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Women who participate in spontaneous screening are not at higher risk for cervical cancer than women who attend programme screening

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Abstract

Up to 1995, programme screening for cervical cancer in The Netherlands was targeted at women between 35 and 54 years of age at 3-yearly intervals. Spontaneous screening in addition to programme screening was common practice. Our aim was to compare the underlying risk for cervical neoplasia for women involved in both types of screening. From the national pathological database, we retrieved all primary smears ($n = 693\,318$) taken in 1994 in The Netherlands. Among the smears registered for screening purposes (39%), 79% was taken within the mass screening programme and 21% was taken for spontaneous screening. The underlying risk was studied from the detection rates of histologically confirmed severe dysplasia or worse, using a multivariate loglinear model, including age and screening history. The detection rate of at least severe dysplasia, adjusted for age and screening history, was equal for women who had a spontaneous smear and for those who had a programme smear (odds ratio (OR): 0.97; 95% Confidence Interval (CI): 0.84–1.14). In our data, women participating in spontaneous screening were not at a higher risk for cervical cancer than women who used programme screening. Therefore, all asymptomatic women in the Netherlands should follow the general guidelines for age-range and screening-interval. © 2002 Published by Elsevier Science Ltd.

Keywords: Cervical cancer; Mass screening; Spontaneous screening

1. Introduction

In The Netherlands, as in many European countries, the efficiency of screening for cervical cancer suffers from an incomplete coverage combined with an excessive use due to spontaneous smear taking [1–3]. The lack of coverage decreases the effectiveness, also due to a higher risk for cervical cancer in non-participants [4]. Excessive use of cervical smears will result in a proportional increase in costs and negative side-effects, while the extra effect on mortality and incidence will be relatively small [5]. The effectiveness of this public health programme depends on the frequency of screening and the age-ranges. The corresponding guidelines were determined to give a favourable balance between negative side-effects (costs and iatrogenic harm) versus the positive effects (reduction of incidence and of mortality from cervical cancer).

Screening for cervical cancer in The Netherlands is organised by sending out personal invitations to all women at specific ages. In this way, the programme aims at a high attendance rate and a limited frequency of smear taking. Spontaneous screening, however, in addition to programme smears, is common practice. Both types of screening are funded by the national health services. In spontaneous screening, preventive smears are taken on the initiative of the women and/or her physician. Usually, there is no specific information available about the motives for these spontaneous smears. In the past, we have estimated the efficiency of spontaneous screening to be low, due to the low starting age and short screening-interval used in spontaneous screening [6,7]. This is in line with international opinion [8,9]. Accordingly, since 1995, the Dutch government has discouraged spontaneous screening by reducing the possibilities for funding. Gustafsson and colleagues [10]

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questioned this point of view, based on a comparison of detection rates of carcinoma *in situ* in smears taken within the mass screening programme with smears taken outside the programme. A factor that could increase the effectiveness of spontaneous screening is that women who use this type of screening might be at higher risk for cervical cancer, in other words, that these women have been selected on individual characteristics for a more frequent screening by themselves or by their physician.

In the present study, our aim was to investigate if there was a difference in the underlying risk of cervical cancer for women who use spontaneous screening compared with women who participate in the screening programme. To this end, we distinguished between programme screening and spontaneous screening on whether or not the smear was registered as a programme smear. From both types of screening, we compared the detection rates for at least high-grade dysplasia, adjusting for age and screening history.

2. Patients and methods

In The Netherlands, all cytological and histological examinations are registered in a centralised database: the Pathological National Automated Archive (PALGA). The PALGA started on a limited scale in 1975. From 1990 onwards, over 95% of the cervical examinations were registered and the coverage had increased by 100% in 1994. We retrieved all relevant information on cervical cytology and histology from this national database. In 1995, the new national screening policy was introduced, targeting women 30–60 years at 5-year intervals. The present study was restricted to smears taken in 1994, because this year was before the introduction of the new screening programme and the high coverage in the years before 1994 guarantees a high degree of completeness in information about the screening history.

In the PALGA, persons are identified by the first four characters of their maiden name, their date of birth and gender. Although this identification method can lead to misclassifications (a proportion of persons will have equal identifying characteristics, and (typing) errors will result in false registrations) it provides the possibility to follow persons over time.

The study material was restricted to all primary smears taken in 1994, being registered as either programme smears or spontaneous smears. Primary smears, as opposed to follow-up smears, were defined as smears with no positive (showing at least atypia) cytology or histology in the previous five years; smears with previous borderline (requiring a repeat smear) and unqualified smears (not suitable for diagnosis) that had a sufficient and negative follow-up were also included. According to the PALGA registry, 932 805 smears were taken in 1994 in The Netherlands, of which 26% had a previous positive or inadequate result in the preceding 5 years. For all primary smears, we assessed whether a previous primary smear was available and if so the 'screening-interval' was calculated, defined as the interval since the last primary smear.

In the PALGA, the indication for taking the smear was registered for 48% of the primary smears taken in 1994. The indication is registered by the general practitioner and imported by the diagnosing pathology laboratory. On the basis of the available categories, we distinguished between 'programme smears', which were taken because of an invitation for mass screening, spontaneous smears, which were taken because of preventive reasons, but outside of the screening programme, and smears taken because of a medical indication. Primary smears for which no information on the indication was available were classified as 'unknown indication'. Smears with a medical indication and those classified as unknown indication were excluded from the analysis.

The detection rates were estimated from the maximum histological diagnosis until 1 April 1998, which was classified as no neoplasia, cervical intra-epithelial neoplasia (CIN) I (mild dysplasia), CIN II (moderate dysplasia), CIN III (severe dysplasia and carcinoma *in situ*) or invasive cervical cancer. We compared the underlying risk for cervical cancer for spontaneous smears with that for programme smears, using the detection rate of histologically-confirmed CIN III or worse, adjusted for age and screening history. Screening history is a combination of rank of the smear and interval since the last smear. The independent effects of type of screening, age and screening-history were estimated by logistic regression, and the interactions between the variables age and screening-history, age and type of screening and screening-history and type of screening were included in the model if they significantly improved the fit. The regressions coefficients of the best fitting model and their standard errors were used to calculate odds ratios (OR) and their 95% confidence intervals (95% CI).

3. Results

In 1994, there were 693 318 primary smears taken in The Netherlands. Among the smears with a registered indication (48% of all primary smears) 64% was taken after an invitation for mass screening, 17% of the smears was taken for spontaneous screening and 19% of the smears was taken for medical indication. Within the mass screening programme, 924 lesions (histologically-confirmed CIN III or worse) were detected, giving a detection rate of 4.3 CIN III or worse per 1000 programme smears. Another 308 lesions were detected by

spontaneous screening, leading to a detection rate of 5.3 CIN III or worse per 1000 spontaneous smears. Table 1 shows the detection rates and the number of smears for spontaneous smears and for mass screening are presented by age and screening history. The distribution of the number of smears by age and screening history differs for the two types of screening. Spontaneous smears were predominantly taken at younger ages and 30% of the spontaneous smears are first smears (rank 1). Although, the crude detection rate is higher for spontaneous smears than for programme smears, the detection rate of the first smears and for repeat screening within 3 years is lower for spontaneous screening compared with programme screening.

In the multivariate model, the OR for the detection of histologically-confirmed CIN III or worse for the variables age and screening-history confirm current knowledge: the detection rate is highest in age-group 30–34 years, is higher for first smears than for repeat smears, and increases with longer screening-intervals (Table 2). An exception is that smears taken within a year of the preceding smear have a relatively high detection rate of CIN III or worse. This was seen for both programme and spontaneous smears (Table 1). Possibly these smears were taken in high-risk women, without specifying this as the indication for smear taking.

The detection rate of histologically-confirmed CIN III or worse of spontaneous screening, adjusted for age and screening history, was equal to that of programme screening (OR: 0.97; 95% CI: 0.84–1.14). The model which best described the data included interaction between age and screening-history. The inclusion of the interaction hardly altered the estimation for the OR (OR: 0.97; 95% CI: 0.83–1.13).

4. Discussion

We compared the detection rates of histologically-confirmed CIN III or worse in spontaneous screening with that of programme screening, as a proxy for the underlying risk for cervical cancer in the women involved. The crude detection rate of histologically-confirmed CIN III or worse was higher for spontaneous smears (5.3 per 1000 smears) compared with programme smears (4.3 per 1000 smears). In a multivariate model, which corrects for age and screening history, the adjusted detection rate was equal for spontaneous screening compared with programme screening. The results indicate that the underlying risk for women who had a spontaneous smear is not higher than for women who had a programme smear.

Table 1
Detection rates of mass screening and of spontaneous screening by age and by screening history, PALGA 1994

Variable category	Mass screening			Spontaneous screening		
	Detection rate	Smears		Detection rate	Smears	
	(CIN III + per 1000 smears)	Number	Percentage	(CIN III + per 1000 smears)	Number	Percentage
Age (years)						
< 25	1.7	2316	1	2.3	4430	8
25–29	6.1	7695	4	7.2	9763	17
30–34	9.3	6694	3	9.4	12 296	21
35–39	6.6	67 280	31	5.5	7813	14
40–44	3.7	55 159	26	3.8	6633	11
45–49	2.7	36 135	17	2.6	6054	10
50–54	1.4	35 953	17	2.0	3981	7
55–59	3.1	1610	1	1.7	2982	5
60–64	3.2	632	0	3.0	1672	3
65 +	12.5	720	0	5.3	2075	4
Total	4.3	21 4194	100	5.3	57 699	100
Screening history						
First smear	8.4	36 333	1	7.8	17 497	30
Rank > 1, interval < 1 year	4.5	17 352	8	3.6	4673	8
Rank > 1, interval 1–2 years	2.5	16 889	8	1.7	7548	13
Rank > 1, interval 2–3 years	2.4	48 237	23	2.0	8006	14
Rank > 1, interval 3–4 years	2.6	52 568	25	4.1	6749	12
Rank > 1, interval 4–5 years	4.3	12 628	6	5.6	4990	9
Rank > 1, interval 5 + years	6.3	30 187	14	8.5	8236	14
Total	4.3	214 194	100	5.3	57 699	100

PALGA, Pathological National Automated Archive; CIN III, severe dysplasia and carcinoma *in situ*.

Table 2
Odds ratios (OR) for detection of CIN III or worse, estimated in a multivariate model for age, screening history and type of screening, PALGA 1994

Variable category	Odds ratio	95% Confidence Interval (CI)
Age (years)		
<25	0.17	0.10–0.29
25–29	0.62	0.49–0.79
30–34	1.00	Reference
35–39	0.75	0.62–0.91
40–44	0.50	0.40–0.62
45–49	0.35	0.27–0.45
50–54	0.20	0.15–0.27
55–59	0.26	0.14–0.50
60–64	0.31	0.15–0.66
65+	0.65	0.41–1.03
Screening history		
First smear	1.00	Reference
Rank >1, interval <1 year	0.55	0.44–0.70
Rank >1, interval 1–2 years	0.29	0.22–0.38
Rank >1, interval 2–3 years	0.33	0.27–0.40
Rank >1, interval 3–4 years	0.40	0.33–0.48
Rank >1, interval 4–5 years	0.58	0.46–0.74
Rank >1, interval 5+ years	0.87	0.74–1.02
Type of screening		
Mass screening	1.00	Reference
Spontaneous screening	0.97	0.84–1.14

CIN III, severe dysplasia and carcinoma *in situ*: PALGA, Pathological National Automated Archive.

Detection rates in this analysis are used as a proxy for underlying risk. However, detection rates could also have been influenced by differences in the management of the smears: the classification criteria of the smears, the quality of the smear (collection of material, fixation and cytological evaluation), the recommendations for an additional smear or referral and in the follow-up. We expect a similar management for spontaneous smears and programme smears in The Netherlands, because the two types of smears are taken by the same general practitioners, classified by the same cytological laboratories, and histological follow-up takes place at the same gynaecology departments. If there are differences in management of the smears, they must reflect differences in the *a priori* expected risk by the physician involved. Since programme smears are in principle taken in asymptomatic women, the expected risk will be low. Possibly, smears taken 'outside the programme' are managed more carefully. This, however, would lead to higher detection rates of spontaneous smears, leading to an overestimation of the underlying risk for women who used spontaneous smears.

More than half of the smears was registered as 'unknown indication'. We explored whether these smears are a selected group, e.g. with relatively many smears taken for medical indication, by comparing the detection rates of histologically confirmed CIN III or worse, adjusted for age and screening history, for smears taken for unknown indication with smears taken for known indication. We found no significant difference (OR: 1.03; 95% CI: 0.98–1.09). This suggests that the underlying risk for cervical cancer for smears taken for unknown indications was not significantly higher.

Is spontaneous screening less efficient than programme screening? In general, spontaneous screening does not follow the recommendations for age range and interval between successive screenings, because younger women are being screened and many smears are taken at too short an interval, which is considered inefficient. In the Dutch data reported here, we also see these differences between the spontaneous and programme screening: 57% of all spontaneous smears were taken in women outside the target age group of 35–54 years of age, and another 20% was taken in the target age group, but within 3 years after the preceding smear. However, 23% of all spontaneous smears were taken in women of 35–54 years of age, after a screening-interval of more than 3 years, which is in agreement with the guidelines of the programme.

However, it has been argued that spontaneous screening catches women at high risk who are identified by physicians on basis of the knowledge of individual characteristics of women. Gustafsson has questioned the inefficiency of spontaneous screening by pointing out that in Sweden the detection rates for high grade cervical neoplasm were on average higher in spontaneous screening compared with programme screening in the period 1969–1988, but with a sharp trend from higher CIN III rates for spontaneous screening in the early years to lower rates in the years 1984–1988 [10].

In the Dutch data as well, the crude detection rates for histologically confirmed CIN III or worse in spontaneous smears are higher than in programme smears. Use of detection rates of (high grade) CIN as a surrogate measure for prevention of cancer and related mortality would favour more screening in younger age, since detection rates of CIN III are relatively high in young age. But the progression rate of (high grade) CIN is rather slow, and a considerable proportion will never progress to invasive cancer, especially in young ages [11]. This means that especially at younger age many CIN is detected and treated without health benefits, and detection is associated with considerable adverse health effects and costs. The (official) Dutch policy is based on the potential impact on the incidence of invasive cancer and on cervical cancer mortality rather than on CIN detection rates and, therefore starts later. Spontaneous screening, before the starting age of the screening programme, reduces the efficiency of smears taken at the target ages.

To analyse whether spontaneous screening, with its smears taken at a younger age and at shorter intervals, is inefficient, the crude detection rates are not relevant,

the question is whether there is an extra risk involved when the spontaneous smears were performed. Such an extra risk can be identified if spontaneous and programme smears are compared on the basis of detection rates that are adjusted for age and interval since the previous smear. Such an extra independent risk would imply that there was a good reason for a more intensive screening than currently recommended. We compared detection rates, while adjusting for differences in age and screening history (number of previous smears, interval since previous smear), and found no difference in the adjusted detection rates between spontaneous and programme smears. We conclude that women who used spontaneous screening have a similar underlying risk for cervical cancer as women who used programme screening. Therefore, there was no reason to depart from the recommended age-range and screening-interval when spontaneous smears were taken.

Having come to this conclusion, we can consider those smears that were performed extra to the recommended schedule as inefficient. For example, an extra spontaneous smear, after a programme smear at age 47 years, taken for example at age 48 years produces a shorter than intended interval for both the spontaneous smear itself and the subsequent programme smear at age 50 years. Nineteen percent of all preventive smears (mass screening and spontaneous screening) were taken in women outside the age-range of 35–54 years. Furthermore, 33% of the smears were taken in women of the target age group, but the screening interval was less than 3 years; the mean interval was 1.9 year. From the point of view of a 3-year schedule ($1–1.9/3 = 0.37$), 37% of these smears can be seen as unnecessary. An estimate for the number of extra smears (on top of the recommended age and interval schedule) is $19\% + 33\% \times 37\% = 31\%$. These extra inefficient spontaneous smears occur in many countries with an organised screening programme.

Smears taken within a year of the preceding smear showed relatively high detection rates in the multivariate model (Table 2). Similar high detection rates for smears taken within a short interval are usually seen in other registrations, such as in Sweden [10] and in British Colombia [4]. These results can be explained by the hypothesis that a considerable proportion of these smears are taken within a short interval because of signs or symptoms, despite the fact that they are registered as preventive smears. If we calculate the smears taken within 1 year not as excessive, the proportion of excessive programme smears becomes 25% of all preventive smears (mass screening and spontaneous screening).

In 1995, new guidelines for the screening programme were introduced, targeting women between 30 and 60 years of age with a screening-interval of 5 years. These new guidelines do not influence our conclusion, that women with spontaneous smears are not at a higher risk for cervical cancer. However, the estimate of the number of inefficient smears is influenced by these new guidelines, because the proportion of smears taken after a short interval, is lower with the new guidelines. Therefore, our estimate of the number of extra smears will be an underestimate of the actual number of extra smears in the new setting.

We conclude that in The Netherlands, spontaneous screening is not selectively used by women at a higher risk for cervical cancer. Therefore, women participating in spontaneous screening do not represent a higher risk group and therefore should not be screened more intensively than according to the programme guidelines on age-range and screening interval, unless symptoms are involved. If all preventive smears are taken following the recommended age-range and screening-interval prescribed by the programme, in The Netherlands the number of primary smears will be reduced by approximately one fourth.

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