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Original Paper

Interaction of Spontaneous and Organised Screening for Cervical Cancer in Turin, Italy

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In a screening programme for cervical cancer, coverage of the target population is a major determinant of effectiveness and cost-effectiveness and is one of the parameters for programme monitoring recommended by the "European Guidelines for Quality Assurance". An organised screening programme was started in Turin, Italy, in 1992. Spontaneous screening was already largely present, but coverage (proportion of women who had at least a test within 3 years) was low (<50%) and distribution of smears uneven. No comprehensive registration of spontaneous smears was available. All women were invited for the first round, independently of their previous test history. Coverage was estimated by integrating routine data from the organised programme with data on spontaneous screening obtained by interviews of a random sample of 268 non-compliers to invitation and 167 compliers. Overall (spontaneous + organised) coverage was estimated to be 74% (95% CI, 71–78%). The proportion of the target population covered as an effect of invitation was estimated to be 17% (95% CI, 15–20%). Invitations were successful in increasing coverage in previously poorly screened groups. Although 20–25% of compliers was estimated to have had further tests before the end of the round, we estimated that switching to a 3-year interval saved approximately 0.26 tests per complier. This suggests that invitations to an organised programme even to previously covered women, can be a cost-effective policy. Our method of estimating overall coverage can be useful in many other European areas where a comprehensive registration of smears is not available. © **1997 Published by Elsevier Science Ltd.**

Key words: cervical cancer, screening, coverage, costs

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INTRODUCTION

IN MANY European countries, screening for cervical cancer has developed spontaneously, in the absence of organised programmes based on active invitation. A frequent result is an inadequate coverage of a large proportion of the female population, and a short interval between tests among regularly screened women [1]. In addition, women not adequately screened tend to be selected, commonly for being of older age, single and of lower social class [2–9], leading to inequalities in access. Therefore, organised programmes have been introduced with the purpose of increasing coverage and improving cost-effectiveness [1, 10, 11]. A further aim is that of reducing inequalities in access [1]. Coverage is defined as the proportion of women who had at least one Papanicolau (Pap) test within a period corresponding to the desired interval between tests.

When an organised screening is implemented in the presence of previous spontaneous activity, it is possible either to invite all women, independently of their previous screening practice, or to invite only those not already covered. This last option is recommended by the EC guidelines [1]. However, it is presumed that nominal lists of all or almost all cervical smears taken in the programme area are readily available to organisers. The same data are needed in order to measure directly coverage of the target population, one

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of the basic parameters for programme monitoring recommended by the EC [1].

In Turin, Italy, an organised programme started in June 1992. Before then, relevant spontaneous screening was present: a population survey conducted in 1986 [12] showed that 48% of women aged 18–70 years had never had a Pap test and that coverage within 3 years was approximately 37%, while 60% of women with at least three tests reported yearly tests. Age, education and marital status were strongly independently associated with having been tested, both ever, and in the last 3 years [13].

In the first screening round, all women in the target age (25–64 years) were invited, independently of their previous test history. The main reason was that, since tests were taken and interpreted in a large number of different centres, almost all without usable computerised files, it was impossible to identify those already screened. This was also done in the hope that, by joining the organised programme, already-screened women would shift to a 3-year interval.

We conducted the present study in order to verify if active invitation did actually result in a substantial increase in coverage and in a reduction of selection. Indeed, it was possible that compliers were almost only women already covered by spontaneous practice. In addition, we wanted to verify whether already-screened women complying with our invitation did actually shift to a 3-year interval, or if they simply added a further test to their usual practice.

Given the lack of census registration of spontaneous activity, we estimated coverage by integrating data obtained by the computerised files of the programme with data of spontaneous activity based on interviews.

PATIENTS AND METHODS

Drawing directly from the computerised population-registry of the Archives Department of the city of Turin (including all women with an official permanent address in Turin), women aged 25–64 years were sent a letter, signed by their general practitioner, with a predefined appointment at a family planning clinic, modifiable by a telephone call. Non-attenders to the appointment were sent a reminder. A mass media campaign was conducted just before the start of the programme, but not repeated.

Data on compliance to invitation in the first 3 years of activity were obtained from the computerised files of the screening programme, including census registrations of all invitations and of all smears taken within the programme.

A random sample of 175 attenders to the invitation in the first screening round, and 347 non-attenders, were obtained at the end of 1994 from the computerised screening files. The sample size was determined in order to have a confidence interval of $\pm 5\%$ in the estimate of spontaneous coverage among non-compliers to invitation (with a true value of 50%, corresponding to the highest variance with the assumed binomial distribution). Sampling lists included all women invited until June 1994. The proportion of attenders in the sample was the same observed until that moment in the invited population, so that the sample was self-weighting. Each subsample (compliers and non-compliers) was independently stratified for age and centre where the women were invited (roughly corresponding to the city district of residence): therefore, the two samples were not matched.

Most interviews were conducted by telephone by one trained interviewer using a standardised questionnaire. In order to avoid interview refusal by non-compliers to invitation, we introduced ourselves as an agency appointed to study screening activities in Turin and no pressure to participate in the screening programme was applied. Women without a telephone, or difficult to trace, were asked by letter to contact us. Repeated attempts were made, on different days and hours. All women who were impossible to contact were sent a reduced self-administered questionnaire to be returned free of charge.

Overall coverage and coverage attributable to the organised programme were estimated as: $a + (1 - a)b$ and $a(1 - d)$, respectively, where: a = measured compliance in invited women, b = proportion of sample non-compliers reporting at least one Pap test in the 3 years before interview and d = proportion of sample compliers reporting at least one test in the 3 years before invitation.

In computing confidence intervals, compliance with the invitation was considered to be without random error. A similar method was used to compute overall coverage and coverage due to screening by education, place of birth and marital status. In such a case, however, compliance was estimated on the basis of sample subjects (all sample subjects, since these data were obtained by linkage with a file available from the population registry; linkage was not extended to the whole population because of computational costs).

Each woman in the sample was also classified as covered (those who either complied or had a spontaneous test within 3 years of interview) or not covered. Adjusted measures of relative coverage were estimated by multiple regression, using generalised linear models with a logarithmic link and a binomial distribution of errors [14] by the SAS GENMOD Procedure [15]. This was possible since the sample was self-weighting. The same was carried out for variables associated with compliance with invitation. Approximate 95% confidence intervals were computed from Wald-type standard errors of the regression coefficients. When a determinant was classified in more than two categories, a test of its overall effect was computed, based on the likelihood ratio test [16]. Checks were performed to ensure that in no subject was the expected probability of the studied event >1 or <0.

RESULTS

Overall, interviews were conducted with 435/522 (83%) sampled women. Among non-attenders to the invitation, 268 (77.2%) were interviewed (10 of them by reduced questionnaire); 27 (7.8%) refused; 43 (12.4%) could not be found despite repeated attempts; 3 had emigrated and 4 were not interviewable. Among attenders 167 (95.4%) were interviewed (1 refused, 6 could not be contacted and 1 was not able to be interviewed).

Compliance with the invitation in the programme was stable around 34% during each year of the first round (Table 1).

The proportion of non-compliers to the invitation reporting at least one Pap test in the 3 years before interview was 61%. Overall coverage (proportion of women who either complied with the invitation or had at least one test in the last 3 years) was estimated to be 74% (95% CI, 71–78%) (Table 2A). Among compliers to the invitation, 49% reported a spontaneous test in the 3 preceding years. The coverage attributable to the organised programme (proportion of women who both complied with the invitation and did not have a spontaneous test in the 3 years

Table 1. Compliance with invitation in the 3-year round

Age class	1st year 1 June 92–30 June 93 Women invited	1st year Compliance (%)	2nd year 1 July 93–30 June 94 Women invited	2nd year Compliance (%)	3rd year 1 July 94–30 June 95 Women invited	3rd year Compliance (%)	Total 1 June 92–30 June 95 Women invited	Total Compliance (%)
25–34	9173	27.4	13 574	27.6	14 115	27.9	36 862	27.7
35–44	9582	34.2	13 876	33.7	14 784	32.7	38 242	33.5
45–54	11 009	37.8	15 389	37.7	16 655	38.0	43 053	37.8
55–65	11 535	33.4	17 271	33.9	20 213	36.9	49 019	35.0
Total	41 229	33.5	60 110	33.4	65 767	34.3	167 176	33.8

before it) was estimated to be 17% (95% CI, 15–20%) of the target population (Table 2B). Coverage among non-compliers increased to 63% if hysterectomised women were excluded. Among non-compliers, 5 women (2.3% of those covered) had their first test after invitation, possibly as an indirect effect of the invitation itself. The data suggest that the organised programme may have reduced differences in coverage, especially between women with middle–low versus women with high education (Table 3). There was, however, no statistically significant difference in the proportion of coverage added by the organised programme, and a statistically significant linear increase of coverage with increasing education was still present (Table 4).

Compliers were interviewed on average 1.5 years after invitation. Some 12% reported at least one spontaneous test after invitation. Approximately half of these were sought due to symptoms and half because of a belief in a shorter interval than the one recommended. This approximately corresponds to 20–25% of women having extra tests in a 3-year round. Data suggest that very few tests were performed in the first year after invitation (Table 5), and that very few women, if any, performed more than one extra test. However, 23% of compliers reported that, before invitation, they usually had tests every year; a further 10% of compliers reported previous tests every 2 years.

DISCUSSION

The present study showed that an organised programme based on personal invitations to all women in the target population was able to increase coverage to a level of 74%. The EC target is 85%, but the actual coverage of EC women was estimated to be 65% in 1991 [1]. The increase seen in this study was very high when compared to the 1986 figure of 37%, which concerned women in the age range 18–70 years [12]. Part of the increase is attributable to a spontaneous trend: in a further survey, conducted in 1991, coverage of women aged 18–70 years was 43%. However, the direct effect of invitation was to increase coverage by at least 17% of the target population. Attention given to this problem by media and by the medical community, and the initial mass media campaign, probably indirectly contributed to increasing the spontaneous activity.

Coverage is one of the most important factors in increasing both effectiveness and cost-effectiveness of cervical cancer screening [17]. The decrease of cervical cancer incidence and mortality in Finland and Sweden has been attributed to nationally organised programmes leading to a better coverage of the population [18–20]. In Denmark, incidence and mortality for cervical cancer were significantly lower, after adjustment for overall smear taking activity, in counties where organised programmes had been

Table 2. Overall coverage (A) and coverage attributed to the organised screening programme (B)

(A)

Age class	Compliance with invitation[a]	Coverage among non-compliers[b]	Overall coverage[c]	(95% CI)
25–34	28%	63%	74%	(66–82%)
35–44	34%	66%	78%	(70–85%)
45–54	38%	62%	76%	(69–84%)
55–65	35%	55%	70%	(63–78%)
Total (25–65)	34%	61%	74%	(71–78%)

(B)

Age class	Coverage of compliers with invitation[d]	Coverage attributed to screening programme[e]	(95% CI)
25–34	50%	14%	(9–19%)
35–44	56%	15%	(10–20%)
45–54	43%	21%	(16–27%)
55–65	48%	18%	(13–23%)
Total (25–65)	49%	17%	(15–20%)

[a]Measured from the computerised programme files.

[b]Estimated by interview from a sample of 268 women who did not comply with invitation. Proportion of sample non-compliers reporting at least one Pap test in the 3 years before interview.

[c]Estimated as $[a + (1 - a)b]$.

[d]Estimated by interview from a sample of 167 compliers with invitation. Proportion of sample compliers reporting at least one test in the 3 years before invitation.

[e]Estimated as $a(1 - d)$.

Table 3. Estimated coverage without organised programme, coverage attributed to the organised programme and overall coverage according to age, education, place of birth and marital status

	Coverage without organised programme[a]	Coverage attributed to organised programme[b]	Overall coverage[c]
Age			
25–34	60%	14%	74%
35–44	63%	15%	78%
45–54	55%	20%	76%
55–	52%	18%	71%
Education			
No qualifications	47%	14%	61%
5th grade	52%	16%	68%
13th grade	54%	22%	76%
Diploma	64%	15%	78%
University degree	75%	13%	88%
Place of birth			
Northern Italy	59%	16%	75%
Southern Italy	53%	19%	71%
Other	64%	22%	85%
Marital status			
Single	55%	13%	67%
Married	58%	19%	77%
Widowed	52%	9%	61%
Divorced	63%	14%	77%

(a) estimated as c–b.
(b) and (c) estimated as in Table 2, but compliance was estimated on the basis of sampled women (data were unavailable for all subjects), not of all invited women.

active for many years than in countries without organised activity [21].

Invitations were also able to increase coverage in subgroups of previously poorly screened populations. Although coverage was still higher in more educated women, this trend was less steep than in 1986. Differences in coverage by age and place of birth were very small, if any, in the present study. Although the traditional belief that women who do not undergo spontaneous screening are at higher risk of cervical cancer has recently been challenged [22], active

Table 4. Relative overall coverage and relative coverage attributed to the organised screening programme

	No. of women covered			Relative coverage			
				Overall		Programme	
	Total	Overall	By programme	RR*	(95% CI)	RR†	(95% CI)
Age							
25–34‡	101	75	15	1		1	
35–44	103	82	18	1.03	(0.89–1.17)	1.14	(0.60–1.17)
45–54	104	82	26	1.05	(0.92–1.21)	1.68	(0.92–3.04)
55+	127	92	26	1.02	(0.88–1.19)	1.65	(0.90–3.05)
Education							
No qualifications‡	34	21	5	1		1	
5th grade	112	79	21	1.10	(0.87–1.39)	1.45	(0.58–3.62)
13th grade	143	112	36	1.20	(0.95–1.50)	2.18	(0.89–5.31)
Diploma	114	91	19	1.21	(0.96–1.52)	1.72	(0.65–4.57)
University degree	32	28	4	1.33	(1.02–1.74)	1.19	(0.33–4.24)
Place of birth							
Northern Italy‡	256	196	45	1		1	
Southern Italy	154	113	33	1.01	(0.91–1.12)	1.32	(0.86–2.02)
Other	25	22	7	1.12	(0.94–1.34)	1.57	(0.79–3.10)
Marital status							
Single‡	55	38	8	1		1	
Married	329	258	70	1.11	(0.95–1.30)	1.25	(0.63–2.46)
Widowed	35	22	4	0.96	(0.75–1.23)	0.63	(0.20–2.00)
Divorced	16	13	3	1.10	(0.82–1.47)	1.11	(0.33–3.72)

*Relative prevalence of women who either complied or had a spontaneous test within 3 years of interview—adjusted for the other variables in this table by multiple regression with loglink and binomial distribution of errors (see Patients and Methods).
†Relative prevalence of women who complied to invitation and did not have a test in the 3 years before invitation. Adjusted as*.
‡-Reference category.
NB: P values, computed by likelihood ratio chi-square, were non-significant for overall effect in all categories. $P < 0.05$ for linear trend for the effect of Education on Overall Coverage.

Table 5. Women with at least one extra test by duration of follow-up

Duration of follow-up	Mean duration (years)	Total women *n*	Women with at least one extra test *n*	%
<1 year	0.83	31	1	(3)
1–2 years	1.53	98	12	(12)
>2 years	2.34	30	6	(20)
Total	1.55	159	19	(12)

invitation could reduce inequalities in access to early diagnosis, and therefore in cancer risk.

Data show that 20–25% of the women who joined the programme also had tests outside the protocol. Such a proportion is higher than that recommended by the EC guidelines. However, entering the organised programme seems to have been effective in convincing many women to change their frequency of test, leading to an overall test saving. Women with negative cytology obtained in the organised programme received a letter stating that they will be re-invited after 3 years and that more frequent tests did not significantly increase protection. Data are consistent with approximately 0.25 extra tests performed per complier. Approximately two extra tests performed outside the protocol were saved in a 3-year round for each complier previously having yearly tests (23% of compliers) and approximately 0.5 tests in the same time interval were saved for each complier previously having tests every 2 years (10% of compliers). Therefore, approximately 0.51 ($0.23 \times 2 + 0.1 \times 0.5$) extra tests per complier were saved as an effect of switching to a 3-year interval. The overall effect of the organised programme was of saving 0.26 tests (0.51 minus 0.25) performed outside the protocol per complier every 3 years. Screening more frequently than every 3 years improves protection only marginally, and leads to low cost-effectiveness [11, 23–25]. Our data show that inviting all women could be a more cost-effective policy than the 'integrated' approach.

Our approach for estimating coverage, based on interviews with a sample of non-compliers to the invitation, provided reasonably precise and reliable estimates and is plausibly the only one applicable in many situations similar to ours.

Our estimate of coverage concerns women invited to the organised programme. Not all the target population had been invited when the sample was drawn. However, the invited population can be considered a random sample of the target population, consistent with the fact that compliance is stable in time. Therefore, our estimate can be considered a reliable projection of coverage when all the target population will be invited.

Non-responders to the interview were 23% among non-attenders to the invitation. When considering just this group, and comparing those interviewed and those not interviewed by socio-demographic variables (available for all from the population registry), small differences were found. Non-respondence could theoretically have led to some overestimate of coverage. However, even under the extreme assumption that none of the non-responders had had a spontaneous Pap test in the previous 3 years, the estimated overall coverage would be 65%. Data suggest that some non-compliers to invitation had an official permanent address in Turin but were probably not present for most of their time (and therefore it was impossible to contact them for the interview). Self-reported tests could have been overestimated, leading to an overestimate of overall compliance, and to an underestimate of the effect of organised screening. We used the same questions asked in the previous survey [12, 13]. Data are therefore comparable. On such occasions, questions were validated and answers found to be consistent with the actual number of tests annually performed in Turin.

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