

# CUGH & NCI Cervical Cancer Webinar 3: Ensuring effective implementation of cervical cancer prevention and control strategies

August 12, 2020

11:00am-12:00pm EDT

Co-Moderator



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Sociedad  
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Co-Moderator



**Isaac F. Adewole, MD,**  
Professor, Obstetrics and Gynaecology  
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# CUGH & NCI Cervical Cancer

*The role of Implementation Science to bridge the gap between research and practice in the implementation of HPV-testing as primary screening in middle income settings*

Silvina Arrossi, Msc, PhD  
CEDES/CONICET

Declaration of Good Standing and Conflict of Interest Disclosure

I do not have a financial interest in any product or service related to my presentation

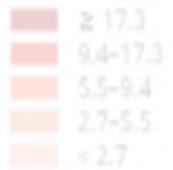
# THE BURDEN OF CERVICAL CANCER

## TECHNOLOGY

HPV-testing  
HPV-self  
collection  
HPV-  
vaccination

Cervical  
cancer  
elimination

ASR (World) per



# THE BURDEN OF CERVICAL CANCER

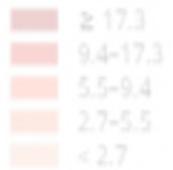
## TECHNOLOGY

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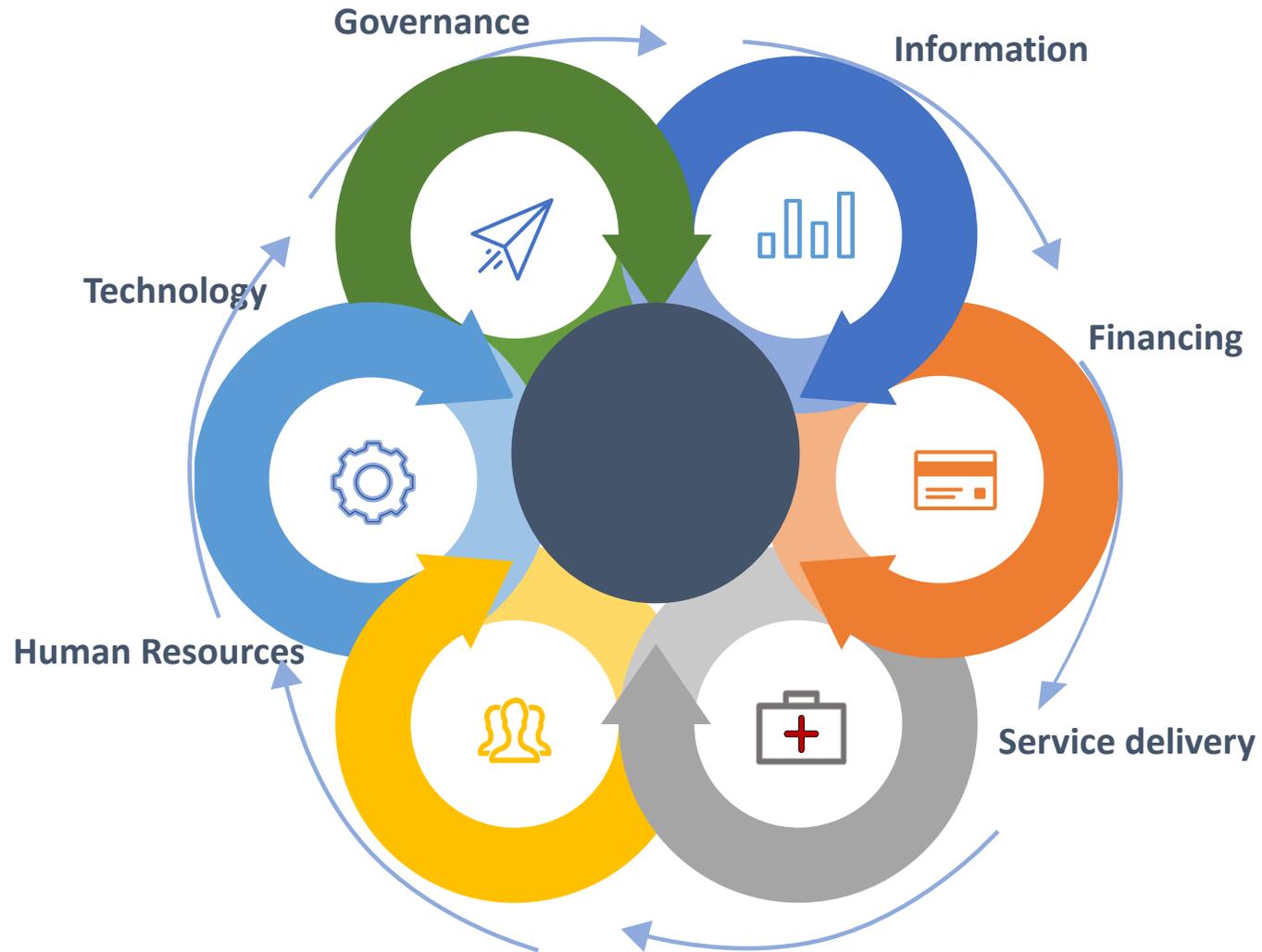
Cervical  
cancer  
elimination

ASR (World) per



# HOW TO IMPLEMENT EVIDENCE-BASED INTERVENTIONS IN REAL WORLD SETTINGS SO WE CAN MAKE THEM WORK?

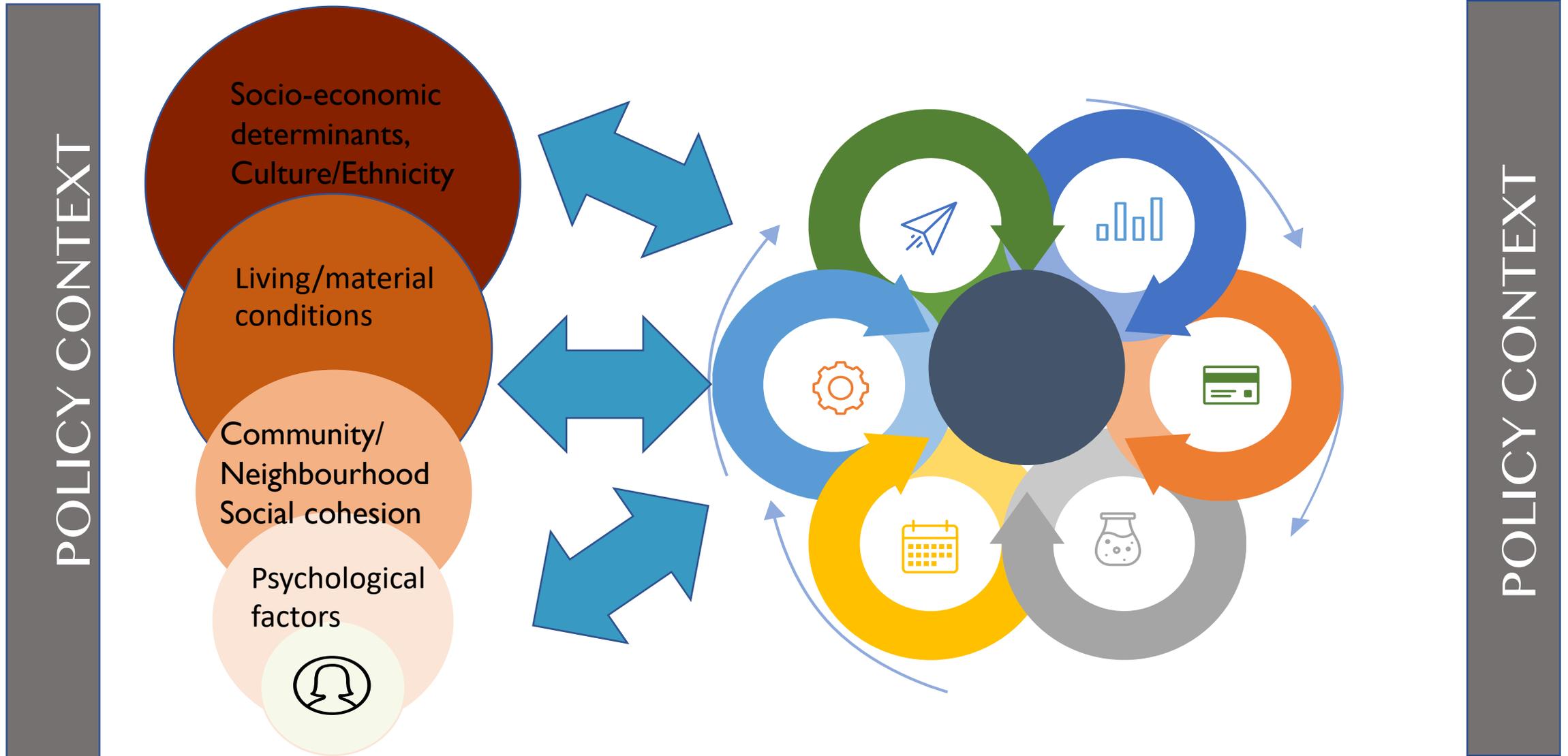
POLICY CONTEXT



POLICY CONTEXT

SOURCE: WHO, 2007

# HOW TO IMPLEMENT EVIDENCE-BASED INTERVENTIONS IN REAL WORLD SETTINGS SO WE CAN MAKE THEM WORK?



POLICY CONTEXT

**WHAT**  
HPV-testing  
HPV-self  
collection  
HPV-  
vaccination



**POLICY CONTEXT**

**WHAT**

HPV-testing  
HPV-self  
collection  
HPV-  
vaccination

**HOW**

Implementation  
strategies

**OUTCOMES**

Reach  
Feasibility  
Acceptability  
Adoption  
Cost  
Uptake  
Fidelity  
Scaling-up  
Barriers  
Facilitators  
Equity

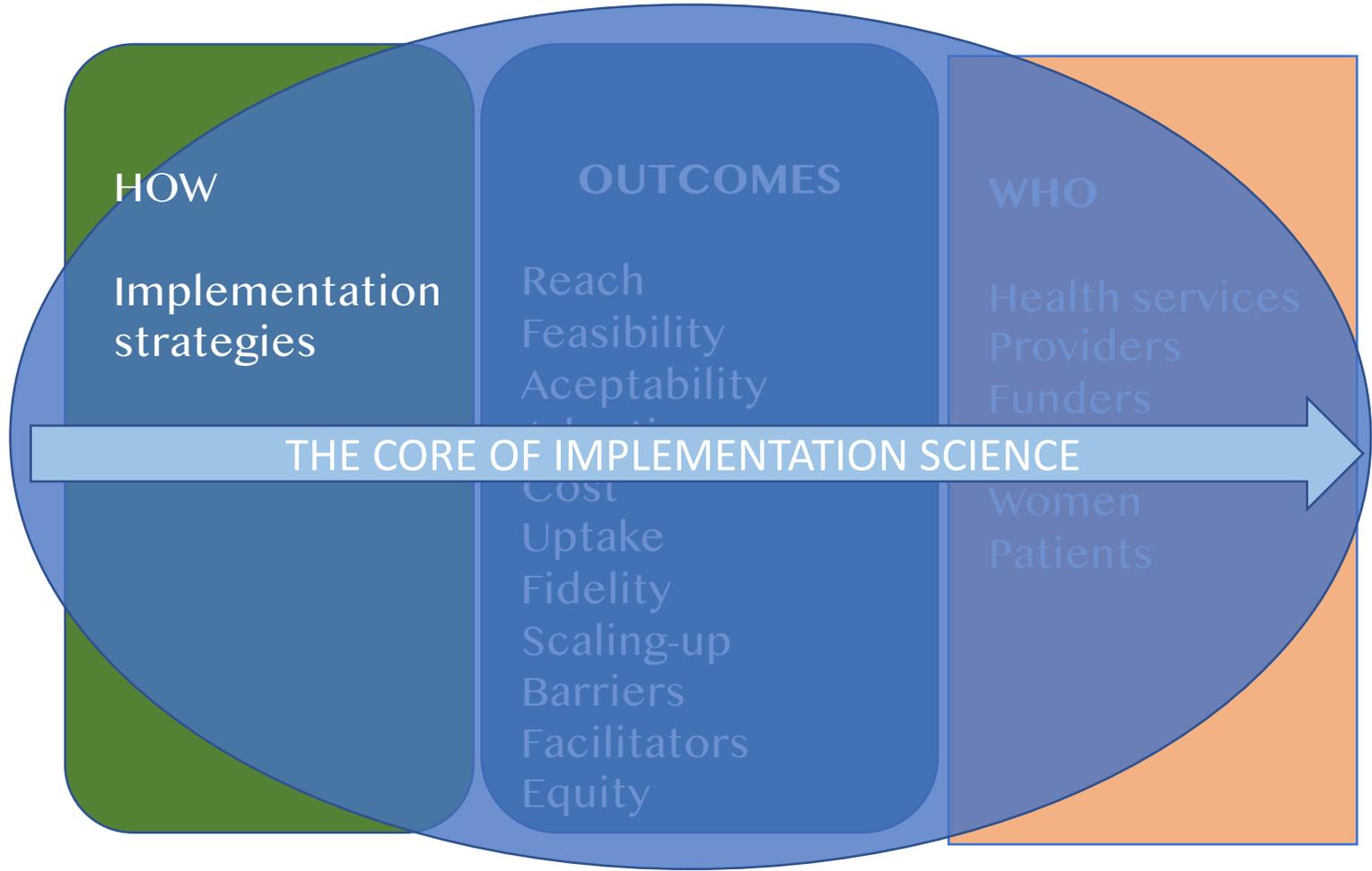
**WHO**

Health services  
Providers  
Funders  
Decision-makers  
Women  
Patients

**Incidence  
Mortality**

**POLICY CONTEXT**

**WHAT**  
HPV-testing  
HPV-self collection  
HPV-vaccination



**Incidence  
Mortality**

## ARGENTINEAN CONTEXT

### HPV SELF-COLLECTION

Highly effective to detect disease

Acceptable

High potential to reduce barriers to screening

- The offer of HPV self-collection: Where, by whom?
- Is it acceptable?
- Is it effective to increase screening uptake?
- What are its core components?
- What are the method main limitations in the local context?

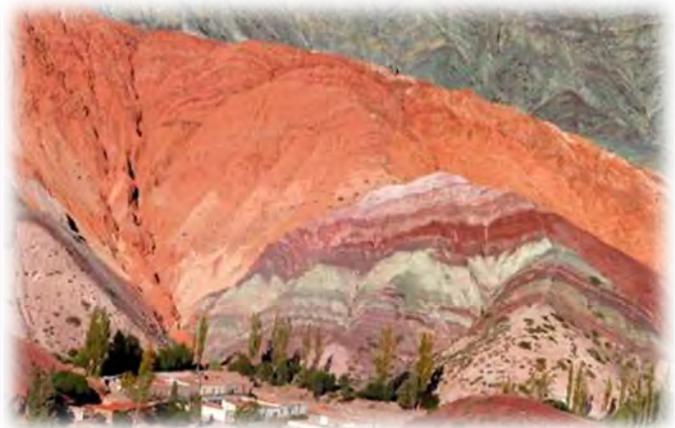




**200 CHWs who routinely visited households for health service provision**



**6000 women**



# EMA STUDY: MAIN RESULTS



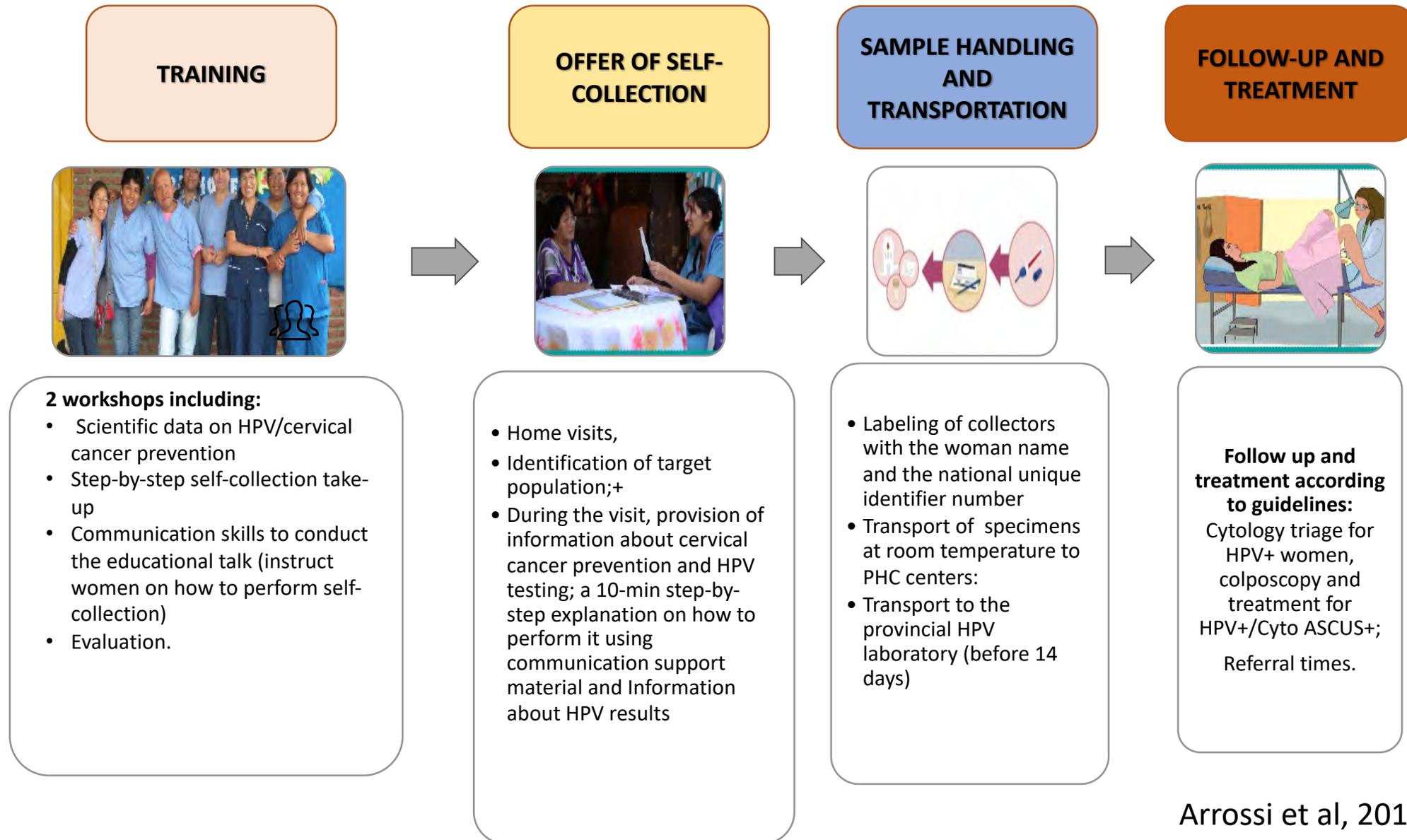
- High acceptability by women, by CHWs and health providers



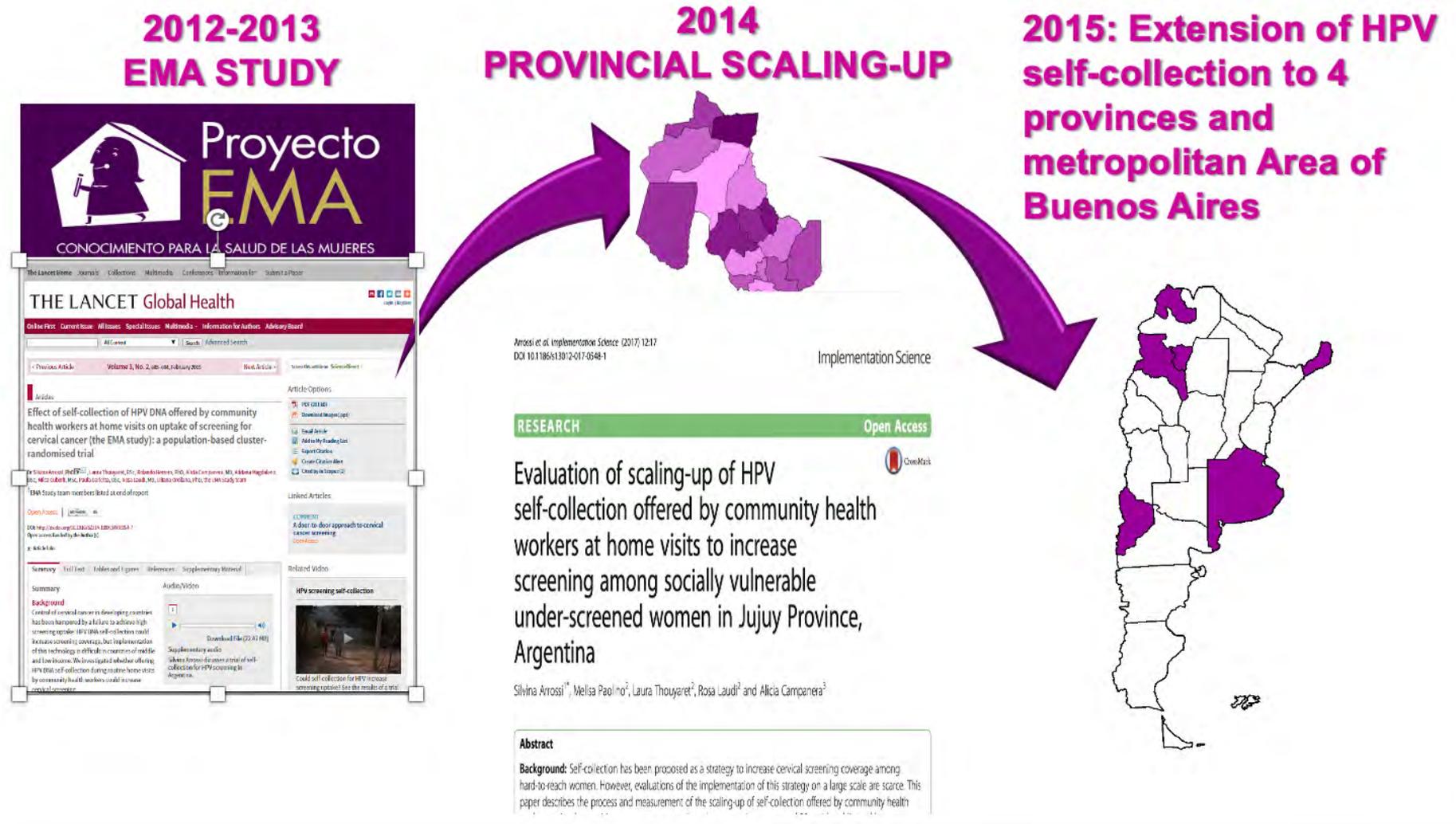
- 4 times more screened women in the intervention group than in the control group (86% vs 20%)

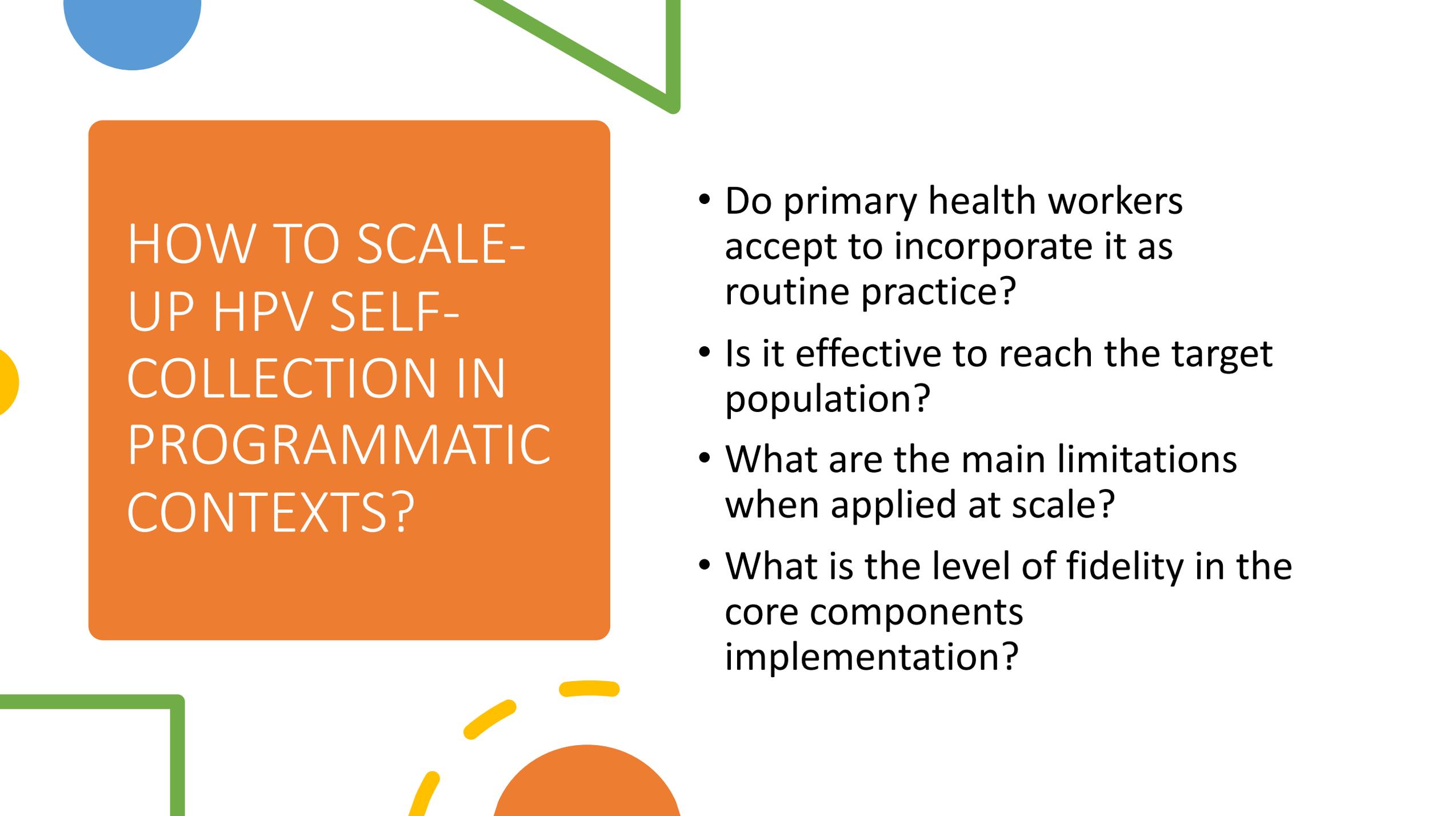


# Self-collection strategy: Core components



# Is the intervention (EMA STRATEGY) being delivered as intended by the program developers and in line with the program model?

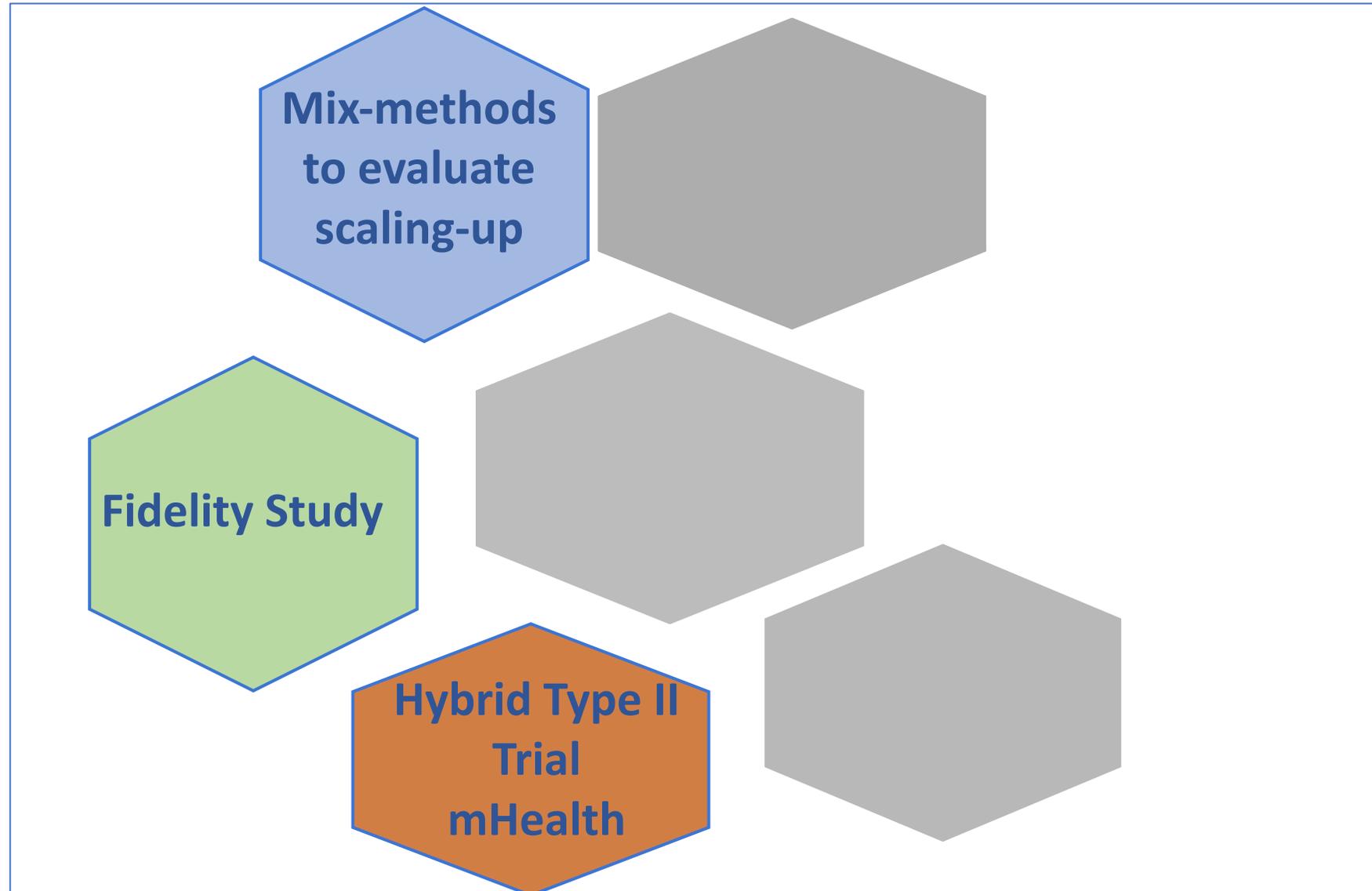




## HOW TO SCALE-UP HPV SELF-COLLECTION IN PROGRAMMATIC CONTEXTS?

- Do primary health workers accept to incorporate it as routine practice?
- Is it effective to reach the target population?
- What are the main limitations when applied at scale?
- What is the level of fidelity in the core components implementation?

# IMPLEMENTATION SCIENCE APPLIED TO SELF-COLLECTION



➤ Evaluation of provincial scaling up

➤ N= 3000 women

**R**

**Reach:** 10 % of screening in target population

**E**

**Effectiveness to increase coverage:**  
40% increase in screening uptake in target population

**A**

**Adoption:** 70% of CHWs offered Self-collection;

**I**

**Implementation:**  
Training: 82%; Discarded samples: 0.2%  
70% triage; 70% DX; Tx: 82%  
CIN2+: 0,9% (EMA: 1,1%)

**M**

**Maintenance:** SC routine practice from 2014 onwards

# FIDELITY STUDY IN LA MATANZA, BUENOS AIRES METROPOLITAN AREA

Self-collection introduced in 2017

Urban municipality with 2 million inhabitants

More than 30% of its population is poor, high insecurity



# FIDELITY STUDY IN LA MATANZA, BUENOS AIRES METROPOLITAN AREA

How far the implemented intervention actually adhered to the prescribed model  
(EMA strategy/core components)?

## METHODS

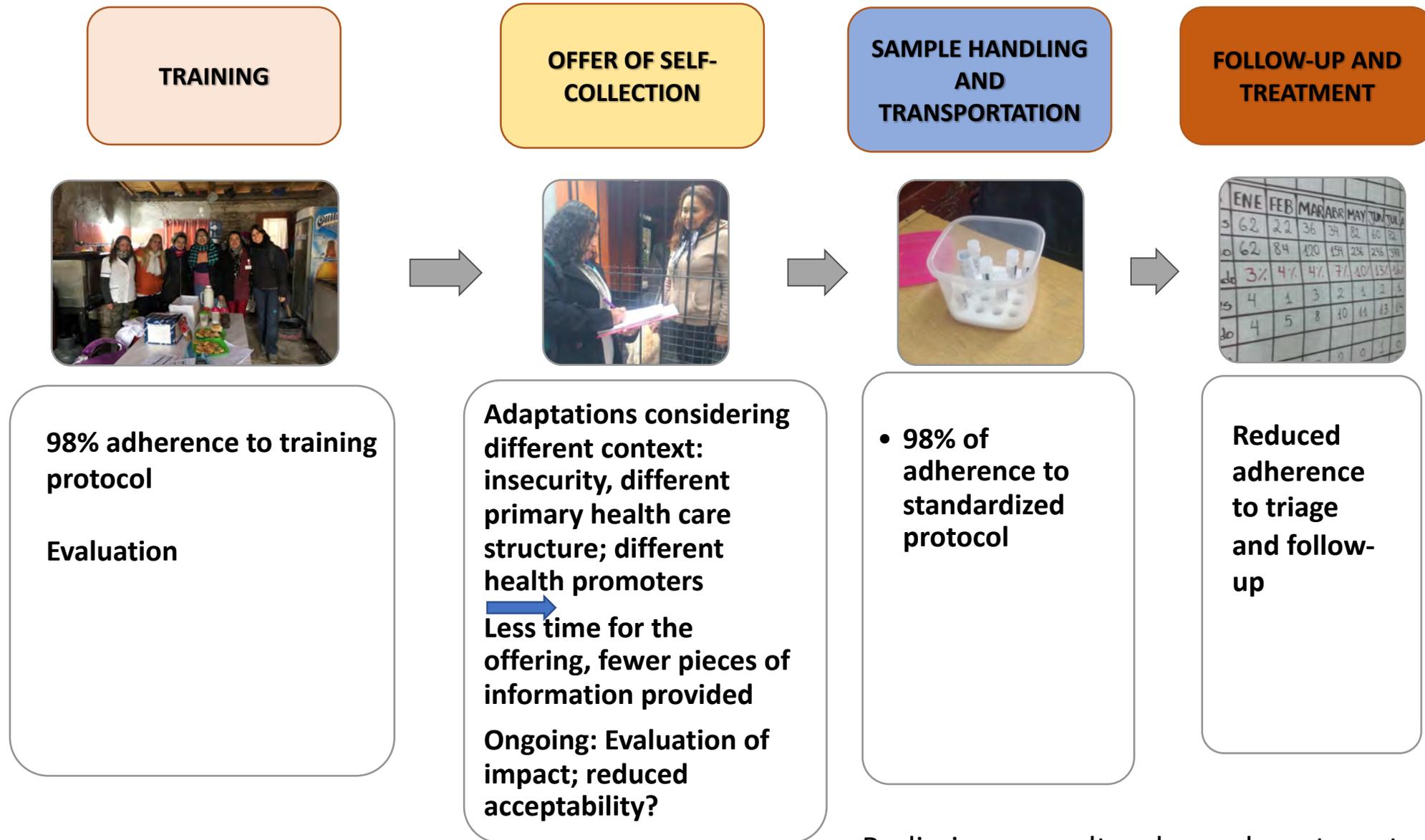
Observations of health promoters during the offering of self collection (n=70)

Evaluation of training (n=171)

Analysis of screening registries (clinical outcomes, follow-up, treatment)

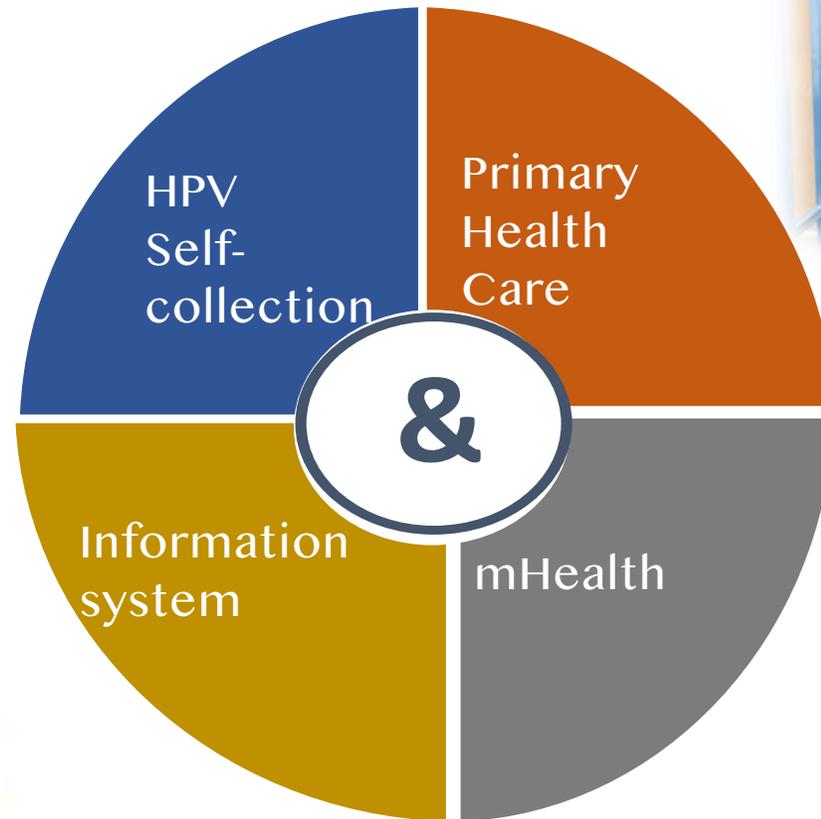


# Fidelity Study in La Matanza, Buenos Aires Metropolitan Area



Preliminary results, please do not quote

# IMPLEMENTATION SCIENCE TO IMPROVE EFFECTIVENESS OF THE FOLLOW-UP PROCESS



# **MIXED-METHODS** EVALUATION OF A MULTI-COMPONENT **MHEALTH** INTERVENTION FOR TRIAGE AFTER HPV **SELF-COLLECTION:** **THE ATICA STUDY**

(APPLICATION OF COMMUNICATION AND INFORMATION TECHNOLOGIES TO SELF-COLLECTION, FOR ITS INITIALS IN SPANISH)

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- ❖ Formative research to design messages: What should be said?, key messages
- ❖ Pragmatic Randomized controlled trial: Is it effective in real world conditions?
- ❖ Evaluation of implementation: decisors, CHWs, women



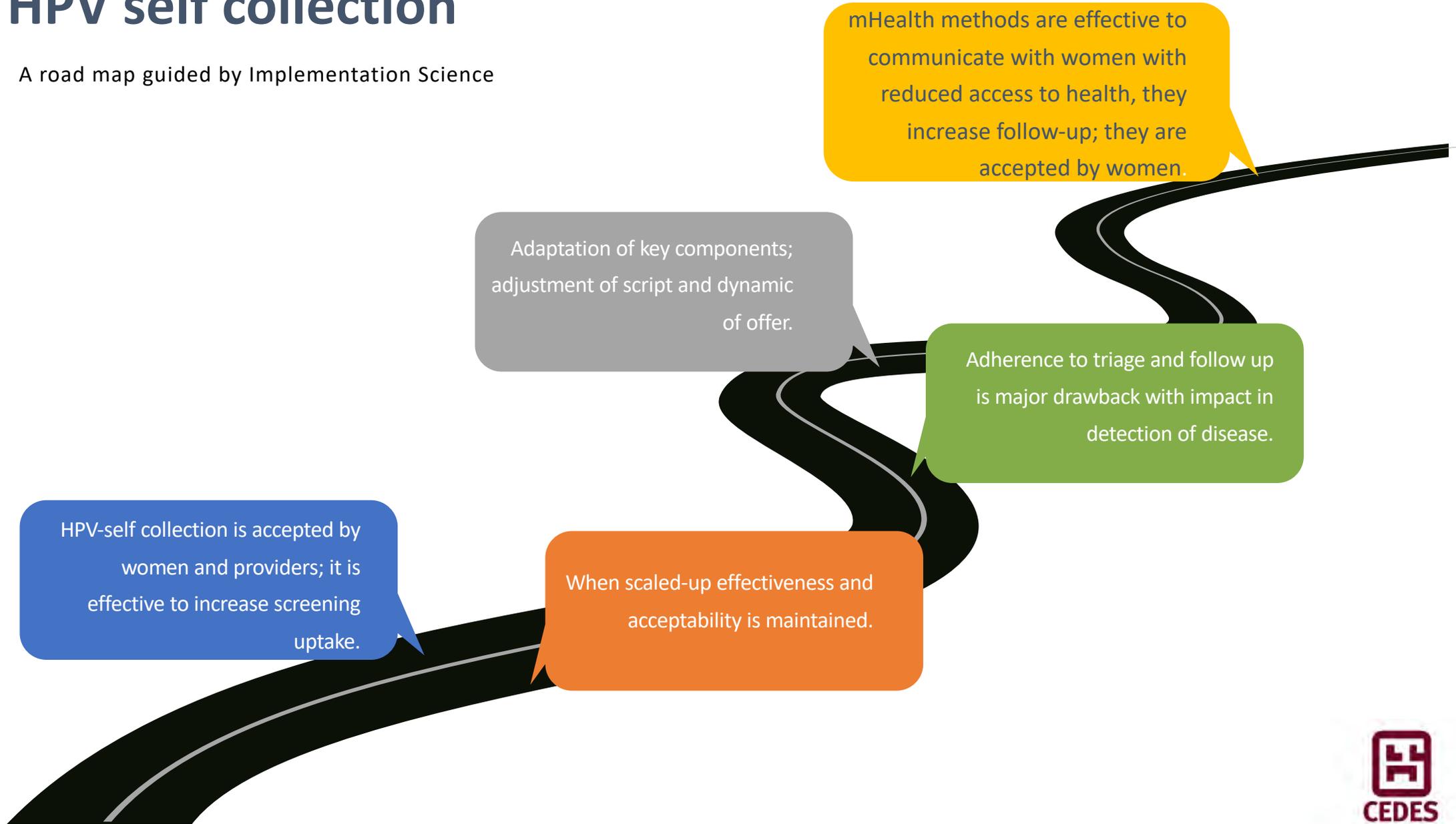
## ATICA PRELIMINARY RESULTS: 5351 participating women

- ❖ Women accept messages; for them they represent the close link with CHWs (Sanchez-Antelo et al, 2019)
- ❖ CHWS consider messages as a facilitator of their work and link with women (preliminary results)
- ❖ Women who received SMS were more likely to be triaged (19% difference; preliminary results)



# HPV self collection

A road map guided by Implementation Science



# **ACKNOWLEDGEMENTS**

Ministerio de Salud de Argentina, for its participation in the EMA study

Instituto Nacional del Cancer, Argentina, for its participation in the EMA study/ATICA project/Fidelity study

Ministerio de Salud de Jujuy, for its participation in the EMA study/ATICA Project

IARC-WHO, for its participation in the EMA Study

Secretaria de Salud de la Matanza, for its participation in the Fidelity Study

Harvard University, for its participation in the ATICA Project

Deakin University Australia, for its participation in the ATICA project

NCI/NIH for its funding of the ATICA Project

**Thanks!**

**Silvina Arrossi**  
**silviarrossi@cedes.org**

# Designing research to guide program implementation: The ASPIRE Program



## CUGH Webinar Series: August 2020

# The ASPIRE program of research

- Partnership between UBC, Makerere University and Uganda Cancer Institute since 2006
- Focused on cervical cancer elimination
- Ongoing consultation with MoH and health care leaders developing National strategy for cervical cancer elimination
- Phased pragmatic research approach to designing cervical cancer screening program



# Designing a research program with an implementation focus

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- 1) Always keep end goal of national scale-up in mind
- 2) Authentic, established partnerships are critical to a pragmatic in trial design
- 3) Responsive to input from partners and stakeholders including patients and health system leaders.
- 4) Plan trial as program implementation - logic model development; consider the entire cascade
- 5) Develop process evaluation strategy using a Implementation Science framework (we used the Reach, Effectiveness, Adoption, Implementation, Maintenance (RE-AIM) framework)

# Assessing women's willingness to collect their own cervical samples for HPV testing as part of the ASPIRE cervical cancer screening project in Uganda

Sheona Mitchell <sup>a</sup>, Gina Ogilvie <sup>a,b,\*</sup>, Malcolm Steinberg <sup>b,c</sup>, Musa Sekikubo <sup>d</sup>,  
Christine Biryabarema <sup>d</sup>, Deborah Money <sup>a,e</sup>

<sup>a</sup> University of British Columbia, Vancouver, Canada

<sup>b</sup> British Columbia Center for Disease Control, Vancouver, Canada

<sup>c</sup> Simon Fraser University, Vancouver, Canada

<sup>d</sup> Makerere University, Kampala, Uganda

<sup>e</sup> British Columbia Women's Hospital, Vancouver, Canada

## Understanding the role of embarrassment in gynaecological screening: a qualitative study from the ASPIRE cervical cancer screening project in Uganda

Flora F Teng,<sup>1</sup> Sheona M Mitchell,<sup>1</sup> Musa Sekikubo,<sup>2</sup> Christine Biryabarema,<sup>2</sup>  
Josaphat K Byamugisha,<sup>2</sup> Malcolm Steinberg,<sup>3,4</sup> Deborah M Money,<sup>1,5</sup>  
Gina S Ogilvie<sup>1,3</sup>

## Understanding Men's Perceptions of Human Papillomavirus and Cervical Cancer Screening in Kampala, Uganda

Erin Moses <sup>1</sup>, Heather N Pedersen <sup>1</sup>, Emily C Wagner <sup>1</sup>, Musa Sekikubo <sup>1</sup>, Deborah M Money <sup>1</sup>,  
Gina S Ogilvie <sup>1</sup>, Sheona M Mitchell-Foster <sup>1</sup>

# Results of a community-based cervical cancer screening pilot project using human papillomavirus self-sampling in Kampala, Uganda

Gina S. Ogilvie <sup>a,\*</sup>, Sheona Mitchell <sup>b</sup>, Musa Sekikubo <sup>c</sup>, Christine Biryabarema <sup>c</sup>, Josaphat Byamugisha <sup>c</sup>, Jose Jeronimo <sup>d</sup>, Dianne Miller <sup>b</sup>, Malcolm Steinberg <sup>e</sup>, Deborah M. Money <sup>b</sup>

<sup>a</sup> Department of Family Practice, University of British Columbia, Vancouver, Canada

<sup>b</sup> Department of Obstetrics and Gynecology, University of British Columbia, Vancouver, Canada

<sup>c</sup> Department of Obstetrics and Gynecology, Makerere University, Kampala, Uganda

<sup>d</sup> Program for Appropriate Technology in Health, Seattle, USA

<sup>e</sup> Faculty of Health Sciences, Simon Fraser University, Vancouver, Canada

## Self-collection based HPV testing for cervical cancer screening among women living with HIV in Uganda: a descriptive analysis of knowledge, intentions to screen and factors associated with HPV positivity

Sheona M Mitchell <sup>1</sup>, Heather N Pedersen <sup>1</sup>, Evelyn Eng Stime <sup>1</sup>, Musa Sekikubo <sup>2</sup>, Erin Moses <sup>3</sup>, David Mwesigwa <sup>4</sup>, Christine Biryabarema <sup>2</sup>, Jan Christilaw <sup>5</sup>, Josaphat K Byamugisha <sup>2</sup>, Deborah M Money <sup>3</sup>, Gina S Ogilvie <sup>6 7 8</sup>

## Uptake of community-based, self-collected HPV testing vs. visual inspection with acetic acid for cervical cancer screening in Kampala, Uganda: preliminary results of a randomised controlled trial

Erin Moses <sup>1</sup>, Heather N Pedersen <sup>2</sup>, Sheona M Mitchell <sup>2</sup>, Musa Sekikubo <sup>3</sup>, David Mwesigwa <sup>4</sup>, Joel Singer <sup>2</sup>, Christine Biryabarema <sup>3</sup>, Josaphat K Byamugisha <sup>3</sup>, Deborah M Money <sup>1 2</sup>, Gina S Ogilvie <sup>1 2</sup>



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# Community-based HPV self-collection versus visual inspection with acetic acid in Uganda: a cost-effectiveness analysis of the ASPIRE trial

Alex K Mezei,<sup>1</sup> Heather N Pedersen,<sup>2</sup> Stephen Sy,<sup>3</sup> Catherine Regan,<sup>3</sup> Sheona M Mitchell-Foster,<sup>4</sup> Josaphat Byamugisha,<sup>5,6</sup> Musa Sekikubo,<sup>5,6</sup> Heather Armstrong,<sup>1</sup> Angeli Rawat,<sup>2</sup> Joel Singer,<sup>7,8</sup> Gina S Ogilvie,<sup>2</sup> Jane J Kim,<sup>3</sup> Nicole G Campos<sup>3</sup>

## Cost-effectiveness of cervical cancer screening methods in low- and middle-income countries: A systematic review

Alex K Mezei<sup>1</sup>, Heather L Armstrong<sup>2</sup>, Heather N Pedersen<sup>2</sup>, Nicole G Campos<sup>3</sup>, Sheona M Mitchell<sup>4</sup>, Musa Sekikubo<sup>5</sup>, Josaphat K Byamugisha<sup>5</sup>, Jane J Kim<sup>4</sup>, Stirling Bryan<sup>6</sup>, Gina S Ogilvie<sup>2</sup>

## Integrated cervical cancer screening in Mayuge District Uganda (ASPIRE Mayuge): a pragmatic sequential cluster randomized trial protocol



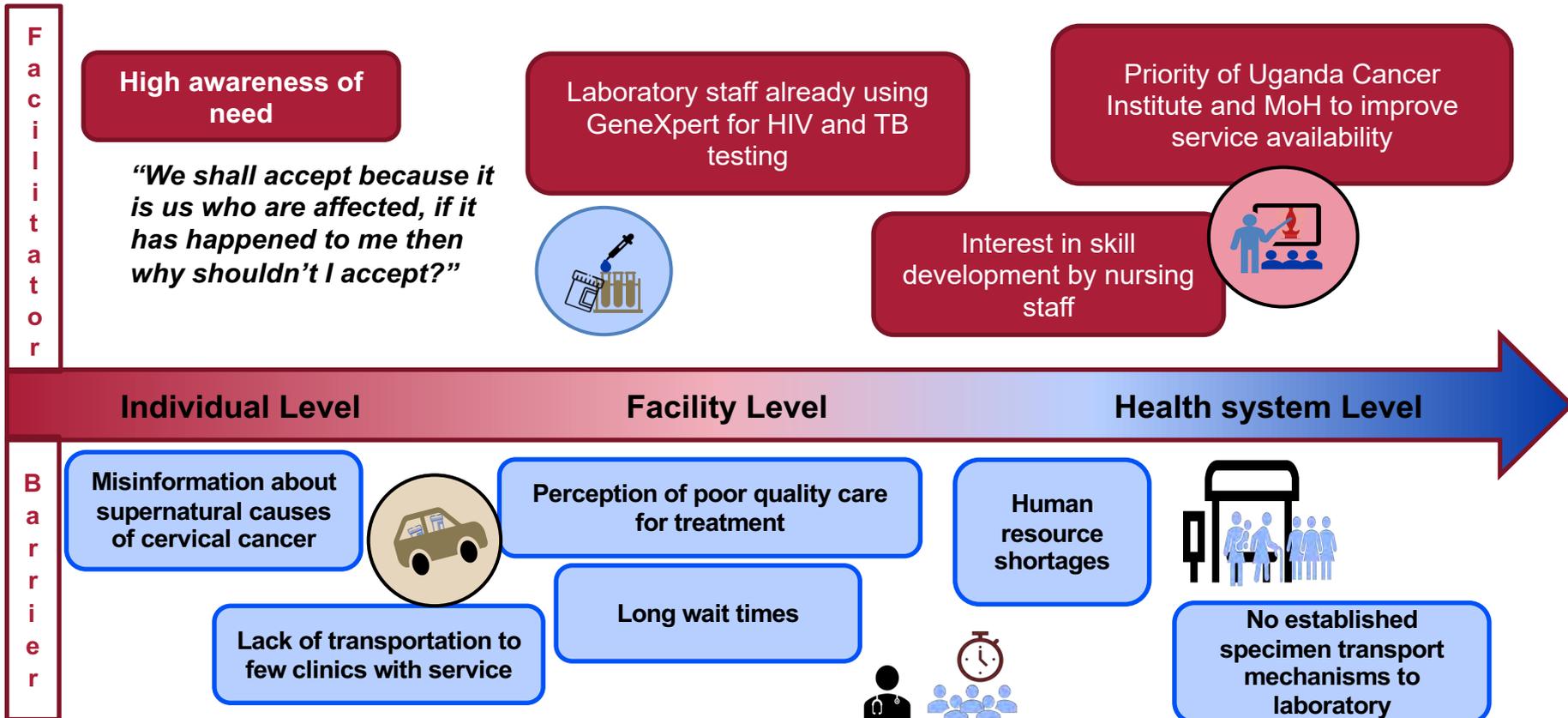
Carolyn Nakisige<sup>1</sup>, Jessica Trawin<sup>1</sup>, Sheona Mitchell-Foster<sup>2,3</sup>, Beth A. Payne<sup>2,4</sup>, Angeli Rawat<sup>1</sup>, Nadia Mithani<sup>2</sup>, Cathy Amuge<sup>1</sup>, Heather Pedersen<sup>5</sup>, Jackson Orem<sup>1</sup>, Laurie Smith<sup>2,6</sup> and Gina Ogilvie<sup>2,4,5\*</sup>



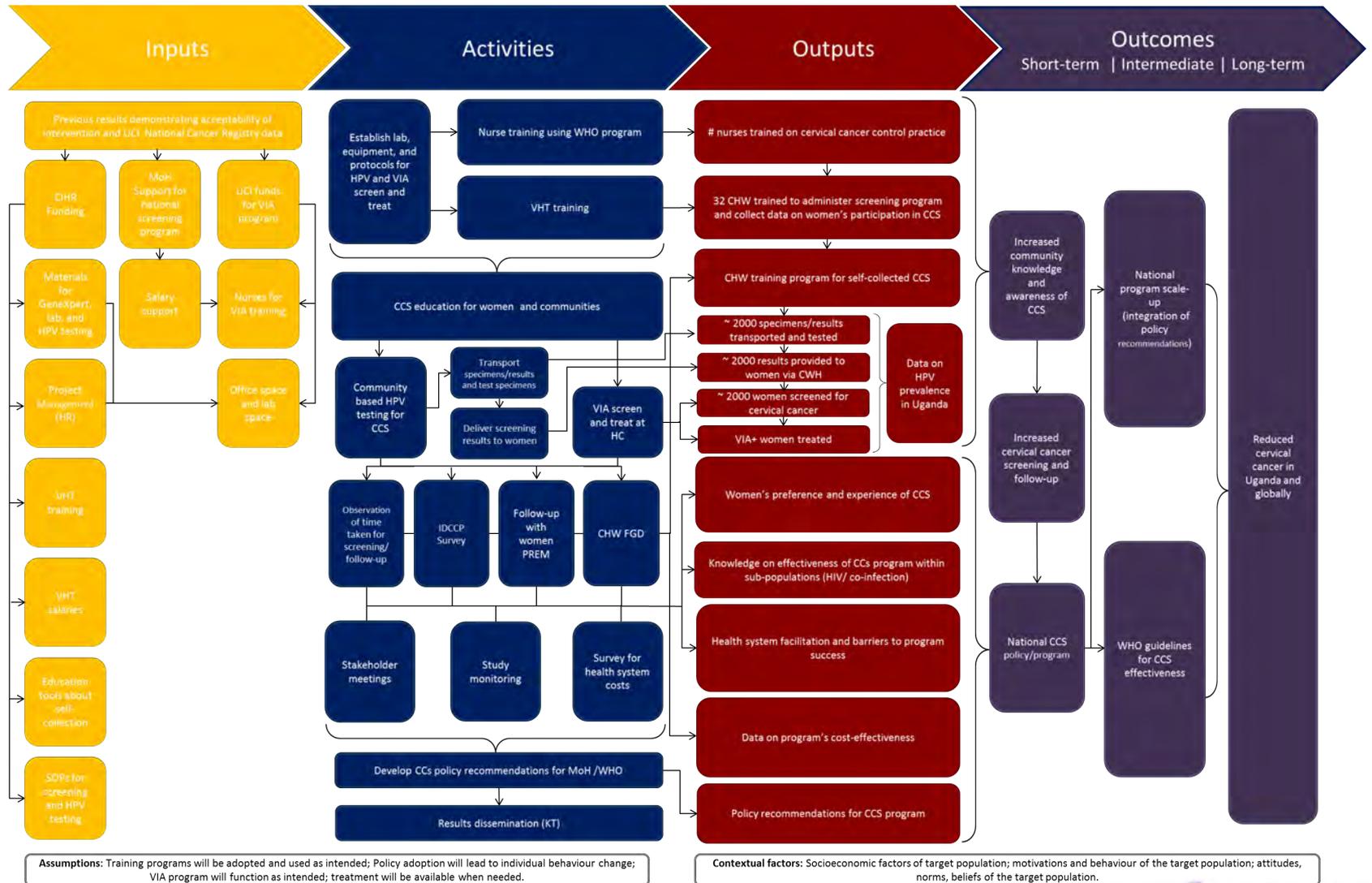
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# Considering rural women's and health care providers preferences



# Program Planning – the ASPIRE Trial Logic Model



a place of mind



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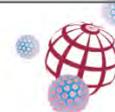


Provincial Health Services Authority Province-wide solutions. Better health.

BC Centre for Disease Control An agency of the Provincial Health Services Authority

BC CANCER Provincial Health Services Authority

CIHR IRSC Canadian Institutes of Health Research



Global Control of HPV Related Diseases and Cancer

# What is the ASPIRE Mayuge trial?

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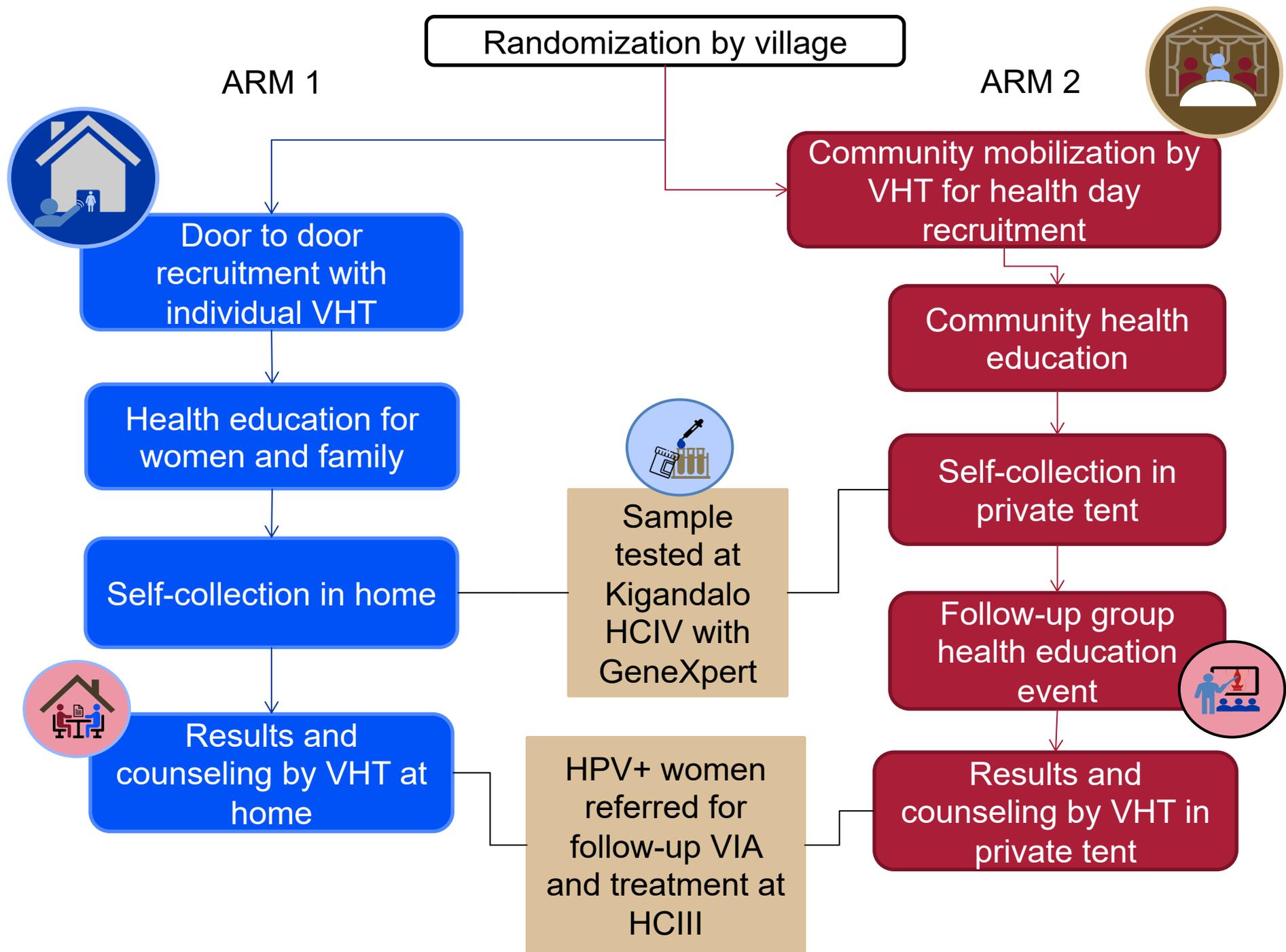
- A sequential, pragmatic, two arm cluster randomized clinical trial
- 31 villages randomized in Mayuge District, Eastern Uganda
- Aim is to determine the most effective method of community based cervical cancer screening for women in rural Uganda
- Secondary objectives to determine cost effectiveness and process evaluation following RE-AIM framework

# Eligibility: Who can participate in sample self-collection for ASPIRE?

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- ✓ women between the ages of 25-49 years old
- ✓ no previous hysterectomy or cervical cancer history
- ✓ who have not previously been treated for cervical cancer







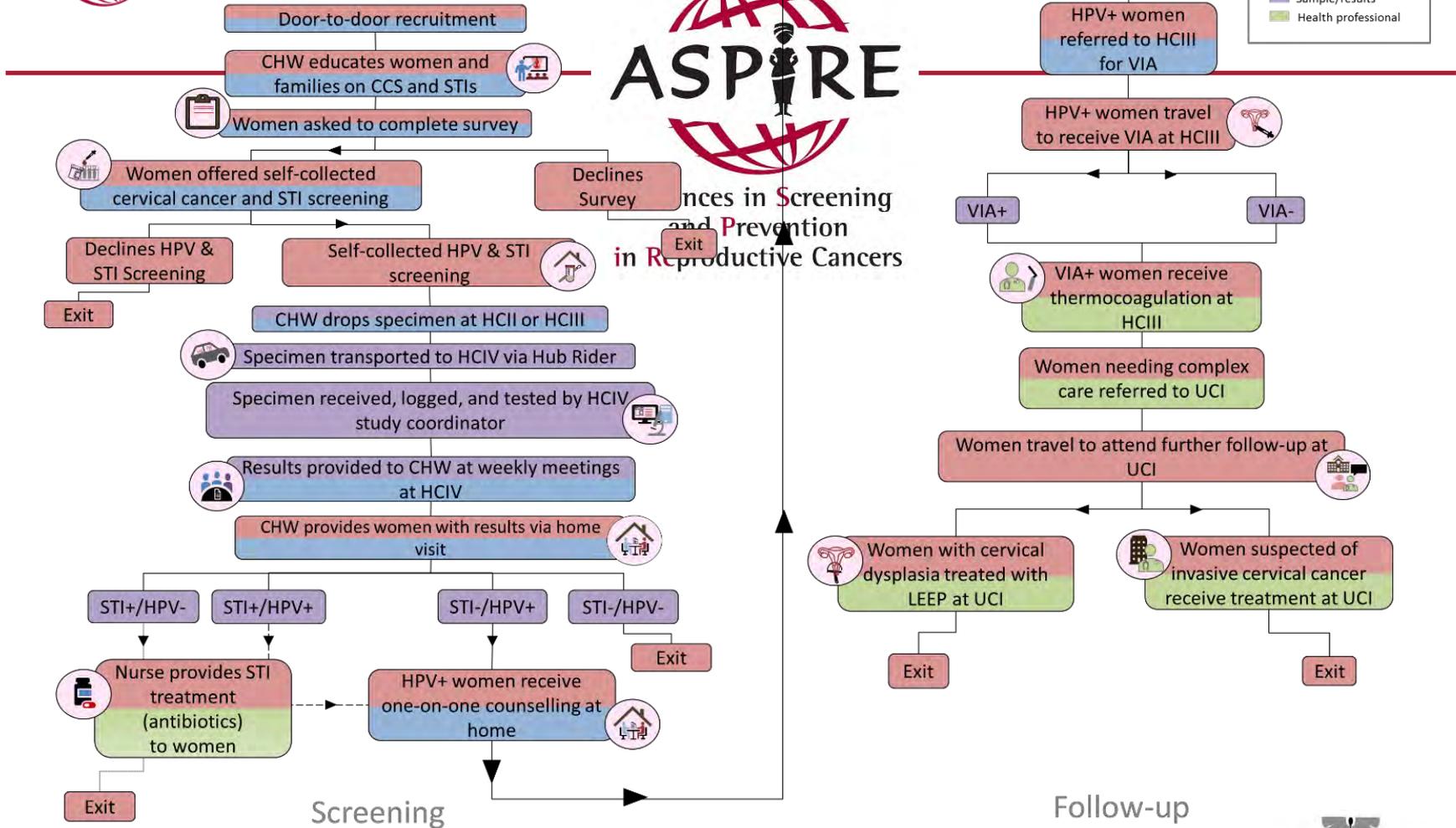
Arm 1



**Pathways Legend**

- Women
- CHW
- Sample/results
- Health professional

### ASPIRE Differences in Screening and Prevention in Reproductive Cancers



Screening

Follow-up



THE UNIVERSITY OF BRITISH COLUMBIA



# Build Local Partnerships And Leverage Existing Resources

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# Adapting to the Agile Nature of the Research Environment and COVID-19

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## Key:

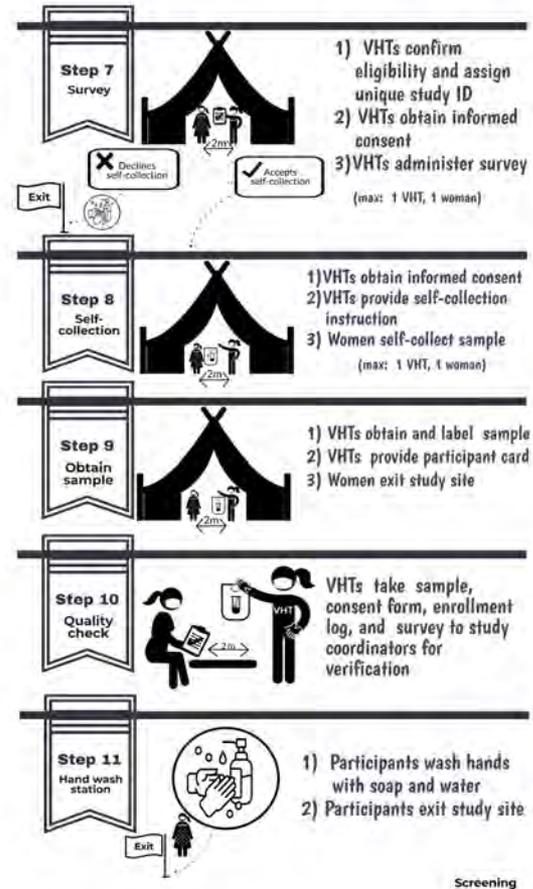
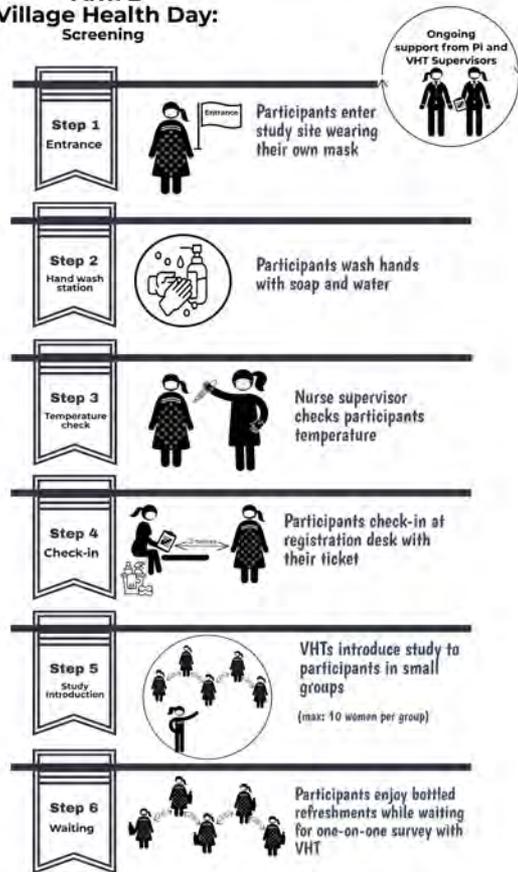
- Strong partnerships at community and health system level

## Example:

- Local partnerships were integral to resumption of research during COVID-19 pandemic
  - Essential updates on local situation and lockdown measures
  - Advocate for resumption with ethics committee
  - Guidance on safety plan development and adjustments to standard operating procedures to meet standards of new research environment
  - Link to both community and health system to ensure plans reflect needs of both and maintain overall research aims

# Arm 2 process adapted to COVID-19

## Arm 2 Village Health Day: Screening



# Status update



- Recruitment for Arm 1 complete between August 7, 2019 – December 20, 2019
- 1055 now enrolled and tested
- Ongoing VIA follow-up being monitored
- Resumption of research now approved and Arm 2 expected to start in September

# Discussion

- Recruitment to Arm 1 exceeded expectations in pace
- Community support is high
- HR-HPV is common and dominated by types not impacted by the use of the quadravalent vaccine
- Suggests screening is critical to Ugandan strategy for elimination of cervical cancer



# Thank you!



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# Background

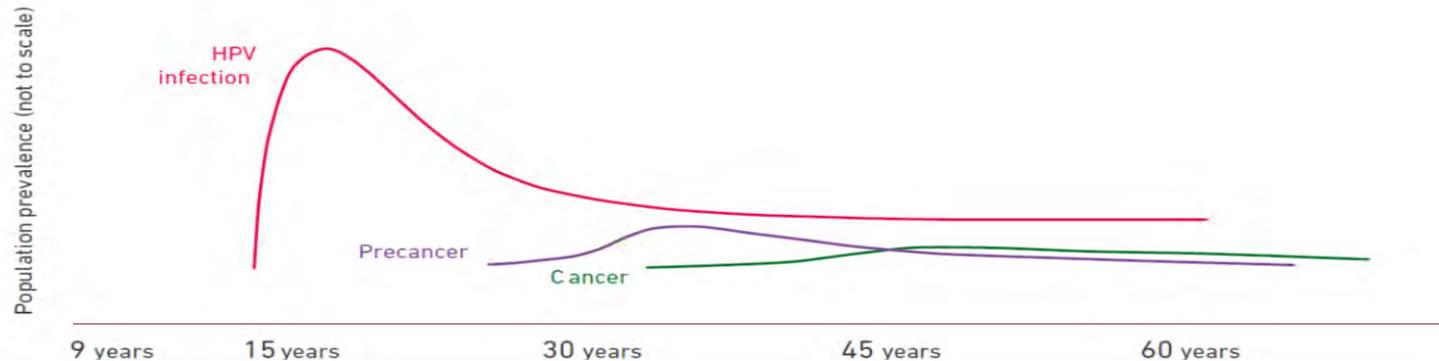
- The World Health Organization has called cervical cancer one of the 'gravest threats to women's lives.'
- Uganda has one of the highest cervical cancer incidence rates in the world (54.8 per 100,000).
- Specific high-risk subtypes of human papillomavirus (HR-HPV) are established as the cause of cervical cancer.



# Process Evaluation Strategy Using RE-AIM Framework

Research Objective	Research Question	RE-AIM Outcome	Outcomes	Data Analysis Approach
Primary Objective				
Self-collected cervical cancer screening effectiveness				
To compare the effectiveness of two self-collected CCS models at improving VIA follow-up: community health worker recruitment (door-to-door) versus community health day.	Which of the two self-collected CCS models is more effective at improving VIA follow-up among screened women: door-to-door screening or community health days?	Effectiveness (Individual level)	Primary Outcome: Follow-up attendance for VIA screening at a designated Health Center after a positive HR-HPV test screened per arm	Quantitative analysis of clinical data: Mixed effect model with cluster as a random intercept and adjusted for all known confounders. Intention to treat and sensitivity analysis; Multivariate logistic regression
	What is the effect of screening model on CCS knowledge retention and follow-up uptake? Are women aware of cervical cancer and how knowledgeable are they about CCS?	Effectiveness (Individual level)	Mean CCS knowledge scores; cervical cancer awareness;	Quantitative analysis of survey data: multi-level Poisson model;

# WHO Life-course Approach To Cervical Cancer Control



## Primary Prevention

### Girls 9-14 years

- HPV vaccination

### Girls and boys, as appropriate

- Health information and warnings about tobacco use
- Sexuality education tailored to age & culture
- Condom promotion/provision for those engaged in sexual activity
- Male circumcision

## Secondary Prevention

### Women > 30 years of age

“Screen and treat” – single visit approach

- Point-of-care rapid HPV testing for high risk HPV types
- Followed by immediate treatment
- On site treatment

## Tertiary Prevention

### All women as needed

Treatment of invasive cancer at any age and palliative care

- Ablative surgery
- Radiotherapy
- Chemotherapy
- *Palliative Care*



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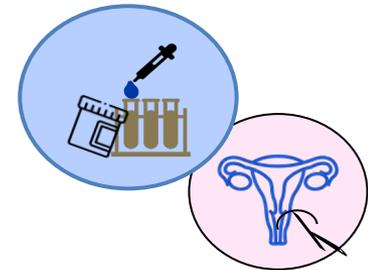
# Current Evidence for Self-collected HPV Testing as Primary Screening Method For LMICs

Three trials: India; Mexico and South Africa

Self-collected HR-HPV testing led to higher screening uptake

3.4 x higher detection of CIN2+ than Pap

Higher specificity for CIN2+ than VIA or Pap

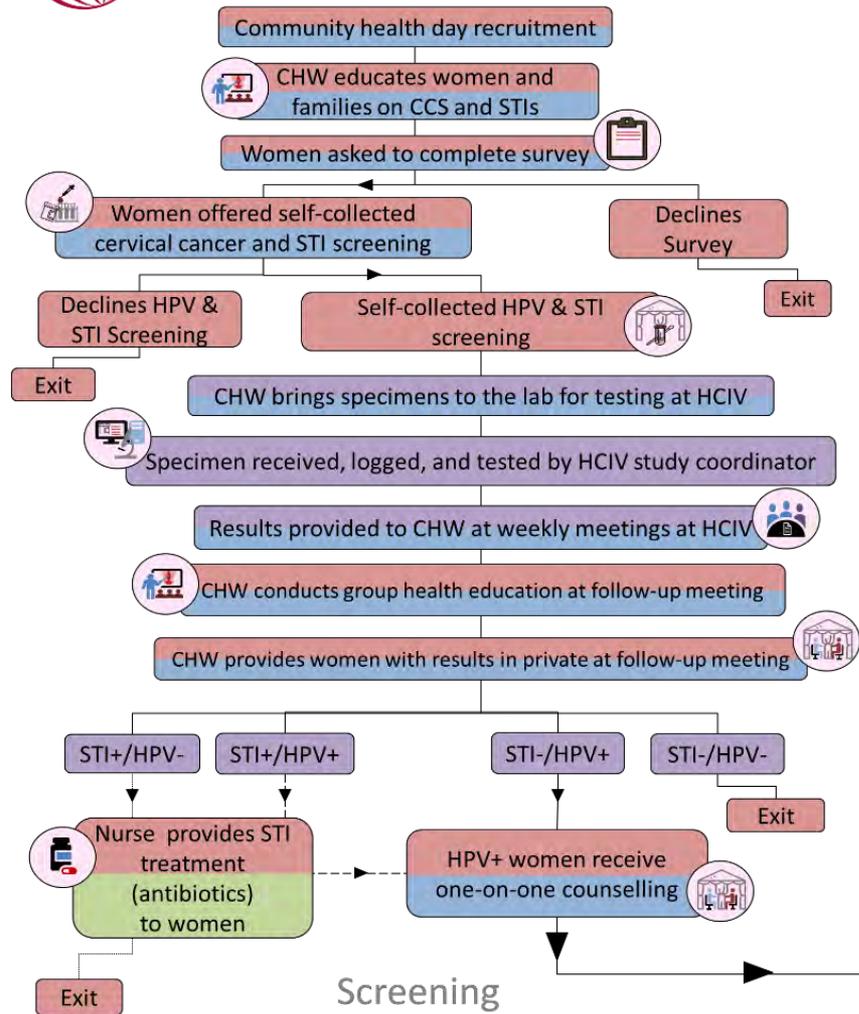




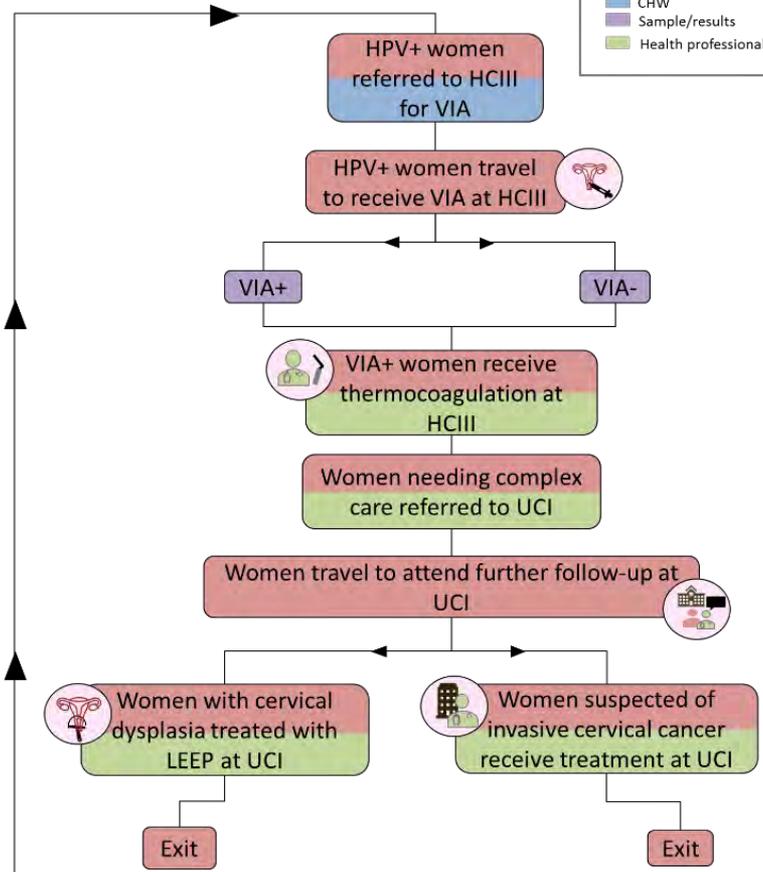
# Arm 2

**Pathways Legend**

- Women (Red)
- CHW (Blue)
- Sample/results (Purple)
- Health professional (Green)



## Screening



## Follow-up



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Better health.



BC Centre for Disease Control  
Provincial Health Services Authority



Provincial Health Services Authority



Global Control of  
HPV Related Diseases  
and Cancer

*Cervical Cancer Prevention in El Salvador (CAPE):  
Lessons in developing and implementing a primary HPV  
screening program in a low-middle-income country*

Karla Alfaro

Basic Health International

August 12th, 2020

## Conflict of Interest

I have no commercial relationship with any corporate entity that produces or sells products related to HPV testing.

## Presentation outline

- *State of cervical cancer control in El Salvador pre-CAPE*
- *Steps leading to the development of CAPE*
- *Steps involved in building and delivering a screening program in a limited-resource setting.*
- *National Scale-up*
- *Challenges*

## *Cervical Cancer Control in El Salvador pre-CAPE*

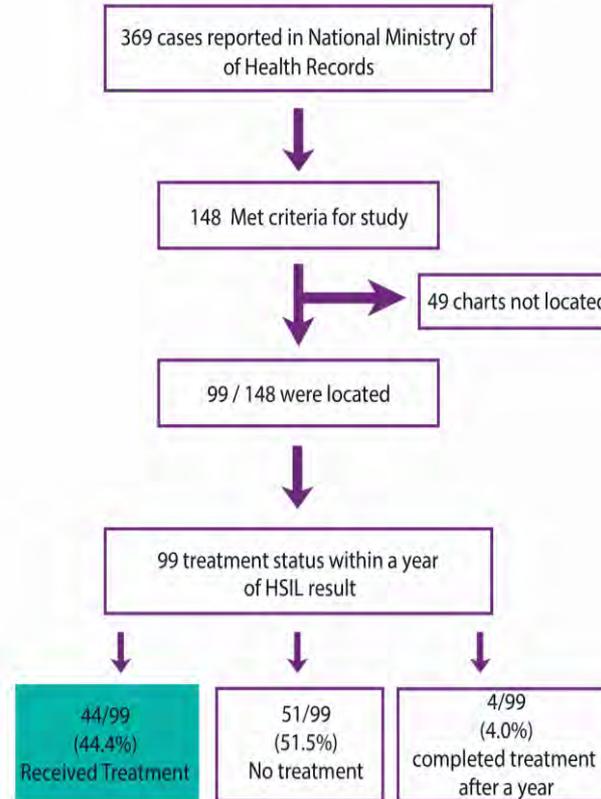
# Cervical cancer in Latin America

**Table 4**  
Cytological screening coverage in Latin America and the Caribbean

Target population			Women interviewed		Screening		Method of estimation
Country	Year	Region or city	Number of women	Age (years)	Coverage (%)	Interval (years)	
Argentina	2005	National	NS	>18	51.6	2	Survey
Belize <sup>a</sup>	1999	National	4,164	13–49	13.4	1	Survey
Brazil	2002–2005	Capital cities	13,282	25–59	63.4	1	Survey
	2003	National	NS	>24	68.7	3	Survey
	2002	National	2,577	18–69	64.8	3	Survey
	2002	Pelotas	1,198	25–59	68.8	3	Survey
	2000	Sao Paulo	1,050	15–49	77.3	3	Survey
Chile	2003	National	27,000	>15	51.4	3	Survey
	2003	National	–	25–64	66.0	1	SP
	2000	National	–	25–64	64.0	3	SP
	2000	Araucania Sur	–	25–64	56.2	3	SP
Colombia	2005	National	34,674	25–69	50.6	1	Survey
Costa Rica	1999–2000	National	1,612	18–44	37.0	1	Survey
	1991	National	NS	25–58	51.3	1	Survey
Cuba	1993–1994	National	–	>20	54.2	2	SP
Dominican Republic	2002	National	1,389	18–69	54.4	3	Survey
Ecuador	2004	National	10,813		31.0		
		Urban	5,876	15–49	35.6	2	Survey
		Rural	4,938		24.9		
El Salvador	2002	National	10,689	15–49	47.0	1	Survey
	1998	National	–	NS	19.0	3	SP

R. Murillo et al. / Vaccine 26S (2008) L37–L48

# Pre-CAPE: 1-year follow-up after cytology-based screening (2010)



## *Steps leading to CAPE*

# Introduction of HPV-based screening in El Salvador



MOH and BHI partnered to present a proposal for the implementation of a low-cost HPV through a donation program .

Consultants from NCI, PAHO, National OBGYN and Pathology societies were involved in the process.

In 2011 we received the approval to implement HPV as part as a pilot project.

## CAPE: Cervical Cancer Prevention in El Salvador



# Building and delivering a screening program in a limited-resource setting

# CAPE Cervical Cancer Prevention in El Salvador

Three phase project:

Phase 1: 2,000 women (2012-2013)

Phase 2: 8,000 women (2013-2014)

Phase 3: 20,000 women (2015-2017)





## Cost-Effectiveness Results

- Screening with a low-cost HPV test provides *greater health benefits* than current Pap smear screening.
- Routine screening with this low-cost HPV test (every 5y) is *cost-effective* compared to Pap testing (every 2y).
- Screening with low cost HPV test followed by visual assessment triage is *more effective and less costly* than low cost HPV test with colposcopy triage

## Presenting results



# Changing the paradigm

Meeting



Meeting



Meeting



Meeting

Meeting



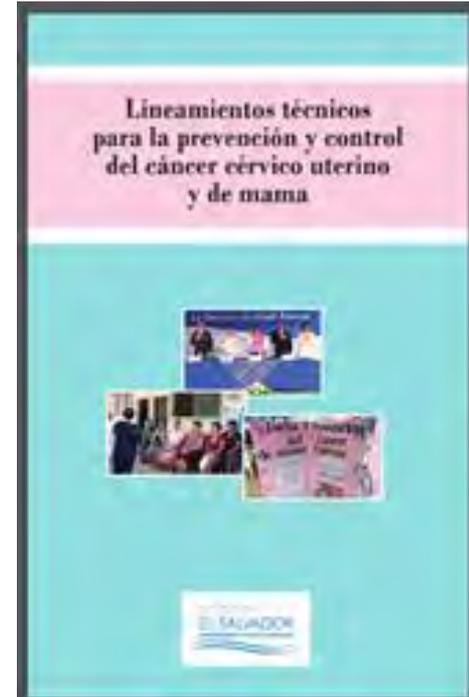
Meeting



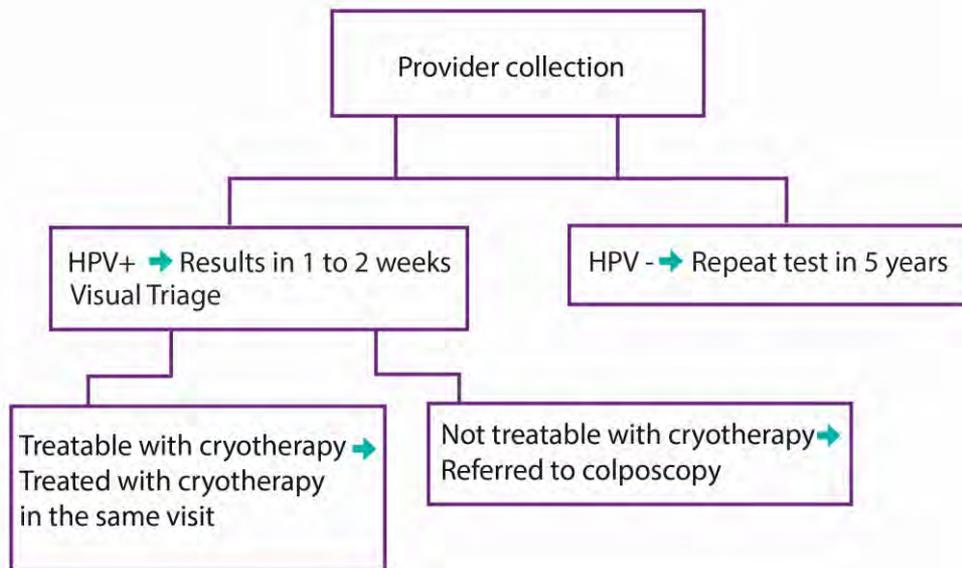
## Sustainable change

December 2015

As a result of CAPE, the El Salvador MOH changed its cervical cancer guidelines to include HPV test and the proposed treatment algorithm.



# Visual Assessment Triage (VAT)





# Building a Surveillance System in El Salvador

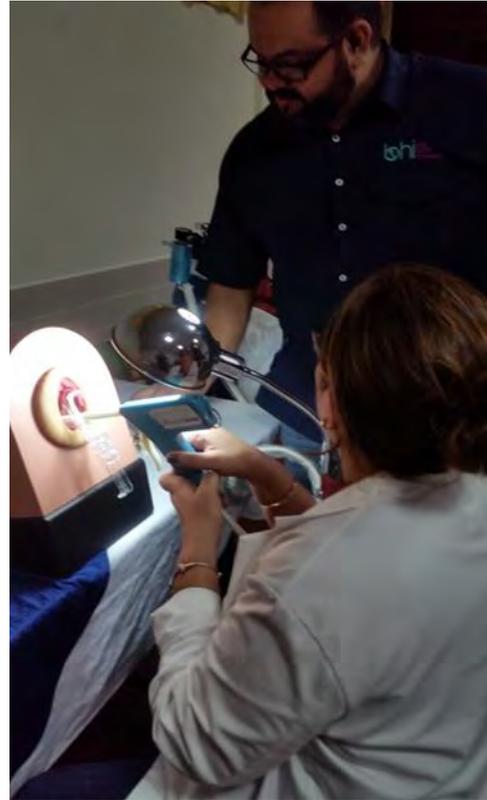


Indicadores	
Indicador	
Numero de mujeres con pruebas de VPH y PAP realizadas	
Numero de mujeres con pruebas de VPH y PAP positivas	
Numero de mujeres con pruebas de VPH positivas que asistieron a evaluacion visual	
Numero de mujeres con pruebas de VPH positivas que fueron elegibles para crioterapias	
Numero de mujeres con pruebas de VPH positivas que fueron referidas a colposcopia	
Numero de mujeres con pruebas de VPH positivas a quienes se les realizo colposcopia	
Numero de mujeres con pruebas de PAP positivas a quienes se les realizo colposcopia	
Numero de mujeres a quienes se les practico crioterapia despues de evaluacion colposcopia	
Numero de mujeres con biopsia cervico uterinas positivas	
Numero de mujeres a quienes se les practico cono leep	

## Training sessions



# Visual assessment triage and cryotherapy



# National scale-up

December 2018

# Expectations

2014-2015



2016



2017



2018



2019



# Reality



## Total of health personnel trained 2012-2020

<b>Health Personnel</b>	<b>Total</b>
Health Promoters	2,655
Nurses	1,230
Doctors	869
<b>Total</b>	<b>4,754</b>

## Total of women screened 2012-2020

<b>Period of time</b>	<b>Total of Screenings</b>
2012-2017 Pilot	29,139
2018-2020(Octubre-Diciembre)	64,690
<b>Total</b>	<b>93,829</b>

# Challenges

-Reluctance by local stakeholders to change cytology-based screening program to HPV testing

-Loss to follow-up increased as program expanded

-Long intervals between program steps

-Advocate for ways to conduct implementation research

in limited resource settings **BASED ON YOUR RESEARCH FINDINGS**

# Impact of COVID19 in Cervical Cancer Program

- Health services are focusing to combat the pandemic.
- Occidental and Oriental Region: women pending of treatment
- Delay implementing HPV testing in Central and continuing in Paracentral region
  - 80,000 women schedule to be screened in 2020
  - New possible target to screen 40,000
  - Self Sampling to be added in the national guidelines

Thank you

# CUGH & NCI Cervical Cancer Webinar 3: Ensuring effective implementation of cervical cancer prevention and control strategies

August 12, 2020

11:00am-12:00pm EDT

**Co-Moderator**



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Centro de Estudios de Estado  
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