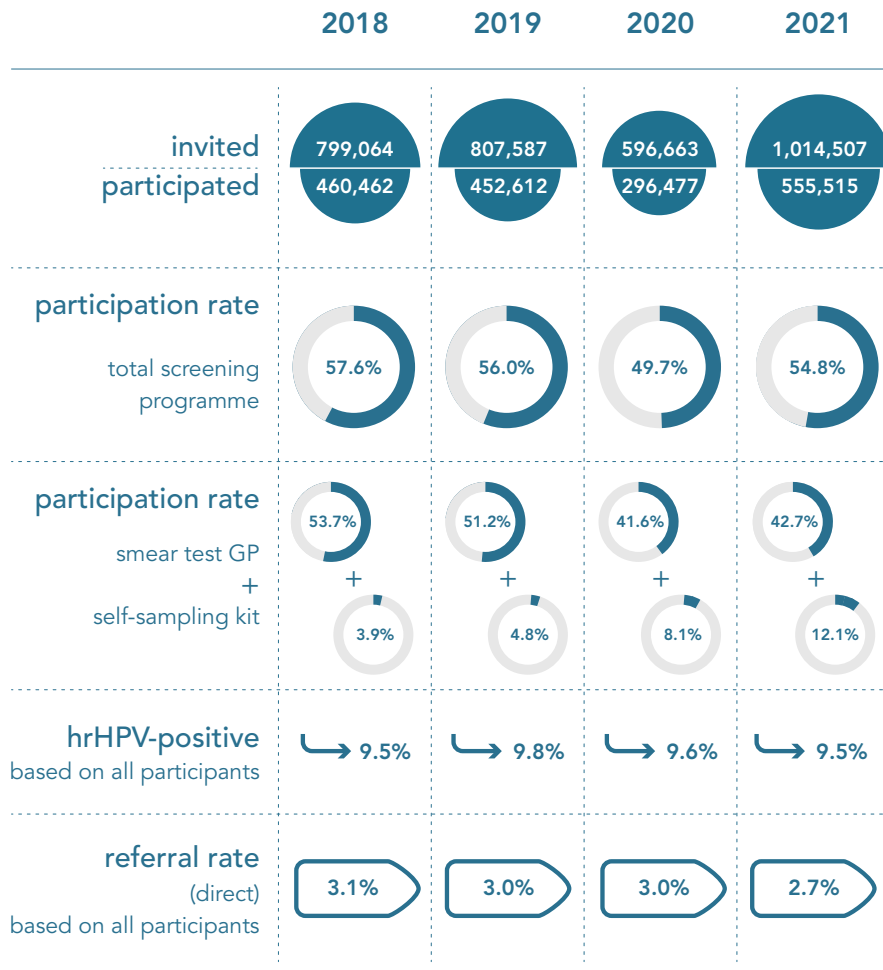
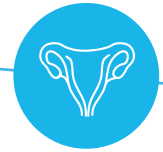


national monitoring of the cervical cancer screening programme in the Netherlands 2021



Reference date of the participation rate, hrHPV-positivity and referral rate is 15 months after the year started.

COVID-19 pandemic

In 2020, due to the COVID-19 pandemic the screening programme was put on hold from 16 March until 1 July. From 1 July onwards the screening programme was slowly restarted. In the fall the invitation rate was upscaled to 120% and the SSK option for participation was emphasized in the invitation letter. In 2021, besides the normal invitations all the delayed invitations were sent to catch up on the backlog.

most important results 2021

In 2021, about 200,000 extra invitations were sent to catch up on the backlog which has arisen during the temporary shutdown of the screening programme due to the COVID-19 pandemic. In total, 555,515 persons participated at the national screening programme.

The participation rate in 2021 was 54.8%; 42.7% participated by a smear test at the general practitioner (GP) and 12.1% participated by a self-sampling kit (SSK). Of all participants 22.1% used a SSK, which is an increase compared to last year (16.3%).

In total, 9.5% of the participants had a high risk Human Papilloma Virus (hrHPV).

The direct referral rate in 2021 was 2.7% based on the total number of participants and 29.2% based on all hrHPV-positive participants with cytology results. This corresponds with 14,973 participants who were directly referred to a gynaecologist.

Finally, 1.1% of all participants had a (pre)cancerous lesion of cervical cancer (CIN2+), which corresponds with 6,246 participants.

introduction

By using the National Cervical Cancer Screening Programme, cervical cancer can be prevented by detecting and treating pre-cancerous lesions. In addition, sometimes early staged cervical cancer is detected which gives a better prognosis. The Dutch National Cervical Cancer Screening Programme is coordinated by the National Institute for Public Health and the Environment (RIVM). The RIVM has commissioned Netherlands Comprehensive Cancer Organization (IKNL) to carry out the annual monitoring of the national

cervical cancer screening programme. Monitoring helps to ensure the quality of the screening programme and identifies trends. Monitoring is conducted using data from Bevolkingsonderzoek Nederland (BVO NL) and the nationwide network and registry of histo- and cytopathology in the Netherlands (PALGA). Furthermore, incidence data is collected from the Netherlands Cancer Registry (NKR). In this monitor the results of persons invited in 2021 are presented.

collaboration

The screening programme cervical cancer is carried out in collaboration with the following parties:



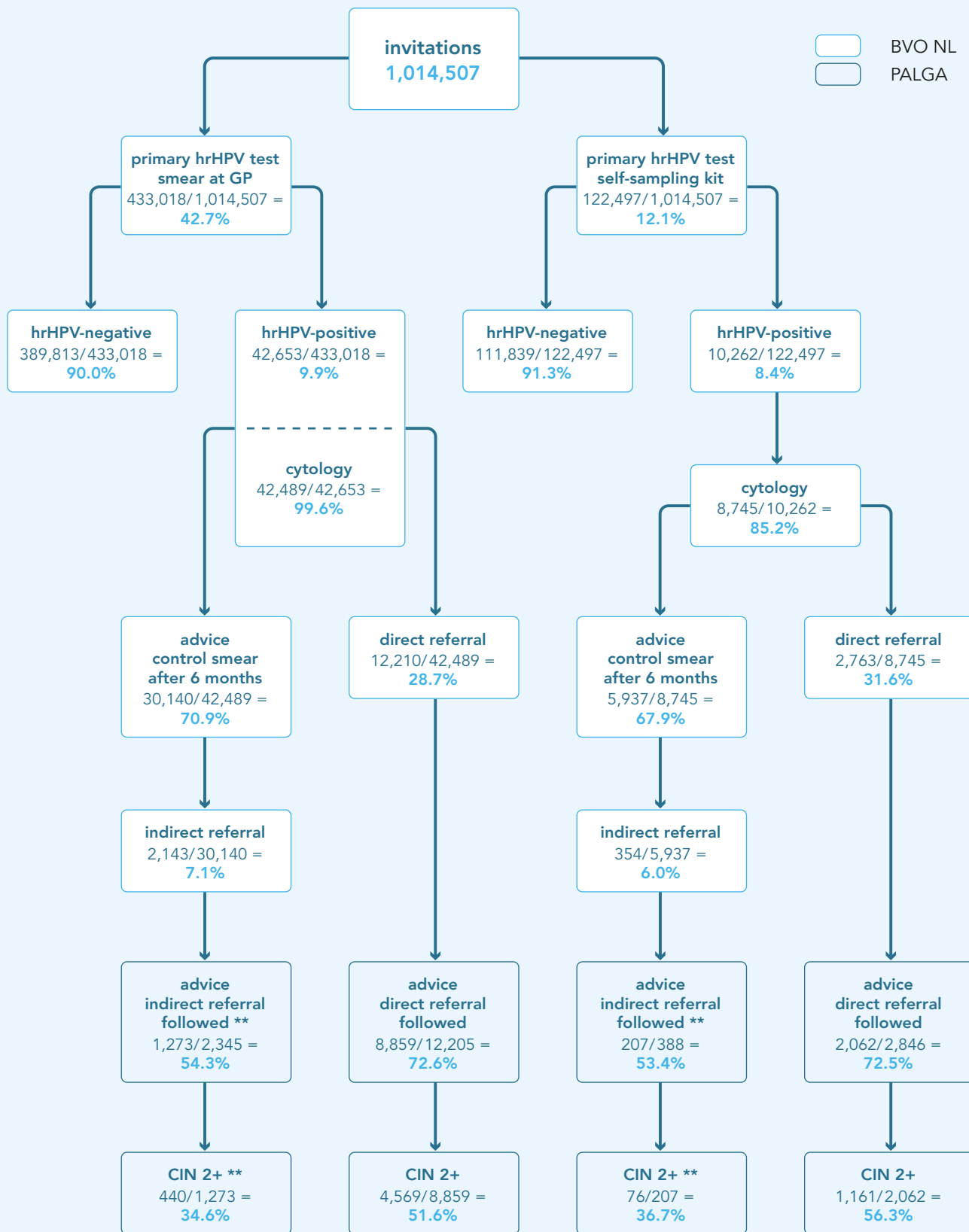
terminology

- **control smear** = smear which is performed after 6 months in hrHPV positive participants without cytological abnormalities in the primary test
- **coverage** = percentage of persons within the range of the screening age group that took at least one cervical smear or hrHPV test in the five years before the reference date
- **cytological assessment** = examination of cells taken from cervical smear
- **detection rate** = percentage of participants in whom CIN2, 3 or a malignancy is detected
- **histological assessment** = examination of tissue obtained from colposcopic biopsy
- **initial target population** = persons that are based upon their year of birth eligible for the national screening programme
- **participation rate** = percentage of participants that in response to an invitation participated in the national screening programme. The reference date is always 1 April of the next year
- **poor quality smear** = specimen that

- cannot be assessed
- **primary test** = hrHPV test and, when a hrHPV positive result, cytological assessment, after being invited for the screening programme. A hrHPV test can be taken by having a smear done by a GP or by using the self-sampling kit
- **referral rate** = percentage of participants that are referred to the gynaecologist. Participants can be referred after the primary test (**direct**) or after the control smear (**indirect**)
- **positive predictive value (PPV)** = participants who are referred to the gynaecologist and where CIN 2+ was detected histologically
- **repeat smear test** = smear is repeated due to poor quality
- **return to screening** = no further follow up is needed. Participant can await the next screening invitation
- **screening programme** = national cervical cancer screening programme
- **SSK** = self-sampling kit

flowchart

total screening process in 2021* (source: BVO NL and PALGA)



* When subdividing the test results, the sum of the numbers of tests is not equal to the total number of tests as some results could not be assessed.

** Numbers of indirect referral are preliminary because not all participants have had an invitation for the control smear at the reference date.

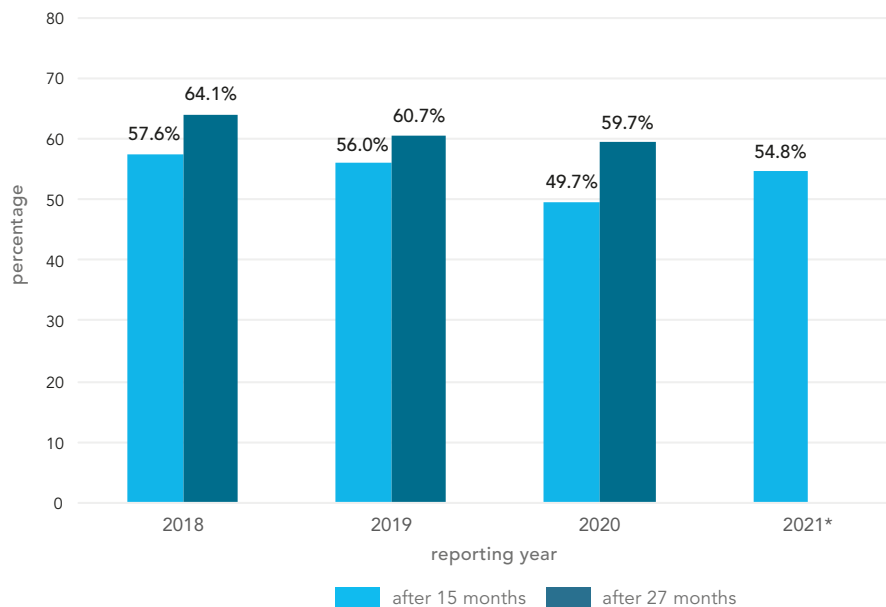
table 1 invitation and participation rate

by year, reference date 1 April of the next year (source: BVO NL)

	2018	2019	2020	2021
invitations sent	799,064	807,587	596,663	1,014,507
participation rate primary test	460,462	452,612	296,477	555,515

figure 1 participation rate

by year, reference date 1 April of the next year (15 months) and 1 year later (27 months) (source: BVO NL)



* For 2021 the participation rate after 27 months is not yet known.

A full screening round lasts 5 years (60 months). For 2017 the participation rate is now 66.1%. For comparison: for 2017

the participation rate was 57.0% after 15 months and it was 63.9% after 27 months.

explanation for participation rate

The participation rate is calculated by dividing the total number of participants by the total number of invited persons. The reference date for the participation rate is always 1 April of the next year (15 months after the start of the reporting year) and also 1 April of the subsequent year (27 months after the start of the reporting year).

In 2020 the screening programme was put on hold on 16 March due to the COVID-19 pandemic and therefore from cohort 2019 as well as cohort 2020 some participants participated outside the reference period. On 1 July 2020, the screening programme restarted slowly and therefore the number of sent invitations is higher than usual.

table 2 participation rate primary test total

by age and year, reported on 1 April of the next year (15 months) and 1 year later (27 months), based on total number of invited persons (source: BVO NL)

	2018	2018	2019	2019	2020	2020	2021*
reference period (months)	15	27	15	27	15	27	15
age							
30 - 34 years	46%	58%	44%	53%	39%	53%	44%
35 - 39 years	51%	60%	50%	57%	44%	56%	49%
40 - 44 years	58%	65%	56%	61%	49%	60%	55%
45 - 49 years	61%	66%	59%	63%	52%	62%	57%
50 - 54 years	62%	67%	61%	64%	54%	63%	59%
55 - 59 years	63%	66%	61%	63%	56%	63%	61%
60 - 64 years	62%	65%	61%	63%	54%	61%	60%
total	58%	64%	56%	61%	50%	60%	55%

* For 2021 the participation rate after 27 months is not yet known.

figure 2a participation rate primary test total

by age and year, reported on 1 April of the next year (15 months), based on total number of invited persons (source: BVO NL)

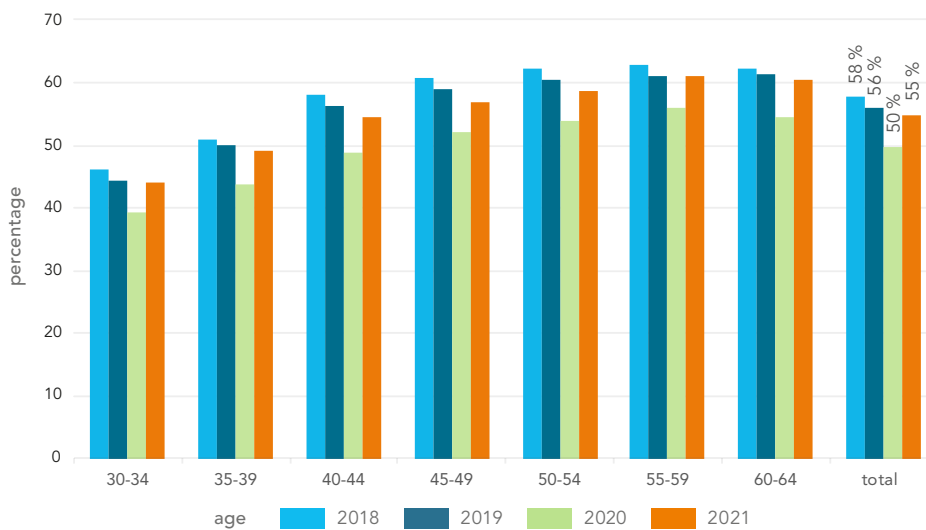


figure 2b participation rate primary test smear by age and year, reported on 1 April of the next year (15 months), based on total number of invited persons (source: BVO NL)

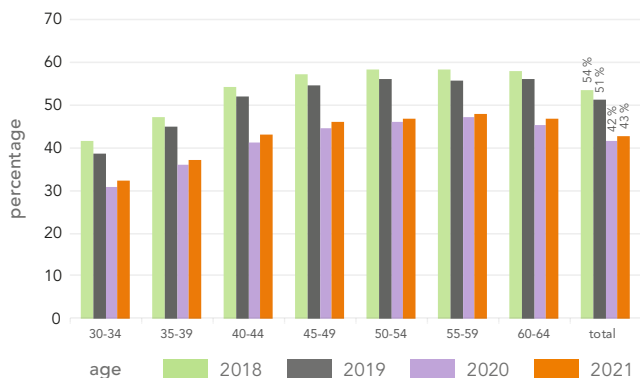
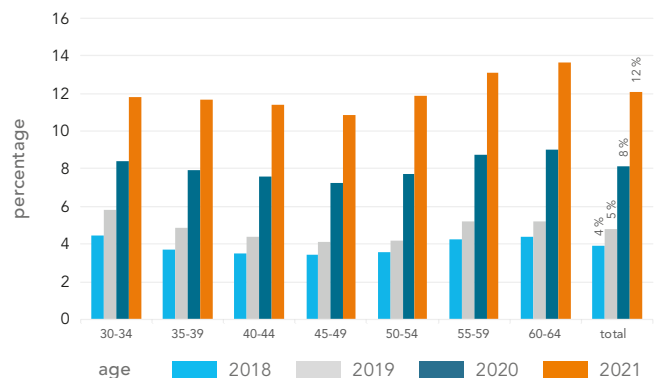


figure 2c participation rate primary test SSK by age and year, reported on 1 April of the next year (15 months), based on total number of invited persons (source: BVO NL)



- In 2021, 54.8% of the invited persons participated in the screening programme, compared to 49.7% in 2020 with the same reference period. For 2020, after 27 months this increased to 59.7%.
- The percentage of participants who underwent a smear test by their GP was 42.7% in 2021 compared to 41.6% in 2020. For using the SSK this was 12.1% and 8.1% respectively.

- The total participation rate was lower among young participants than among older participants. After 27 months the highest increase was seen in the younger age groups.
- Use of the SSK was highest among the oldest participants and after that in the youngest age groups. In 2021, this was higher in all age groups compared to earlier years.

table 3 participation rate smear after hrHPV-positive self-sampling kit by age and year (source: BVO NL) *

	2018	2019	2020	2020	2021
reference period (months)	51	39	27	15	15
age					
30 - 34 years	93%	92%	93%	80%	87%
35 - 39 years	89%	90%	93%	80%	85%
40 - 44 years	91%	87%	92%	79%	85%
45 - 49 years	90%	87%	92%	76%	86%
50 - 54 years	87%	91%	91%	80%	86%
55 - 59 years	87%	85%	92%	76%	85%
60 - 64 years	87%	86%	93%	80%	85%
total	90%	89%	92%	79%	86%

table 4 participation rate after invitation for a control smear after 6 months by age and year (source: BVO NL) *

	2018	2019	2020	2020	2021
reference period (months)	51	39	27	15	15
age					
30 - 34 years	77%	74%	77%	55%	60%
35 - 39 years	79%	76%	78%	54%	61%
40 - 44 years	85%	81%	85%	60%	66%
45 - 49 years	87%	83%	86%	59%	69%
50 - 54 years	88%	84%	88%	60%	69%
55 - 59 years	90%	87%	89%	65%	73%
60 - 64 years	91%	87%	90%	66%	75%
total	84%	80%	83%	59%	66%

* Reference date for all results is 1 April 2022. Therefore, the reference period for 2020, for example, is 12 months longer than for 2021 (27 months and 15 months, respectively), which makes the years incomparable. For that reason an extra column of 2020 with a reference period of 15 months is added for comparison. The numbers of the reference period of 15 months are preliminary and printed in italic.

- The participation rate for taking a cervical smear after a hrHPV-positive SSK was 86% in 2021 (preliminary result). In 2020 with a 15 months reference period this was 79% which increased to 92% at 27 months.
- The participation rate for control smears (after hrHPV-

- positive + Pap 1) was 66% in 2021 (preliminary result). In 2020 with a 15 months reference period this was 59%, which increased to 83% at 27 months.
- The participation rate for control smears increased with higher age.

figure 3a hrHPV-positive participants for cervical smear by age and year (source: BVO NL)

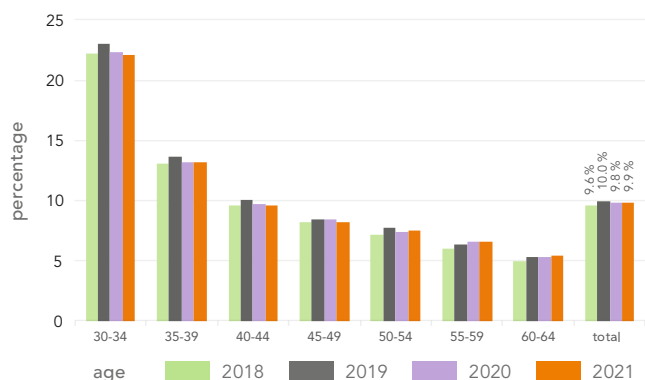
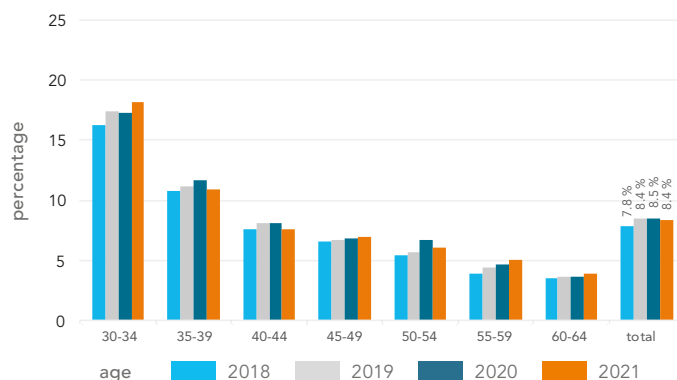


figure 3b hrHPV-positive participants for SSK by age and year (source: BVO NL)



- In 2021, hrHPV was found in 9.5% of all participants. Most hrHPV positive results were found in young participants.
- In 2021 9.9% of participants who underwent a smear test were hrHPV positive, compared to 9.8% in 2020. For the SSK this was 8.4% compared to 8.5% in 2020.
- For participants that used the SSK the percentage of hrHPV positivity was lower (8.4%) than for participants who underwent a smear test (9.9%). This was also observed in earlier years.

table 5a cytology primary test total

by year (source: BVO NL)

	2018	2019	2020	2021
normal smear (Pap 1)	67.3%	68.8%	67.9%	70.4%
ASC-US (Pap 2)	12.8%	13.2%	12.6%	11.0%
LSIL (Pap 3A1)	8.8%	8.6%	8.9%	8.0%
HSIL (Pap 3A2 - Pap 4)	10.9%	9.2%	10.3%	10.2%
invasive carcinoma (Pap 5)	0.03%	0.02%	0.01%	0.03%
indication for referral to gynaecologist (ASC-US-invasive carcinoma)	31.8%	31.0%	31.9%	29.2%

table 5b cytology primary test cervical smear

by year (source: BVO NL)

	2018	2019	2020	2021
normal smear (Pap 1)	67.4%	69.0%	68.2%	70.9%
ASC-US (Pap 2)	12.9%	13.2%	12.9%	11.1%
LSIL (Pap 3A1)	8.8%	8.6%	8.8%	7.9%
HSIL (Pap 3A2 - Pap 4)	10.7%	8.9%	9.9%	9.7%
invasive carcinoma (Pap 5)	0.02%	0.02%	0.01%	0.02%
indication for referral to gynaecologist (ASC-US-invasive carcinoma)	32.4%	30.8%	31.6%	28.7%

table 5c cytology primary test SSK

by year (source: BVO NL)

	2018	2019	2020	2021
normal smear (Pap 1)	65.8%	65.0%	66.1%	67.9%
ASC-US (Pap 2)	11.7%	12.5%	10.8%	10.6%
LSIL (Pap 3A1)	8.3%	8.9%	9.6%	8.3%
HSIL (Pap 3A2 - Pap 4)	13.7%	13.3%	13.2%	12.6%
invasive carcinoma (Pap 5)	0.14%	0.03%	0.03%	0.05%
indication for referral to gynaecologist (ASC-US-invasive carcinoma)	33.8%	34.7%	33.6%	31.6%

- In 2021, 29.2% of the hrHPV-positive participants were directly referred to a gynaecologist (ASC-US – invasive carcinoma), which were 14,973 persons. In 2020 this was 31.9%.
- Participants that used the SSK and were hrHPV-positive seem to have a higher HSIL result than participants who underwent a cervical smear at the GP. This was also observed in earlier years.

table 6 advices based on primary test

by year (source: BVO NL) *

	2018	2019	2020	2020	2021
reference period (months)	51	39	27	15	15
direct referral	3.1%	3.0%	3.0%	2.9%	2.7%
repeat smear due to smear material that cannot be assessed (Pap 0) or hrHPV could not be determined (no follow up)	0.23%	0.31%	0.27%	0.26%	0.29%
control smear after 6 months	6.3%	6.7%	6.5%	6.2%	6.5%
return to screening programme	90.5%	90.1%	90.4%	90.1%	90.3%
cytology after positive SSK (no follow up)	0.05%	0.08%	0.11%	0.29%	0.26%

* Reference date for all results is 1 April 2022. Therefore, the reference period for 2020, for example, is 12 months longer than for 2021 (27 months and 15 months, respectively), which makes the years incomparable. For that reason an extra column of 2020 with a reference period of 15 months is added for comparison. The numbers of the reference period of 15 months are preliminary and printed in italic.

explanation for referral and advice

In the screening programme, participants with hrHPV positivity and ASC-US or higher result are directly referred to a gynaecologist.

In the screening programme, participants are advised to take a control smear after a hrHPV-positive and normal smear.

- In 2021, the percentage of participants with direct referral (of the total participants) was 2.7%, compared to 2.9% in 2020 with the same reference period.
- In 2021, the percentage of participants that was invited for a control smear after 6 months was 6.5%, compared to 6.2% in 2020 with the same reference period.

figure 4a referral (direct and indirect) by age and year (source: BVO NL) * based on the total number of participants

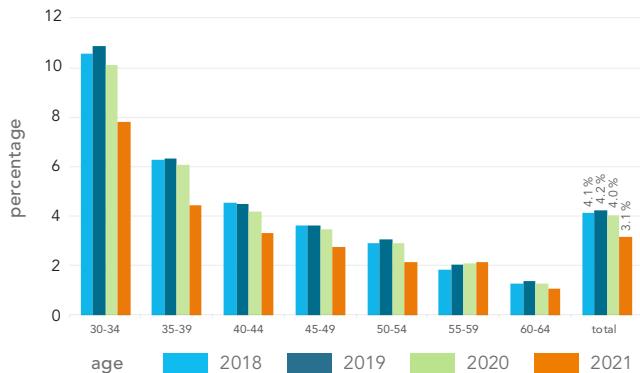
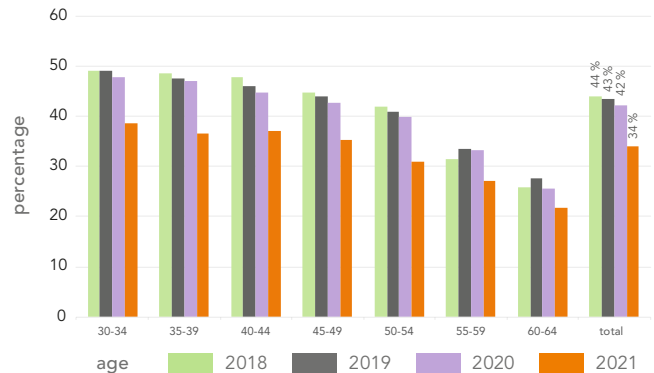


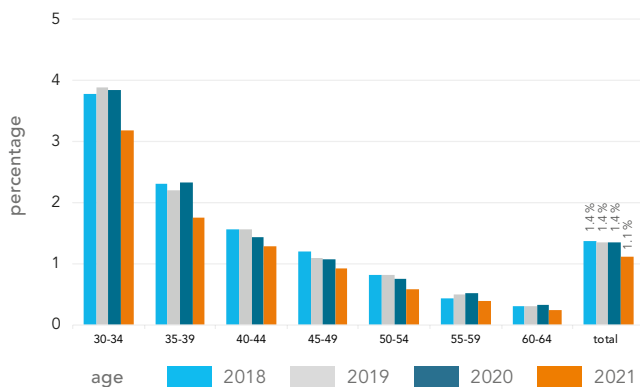
figure 4b referral (direct and indirect) by age and year (source: BVO NL) * based on the total number of hrHPV-positive participants with cervical smear



- Similar to earlier years, in 2021 younger participants are more often referred to the gynaecologist.
- The total referral rate, the percentage of participants that was referred to a gynaecologist, in the group of hrHPV-

positive participants and for whom cytology is assessed, was 34% in 2021. For 2020, this was 42% with a reference period of 27 months.

figure 4c detection (direct and indirect) by age and year (source: BVO NL and PALGA) * based on the total number of participants



* Reference date for all results is 1 April 2022. Therefore, the reference period for 2020, for example, is 12 months longer than for 2021 (27 months and 15 months, respectively), which makes the years incomparable. Due to the shorter reference period the 2021 numbers are preliminary.

- The total detection rate, the percentage of participants with a screen-detected (pre-)malignancy (CIN 2+) was 1.1% in 2021 (preliminary data). In 2020 this was 1.4% with a reference period of 27 months.
- Due to the short follow-up time, the indirect detection rate is preliminary and the (total) detection rate might therefore increase over time.

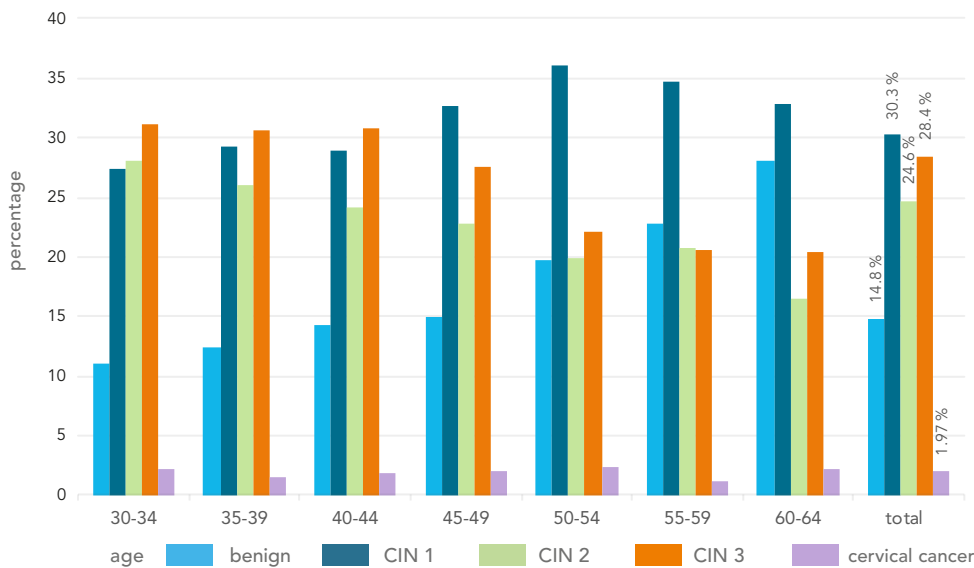
table 7 detection after direct referral in 2021, within 150 days after the primary test (source: PALGA)

	primary test cervical smear	primary test SSK	total
no histology assessed	0.01%	1.21%	0.24%
benign	14.6%	12.2%	14.1%
CIN 1	29.9%	26.1%	28.9%
CIN 2	23.6%	22.8%	23.5%
CIN 3	26.2%	31.0%	27.1%
malignant, primary cervix carcinoma	1.8%	2.4%	1.9%
malignant, other	0.00%	0.05%	0.01%
poor quality	2.4%	2.5%	2.4%
subtotal	98.5%	98.3%	98.2%
unknown	1.5%	2.9%	1.8%
total	100%	101%	100%

- The percentage of participants with CIN3+ was higher among participants using SSK than among participants going to the GP.

figure 5 detection after direct referral

in 2021, by age, within 150 days after the primary test (source: PALGA)



- In the oldest age groups more low lesions (CIN 1) were observed, while in the youngest age groups higher lesions (CIN 2+) were found.

table 8 referral rate, followed referral, detection and positive predictive value (PPV) by year (source: BVO NL and PALGA) *

	2018	2019	2020	2020	2021
reference period (months)	51	39	27	15	15
referral rate total	4.1%	4.2%	4.0%	3.2%	3.1%
referral rate direct	3.1%	3.0%	3.0%	2.9%	2.7%
referral rate indirect	1.1%	1.2%	0.99%	0.24%	0.45%
followed referral total	74%	73%	73%	69%	70%
followed referral direct	75%	75%	75%	71%	73%
followed referral indirect	70%	67%	68%	50%	54%
detection total	1.4%	1.4%	1.4%	1.1%	1.1%
detection direct	1.1%	1.1%	1.1%	1.0%	1.0%
detection indirect	0.27%	0.28%	0.24%	0.04%	0.09%
PPV total	35%	33%	34%	34%	35%
PPV direct	38%	36%	38%	35%	38%
PPV indirect	4.6%	4.3%	3.8%	0.69%	1.4%

* Reference date for all results is 1 April 2022. Therefore, the reference period for 2020, for example, is 12 months longer than for 2021 (27 months and 15 months, respectively), which makes the years incomparable. For that reason an extra column of 2020 with a reference period of 15 months is added for comparison. The numbers of the reference period of 15 months are preliminary and printed in italic.

explanation for histology

In table 7 and 8 the percentage of participants in which a cytological or histological sample (cervical smear or biopsy) was taken due to referral, was used as proxy for compliance, instead of the number of consultations.

- The total referral rate, the percentage of participants that were referred to a gynaecologist, was 3.1% for 2021 and for 2020 3.2% with a reference period of 15 months.
- Due to the temporary shutdown of the screening programme, the data concerning the indirect referral (followed) and the indirect positive predictive value in 2021 were not comparable to 2020.
- The indirect referral for 2019 at a reference period of 15 months was 0.45% and this was comparable to 2021.
- The percentage of followed indirect referral was 70% for 2021, while for 2020 this was 69% (same reference period). The numerator is the number of participants from whom cells or tissue was taken, not the number of consultations. See also 'explanation for histology'.
- The percentage of participants that followed the indirect referral was 54% for 2021, and this was 56% in 2019 at the same reference period.
- The positive predictive value of the screening programme, the chance that a person is correctly referred to the gynaecologist for further examination, was 35% and comparable with 2020.
- The indirect positive predictive value for 2021 was 1.4%, and this was 1.3% in 2019 at the same reference period.

table 9 **histological test** by year (source: PALGA) *

	2018	2019	2020	2020	2021
reference period (months)	51	39	27	15	15
percentage of persons with histological sample	72.9%	71.6%	72.0%	67.1%	68.5%
positive predictive value of histology at colposcopy	53.1%	50.5%	49.5%	49.3%	51.0%

* Reference date for all results is 1 April 2022. Therefore, the reference period for 2020, for example, is 12 months longer than for 2021 (27 months and 15 months, respectively), which makes the years incomparable. For that reason an extra column of 2020 with a reference period of 15 months is added for comparison. The numbers of the reference period of 15 months are preliminary and printed in italic.

- The positive predictive value of histology at colposcopy is determined as the proportion of persons for whom the histology was justified.
- The percentage of persons from whom a histological sample was taken decreased to 69% in 2021. In 2020, 2019 and 2018, looking at a longer reference period, this percentage was higher (73%).
- The positive predictive value of taking a histological sample (the number of persons diagnosed with CIN 2+) was 51%.

PART 3 coverage

explanation for coverage

Coverage or the 5-year coverage rate is the percentage of persons at risk (i.e. persons whose cervix is not removed) within the range of the screening age group that took at least one cervical smear or hrHPV test in the five years before the reference date (in or out of the screening programme). To calculate

the 5-year coverage rate, we analysed the data for periods of five consecutive years. The outcomes of a particular year are based on the five-year period up to, and including that year. For example: the 5-year coverage rate of 2018 is based on tests performed during the period 2014-2018.

table 10 **coverage (5-year coverage rate in percentage)**

by age and year (source: PALGA)

	2017	2018	2019	2020	2021
age					
30 - 34 years	65.4%	65.2%	65.0%	61.7%	64.2%
35 - 39 years	72.5%	71.2%	71.0%	67.4%	69.7%
40 - 44 years	73.4%	74.0%	74.1%	71.0%	72.8%
45 - 49 years	77.3%	75.4%	73.6%	69.4%	70.9%
50 - 54 years	78.5%	77.9%	77.9%	73.4%	75.3%
55 - 59 years	80.0%	78.9%	78.1%	73.0%	75.0%
60 - 64 years	76.9%	76.8%	77.0%	71.7%	74.3%
total	75.0%	74.3%	73.8%	69.7%	71.7%
primary tests (screening programme)	66.5%	65.9%	65.5%	60.8%	63.2%
other *	8.5%	8.4%	8.4%	9.0%	8.6%

* Opportunistic, indicative and secondary smears.

- The 5-year coverage rate decreased in the period 2017 to 2021. The largest decrease is in 2020. In 2020 the screening programme was temporarily put on hold and therefore less persons were invited and less persons participated. In 2021 more persons are invited to catch up on the backlog. The coverage rate, however, includes the at risk population and not the real invited persons. This distorts the 2020 coverage rate.

figure 6 incidence and mortality

by year (source: NCR: (incidence) and CBS (mortality))

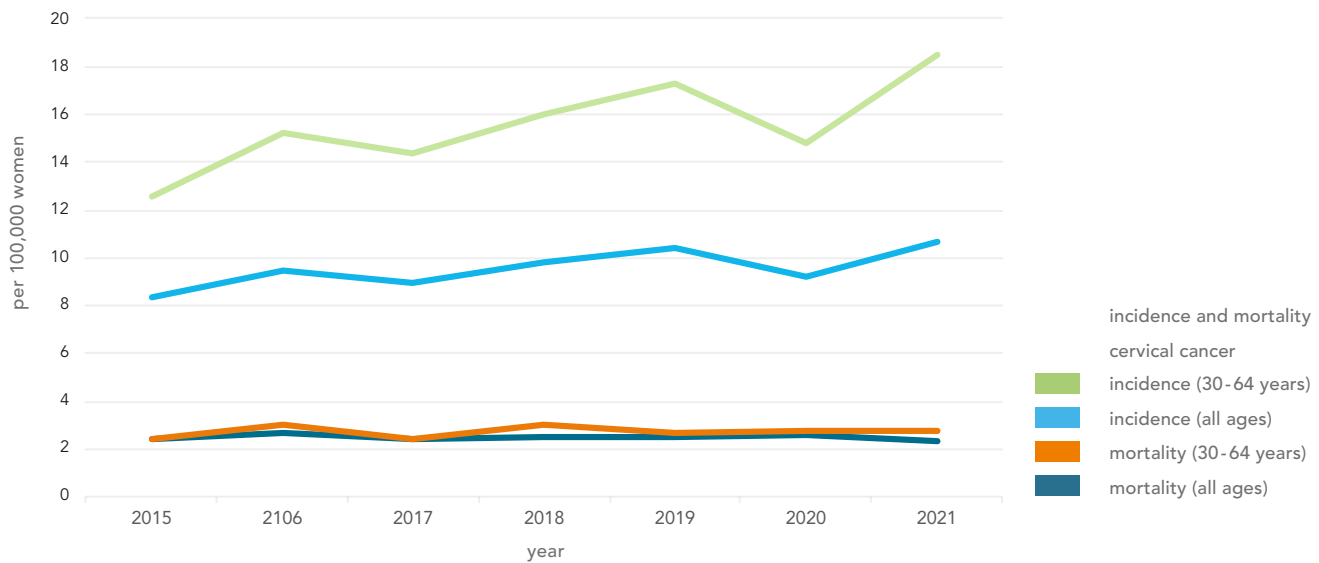


table 11 incidence and mortality

by year (source: NCR (incidence) and CBS (mortality))

	2015	2016	2017	2018	2019	2020	2021
incidence cervical cancer/100,000 women 30-64 years							
squamous cell carcinoma	9.4	11.2	10.9	11.9	12.6	11.2	13.4
adenocarcinoma	2.5	3.2	2.8	3.3	3.6	3.0	4.2
other	0.7	0.9	0.6	0.8	1.1	0.6	0.8
total	12.6	15.3	14.4	16.0	17.3	14.8	18.5
incidence cervical cancer/100,000 women all ages							
squamous cell carcinoma	6.2	6.9	6.7	7.2	7.7	6.8	7.7
adenocarcinoma	1.6	2.0	1.7	2.0	2.0	1.9	2.4
other	0.5	0.6	0.5	0.6	0.7	0.5	0.6
total	8.3	9.4	9.0	9.8	10.4	9.2	10.7
mortality cervical cancer/100,000 women 30-64 years							
total	2.4	2.9	2.4	2.9	2.7	2.8	2.7
mortality cervical cancer/100,000 women all ages							
total	2.5	2.7	2.4	2.5	2.5	2.6	2.3

Incidence and mortality are standardized for the Dutch population. 2021 are preliminary results and therefore in italic.

- The nationwide incidence of cervical cancer varied from 8.3 to 10.7 per 100,000 women.
- This incidence varied from 12.6 to 18.5 per 100,000 women within the screening age.
- The nationwide mortality varied from 2.3 to 2.7 per 100,000 women.

This monitor is available on: www.iknl.nl/en/screening and on: www.rivm.nl/en/cervical-cancer-screening-programme

Disclaimer: the information in this monitor has been carefully compiled. The results of previous years have been updated with recent data. Therefore, these may differ from previously reported results.