HPV screening and treatment challenges in Eastern and Central Europe:

part of Europe with highest burden of cervical cancer

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No conflicts of interest to declare.

Source: Globocan 2018

World-age-standardised rates of incidence and mortality from cervical cancer (/100,000 women-years), in Europe, estimates for 2018

28 countries included in the regional report

"Comprehensive Control of HPV Infections and Related Diseases in the Central and Eastern Europe and Central Asia Region"
Albania, Bosnia and Herzegovina, Bulgaria, Croatia, Czech Republic, Estonia, Republic of North Macedonia, Hungary, Latvia, Lithuania, Montenegro, Poland, Romania, Serbia, Slovenia, Slovakia.

Organized CC screening
Opportunistic CC screening

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November 2019

- 10 countries organized cervical screening
- 5 countries opportunistic cervical screening
- cervical screening mainly based on conventional cytology

Slovenia
- national organized screening programme since 2003
- the coverage reached 82.5% in the first 6-year period

Hungary
- implemented organized screening in 2004
- low coverage of target population in organized settings and more than 60% attendance outside the programme
- pilot programme started in 2011 aiming to improve the coverage

Czech Republic, Estonia, Lithuania, Latvia
- at least partially functioning organized screening programs
- low coverage reported

Romania
- organized screening started in 2012, low coverage reported

Montenegro
- implemented population based nationwide organized screening programme in February 2018 (pilot started in July 2016)
- target population: 30-49 years
- HPV-based (the only HPV-based screening programme in the region)
- the coverage reached 5.2% in the first 2-year period

Bulgaria
- implemented organized screening programme at the end of 2018
- target population: 30-60 years; coverage rates not available

Slovakia
- implemented organized screening programme in November 2019
- target population: 23 - 64 years; coverage rates not available

Croatia
- implemented organized screening in December 2012
- the coverage reached 29.6% in 2015
- stopped organized screening in January 2016 and has since then reorganizing it
- widespread opportunistic screening

Poland
- started organized screening in 2004
- coverage around 17%
- invitations stopped in 2016 by the decision of the Ministry of Health
- widespread opportunistic screening

Conclusions - November 2019 situation

officially proclaimed “organized” cervical cancer screening in 10/15 countries; only in single country coverage over 70% in great majority of countries with “organized” screening coverage data not available, assumed substantial attendance outside the official national screening program (opportunistic settings)

5/15 countries opportunistic screening only; insufficient funding and infrastructure; low population coverage, moderate to poor quality cytology

national HPV-based organized cervical screening implemented in single country but with extremely low coverage, in the remaining countries still cytology-based

over-screening and under-screening: relatively high coverage in women below 40 and poor coverage in older women

lack of financial resources; cervical cancer (women health) not high on political agenda; several country-specific problems e.g. population registry lacking (BiH)
Slovenia

effective nationally organized cervical cancer screening programme with the three years coverage over 70%

+ HPV vaccination integrated into national immunization programme and provided free of charge to the primary target population with coverage over 60%

ZORA (Zgodnje odkrivanje raka materničnega vratu)

- screening women 30-64 years
- screening every three years (after two consecutive negative results in one year period)
- conventional cytology, cytology interpreted by certified cytologists
- cross sectional sensitivity of cytology: CIN2+ = 66.2 %, CIN3+ = 80.6 %
- HPV reflex testing for five indications

Integration of:
1. Central national registry of cytology, histology and HPV-test results
2. Central national population registry
3. National cancer registry

Incidence of cervical cancer in Slovenia 2003-2018

<table>
<thead>
<tr>
<th>Year</th>
<th>New cases</th>
<th>Crude incidence rate/100,000</th>
<th>ASR (W)</th>
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<td>211</td>
<td>20.7</td>
<td>15.3</td>
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<td>19.4</td>
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<tr>
<td>2018</td>
<td>106</td>
<td>10.2</td>
<td>6.6</td>
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</tbody>
</table>

opportunistic screening
- coverage approx. 40%
- 170,000 smears/year

organised screening
- coverage above 70%
- 170,000 smears/year

ASR (W): age-standardized rate by world population

Three years coverage in national organized cervical cancer screening programme in Slovenia in different age groups (2007-2019)

conventional cytology-based screening
HPV-based screening

HPV-based screening
HPV-based screening (conventional and HPV-based triple triage)

HPV-based screening
HPV-based screening (conventional and HPV-based triple triage)
Slovenian Primary Cervical Cancer Screening Cohort Study

First screening round
4,507 unselected women aged 20-64 years, who attended routine PAP screening with local gynecologists (Dec 2009-Aug 2010)

Second screening round
3,920 women that had 36-to 48-month follow-up result of hrHPV DNA and/or cytology after a baseline screening round (Dec 2012-Dec 2014)

Prevalence of infection with 14 hr-HPV types with 95% confidence intervals according to age among 4,431 women screened for cervical cancer, Slovenia, 2010

Time trends of incidence CIN2+ cases according to different baseline characteristics in women 20-65 years; Slovenia 2010-2014

Conventional cytology-based screening
HPV-based borderline cytology triage; HPV test of cure (2010)

Liquid based cytology screening (HPV triage)
HPV-based screening (cytology triage)
Before we start...

performing local HPV genotype distribution studies in women with normal cytology, HSIL, and/or cervical cancer prior to implementation of primary HPV screening is not necessary any more — use available regional data

- do not complicate, do not reinvent the wheel, trust more experienced colleagues and their results
- do not waste time — in several CEECA countries at least one woman in 50 will develop cervical cancer in 2020

COVID-19-related problems arising:
- shifted interest of public and politicians
- testing is important but availability limited
- keeping pace of clinical cancer screening program; manufacturers shifted to new niche market with unprecedented market growth opportunity: “new normal” with unclear future

Prepare fractions of cervical cancer screening in six Baltic, central, and Eastern European countries 2017-2040: a population-based study

- more genotypes = better HPV test
- higher price = better HPV test
- manufacturers’ rumors (bizarre case reports, biased evaluations, L1 deletion story . . . )
- long screening rounds are unsafe (even with shorter rounds they missed carcinomas . . . )
- lobbies (cytologists, gynecologists, colposcopists . . . new role for all should be identified)
- experiment serving diagnostic companies
- general mistrust in the ineffective public health system

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