Optimizing Cervical Cancer Screening among Women Living with HIV

Estudio Oportunidad in the Dominican Republic

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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.

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

Viral suppression

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**

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

Accelerating evidence-based strategies and technologies across the life course
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

**Sampling target population**
Opportunistic and programmatic

- Women in the community
- Women at medical center

**Screening**
Results same day with point-of-care (POC) testing, up to 2 months with batch testing

- Rescreen in 5 years
- HPV lab test
- POC testing
- Batch testing
- Results to patient
- Positive
- Negative

**Clinical management**
Triage and treatment in 1 month or less

- Follow-up in 1 year
- Treatment
- Positive
- Negative

Bottlenecks noted represent only a selection of possible bottlenecks and may vary across countries and regions.

Source: de Sanjose, S. and Home, F. Papillomavirus research, 2019
Latin America & Caribbean (LAC)

Dual HIV / Cervical Cancer Burden

- LAC region has second highest HIV prevalence in the world, second to sub-Saharan Africa\(^1\)

Dominican Republic

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

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

https://prevention.cancer.gov/major-programs/us-latin-american-caribbean-u54
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*

Icons: Peru by Ted Grajeda, Brazil & Dominican Republic by Tom Walsh from the Noun Project
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” / 2nd 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

<table>
<thead>
<tr>
<th>Test</th>
<th>General population (1-5% CIN2+)</th>
<th>WLHIV (20-25% CIN2+)</th>
<th>Low sensitivity = missed cases</th>
<th>Low specificity = overtreatment</th>
<th>Burden on health system?</th>
<th>Disruption to reproductive tract in WLHA?</th>
</tr>
</thead>
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<tr>
<td><strong>Visual Inspection (VIA)</strong></td>
<td>Sensitivity 79% Specificity 85%</td>
<td>Sensitivity 56-65% Specificity 65-78%</td>
<td>Requires frequent training &amp; supervision</td>
<td>Improves treatment rates in WLHIV in South Africa</td>
<td>Screen and treat</td>
<td><strong>“Screen and treat”</strong> Requires frequent training &amp; supervision</td>
</tr>
<tr>
<td><strong>Cervical cytology (≥LSIL)</strong></td>
<td>Sensitivity 51% Specificity 95%</td>
<td>Sensitivity 73-98% Specificity 13-80%</td>
<td>Observer-dependent++ Can be automated (LBC)</td>
<td></td>
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</tr>
<tr>
<td><strong>Hybrid Capture II</strong></td>
<td>Sensitivity 90% Specificity 89%</td>
<td>Sensitivity 92% Specificity 51%</td>
<td>Single round halved rate of advanced cervical cancer (HR 0.47) and death from ICC (HR 0.52) compared to VIA and vs. cytology in Europe</td>
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<tr>
<td><strong>CareHPV (clinician-collected)</strong></td>
<td>Sensitivity 88% Specificity 84%</td>
<td>Sensitivity 93% Specificity 58%</td>
<td>Potential for increased coverage in LMIC</td>
<td></td>
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</tr>
<tr>
<td><strong>CareHPV (self-collected)</strong></td>
<td>Sensitivity 74% Specificity 88%</td>
<td>- Specificity -</td>
<td>As a repeat test, its specificity and PPV for detection of CIN2+ has shown to increase among WLHIV</td>
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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

Instituto Dermatologico Dominicano y Cirugia 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

* Draft protocol as of March 2020
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