ESMO SUMMIT
LATIN AMERICA 2019

Gynaecological Cancer in Latin America

Andréia Melo, MD, PhD
INCA, Grupo Oncoclínicas
CONFLICT OF INTEREST

Research Support: BMS, Roche, Novartis, MSD, Clovis, AstraZeneca, Amgen, Abbvie

Speaker Bureau: BMS, Roche, Novartis, MSD

Advisory board: Roche, MSD, Novartis
AGENDA

- Epidemiology
- Cervix Cancer Screening
- Treatment Access
- HPV Vaccination
- Perspectives
Challenge #1

Gynecological cancer epidemiology in Latin America
POPULATION

8.5% of world population
~640 million

20 aggregated areas – United Nations

World area (% of population)

- Americas (13.3%)
  - Northern (4.8%)
  - Central (2.3%)
  - Caribbean (0.6%)
  - South (5.6%)

- Africa (16.9%)
  - Northern (3.1%)
  - Western (5.0%)
  - Middle (2.2%)
  - Eastern (5.7%)
  - Southern (0.9%)

- Europe (9.8%)
  - Western (2.6%)
  - Northern (1.4%)
  - Southern (2.0%)
  - Eastern (3.8%)

- Asia (59.5%)
  - Western (3.5%)
  - South Central (25.7%)
  - Eastern (21.7%)
  - South-Eastern (8.6%)

- Oceania (0.5%)
  - Australia/New Zealand (0.4%)
  - Melanesia (0.1%)
  - Micronesia/Polynesia (0.02%)

No data  Not applicable
LATIN AMERICA

- Demographic transition, ageing of populations

- Rapid industrialization and *westernization* of lifestyle

- A region marked by socioeconomic inequalities
CANCER REGISTRIES
IN LATIN AMERICA

- Necessary to enhance cancer registration
- Population-based cancer registries covering <10% of population
- Diversity of populations and risk factors between and within countries
- To better target populations at risk, with cancer control programs
- To evaluate public policies and cancer control activities
CANCER INCIDENCE

- Changes in life expectancy and age distribution of population structure
- Inequalities in economic development
- Socio-economic factors
- Demographic and epidemiological transition
- Changes in lifestyle and dietary patterns
- Infectious risk factors
CASES AND DEATHS IN 2018

BOTH SEXES

17 M and 9.5 M excluding NMSC
CASES AND DEATHS IN 2018

FEMALES

Incidence
- Americas: 21.3%
- Asia: 47.5%
- Europe: 23.0%
- Oceania: 1.2%

Mortality
- Americas: 15.8%
- Europe: 20.6%
- Oceania: 0.7%

8.6 million new cases
4.2 million deaths
## ESTIMATED NUMBER OF NEW CASES IN 2018

Latin America and the Caribbean

<table>
<thead>
<tr>
<th>ICD</th>
<th>Cancer</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>C00-97</td>
<td>All cancers</td>
<td>1412732</td>
</tr>
<tr>
<td>C53</td>
<td>Cervix uteri</td>
<td>56187</td>
</tr>
<tr>
<td>C54</td>
<td>Corpus uteri</td>
<td>29353</td>
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<tr>
<td>C56</td>
<td>Ovary</td>
<td>23285</td>
</tr>
<tr>
<td>C51</td>
<td>Vulva</td>
<td>3983</td>
</tr>
<tr>
<td>C52</td>
<td>Vagina</td>
<td>1925</td>
</tr>
</tbody>
</table>

http://gco.iarc.fr/
Estimated age-standardized incidence rates (World) in 2018, cervix uteri, all ages

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Data source: GLOBOCAN 2018
Graph production: IARC
(http://gco.iarc.fr/today)
World Health Organization
Estimated age-standardized incidence rates (World) in 2018, ovary, all ages

Estimated age-standardized incidence rates (World) in 2018, corpus uteri, all ages
## ESTIMATED NUMBER OF DEATHS IN 2018
### Latin America and the Caribbean

<table>
<thead>
<tr>
<th>ICD</th>
<th>Cancer</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>C00-97</td>
<td>All cancers</td>
<td>672758</td>
</tr>
<tr>
<td>C53</td>
<td>Cervix uteri</td>
<td>28318</td>
</tr>
<tr>
<td>C56</td>
<td>Ovary</td>
<td>13668</td>
</tr>
<tr>
<td>C54</td>
<td>Corpus uteri</td>
<td>7493</td>
</tr>
<tr>
<td>C51</td>
<td>Vulva</td>
<td>1265</td>
</tr>
<tr>
<td>C52</td>
<td>Vagina</td>
<td>582</td>
</tr>
</tbody>
</table>

http://gco.iarc.fr/
ADJUSTED INCIDENCE AND MORTALITY RATE IN BRAZIL

CERVIX UTERI

y = -0.7872x + 22.743
R² = 0.9548

y = -0.0288x + 5.2067
R² = 0.4029

Manuscript in preparation – unpublished data
Comparison of adenocarcinoma (ACA) and squamous cell carcinoma (SCC) of the uterine cervix in a sub-optimally screened cohort: A population-based epidemiologic study of 51,842 women in Brazil

Angélica Nogueira-Rodrigues a,b,*, Carlos Gil Ferreira b, Anke Bergmann b,c, Suzana Sales de Aguiar b, Luiz Claudio Santos Thuler b,d

- Retrospective cohort study was conducted using information from Brazilian hospital-based cancer registries
- 239 hospital units in 25 states of Brazil and the Federal District
- >70% locally advanced
- An increase of 55.9% in adenocarcinoma was observed over 10 years.
ADJUSTED INCIDENCE AND MORTALITY RATE IN BRAZIL

ENDOMETRIAL CANCER

\[ y = 0.0676x + 6.1852 \]

\[ R^2 = 0.5051 \]

\[ y = -0.0368x + 3.4866 \]

\[ R^2 = 0.6366 \]
Challenge # 2

Cervix cancer screening
Cervical Cancer Control in Latin America: A Call to Action

Brittany L. Bychkovsky, MD, MS; Mayra E. Ferreyra, MD; Kathrin Strasser-Weipol, MD; Christina I. Herold, MD; Gilberto de Lima Lopes Jr, MD; Don S. Dizon, MD; Kathleen M. Schmeier, MD; Marcela Del Carmen, MD; Tom C. Randall, MD; Angelica Nogueira-Rodrigues, MD, PhD; Aknar Freire de Carvalho Calabrich, MD; Jessica St. Louis, BA; Caroline M. Vail, BS; and Paul E. Goss, MD, PhD.

TABLE 1. Cervical Cancer Incidence, Mortality, Mortality to Incidence Ratio, and HPV Vaccination Status by Country in Latin America and the Caribbean

<table>
<thead>
<tr>
<th>Country</th>
<th>Incidence per 100,000 Women</th>
<th>Mortality per 100,000 Women</th>
<th>Mortality to Incidence Ratio</th>
<th>Cytology Available in the Public/Private Sector</th>
<th>VIA Available in the Public/Private Sector</th>
<th>Presence of National Immunization Program (Year Initiated)</th>
<th>Sex/Age</th>
<th>Vaccine Type and Dosing Schedule</th>
<th>Estimated Coverage for First Dose (Year)</th>
<th>Estimated Coverage for Completing the Series (Year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argentina</td>
<td>25.6</td>
<td>8.3</td>
<td>0.40</td>
<td>Both</td>
<td>Both</td>
<td>Yes (2011)</td>
<td>Girls&lt;11 y</td>
<td>Bivalent, 0-1-5 mo</td>
<td>80% (2011)</td>
<td>50% (2011)</td>
</tr>
<tr>
<td>Belize</td>
<td>32.7</td>
<td>14.9</td>
<td>0.85</td>
<td>Both</td>
<td>Private</td>
<td>Yes (2014)</td>
<td>Girls&lt;9-13 y</td>
<td>Bivalent, 0-6-12 mo</td>
<td>92% of girls aged 11-13 y (2014 overall)</td>
<td>53% received 2nd dose of girls aged 11-13 y (2016)</td>
</tr>
<tr>
<td>Bolivia</td>
<td>47.7</td>
<td>21</td>
<td>0.44</td>
<td>Both</td>
<td>Both</td>
<td>Yes (2014)</td>
<td>Girls&lt;9-10 y</td>
<td>Quadrivalent, 0-12 mo</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Brazil</td>
<td>16.3</td>
<td>7.3</td>
<td>0.45</td>
<td>Both</td>
<td>Both</td>
<td>Yes (2012)</td>
<td>Girls&lt;9-10 y</td>
<td>Bivalent, 2-dose schedule</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Chile</td>
<td>12.8</td>
<td>6</td>
<td>0.47</td>
<td>Both</td>
<td>No</td>
<td>Yes (2016)</td>
<td>Girls&lt;11 y</td>
<td>Bivalent, 2-dose schedule</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Colombia</td>
<td>16.7</td>
<td>8</td>
<td>0.43</td>
<td>Both</td>
<td>Both</td>
<td>Yes (2015)</td>
<td>Girls&lt;9-10 y</td>
<td>Bivalent, 2-dose schedule</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Costa Rica</td>
<td>11.4</td>
<td>4.4</td>
<td>0.39</td>
<td>Both</td>
<td>No</td>
<td>Yes (2014)</td>
<td>Girls&lt;9-10 y</td>
<td>Bivalent, 2-dose schedule</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Cuba</td>
<td>17.1</td>
<td>8.7</td>
<td>0.39</td>
<td>Both</td>
<td>No</td>
<td>Yes (2014)</td>
<td>Girls&lt;9-10 y</td>
<td>Bivalent, 2-dose schedule</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Dominican Republic</td>
<td>30.7</td>
<td>12.3</td>
<td>0.80</td>
<td>Both</td>
<td>No</td>
<td>Yes (2011)</td>
<td>Girls&lt;9-11 y</td>
<td>Bivalent, 2-dose schedule</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>Ecuador</td>
<td>39.0</td>
<td>14</td>
<td>0.36</td>
<td>Both</td>
<td>No</td>
<td>Yes (2016)</td>
<td>Girls&lt;9-11 y</td>
<td>Bivalent, 2-dose schedule</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>El Salvador</td>
<td>24.8</td>
<td>11.0</td>
<td>0.46</td>
<td>Both</td>
<td>Both</td>
<td>Yes (2013)</td>
<td>Girls&lt;10-13 y</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Guatemala</td>
<td>25.3</td>
<td>12.2</td>
<td>0.55</td>
<td>Private</td>
<td>Public</td>
<td>Yes (2015)</td>
<td>Girls&lt;10-13 y</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Guatemala</td>
<td>40.0</td>
<td>21.0</td>
<td>0.67</td>
<td>Public</td>
<td>Public</td>
<td>Yes (2010)</td>
<td>Girls&lt;9-12 y</td>
<td>Both vaccines, 0-6-12 mo</td>
<td>98% (2010)</td>
<td>67% (2016)</td>
</tr>
<tr>
<td>Haiti</td>
<td>24.9</td>
<td>14.6</td>
<td>0.36</td>
<td>Both</td>
<td>No</td>
<td>Yes (2014)</td>
<td>Girls&lt;9-10 y</td>
<td>Bivalent, 0-1-12 mo</td>
<td>96% (2015)</td>
<td>67% (2016)</td>
</tr>
<tr>
<td>Honduras</td>
<td>29.4</td>
<td>14.1</td>
<td>0.51</td>
<td>Both</td>
<td>No</td>
<td>Yes (2008)</td>
<td>Girls&lt;9-12 y</td>
<td>Both vaccines, 0-6-12 mo</td>
<td>98% (2010)</td>
<td>67% (2016)</td>
</tr>
<tr>
<td>Mexico</td>
<td>25.3</td>
<td>8</td>
<td>0.34</td>
<td>Both</td>
<td>No</td>
<td>Yes (2008)</td>
<td>Girls&lt;9-10 y</td>
<td>Bivalent, 0-1-12 mo</td>
<td>96% (2015)</td>
<td>67% (2016)</td>
</tr>
<tr>
<td>Nicaragua</td>
<td>36.2</td>
<td>18.3</td>
<td>0.51</td>
<td>Both</td>
<td>No</td>
<td>Yes (2008)</td>
<td>Girls&lt;9-12 y</td>
<td>Both vaccines, 0-6-12 mo</td>
<td>98% (2010)</td>
<td>67% (2016)</td>
</tr>
<tr>
<td>Panama</td>
<td>18.7</td>
<td>7.1</td>
<td>0.38</td>
<td>Both</td>
<td>No</td>
<td>Yes (2008)</td>
<td>Girls&lt;9-12 y</td>
<td>Both vaccines, 0-6-12 mo</td>
<td>98% (2010)</td>
<td>67% (2016)</td>
</tr>
<tr>
<td>Paraguay</td>
<td>31.2</td>
<td>15.7</td>
<td>0.66</td>
<td>Both</td>
<td>No</td>
<td>Yes (2015)</td>
<td>Girls&lt;9-11 y</td>
<td>Bivalent, 0-1-6 mo</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Peru</td>
<td>52.7</td>
<td>12</td>
<td>0.27</td>
<td>Both</td>
<td>Yes (2013)</td>
<td>Girls&lt;9-12 y</td>
<td>Bivalent, 2-dose schedule</td>
<td>NA</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Saint Lucia</td>
<td>36.0</td>
<td>16.7</td>
<td>0.47</td>
<td>Both</td>
<td>No</td>
<td>Yes (2014)</td>
<td>Girls&lt;11-12 y</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Trinidad and Tobago</td>
<td>35.3</td>
<td>12</td>
<td>0.49</td>
<td>Both</td>
<td>No</td>
<td>Yes (2015)</td>
<td>Girls&lt;9-12 y</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Uruguay</td>
<td>18.9</td>
<td>7.1</td>
<td>0.38</td>
<td>Both</td>
<td>Private</td>
<td>Yes (2013)</td>
<td>Girls&lt;12 y</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Venezuela</td>
<td>32.9</td>
<td>12.3</td>
<td>0.38</td>
<td>Both</td>
<td>No</td>
<td>Yes (2008)</td>
<td>Girls and women&lt;9-26 y Boys and men&lt;15-21 y if did not receive it previously, Girls and women&lt;13-26 y</td>
<td>Both vaccines, 3-dose schedule</td>
<td>57.3% for girls aged 13-17 y (2013), 51.6% for boys aged 13-17 y (2013)</td>
<td>37.8% for girls aged 13-17 y (2013), 15.9% for boys aged 13-17 y (2013)</td>
</tr>
<tr>
<td>United States</td>
<td>8.6</td>
<td>2.7</td>
<td>0.35</td>
<td>Both</td>
<td>No</td>
<td>Yes (2008)</td>
<td>Girls and women&lt;9-26 y Boys and men&lt;15-21 y if did not receive it previously, Girls and women&lt;13-26 y</td>
<td>Both vaccines, 3-dose schedule</td>
<td>57.3% for girls aged 13-17 y (2013), 51.6% for boys aged 13-17 y (2013)</td>
<td>37.8% for girls aged 13-17 y (2013), 15.9% for boys aged 13-17 y (2013)</td>
</tr>
<tr>
<td>Canada</td>
<td>5.3</td>
<td>1.7</td>
<td>0.27</td>
<td>Both</td>
<td>No</td>
<td>Yes (2008)</td>
<td>Girls and women&lt;9-26 y Boys and men&lt;15-21 y if did not receive it previously, Girls and women&lt;13-26 y</td>
<td>Both vaccines, 3-dose schedule</td>
<td>85% for girls in grade 9 (2013), 79% for boys in grade 9 (2013).</td>
<td></td>
</tr>
</tbody>
</table>
- Data from health surveys in LA have demonstrated that <55% of eligible women received a recent Pap test
  - Especially for urban poor and rural population

- Poor infrastructure and staff
  - Poor-quality tests, suboptimal due to issues with sampling, preparation or interpretation
  - In Brazil: 10% of all samples were not interpretable
Challenge # 3

Treatment access
Massuda and colleagues have recently published at BMJ Global Health a paper entitled “The Brazilian health system at crossroads: progress, crisis and resilience” describing the Brazilian health system and its challenges in health system financing, coverage, resource allocation and the impact over the regional disparities in access to healthcare services and health outcomes.

Brazil is a large country with an estimated population of approximately 209 million inhabitants. The Universal Health Coverage provided by Brazilian Unified Health System (SUS) is a constitutional right of every citizen. According to the National Supplementary Health Agency (ANS) in May 2018 only 22.7% of Brazilians had private insurance plans, with a 12% decrease in relative numbers during the last 30 months due to the local political and economic crisis [1].

Every two years the Brazilian National Cancer Institute generates data on cancer. According to the last publication 600,000 new cases are expected for 2018 [2]. Currently cancer is the second most common cause of death in Brazil [2]. Since the middle of the last century, the scientific understanding of cancer began to rise. This enabled the development of novel therapeutic interventions, such as new surgical techniques, modern radiotherapy, cytotoxic agents and more recently, targeted therapy and immunotherapy, giving place to a growing number of oncological interventions to combat cancer, improving quality of life, overall survi...
In 2012 the Federal Government decreed the “Law of 60 days”
This law came into effect in 2013
Delays in scheduling medical appointments and exams results
- Shortage in chemotherapy
- Shortage of radiotherapy
- Lack of equipped hospitals
- In Latin America physicians may overuse NACT for AOC

- Lack of expertise and infrastructure
- Overweight and obesity
  - IBGE in the past 5 decades the % of women >20 years old who are overweight or obese increased from 29 to 48% and 8 to 17%
  - 38.2% of Brazilian women will be obese by 2022
- Older age
  - Life expectancy increased from 73.9 in 2000 to 78.8 in 2014
- Training of gyneco-oncologists

- Preventive strategies

- Number or radiotherapy machines/sites
A systematic review of radiotherapy capacity in low- and middle-income countries

Surbhi Grover¹*, Melody J. Xu¹, Alyssa Yeager¹, Lori Rosman², Reinou S. Groen³, Smita Chackungal⁴, Danielle Rodin⁵, Margaret Mangaali¹, Sommer Nurkic², Annemarie Fernandes¹, Lilie L. Lin¹, Gillian Thomas⁵ and Ana I. Tergas⁶

- Number of radiation machines in Latin America has increased over the past 30 years, especially in countries with greater population
  - From 1989 to 2004 – Brazil 165 to 270 (64% increase), Venezuela 18 to 44 (144% increase)
- The distribution varies widely from country to country
- The capacity remains insufficient, older machines
- Insufficient number of full-time radiation oncologists and radiation technologists
- At the time of publication only Bolivia and Venezuela had > 1 radiation oncologist per 1000 cancer cases
- Formal training programs for radiation oncology are rising
Challenge # 4

HPV vaccination
Efficacy, immunogenicity, and safety of a 9-valent human papillomavirus vaccine in Latin American girls, boys, and young women


Background: A 9-valent human papillomavirus (HPV6/11/16/18/31/33/45/52/58; 9vHPV) vaccine was developed to expand coverage of the previously developed quadrivalent (HPV6/11/16/18; qHPV) vaccine. Methods: Efficacy, immunogenicity, and safety outcomes were assessed in Latin American participants enrolled in 2 international studies of the 9vHPV vaccine, including a randomized, double-blinded, controlled with qHPV vaccine, efficacy, immunogenicity, and safety study in young women aged 16–26 years, and an immunogenicity and safety study in girls and boys aged 9–15 years. Participants (N=5312) received vaccination at Day 1, Month 2, and Month 6. Gynecological swabs were collected regularly in young women for cytological and HPV DNA testing. Serum was analyzed for HPV antibodies in all participants. Adverse events (AEs) were also monitored in all participants.

Results: The 9vHPV vaccine prevented HPV 31-, 33-, 45-, 52-, and 58-related high-grade cervical, vulvar, and vaginal dysplasia with 92.3% efficacy (95% confidence interval 54.4, 99.6). Anti-HPV6, 11, 16, and 18 geometric mean titers at Month 7 were similar in the 9vHPV and qHPV vaccination groups. Anti-HPV antibody responses following vaccination were higher among girls and boys than in young women. Most (> 99%) 9vHPV vaccine recipients seroconverted for all 9 HPV types at Month 7. Antibody responses to the 9 HPV types persisted over 5 years. The most common AEs were injection-site related, mostly of mild to moderate intensity.

Conclusions: The 9vHPV vaccine is efficacious, immunogenic, and well tolerated in Latin American young women, girls, and boys. These data support 9vHPV vaccination programs in Latin America, a region with substantial cervical cancer burden.
- Panama and Mexico were the first countries in Latin America to include HPV vaccination in their immunization programs (2008/2009)
- In Brazil the vaccine was introduced in 2014
- PAHO stated that immunization is available to >80% girls the Americas
An Alert to Latin America: Current Human Papillomavirus Vaccination Trends Highlight Key Barriers to Successful Implementation

Angelica Nogueira-Rodrigues, MD, PhD1,2,3,4; Alexandra Bukowski, BA1,2; Eduardo Paulino, MD1,2,4,5,6; Jessica St. Louis, BA1,2; Adriana Barrichello, MD1; Clithya Sternberg, PhD7,8; Markus A. C. Gifoni, MD7; Silvana Luciani, MHSc9; and Paul E. Goss, MD, PhD1,2,10

Latin American countries with national recommendations for HPV vaccine

Figure 1. Latin American countries with national recommendations for the human papillomavirus vaccine. The countries not shown are Saba and St. Maarten.
- Reduction in vaccine uptake
  - Brazil: >=1 dose decreased from 92% of target population in 2014 to 69.5% in 2015
  - Similar trend in others Latin America countries
Perspectives
Disparities in Breast, Lung, and Cervical Cancer Trials Worldwide

Geographic distribution of clinical trials for cervical cancer
ClinicalTrials.gov or the WHO International Clinical Trial Registry Platform between 2010 and 2017

jgo.org on April 11, 2018.
Clinical Cancer Advances

Nine Research Priorities to Accelerate Progress Against Cancer

6. Increase Equitable Access to Cancer Clinical Trials

Certain patient populations are consistently under-represented in cancer clinical trials. These include patients from racial and ethnic minorities, rural areas, lower socioeconomic groups, and people older than 65 years as well as adolescents and young adults age 15–39 years. Decreased representation among these groups can limit access to the promising treatments offered through these trials and means that research findings may not fully account for the diversity of biological, social, and cultural factors that influence outcomes. Additional research is needed to ensure that every patient with cancer, regardless of race, ethnicity, age, geographic location, or socioeconomic status, benefits from research advances.
TAKE HOME MESSAGES

- Geographic coverage by population-based cancer registries in Latin America remains low
- Cervical cancer incidence rates observed in Latin America are among the highest in the World
- Improve quality of cervical cancer screening and also the treatment access to gynecological cancer
- Improve the number of clinical trials in the field
Thank you!

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