



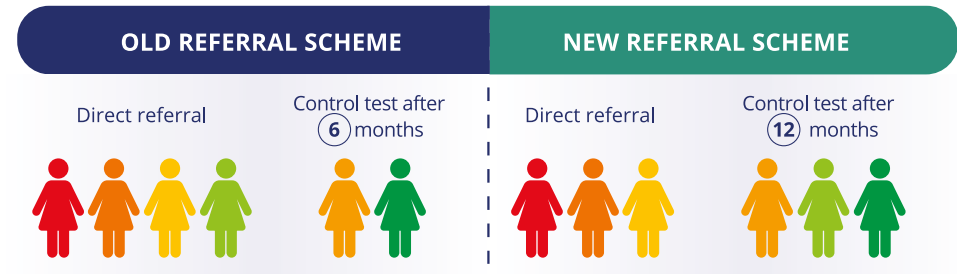
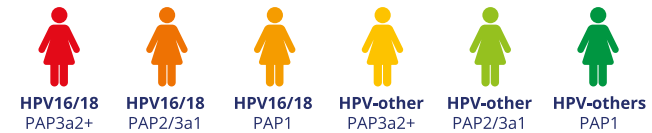
# Impact of the New Referral Scheme on the Cervical Cancer Screening Program

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## Background

By conducting a screening test within the cervical cancer screening program, individuals are identified who need to be seen by a gynecologist for further diagnostic investigation. The referral scheme indicates under which screening result someone should be referred to a gynecologist. A disadvantage of screening is that some people are referred for further examination by a gynecologist even though they are not ill ('unnecessary referrals'). The introduction of primary human papillomavirus (HPV) screening in 2017 provides more health benefits, but also resulted in more participants being referred to the gynecologist. More than half of these turned out not to have a precancerous stage of cervical cancer ('unnecessarily referred'). To reduce the number of unnecessary referrals, the referral scheme of the screening program was adjusted on July 11, 2022 (see Figure 1). It was expected that with this referral scheme the number of unnecessary referrals would decrease by about half.



**Figure 1** Overview of different risk groups in the screening program (HPV-positive participants) and referral advice in the old and new situation

In the old referral scheme, all HPV-positive participants with abnormal cervical cells (from Pap 2 onward) were referred to the gynecologist. In the new referral scheme, HPV genotyping is used. A distinction is made between HPV types 16/18 and the other HPV types (HPV-other). Participants with HPV16/18 are referred directly from Pap 2 onward. When no cell abnormalities are visible (Pap 1), these participants receive an invitation for a control test. Participants with HPV-other are referred directly only if cytological abnormalities from Pap 3a2 (moderate/severe cell abnormalities) are present. When no or minor cell abnormalities are visible (<Pap 3a2), these participants receive an invitation for a control test. Participants in whom abnormal cells (from Pap 2 onward) are found during the control test are still referred to the gynecologist (indirect referral). In the new referral scheme, the interval for this follow-up test has been extended from 6 to 12 months.

## Aim of the study

The impact of the adjusted referral scheme on the cervical cancer screening program has been investigated. This was done by comparing the participation rate and the results of the control test, the referral rate to the gynecologist, and the detected cervical abnormalities before and after the introduction of the new referral policy. Clients who participated in the period July 11, 2022 through June 30, 2023 were compared with clients invited in the period January 1, 2022 through June 30, 2022. The follow-up for both groups continued until August 31, 2024.

## Participation in Follow-Up Testing

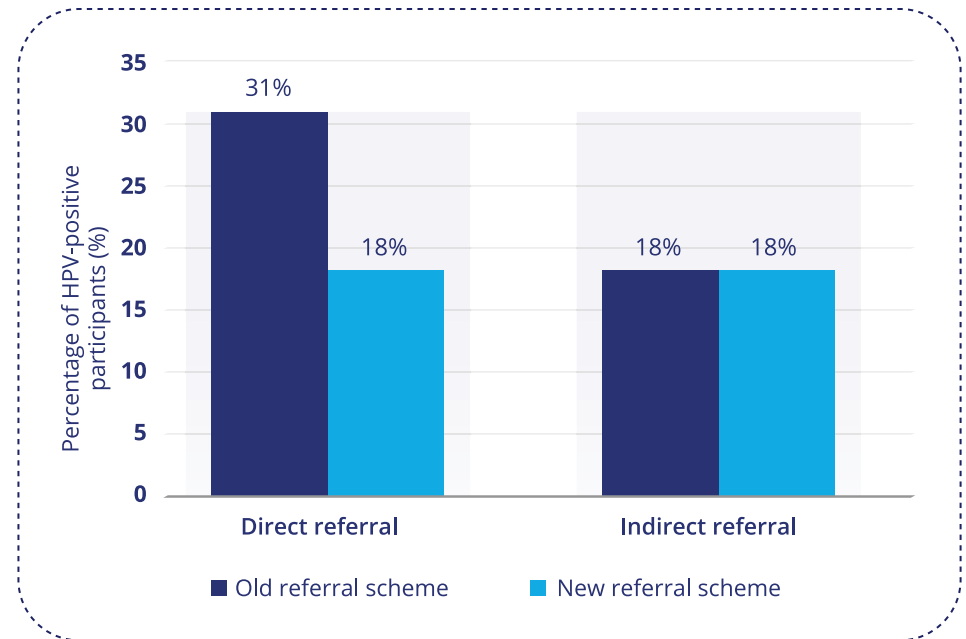
Because the interval for the follow-up test has been extended from 6 to 12 months, participation in follow-up testing may have changed. After the introduction of the new referral scheme, overall participation in the follow-up test was lower (82%) than before the introduction of the new scheme (89%). What makes comparison difficult is that participants in the period before the introduction of the new referral scheme had more time to participate than after the introduction (a maximum of 26 vs. 14 months). The expectation is that the percentage of participants in the more recent period will still increase over time.

## Follow-Up Results

Due to the new referral scheme, more clients, and with an average slightly higher risk (not only Pap 1, but also Pap 2/3a1 in combination with HPV-other), receive a control test instead of a direct referral (see Figure 1). As a result, it is expected that relatively more abnormal smears will be found during control testing. In addition, extending the follow-up interval (from 6 to 12 months) may also play a role, as abnormalities have more time to develop. At the control test, there was indeed a small decrease in normal smears ('Pap 1') (from 79% to 76%) and a small increase in mildly abnormal smears (Pap 2/3a1; from 17% to 19%) and severely abnormal cells (Pap 3a2+; from 4% to 5%).

## Referrals to Gynecologists

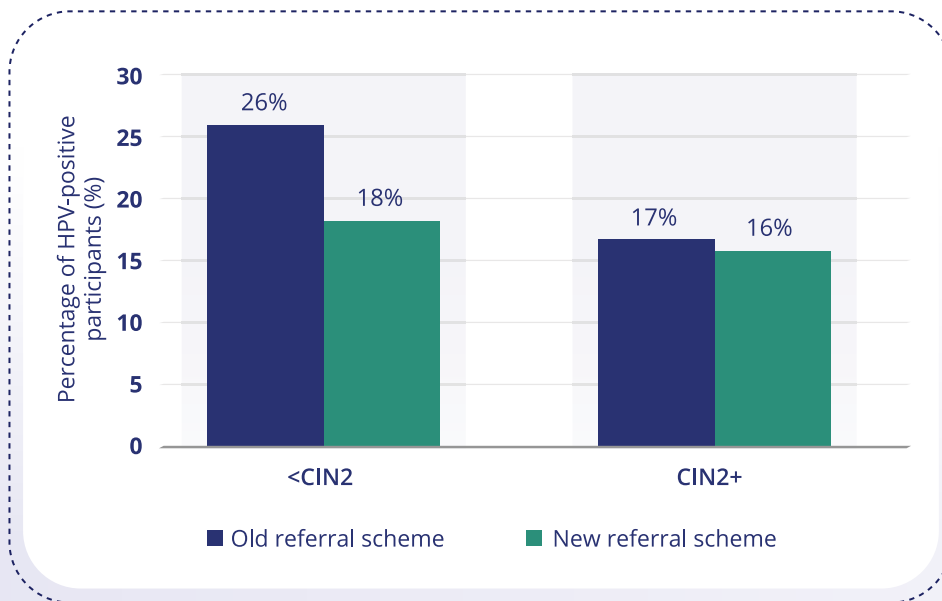
It was expected that the new referral scheme would lead to fewer referrals to the gynecologist. The direct referral rate indeed dropped sharply, from 31% to 18%, which can be explained by the fact that now only clients with a higher risk are referred directly (Figure 2). The increase in abnormal smears during the control test caused a small increase in the number of participants who, after a control test, were still ('indirectly') referred to the gynecologist (from 17.5% to 18.4%). However, in total, the number of referrals to the gynecologist decreased (from 43% to 33% of HPV-positive participants).



**Figure 2** HPV-positive participants with direct or indirect referral under old vs. new referral scheme

## Detected Abnormalities After Referral

Because after the adjustment of the referral scheme only clients with high-grade cell abnormalities, or HPV16/18 (in combination with cell abnormalities) are referred, it was expected that relatively more abnormalities would be found after direct referral. After direct referral, indeed, relatively more cervical abnormalities that need to be treated by the gynecologist were found following the change in the referral scheme. A relevant abnormality means a CIN2 diagnosis or more severe (CIN2+). Before the change, 44% of directly referred participants had CIN2+, after the change 61%. The total percentage of referred participants in whom no relevant abnormality was found (i.e., false positives; both after direct and indirect referral) decreased significantly after the change (from 26% to 18%).



**Figure 3** HPV-positive participants with no relevant abnormality (<CIN2) vs. relevant abnormality (CIN2+) under old vs. new referral scheme.

When looking at all HPV-positive participants instead of the referred participants, the percentage of detected CIN2+ (from 17% to 16%) and CIN3+ (from 9.4% to 8.9%) is slightly lower under the new referral scheme (Figure 3). Because participants in the more recent period were followed for a shorter time, the detected abnormalities will still increase somewhat over time. In that case, the percentages of CIN2+ will not be lower but equally high, and it therefore appears that among HPV-positive participants ultimately about the same number of clinically relevant abnormalities are found, and the effectiveness of the program is maintained. The decrease in unnecessary referrals (<CIN2) can be attributed to more effective risk selection, which means fewer women with a low risk of abnormalities are unnecessarily referred.

## Conclusion

The new referral scheme appears to contribute to a more efficient screening program. It ensures better selection of clients for referral to examination by a gynecologist, resulting in fewer clients being unnecessarily referred to the gynecologist while still detecting the same number of abnormalities.