Epidemiology of HPV related disease of the lower genital tract: a European perspective

Controversies in Obstetrics Gynecology & Infertility

Barcelona March 2007
F. Xavier Bosch
Catalan Institute of Oncology
THE BURDEN OF HPV
THE EUROPEAN PERSPECTIVE

F. XAVIER BOSCH
Catalan Institute of Oncology
THE PREVALENCE OF HPV DNA:
LITERATURE REVIEW


- Reports with cross sectional data with at least 100 women with normal cytology
- PCR or HC2
- Entered: 108 studies (n= 169,341)
  - 78 studies with normal cytology (n=157,879)

- Results on HPV DNA Prevalence: Crude, crude in women with normal cytology, adjusted in women with normal cytology, type distribution.

DE SANJOSÉ ET AL. 2007, 2007 IN PRESS
### HPV DNA Prevalence in Women with Normal Cytology (Adjusted Model)

<table>
<thead>
<tr>
<th>Region</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global</td>
<td>10.4% (10.2-10.7)</td>
</tr>
<tr>
<td>Africa</td>
<td>22.1% (20.9-23.4)</td>
</tr>
<tr>
<td>America</td>
<td>13.0% (12.4-13.5)</td>
</tr>
<tr>
<td>Europe</td>
<td>8.1% (7.8-8.4)</td>
</tr>
<tr>
<td>Asia</td>
<td>7.9% (7.5-8.4)</td>
</tr>
</tbody>
</table>
WORLD-WIDE AGE-SPECIFIC CERVICAL HPV DNA PREVALENCE AMONG WOMEN WITH NORMAL CYTOLOGY

DE SANJOSÉ ET AL. 2007, 2007 IN PRESS
GEOGRAPHICAL AREA COVERED BY CANCER REGISTRIES

- 82.1%
- 16.7%
- 11.9%
- 1.3%
- 3.4%
- 18.6%
- 23.2%

GLOBOCAN 2002
ESTIMATED NUMBER OF CASES OF CERVICAL CANCER (2002)

- **N. AMERICA**: 14,670
- **C-S. AMERICA**: 71,862
- **AFRICA**: 78,897
- **EUROPE**: 59,931
- **ASIA**: 265,884

*per 100,000*
The most frequent cancers in women: Incidence & Mortality

Europe

Incidence

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>24.2</td>
</tr>
<tr>
<td>Colon/Rectum</td>
<td>24.2</td>
</tr>
<tr>
<td>Corpus</td>
<td>12.1</td>
</tr>
<tr>
<td>Cervix</td>
<td>11.9</td>
</tr>
<tr>
<td>Lung</td>
<td>11.3</td>
</tr>
<tr>
<td>Ovary</td>
<td>10.8</td>
</tr>
<tr>
<td>Stomach</td>
<td>9.5</td>
</tr>
</tbody>
</table>

Mortality

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>19.7</td>
</tr>
<tr>
<td>Colon/Rectum</td>
<td>12.8</td>
</tr>
<tr>
<td>Lung</td>
<td>9.8</td>
</tr>
<tr>
<td>Ovary</td>
<td>7.6</td>
</tr>
<tr>
<td>Pancreas</td>
<td>6.1</td>
</tr>
<tr>
<td>Cervix</td>
<td>5.0</td>
</tr>
</tbody>
</table>
### Incidence and Mortality of Cervical Cancer in Europe

<table>
<thead>
<tr>
<th>Region</th>
<th>Incidence ASR</th>
<th>Incidence Cases</th>
<th>Mortality ASR</th>
<th>Mortality Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervix uteri (All ages)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eastern Europe</td>
<td>14.5</td>
<td>30897</td>
<td>7.1</td>
<td>17198</td>
</tr>
<tr>
<td>Northern Europe</td>
<td>9.0</td>
<td>5647</td>
<td>3.6</td>
<td>2814</td>
</tr>
<tr>
<td>Southern Europe</td>
<td>10.7</td>
<td>10641</td>
<td>3.3</td>
<td>4131</td>
</tr>
<tr>
<td>Western Europe</td>
<td>10.0</td>
<td>12744</td>
<td>3.4</td>
<td>5671</td>
</tr>
<tr>
<td><strong>EUROPE</strong></td>
<td>11.9</td>
<td>59931</td>
<td>5.0</td>
<td>29812</td>
</tr>
</tbody>
</table>
INCIDENCE OF THE SEVEN MOST COMMON CANCERS IN WOMEN

**Northern Region**
- Breast: 82.5%
- Colon & Rectum: 26.4%
- Lung: 21.3%
- Ovary Etc.: 13.3%
- Corpus Uteri: 12.2%
- Melanoma: 10%
- Cervix Uteri: 9%

**Western Region**
- Breast: 84.6%
- Colon & Rectum: 29.8%
- Corpus Uteri: 12.5%
- Lung: 12%
- Ovary Etc.: 11.3%
- Melanoma: 10.3%
- Cervix: 10%

**Southern Region**
- Breast: 62.4%
- Colon & Rectum: 23.5%
- Corpus Uteri: 11.8%
- Cervix Uteri: 10.7%
- Ovary Etc.: 9.7%
- Lung: 9.2%
- Stomach: 8.7%

**Eastern Region**
- Breast: 42.6%
- Colon & Rectum: 20.1%
- Cervix Uteri: 14.5%
- Stomach: 12.5%
- Corpus Uteri: 11.8%
- Ovary Etc.: 10.2%
- Lung: 8.7%

GLOBOCAN 2002
MORTALITY OF THE SEVEN MOST COMMON CANCERS IN WOMEN IN EUROPE

GLOBOCAN 2002

NORTHERN

BREAST 22,6
LUNG 18,2
COLON AND RECTUM 12,7
OVARY ETC. 7,9
PANCREAS 5,8
STOMACH 4,6
CERVIX UTERI 3,6

SOUTHERN

BREAST 18,1
COLON AND RECTUM 11
LUNG 7,5
STOMACH 6,3
PANCREAS 4,7
OVARY ETC. 4,5
LIVER 4,1

WESTERN

BREAST 22,3
COLON AND RECTUM 14
LUNG 10,3
OVARY ETC. 6,3
PANCREAS 5,9
OVARY ETC. 4,5
LIVER 4,1

EASTERN

BREAST 17,9
COLON AND RECTUM 12,9
STOMACH 10,8
LUNG 7,8
CERVIX UTERI 7,1
OVARY ETC. 6
PANCREAS 4,5
INCIENCE OF CERVICAL CANCER IN EUROPE

- Eastern Europe
  - Romania
  - Bulgaria
  - Slovakia
  - Poland
  - Moldova
  - Czech Republic
  - Hungary
  - Ukraine
  - Belarus
  - Russian Federation

- Northern Europe
  - Lithuania
  - Estonia
  - Latvia
  - Denmark
  - Norway
  - Iceland
  - United Kingdom
  - Sweden
  - Ireland
  - Finland

- Southern Europe
  - Serbia and Montenegro
  - Albania
  - Bosnia and Herzegovina
  - Slovenia
  - Macedonia
  - Portugal
  - Croatia
  - Italy
  - Greece
  - Spain
  - Malta

- Western Europe
  - Austria
  - Germany
  - France
  - Belgium
  - Luxembourg
  - Switzerland
  - The Netherlands

GLOBOCAN 2002
AGE-SPECIFIC INCIDENCE RATES OF CIN-3 / CARCINOMA IN SITU AND INVASIVE CERVICAL CANCER IN SELECTED POPULATIONS

(A) FINLAND*

(INVASIVE (1998))

(IN SITU (1998))

RATIO: 1.57

(B) EAST-ANGLIA (United Kingdom)*

(INVASIVE (1998))

(IN SITU (1998))

RATIO: 12.96

(C) ICELAND*

(CIN-3 (2001))

(INVASIVE (1997 - 2001))

RATIO: 16.23

*Data provided courtesy of the Finnish Cancer Registry, East Anglian Cancer Registry, and the Iceland Cancer Registry.

CERVICAL CANCER AGE SPECIFIC INCIDENCE & MORTALITY RATES

FRANCE

SPAIN

ITALY

PORTUGAL

INCIDENCE

MORTALITY

Tasas x 100.000

0-14 15-44 45-54 55-64 65+

GLOBOCAN 2002
CERVICAL CANCER: TRENDS IN THE AGE-STANDARDIZED INCIDENCE RATES

Eastern Europe

AGES: 0 – 85+

AGES: 20 - 34

ASR (0-85+) PER 100,000 (WORLD)

ASR (20-34) PER 100,000 (WORLD)

Belarus
Czech Republic
Slovakia
CERVICAL CANCER: TRENDS IN THE AGE-STANDARDIZED INCIDENCE RATES

Southern Europe

**AGES: 0 – 85+**

**AGES: 20 - 34**

- Croatia
- Italy
- Spain

ASR (0-85+) PER 100,000 (WORLD)

ASR (20-34) PER 100,000 (WORLD)
CERVICAL CANCER: TRENDS IN THE AGE-STANDARDIZED INCIDENCE RATES

Northern Europe

AGES: 0 – 85+

AGES: 20 - 34

ASR (0-85+) PER 100,000 (WORLD)

- DENMARK
- FINLAND
- LATVIA
- UK

ASR (20-34) PER 100,000 (WORLD)

- DENMARK
- FINLAND
- LATVIA
- UK
CERVICAL CANCER: TRENDS IN THE AGE-STANDARDIZED INCIDENCE RATES

Western Europe

AGES: 0 – 85+

AGES: 20 – 34
## Predicted Number of Cervical Cancer Cases in 2020 by World Area and Age

<table>
<thead>
<tr>
<th></th>
<th>2002</th>
<th>2020* (% Change)</th>
<th>2020* (% Burden)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>World</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women aged &lt;65</td>
<td>396,500</td>
<td>549,000 (38%)</td>
<td>78%</td>
</tr>
<tr>
<td>Women aged ≥ 65</td>
<td>96,500</td>
<td>153,500 (59%)</td>
<td>22%</td>
</tr>
<tr>
<td><strong>Less Dev. Areas</strong></td>
<td>409,000</td>
<td>639,500 (56%)</td>
<td>83%</td>
</tr>
<tr>
<td>Women aged &lt;65</td>
<td>336,000</td>
<td>507,500 (51%)</td>
<td>79%</td>
</tr>
<tr>
<td>Women aged ≥ 65</td>
<td>73,000</td>
<td>132,000 (80%)</td>
<td>21%</td>
</tr>
<tr>
<td><strong>More Dev. Areas</strong></td>
<td>83,000</td>
<td>92,500 (11%)</td>
<td>17%</td>
</tr>
<tr>
<td>Women aged &lt;65</td>
<td>60,000</td>
<td>62,500 (30%)</td>
<td>67%</td>
</tr>
<tr>
<td>Women aged ≥ 65</td>
<td>23,000</td>
<td>30,000 (31%)</td>
<td>33%</td>
</tr>
</tbody>
</table>

*Projections assume that rates estimated for 2002 continue into the future*
### PREDICTED NUMBER OF CERVICAL CANCER CASES IN 2020 BY EUROPE AREA AND AGE

<table>
<thead>
<tr>
<th></th>
<th>2002</th>
<th>2020*</th>
<th>2020*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>(% CHANGE)</td>
<td>(% BURDEN)</td>
</tr>
<tr>
<td><strong>Eastern</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women aged &lt;65</td>
<td>22534</td>
<td>53744 (139%)</td>
<td>85%</td>
</tr>
<tr>
<td>Women aged +65</td>
<td>8363</td>
<td>9593 (15%)</td>
<td>15%</td>
</tr>
<tr>
<td><strong>Northern</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women aged &lt;65</td>
<td>3966</td>
<td>4067 (3%)</td>
<td>66%</td>
</tr>
<tr>
<td>Women aged +65</td>
<td>1681</td>
<td>2069 (23%)</td>
<td>34%</td>
</tr>
<tr>
<td><strong>Southern</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women aged &lt;65</td>
<td>7702</td>
<td>8080 (5%)</td>
<td>69%</td>
</tr>
<tr>
<td>Women aged +65</td>
<td>2939</td>
<td>3563 (21%)</td>
<td>31%</td>
</tr>
<tr>
<td><strong>Western</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women aged &lt;65</td>
<td>8892</td>
<td>9320 (5%)</td>
<td>66%</td>
</tr>
<tr>
<td>Women aged +65</td>
<td>3852</td>
<td>4849 (26%)</td>
<td>34%</td>
</tr>
</tbody>
</table>

*Projections assume that rates estimated for 2002 continue into the future*
## HPV ATTRIBUTABLE CANCER IN 2002

<table>
<thead>
<tr>
<th>SITE</th>
<th>DEVELOPED COUNTRIES</th>
<th>DEVELOPING COUNTRIES</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ATTRIB TO HPV (%)</td>
<td>TOTAL CANCERS</td>
</tr>
<tr>
<td>CERVIX</td>
<td>100</td>
<td>83,400</td>
</tr>
<tr>
<td>PENIS</td>
<td>40</td>
<td>5,200</td>
</tr>
<tr>
<td>VULVA, VAGINA</td>
<td>40</td>
<td>18,300</td>
</tr>
<tr>
<td>ANUS</td>
<td>90</td>
<td>14,500</td>
</tr>
<tr>
<td>MOUTH</td>
<td>3</td>
<td>91,200</td>
</tr>
<tr>
<td>OROPHAR</td>
<td>12</td>
<td>24,400</td>
</tr>
<tr>
<td>ALL SITES</td>
<td></td>
<td>5,016,100</td>
</tr>
</tbody>
</table>

PARKIN M ET AL. INT J CANCER 2006
THE ROLE OF HPV IN CERVICAL CANCER

Causality established
HPV DNA PREVALENCE IN CERVICAL CANCER
BY HISTOLOGY

AFRICA
SOUTH-SAHARAN
NORTHERN
C-S. AMERICA
S. ASIA
EUROPA & N. AMERICA
TOTAL

0 10 20 30 40 50 60 70 80 90 100
HPV POSITIVE (%)

squamous (N=2281)
adeno/mixed (N = 196)

FALSE NEGATIVES
POOR SPECIMEN HPV TEST

MUÑOZ N, ET AL. INT J CANCER
CASTELLSAGUÉ X, ET AL., J NATL CANCER INST
PREVALENCE OF HPV DNA AND OR BY COUNTRY

SQUAMOUS CELL CARCINOMA

*OR ADJUSTED BY COUNTRY AND AGE-GROUP OR (LOGARITHM)

OR* (95% CI)

ALGERIA 110.1 (45.1-268.9)
BRAZIL 177.0 (65.5-478.3)
INDIA 64.1 (28.1-146.3)
MALI 109.2 (10.6-1119.0)
MOROCCO 113.7 (42.3-305.3)
PARAGUAY 208.1 (46.4-932.8)
PERU 115.9 (48.6-276.4)
PHILIPPINES 276.8 (139.7-548.3)
THAILAND 163.5 (82.0-325.9)
COLOMBIA 18.4 (9.4-36.0)
SPAIN 67.4 (30.3-149.8)
COLOMBIA 90.0 (71.3-113.5)
HPV TYPE SPECIFIC ODDS RATIOS FOR CERVICAL CARCINOMA

*OR ADJUSTED BY COUNTRY AND AGE

VACCINE HPV MONOGRAPH, 2006
CUMULATIVE INCIDENCE OF CIN 3+ AMONG 13,000 WOMEN OVER A TEN YEAR PERIOD (AS A FUNCTION OF A SINGLE HPV TEST RESULT AT ENROLMENT)

Khan et al, JNCI, 2005
TYPE-SPECIFIC HPV PREVALENCE IN CERVICAL CANCER CASES

Europe & North America

<table>
<thead>
<tr>
<th>Type</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>65.4%</td>
</tr>
<tr>
<td>+ 18</td>
<td>71.5%</td>
</tr>
<tr>
<td>+ 33</td>
<td>77.1%</td>
</tr>
<tr>
<td>+ 31</td>
<td>81.2%</td>
</tr>
<tr>
<td>+ 45</td>
<td>84.1%</td>
</tr>
<tr>
<td>+ 56</td>
<td>85.6%</td>
</tr>
<tr>
<td>+ 35</td>
<td>86.8%</td>
</tr>
<tr>
<td>+ 52</td>
<td>87.8%</td>
</tr>
</tbody>
</table>
PREVALENCE OF THE 11 MOST COMMON HPV TYPES WORLDWIDE IN 2855 HPV POSITIVE CERVICAL CANCER CASES & RANK BY REGION

<table>
<thead>
<tr>
<th>HPV type</th>
<th>%</th>
<th>HPV type</th>
<th>%</th>
<th>HPV type</th>
<th>%</th>
<th>HPV type</th>
<th>%</th>
<th>HPV type</th>
<th>%</th>
<th>HPV type</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV 16</td>
<td>47.7</td>
<td>HPV 16</td>
<td>67.6</td>
<td>HPV 16</td>
<td>57.0</td>
<td>HPV 16</td>
<td>52.5</td>
<td>HPV 16</td>
<td>69.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPV 18</td>
<td>19.1</td>
<td>HPV 18</td>
<td>17.0</td>
<td>HPV 18</td>
<td>12.6</td>
<td>HPV 18</td>
<td>25.7</td>
<td>HPV 18</td>
<td>14.6</td>
<td></td>
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</tr>
<tr>
<td>HPV 45</td>
<td>15.0</td>
<td>HPV 45</td>
<td>5.6</td>
<td>HPV 31</td>
<td>7.4</td>
<td>HPV 45</td>
<td>7.9</td>
<td>HPV 45</td>
<td>9.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPV 33</td>
<td>3.2</td>
<td>HPV 33</td>
<td>4.0</td>
<td>HPV 45</td>
<td>6.8</td>
<td>HPV 52</td>
<td>3.1</td>
<td>HPV 31</td>
<td>4.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPV 58</td>
<td>3.2</td>
<td>HPV 31</td>
<td>3.4</td>
<td>HPV 33</td>
<td>4.2</td>
<td>HPV 58</td>
<td>3.0</td>
<td>HPV 56</td>
<td>2.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPV 56</td>
<td>2.7</td>
<td>HPV 56</td>
<td>2.2</td>
<td>HPV 52</td>
<td>3.6</td>
<td>HPV 33</td>
<td>2.2</td>
<td>HPV 52</td>
<td>1.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPV 31</td>
<td>2.3</td>
<td>HPV 35</td>
<td>1.9</td>
<td>HPV 35</td>
<td>3.1</td>
<td>HPV 59</td>
<td>2.0</td>
<td>HPV 35</td>
<td>1.1</td>
<td></td>
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</tr>
</tbody>
</table>
### COMPARISON OF TYPE-SPECIFIC HPV PREVALENCE BETWEEN SCC AND HSIL CASES

<table>
<thead>
<tr>
<th>HPV TYPE</th>
<th>SCC</th>
<th>HSIL</th>
<th>SCC: HSIL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>HPV (%)</td>
<td>N</td>
</tr>
<tr>
<td>ALL</td>
<td>8550</td>
<td>87.6</td>
<td>4338</td>
</tr>
<tr>
<td>16</td>
<td>8594</td>
<td>54.3</td>
<td>4338</td>
</tr>
<tr>
<td>18</td>
<td>8502</td>
<td>16.6</td>
<td>4338</td>
</tr>
<tr>
<td>33</td>
<td>8449</td>
<td>4.3</td>
<td>4302</td>
</tr>
<tr>
<td>45</td>
<td>5174</td>
<td>4.2</td>
<td>2214</td>
</tr>
<tr>
<td>31</td>
<td>7204</td>
<td>4.2</td>
<td>4036</td>
</tr>
<tr>
<td>58</td>
<td>5646</td>
<td>3.0</td>
<td>2175</td>
</tr>
<tr>
<td>52</td>
<td>5304</td>
<td>2.5</td>
<td>2153</td>
</tr>
</tbody>
</table>

CLIFFORD GM ET AL. BR J CANCER 2003; 89:101-105
PREDICTED IMPACT OF A VACCINE INCLUDING HPV TYPES 16 & 18

Decade(s) →

Potential Reduction

ICC: 67-71%

Years

HSIL: 52-60%

Months

LSIL: 14-25%

ASCUS: 20%
Europe generates an estimated number of 60,000 new cases of cervical cancer per year. The number of HSIL lesions diagnosed and treated is likely to double this figure. Eastern Europe represents a group of countries at very high risk of cervical cancer. All cervical cancer cases are related to persistent HPV infections. HPV 16 & 18 account for 70% of cases worldwide.
GRACIAS POR SU ATENCIÓN