Results of the second round of the Dutch primary HPV screening programme

Ellen MG Olthof, Inge MCM de Kok
Erasmus MC, department of Public Health

Background

January 1, 2022, the second screening round of the reorganized Dutch cervical cancer population programme, using primary HPV screening, has started. From this date, people with a known HPV result from the previous round will be invited for screening. All persons aged 30, 35, 40, 50 and 60 years are invited by default (i.e. *the base population*; Figure 1). In addition, three *high-risk population*s aged 45, 55 and 65 are invited. Clients aged 45 and 55 are invited if they have not participated or if they were HPV positive 5 years before. Clients aged 65 are only invited if they were HPV positive 5 years earlier and have not been referred. In addition to these changes in invitation policy, we expect that we will also see differences with the previous round due to the so-called 'second round effect' (see Box 1).

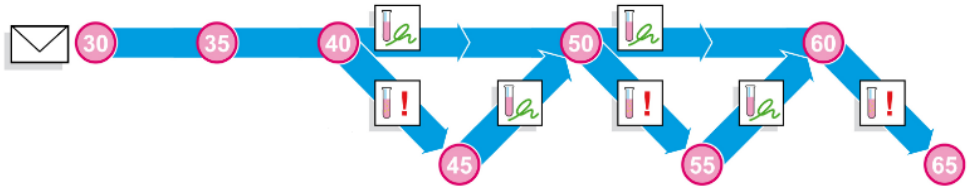

Figure 1: The new invitation schedule for the population-based cervical cancer screening programme

The **"second round effect"** in cancer screening refers to changes in risk in the screening population in the initial round of screening (i.e. prevalence screening) versus subsequent rounds (i.e. incidence screening):

- **Prevalence Screening:** Prevalence screening identifies individuals who may have developed CIN or cancer long before screening.
- **Incidence Screening**: Incidence screening mainly finds cases that have developed recently (after the previous screening). New cases are often diagnosed at an earlier stage of the disease.

As a result of prevalence screening, the detection rate of (pre-)cancer in the screened population is higher in the first round compared to subsequent rounds.

Box 1. Explanation of the 'second round effect' in screening

We evaluated the effects of these changes by evaluating the size of the screening programme and screening behaviour, and the results of screening. We specifically looked at the differences between the base population and the high-risk populations in 2022, and the differences between the base populations in 2017 vs 2022.

Size of the screening programme and screening behaviour

The numbers of invitations and HPV analyses decreased in the second round of the HPV-based programme. The Monitor from 2022 observed a lower participation rate in 2022 compared to previous years. We have shown that the participation rate is significantly lower in the high-risk populations (31.0%) compared to the base population in 2022 (52.1%). This low participation rate is mainly observed in 45 and 55 year olds of which a large proportion (approximately 85%) of the invitees did not participate in the previous screening round (and do not participate in the second round as well) (Figure 1). In contrast, the participation rate in people who were HPV positive in the previous round, was higher compared to the other age categories in 2022, for both 45, 55 and 65 year olds. However, if we compare the base populations of 2022 and 2017 we see that the participation rate overall is lower in 2022 (Figure 1). This shows that the lower participation rate is not only caused by the changed invitation schedule, but that probably additional factors play a role. More research is needed to understand the decrease in participation.

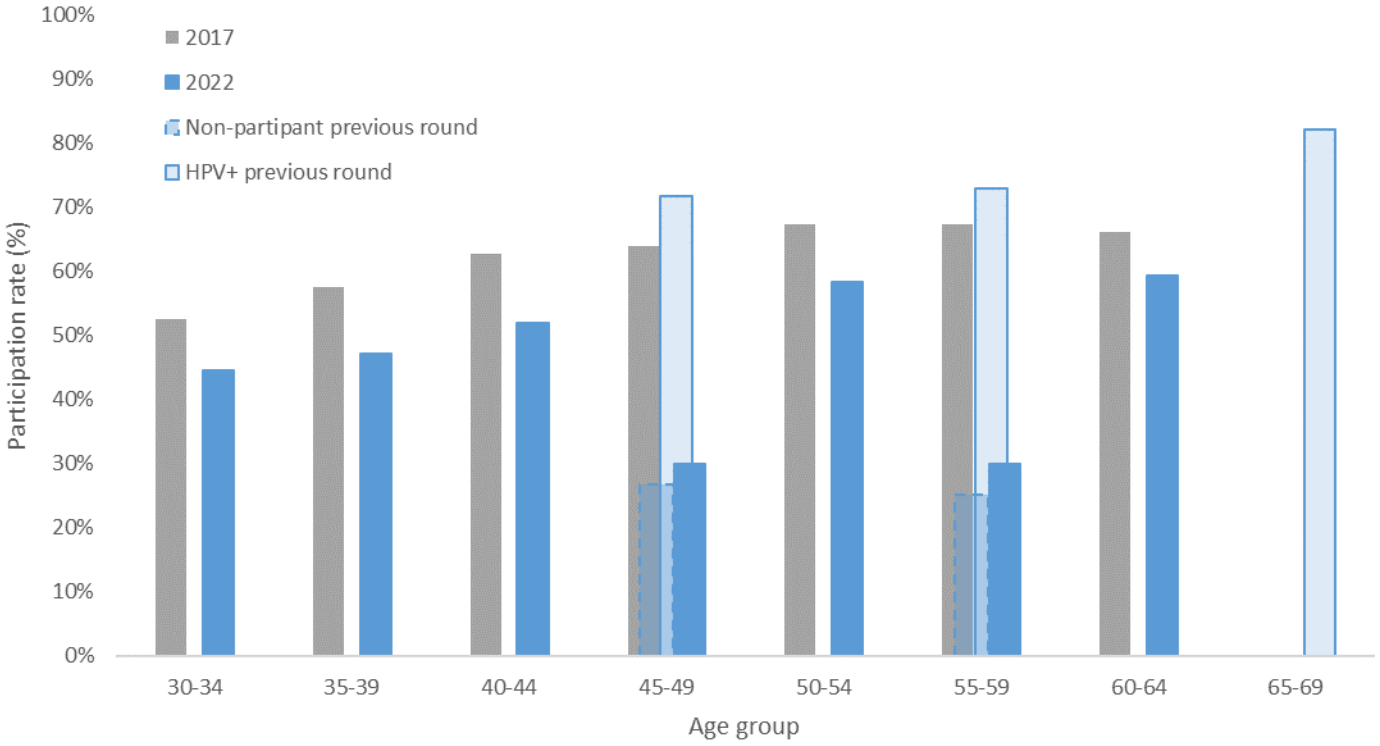

Figure 1. *Participation rate (i.e. number of persons invited and participated / number of persons invited) in the base populations 2017 and 2022, broken down by the two different high-risk populations (i.e. number of persons invited and participated in that specific high-risk group / number of persons invited in that specific high-risk group) in 2022 for the ages where this applies (1) Non-participant in 2017 or 2) HPV positive in 2017, for 45, 55 and 65 year olds)*

The use of the self-sampling kit (SSK) is higher in 2022 compared to 2017, in every age group. Participation using a SSK was higher in the high-risk populations, but if people were HPV positive in the previous round, the majority preferred the smear test (Figure 2). Those who did not participate in the previous round, but did participate in the second round, preferred the SSK relatively more often (compared to participants in the previous round). This indicates that the SSK also reaches some of the people who did not participate before and can potentially increase the overall participation rate.

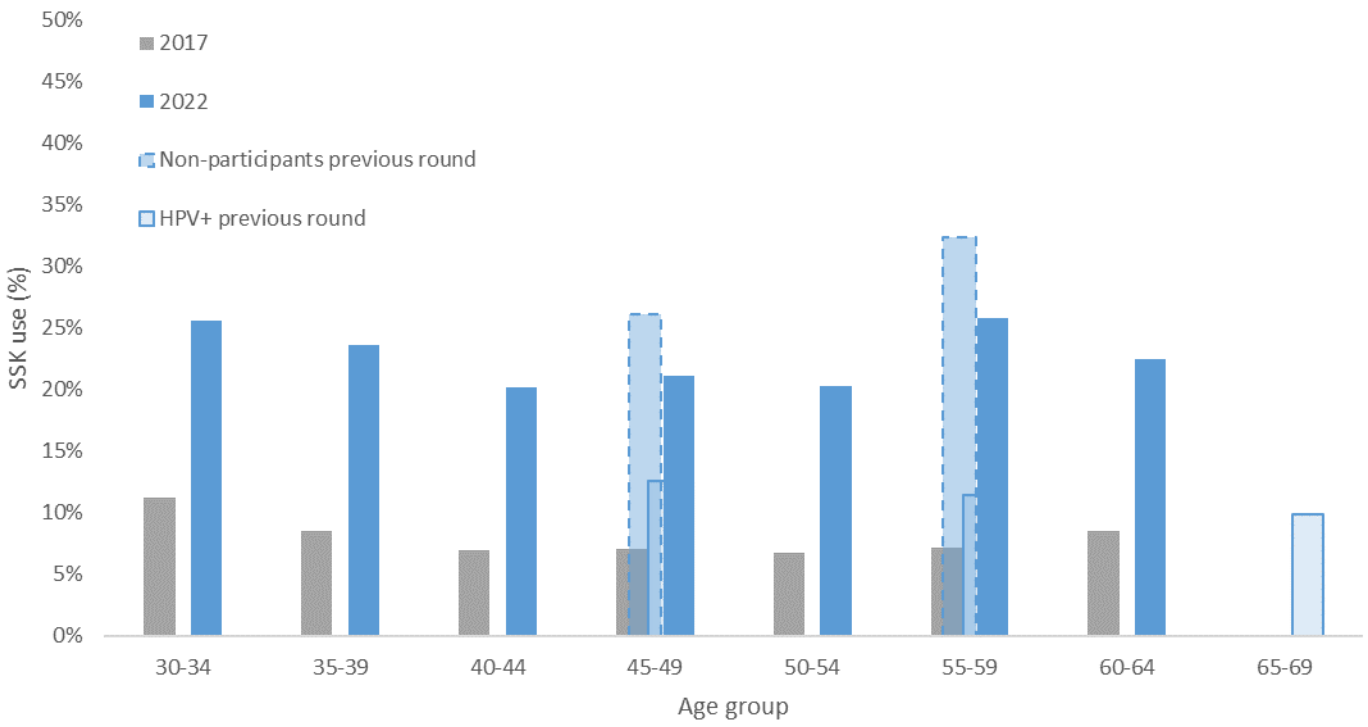

Figure 2. *Percentage of participants using a self-sampling kit (SSK) (i.e. number of people participating using a SSK / number of people participating) in the 2017 and 2022 base populations, broken down by the two different high-risk populations (i.e. number of participants and SSK users in that specific high-risk group / number of persons participating in that specific high-risk group) in 2022 for the ages where this applies (1) Non-participant in 2017 or 2) HPV positive in 2017, for 45-, 55- and 65 year olds)*

Results of screening

The 2022 Monitor showed that the HPV positivity rate was higher in 2022 compared to previous years. We have found that HPV positivity rates are higher in all high-risk populations compared to the base population and highest in participants who were also HPV positive in the previous round (Figure 3). We also found that the HPV positivity rate in the base population is similar in 2017 (10.4%) and 2022 (10.1%). This means that the 'second round effect' had no impact on the HPV positivity rate.

If we compare the cytology results in 2022 to 2017, we did see a small shift towards less high-grade abnormal cells in all HPV-positive participants in the second round (Table 1). We also found relatively fewer high-grade histological confirmed abnormalities (i.e. CIN 2/3+) after referral in the base populations (Table 2). A similar pattern was found in 30-year-old people after referral. Since this cannot be an effect of the second round of HPV (because women aged 30 are screened for the first time), this may indicate a different trend in screening effectiveness (which may also have an effect at other ages). It is therefore probable, that the trends described is this paragraph can only partly be attributed to 'the second round effect'.

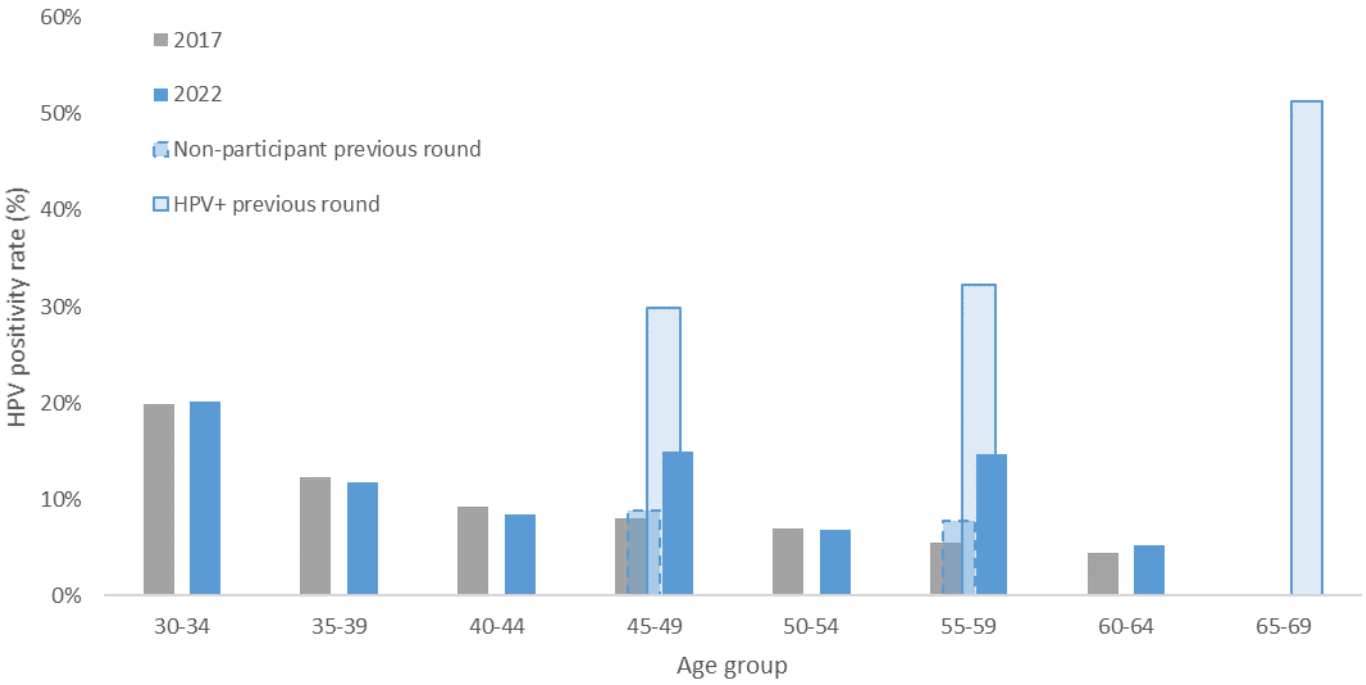

Figure 3: *HPV positivity rate (i.e. number of HPV positive participants / number of persons participated) in the base populations 2017 and 2022, broken down by the two different high-risk populations (i.e. number of HPV positive participants in that specific high-risk group / number of participants in that specific high-risk group) in 2022 for the ages where this applies (1) Non-participant in 2017 or 2) HPV positive in 2017, for 45, 55 and 65 year olds)*

Table 1: *Percentage of HPV positive women with high-grade abnormal cells (Pap3a2+; i.e. HSIL), in 2017 compared to 2022, by age*

Age group	2017	2022	Difference
30-34	14.7%	13.2%	**-1.5%**
35-39	13.5%	9.6%	**-4.0%**
40-44	11.9%	10.5%	**-1.4%**
45-49	10.0%	11.9%	1.9%
50-54	8.6%	5.8%	**-2.8%**
55-59	6.4%	7.3%	0.9%
60-64	5.6%	5.0%	**-0.6%**
65-69	n.a.	3.8%	n.a.
Total	11.4%	9.8%	**-1.6%**

Table 2: *Percentage of CIN2+/3+ found after direct referral, in the basic population in 2022 compared to 2017*

Round	CIN2+	CIN3+
First (2017)	62%	39%
Second (2022)	58%	33%
Difference	**-3%**	**-6%**

Conclusion

A lower participation rate is seen in the high-risk populations (with the exception of people who were HPV positive in the previous round), but is also visible to a lesser extent in the base population in the second round (compared to 2017). An HPV-positive test in the previous screening round appears to be an important predictor for an HPV-positive test in the next screening round. Comparing the first and second rounds, we saw a small shift towards fewer high-grade abnormal cells in all HPV-positive participants. The second round of HPV screening also appears to have led to a slightly reduced prevalence of cervical abnormalities in the screening population. The same pattern of fewer high-grade abnormalities observed in the 30-year-olds indicates (in addition to the 'second round effect') an additional change in screening effectiveness. The SSK appears to have a promising role in increasing participation rates in high-risk women who have not previously participated.