scalable unit or the microsystem that can be replicated under appropriate conditions, test the scale-up, and go to full scale); (2) articulating the context and environmental factors, or mechanisms, that will foster scale-up of best practices; and (3) describing the infrastructure that is required to successful support scale-up. Barker integrates the Plan-Do-Study-Act process improvement approach as a core strategy that involves iterative testing and modification to enhance feasibility and fit as an EBI is scaled across systems and settings. Similarly, Zamboni et al<sup>64</sup> described a model that includes five phases (preparatory, initial planning, stakeholder workshop, follow-up, and scale-up). Both models emphasize testing/piloting and adoption and support system requirements (leadership, communication, social networks, data systems, human capacity, capability

for scale-up) that are subsequently complemented by individual-level strategies.<sup>17</sup>

Implementation and scale-up frameworks provide a structure for analyzing potential barriers and selecting theory-driven strategies on the basis of expected mechanisms needed to achieve large-scale programming. Three studies in our review used IS frameworks and specifically commented on organization-level strategies.<sup>33,42</sup> Soi et al<sup>50</sup> used the Consolidated Framework for Implementation Research (CFIR) to evaluate the implementation of HPV vaccine delivery in Mozambique, revealing several significant determinants of implementation successes and failures. They noted that CFIR was a useful and practical tool for researching health system implementation success determinants and that its unique methodology allowed for the comparison of constructs across different implementation efficiencies. Arrossi et al,<sup>42</sup> using the RE-AIM framework,



noted that facilitators of scaling-up HPV self-collection in Argentina included the organizational capacity of the provincial health system, sustainable funding for HPV testing, and local consensus about the value of the technology. Johnson et al,<sup>33</sup> who compared nurses' adherence between the pilot and scaled-up sites and determined main drivers of nonadherence across all sites, noted that successful scale-up might have been attributable to the program's intensive quality assurance monitoring. The approach or theory, as well as a focus on understanding multilevel contextual determinants of implementation, sustainability, and scale-up, is grounded in relevant intermediate outcomes such as acceptability, appropriateness, and cost. Together, these can help create the foundation for real-world relevant partnerships to translate research into practice at scale.

To this end, there are research funding opportunities such as those provided by institutions like the Center for Global Health at the National Cancer Institute to support IS for cancer prevention and control in LMICs. These opportunities support research to address the challenges of implementing EBIs and policies in LMIC settings<sup>65</sup> although even these funds are limited in comparison with what is needed to achieve broad scale-up. Identifying and addressing the gap in funding for broader, long-term, sustainable scale-up is needed to be able to move cancer prevention and early detection scale-up forward and will likely require a multisectoral approach.

This review summarizes the state of the science of scale-up of EBIs for cancer prevention and early detection in LMIC settings. An important limitation is that only English language studies and those published in the scientific literature

were included, and thus, it is likely that publications in other languages were missed. In addition, there are numerous efforts globally to close the gap between evidence and practice for cancer prevention and control that are never published or are disseminated through other sources than those used here. That said, our scoping review process included expert consultation to identify relevant literature and select studies, which reflects the available state of research.

In many LMICs, limited access to cancer screening and treatment options perpetuates poor outcomes and high rates of preventable cancer-related deaths. By 2040, 69% of cancer deaths will occur in LMICs compared with 6% in the United States. Despite the extensive literature on pilot programs and demonstration projects, there are relatively few published reports on the scale-up of cancer prevention and early detection interventions in LMICs. The review suggests a disproportionate emphasis on cervical cancer as compared with other cancers such as breast and colon. Findings point to areas for further study including testing a broader range of strategies that address multilevel determinants of scale-up such as organizational infrastructure and payment policies.

There is an urgent need to fill gaps in research to guide best practices for bringing the implementation of cancer prevention and early detection EBIs to scale in LMICs to reduce the disproportionate mortality experienced in these countries. This review summarizes the evidence to date and provides insight into current practices for scale-up, while emphasizing that utilization of IS frameworks could streamline interventions to maximize efficiency and effectiveness.

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## APPENDIX

TABLE A1. Search Strategy

Concept	Search	Block
Concept 1: prevention	1	Block 2—interventions type—clinical primary and secondary preven Screen Early detect Early diagnosis
Concept 2: scale-up	2	Block 3—scale-up scale Scalability Scaling Scalable Spread Scale-up Scale-up Sustainability Scale out scale-out Expand Expanding Uptake
Concept 3: cancer	3	Block 4—cancer Cancer Cancerous Carcinogen Carcinoma Malignan (eg, malignancy, malignant, malignancies) Malignant tumor Neoplasm Tumor Tumor
Limit to LMICs	4	LMICs on the basis of World Bank categories linked to full search terms
Merge	5	Block 5—1, 2, 3, and 4
Exclusion—date	6	Block 6—publication date limitation to articles 2012 and over
Exclusion—language	7	Block 7—English language and human participants

Abbreviation: LMICs, low- and middle-income countries.

TABLE A2. Inclusion and Exclusion Criteria

Criteria Area	Inclusion	Exclusion
Scale-up	Studies must meet both these definitions of scaling-up Scaling-up is..."deliberate efforts to increase the impact of successfully tested health innovations so as to benefit more people and to foster policy and program development on a lasting basis" <sup>18</sup> In the health sector, scalability is "...the ability of a health intervention shown to be efficacious on a small scale and or under controlled conditions to be expanded under real-world conditions to reach a greater proportion of eligible population, while retaining effectiveness" <sup>19</sup>	Policy studies
Study designs	Protocol, scale-up component/project report (not study); programs/ interventions (RCTs and non-RCTs), empirical studies (including RCTs, cohort, case-control, cross-sectional, qualitative, and mixed-methods studies), observational studies natural experiments, modeling studies, secondary analysis; and before v after interventions	Reviews; commentary/opinion articles; data/statistics from monitoring and surveillance that are not directly linked to a specific/scale-up/intervention. Abstract-only studies, study protocols, and gray literature such as reviews, unpublished work, editorials, and personal perspective papers
Interventions	Primary preventions (eg, HPV vaccine); secondary prevention (eg, HPV test)	
Country type	LMICs as defined by the World Bank for the current 2022 fiscal year calculated using the World Bank Atlas method for year 2020 with gross national income per capita Low-income economies = ≤\$1,045 USD Lower-middle-income economies = \$1,046-\$4,095 USD Upper-middle-income economies = \$4,096-\$12,695 USD	High-income economies = ≥\$12,696 USD or over
Populations	All age groups from all populations	Studies conducted in special populations with major underlying disease
Pilots		Studies that conducted a pilot of an intervention with the intent to scale-up regardless of the size of the pilot sample
Timeframe	Articles published between 2012 and 2022	Articles older than 10 years
Language	English	Non-English texts

Abbreviations: HPV, human papillomavirus; LMICs, low- and middle-income countries; RCTs, randomized controlled trials; USD, US dollars.

TABLE A3. Detailed Study Characteristics of the 24 Included Scale-Up Studies

Study ID	Country	World Bank Classification—LMIC Tier	IS Scale-Up Framework/Theories/Methods Used	Is Scale-Up Explicitly Mentioned?	Implementation Strategies (organized by cluster)	Implementation Strategy Design	Stage of Implementation/Integration	Level of Scale-Up	Scale-Up Setting	Scale-Up Target	Scale-Up Strategy Target Population	EBI/Cancer-Related Intervention Target Phase in Cancer Care Continuum	EBI Target Level	EBI Target Cancer Type	Study Type/Design	Qualitative Data	Duration of Scale-Up	Quantitative Data Collection	Did This Study Use IS Outcome Definitions?	IS Outcomes Mentioned
Khozaim et al <sup>14</sup>	Kenya	LM	No	No	Evaluative and iterative strategies, provide interactive assistance, develop stakeholder inter-relationships, train and educate stakeholders, engage consumers	Bottom-up	Post, evaluation	Regional	Rural	Health clinics (community health centers), communities	Providers, patients	Early detection/secondary prevention	Health system	Cervical	Retrospective; descriptive	No	29 months	Yes	No	Other: text mentions that program must be measurable and sustainable—and feasibility and acceptability of cervical cancer screening
Li et al <sup>15</sup>	China	UM	No	No	Evaluative and iterative strategies, provide interactive assistance, develop stakeholder inter-relationships, train and educate stakeholders, use financial strategies, other: engage providers	Bottom-up	Evaluation	Other: district level	Rural, urban, periurban (suburban)	Communities, other: community health centers	Providers, patients	Early detection/secondary prevention	Individual	Colon	Prospective; evaluation	No	3 years	Yes	No	Penetration
Kury et al <sup>16</sup>	Brazil	UM	No	No	Train and educate stakeholders, engage consumers, change infrastructure	Bottom-up	Implementation	Other: city level	Urban	Schools	Patients	Primary prevention	Individual	Cervical	Evaluation	Yes	2 years	Yes	Yes	Costs
Binagwaho et al <sup>17</sup>	Rwanda	L	No	Yes	Develop stakeholder inter-relationships, train and educate stakeholders, use financial strategies, change infrastructure	Top-down	Scale-up	National	Rural, urban, periurban (suburban)	Hospitals, health clinics (community health centers), communities	Patients	Primary prevention, early detection/secondary prevention	Community health system	Cervical	Evaluation	No	2 years	Yes	Other: no	Costs, penetration, sustainability
Chary and Rohloff <sup>18</sup>	Guatemala	UM	No	Yes	Evaluative and iterative strategies, develop stakeholder inter-relationships, train and educate stakeholders, change infrastructure, engage consumers	Bottom-up	Post, evaluation	National	Rural; other: mostly rural	Other: NGOs	Providers	Early detection/secondary prevention	Community	Cervical	Qualitative	Yes	16 months	No	Yes	Sustainability, other: mention sustainability in discussion (. . . points to needing “strategies for improving service delivery, sustainability, and resource allocation”)
Holme et al <sup>19</sup>	Guatemala, Honduras, and Nicaragua	LM, UM	No	Yes	Evaluative and iterative strategies, adapt and tailor to concept, develop stakeholder inter-relationships, engage consumers, change infrastructure	Top-down	Post, evaluation	National	Rural, urban	Health clinics (community health centers), primary health care (provide health care and services in a variety of settings), communities, other: health workers offered HPV screening tests free of charge in a mixture of outreach models, either at health clinics (the majority) or community-based locations	Providers, patients, health care leadership	Early detection/secondary prevention	Health system	Cervical	Evaluation	No	3 years, 8 months	Yes	No	Other: mentioned acceptability, adoption, and feasibility in discussion—but not explicitly as outcomes
Johnson et al <sup>20</sup>	Botswana	UM	No	Yes	Evaluative and iterative strategies, provide interactive assistance, develop stakeholder inter-relationships, change infrastructure	Bottom-up	Evaluation	Other: five sites around the country	Urban	Other: health centers, sites; clinics	Providers	Early detection/secondary prevention	Health system	Cervical	Retrospective; evaluation	No	20 months	Yes	Yes	Fidelity
Quedraogo et al <sup>21</sup>	Burkina Faso	L	No	No	Evaluative and iterative strategies, provide interactive assistance, adapt and tailor to concept, develop stakeholder inter-relationships, train and educate stakeholders, engage consumers, use financial strategies, change infrastructure, other: see Table	Bottom-up	Evaluation	Regional, other: nine regional hospitals and three district hospitals	Other: does not specify?	Hospitals	Providers, patients, other: institutional capacity	Early detection/secondary prevention	Health system	Cervical	Retrospective; descriptive; evaluation	No	48 months	Yes	No	Other: mentions acceptability and feasibility in abstract and in discussion mentions acceptability and feasibility, sustainability, and reach, discussion mentions IS without mentioning IS: “some components are likely setting-specific and should be adapted to consider local contexts”

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**TABLE A3.** Detailed Study Characteristics of the 24 Included Scale-Up Studies (continued)

Study ID	Country	World Bank Classification—LMIC Tier	IS Scale-Up Framework/Theories/Methods Used	Is Scale-Up Explicitly Mentioned?	Implementation Strategies (organized by cluster)	Implementation Strategy Design	Stage of Implementation/Integration	Level of Scale-Up	Scale-Up Setting	Scale-Up Target	Scale-Up Strategy Target Population	EBI/Cancer-Related Intervention Target Phase in Cancer Care Continuum	EBI Target Level	EBI Target Cancer Type	Study Type/Design	Qualitative Data	Duration of Scale-Up	Quantitative Data Collection	Did This Study Use IS Outcome Definitions?	IS Outcomes Mentioned
Majumbara et al <sup>42</sup>	Malawi	L	No	Yes	Train and educate stakeholders, change infrastructure, other: did not really detail any strategies—just reports on quantitative outcomes	Bottom-up	Post, evaluation	National	Rural, urban	Hospitals, health clinics (community health centers), primary health care (provide health care and services in a variety of settings)	Providers, patients	Early detection/secondary prevention	Health system	Cervical	Retrospective, cohort	No	5 years	Yes	No	
Korn et al <sup>43</sup>	Namibia	UM	No	No	Train and educate stakeholders	Top-down	Scale-up	National	Rural, urban, periurban (suburban)	Hospitals, health clinics (community health centers), primary health care (provide health care and services in a variety of settings)	Providers, patients	Early detection/secondary prevention	Individual	Cervical	Evaluation	No	3 years	Yes	Acceptability, feasibility, penetration	
Wang et al <sup>44</sup>	China	UM	No	No	Develop stakeholder inter-relationships, train and educate stakeholders, change infrastructure	Bottom-up	Implementation	Other: city level	Urban	Hospitals, communities	Patients	Early detection/secondary prevention	Health system	Cervical	Evaluation	No	3 months reported; estimated for the past 2 years	Yes	Penetration	
Wu and Hoffman <sup>45</sup>	Philippines	LM	No	No	Develop stakeholder inter-relationships, train and educate stakeholders, change infrastructure	Top-down	Implementation, evaluation	Other: cross country	Rural, urban, periurban (suburban)	Health clinics (community health centers), other: community health infrastructure (community health centers)	Providers, patients	Early detection/secondary prevention	Community	Breast	Descriptive	Yes	2 years	No	Yes	Sustainability
Said and Sutan <sup>46</sup>	Malaysia	UM	No	No	Evaluative and iterative strategies, use financial strategies	Top-down	Evaluation	National	Rural, urban, other: national	Primary health care (provide health care and services in a variety of settings)	Patients	Early detection/secondary prevention	Health system	Breast	Retrospective	No	5 years	Yes	No	Other: mentions sustainability and accessibility, measures process (reach) and performance (fidelity?) indicators
Soi et al <sup>47</sup>	Mozambique	L	CFIR	Yes	Develop stakeholder inter-relationships	Bottom-up	Implementation, evaluation	National	Rural, urban, periurban (suburban)	Schools	Patients	Primary prevention	Individual	Cervical	Evaluation	Yes	2 years	No	No	Other: adaptability
Shikha et al <sup>48</sup>	India	LM	No	Yes	Evaluative and iterative strategies, develop stakeholder inter-relationships, train and educate stakeholders, engage consumers, use financial strategies	Bottom-up	Scale-up, evaluation	Regional, other: cities	Urban	Hospitals	Providers, other: community health workers	Early detection/secondary prevention	Health system	Cervical	Prospective, evaluation	No	12 months	Yes	No	Other: mentions feasibility, safety, and acceptability
Oluwole et al <sup>49</sup>	Botswana, Zambia	L, UM	No	Yes	Adapt and tailor to concept, train and educate stakeholders, engage consumers, change infrastructure	Bottom-up	Scale-up	National	Rural, urban, periurban (suburban)	Health clinics (community health centers), communities	Providers, patients	Early detection/secondary prevention	Community	Cervical, breast	Descriptive	No	2 years Zambia; 6 months Botswana	Yes	Yes	Penetration
Mwanahamuntu et al <sup>50</sup>	Zambia	LM	No	Yes	Train and educate stakeholders, engage consumers, change infrastructure	Top-down	Scale-up, evaluation	National	Rural, urban, periurban (suburban)	Health clinics (community health centers)	Patients	Primary prevention, early detection/secondary prevention	Health system	Cervical	Evaluation	No	7 years	Yes	Adoption, sustainability	
Lemone et al <sup>51</sup>	The Gambia	L	No	No	Develop stakeholder inter-relationships, engage consumers, change infrastructure	Bottom-up	Implementation	Regional	Rural, urban	Hospitals, communities	Patients	Primary prevention, early detection/secondary prevention, other: screening and treating HBV—before liver cancer can develop	Community, health system	Liver	Mixed methods, descriptive	Yes	3 years	Yes	Yes	Acceptability, feasibility
Kumar et al <sup>52</sup>	India	LM	No	Yes	Evaluative and iterative strategies, train and educate stakeholders, engage consumers, change infrastructure, other: see Table 1: breast health implementation strategies and key interventions	Top-down	Post, evaluation	National, other: intervention in two states (Uttar Pradesh and Jharkhand) but says it is a national program	Rural, urban	Hospitals, primary health care (provide health care and services in a variety of settings)	Providers	Early detection/secondary prevention	Health system	Breast	Prospective, other: situational assessment	No	18 months	Yes	No	Feasibility, fidelity, other: feasibility and effectiveness (also used adherence/fidelity)—terms are mentioned in the abstract and discussion—but not as explicitly IS

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**TABLE A3.** Detailed Study Characteristics of the 24 Included Scale-Up Studies (continued)

Study ID	Country	World Bank Classification—LMIC Tier	IS Scale-Up Framework/Theories/Methods Used	Is Scale-Up Explicitly Mentioned?	Implementation Strategies (organized by cluster)	Implementation Strategy Design	Stage of Implementation/Integration	Level of Scale-Up	Scale-Up Setting	Scale-Up Target	Scale-Up Strategy Target Population	EBI/Cancer-Related Intervention Target Phase in Cancer Care Continuum	EBI Target Level	EBI Target Cancer Type	Study Type/Design	Qualitative Data	Duration of Scale-Up	Quantitative Data Collection	Did This Study Use IS Outcome Definitions?	IS Outcomes Mentioned
Chigbu et al <sup>17</sup>	Nigeria	LM	No	No	Train and educate stakeholders, engage consumers, change infrastructure	Bottom-up	Implementation	Regional	Rural	Health clinics (community health centers), communities	Providers, patients	Primary prevention	Individual	Cervical, breast	Cohort	No	2 years	Yes	Yes	Adoption, sustainability
Borja-Aburto et al <sup>18</sup>	Mexico	UM	No	No	Train and educate stakeholders, engage consumers, change infrastructure	Top-down	Post, evaluation	National	Urban	Hospitals, primary health care (provide health care and services in a variety of settings), other: IMSS health care benefits comprise preventive, curative, and rehabilitation care provided in 1,521 primary care clinics, 251 secondary hospitals, and 25 tertiary care hospitals	Providers, patients; other: in 2002, IMSS began a process to strengthen primary care by instituting a training course for 14,000 family care physicians, designing and publishing clinical care guidelines for major diseases, introducing an electronic medical record, and integrating a preventive strategy called PREVENIMSS	Primary prevention, early detection/secondary prevention	Individual, community, health system	Cervical, breast	Retrospective, other: differences in incidence and mortality	No	14 years	No	No	
Boni et al <sup>16</sup>	Cote d'Ivoire	LM	No	Yes	Evaluative and iterative strategies, train and educate stakeholders, change infrastructure	Bottom-up	Post, evaluation	Regional	Urban	Health clinics (community health centers), primary health care (provide health care and services in a variety of settings), other: health centers	Patients	Early detection/secondary prevention	Health system, other: 27 registered health care facilities from the government and private sector	Cervical	Retrospective	No	4 years	Yes	No	Acceptability, appropriateness, feasibility, other: it says these words in the discussion—but not predefined as an outcome
Arrossi et al <sup>15</sup>	Argentina	UM	RE-AIM	Yes	Provide interactive assistance, train and educate stakeholders, use financial strategies	Bottom-up	Scale-up	Regional	Rural, urban, periurban (suburban)	Primary health care (provide health care and services in a variety of settings)	Providers, patients	Early detection/secondary prevention	Individual	Cervical	Evaluation	No	3 years	No	Other: yes	RE-AIM, acceptability, adoption, feasibility, sustainability
Alfaro et al <sup>19</sup>	El Salvador	LM	No	Yes	Develop stakeholder inter-relationships, train and educate stakeholders, engage consumers, change infrastructure	Bottom-up	Post, evaluation	Regional	Rural, urban; other: primarily rural, 76.8% rural, 23.2% urban	Hospitals, health clinics (community health centers), other: 63 health units	Providers, patients, health care leadership	Early detection/secondary prevention	Individual, community, health system	Cervical	Other: demonstration project	No	2 years	Yes	No	Feasibility, penetration

Abbreviations: CFIR, Consolidated Framework for Implementation Research; EBI, evidence-based intervention; HBV, hepatitis B virus; ID, identification number; IMSS, Mexican Institute for Social Security; IS, implementation science; L, low; LM, lower-middle; LMIC, low- and middle-income country; NGO, nongovernmental organization; NOS, not otherwise specified; RE-AIM, Reach, Effectiveness, Adoption, Implementation and Maintenance; UM, upper-middle.

**TABLE A4. All Implementation Science Strategies**

Strategies According to	All Strategies Cited
Develop stakeholder inter-relationships	Community-level stake holder engagement (we organized a meeting in each enumeration area with the help of the village head) <sup>41</sup> ; support from the NIP throughout all demonstration project implementation phases <sup>50</sup> ; hospitals formed collaborations with the local Women's Federation, Family Planning Commission, and the Community Board to develop outreach mechanisms that promote participant recall and periodical follow-up with high-risk individuals <sup>29</sup> ; network of private practitioners <sup>30</sup> ; The MOH, in collaboration with the BUP, began scale-up of see-and-treat in 2014 with support of the PEPFAR funding <sup>33</sup> ; collaborative project <sup>45</sup> ; NGOs approached local MOH administrators in three of the 24 MOH-designated national health districts who agreed to have staff at selected clinics participate in NGO-sponsored VIA cryotherapy training and screening campaigns monitored and evaluated by the NGOs <sup>31</sup> ; enlisted teachers and village leaders in sensitization efforts and mobilized the country's 45,000 community health workers to trace out-of-school girls <sup>34</sup> ; a formal letter requesting verbal approval <sup>35</sup> ; PATH partnered with local nongovernmental organizations to aid the MOHs in implementing the project through planning, advocacy, coordination of screening and follow-up, development of community outreach strategies, and data collection <sup>44</sup> ; STMM volunteers arrived early and personally met with stakeholders <sup>35</sup> ; the implementation relied on the existing resources of the national public health system, with BHI providing technical support and training to MOH personnel <sup>38</sup> ; AMPATH MUSOM collaboration provided the regional logistic support, supply chain management, and screening rooms <sup>43</sup>
Train and educate stakeholders	Participating hospitals established independent management systems to conduct the program using personnel dedicated for the purpose <sup>29</sup> ; trained private practitioners and community health workers <sup>30</sup> ; the municipality staff was trained to vaccinate in schools and public sites <sup>52</sup> ; training CHW and laboratory technicians <sup>34</sup> ; highly skilled healthcare providers who delivered capacity-strengthening training to a small group of STMM volunteers who became trainers in the Philippines and proceeded to transfer those skills to local healthcare providers. As a result, upskilling through training becomes self-sustaining over time; disseminated information to all stakeholders <sup>35</sup> ; train providers <sup>36</sup> ; train community health educators on cancer prevention <sup>37</sup> ; throughout CAPE, training was provided to a total of eight laboratory technicians, 610 CHPs, 360 nurses, and 223 physicians <sup>38</sup> ; training for physicians <sup>39</sup> ; training and certification of health care providers in VIA and cryotherapy <sup>40</sup> ; national and provincial team members led 18 workshops <sup>42</sup> ; training health care providers: Training of providers in counseling, VIA, cryotherapy, and LEEP <sup>45</sup> ; there were a total of 395 VIA and cryotherapy providers who were trained during the period 2011-2015 <sup>47</sup> ; train nurses <sup>48</sup> ; IMSS began a process to strengthen primary care by instituting a training course for 14,000 family care physicians; nurses were trained in the new model <sup>49</sup> ; NGO sponsored VIA trainings for MOH staff <sup>31</sup> ; train female community health workers <sup>32</sup> ; the program used a training curriculum adapted from the WHO's IARC, and key nurses underwent additional training in cryotherapy and cervicography in Lusaka, at the Centre for Infectious Disease Research in Zambia. These key nurses then trained (using IARC-based materials) and mentored other local MOH nurses who staffed the cervical cancer screening services in their clinics <sup>43</sup> ; followed WHO recommended screening <sup>46</sup> ; learning strategies were used, including Microsoft PowerPoint presentations, role-plays, and case studies <sup>35</sup> ; at the beginning of 2015, a refresher training was provided to all CHWs <sup>42</sup> ; designing and publishing clinical care guidelines for major diseases <sup>49</sup> ; a pictorial booklet was prepared for the CHW to be used in the community for educating women <sup>30</sup> ; MOH now is national and has trained thousands of providers in VIA or VIA cryotherapy since 2008 <sup>31</sup> ; a hands-on session on how to perform a CBE and teach BSE was also included <sup>35</sup> ; development of standardized screening and treatment algorithms to ensure the same quality of care at all locations <sup>43</sup> ; community involvement and continued training of non-physician community mobilizers and care givers <sup>48</sup> ; train female community health workers <sup>32</sup>
Change infrastructure	Each site was staffed with MOH nurses to conduct VIA and equipped with adequate supplies of liquid nitrogen gas for cryotherapy <sup>33</sup> ; build up equipment capacity (discounts and donations)—consumables, building supply chain capacity <sup>34</sup> ; went home to home <sup>37</sup> ; referral system <sup>29,36,40,41,48,50</sup> ; functional cryotherapy sites <sup>47</sup> ; electronic records <sup>48</sup> ; introducing an electronic medical record and integrating a preventive strategy called PREVENIMSS <sup>49</sup> ; in 2004, in an effort to overcome problems with cytology-based screening, a small group of NGOs began pilot-testing VIA cryotherapy in their own clinics <sup>31</sup> ; systems created for tracking and follow-up of patients across the care pathway <sup>32</sup> ; permanent public sites for HPV vaccination <sup>52</sup> ; add point-of-care screening <sup>36</sup> ; in phases II and III, the CAPE online database was completed and management was transferred to the MOH <sup>38</sup> ; development of data collection tools: individual client form, client registry, and monthly summary sheet. Provision of initial equipment for VIA, cryotherapy, and LEEP including parts and supplies <sup>45</sup> ; dedicated data clerks entered the data from the forms during a 4-month period using the EpiData V3.1 software <sup>46</sup> ; the hospitals developed the necessary software to establish a patient database <sup>29</sup> ; equipment provided to health facilities <sup>37</sup> ; a unique ID was generated for each participant on the basis of their full name and date of birth <sup>46</sup> ; to implement the program, the appointment booklet for individual IMSS members was redesigned to include registries and details of preventive services and reminders tailored to each programmatic age/sex group <sup>49</sup> ; three databases were built specifically for the study <sup>42</sup> ; referral for women who are not eligible for immediate cryotherapy <sup>46</sup> ; vaccination data were inserted in a specific vaccination program database, named SIVAC, which functions as an electronic vaccination notebook, informing when the next vaccination routine for adolescents will be held <sup>52</sup> ; patient tracking, and data management systems <sup>36</sup> ; the infrastructure to accommodate preventive services in each primary care facility was also remodeled <sup>49</sup> ; participating hospitals established independent management systems to conduct the program using personnel dedicated for the purpose <sup>29</sup>
Engage consumers	Engage parents and guardians who did not have children at school <sup>52</sup> ; during the visit, CHWs provided women with information about cervical cancer prevention and HPV testing and then offered them HPV self-collection, followed by a 10-minute step-by-step explanation on how to perform it using communication support material <sup>42</sup> ; raising awareness at the community level <sup>44</sup> ; facilitating adoption and encouraging procurement of HPV testing <sup>44</sup> ; awareness campaigns <sup>35</sup> ; communication campaign <sup>34</sup> ; fieldworkers did a census by visiting all households to register the name, age, and sex of all eligible people and to invite them for screening <sup>41</sup> ; Information Education Campaign was implemented by means of health talks, T-shirts, and print media to raise awareness about the necessity of screening <sup>43</sup> ; frontline health workers increase breast health awareness and encourage and facilitate women who have breast symptoms to present to the nearest primary-level health facility for CBE by trained health care staff <sup>32</sup> ; media campaign to reach girls who did not yet received the first or the second dose of vaccine <sup>52</sup> ; a series of lectures given in public and private schools on HPV <sup>52</sup> ; increase knowledge, awareness, and understanding of cervical cancer services <sup>36</sup> ; recruitment of participants was conducted by CHPs <sup>38</sup> ; the providers were

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**TABLE A4.** All Implementation Science Strategies (continued)

Strategies According to	All Strategies Cited
	<p>expected to send out CRC screening invitations to the entire target population by the end of the second round of the program<sup>39</sup>; people who were invited, but did not attend screening were reminded by the fieldworkers up to three times<sup>41</sup>; group education in facilities about cervical cancer and CECAP services. Television programs about cervical cancer and CECAP services<sup>45</sup>; PREVENIMSS provides written information to motivate health self-care and to empower users<sup>49</sup>; large number of women are mobilized for screening; these CHWs mobilized clients to the doctors hospitals/outpatient clinics either on designated days or as a walk-in facility<sup>30</sup>; unit nurses visited HPV-positive women at home to deliver their results<sup>38</sup> and to address potential losses to follow-up along the continuum of care, an appointment system was implemented, and the cell phone network in the region was used to provide reminder calls and text messages before scheduled appointments. Lay person clinic assistants were hired to help nurses with filing medical records, recording upcoming appointments, and calling patients in advance to remind them of upcoming follow-up appointments<sup>43</sup>; in November 2010 and 2012, two mobilization days (Saturdays) were set to either update vaccination for girls who already took the first or second doses or to vaccinate girls who missed the first vaccination. Five hundred nurses and 10 doctors to conduct the interviews were recruited, and the project holidays HPV-free was launched<sup>52</sup>; an intense social communication campaign was launched with radio and television advertisements to increase awareness regarding these preventive services among IMSS affiliates<sup>32</sup>; the program used a training curriculum adapted from the WHO's IARC<sup>43</sup>; women in each household reached was educated on cervical and breast cancer prevention and HPV<sup>37</sup></p>
Use evaluative and iterative strategies	<p>The program used a training curriculum adapted from the WHO's IARC<sup>43</sup>; developed indicators to be monitored throughout the activity<sup>44</sup>; assessed data from women attending CC screening; this paper highlights the essential performance findings of the program with regards to the participation and performance indicators for the past 5 year<sup>53</sup>; SSV was to identify any gaps in the beginning of the program and find any appropriate solution<sup>30</sup>; review progress of each community health center; the CHCs were also required to submit monthly progress reports to the CDC of the district. The local CDC was responsible for the quality control of the whole process of the screening program<sup>39</sup>; capacity building in monitoring and evaluation<sup>45</sup>; created a context-appropriate implementation plan for breast cancer care delivery<sup>32</sup>; we have conducted a situational assessment of breast health services in both states using the BHGI BC12.5 toolkit<sup>32</sup>; we established a robust monitoring and evaluation system at the onset of the program, so that all key data needed for decision-making could be captured in a timely and reliable manner. A centralized digital dashboard allowed for real-time monitoring of key indicators<sup>32</sup>; all sites participated in intensive QA monitoring<sup>33</sup>; conducted semi-structured interviews with 36 staff members of 20 NGO-based VIA programs<sup>31</sup>; assessed data from women attending CC screening<sup>46</sup></p>
Provide interactive assistance	<p>An experienced gynecologist conducted monitoring visits at the triage centers to ensure adequate implementation of clinical procedures<sup>38</sup>; experts from the pilot site reviewed all cervical images centrally and mentored providers during monthly site visits. Each scaled-up site was monitored monthly<sup>33</sup>; BHI personnel monitored program logistics<sup>38</sup>; core group of local gynecologists from MUSOM underwent specialized training and continuous mentorship from visiting North American gynecologists to become skilled at colposcopy, biopsy, and LEEP<sup>43</sup>; supportive supervision visits to mentor and support providers; training of data managers on data extraction and cross-check methodology to improve data quality. Training of providers on utilization of data to track program progress<sup>45</sup>; to balance the workloads, each designated hospital took charge of the referrals from several community health centers, which were determined according to the average travel distance of the participants to the hospital and the COL service capacity of the hospital<sup>39</sup>; a training and mentorship program in medical and surgical gynecologic oncology was developed<sup>43</sup></p>
Use financial strategies	<p>Build up equipment capacity (discounts and donations)—consumables, building supply chain capacity<sup>34</sup>; subsidized mammography program<sup>53</sup>; increase incentives for physicians, paid with subsidies, the amount of which were associated with the quality control outcomes<sup>39</sup>; negotiate donations and prices of vaccine<sup>34</sup>; in each screening round of the C-CRCSP, a budget was allocated by the government of the district. Funds were then distributed to each of the 46 communities within the district<sup>39</sup>; all funding for this project was provided by the regular mechanisms of public health system financing. Thus, scaling-up was guaranteed and stewardship strengthened, sending also a strong message to the community about the government commitment with its implementation in the context of the national policy for cervical cancer prevention<sup>42</sup>; the private practitioners provided cervical cancer screening at subsidized rates<sup>30</sup>; next, primary screening that includes RA and FOBt (colloidal gold) was provided for free<sup>39</sup>; adapt user fees<sup>45</sup></p>
Adapt and tailor to context	<p>Adapt model by country<sup>36</sup>; using vaginal self-sampling for test specimens to facilitate rapid screening uptake<sup>44</sup>; sessions were adapted to focus on the trainees' weaknesses identified through an initial assessment of baseline knowledge and skills<sup>45</sup></p>
Support clinicians	<p>Increase incentives for physicians, paid with subsidies, the amount of which was associated with the quality control outcomes<sup>39</sup></p>

Abbreviations: AMPATH, Academic Model Providing Access to Healthcare; BHI, Basic Health International; BSE, breast self-examination; BUP, Botswana-UPenn Partnership; CAPE, Cervical Cancer Prevention in El Salvador; CBE, clinical breast examinations; CC, cervical cancer; C-CRCSP, community-based colorectal cancer screening program; CDC, Center for Disease Control and Prevention; CECAP, cervical cancer prevention; CHPs, community health promoters; CHW, community health worker; CRC, colorectal cancer; FOBt, fecal occult blood test; HPV, human papillomavirus; IARC, International Agency for Research on Cancer; ID, identification number; IMSS, Mexican Institute for Social Security; LEEP, loop electrical excision procedure; MOH, Ministry of Health; MUSOM, Moi University School of Medicine; NGOs, nongovernmental organizations; PEPFAR, President's Emergency Plan for AIDS Relief; QA, quality assurance; RA, risk assessment; SSV, supportive supervision visit; STMM, short-term medical missions; VIA, visual inspection with acetic acid.