NATIONAL CERVICAL CANCER SCREENING PROGRAMME

Monitor 2017

Nationwide monitoring of the National Cervical Cancer Screening Programme

Erasmus MC – PALGA

FIRST RESULTS OF THE RENEWED CERVICAL CANCER SCREENING PROGRAMME

Summary

- The new National Cervical Cancer Screening Programme began on 1 January 2017. The current monitor presents the first results.
- The participation rate was 57.4% on 31 March 2018 and 61.1% on 30 June 2018.
- In the total group of screened women, 9% had a positive test result for the high-risk human papillomavirus (hrHPV).
- 6.9% of all participating women used the self-sampling kit.
- The hrHPV positivity rate was lower (7.4%) among participants who used the self-sampling kit than among participants who had a smear taken with the General Practitioner (GP) (9.1%).
- The percentage of women who were referred to the gynaecologist and the percentage of women who were recommended to have a follow-up smear after 6 months has strongly increased compared with the period 2012-2016 (2.9% and 6.0%, respectively, in 2017 vs. 0.9% and 3.7% in 2012-16).
- The percentage of referrals was higher in women with the self-sampling test (36.6%) than in women having a smear at the GP (31.8%).
- The number of detected CIN2+ lesions has strongly increased compared with the period 2012-2016 (1036 vs. 630 per 100,000 screened women).

Introduction

The Dutch Cervical Cancer Screening Programme is coordinated by the National Institute for Public Health and the Environment (RIVM). The RIVM has commissioned Erasmus MC to carry out the annual monitoring of the national cervical cancer screening programme. Monitoring helps ensure quality of the screening programme and identifies issues, such as unexpected changes in participation or referral rates. Monitoring is conducted using data from the nationwide network and registry of histo- and cytopathology in the Netherlands (PALGA).

The new National Cervical Cancer Screening Programme began on 1 January 2017. The current monitor presents the first results and compare these with the old National Cervical Cancer Screening Programme. This monitor is different from previous editions due to the changes made to the programme. Information about the old and new National Cervical Cancer Screening Programme can be found in the frames on the next page.

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Frame 1. The new National Cervical Cancer Screening Programme (since 1 January 2017)

From 1 January 2017 onwards, the new National Cervical Cancer Screening Programme Programme based on primary hrHPV screening was implemented. HrHPV screening can be performed either by a clinician or by using self-sampling devices.

Self-sampling kit

Women aged 30, 35, 40, 45, 50, 55 and 60 years are invited by letter to make to an appointment for screening with their general practitioner (GP). Women who do not want to go to the GP can request a self-sampling kit from their regional screening organisation. The test kit is sent to the woman's home address approximately four months after the initial invitation letter is sent. If women do not respond to the invitation a reminder is sent four months after the initial invitation, a reminder which also contains information about how to obtain the self-sampling kit. Women who use the request form from the reminder letter receive their self-sampling kit immediately.

Primary hrHPV screening

First, the primary smear is tested for hrHPV positivity (primary screening test). Then, cytology is assessed if women have an hrHPV-positive result. Women who use the self-sampling kit and have a hrHPV-positive result are asked to make to an appointment with their GP for cytological assessment.

Women with cytological abnormalities are referred to the gynaecologist, while women with normal cytology are invited for control cytology testing after six months.

The total number of hrHPV based primary screening and cytological examinations of hrHPV positive samples are performed in five laboratories.

Frame 2. The old National Cervical Cancer Screening Programme (before 2017)

Women aged 30 to 60 years were invited for cervical cytology screening once every five years. Women were asked to make an appointment for screening with their general practitioner (GP). Women with severe cervical cytological abnormalities were referred by their GP to a gynaecologist for further assessment. Women with mild cervical cytological abnormalities were advised to make an appointment with their GP after six months for a follow-up smear. The follow-up smear could be followed by an hrHPV test, depending on policy of the laboratory assessing the smear.

Frame 3.
Results and recommendations

Primary test

hrHPV test

Result	Recommendation in old screening programme	Recommendation in new screening programme
hrHPV-	Not applicable (NA)	Return to screening programme
hrHPV+	NA	Cytological assessment

Cytological assessment

Result	Recommendation in old screening programme (without hrHPV test)	Recommendation in new screening programme (with hrHPV test)
PAP 0	Repeat smear due to poor quality smear	Repeat smear due to poor quality smear
PAP 1	Return to screening programme	Control smear after 6 months
PAP 2/3a1	Follow-up smear after 6 months	Referral to gynaecologist
PAP3a2+	Referral to gynaecologist	Referral to gynaecologist

Triage after 6 months

Result	Old screening programme			New screening programme
	Triage without hrHPV test	Triage with hrHPV-positive test result	Triage with hrHPV-negative test result	
PAP 0	Repeat smear due to poor quality smear	Repeat smear due to poor quality smear	Repeat smear due to poor quality smear	Repeat smear due to poor quality smear
PAP 1	Follow-up smear after 12 months	Follow-up smear after 12 months	Return to screening programme	Return to screening programme
PAP 2/3a1	Referral to gynaecologist	Referral to gynaecologist	Follow-up smear after 12 months	Referral to gynaecologist
PAP3a2+	Referral to gynaecologist	Referral to gynaecologist	Referral to gynaecologist	Referral to gynaecologist

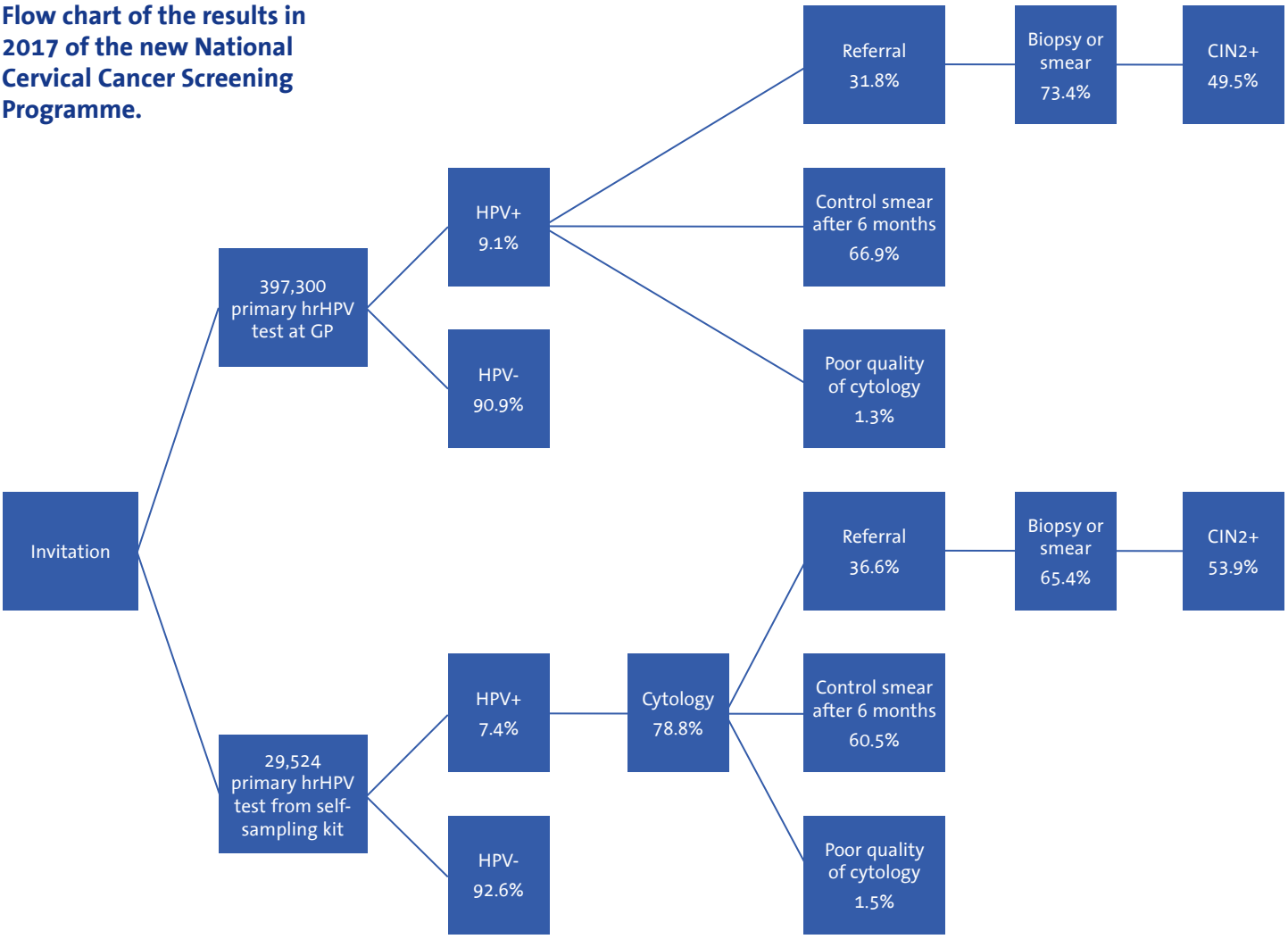
Triage after 12 months

Result	Old screening programme			New screening programme
	Triage without hrHPV test	Triage with hrHPV-positive test result	Triage with hrHPV-negative test result	
PAP 0	Repeat smear due to poor quality smear	NA	NA	NA
PAP 1	Return to screening programme	NA	NA	NA
PAP 2+	Referral to gynaecologist	NA	NA	NA

Terminology

New screening programme = Renewed National Cervical Cancer Screening Programme (since 2017).
Old screening programme = Old National Cervical Cancer Screening Programme (before 2017).
SSK = Self-sampling kit.
Primary test (new screening programme) = hrHPV test and, with a hrHPV positive result, cytological assessment, which is performed from the screening invitation. A hrHPV test can be taken by having a smear taken with the GP or by using the self-sampling kit.
Primary test/smear (old screening programme) = Smear at the GP which is performed as a result of invitation for screening.
Repeat smear = Smear is repeated due to a poor quality smear.
Poor quality smear = Specimen that cannot be assessed.
Control smear (old and new screening programme) = Smear which is performed after 6 months, due to the results of the primary test.
First follow-up smear/first triage (old screening programme) = Smear which is performed after 6 months, due to the results of the primary test. In addition to the first follow-up smear, an hrHPV test could be performed, depending on policy of the laboratory assessing the smear.
Second follow-up smear/second triage (old screening programme) = Smear which is performed after 12 months, due to the results of the first follow-up smear.
Referral = Women are referred to the gynaecologist. Women can be referred from primary screening, first follow-up smear/control smear (old and new screening programme) or second follow-up smear (old screening programme).
Return to screening = No further follow-up examinations are needed. Women can await the next screening invitation.

Flow chart of the results in 2017 of the new National Cervical Cancer Screening Programme.



MONITORING PARTICIPATION AND SHORT-TERM FOLLOW-UP

Part 1 shows the results of the new National Cervical Cancer Screening Programme in comparison with the old screening programme. The results of the old screening programme are based on the averaged values over the last five years (2012 – 2016), as the results over this period were fairly stable. The participation rate in the old screening programme was calculated over the period 2012-2015, as 2016 was not representative due to the finalisation of the old screening programme. Results which are specific for the new screening programme are also presented, such as outcomes by type of primary test, i.e. GP smear or self-sampling kit.

1. Participation

Of all participants in the new screening programme, 6.9% chose the self-sampling kit. The total participation rate in 2017 was 57.4% (on reference date 31 March 2018). During the period 2012-2015, the average participation rate was 65.1% (figure 1).

In both the period 2012-2015 and 2017, the participation rate was lower for younger women than older women (figure 2).

From January 2017, there was a phased roll-out of the new screening programme by each geographical region covered by one of the five screening laboratories. By April, the roll-out was complete with all laboratory regions participating. As a result, women had less time to participate than in the previous years.

Another possible explanation for the lower participation rate is that women who requested the self-sampling test received the test four months (or later) after the screening invitation. It is possible that women who want to participate are still waiting for the self-sampling kit.

For these reasons, an extra reference date has been added to figure 1. We found that there were relatively more women in 2017 who participated late (in the first months of 2018) than in previous years (data not shown). From April 2017, all laboratory regions were fully participating in the new screening programme. With the extra reference date of 30 June 2018, all women have the same time period (15 months) to participate as in previous years. By 30 June 2018, the participation rate had increased to 61.1% (figure 1).

2. hrHPV positivity

In total, 9% of the participating women had a positive hrHPV test. As expected, the percentage of hrHPV positives is highest in the youngest age group and decreased with age (figure 3). The hrHPV positivity was 21.3% in the youngest age group. HrHPV positivity was higher among participants who opted for the GP smear (9.1%) than among participants who used the self-sampling test (7.4%) (see flowchart on p. 3). Further research into the causes of these differences is underway.

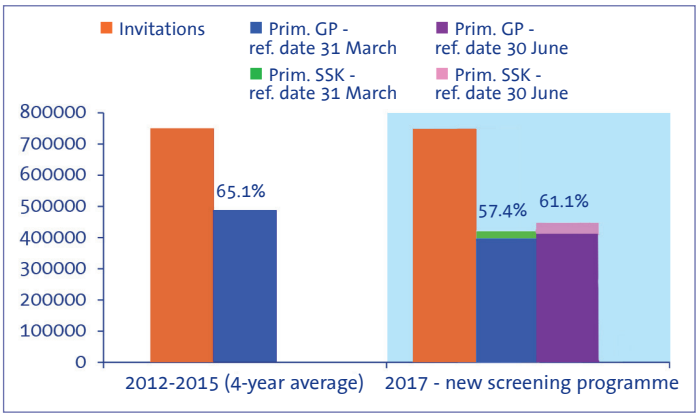


Figure 1. Number of invitations (i.e. population at risk; based on CBS Netherlands, corrected for the risk of hysterectomy) and number of primary smears (PALGA), between 1 January of the invitation year through 31 March of the following year (reference date 31 March) and through 30 June 2018 (reference date 30 June 2018, for new screening programme).

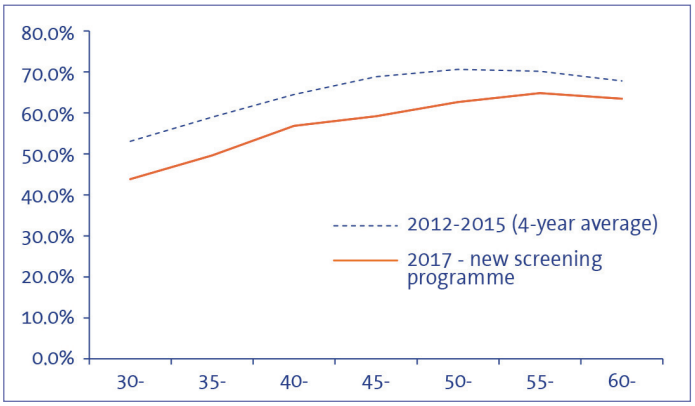


Figure 2. Participation rate by age (PALGA; CBS, corrected for the risk of hysterectomy).

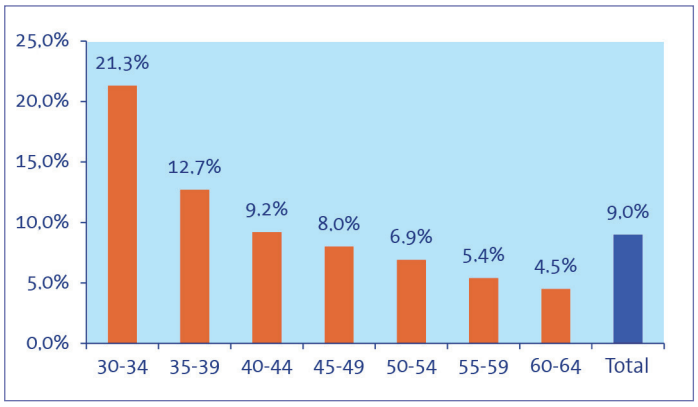


Figure 3. Percentage of women with an hrHPV-positive result according to age (PALGA).

3. Advice given as a result of the primary test

Important differences between the new and old screening programme

Referral:
- The new screening programme uses a broader referral criterion: hrHPV positives with a PAP2+ result.
- In the old screening programme only women with PAP3a2+ were referred.

Control smear:
- In the new screening programme, hrHPV-positive women with normal cytology are recommended to have a control smear after 6 months.
- In the old screening programme, women with a PAP2 or PAP3a1 result are recommended to have a follow-up smear after 6 months.

Repeat smear (due to poor quality of cytology):
- In the new screening programme, cytology is assessed in hrHPV positives only.
- In the old screening programme, cytology was assessed in all women.

See also frames 1 and 2.

As a result of the changes in the new screening programme, including broader criteria for referral, screened women in 2017 were referred three times more often to the gynaecologist and there were almost twice as many women who were invited for a follow-up/control smear than in the period 2012-2016 (figure 4). Less women were recommended to have a repeat smear because of poor quality cytology. So, the percentage of poor quality cytology in the total group of participants has decreased. However, cytology is taken place less often in the new screening programme, as it is performed only with a hrHPV-positive result, whereas cytology was assessed in all women in the old screening programme. In women with a cytology test, the percentage of cytology of poor quality was fairly similar in the new and old screening programme.

Table 1 shows the proportion of advice given on the basis of primary screening in two groups for hrHPV-positive women with a cytology result and the total group of participants, respectively. Of all hrHPV positive women, 32.1% were referred to a gynaecologist because of cytological abnormalities of low-grade or worse. The percentage of cytological abnormalities, in particular high-grade abnormalities (i.e. ≥Pap3a2), was higher in women who used the self-sampling kit than in women who had a smear taken at the GP. Research is underway into the causes of this difference. In total, 66.6% of all hrHPV-positives had normal cytology. This group was recommended to have a control smear after six months. In 1.3% of cases, the cytology material was of poor quality.

Table 1 also shows the proportion of advice given on the basis of primary screening in the total group of participants. In total, 2.9% of all participants were referred as a result of the primary test (direct referral) and 5.9% were recommended to have a control smear after 6 months. As explained above, the percentage of referrals was higher in women who used the self-sampling kit (36.6%) than in women having a smear at the GP (31.8%). In the total screened group this was the other way round because some cytology results of hrHPV-positive women who used the self-sampling kit are still unknown. These women need go to the GP to have a smear taken in order for cytology to be assessed. Table 1 shows that of all women who participated with the self-sampling kit, 1.5% did not have a smear yet.

In hrHPV-positive women, the percentage of direct referrals decreases with age (figure 5).

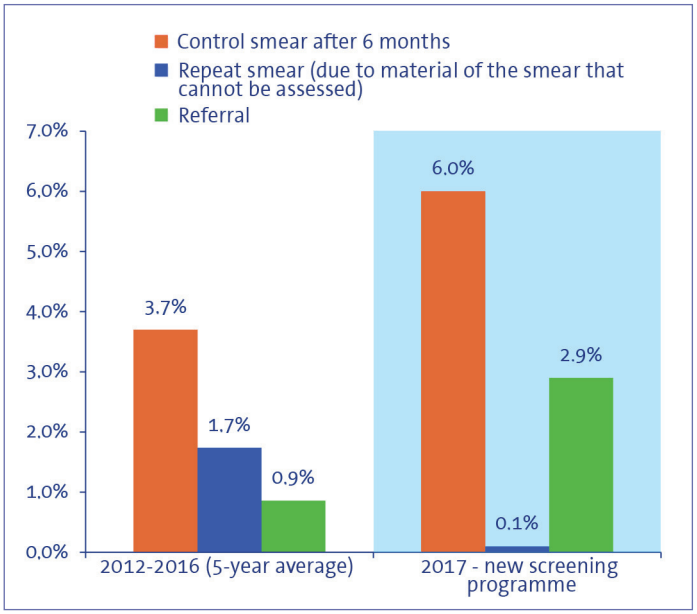


Figure 4. Advice given as a result of the primary test (percentage of total number of primary tests (PALGA).

Table 1. New screening programme: Advice given as a result of the primary test (based on primary tests taken between 1-1-2017 and 31-3-2018) (PALGA).

	hrHPV-positives with cytological result			All participants		
Advice	**Primary test GP**	**Primary test SSK***	**Total**	**Primary test GP**	**Primary test SSK**	**Total**
Referral	31.8%	36.6%	32.1%	2.9%	2.1%	2.9%
High-graded (≥PAP 3a2)	*10.8%*	*15.9%*	*11.0%*	*1.0%*	*0.9%*	*1.0%*
Low-graded (PAP 2 or PAP 3a1)	*21.1%*	*20.8%*	*21.1%*	*1.9%*	*1.2%*	*1.9%*
Control smear after 6 months	66.9%	60.5%	66.6%	6.1%	3.5%	5.9%
Return to screening programme	NA	NA	NA	90.9%	92.7%	91.0%
Repeat smear (due to material of the smear that cannot be assessed)	1.3%	1.5%	1.3%	0.1%	0.1%	0.1%
Cytology because of a hrHPV positive result with the self-sampling kit, but which was not (yet) assessed	NA	NA	NA	NA	1.5%	0.1%
Total	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

*) 78.8% had cytology assessed

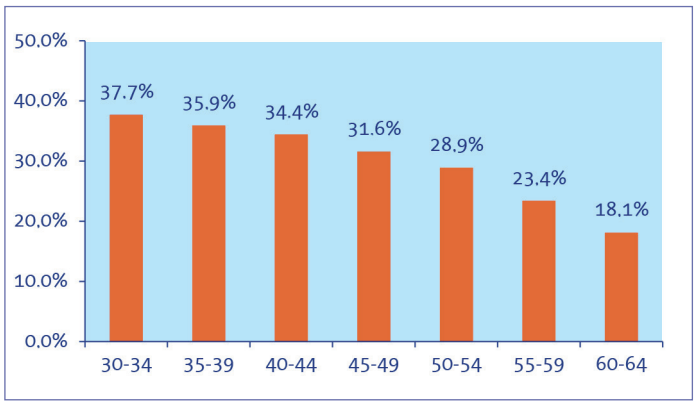


Figure 5. New screening programme: Percentage of direct referrals according to age (in hrHPV-positives with a cytological result) (2017) (PALGA)

4. Percentage where a cytological or histological sample was taken due to direct referral

Colposcopies without accompanying cytology or histology tests being taken are not registered in PALGA. Therefore, we used the percentage of women who had a cytology or histology test taken at colposcopy, due to direct referral, as a proxy for the compliance of referrals, instead of the number of consultations.

Table 2 shows the percentage of colposcopies with either cytology or histology as a result of direct referral. In 2017, this percentage was 90.0% among referred women due to PAP3a2+, which was similar to the period 2012-2016 (91.7%). The percentage of colposcopies with histology/cytology is lower (64.1%) in women referred for low-grade cytological abnormalities (due to new referral criteria in the new screening programme). The reason is, probably, that cytology/histology samples are taken less often from women referred with low-grade cytological abnormalities.

5. Outcome from direct referral (due to the primary test)

In 2017, the detection of clinically relevant findings (i.e. CIN2+) has increased compared with the period 2012-2016 (figure 6). The detection of not-clinically relevant findings (i.e. 'benign' and CIN1) has also increased in 2017 compared with the previous period.

In the new screening programme, in total 49.7% clinically relevant findings (CIN2+) were detected from direct referral, 49.5% in women who had a smear taken at the GP and 53.9% in women who used the self-sampling kit (table 3). Not clinically relevant findings (benign, CIN1 and 'No histology, only cytology by gynaecologist') were found in 48.4% of directly referred women (48.6% in participants with the GP smear and 45.3% in participants who used the self-sampling kit). It is possible that the percentage of clinically relevant findings is underestimated. There was no cytology or histology taken at colposcopy in 27% of the referred women (table 2), possibly because there was no need for it according to the gynaecologist. Another reason might be that the woman has not complied to the referral advice or intends on complying at a later date.

Figure 7 shows the detection of CIN2+ due to direct referral in the new screening programme, according to age. The proportion of benign and, to a lesser extent, CIN1 abnormalities increased with age. The proportion of CIN2 and CIN3 decreased with age. The proportion of cervical cancer is fairly stable from ages 30-34 to ages 45-49 and declines slightly in the older age groups

Table 2. Percentage colposcopies where a cytological or histological sample was taken due to direct referral (PALGA).

	2012-2016 (5-year average)	2017 New screening programme*
Referral		
High-graded (≥PAP 3a2)	*91.7%*	*90.0%*
Low-graded (PAP 2 or PAP 3a1)	*NA*	*64.1%*
Total	91.7%	73.0%

* based on the currently available follow-up time; is expected to increase.

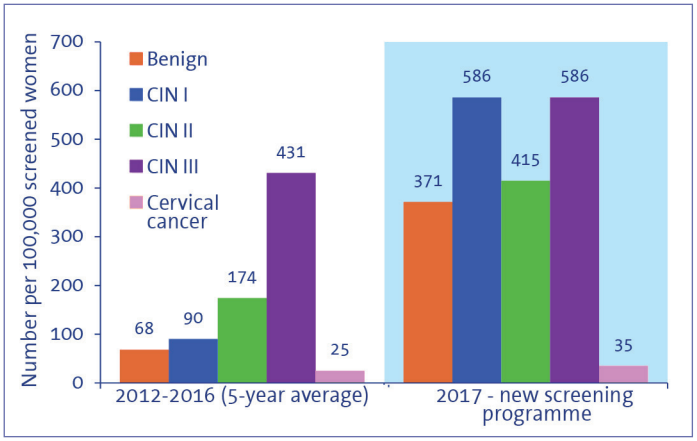


Figure 6. Outcomes from direct referral (number per 100,000 screened women) (PALGA). Outcomes from direct referral in 2017 are preliminary.

Table 3. New screening programme: Detection from direct referral* (within 150 days after the primary test)(2017)(PALGA)

	Primary test GP	Primary test SSK	Total
No histology assessed**	2.3%	8.0%	2.5%
Benign	17.9%	15.1%	17.8%
CIN 1	28.4%	22.2%	28.1%
CIN 2	19.9%	19.8%	19.9%
CIN 3	27.9%	32.4%	28.1%
Malignant, primary cervix carcinoma	1.7%	1.7%	1.7%
Maligne, other	0.0%	0.0%	0.0%
Poor quality	1.9%	0.7%	1.9%
Total	100.0%	100.0%	100.0%

*) First indication of the outcomes based on the available follow-up time.
**) Cytology assessment by the gynaecologist, but no histology assessment.

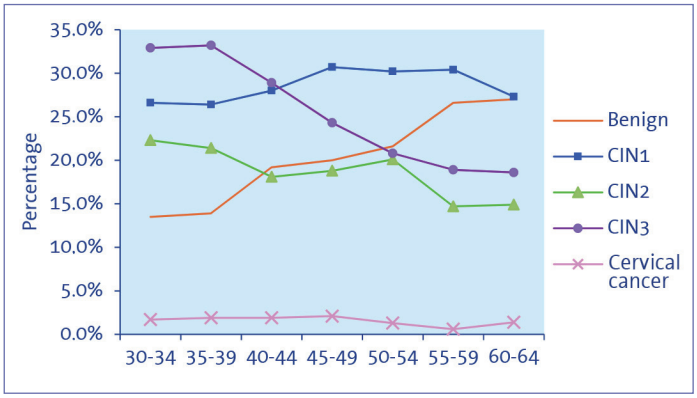


Figure 7. New screening programme: Detection from direct referral according to age (2017) (PALGA)

MONITORING LONG-TERM FOLLOW-UP

The available follow-up time is too short to assess long-term follow-up outcomes of the new National Cervical Cancer Screening Programme in 2017.

*This part shows a brief overview of the long-term follow-up outcomes of the **old National Cervical Cancer Screening Programme.** Findings are based on the screening rounds of women invited in 2009 – 2013.*

The purpose of this analysis is to evaluate the outcomes in a full screening round, from primary smear until the second follow-up smear. Women who participated in the first two years after the invitation (which is approximately 97-98% of all participating women per each invitation round) are followed for a maximum of four years from the time of the primary smear.

1. Percentage where a cytological or histological sample (cell or tissue material) was taken due to referral or follow-up smear

We used the percentage of women in which a cytological or histological sample (biopsy or smear) was taken due to referral, as a proxy for compliance, instead of the number of consultations. Colposcopies without a cytological or histological sample taken are not registered in PALGA.

From 2011 the percentage of colposcopies with histology/cytology resulting from the recommendations remains fairly stable (figure 8). Cytological or histological samples were taken in almost all referred women. However, fewer women who were referred as a result of the second follow-up smear had cytological or histological samples taken. This may be due to the fact that low-grade cytology abnormalities are referred at the second follow-up smear, meaning that they may not require intervention at colposcopy .

Smears were taken more often as a result of the recommendation for the first follow-up smear than for the second follow-up smear. Almost all women with a smear of poor quality had a repeat smear taken.

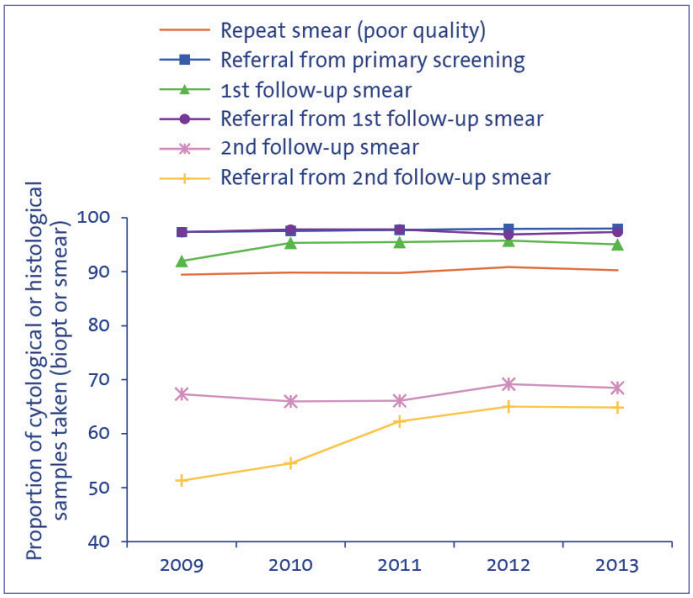


Figure 8. Percentage where a cytological or histological sample (cell or tissue material) was taken due to referral or follow-up smear, 2009-2013 (PALGA)

2. Findings based on the total follow-up route

The trends in the number of different recommendations from first and second follow-up smear were fairly stable during the period 2009-2013.

Figure 9 and table 4 show the total detection of abnormalities from screening in the total follow-up route (i.e. as a result of the primary test, and the first and second follow-up smear). In general, the trends in detected abnormalities were stable in the period 2009-2012.

Table 4. Total share of detected anomalies (PALGA).

	2009	2010	2011	2012	2013
Benign	98.60%	98.55%	98.49%	98.54%	98.50%
CIN 1	0.36%	0.38%	0.39%	0.37%	0.40%
CIN 2	0.37%	0.39%	0.41%	0.40%	0.42%
CIN 3	0.63%	0.64%	0.66%	0.66%	0.65%
Malignant, primary cervix carcinoma	0.03%	0.03%	0.04%	0.03%	0.03%

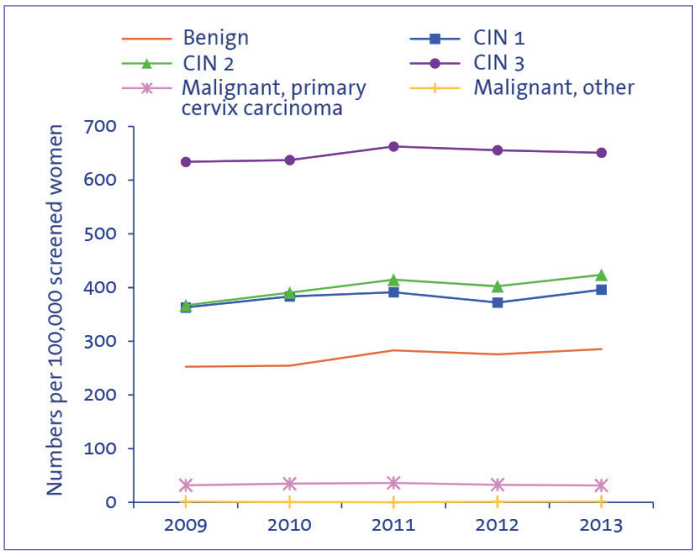


Figure 9. Outcomes of referral in the total follow-up route (numbers per 100,000 screened women) (PALGA).

Part 3

COVERAGE

Coverage indicates the extent to which women who are eligible for cervical cancer screening have had some sort of testing for cervical abnormalities in a specified period. The 5-year coverage is the proportion of women at risk (women with a cervix) in the age group eligible for screening who had at least one test in the previous five years.

Data sources

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 2011 is based on testing during the period 2007-2011.

Table 5 shows the 5-year coverage rate (%) of women in the screening age group in the period 2011 through 2017. The 5-year coverage declined by approximately 2% during this period, particularly in women aged 30 to 40 years and aged 40 to 44 years. This decline was caused by a decline in the number of primary tests both within and outside of the screening programme.

In 2017, the coverage rate is approximately 3% lower than in 2016, as a result of the lower participation rate in 2017 (see section 1 of part 1 where the participation rate is discussed). The coverage of other smears/hrHPV tests (outside the screening programme) in 2017 was comparable with 2016 and 2015.

Table 5. 5-year coverage in 2011-2017 (PALGA).

Age	2011	2012	2013	2014	2015	2016	2017
30-34	72.0	70.6	69.8	69.2	68.0	67.6	64.1
35-39	74.8	74.3	75.3	74.7	75.0	74.2	71.0
40-44	79.3	78.0	76.2	74.5	73.8	73.9	71.8
45-49	81.0	80.5	80.2	80.1	79.2	78.2	75.1
50-54	82.8	81.7	81.7	81.2	80.4	79.2	76.0
55-59	79.4	79.7	79.8	80.1	79.8	79.9	77.4
60-64	74.0	75.0	76.4	76.2	76.8	77.6	74.6
Total*	**77.8**	**77.3**	**77.2**	**76.7**	**76.3**	**75.9**	**73.0**
Primary tests (screening programme)	*68.4*	*67.9*	*67.9*	*67.7*	*67.5*	*67.4*	*64.3*
*Other***	*9.4*	*9.4*	*9.2*	*8.9*	*8.6*	*8.4*	*8.5*

*Including unknown smears.
**Opportunistic, indicative and secondary smears.

Part 4

NATIONWIDE INCIDENCE AND MORTALITY

Table 6 presents the incidence of, and mortality from, cervical cancer in the Netherlands during the period 2012-2016, in women aged 30 through 64 years (the eligible ages for the cervical cancer screening programme) and for the entire Dutch female population [between brackets]. The figures are age-standardised (based on the Dutch female population in 2016).

In the ages 30-64, as well as the total female population, the incidence of CIN1, CIN2 and CIN3 slightly increased. Remarkably, there was a relatively large increase in CIN1 diagnoses in 2016 compared with the period 2012-2015. The incidence of cervical cancer was fairly stable during the period 2012-2015. However, in 2016, the incidence of cervical cancer has increased compared with 2012-2015. The mortality from cervical cancer declined between2013 and 2015, followed by a slight increase in 2016 (figures of 2016 are preliminary).

Table 6. Nationwide incidence and mortality, standardised by age, per 100,000 women (PALGA, NKR).

2012	2013	2014	2015	2016
CIN I				
89 [51]	81 [48]	83 [49]	88 [51]	97 [56]
CIN II				
78 [45]	77 [45]	78 [45]	82 [47]	88 [49]
CIN III				
119 [64]	116 [63]	119 [64]	124 [66]	128 [68]
Primary cervix carcinoma (squamous-cell carcinoma)				
9.8 [6.5]	8.7 [5.8]	9.8 [6.3]	9.3 [6.1]	11.3 [6.9]
Primary cervix carcinoma (adenocarcinoma)				
2.4 [1.6]	2.2 [1.5]	3.0 [1.8]	2.5 [1.7]	3.3 [2.0]
Primary cervix carcinoma (otherwise)				
0.9 [0.7]	0.8 [0.6]	0.9 [0.7]	0.7 [0.6]	0.8 [0.6]
Primary cervix carcinoma (total)				
13.0 [8.8]	11.7 [7.9]	13.8 [8.8]	12.6 [8.4]	15.3 [9.5]
Mortality from cervical cancer				
2.6 [2.7]	2.7 [2.7]	2.4 [2.4]	2.4 [2.4]	2.9 [2.7]*

*The mortality data of 2016 are preliminary.