Implementation of regional HPV-based screening; Challenges and way forward to national implementation. The Italian policy.

Francesca Maria Carozzi
Responsible
Responsible for hpv implementation in Tuscany Region
Director Regional Laboratory For Cancer Prevention
ISPRO- Florence -Italy
Contents

• Background: Cervical Cancer screening in Italy
• The HPV- primary test strategy in Italy: protocol, age, interval.
• Where we are today
• Data from 2° round of HPV screening
• The LABs in the regional programs and LABs quality control.
• COVID19 and HPV-primary testing.
Cervical Cancer Screening: target Age 25-64 y
Different protocols by age

Active invitation by Letter

HPV screening test >=30-64 years

HPV Positive

HPV Negativo

HPV test negative

Citology Neg

Recall after 1 year to repeat HPV Test

New screening round after 5 years

HPV test Positive (persistence)

Referral to colposcopy

Pap TEST screening test 25-30/34

Citology ASC-US+

HPV Negative

New screening round after 3 anni

HPV Positive

Referral to Colposcopy

Citology NEG

Pap >ASC-US+

HPV Negative

Referral to colposcopy

If HPV positive pap test is always performed, but only to guide follow-up recall;
HPV Screening In Italy: 19 regions out of 21
Different models of lab centralisation by region

<table>
<thead>
<tr>
<th>Year</th>
<th>Regioni</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>10</td>
</tr>
<tr>
<td>2013</td>
<td>10</td>
</tr>
<tr>
<td>2014</td>
<td>12</td>
</tr>
<tr>
<td>2015</td>
<td>12</td>
</tr>
<tr>
<td>2016</td>
<td>15</td>
</tr>
<tr>
<td>2017</td>
<td>16</td>
</tr>
<tr>
<td>2018</td>
<td>17</td>
</tr>
<tr>
<td>2019</td>
<td>19</td>
</tr>
</tbody>
</table>

All screening programs use HPV validated test

Implementation started from older women
1 year 55-64
2° year 45-54
3° year 30/34-44
Documents for HPV screening Implementacion

- List of HPV test Validated for Cervical Cancer Screening according to the European Guidelines
- ONS-GISCiReport N°. 4 31 January 2019
- Document is updated annually and available on the web site www.gisci.it

External Quality assurance programs for HPV and cytology triage

HPV test EQA
Pap Triage EQA
Women invited to HPV screening from 2015 to 2018

- 2015: 654,143
- 2016: 905,007 (+190,000)
- 2017: 1,196,843 (+260,000)
- 2018: 1,458,102
Compliance to screening invitation by year and MACROAREA

![Graph showing compliance to screening invitation by year and MACROAREA.](image-url)
HPV screening tests ≥30-64 years old

Protocol HPV Cervical Cancer Screening

HPV Negative

- HPV Positive
  - Cytology ASC-US+ or unsatisfactory
    - Colposcopy
  - HPV test still positive
    - Invited after 1 year for new HPV test
  - HPV test negative
    - Referred to New screening round After 5 Year

PAP TEST TRIAGE

Citology WNL

Liquid based samples

Relevant variability of HPV positivity by region and cities 5.4%-12.1%

Relevant variability on pap triage positivity 16%-37.1%

Clearance less than expected 46%-61%

Data from Italian Nationale Gisci Meeting May 2020
HPV Screening In Italy: 19 regions out of 21
Different models of lab centralisation by region

All screening programs are using HPV validated test
DATI SURVEY HPV 2018 REGIONE TOSCANA
Positività Test HPV Primario

Standard ONS-Gisci
HPV 5-9%

Survey Italia* 2017: 5,4%-13,1%

Survey Toscana 2018: 5,7%-12,6%

% HPV inadeguati RT
Italia 0,02%
0,14
### Preliminary Results in Florence Area

**HPV primary test (Cobas4800) – partial genotyping**

<table>
<thead>
<tr>
<th></th>
<th>Enrolled women</th>
<th>HR-HPV n</th>
<th>HR-HPV %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccinated</td>
<td>1,605</td>
<td>281</td>
<td>17.5</td>
</tr>
<tr>
<td>Unvaccinated</td>
<td>457</td>
<td>121</td>
<td>26.5</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>2,062</strong></td>
<td><strong>402</strong></td>
<td><strong>19.5</strong></td>
</tr>
</tbody>
</table>

*p value < 0.01*

La positività del test HPV fra le donne vaccinate è circa 32% inferiore rispetto a quella delle donne non vaccinate (17.9% vs. 26.4%; p<0.01)
Stop of screening programs 15 march 2020 at national level

In 2020, the screening tests are about 55.3% less than in 2019. There are small fluctuations between the Regions, however no Region at the end of May 2020 has accumulated delays of less than 40%.

This value transformed into time becomes an average delay of 2.8 standard months (with fluctuations ranging from 2.1 to 3.2 standard months).

The number of undiagnosed CIN 2 or more severe injuries is estimated at 1,676.

Fortunately, at the moment the accumulated mean diagnostic delay is quite limited and the clinical consequences are probably not particularly pronounced.

The screening is now re-opened (from 15 May 2020) but the compliance is lower than expected and from September we re-start with usual overbooking (4 women every 15 min).

Self-sampling option is under evaluation not only for not-responder but especially for women in HPV program at 2° round of screening.
Thanks for your attention

f.carozzi@ispro.toscana.it