QA and Quality Indicators for Cervical Cancer Screening Programs

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Disclosures

• No financial relationships or conflict of interest to disclose
Organised screening programs

- Active invitation (all or “integrated”)
- Defined (evidence-based) protocols for all phases
- Fail safe system for women with non normal primary test (guarantee diagnostic work-up)
- Fail safe system for women needing treatment
- Registration of all screening events (linkage with cancer registry)
- QA and monitoring.
**Objective**

- Increasing effectiveness
  - Reducing cancer incidence and mortality in population
- Controlling undesired effects and costs

**QA and Monitoring**

**Approaches**

- Define “rules” (standard behaviour) – measure if followed
  Does following the rules improve the desired final result?
- Monitor to measure intermediate results and costs – correct situation if needed
Organization of cytology-based and HPV-based cervical cancer screening

A. Anttila, G. Ronco, F. Nicula, P. Nieminen, M. Primic Žakelj
EU guidelines
Screening intensity

• Programme extension
• Coverage of the target population by invitation
• Coverage of the target population by smear/HPV test
• Compliance to invitation
• Smear/HPV primary test consumption
• Incidence of invasive cancer in unscreened and underscreened women in a given interval (3.5 and 5.5 years for cytology; 5.5 and 7.5 for HPV)
EU guidelines
Screening test performance

• Proportion of women positive at the primary screening test
• Referral for triage test
• Referral for colposcopy
• Positive Predictive value for referral to colposcopy
• Detection of CIN (particularly CIN2 and CIN3)
• Cancer incidence after normal primary test result
What cannot be measured in routine practice

- **Sensitivity**
  - Measuring them entails referring to second level all or a relevant number of subjects negative to primary test
  - If not, possibly relevant bias

- **Detection rate not surrogate measure of sensitivity except**
  - Risk can be assumed as uniform
    - in Italy high variability of %HPV+ in areas covered by same lab
  - Related to an external risk measure
    - Incidence in absence of screening (impossible to compute correctly)
    - Risk quite stable in HPV+ women given screening history (cfr. triage tests)
Detailed indicators depend on protocol.

- Italian guidelines give one precise protocol for management of HPV+ women. Process indicators very detailed.
- EU guidelines allow different approaches. Less detailed
HPV based screening - Italy

Samples for HPV and cytology taken

- HPV test
  - Negative
    - Referred to New screening round
  - Positive
    - Cytology ASC-US+ or unsatisfactory
      - Referred to colposcopy
    - Cytology WNL
      - Invited after 1 year for new HPV test
        - HPV test negative
          - Referred to New screening round
        - HPV test still positive
          - Referred to colposcopy
    - Cytology stained and interpreted
      - INFORMED OF HPV POSITIVITY
EU guidelines
Diagnostic assessment and treatment

• Compliance to referral for colposcopy
• Treatment of high-grade intraepithelial lesions
• Proportion of women hysterectomised on screen-detected CIN
• Proportion of women treated on CIN1
• Proportion of women with cytology negative for SIL 6 months after treatment
Italy, survey 2014

- Compliance to referral for colposcopy
  - Any reason 87.0% HSIL 91.2%

- Treatment of high-grade intraepithelial lesions
  - Recommended but not treated 3.8% (2.7% > 3 mths.)
  - Unknown if treated 7.1%

- Proportion of women hysterectomised on screen-detected CIN
  - 0.0% of CIN1, 0.3% of CIN2, 1.4% of CIN3

- Proportion of women treated on CIN1
  - 82% follow-up first recommended
Italy 2014 survey
Distribution of histology at excisional treatment by histology on biopsy

<table>
<thead>
<tr>
<th>Biopsy</th>
<th>No CIN</th>
<th>CIN1</th>
<th>CIN2/3</th>
<th>AdenoCa IS</th>
<th>Inv Ca</th>
<th>Not available</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIN1</td>
<td>18.6%</td>
<td>41.4% (143)</td>
<td>29.3% (101)</td>
<td>0.6% (2)</td>
<td>0.3% (1)</td>
<td>9.9% (34)</td>
</tr>
<tr>
<td>CIN2/3</td>
<td>3.4% (102)</td>
<td>8.7% (261)</td>
<td>81.1% (2432)</td>
<td>0.5% (15)</td>
<td>2.7% (83)</td>
<td>3.6% (107)</td>
</tr>
<tr>
<td>AdenoCa IS</td>
<td>6.4% (3)</td>
<td>2.1% (1)</td>
<td>6.4% (3)</td>
<td>59.6% (28)</td>
<td>17.0% (8)</td>
<td>8.5% (4)</td>
</tr>
<tr>
<td>Inv Ca</td>
<td>1.9% (1)</td>
<td>0% (0)</td>
<td>18.5% (10)</td>
<td>7.4% (4)</td>
<td>66.7% (36)</td>
<td>5.6% (3)</td>
</tr>
<tr>
<td>No Biopsy (see and</td>
<td>6.7% (14)</td>
<td>21.0% (44)</td>
<td>54.3% (114)</td>
<td>3.8% (8)</td>
<td>1.4% (3)</td>
<td>12.9% (27)</td>
</tr>
<tr>
<td>treat)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Percents are on rows
## 2014 Survey Italy

Free endocervical margins in excisional treatments

<table>
<thead>
<tr>
<th>Method</th>
<th>Tot</th>
<th>Yes</th>
<th>%</th>
<th>No</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radio frequency device (LLETZ needle)</td>
<td>2352</td>
<td>1758</td>
<td>92.8%</td>
<td>136</td>
<td>7.2%</td>
</tr>
<tr>
<td>Cold knife conization</td>
<td>407</td>
<td>170</td>
<td>93.9%</td>
<td>11</td>
<td>6.1%</td>
</tr>
<tr>
<td>Laser conization</td>
<td>455</td>
<td>396</td>
<td>91.7%</td>
<td>36</td>
<td>8.3%</td>
</tr>
<tr>
<td>Total</td>
<td>3214</td>
<td>2324</td>
<td>92.7%</td>
<td>183</td>
<td>7.3%</td>
</tr>
</tbody>
</table>
Reference values

- **What is best for effectiveness and cost**
  - In some case relation with effect direct: the highest participation to screening the greatest effectiveness taking everything else stable. Logical relation. No extra evidence needed.
  - In some case relation can be complex, evidence needed – modelling.

- **What is feasible.**
  - Given the highest participation the best, which participation is it possible to reach?
  - What has been reached?
  - “External validity”

- **Evaluate variability between programs**
  - Explainable by different prevalence of searched condition?
• The most difficult is making changes when a problem is identified
• Sometimes simply showing variability reduces it
% Referral rate to colposcopy
Italy Surveys 2002 (blue) and 2014 (red)

Each bar is a local program