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Integrative Systems Praxis for Implementation Research (INSPIRE): An Implementation Methodology to Facilitate the Global Elimination of Cervical Cancer

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ABSTRACT

Background: The World Health Organization (WHO) has called for a systems thinking approach to health systems strengthening to increase adoption of evidence-based interventions (EBI). The Integrative Systems Praxis for Implementation Research (INSPIRE) methodology operationalizes the WHO systems thinking framework to meet cervical cancer elimination–early detection and treatment (CC-EDT) goals.

Methods: Using a systems thinking approach and grounded in the consolidated framework for implementation research, INSPIRE integrates multiple research methodologies and evaluation frameworks into a multilevel implementation strategy.

Results: In phase I (creating a shared understanding), soft systems methodology and pathway analysis are used to create a shared visual understanding of the CC-EDT system, incorporating diverse stakeholder perspectives of the "what, how, and why" of system behavior. Phase II (finding leverage) facilitates active stakeholder engagement in knowledge transfer and decision-making using deliberative dialogues and multiple scenario analyses. Phase III (acting strategically) represents stakeholder-engaged implementation planning, using well-defined implementation strategies of education, training, and infrastructure development. In phase IV (learning and adapting), evaluation of key performance indicators via a reach, effectiveness, adoption, implementation, and maintenance framework is reviewed by stakeholder teams, who continuously adapt implementation plans to improve system effectiveness.

Conclusions: The INSPIRE methodology is a generalizable approach to context-adapted implementation of EBIs.

Impact: Replacing static dissemination of implementation "roadmaps" with learning health systems through the integration of systems thinking and participatory action research, INSPIRE facilitates the development of scalable and sustainable implementation strategies adapted to local contexts.

Introduction

In 2018, World Health Organization (WHO) Director General Dr. Tedros Adhanom Ghebreyesus called for the elimination of cervical cancer. In December 2019, a draft strategy for elimination was released and included the following targets to be met by 2030: (i) 90% coverage of human papillomavirus (HPV) vaccination of girls by age 15 years, (ii) 70% coverage of screening, and (iii) management of 90% of precancers and invasive cancer cases (1). It is well recognized that meeting these targets, especially the early detection and treatment (EDT) goals, will require significant changes in the approach to implementation of context-adapted programs into regions with the highest burden of cervical cancer (2–8).

EDT programs, even when implemented in regions with strong primary health care systems, face several unique and complex challenges. These challenges can be mapped to specific implementation outcomes: adoption, acceptability, appropriateness, feasibility, fidelity, cost, penetration, and sustainability (9). In the early- to mid-phase of implementation, new evidence-based interventions (EBI) must be considered acceptable and appropriate by a range of stakeholders across the health system structure, from national ministries and professional societies to health professionals and the population intended to benefit from the intervention. Health authorities and health professionals must be willing to adopt new EBIs and abandon ineffective practices and must consider the new EBIs to be feasible to use within their public health system. Health information systems must be robust and accessible to ensure accurate patient monitoring throughout the care cascade, or the program design must be significantly simplified (e.g., use single visit screen-and-treat approaches). The health professionals must be sustainably trained to use the EBIs as they were intended and, in the context of the care cascade, ensure that all elements of the continuum of care can be completed. Finally, cost is a paramount consideration, especially to regional systems struggling to balance budgets for the delivery of multiple public health strategies, including infection control, maternal and child mortality, and chronic disease prevention. To that end, new EBIs must not only be a cost-effective alternative to existing programs but must be deemed affordable to deliver with high fidelity by the program administrators and within the national public system. Ultimately, implementation strategies must be designed to allow rapid scale-up and sustainability to

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meet elimination goals by 2030. This includes development or strengthening of health information systems, technology supply chains, distribution networks, and a local capacity for training and quality assurance.

From an implementation research perspective, we will not meet the ambitious elimination strategy timelines if each of these implementation outcome challenges are evaluated individually; a comprehensive approach is essential. The Integrative Systems Praxis for Implementation Research (INSPIRE) methodology was designed to meet this challenge by operationalizing implementation research methods and frameworks into a logical sequence of rapid, mixed methods research activities, which are funneled back into stakeholder-owned adaptation of implementation plans and prevention strategies based on the INSPIRE-derived, practice-based evidence. It is a blended implementation strategy, which can be applied in any context to ensure that the WHO-recommended EDT programs are locally adapted to meet the implementation outcome requirements described above.

Materials and Methods

INSPIRE represents an operational methodology that systematically integrates a set of implementation research frameworks, approaches, conceptual models, research methods, and implementation strategies with a purposeful goal of improving performance of multi-level complex adaptive cervical cancer EDT systems. Specifically, INSPIRE is grounded on the following five theoretical and methodologic approaches: systems thinking, participatory action research (PAR), soft systems methodology (SSM), the consolidated framework for implementation research (CFIR), and the reach, effectiveness, adoption, implementation, and maintenance (RE-AIM) evaluation framework.

Systems thinking

In contrast to the reductionist approach taken by the biomedical science community in much of the twentieth century, systems thinking takes a holistic view of complex adaptive systems (10–17). The focus of systems thinking involves defining and localizing the problems leading to poor performance of existing EDT programs and then acting strategically to address the problems including, but not limited to, introduction of the new EBIs, such as HPV testing and ablative therapies. Systems thinking acknowledges that while EBIs solve some core problems, introducing new and/or improved technologies will not fundamentally change health outcomes if other critical system functions are not working properly. For example, high turnover and reassignment of health professionals creates instability in a health system regardless of the technologies being employed for screening and treatment. Understanding and adapting the implementation of the new EBIs to this and other similar realities is thus essential.

INSPIRE is modeled using the WHO framework for systems thinking to improve health systems strengthening (18) and the systems practice framework developed by the Omidyar Group (19). Designed to close a gap between the "promise of a systems approach for making social change" and putting this promise into practice, the Omidyar Systems Practice model progresses through iterative phases of understanding the system and creating shared visual understanding of the system forces and behaviors (phase I), finding leverage in the most promising alternatives for change (phase II), acting strategically to implement the highest leverage opportunities for sustainable change (phase III), and learning and adapting by continuous monitoring and evaluation (M&E) of system performance (phase IV). The systems thinking model emphasizes continual progress, not an idealized and unrealistic "single solution," as well as the interconnectedness between multiple layers of the health system involved in sustainable delivery of cervical cancer elimination–EDT (CC-EDT) programs.

PAR

Sustainable adoption of any EBI will be enhanced if the intervention is internally derived (20). In other words, stakeholders are more likely to adopt, adapt, and use an intervention if they are involved in the selection, the planning for its implementation, and the M&E of the postimplementation experience. PAR establishes local ownership of the implementation success and in the process, establishes a "colearning" environment, which has been shown to result in increased adoption and sustainability (21–23).

SSM

Checkland and Poulter summarize SSM as follows: "SSM is an action-oriented process of inquiry into problematical situations in the everyday world; users learn their way from finding out about the situation to defining/taking action to improve it. The learning emerges via an organized process in which the real situation is explored, using intellectual devices, which serve to provide structure to discussion, as models of purposeful activity built to encapsulate pure, stated worldviews" (24, 25). Application of SSM aims to establish a learning health system (26), which ensures that diverse stakeholder perspectives and values are clearly understood and considered when adapting EBIs to local context, maximizing broad acceptability and adoption over time. SSM provides a systems framework for using the results of mixed methods research to visualize and discuss systems structures, interrelationships, historic context, and values/perspectives for more focused and productive problem-solving activities.

CFIR

The CFIR is used to anchor the systems thinking in a multilevel context, providing a macrolevel theoretical framework to guide research activities (20). CFIR guides boundary setting in the systems approach and facilitates the identification of stakeholders at all levels involved in or influencing cervical cancer EDT, ensuring a more complete elucidation of the system behavior. The relative impact of each CFIR domain on implementation success is naturally surfaced or probed in each phase of INSPIRE (see **Table 1**). References to specific CFIR domains by stakeholders are qualitatively coded in meeting and workshop transcripts and this information is mapped back to visual representations of the system structure and used in dialectic discussions directed toward the identification of high leverage change opportunities.

RE-AIM

The RE-AIM evaluation framework is used to both quantitatively and qualitatively assess the impact of the INSPIRE methodology as an implementation strategy in an interrupted time series design (**Table 2**; refs. 27, 28).

Results

The INSPIRE methodology

The full concept for INSPIRE is illustrated in **Fig. 1**. As in the Omidyar Systems Practice, it is an operational methodology which informs a logical sequence of purposeful research activities that collectively lead toward an implementation plan appropriately adapted and tailored to the local context. Each phase of INSPIRE is approached using a mixture of rapid mixed methods research to

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Table 1. Integration of research methods, IR frameworks, and implementation strategies by phase of INSPIRE.

	INSPIRE action	Research methods utilized	IR frameworks	Implementation strategies
Hub	1. Define problem situation with stakeholders 2. Launch the project	SSM	CFIR-1: intervention source CFIR-5: engaging	Build buy-in (involve existing governance structures, ID champions) Develop relationships (build coalitions, resource-sharing agreements, formal commitments, academic partnerships)
Phase I	3. Develop mental models of the system 4. Establish narrative and stakeholder perceptions of the system 5. Make the system visible	AIIM SAST stage 1 with key informant interviews and FGDs KAP surveys Audits of current system outcomes Pathway analysis visually represented by flow charts and swim-lane diagrams	CFIR-2/HSF: defining structural characteristics, networks, and communications CFIR-2: culture and implementation climate CFIR-3: patient needs and resources CFIR-3: external policies and incentives CFIR-4: knowledge and beliefs about the intervention CFIR-4: understand self-efficacy, individual stage of change and other attributes	Gather information (needs assessment, readiness to change) Involve patient/consumers and family members Audit current system behavior Capture and share local knowledge
Phase II	6. Engage stakeholders in group model building 7. Share, test, revise system/process maps 8. Define and localize system behaviors contributing to problem situation 9. Find leverage for change	SAST stage 2 – DWs Dialectic debate and group model building (facilitated with goal to balance desirability and feasibility guided by reflection on implementation outcomes such as feasibility, cost, acceptability, sustainability, etc.) Scenario analysis	CFIR-1: review characteristics of the intervention and options (evidence strength and quality, relative advantage, complexity, cost) and assess adaptability and trialability of alternatives CFIR-3: assess cosmopolitanism, peer pressure, influence of external policies/incentives CFIR-4: assess KAB about intervention options CFIR-4: group-level stage of change	Assess readiness and identify barriers Get feedback from audit of current system behavior Purposefully reexamine the intervention Tailor strategies to overcome barriers and honor preferences Model and simulate change Conduct local consensus discussions Distribute educational materials and conduct educational meetings Make training/education dynamic and participatory Inform local opinion leaders Create a learning collaborative Consider restructuring strategies as leverage opportunities Consider financing strategies as leverage opportunities Mandate change
Phase III	10. Stakeholder-designed implementation plan 11. Infrastructure modifications, training, dissemination plan development 12. Implement changes	Work group SSM with research team facilitation	CFIR-1: design quality CFIR-1: complexity CFIR-5: planning CFIR-5: executing	Develop a formal implementation blueprint Tailor strategies to overcome barriers and honor preferences Stage implementation scale-up Involve patients/consumers and family members Recruit, designate, and train for leadership Obtain formal commitments Develop effective educational materials relevant to mandated change

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Table 1. Integration of research methods, IR frameworks, and implementation strategies by phase of INSPIRE. (Cont'd)

	INSPIRE action	Research methods utilized	IR frameworks	Implementation strategies
				Develop a glossary of implementation (including new models) Distribute educational materials Conduct ongoing, dynamic training Conduct educational outreach visits Use train-the-trainer strategies Provide ongoing consultation Place new interventions on fee for service lists/formularies Develop supply chain management Revise professional roles Create new clinical teams Change services sites Change equipment Change records systems Develop and organize quality monitoring systems Develop tools for quality monitoring Use advisory boards and work groups Conduct cyclical tests of change Create or change credentialing and/or licensure standards
Phase IV	13. Ongoing M&E using stakeholder-defined implementation outcome metrics 14. Share M&E with stakeholder group 15. Reinitiate INSPIRE cycle where indicated by identification and localization of new or unresolved problem situation	M&E for primary implementation outcomes SAST with KII and FGD DWs	RE-AIM CFIR-5: reflecting and evaluating	Provide ongoing consultation Sustain a learning collaborative Use mass media to increase reach (only after system behavior is stabilized postimplementation) Use advisory boards and working groups Organize clinical implementation team meetings

Abbreviations: AIIM, alignment, influence, and interest matrix; DW, design workshop; FGD, focus group discussions; HSF, health systems framework; KAB, knowledge, attitudes, and beliefs; KAP, knowledge, attitudes, and practices; KII, key informant interview; SAST, strategic assumption surfacing and testing.

facilitate timely feedback to collaborators. Application of INSPIRE naturally addresses different domains of the CFIR (29) and uses multiple discrete evidence-based implementation strategies to meet the objectives of each INSPIRE phase (**Table 1**; ref. 29).

Steps 1 and 2 (phase 0) define the initial engagement of all stakeholders in the change initiative, collaboratively defining their core vision and mission and formally launching the project. These are the steps where champions are identified, and "buy-in" from the local stakeholders is established. It is critical in this early step to formalize the research–stakeholder relationships with authorized written commitments (i.e., memorandums of collaboration between institutions, including the Ministry of Health), establish roles and responsibilities, and develop initial resource-sharing agreements (with an understanding that this process itself is rarely static and will need to be iteratively addressed as health authorities, professionals, and environments change over time).

The three steps in phase I of INSPIRE aim to create a shared understanding of the current EDT program. This phase is more research intensive than the other phases but is essential to surface the critical nuances of system behavior that are context specific and thus rarely predictable from previous research. SSM emphasizes that stakeholders may have vastly different "worldviews" or understanding of how their program works (24, 25). Each stakeholder harbors a different "mental model" of the system and thus, will approach problem solving during implementation planning from their unique perspective. It is easy to see how differences in mental models between individuals will result in difficult and unproductive planning discussions; thus, it is important to bring the stakeholders into closer alignment as a first step to program design and planning by agreeing to a shared mental model and then visualizing the system that has integrated all of the perspectives in detail. This can be facilitated by starting with a general mental model of the current screening system (step 3), such as the one illustrated in **Fig. 2**. From this model, several key features of a successful cervical cancer EDT program are clear: (i) women must have access to and attend screening, (ii) the screening test must be reasonably sensitive, specific, and reliable, (iii) women

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Table 2. Proyecto PreCancer RE-AIM quantitative and qualitative evaluation metrics.

RE-AIM dimension	Quantitative evaluation metric(s)	Qualitative evaluation metric(s)
Reach	% of eligible women screened Preimplementation: VIA Postimplementation: HPV testing	FGD/KII of women screened vs. unscreened KAP survey
Effectiveness	% of women completing continuum of care Preimplementation: % of screen-positive women attending colposcopy, % with colposcopy/histology-confirmed CIN2^{+} receiving treatment Postimplementation: % of screen-positive women attending TVT, % of ablation-eligible women receiving ablation, % of ablation-ineligible women attending colposcopy, and % of ablation-ineligible women receiving treatment	Clinical observation (counseling content and quality) Time-and-motion studies (36) FGD/KII of women completing and not completing continuum of care FGD/KII of staff delivering the program Assess acceptability of receiving immediate treatment vs. triage management by women Assess acceptability of self vs. clinician sampling, lack of visual exam at primary screen
Adoption	% of midwives screening ages 30–49 women by HPV testing Compare %VIA/total screens to %HPV/total screens over time	FGD/KII with high and low adopters of HPV testing
Implementation	Time from sample collection to testing, result delivery to patient, result delivery to follow-up visit, etc.	Time-and-motion studies
Maintenance	Quarterly change in reach and effectiveness measures over time	Note major events that can influence time trends (health strikes, flooding, transportation strikes, supply chain disruptions, political turnover) Assess unexplained changes (increases or decreases) in reach and effectiveness measures

Abbreviations: TVT, Triaje Visual para Tratamiento; VIA, visual inspection with acetic acid.

screening positive and referred for diagnosis of neoplasia must have access to and complete the diagnostic procedures, (iv) the diagnostic test must be reasonably sensitive, specific, and reliable, (v) women with confirmed neoplasia must have access to and complete treatment, and (vi) the treatment provided must be reasonably effective.

These mental models can be used to guide qualitative assessments of the stakeholders by probing for details such as the "who, what, when, where, and how" for each step of the EDT process, as well as evaluating stakeholders' readiness to change (step 4). While this can be done in 1–2 focus groups representing many stakeholders, power differentials and hierarchies operate in most health systems, and thus, it is critical to elicit the mental models of all stakeholders, not just those of the authorities. This can be achieved by employing an SSM approach called strategic assumption surfacing and testing (SAST). This

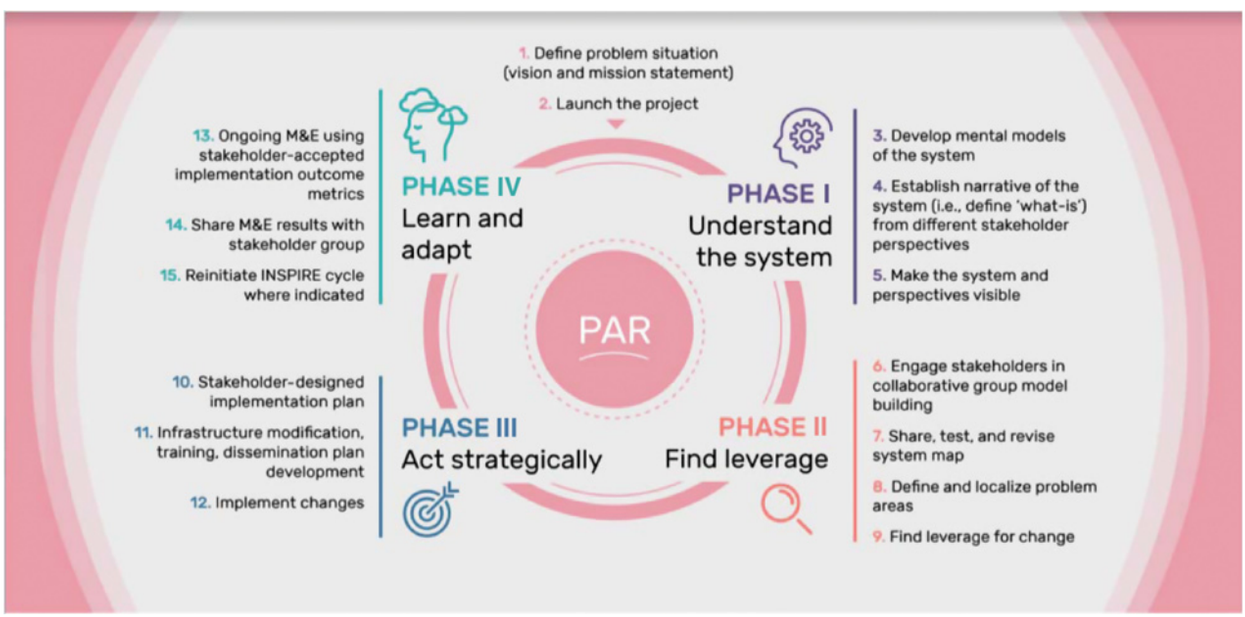

Figure 1.
Conceptual model of INSPIRE, adapted from the Omidyar Group Systems Practice (19).

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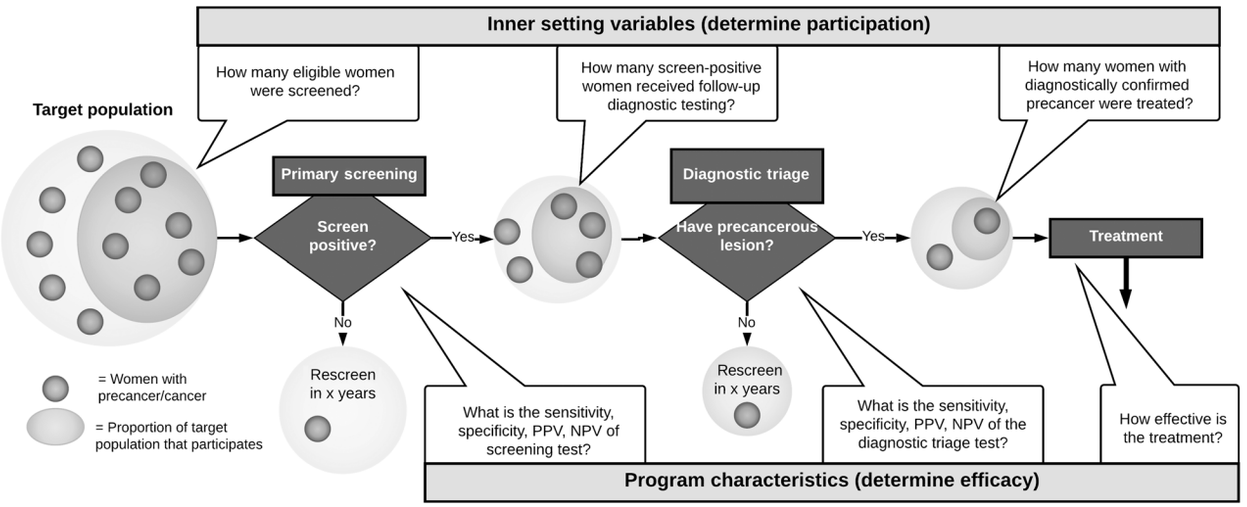

Figure 2.

Mental model of key elements for effective EDT programs for the secondary prevention of cervical cancer. NPV, negative predictive value; PPV, positive predictive value.

approach is deployed in two stages (12). The first SAST stage (conducted in phase I) stratifies stakeholders according to shared characteristics, maximizing the within-group similarities and between-group differences in function/hierarchy. The second SAST stage (conducted in phase II) brings representative stakeholders together for facilitated discussion of the system structure, function, and perspectives elicited in SAST stage 1.

This qualitative work is complemented with quantitative assessments: (i) an audit of the key performance indicators from the current system (e.g., number and percent of women screened, prevalence of screen positives, diagnostic and treatment completion rates, etc.) and (ii) assessment of the knowledge, attitudes, and practices (KAP) regarding cervical cancer screening of a representative sample of community women. The audit will not only measure system performance but will also uncover strengths and deficiencies in data capture, data flow, and overall quality of existing surveillance efforts. The KAP survey can be further complemented with GPS data to estimate distances and time required for women to access services.

Step 5 operationalizes the goal of phase I of INSPIRE, to create a common visual understanding of current system behavior. This requires pathway analysis, which is accomplished through triangulation of mixed method research findings, including semistructured interviews, focus group discussions (FGD), and a KAP survey of community women. The program impact of the elucidated pathways is derived from the system audit. Visualizing the results may take multiple forms depending on the information to be shared (30). For example, flow charts are useful for depicting overall system structure, with annotations and symbols to localize delays, bottlenecks, redundancies, and fragmentation. Alternatively, swim-lane diagrams are better suited for outlining detailed movement of patients, data, and/or specimens through the multiple levels (or sectors) of the system and can highlight inefficiencies or inequalities in the burden of EDT implementation or utilization (Supplementary Fig. S1).

The objective of phase II of INSPIRE is to find leverage. This involves a series of four steps, which can be accomplished during a 1.5- to 2-day carefully planned stakeholder workshop, or "design workshop" (DW). The DWs operationalize the second stage of SAST (12), which seeks to use the information collected and made visible in SAST stage 1 to facilitate a dialectical debate about the current problem situation among a fully representative set of stakeholders (including health authorities, administrators, health professionals at all levels, and community representatives; step 6). There are three primary goals for a DW: (i) facilitate discussion to elicit feedback regarding the results of the system audit (step 7); (ii) debate the problem areas (step 8; ref. 31), and (iii) transfer evidence-based knowledge (32) and use multiple scenario analysis to find leverage points for positive change (step 9; ref. 33).

Scenario analysis tools are applied to help fully appreciate the "what-if" consequences of one possible change over another. Simple simulations of changes to the system in terms of coverage at each step in the care cascade, test sensitivity and specificity, loss to follow-up, and treatment efficacy are set-up to generate a comparative impact on health outcomes and resource needs from each implementation scenario. The scenario analysis is an interactive exercise, where stakeholders come up with the "what-if" scenarios, make and justify their model assumptions, and then discuss the simulation output. DW facilitators probe stakeholders for evidence and/or certainty regarding their assumptions (which will facilitate useful debate) and probe each scenario regarding its ability to meet the full spectrum of implementation requirements, such as acceptability, adoption, etc. (see **Table 3**; ref. 9). A key principle of both the scenario analysis exercise and SSM is that there is no single best or "right" solution. Workshop facilitators emphasize that any chosen intervention will come with some costs and some benefits; the aim of the DW is to select the choice that best fits the stakeholder's context and optimizes program impact for reduction in cervical cancer incidence and mortality.

The DW is intended to reach an agreed upon action for change in the screening system (24, 25). The goal is not to achieve 100% consensus, but rather to reach a general agreement in an option that maximally balances desirable and feasible change among most stakeholders and is agreeable to the governing authorities. From **Table 1**, phase II of INSPIRE can blend at least 13 discrete, evidence-based implementation strategies (29) into a 2-day DW, increasing the efficiency of implementation research and covering multiple CFIR implementation domains (20).

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Table 3. Implementation considerations in implementation planning and decision-making.

Acceptability
How acceptable is this option to health providers, patients, and the administration?
Adoption
How likely is it that all health centers will be willing to change their behaviors to enact this plan?
Feasibility
How likely is it to acquire the resources necessary for this option?
Fidelity
How likely is it to complete all trainings necessary for this option?
How likely is it that the established processes will be followed without external support?
Implementation cost
How likely is it that the DIRESA/health system can finance this option?
Coverage
How likely is it that this option will increase the percentage of women screened and women who adhere to the continuum of care from screening until treatment (if necessary)?
Sustainability
How likely is it that this option will continue once the project withdraws?
How likely is it that this option will survive changes in the government/administration?

INSPIRE's third phase, acting strategically, is the phase most familiar in implementation research. This phase represents the "do" phase of implementation and bundles together at least 25 evidence-based discrete implementation strategies (29) into a series of three steps. In step 10, stakeholders drive the implementation planning. This planning is extensive and must involve stakeholders at all levels of the health system structure (**Fig. 3**). Planning is guided by a new shared mental model that is derived from the DW decisions (Supplementary Fig. S2) and uses similar visual aids as in phase I, including flowcharts and swim-lane diagrams to create a shared understanding of how processes will change. Facilitators of the planning workshops guide stakeholders in specifying the who, when, where, how, and why for each process step, and these decisions are annotated and reflected in the shared visual. Multiple scenario analysis is again useful to simulate the impact of different choices in staffing and resourcing to maximize program efficiency, feasibility, and cost-effectiveness. The key in INSPIRE phase III is the facilitation of stakeholders in shared decision-making, rather than prescriptive transfer of implementation guides to ensure locally adapted, acceptable, feasible, and affordable program design.

Step 11 involves the known requirements of implementing a new innovation and includes making (and financing) any infrastructural modifications, arranging for training and development of a sustainable training plan for counseling, new laboratory and clinical procedures, disseminating changes and new processes through all levels of the health system, and ensuring a quality data collection and monitoring plan.

INSPIRE phase IV, learn and adapt, involves ongoing M&E and iterative evaluation of the key implementation outcome metrics (as described in **Table 2**) through periodic stakeholder meetings, or "redesign workshops." Step 13 emphasizes that the key performance indicators measuring intermediate program success (RE-AIM metrics; **Table 2**) are established and agreed upon in advance with the stakeholders and should ensure monitoring through the care cascade (e.g., through treatment where necessary). Redesign workshops operate similarly to DWs, but with knowledge transfer coming more from internally derived data and experience than from external experience and literature (23). New problem situations, as well as unexpected positive system behavior, may emerge postimplementation. The goal of the redesign workshop and step 15

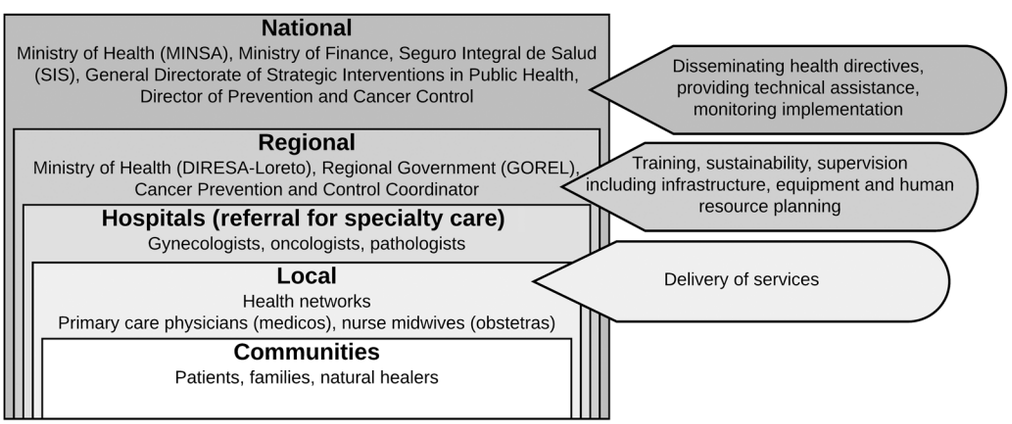

Figure 3.
Multilevel sectors of cervical cancer control through EDT in Peru.

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in phase IV is to find leverage to improve problematic areas and to capitalize on emergent opportunities to collectively strengthen the screening system. Phase IV represents the establishment of an ongoing learning health system process, which may strengthen overall health system functions and may increase feasibility of additional implementation strategies to further sustain the intervention over the long term.

Discussion

A global resolution for elimination of cervical cancer is a tribute to the unprecedented success in the discovery and development of EBIs for the prevention and control of a cancer, which remains one of the leading causes of cancer-related incidence and mortality in women worldwide. There is ample cause to celebrate the biomedical progress that paved the way for the elimination initiative. However, meeting ambitious elimination goals will not occur if we accept the historically long lag between discovery and widespread adoption of EBIs into practice.

The INSPIRE methodology was developed with an acute understanding that the translational challenges are complex and center as much around the challenges related to health systems' organizational structure and human agency as the availability, adoption, and affordability of new technologies. While standard implementation research, focused on specific elements of individual or organizational behavior change are methodologically rigorous and thus, academically desirable, it is readily evident from a program-planning perspective that any of the discrete implementation strategies in **Table 1**, enacted alone, would be unlikely to facilitate the system-level change required to introduce and sustain HPV-based screen-and-treat programs in low- and middle-income contexts by 2030. We, therefore, hypothesize that a generalizable approach to context-adapted implementation of EBIs, rather than static dissemination of concrete implementation roadmaps, will more rapidly facilitate scalable and sustainable EDT program development.

This article is intended to describe the foundational underpinnings of this participatory systems approach to implementation of cervical cancer EDT programs and to discuss preliminary evidence of the success of the approach; more detailed analysis of the implementation research is in progress and will be reported separately. In brief, we (Proyecto PreCancer) have applied the approach in a single-health network in the Amazonian city of Iquitos, Peru, which provides basic health care and preventative services to approximately 20,000 women ages 30–49 years who are the primary targets for cervical screening.

Using a small research staff, we have successfully and sustainably engaged over 90 stakeholders across multiple health system levels involved in and/or influencing cervical cancer prevention in Peru since introducing the INSPIRE approach to participatory development of improved cervical cancer EDT programs in 2016. These stakeholders have served dual roles in the implementation process. As research subjects in phase I of INSPIRE, they were instrumental in providing the necessary data regarding systems processes, values, and perspectives critical to creating a shared visual understanding of the actual, not just the intended, behavior of the EDT system in their context.

Application of SSM in DWs in INSPIRE phase II facilitated shared decision-making across a broad spectrum of stakeholders acting as collaborators in the implementation planning. This was guided by: (i) a shared understanding of their current system; (ii) facilitated debate on the system's strengths and failures, as well as historic precedents or habituation that might have contributed to system behavior; (iii) knowledge transfer of alternative processes, technologies, and strategies tested in other settings; and (iv) use of simple, interactive simulation models to evaluate different intervention options in terms of program effectiveness by simultaneously considering the efficacy of screening, diagnostic tests, and treatment strategies with the likelihood of accessibility, adoption, and ability to deliver the EBI as designed. As a result of this process, stakeholders in the Iquitos-South health network elected to move away from Pap- or visual inspection with acetic acid (VIA)–based screening with colposcopic evaluation of all positive tests to an HPV-based screening with visual evaluation and ablative treatment of all positives, if eligible, referring only ablation-ineligible women to severely constrained colposcopy/pathology services.

Research staff and stakeholder collaborators worked together from February 2019 through June 2019 to prepare the system for implementation of several new activities, including HPV-based screening and thermal ablation treatment at the primary level. Implementation of this new strategy included efforts to deimplement existing Pap-based strategies. The research team, guided by the CFIR framework (20) and health systems models (15), worked to ensure that the required infrastructure, training, knowledge dissemination, reporting, procurement, and M&E plans were adapted to the new system (**Table 2**). In July 2019, a phased approach to launching the new HPV-based screen-and-treat program was launched in two health centers, expanding over the next 5 months to 14 of the 17 largest health facilities in the network.

Adoption of the strategy and deimplementation of prior strategies targeted for women 30–49 years has been achieved in all health centers, and screening coverage increased from 19% of annual goals in 2018 using Pap/VIA to 86% average monthly coverage in the first 8 months of the HPV screen-and-treat program implementation (screening coverage calculated as an average of monthly targets given a goal of 20% coverage per year in 5-yearly HPV-based screening and 33.3% coverage per year in 3-yearly Pap- or VIA-based screening). Work is ongoing to monitor the changes in screening coverage over time as the system stabilizes and to strengthen the plans to ensure all HPV-positive women are evaluated and treated as appropriate within 30 days of screening. Acceptability of the new program by health professionals and the community is being evaluated through mixed methods approaches in phase IV and is communicated back to the stakeholder groups for ongoing program delivery adaptation (23).

A key next step in the evaluation of the INSPIRE methodology for implementation of cervical cancer EDT programs is evaluation of the scalability and sustainability. The Peruvian Ministry of Health has documented plans for phased scale-up in the region beyond the Iquitos-South health network, as well as other regions in Peru. Using the experience from the Proyecto PreCancer, we are developing a model of 1- to 2-day DWs to facilitate context-adapted implementation planning, including the review of M&E results in quarterly or biannual redesign workshops, which allows for ongoing adaptation.

Certainly, the INSPIRE-driven implementation strategy requires further testing to establish its value as a generalizable implementation approach. However, early evidence from the Proyecto PreCancer suggests that the ownership and understanding of the complex system behavior–driving program impact instilled through INSPIRE can influence sustainability. Specifically, it is known that most EBIs implemented within complex, government-operated, adaptive health systems must be resilient to frequent staff and management turnover at

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all levels of the health system, from the National and Regional Ministries to the health care professionals trained to deliver the intervention at the local level.

Since the initiation of Proyecto PreCancer, Peru has had two Presidents, five Ministers of Health, five Directors of the National Cancer Control Program, and three Regional Directors of Health. A result of some of this turnover has been a national change in cervical cancer screening policy, affecting the compliance of the screen-and-treat program with national guidelines, which state a clear preference for treatment only after histologic confirmation of precancerous lesions (34, 35). A sense of ownership and understanding of the choices they made through rigorous system evaluations in INSPIRE has led the Regional Ministry and the Iquitos-South health system to codify their decisions to use the most appropriate context-adapted strategy, through a regional "ordenanza," to ensure meaningful reduction in cervical cancer in their region, which has the highest burden of cervical cancer in Peru.

In summary, INSPIRE recognizes that implementation strategies must be adapted to both engineered systems processes and technologies as well as the human agency and interactions, which are essential elements in ensuring that an EDT system achieves its intended purpose of reducing cervical cancer incidence and mortality. By anchoring INSPIRE on participatory systems thinking, the approach is hypothesized to result in establishment of a sustainable learning system, which will be critical to achieve sustainable program implementation in complex adaptive health system environments. Standardized reporting of both successful and unsuccessful implementation interventions and program adaptations in each INSPIRE phase, as well as accessible warehousing of evidence-based tools and resources, will facilitate global expansion of the learning system. In this respect, INSPIRE represents an operational methodology to move implementation research out of reductionist thinking and academic silos by providing a feasible methodology that allows research and implementation teams to "keep the big in mind when you can only handle the small" (12).

Disclosure of Potential Conflicts of Interest

P.E. Gravitt reports receiving other commercial research support from Cepheid. A.F. Rositch is a consultant for UE LifeSciences. J. Jeronimo is a consultant for Merck. No potential conflicts of interest were disclosed by the other authors.

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The views expressed in this article are those of the authors and do not represent the official positions of the NCI or NIH.

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