Storia di screening delle donne con cancro della cervice in Friuli Venezia Giulia

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Cervical cancer screening programs, through Papanicolaou (Pap) smear, allow the identification of pre-invasive lesions which can be adequately treated:

- reduced incidence and mortality rates for invasive cervical cancer (up to 80%)

1995-1999: an investigation conducted by Friuli Venezia Giulia (FVG) Cancer Registry

- 72% of invasive cervical cancer cases had no previous Pap-smear
Background

- 1999: Organized Cervical Cancer Screening Program (OCSP) in Friuli Venezia Giulia
  - Whole region covered
  - Target population: women aged 25-64 years
  - Personal invitation letter
  - A Pap-smear, free of charge, every 3 years

In 2005:
- 90% coverage of target population
- 55% compliance to screening invitation
Background

- FVG is one of Italian regions with the highest use of Pap-smear tests (survey ISTAT, 2004-2005)
  - 86% of the women aged ≥25 years, received at least one Pap-smear in their life
  - 64% of women living in North-East Italy perform opportunistic Pap-smears outside the OCSPs
Rationale

- Why do women develop invasive cervical cancer in FVG, despite the existence of an OCSP and the widespread use of opportunistic screening?
  - Std (EU pop) incidence rates x100,000:
    - 8.7 in 1999-2003
    - 6.7 in 2004-2005

- Feasibility: FVG region has both OCSP and Cancer Registry covering the whole area
Objectives

- To evaluate screening history of women diagnosed with invasive cervical cancer according to demographic variables and tumor characteristics
- To determine reasons of missed prevention
- To identify possible limitation of the effectiveness of OCSP
Material and Methods

- 438 invasive cervical cancer cases occurred between 1999 and 2005 (FVG Cancer Registry)

- Computerized databases were employed to track screening histories, using an anonymous regional identification code:
  - Pathological Archives: cytological (e.g., Pap-smear dates and results) and histological information (e.g., tumor stage and histology)
  - OCSP: invitation and compliance to OCSP (e.g., invitation date, reason of non invitation)
  - Other (Colposcopy, Hospital discharge)
Material and Methods

Cervical cancer cases were categorized as:

> Without information about Pap-smears
  - Not invited by OCSP
  - Not compliant with OCSP invitation

> Ever screened (inside/outside OCSP)
  - Last Pap-smear NEGATIVE
    - test misread as negative
    - sub-optimal time schedule of tests
  - Last Pap-smear POSITIVE or inadequate
    - detected at screening
    - inadequate follow-up (diagnosis >1.5 years after abnormal Pap-smear)
Results

438 Cervical cancer cases

- 273 (62.3%) Ever Screened
  - 201 (45.9%) Last Pap-smear: not negative
  - 72 (16.4%) Last Pap-smear: negative

- 165 (37.7%) No information on Pap-smear
  - 71 (16.2%) Not compliant to OCSP invitation

- 94 (21.5%) Not invited by OCSP

- 69 (15.8%) Because of age >64 years
  - 25 (5.7%) For other reasons

- 34 (7.8%) >3 years before diagnosis
- 38 (8.7%) ≤3 years before diagnosis
- 193 (44.1%) Detected at Screening
- 8 (1.8%) Inadequate follow-up
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### Distribution of 438 cervical cancer cases according to screening - FVG Italy, 1999-2005

<table>
<thead>
<tr>
<th></th>
<th>Ever screened</th>
<th>Never screened</th>
<th>OR° (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>No. (%)</td>
<td></td>
</tr>
<tr>
<td><strong>Age at diagnosis (years)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>26-45</td>
<td>89 (32.6)</td>
<td>22 (13.3)</td>
<td>1#</td>
</tr>
<tr>
<td>45-64</td>
<td>110 (40.3)</td>
<td>61 (37.0)</td>
<td>2.24 (1.28 -3.94)</td>
</tr>
<tr>
<td>≥65</td>
<td>74 (27.1)</td>
<td>82 (49.7)</td>
<td>4.48 (2.55 -7.87)</td>
</tr>
<tr>
<td><strong>National ity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Italian</td>
<td>258 (94.5)</td>
<td>158 (95.8)</td>
<td>1#</td>
</tr>
<tr>
<td>Non Italian</td>
<td>15 (5.5)</td>
<td>7 (4.2)</td>
<td>1.27 (0.49 -3.33)</td>
</tr>
<tr>
<td><strong>Tumor stage (FIGO)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IA–microinvasive</td>
<td>88 (32.2)</td>
<td>18 (10.9)</td>
<td>1#</td>
</tr>
<tr>
<td>IB</td>
<td>75 (27.5)</td>
<td>26 (15.8)</td>
<td>1.55 (0.78 -3.07)</td>
</tr>
<tr>
<td>II</td>
<td>34 (12.5)</td>
<td>33 (20.0)</td>
<td>3.73 (1.82 -7.63)</td>
</tr>
<tr>
<td>III-IV</td>
<td>51 (18.7)</td>
<td>55 (33.3)</td>
<td>3.96 (2.05 -7.67)</td>
</tr>
<tr>
<td>Unk</td>
<td>25 (9.2)</td>
<td>33 (20.0)</td>
<td>4.17 (1.91 -9.11)</td>
</tr>
<tr>
<td><strong>Tumor histology</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Squamous</td>
<td>204 (74.7)</td>
<td>126 (76.4)</td>
<td>1#</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>54 (19.8)</td>
<td>27 (16.4)</td>
<td>0.74 (0.43 -1.26)</td>
</tr>
<tr>
<td>Other</td>
<td>15 (5.5)</td>
<td>11 (6.7)</td>
<td>0.85 (0.37 -1.98)</td>
</tr>
</tbody>
</table>

° Odds Ratio (OR) and 95% confidence intervals (CI) estimated using logistic regression model adjusted for age at diagnosis. - # Reference category.
### Distribution of 273 of cervical cancer cases screened inside and outside the organized program (OCSP) - FVG Italy, 1999-2005

<table>
<thead>
<tr>
<th>Inside O CSP (n=132)</th>
<th>Outside O CSP (n=141)</th>
<th>OR° (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age at diagnosis (years)</strong></td>
<td><strong>No. (%)</strong></td>
<td><strong>No. (%)</strong></td>
</tr>
<tr>
<td>26-45</td>
<td>61 (46.2)</td>
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</tr>
<tr>
<td>45-64</td>
<td>62 (47.0)</td>
<td>48 (34.0)</td>
</tr>
<tr>
<td>≥65</td>
<td>9 (6.8)</td>
<td>65 (46.1)</td>
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<tr>
<th><strong>Nationality</strong></th>
<th><strong>No. (%)</strong></th>
<th><strong>No. (%)</strong></th>
<th><strong>OR° (95%CI)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Italian</td>
<td>120 (90.9)</td>
<td>138 (97.9)</td>
<td>1#</td>
</tr>
<tr>
<td>Non Italian</td>
<td>12 (9.1)</td>
<td>3 (2.1)</td>
<td>0.41 (0.11-1.55)</td>
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<tr>
<th><strong>Tumor stage (FIGO)</strong></th>
<th><strong>No. (%)</strong></th>
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<tr>
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<td>1.90 (0.95-3.80)</td>
</tr>
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<td>4.23 (1.65-10.83)</td>
</tr>
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<tr>
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<tr>
<td>Other</td>
<td>2 (1.5)</td>
<td>13 (9.2)</td>
<td>3.08 (0.59 -16.0)</td>
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° Odds Ratio (OR) and 95% confidence intervals (CI) estimated using logistic regression model adjusted for age at diagnosis. - # Reference category.
Discussion

Causes of missed prevention:

- 38% of cases never screened
  - vs. 72% in the period before OCSP introduction

- 56% of cases detected at FIRST Pap-smear
  → never screened before
Discussion

Possible limitations of the OCSP:

- 28% of cases not invited because of age (>64 years)
- 4% of cases not invited because of opportunistic screening in the previous 3 years

- Among 132 women screened inside OCSP:
  - 11% false-negative Pap-smears (mostly adenocarcinomas)
  - 5% inadequate follow-up after abnormal Pap-smear

- 16% of cases were not compliant to OCSP invitation
Conclusions

- Nonattendance is the main limitation for the effectiveness of OCSP among women in the target population
  - Unknown percentage of cases screened in private physician practices, but the estimates are very low in FVG

- Screened cases, in particular inside OCSP, have lower tumor staging
  - What about pre-invasive cancers? FVG Cancer Registry has incomplete registration of pre-invasive cervical cancer (CIN3-In situ)
Thanks to....

- Grant: Italian Association for Research on Cancer (AIRC)