



Državni program zgodnjega odkrivanja
predrakavih sprememb
materničnega vratu

National programme ZORA

The NP ZORA was implemented in 2003 with conventional cytology in three-year screening intervals in the 20–64 age group. The three-year coverage of the target population with a screening test is just above 70%, and its five-year coverage is just above 80%. Higher coverage is observed in younger women and reaches 80% in the 20–24 age group. It drops below 70% in women above 50 and is just below 55% in the oldest age group of women aged from 60 to 64. Coverage also varies between administrative units. Slovenia is among the European countries with the highest historical cervical cancer incidence rates but is also among the countries with the most pronounced decline in cervical cancer incidence rates over time. The steepest decline was observed after the implementation of the NP ZORA, in 2003–2015, with the annual percentage change being –5.8. Non-attenders in the NP ZORA account for 50–60% of new cervical cancer cases, among which more than 80% are diagnosed at FIGO stage II or higher, compared to regular attenders where only 20% of cancers are diagnosed at stage II or higher.

Responsible institution: Institute of Oncology Ljubljana

Website of the programme: <http://zora.onko-i.si> (in Slovene language only)

Screening examination

- Cervical smear for conventional cytological examination (Pap test)
- Results are classified according the Bethesda 2001 system

Screening interval

- Three years, after two consecutive smears in one year are negative

Target group of population

- Female residents of the Republic of Slovenia aged from 20 to 64 years
- Women older than 64 may attend screening, but they are no longer invited
- Women are not eligible for screening if they had cervical cancer diagnosed at any time in the past; are currently treated for cervical pathology or are in the process of follow-up after treatment or if they had hysterectomy with cervix removed in the past

Programme providers

- Personal gynaecologists teams at the primary level (screening and management of women with low-grade lesions of cervix)
- Gynaecological teams on secondary and tertiary levels for diagnostics and treatment of high grade cervical lesions and cervical cancer
- Laboratories (cytopathology, histopathology laboratories, HPV)
- Regional offices of the National Institute of Public Health for cancer screening promotion
- ZORA programme and registry department at the Institute of Oncology Ljubljana.

Invitation method

- With free access to their personal gynaecologist (PG), women do not need a special invitation to schedule a screening appointment. If a woman fails to make an appointment on time, her PG should invite her to make one, according to the rules on carrying out preventive healthcare at the primary healthcare level. In case she does not respond, the PG should send her another invitation. The ZORA registry serves as a final supervisor of screening attendance. Where a woman has not had cytology result registered for four years, she receives a status of non-attender and is as such eligible for central invitation, which is sent to her in the fifth year by the Institute of Oncology Ljubljana.
- The central invitation package includes an invitation letter, an informational leaflet about the ZORA programme and detailed information about gynaecologists working in the region of the woman's place of residence. Women are encouraged to call their PG to make a screening appointment. Women who do not have a PG are encouraged to call one of the gynaecologists from the national list. If a cytology result is not registered after the first central invitation, a second central invitation is sent one to two years after the first one. If the woman fails to respond, she receives the status of "final non-attender" and is not invited by the central coordination office again until a new cytology result is registered. However, GPs should still send regular invitations to such women.

Management of women with cervical pathology

- Women with pathological screening results or with histologically confirmed cervical lesions are managed according to national guidelines for the management of women with precancerous lesions and cervical cancer
- Women with atypical squamous cells of undetermined significance (ASC-US) or low grade squamous intraepithelial lesion (LSIL) are invited back to their PG after six months for a triage HPV test and repeat cytology. In women with LSIL younger than 35 years, only repeat cytology is performed
- Women with other pathological screening results are referred to colposcopy. Following treatment of precancerous lesion, a control follow-up cytology is recommended six months later and both HPV testing and a repeat cytology 12 months after treatment. If both tests are negative, the woman is invited back 24 months after treatment for another HPV test and cytology. If both tests are again negative, women can return to a three-year screening interval. All PGs in Slovenia are involved in screening.
- Screening and diagnostic samples are evaluated by certified laboratories (nine for cytology, nine for pathology and two for HPV testing).

Quality assurance and control

- Legal framework supports the central screening registry and quality assurance and control schemes
- Standardised and personalised screening invitation letters and reminders, information booklets for women in Slovenian, Italian and Hungarian language
- Professional guidelines for providers of screening (gynaecology, cytopathology, histopathology)
- Standardised laboratory reports
- Guidelines for management of women with cervical pathology and cervical cancer
- Fail-safe mechanism: notification of gynaecologists about missed follow-up exams after pathological smears by the screening registry
- Regular specialised training of experts involved in screening programme;
- Regular revision of pap smears and (planned) revision of histology of women diagnosed with cervical cancer
- Annual feedback to providers (gynaecologists and laboratories) about their results and quality of work
- High quality screening registry: regular monitoring of data quality, inquiries for missing or incorrect data

Information system of the programme

- Centralised national screening registry ZORA at the Institute of Oncology Ljubljana
- All providers have legal obligation to send standardised data to the screening registry
- Registry is linked to Central population register and Spatial unit register (nightly synchronisation), Cancer Registry of the Republic of Slovenia, in the near future also to the Electronic registry of vaccinated persons and Health insurance institute of Republic of Slovenia and national eHealth platform
- Registry records personal data of women, personalised data about screenings and diagnostic examinations and treatment; data on central invitations to screenings and responses of women to these invitations
- The information system is currently in the process of renewal

Key indicators of the ZORA national programme

Screening results

- According to the data from the screening registry, 154.747 women in the target age group (20–64 years) had a screening smear in 2017.
- According to the Bethesda classification 99,9 % of all screening smears were satisfactory for the evaluation
- Majority of the smears were negative for intraepithelial lesion or malignancy (90,4% normal results and 4,5% non-neoplastic findings), these women did not need further diagnostics and were returned to the regular screening
- Epithelial cells abnormalities were found in 4,9% of the screening smears, these women were invited to further diagnostic evaluation
- There was 9.340 either diagnostic or therapeutic procedures registered in the screening registry in 2017, but since pathological reports from this year are still in the process of collection and registration, this number is not yet final

Coverage

- One of the most important conditions to be fulfilled for the effective operation of screening programmes is a good coverage of the target population by the screening test (coverage). Coverage represents a proportion of women with at least one smear among all the women in the target population (residents of Republic of Slovenia aged 20-64 years). The targeted three-year coverage is 70 %.
- A three-year coverage of the target population has been monitored in ZORA since the beginning of the programme in 2003. In the last three-year period (July 1st 2014 – June 30th 2017), coverage has again exceeded 70%.
- Coverage is above 70 % in women aged 20 to 49, where the number of newly diagnosed cervical cancer is high; nevertheless, the coverage is still below 70 % in older women (50 to 64 years old) (**Figure 1**).
- The coverage is above 70% in all health regions of Slovenia except in Koper, Maribor, Novo Mesto and Murska Sobota (**Figure 2**).
- If we compare Slovenian results with countries with well organised screening programmes from abroad which have a five-year screening interval, such as Finland and the United Kingdom, the five-year coverage in Slovenia is above 80%, which places Slovenia among the countries with the highest coverage in Europe.

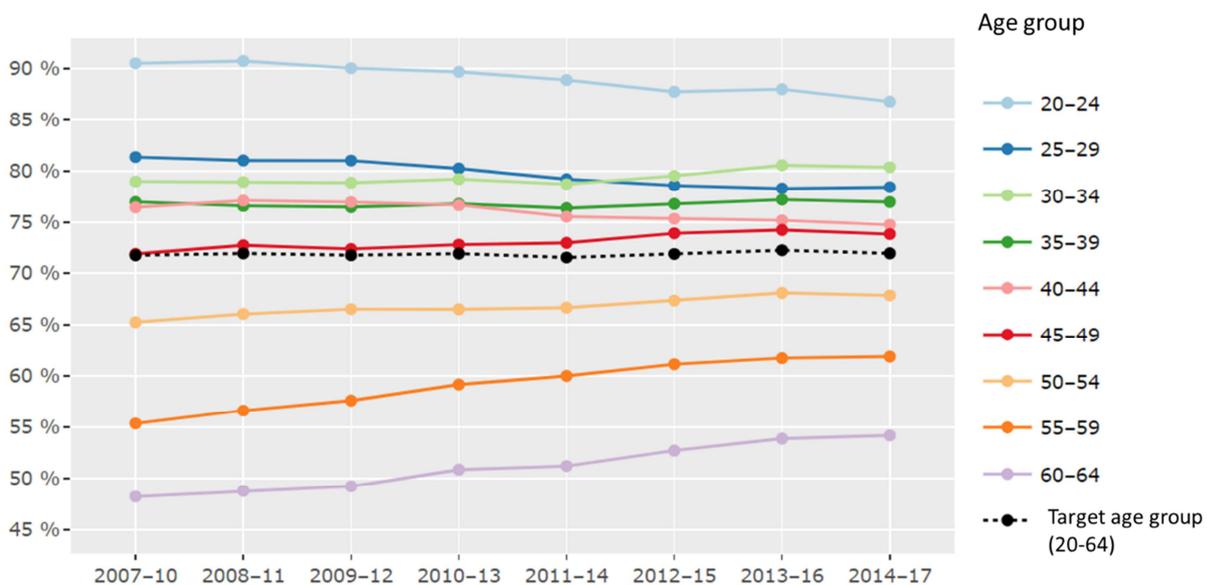


Figure 1: Three-year coverage of the target population by smear within cervical cancer screening programme ZORA, by five-year age groups, last eight three-year periods. Source: Screening registry ZORA. Available at: <https://zora.onko-i.si/publikacije/kazalniki/>

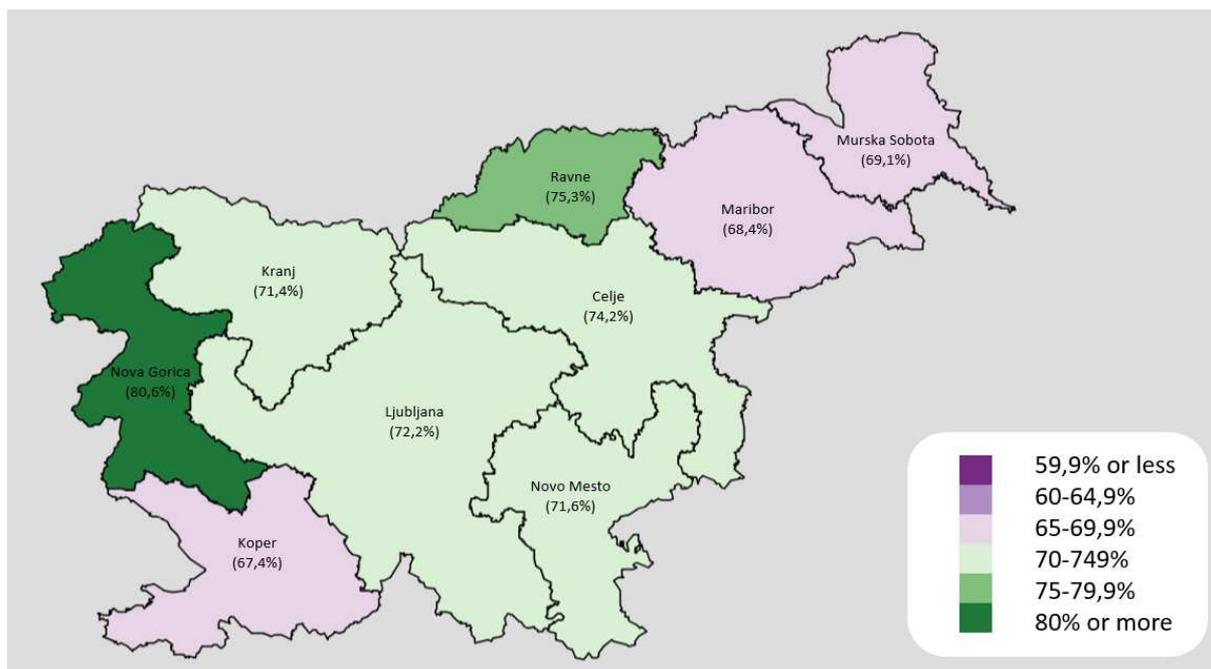
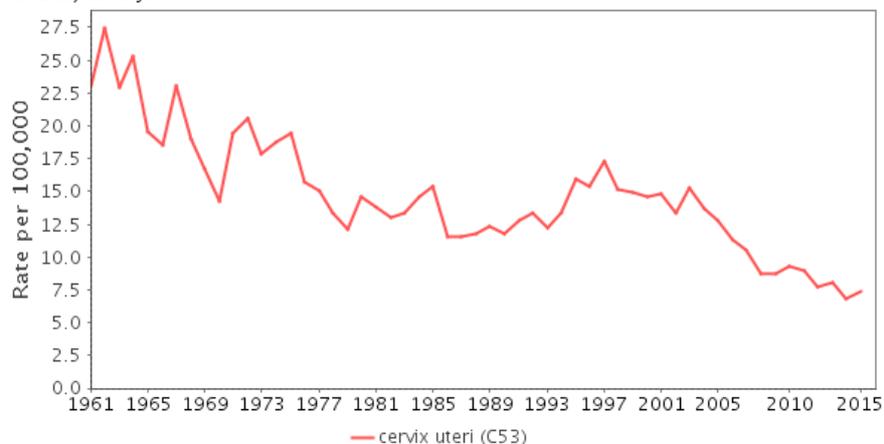


Figure 2: Three-year coverage of the target population by smear within NP ZORA, by health regions, last five three-year periods. Source: Screening registry ZORA. Available at: <https://zora.onko-i.si/publikacije/kazalniki/>

Main results and achievements

- Slovenia is among the European countries with the highest historical cervical cancer incidence rates but is also among the countries with the most pronounced decrease in cervical cancer incidence rates over time. The steepest decrease was observed after the implementation of the NP ZORA, in 2003–2015, with the annual percentage change being -5.8 .
- The most important achievement of the ZORA programme is undoubtedly the desired decrease in cervical cancer incidence; from the introduction of the programme in 2003 to present the incidence fell by almost 50% (**Figure 3**). Praise goes to the gynaecological teams who regularly invite women to their screening exams, which certainly contributes to a good coverage which is one of the key factors for the success.
- Non-attenders in the NP ZORA account for 50–60% of new cervical cancer cases, among which more than 80% are diagnosed at FIGO stage II or higher, compared to regular attenders where only 20% of cancers are diagnosed at stage II or higher.
- Slovenia has already conducted a large-scale randomised trial of HPV self-sampling among non-responders and will decide in the next few years if self-sampling for non-responders will be implemented into the renewed cervical cancer screening programme.

Age standardized
incidence rate (world standard)
cervix uteri (C53)
world standard, female
1961–2015, Slovenija



Institute of Oncology Ljubljana, Cancer Registry of Slovenia, 25.11.2018

Figure 3: Cervical cancer incidence, crude and age standardised (world standard) rates, Slovenia 2003–2016. Source: Cancer registry of Republic of Slovenia. Available at: <http://www.slora.si/en/>

Future challenges

- *Renewal of the Programme guidelines for the quality assurance and quality control in the national cervical cancer screening programme ZORA (2019)*

Comprehensive programme guidelines will be revisited and published by the screening program in collaboration with broad panel of experts that will cover the field of cervical gynaecology, gynaecology cytopathology and pathology and HPV diagnostics – for screening, diagnostics, treatment and follow up.

- *The project of the renewal of the cervical cancer screening information system (2018—2020):*

Organised, population based screening programmes are entering the era where innovative technology solutions and new evidence from research are accumulating rapidly. This may change the traditional role of cancer screening registries from being used as an additional system within the screening programmes that allows for monitoring and evaluation of the programme, to the central communication and decision supporting tool between the professionals involved in screening, diagnostic, follow-up and treatment of women. Such active system also enables real-time monitoring and evaluation of the programme. The concept of upgraded central cervical cancer screening information system was developed with the objective that this information will be available to the professionals involved in screening and management of the women, together with the guidance tool for the clinical decisions based on current screening and management guidelines of Slovenian cervical cancer screening programme ZORA.

- *The project of the renewal of the screening policy (2020—2021) – toward cervical cancer elimination:*

In April 2018 World Health Organisation made a global call for action towards the elimination of cervical cancer with HPV vaccination, early detection and effective management of cervical lesions. In

Slovenia, school-based HPV vaccination of 12 year-old girls in the 6th grade of primary school was implemented in year 2009 and is coordinated by the National institute of public health. Vaccination coverage is around 50 %. The future challenges that Slovenia has to face in the way to cervical cancer elimination are the increase in HPV vaccination rates and renewal of cervical cancer screening programme. Decision and an action plan will be prepared regarding the implementation of HPV-screening for women of certain age and for vaccinated women, HPV self-sampling for non-responders, liquid-based cytology and triage of screen-positive women.