Review of HPV\cervical cancer Screening and treatment challenges in Eastern Europe and Central Asia: 
Russia, Georgia, Belorussia, Ukraine, Moldova, Armenia, Azerbaijan, Uzbekistan, Kazakhstan, Kirgizstan.

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(RUSSIAN ASSOCIATION FOR GENITAL INFECTIONS AND NEOPLASIA)
nothing to declare
Basic facts

• No system of epidemiological observation of HPV

• State statistics exists for anogenital warts and malignancy (somewhere CIS). No correlation with HPV. The cancer register is mainly based on oncological institutions data

• Data of HPV types are based on selective researches with various methodology and tools.

• Impact of HPV -46.7% are accounted for anogenital warts, cervical cancer - 19.5%, anal cancer - 15.6%, vulvar cancer - 2.3%, vaginal cancer - 0.5%, CIN- 15.5% (Chernova, 2018)

• System should consider psychosocial damage of patient with positive test results, additional clinical visits, overtreatment, risk of lost to follow up, etc.
**AGW – the interdisciplinary problem**

<table>
<thead>
<tr>
<th>Country</th>
<th>Incidence anogenital warts</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Russia</td>
<td>18.8 cases per 100,000 population</td>
<td>Clinical guidelines, RODVK 2019</td>
</tr>
<tr>
<td></td>
<td>It is noted less intensive decrease in the incidence of anogenital venereal warts - 38.2%</td>
<td>Briko N.I., Kaprin A.D 2019; 21 (1): 45–50. DOI: 10.26442/18151434.2019.190199</td>
</tr>
<tr>
<td>Belorussia</td>
<td>30 cases per 100,000 population (10.4%)</td>
<td>A.Navrotsky, M.Romashko et al, 2015</td>
</tr>
</tbody>
</table>

**Georgia, Ukraine, Moldova, Armenia, Azerbaijan, Uzbekistan, Kazakhstan, Kirgizstan** - official statistics are not available

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Tests applied in screening and clinic

Pap tests
- LBC
- Papanicolau test (wet smear)
- Pappenheim test (dry smear)

HPV tests
More than 90 tests are licensed
HR-HPV DNA tests, rare
HPV DNA -PCR Real-time (AmpliSens,Russia, Anyplex™, domestic tests) mainly
Hybrid Capture 2 HPV DNA-Test, expensive
HR-HPV E6/E7 mRNA tests, rare
The burden of HPV infection in women with normal cytology by country (2015-2020)

<table>
<thead>
<tr>
<th>Country</th>
<th>Prevalence range of HPV (%)</th>
<th>Population description</th>
<th>HPV test, Genotyping</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Russia</td>
<td>20.7%</td>
<td>General population</td>
<td>RT-PCR, AmpliSens</td>
<td>Ministry of Health Rosstat, 2016</td>
</tr>
<tr>
<td>Ukraine</td>
<td>40%</td>
<td>General population</td>
<td>RT-PCR, Anyplex™</td>
<td>Suhanova, 2016</td>
</tr>
<tr>
<td>Moldova</td>
<td>15-20 %</td>
<td>General population</td>
<td>RT-PCR</td>
<td>Jarynowski, 2019</td>
</tr>
<tr>
<td>Armenia</td>
<td>no data available</td>
<td>no data available</td>
<td>no data available</td>
<td>no data available</td>
</tr>
<tr>
<td>Georgia</td>
<td>11.5%</td>
<td>General population</td>
<td>no data available</td>
<td>ICO/IARC Information Centre on HPV and Cancer</td>
</tr>
<tr>
<td>Azerbaijan</td>
<td>8.7%</td>
<td>General population</td>
<td>RT-PCR, AmpliSens</td>
<td>Gadzhieva, 2016</td>
</tr>
<tr>
<td>Uzbekistan</td>
<td>18.1%-19.4%</td>
<td>General population</td>
<td>RT-PCR, AmpliSens</td>
<td>Rackmanova, 2020</td>
</tr>
<tr>
<td>Kazakhstan</td>
<td>25%-55.8%</td>
<td>General population Gynecological patients</td>
<td>RT-PCR, AmpliSens</td>
<td>Bekmukhambetov et al, 2016 Balmagambetova et al, 2019 Junerbayeva et al., 2015 Niyazmetova et al., 2017</td>
</tr>
<tr>
<td>Kirgizstan</td>
<td>no data available</td>
<td>no data available</td>
<td>no data available</td>
<td>no data available</td>
</tr>
</tbody>
</table>
Comparison of the HPV oncogenic types among women with normal cytology and cervical cancer in RF, Belarus, Ukraine (Modified from ICO/IARC Information Centre on HPV and Cancer, 2019)

Normal cytology

- Russia: HPV-16 (7.7%), HPV-39 (4%), HPV-31 (1.8%)
- Belarusia: HPV-31 (1.9%), HPV-39 (0.6%)
- Ukraine: HPV-16 (7.1%)

Cervical cancer

- Russia: HPV-16 (64.6%), HPV-31 (3.8%)
- Belarusia: HPV-31 (65.4%)
- Ukraine: HPV-16 (92%)

Prevalence (%) for each HPV type is shown in the bar charts.
New cases cervical cancer (% from all cancers)

- Armenia: 2.7%
- Russian Federation: 3.3%
- Uzbekistan: 6.4%
- Kyrgyzstan: 9.2%
- Kazakhstan: 5.1%
- Ukraine: 3.4%
- Belarus: 2.3%
- Republic of Moldova: 4.2%
- Georgia: 3.2%

Modified The Global Cancer Observatory May, 2019
Epidemiology of cervical cancer in Central and Eastern Europa

Age-standardized incidence rates (World) in 2018, cervix uteri, females, all ages

1. Average number of cases:
- Belarus, Republic of Moldova, Russian Federation, Ukraine, females, all ages

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Epidemiology of cervical cancer in Western Asia

Estimated age-standardized incidence rates (World) in 2018, cervix uteri, females, all ages, Western Asia

- Georgia
- Armenia
- Azerbaijan
- United Arab Emirates
- Oman
- Lebanon
- Cyprus
- Israel
- Turkey
- Qatar

Average number of cases Armenia, Georgia, Azerbaijan, females, all ages

- Breast
- Colorectum
- Corpus uteri
- Stomach
- Cervix uteri

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1The Global Cancer Observatory - All Rights Reserved - May, 2019
2The Global Cancer Observatory - All Rights Reserved - May, 2019
Epidemiology of cervical cancer in South-Central Asia

**Estimated age-standardized incidence rates (World) in 2018, cervix uteri, females, all ages, South-Central Asia**

- Maldives
- Nepal
- Kyrgyzstan
- Kazakhstan
- India
- Bhutan
- Turkmenistan
- Bangladesh
- Uzbekistan
- Sri Lanka

**Average number of cases Uzbekistan, Kazakhstan, Kirgizstan, females, all ages**

- Breast
- Cervix uteri
- Colorectum
- Stomach
- Corpus uteri

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1. The Global Cancer Observatory - All Rights Reserved - May, 2019
2. The Global Cancer Observatory - All Rights Reserved - May, 2019
Cervical cancer incidence (2018)

ANNUAL NUMBER OF NEW CANCER CASES

- Russia: 18,164
- Belorussia: 979
- Ukraine: 5,733
- Georgia: 297
- Moldova: 639
- Armenia: 196
- Azerbaijan: 397
- Kazakhstan: 1,729
- Kirgizstan: 601
- Uzbekistan: 1,608
- Kazakhstan: 1,729
- Kirgizstan: 601

Crude incidence rate*

- Russia: 30.4%
- Belorussia: 24.2%
- Ukraine: 19.4%
- Georgia: 14.5%
- Moldova: 12.6%
- Armenia: 9.9%
- Azerbaijan: 8.0%
- Uzbekistan: 18.2%
- Kirgizstan: 19.4%

*Rates per 100,000 women per year

Modified The Global Cancer Observatory May, 2019.
Estimated number of prevalent cases (5-year) as a proportion in 2018, cervix uteri, all ages

Proportions per 100 000

- ≥ 62.2
- 45.8-62.2
- 32.7-45.8
- 22.0-32.7
- < 22.0

Not applicable
No data

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Data source: GLOBOCAN 2018
Graph production: IARC
(http://gco.iarc.fr/today)
World Health Organization
<table>
<thead>
<tr>
<th>Countries</th>
<th>*Prevalence HPV</th>
<th>**Rates cervical cancer per 100,000</th>
<th>Free HPV tests* **</th>
<th>free PAP-test * **</th>
<th>National HPV Immunization programme* **</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belorussia</td>
<td>30%</td>
<td>13.3/3.8 16,3/6,1</td>
<td>NO</td>
<td>Yes</td>
<td>NO</td>
<td>Globocan: Cancer incidence 2018 ICO/IARC HPV Information Centre 2019 Personal communication Mavrichev S.A. 2018</td>
</tr>
<tr>
<td>Ukraine</td>
<td>40% (n=10 000)</td>
<td>17.0/6.6 14.7/5.1</td>
<td>NO</td>
<td>Yes</td>
<td>NO</td>
<td>ICO/IARC HPV Information Centre 2019 Kolesnik O.O.2018 Bulletin of the national stationery-register of Ukraine no. 21 2020 Personal communication T Tatarchuk</td>
</tr>
<tr>
<td>Moldova</td>
<td>43.2%</td>
<td>21.4/7.9 16.2 \ 8.4</td>
<td>NO</td>
<td>Yes</td>
<td>NO Partial program</td>
<td>ICO/IARC HPV Information Centre 2019 Andrzej Jarynowski 2019 do: <a href="https://doi.org/10.1101/19009886">https://doi.org/10.1101/19009886</a> Personal communication Vetrichyan Nadezhda 2018 Ulyana Tabulka 2018</td>
</tr>
<tr>
<td>Armenia</td>
<td>30%</td>
<td>8.4/5.6</td>
<td>NO</td>
<td>Yes</td>
<td>NO</td>
<td>ICO/IARC HPV Information Centre 2019 Kujoyan L. S. 2019 <a href="http://www.nih.am">www.nih.am</a> 2019 Personal communication L Kujoyan</td>
</tr>
<tr>
<td>Georgia</td>
<td>9.8/5.5</td>
<td></td>
<td>NO</td>
<td>Yes</td>
<td>NO</td>
<td>ICO/IARC HPV Information Centre 2019 Personal communication SH Aliyev</td>
</tr>
<tr>
<td>Azerbaijan</td>
<td>8,7% (n=206)</td>
<td>6,5/4.6 9,3</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>ICO/IARC HPV Information Centre 2019 Personal communication SH Aliyev</td>
</tr>
<tr>
<td>Uzbekistan</td>
<td>18,1% (n=6431)</td>
<td>9.9/5.4</td>
<td>NO</td>
<td>Yes</td>
<td>2019</td>
<td>ICO/IARC HPV Information Centre 2019 According to the statistics of the Ministry of the Republic of Uzbekistan 2018 <a href="https://www.who.int/countries/uzb/en/">https://www.who.int/countries/uzb/en/</a> Rakhmanova, J. A. 2020</td>
</tr>
<tr>
<td>Kazakhstan</td>
<td>28.3</td>
<td>15.7/7.5 18.1</td>
<td>yes</td>
<td>Yes</td>
<td>NO/Partial program 2013 Planning in 2021</td>
<td>Personal communication Lokshin V.N. 2019 Gulzhanat Aimagambetova 2018</td>
</tr>
<tr>
<td>Kirgizstan</td>
<td>NO</td>
<td>19.9/10.9</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>ICO/IARC HPV Information Centre 2019</td>
</tr>
<tr>
<td>Russia</td>
<td>25</td>
<td>15.08/5.07</td>
<td>NO/Partial program</td>
<td>Yes</td>
<td>NO/Partial program 2013</td>
<td>Каприн А.Д., Старынкин В.В., 2018 RAGIN, 2020 <a href="https://www.hse.ie/eng/health/immunisation/infomaterials/leaflettranslations/russianhpv.pdf">https://www.hse.ie/eng/health/immunisation/infomaterials/leaflettranslations/russianhpv.pdf</a></td>
</tr>
<tr>
<td>Country</td>
<td>Screening age</td>
<td>Screening interval</td>
<td>Screening methods</td>
<td>Screening system</td>
<td>Registries</td>
<td>Coverage</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>-------------------------------------------------------------</td>
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<td>-------------------------------------------------------</td>
<td>--------------------------------------------------------</td>
<td>----------------------------------------------------------------------------</td>
<td>-------------</td>
</tr>
<tr>
<td>Russian Federation</td>
<td>First intercourse or 18 years– No upper</td>
<td>Annually</td>
<td>Pap test with basic Romanowsky or H&amp;E staining</td>
<td>Opportunistic; call-recall in few</td>
<td>National Cancer Registry, national and regional population registry</td>
<td>20–25%</td>
</tr>
<tr>
<td>Moscow</td>
<td>age limit 35–69 years</td>
<td>Every 3 years</td>
<td>Pap test with basic Romanowsky or MGG staining</td>
<td>regions on irregular basis Opportunistic screening program;</td>
<td>Moscow Cancer Registry, population registry</td>
<td>40–90%</td>
</tr>
<tr>
<td>Belarus</td>
<td>18 years– No upper age limit</td>
<td>Annually</td>
<td>Pap test</td>
<td>call-recall in few regions on irregular basis</td>
<td>National Cancer Registry, population registry</td>
<td>75–80%</td>
</tr>
<tr>
<td>Republic of Moldova</td>
<td>20 years– No upper age limit</td>
<td>Every 2 years</td>
<td>Pap test</td>
<td>Opportunistic; no call-recall system</td>
<td>National population registry</td>
<td>Not available</td>
</tr>
<tr>
<td>Ukraine</td>
<td>18–65 years</td>
<td>Annually</td>
<td>Smear test with basic Romanowsky and Papanicolaou staining</td>
<td>Opportunistic; no call-recall system</td>
<td>National Cancer Registry, national population registry; registration in a computerized system in two regions</td>
<td>20–30%</td>
</tr>
</tbody>
</table>

Rogovskaya et al, 2013
Cervical cancer screening activities in RF and former SU (HPVcenter 2019)

<table>
<thead>
<tr>
<th>Country</th>
<th>Screening age</th>
<th>Screening interval</th>
<th>Screening methods</th>
<th>Screening system</th>
<th>Registries</th>
<th>Coverage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Armenia</td>
<td>30–60 years</td>
<td>Every 3 years</td>
<td>Pap test</td>
<td>Opportunistic, management by local, regional and national health authorities, no call-recall system</td>
<td>Pap smear results centrally recorded in a national database</td>
<td>10–20%</td>
</tr>
<tr>
<td>Azerbaijan</td>
<td>Not available</td>
<td>Not available</td>
<td>Pap test</td>
<td>Opportunistic screening</td>
<td>Not available</td>
<td>Not available</td>
</tr>
<tr>
<td>Georgia</td>
<td>25–60 years</td>
<td>Every 3 years</td>
<td>Pap test</td>
<td>Opportunistic with some elements of call-recall system</td>
<td>Not available</td>
<td>20%</td>
</tr>
<tr>
<td>Kazakhstan</td>
<td>30–60 years</td>
<td>Every 5 years</td>
<td>Conventional</td>
<td>Call-recall system in few regions on unregular basis</td>
<td>National Cancer</td>
<td>75%</td>
</tr>
<tr>
<td>Uzbekistan</td>
<td>20 years - No upper age limit</td>
<td>Not available</td>
<td>Pap test</td>
<td>Organized cervical cancer screening in four pilot regions (dated 2011)</td>
<td>Not available</td>
<td>Not available</td>
</tr>
<tr>
<td>Kyrgyzstan</td>
<td>Not available</td>
<td>Every 5 years</td>
<td>Pap test and HPV test</td>
<td>Not available</td>
<td>Not available</td>
<td>Not available</td>
</tr>
</tbody>
</table>

Rogovskaya et al, 2013
HPV and related diseases trends in countries

- The incidence of cervical cancer trend - no tendency to decline
- Genital wart trend - no tendency to decline
- Cervical cancer - rejuvenation of pathology
- High proportion of advanced cervical cancer
- High mortality rate
- Screening is generally available with Pap
- Treatment mainly is not available for free

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Conclusion

- Organized cervical cancer screening and National programmes are needed
- In our opinion, the basis of organized screening currently, due to its economic feasibility, should be the traditional PAP test, trend – to LBC with automated staining of smears.
- Integration of HPV tests into screening on the basis of domestic economical technologies, as an addition to the already formed system of organized screening. No validity
- Epidemic studies are needed using validated tests with genotyping and a clear distribution of populations
- Implementing e-registry for HPV associated diseases cases and HPV carrying into state system of diseases
- Implementing info about HPV and its prevention into educational programs for medical staff and population.
- RAGIN project for education is ongoing

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Thank you for attention!