

March 19, 2020

TOGETHER for Health

# Optimizing Cervical Cancer Screening among Women Living with HIV

Estudio Oportunidad in the Dominican Republic

Kerry A. Thomson, PhD, MPH



# Today's outline

1. PATH's work in HIV and cervical cancer screening
2. Focus on Latin America & Caribbean region
3. Structure for new NIH-funded ULAC-NET
4. Unanswered questions to optimize cervical cancer screening for WLWH
5. Estudio Oportunidad
  1. Aim
  2. Study design
  3. Additional study possibilities

# PATH's work in HIV: 3 decades across 32 countries

## Prevention



**11,123,240** individuals provided with prevention services, including **VMMC** to more than **386,899**; enrolled more than **11,438** high-risk individuals on **PrEP**; and distributed millions of condoms.

## Awareness of HIV status



**10,724,882** individuals **tested for HIV** in facilities, communities, workplaces, and homes.



**292,395** individuals **newly diagnosed** HIV-positive.

## Linkage to sustained ART



**93%** of newly-diagnosed people living with HIV (PLHIV) **newly enrolled on antiretroviral therapy (ART)** in DRC, Kenya, Ukraine, and Vietnam since 2015.



**63,547** PLHIV currently supported to remain adherent to **ART** in DRC, Kenya, Ukraine, and Vietnam.

**45%** receiving differentiated treatment services.

## Viral suppression









**88%** of PLHIV on ART with active viral load counts achieved **viral suppression** in DRC, Kenya, and Ukraine.

Engage women of reproductive age in HIV care and on ART  
Kenya & DRC

# PATH's work in cervical cancer: 3 decades across the life course

← Accelerating evidence-based strategies and technologies across the life course →

HPV vaccination for adolescents	Cervical cancer screening and treatment for adult women	Health systems and policy
<p>Technical assistance for 27 demonstration projects and national introduction of HPV vaccine in 19 countries</p>  <p>Health economic and costing studies on vaccine delivery</p> 	<p>Multi-country validation of a low-cost HPV test</p>  <p>Bench and end-user testing of portable non-gas treatment devices</p> 	<p>Introduction of HPV testing in Central American Region</p>  <p>Laboratory training and quality assurance program for HPV testing</p> 

# Scale-Up Project (2014 – 2020)

**Purpose:** Rapidly introduce and scale up HPV testing in selected provinces in four Central American countries (Guatemala, Honduras, Nicaragua, El Salvador), with > 260,000 women screened to date

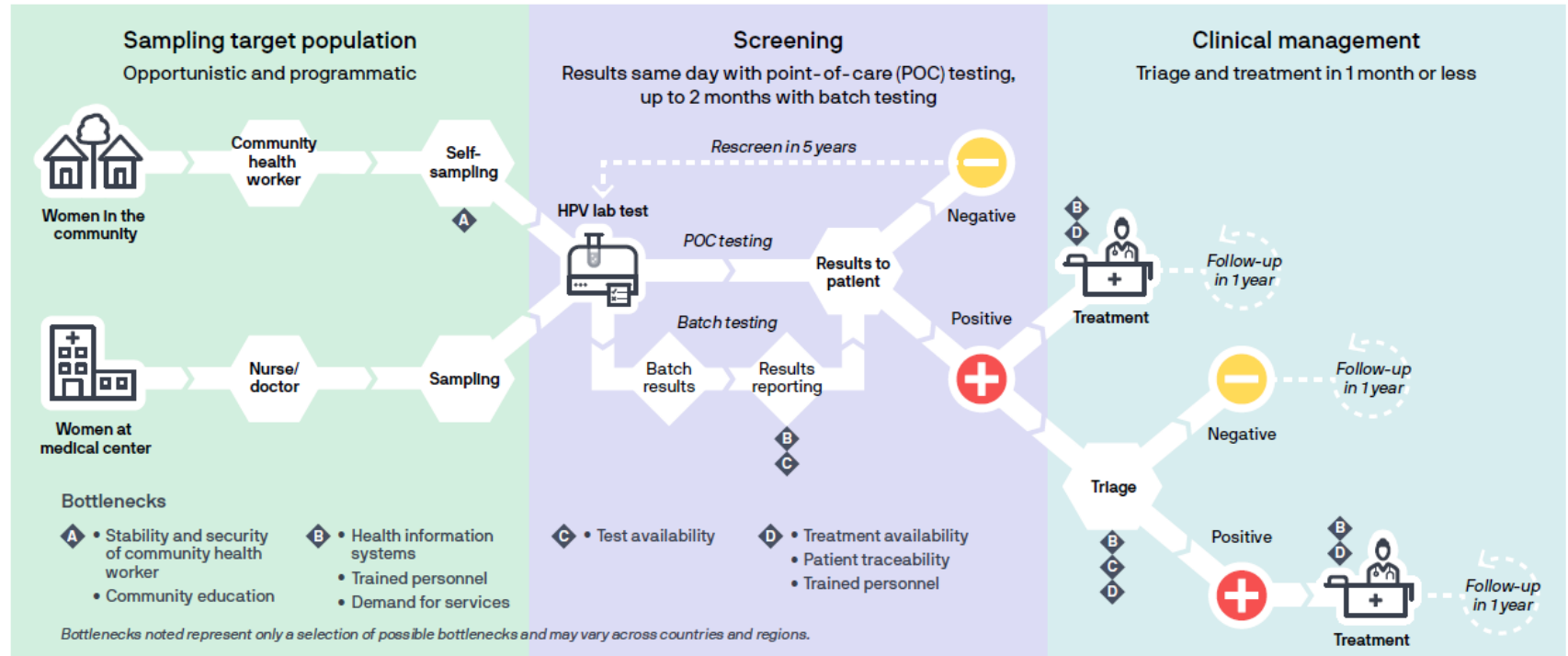
## Activities:

- Transitioning from pap smears/visual inspection with acetic acid (VIA) to HPV testing
- Updating national guidelines and strategies
- Training MOH personnel to implement HPV testing
- Introduce self-sampling as a viable alternative to clinician sampling



# HPV-based cervical cancer screening program

## Main interventions, timelines, and bottlenecks



# Latin America & Caribbean (LAC)

## Dual HIV / Cervical Cancer Burden

- LAC region has second highest HIV prevalence in the world, second to sub-Saharan Africa<sup>1</sup>

## Dominican Republic

- Estimated 34,000 WLWH<sup>2</sup>
- Cervical cancer incidence: 17 /100,000 women<sup>3</sup>
- Cervical cancer is the leading cause of death among women of reproductive age<sup>4</sup>
- Standard of care for screening is pap and/or VIA



Regional experience

HIV

Cervical cancer

1. UNAIDS 2019, 2 UNIADS 2019 3. Global Cancer Observatory, Interagency Group on Cancer, 2018, 4 Bruni, et al. HPV Information Center, Dominican Republic 2019. Icon: by Milo Miloezger for the Noun Project

# US-Latin American-Caribbean Clinical Trials Network (ULACNet) for Prevention of HPV-related Cancers in People Living with HIV

3

Partnership Centers comprised of academic research institutions & NGOs.  
**Emphasis on capacity building for clinic research**

5

Countries: Dominican Republic, Mexico, Puerto Rico, Brazil, United States

3

Scientific areas:

1. Optimize dosing and delivery and evaluating new indications for HPV prophylactic vaccines
2. Evaluate new biomarkers and technologies for improving accuracy of cervical and anogenital cancer screening and triage
3. Evaluate novel non-excisional treatments for HPV-related precancerous lesions



# Colaboración Evita

*PIs: Drs. Margaret Madeleine, Ann Duerr, Robinson Cabellos*

## OPTIMO Trial

**Focus: Primary prevention  
through HPV Vaccination (9-12 yo)  
Peru & Brazil**

Multicenter, Randomized, Open-Label  
Trial to Establish Optimal Number of  
Doses for HPV Vaccination in Children  
and Adolescents Living with HIV

*PIs: Drs. Duerr, Galloway, Kolevic*



## Estudio Oportunidad

**Focus: Secondary prevention  
through screening  
Dominican Republic**

Optimizar el tamizaje y tratamiento del cáncer  
de cuello uterino  
(Optimize screening and treatment  
of cervical cancer)

*PIs: Drs. Silvia de Sanjosé, Yeycy Donastorg*



## Trial 3

**Focus: Non-surgical treatment  
Under Development**

*PIs: Drs. Uldrick, Grinsztejn, Madeleine*



# Opportunities & Challenges for Integrating CC Screening into HIV Care



- WHO Call for Elimination: less frequent screening with higher precision tests
  - Dual HIV/CC burden calls for more frequent testing
- Differential performance of screening testing among WLWH
  - Role of “triage” / 2<sup>nd</sup> test
- WLWH [on ART] presumably have more frequent touchpoints with the health care system
- Judicious use of resources
  - Test supplies
  - Provider time
  - Lab infrastructure

# Performance of screening tests for CIN2+ detection

	General population (1-5% CIN2+)		WLHIV (20-25% CIN2+)		
	Sensitivity	Specificity	Sensitivity	Specificity	
Visual Inspection (VIA) <sup>1-3</sup>	79%	85%	<b>56-65%</b>	<b>65-78%</b>	“Screen and treat” Requires frequent training & supervision Improves treatment rates in WLHIV in South Africa <sup>7</sup>
Cervical cytology (≥LSIL) <sup>2-4</sup>	51%	95%	<b>73-98%</b>	<b>13-80%</b>	Observer-dependent++ Can be automated (LBC)
Hybrid Capture II <sup>2, 4</sup>	90%	89%	<b>92%</b>	<b>51%</b>	Single round halved rate of advanced cervical cancer (HR 0.47) and death from ICC (HR 0.52) compared to VIA <sup>8</sup> and vs. cytology in Europe
CareHPV (clinician-collected) <sup>5,6</sup>	88%	84%	<b>93%</b>	<b>58%</b>	Potential for increased coverage in LMIC
CareHPV (self-collected) <sup>5</sup>	74%	88%	-	-	As a repeat test, its specificity and PPV for detection of CIN2+ has shown to increase among WLHIV



**Low specificity = overtreatment  
Burden on health system?  
Disruption to reproductive tract  
in WLHA?**

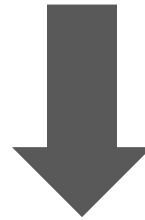
<sup>1</sup>Arbyn M, *Int J Cancer* 2008; <sup>2</sup>Firnhaber C, *PLoS One* 2013; <sup>3</sup>Mayaud P, *IPV* 2015; <sup>4</sup>Arbyn M, *Vaccine* 2012;

<sup>5</sup>Kelly H, *Sex Transm Infect* 2017; <sup>6</sup>Segondy M, *Brit J Cancer* 2016; <sup>7</sup>Denny L, *N Engl J Med* 2007; <sup>8</sup>Sankaranarayanan R, *New Engl J Med* 2009

# Estudio Oportunidad: Research to inform implementation

## Public Health Need

Cervical cancer screening and triage among WLWH needs to be refined to improve detection of precancerous lesions, reduce overtreatment, and facilitate implementation



## Study Aim

To develop an efficient algorithm for primary screening (and triage of screen-positives) that accurately and reliably identifies CIN2+ among women living with HIV

*Examine differences by age, HIV viral load, time on ART*

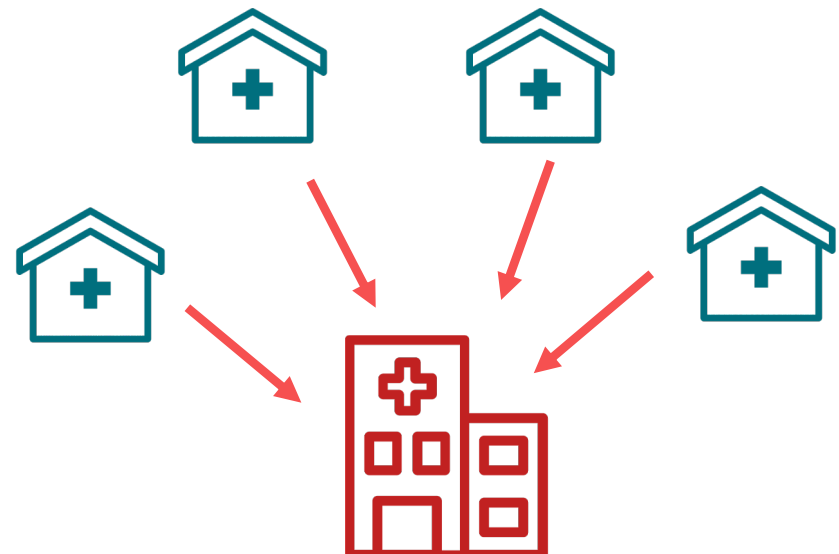
# Estudio Oportunidad: Eligibility criteria\*

1. *Age 23 to 49*
2. *Have ever sexually active*
3. *Evidence of HIV infection*
4. *Not pregnant at baseline*
5. *No prior history of cervical cancer or hysterectomy*
6. *On ARV  $\geq$  3 months*
7. *Stable residency near Santo Domingo*
8. *Able to communicate and willing to sign informed consent*

**600 women living with HIV**

Recruitment at Primary Care / HIV Clinics

Santo Domingo Area

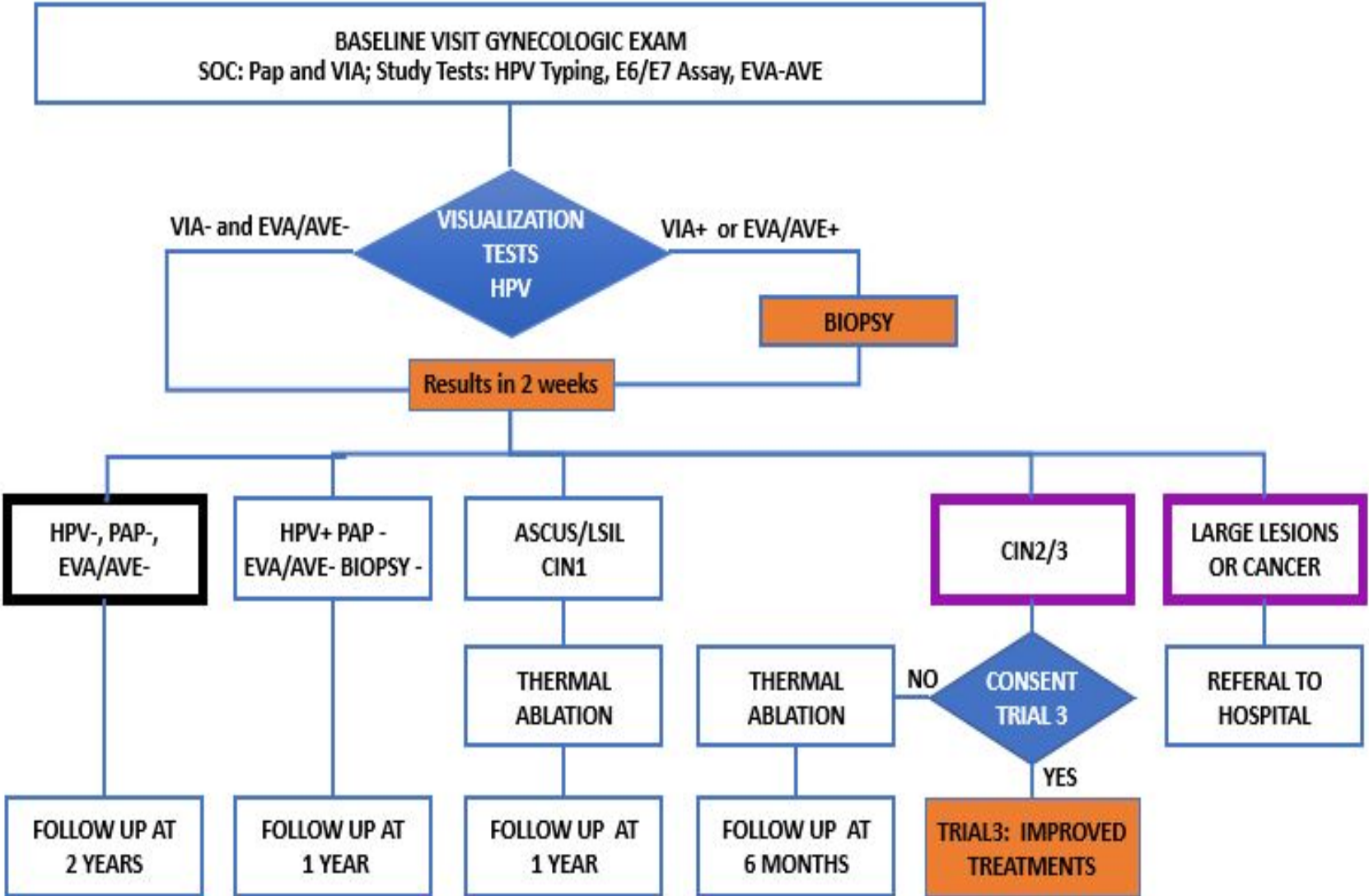


Confirm Eligibility & Study Visits

Instituto Dermatológico Dominicano y Cirugía de Piel (IDCP)

\* Draft protocol as of March 2020. Icons: Nociconist from the Noun Project

# Estudio Oportunidad: Study design\*



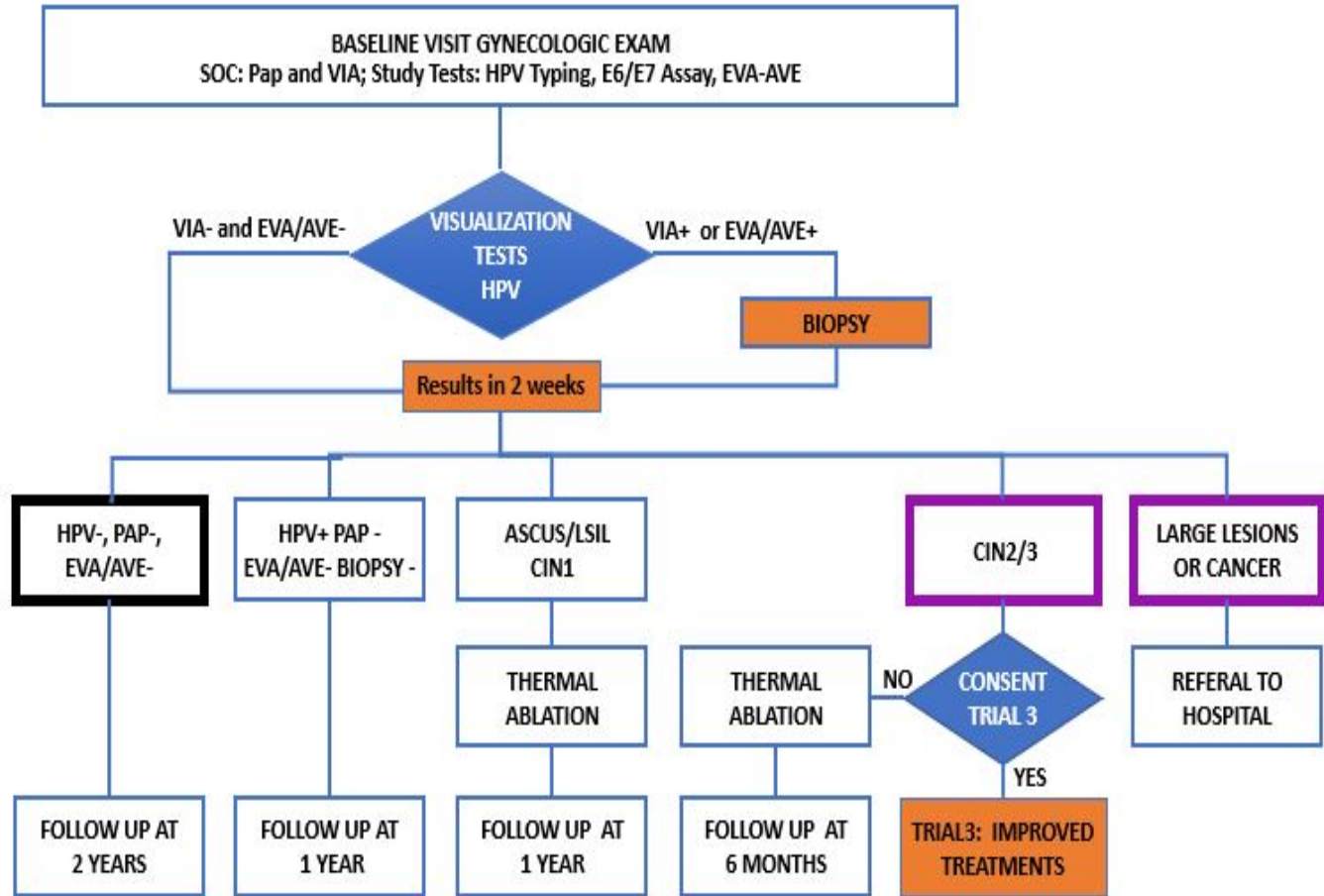
\* Draft protocol as of March 2020

# Estudio Oportunidad: Study design\*

- Candidate Screening Tests
- Papanicolaou
- VIA
- Automated Visual Evaluation
- HPV DNA genotyping
- Onco E6/E7
- Methylation

---

- Biopsy confirmation

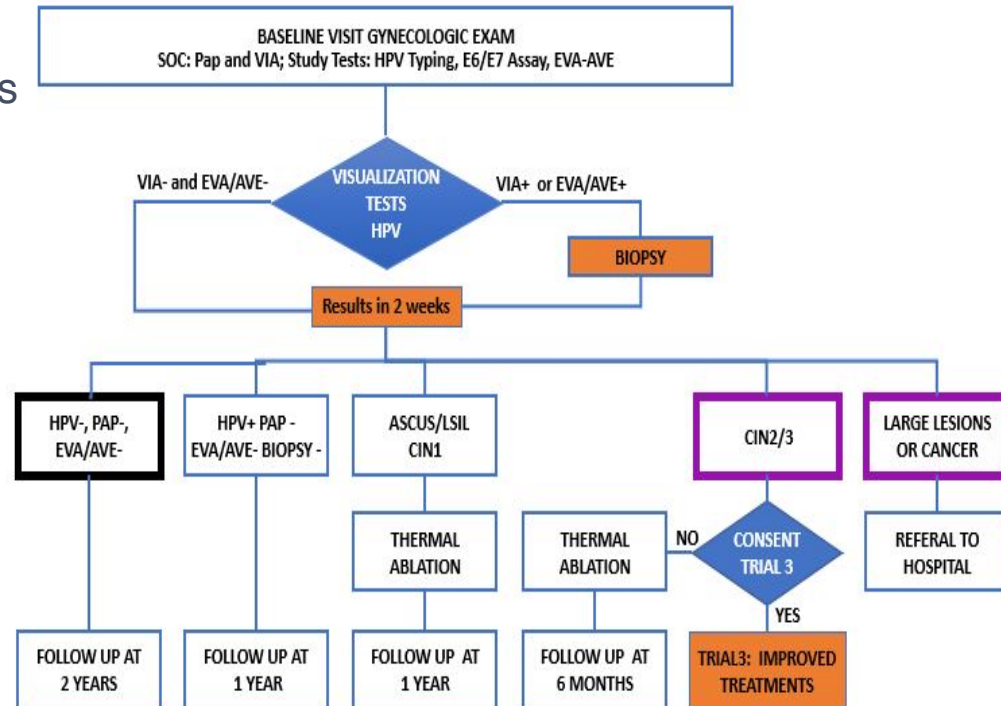


\* Draft protocol as of March 2020



# Estudio Oportunidad\*: additional possibilities

- Increase to study visits every 6 months
- HPV acquisition among initial HPV-
- Role of artificial intelligence
- Thermal ablation
- Qualitative study of perceived risk & screening preferences
- Cost effectiveness
- Vaccine





For more  
information  
contact:

**Kerry Thomson**

[kthomson@path.org](mailto:kthomson@path.org)

**Silvia de Sanjosé**

[sdesanjose@path.org](mailto:sdesanjose@path.org)

**Margaret Madeleine**

[mmadelei@fredhutch.org](mailto:mmadelei@fredhutch.org)



**PATH**  
▶◊::▲○◆//☹◻◉