PERGAMON

European Journal of Cancer 36 (2000) 2177–2188

European Journal of Cancer

www.ejconline.com

Overview of important cervical cancer screening process values in European Union (EU) countries, and tentative predictions of the corresponding effectiveness and cost-effectiveness

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Abstract

The objective was the evaluation of the (cost-)effectiveness of cervical cancer screening in the European Union (EU) countries. Data were collected on recommended screening age ranges and intervals, coverage, proportion of non-negative smears and smear use. Estimates reported by representatives of each participating Member State were compared, and used as input for model based on (using the MISCAN simulation model for cancer screening) effectiveness and cost-effectiveness calculations. Differences in coverage from below 50 to 82% resulted in more or less proportional differences in expected percentage life-years lost reduction, almost regardless of differences in 7–50+ smears recommended in a lifetime. Differences in screening intensity (resulting from the recommended number of smears per lifetime and the number of excess smears on top of these recommendations) resulted in more than 2-fold difference in the expected number of smears per percentage life-years lost reduction. (Cost-)effectiveness predictions would have greatly improved if estimates of long-term coverage had also been available. To conclude, estimates for a restricted set of well defined parameters — a few for short and long-term coverage and one for the total number of smears — are quite useful for country-specific (cost-)effectiveness evaluations. The main, and to some extent, unsolvable problem for further improvement of the analysis is the lack of reliable country-specific estimates for the background risk of cervical cancer in women eligible for screening in the near future.

Keywords: Cervical cancer screening; Coverage; Smear use; Mortality reduction; Cost-effectiveness; Simulation (model)-based analysis

1. Introduction

The usefulness of cervical cancer screening depends on the positive and negative health effects and the costs. Therefore, we collected estimates for the values of a set of key process parameters for each participating country or region of the European Union (EU). This restricted set — coverage, proportion of non-negative smears, and total number of smears for the (excess) smear use — were chosen because of their impact in predicting the effectiveness and cost-effectiveness of screening in the countries. The first objective was to describe the screening activities in EU countries quantitatively, following the publication of the "European Guidelines for Quality Assurance in Cervical Cancer Screening" in 1993 [1]. The second objective was to try to use the data for assessing the effectiveness and cost-effectiveness of screening in the respective situations. The overall aim was to provide data for rational decision making concerning cervical cancer screening on a national, regional or local level.

Coverage, proportion of positive smears and excess smear use are closely related to each other and to the effects and costs of Papanicolaou (Pap) smear screening. Smears either contribute to coverage, or they are excess smears. Those contributing to coverage help to reach the potential effectiveness of the screening programme. Excess smears consist of smears outside the target age range or those taken after too short an interval. They add little to the effectiveness of the regular programme

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0959-8049/00/$ - see front matter
PII: S0959-8049(00)00330-0

smears and therefore decrease the cost-effectiveness of the screening activities. Follow-up smears, which can be regarded as diagnostic excess smears, depend on the proportion of positive (or at least non-negative) smears. Positive smears are the key to positive health effects, but they also generate negative health effects.

2. Materials and methods

2.1. The working group

The Epidemiology Working Group of the European Cervical Cancer Screening Network consists of representatives of 13 of the 15 European Community (EC) Member States (there was no representative from Austria and Luxembourg). The working group came together twice in 1998 in Rotterdam. A set of quantitative data to be collected from each country or region was discussed and agreed upon. The data were chosen to describe important aspects of the (cost-)effectiveness of screening. In addition, the definitions of the concepts behind the data were decided upon. It was agreed that the most recent data available should be used. Where the data sources are not mentioned in the presentation here, they can be found in the country-specific contributions to this issue.

2.2. The age range and screening interval

Evaluation of the screening process values studied requires knowledge of the recommended age range and screening interval. These recommendations differ between countries and regions (Table 1).

Table 1
Policies or recommendations for cervical cancer screening by EU country

Country	Screening age range (years)	Screening interval in years	Smears per woman in a lifetime
Belgium (B)	25–64	3	14
Denmark (DK)	23–59	3	13
Finland (FIN)	30–60	5	7
France (F)	25–65	3	14
Germany (G)	$\geqslant 20$	1	50+
Greece[a] (Ormylia) (GR)	25–64	3	14
Ireland (IRL)	25–60	5	8
Italy (I)	25–64	3	14
The Netherlands (NL)	30–60	5	7
Portugal[a] (Midregion) (P)	20–65	3	16
Spain[a] (C. y. León) (E)	25–65	3	14
Sweden (S)	20–59	3	14
UK (England) (UK)	20–65	3 or 5	16–10

EU, European Union.

[a] Of Greece, Portugal and Spain, no national recommendations were available.

2.3. Process values: definitions

In order to collect comparable and coherent estimates for the respective process parameters, the following definitions have been agreed upon.

2.3.1. Coverage

We will consider the *3-year coverage* for direct comparison between countries, and the so-called *interval coverage* for the policy-specific model predictions. In both cases, the denominator is the number of women in the target age group in the population of the area in question. The numerator is the number of women in the target age group that had at least one smear in the period preceding the moment of evaluation. For the 3-year coverage this period is fixed at 3. For the interval coverage the last i, years are considered, where i is the length in years of the recommended screening interval.

2.3.2. Positive screening results

The *percentage screen positives* only concerns the primary (as opposed to follow-up) programme smears. It is the percentage of non-negative adequate smears. Positive is defined as having a more stringent follow-up recommendation than the normal screening policy. Thus, results that require a repeat smear, e.g. after 6 months (e.g. atypical squamous cells of undetermined significance (ASCUS)) are included in the percentage.

2.3.3. Excess smear use

We will call all smears not contributing to the coverage 'excess smears'. Some of these smears are follow-up smears after non-negative screening results or are taken because of signs or symptoms. Smears following signs or symptoms would also occur without screening (although their number can be influenced by screening). The reason we had to add them to preventive excess smears is that they can often not be discerned from each other in registrations. In order to obtain comparable figures for all countries, we therefore chose to count all smears for calculating the excess smear use.

We considered the excess smears per year related to the 3-year interval for direct comparison between countries, and the excess smear related to the recommended screening interval for the policy-specific model predictions. The former is expressed in number of excess smears per year per thousand women, the latter as a percentage of excess smears considering all smears. The formulas used are as follows (for an example, see the footnotes of Table A2 in the Appendix).

The number of excess smears per year per 1000 women [related to the 3-year interval] = (total yearly number of smears − number of smears needed yearly to reach the observed 3-year coverage) × 1000/number of women in the target population where the yearly number of

smears needed to reach the observed coverage is: the population in the target age range × 3-year coverage/3.

The percentage excess smear use [related to the recommended screening interval] = the percentage of excess smears of the total number of smears = (total number of smears × 100/number of smears needed to reach the observed coverage) − 100% where the number of smears needed to reach the observed coverage is: (the population in the target age range × *i*-year coverage)/*i*, where *i* = the length in years of the recommended screening interval.

2.3.4. Target population

The number of women in the target population is defined as the number of eligible women in the country or region in a screening round (a period of screening that lasts the recommended screening interval). For the last previous round, this is the number of women in the age range beginning with the recommended starting age and ending with the recommended ending age plus the number of years in the screening interval minus one year (e.g. 25 up to but not including 67 years of age for the '25–64 every 3 year' policy).

2.3.5. Cumulative risk

The cumulative risk is defined as the cumulative (background) incidence to age 100 years in the hypothetical situation without screening.

2.4. Model calculations: predicted effects and costs

We used the MISCAN cervical cancer screening simulation model to exploratively predict effects and costs of screening in EU Member States. MISCAN is a microsimulation model described extensively elsewhere [2,3]. The principal predicted effect measure presented is percentage life-years lost reduction. The number of smears is used as an approximate proportionality factor for the costs. Accordingly, the number of smears per percentage life-years lost reduction is the cost-effectiveness measure presented. The number of life-years gained per 1000 women and the number of smears per life-year gained are also discussed. Calculations were made for different screening policies (age range and interval combinations) and different coverage and excess smear rates. More precisely, the *interval* coverage rates and the *interval related* percentages of excess smears are used as input for the predictive calculations. The impact of different risk levels is also discussed.

Fixed parameters in this exploration, and thus parameters for which eventual differences between countries and regions are not accounted for, are:

1. The natural history of cervical cancer, especially the mean and variance of the duration of preclinical (pre-invasive and invasive) detectable disease.
2. The sensitivity (of the combination of screening test and follow-up).
3. The stage-specific prognosis after treatment.

These fixed parameters determine the incidence and mortality reducing potential of Pap smear screening. Compared with other models in the literature (the one of Eddy [4] and of Gustafsson and Adami [5]) the mortality reduction predicted by the MISCAN model in women participating in screening is at the same level (approximately 75% for a 30–60 every 5-year policy and approximately 90% for e.g. 16 smears between age 20 and 70 years). We used the MISCAN model because it can be easily tuned to different screening situations in different countries.

The age distribution of the incidence of cervical cancer was also fixed. As Gustafsson and colleagues showed by studying age-specific incidence rates from different countries in periods before screening started, these distributions follow very much the same pattern for many Western European countries (among others Denmark, Germany, The Netherlands and Sweden with a peak age at 44–47 years), although some countries seem to have a slightly different distribution (Finland with a peak age at 53.5 years; the UK with somewhat later onset, a peak age of 48 years and a slower decline after the peak) [6].

The calculations presented in this paper concern a complete screening of a birth cohort of women following the recommended policy. Therefore, the results represent a steady-state situation in which screening has and will run forever, and in which all birth cohorts have the same cumulative risk of cervical cancer. What cumulative risk to consider when in several Western countries an increased risk is observed for cohorts born after, e.g. 1940 or thereabouts is a subject of discussion. Hysterectomies for reasons other than the management of (precursors of) cervical cancer are not taken into account.

For each combination of age range and recommended screening interval, the influence on (cost-) effectiveness was computed for various coverage and excess smear rates.

3. Results

3.1. Estimates for screening process values in countries and regions

In Table 1 we describe the screening policies in the EU countries or regions, and in Table 2 we present the estimates for the screening process parameters resulting from the collected data. For information on other regional pilot projects and further details see Tables A1 and A2 in the Appendix. Although the definitions to be

used in this paper were well set, the available data did not always make it possible to exactly meet these definitions. Therefore, the tables should not be interpreted without studying the country- and region-specific remarks in the Appendix. (Differences with figures reported in the country-specific papers are due to differences in definitions.)

Although all policies are mainly in line with the European recommendations (screening women every 3–5 years), there is a large variation in screening intensity that is a consequence of these policies. This intensity varies from 7–16 smears per woman in a lifetime, with the exception of Germany where there is a 1-year screening interval and over 50 smears taken in a lifetime. The 3-year coverage in the participating countries varies from 50 to 82% in the national programmes. The figures for the regions of Portugal and Spain involved in the screening programmes are lower, possibly because in these cases coverage by other than programme smears is not accounted for. For France and Ireland, no data on 3-year (or 5-year) coverage were available. The excess smear use varies strongly. However, as has been explained for each country in the Appendix, there are many reasons why these figures are not always comparable. The percentage screen positives varies from 3 to 8% of the screened women. This may reflect differences in the prevalence of neoplastic lesions or differences in cut-off points between negative and positive smears (between 'no follow-up required' and 'at least a repeat smear recommended'). In any case, the percentage of screened women that undergo some kind of negative effect of screening due to follow-up varies accordingly.

Altogether, the data summarised in Table 2 plus the details in the Appendix, show how far we have got in estimating the respective parameters in EU Member States, and how much work remains to be done.

3.2. Model-based predictions

On the basis of the data collected, effectiveness and cost-effectiveness were predicted for a variety of screening situations, differing in screening strategy, coverage and smear use.

3.2.1. Life-years lost reduction

We focused on the reduction in life-years lost from cervical cancer as the effect measure of screening. (In Table A3 in the Appendix, the predicted percentage in incidence and mortality reduction is also presented.) First, we predicted the effectiveness at 100% coverage (and no excess smear use), see the bottom line of Table 3. We did so for three screening policies, including the least and most intensive policy and the intermediate EU recommended policy (see Table A3 for all policies). Because we assume an identical age distribution of incidence across countries, these numbers are applicable to any country with the policy under consideration. The number of life-years lost because of cervical cancer is reduced by between 84% and 94% when screening women between 7 and 14 times, respectively. The

Table 2
Estimates for outcome parameter values of cervical cancer screening by EU country

Country	3-year or [5-year][b] coverage (%)	Screen-positives	3-year excess smears (per 1000 women)	Population subjected to formal programme (%)
Belgium (B)	78	3	167	58
Denmark (DK)	75	5	205	90
Finland (FIN)	[93][b]	5	121[b]	100
France (F)	n.r.e.	5	n.r.e.	< 5
Germany (G)	80	7	248	90
Greece[a] (Ormylia) (GR)	71	5	117	88
Ireland (IRL)	n.r.e.	3	n.r.e.	
Italy (I)	50	n.r.e.	77	13
The Netherlands (NL)	[77][b]	5	24[b]	100
Portugal[a] (Midregion) (P)	37	5	86	100
Spain[a] (C. y. León) (E)	27	15	14	86
Sweden (S)	82	1.5	140	100
UK (England) (UK)	61	8	90	100
Average[c]	75	5	134	

For definitions of the outcome parameters, see the text. EU, European Union; n.r.e., No reliable estimate. For France and Ireland the coverage ever was estimated at 60% and 65%, respectively. If these rates were used as 3-year coverage rates, the calculated number of 3-yearly excess smears would be 133 and −10 per year per 1000 women, respectively.

[a] Of Greece, Portugal and Spain, no national data were available.

[b] For Finland and The Netherlands, only 5-year coverage rates were available. Therefore, the number of excess smears was calculated with the 5-year coverage.

[c] Unweighted average.

German policy with over 50 smears a lifetime is predicted to result in an almost 100% reduction (99.9%). The actual percentage life-years lost reduction depends on the coverage. Therefore, the predicted percentages are given by the coverage rate. This was done for two assumptions on the long-term coverage: (1) it is always the same women who participate at screening in successive rounds (participants–participation is 100% systematic), and (2) participation is independent of previous participation (participants–participation is random). In the first assumption, long-term coverage is equal to coverage within one screening round. With random participation, the long-term coverage increases every screening round. Therefore the mortality reduction is higher with random participants–participation. Assumption (1) is extremely unfavourable and (2) extremely favourable for screening, especially for frequent screening and a low (short-term) interval coverage (see the predictions for the German policy). In fact, with random participants–participation and a low interval coverage, the average screening interval becomes much longer than the recommended one, so

Table 3
Percentage life-years lost reduction by policy, coverage and two assumptions on long-term distribution of participation in the population: the same women participate in all rounds (i.e. participants–participation is systematic) or participation is independent of previous participation (i.e. participants–participation is random)

Policy[a]	NL/FIN 30(5)60[#7]		B/F[b]/GR/I/E 25(3)64[#14]		G 20(1)72[#53]	
Participants-participation	Systematic	Random	Systematic	Random	Systematic	Random
Interval coverage (%)	% Life-years lost reduction					
25	21	36	24	56	25	90
50	42	60	47	80	50	98
75	63	75	71	90	75	99
100	84	84	9	94	99.9	99.9

NL, The Netherlands; FIN, Finland; B, Belgium; F, France; GR, Greece; I, Italy; E, Spain, G. Germany.
[a] Starting age (interval) ending age [number of smears in a lifetime], policies ranked by increasing number of smears in a lifetime.
[b] For France, the stopping age is 65 years.

Table 4
Predicted percentage life-years lost reduction by policy and coverage, assuming systematic participants–participation[a]

Policy[b]	NL/FIN 30(5)60[#7]	IRL 25(5)60[#8]	UK(5) 20(5)64[#10]	DK 23(3)59[#13]	S 20(3)59[#14]	B/F[c]/GR/I/E 25(3)64[#14]	UK(3)/P 20(3)64[#16]	G 20(1)72[#53]
Interval coverage (%)	Life-years lost reduction							
20	17	18	19	18	18	19	19	20
25	21	22	23	23	23	*24* E	24	25
30	25	27	28	28	28	28	29	30
35	29	31	33	32	32	33	*34* P	35
40	34	36	37	37	37	38	38	40
45	38	40	42	41	42	42	43	45
50	42	44	47	46	46	*47* I	48	*50* G[a]
55	46	49	51	51	51	52	53	55
60	50	53	56	55	55	*56* F (max)	*58* UK(3)	60
65	55	*58* IRL (max)	61	60	60	61	62	65
70	59	62	65	64	65	*66* GR	67	70
75	*63* NL	67	*70* UK(5)	*69* DK	69	*71* B	72	75
80	67	71	75	74	*74* S	75	77	80
85	71	75	79	78	79	80	82	85
90	76	80	84	83	83	85	87	90
95	*80* FIN	84	88	87	88	89	91	95
100	84	89	93	92	92	94	96	100

For each country, the prediction resulting from using the estimates on coverage presented in Table A2 are indicated. The values for Greece, Portugal and Spain concern only part of these countries, see Table A2. (max), For Ireland and France, the indicated value is a maximum since it is based on the 'coverage ever' as if it was the interval coverage. Italicised values are those where estimates of interval coverage are applied. For country abbreviations, see Table 1.
[a] Assuming systematic participants–participation is relatively unfavourable for policies with frequent screening. This is especially the case for Germany (see Table 3 and text).
[b] Starting age (interval) ending age [number of smears per women in a lifetime], policies ranked by increasing number of smears in a lifetime.
[c] For France the stopping age is 65 years.

that results are in some sense no longer representative for the screening interval under consideration. In Table 4, the results are given for all policies for the conservative assumption (1). Differences in coverage resulted in more or less proportional differences in expected percentage life-years lost reduction, with much less impact for the number of smears recommended in a lifetime, which varies from 7 to over 50 smears. For example, for a 7 smears per lifetime policy, increasing the coverage from 50 to 75% (which will increase the number of smears by approximately 50%) will add (63−42=) 21% extra life-years lost reduction, while intensifying screening to 14 smears in a lifetime (twice as many smears) will only add (47−42=) 5% life-years lost reduction. In the table, we italicised the predictions per EU Member State if the estimates for the interval coverage (see Table A2 in the Appendix) are applied.

3.2.2. Numbers of smears per percentage life-years lost reduction

The number of smears per percentage life-years lost reduction depends on the policy and the excess smear use. Predictions are given in Table 5 for each policy, with the results per EU Member State if the data collected on excess smear use are applied. Policies with a low smear-taking intensity (fewer smears recommended a lifetime and fewer excess smears in addition to the recommended smears) have a more favourable cost-effectiveness ratio compared with policies with many smears in a lifetime. Differences in +40–130% excess smears and in 7–16 of smears recommended in a lifetime resulted in approximately 2-fold differences in the expected number of smears per percentage life-years lost reduction. If always the same women participate, as was assumed here (i.e. participators–participation is 100% systematic), the predicted cost-effectiveness is independent of the coverage. Especially for Germany, where we know that the coverage after three 1-year screening rounds is considerably higher (80%) than after one round (50%), these predictions are underestimating the life-years lost reduction from screening (Table 4) and thus overestimating the number of smears per percentage life-years lost reduction (Table 5). Obviously, many participating women are not screened every year as recommended, but at a longer interval, which improves cost-effectiveness.

It should be noticed that the extra mortality reduction resulting from preventive smears outside the target age range and recommended screening interval is neglected in these predictions. The expected influence of this simplification will be limited (see Table 3).

3.2.3. Negative side-effects

In order to produce a measure for the negative side-effects, one could calculate the predicted number of screen-positives by per cent life-years lost reduction (by multiplying the number of smears per percentage life-years lost reduction in Table 4 by the proportion of

Table 5
Predicted number of smears (×mln) per % life-years lost reduction by policy and excess smear use, assuming systematic participants–participation[a]

Policy[b]	NL/FIN 30(5)60[#7]	IRL 25(5)60[#8]	UK(5) 20(5)64[#10]	DK 23(3)59[#13]	S 20(3)59[#14]	B/F[c]/GR/I/E 25(3)64[#14]	UK(3)/P 20(3)64[#16]	G 20(1)72[#53]
Excess smear use (%)	Number of smears per % life-years lost reduction							
0	1.9	2.1	2.4	3.2	3.5	3.3	3.7	*11.3* G[a]
10	2.1	2.3	2.7	3.5	3.8	3.7	4.1	12.5
20	2.3	2.5	2.9	3.9	4.2	*4.0* E	4.5	13.6
30	2.5	2.7	3.2	4.2	4.5	4.3	4.9	14.7
40	2.7	2.9	3.4	4.5	4.8	4.7	*5.2* UK(3)	15.9
50	2.9	3.1	3.7	4.8	*5.2* S	*5.0* GR/I	5.6	17.0
60	3.1	*3.3* IRL(min)	3.9	5.2	5.5	*5.3* B	6.0	18.1
70	3.3	3.5	4.1	5.5	5.9	*5.7* F(min)	*6.4* P	19.3
80	*3.5* NL	3.7	4.4	*5.8* DK	6.2	6.0	6.7	20.4
90	3.7	3.9	*4.6* UK(5)	6.1	6.6	6.3	7.1	21.5
100	3.9	4.1	4.9	6.5	6.9	6.7	7.5	22.7
110	4.1	4.4	5.1	6.8	7.3	7.0	7.9	23.8
120	4.2	4.6	5.4	7.1	7.6	7.4	8.2	24.9
130	*4.4* FIN	4.8	5.6	7.4	8.0	7.7	8.6	26.1
140	4.6	5.0	5.9	7.7	8.3	8.0	9.0	27.2

For each country, the prediction resulting from using the estimates on coverage presented in Table A2 are indicated. The values for Greece, Portugal and Spain concern only part of these countries, see Table A2. (min), For Ireland and France, the indicated value is a minimum since it is based on the excess smear use calculated with the 'coverage ever' as if it was the interval coverage. Italicised values are those where estimates of interval coverage are applied. mln, million. For country abbreviations, see Table 1.

[a] Assuming systematic participants–participation is relatively unfavourable for policies with frequent screening. This is especially the case for Germany (see Table 3 and text).

[b] Starting age (interval) ending age [number of smears per women in a lifetime], policies ranked by increasing number of smears in a lifetime.

[c] For France the stopping age is 65 years.

screen-positives in Table 2). However, the percentage of screen-positives is no more than an initial very approximate approach to quantify negative side-effects. The next necessary step would be to divide this percentage into women who are and women who are not referred to colposcopy/biopsy before the end of the follow-up episode. One would also have to describe how long (how many years) follow-up occurs in the respective groups, accounting for the period until a woman resumes regular screening, and what medical procedures (from repeat smears to conisation and hysterectomy) take place during this period.

4. Discussion

The EU Member States have implemented a variety of screening policies. The screening interval varies from 3 to 5 years and the number of smears offered in a lifetime varies from 7 to 16 (Table 1). Germany uses recommendations that strongly differ from those from other countries, with a 1-year screening interval and over 50 smears per women in a lifetime. Screening process values also differ between the countries (Table 2). The 3-year coverage varies from below 50% to over 82%, the excess smear use from less than 100 to over 200 per year per 1000 women, and the percentage screen-positives from 1.5% to 8%.

The predicted (cost)-effectiveness varied accordingly. Differences in coverage of 50–90% resulted in more or less proportional differences in the expected percentage life-years lost reduction, with a much smaller impact for differences from 7 to 16 in the number of smears recommended in a lifetime. Differences from 40 to 130% in excess smear use combined with the already mentioned differences in the number of smears in a lifetime, resulted in at least 2-fold difference in the expected number of smears per percentage life-years lost reduction.

The fact that an association between high risk and non-attendance has been repeatedly observed [7–9] makes the predictions too favourable.

Hysterectomy rates can be substantial. In the UK the rate is 25% under the age of 55 years (data not shown). By including women without a cervix uteri in the denominator of the coverage rate, this rate is more seriously underestimated in countries with high hysterectomy rates than elsewhere.

The values for the parameters presented in Tables 2 and A2 represent the best available estimates at the time they were collected by the working group. Some are based on (almost) nationwide registrations, others on more or less thorough surveys, or are the best guesses of experts. Sometimes, as explained in the text, the figures are minimum or maximum estimates. The potential biases are notified in the country-specific remarks in the Appendix. The lack of data on opportunistic screening is often a problem. Programme screening aims for early detection and treatment of cervical cancer. However, other smears have the same aim. The total performance of early detection in a country is the aggregate of programme screening and other smears taken. Our analysis shows that the high rate of excess screening in most countries or regions (well over 60% in most cases), caused by opportunistic screening either running alone or along with programme screening, results in cost-ineffective situations. In order to improve these situations, it is necessary to monitor the opportunistic screening activities together with the organised screening activity.

A next step in the cost-effectiveness analysis of cervical cancer screening is to go from the percentage life-year lost reduction to the number of life-years gained as the effect measure, and consequently also to the number of smears per life-year gained as the cost-effectiveness measure. To this end, country-specific knowledge is required on the cumulative risk: the cumulative incidence in situations without screening. Taking into account this cumulative risk is conditional for a judgement on how many smears in a lifetime is acceptable for a given country or region. We presented predicted numbers of life-years gained and number of smears per life-year gained for a background cumulative risk of 1% in Tables A4 and A5 in the Appendix. The results in these tables can easily be adjusted to any specific estimate for the cumulative risk (see footnotes to the respective tables). The percentage for women currently eligible for screening in the EU probably varies between 1 and 4%, depending on the birth cohort and geographic area under consideration. However, cervical cancer is not a very stable disease as far as risk over time is concerned. In most countries, screening started decades ago. This means there is a lot of uncertainty about the cumulative risk, especially for young birth cohorts, and that it will be more and more difficult (if not impossible) to estimate the cumulative risk in the future, even with new high quality data. This has consequences as to how to proceed with the work presented. The predictions could be improved in their accuracy in many ways, as has been pointed out earlier in this paper. For instance, one could account for the age dependency of coverage or for the hysterectomy rates. But is this worthwhile if these uncertainties and simplifications in the analysis are dominated by the uncertainty about the cumulative risk? This will be subject to further discussion among the evaluators of cervical cancer screening.

5. Conclusions

The results stress the impact of cervical cancer screening evaluation to provide reliable estimates for a restricted set of parameters: the short- and long-term coverage of screening (including opportunistic

screening) and the total amount of smears (including opportunistic smears). The results also show the importance of a high coverage for the effectiveness of screening, and of a restricted intensity of smear taking for cost-effectiveness. Intensity of screening is derived from the combination of the recommended number of smears in a lifetime and the number of (excess) smears taken on top of these recommendations. In some countries, one might consider de-intensifying the recommended cervical cancer screening policy (i.e. fewer smears in a lifetime). These latter conclusions are not new. The presentation in this paper is highly individualised to participating countries and will therefore hopefully have its own impact on the improvement of cervical cancer screening in the respective countries and regions.

Appendix. Details on estimates for screening process values in countries and regions

The following section contains country- and region-specific remarks on Tables A1 and A2. These tables contain more details than the corresponding Tables 1 and 2 in the text.

Belgium

In Belgium, there is a nationwide consensus about the age range and screening interval, but a formal screening programme has only been implemented in Flanders (covering 58% of the Belgium population). In a telephone interview the 3-year coverage in Flanders was estimated at 82%. According to a Health Interview Survey the 3-year coverage in Flanders was almost 10% higher than in the other part of the country. Therefore, the coverage on a national level was estimated to be $0.58\times82\% + 0.42\times72\% = 78\%$. The difference between Flanders and the other part of the country in the percentage of screen-positives and in the number of excess smears is not known. The percentage of screen-positives (3%) is only known for the Flemish region (for programme and opportunistic screening, excluding smears with a clinical indication and follow-up smears [10]). This percentage was also used for the national estimate (Table 2). The total number of Pap smears (opportunistic and organised) is known only for the whole country. The data presented for the Flemish Region are based on estimation.

Denmark

In 1997, the screening programme with personal invitations covered 90% of the 23–59-year-olds and 46% of the 60–74 year age group of women. According to the national guidelines, the latter age group had to be invited once. The 75% 3-year coverage and the 5% screen-positives were estimated on the basis of data from 1994 to 1996 from the Copenhagen and Frederiksberg

Table A1
Policies for cervical cancer screening by European Union (EU) country or region

	Policy/recommendations			Period described	Number of women in target population (×1000)	Population subjected to formal programme (%)
	Age range (years)	Interval (years)	Smears per woman			
(a) National data[a]						
Belgium	25–64	3	14	1995/6/7	2712	58
Denmark	23–59	3	13	1997/98	1429	90
Finland	30–60	5	7	1996	1275	100
France	25–65	3.5	14	1998	18 000	<5
Germany	⩾20	1	50+	1996	33 000	90
Ireland	25–60	5	8	1996/7	792	–
Italy	25–64	3	14	1994/5/6	15 369	13
The Netherlands	30–60	5	7	1997	3692	100
Sweden	20–59	3	14	1994	2300	100
UK (England)	20–64	3 or 5	16–10	1996/7	15 049	100
(b) Regional data (regions with programme screening/ pilot projects)						
Flanders (B)	25–64	3	14	1995/6/7	1573	100
Copenhagen (DK)	23–59	3	13	1998	165	100
Bas-Rhin (F)	25–64	3	14	1998	255	100
Ormylia (GR)	25–64	3	14	1997	13	88
Florence (I)	25–64	3	14	1997	206	100
Turin (I)	25–64	3	14	1996/97	271	80
Midregion (P)	20–64	3	16	1995/97	292	100
C. y. León (E)	25–65	3	14	1990+	628	86

B, Belgium; DK, Denmark; F, France; GR, Greece; I, Italy; P, Portugal; E, Spain.
[a] Of Greece, Portugal and Spain, no national data are available.

municipalities (see Table 2, 9% of Danish population) (data not shown).

Finland

Programme screening covers over 100% of the country, although ages targeted since the late 1980s (55,60) makes that overall only 87% of the target population. The percentage invited women among 30-year-old women has been approximately 70%. The 5-year coverage on the basis of an annual population survey was estimated to be 93% for any Pap smear. There is no direct estimate of the 3-year coverage, but 18% of the women had a smear once every 5 years, and 27% every 3–4 years, so that the 3-year coverage could be (93-18-27/2=) 62%. The estimated annual number for all smears (including opportunistic and diagnostic smears and all age groups) is 500 000–600 000 (data not shown).

France

In France in 1998, except for three pilot cervical cancer programmes covering less than 5% of the country, screening was opportunistic. It is estimated that 60% of the 20–69 year age group of women in France had a cervical smear (no separate data are available for the target age group of 25–64 years). In the region of Bas-Rhin (with programme screening on the basis of public announcements), the 3-year coverage in the target age group was 69% and the 3.5-year coverage 75%. For the percentage of positive smears national data were not available. In Bas-Rhin it was 5% (follow-up smears

Table A2
Estimates for outcome parameter values of cervical cancer screening by European Union (EU) country or region

	Coverage (%)		% Screen-positive	Annual number of smears (×1000)	Excess smears		Women in target population[d] (×1000)
	3-year	Recommended interval			3-year (per 1000 women)[b]	Recommended interval (%)[c]	
(a) National data[a]							
Belgium	78	78	3	1158	167	64	2712
Denmark	75	75	5	650	205	82	1429
Finland	n.r.e.	93	5	550	121[f]	132	1275
France	n.r.e.	n.r.e.	5	6000	133[g]	67[g]	18 000
Germany	80	50	7	17 000	248	3	33 000
Ireland	n.r.e.	n.r.e.	3	164	−10[g]	59[g]	792
Italy	50	50	n.r.e.	3750	77	46	15 369
The Netherlands	n.r.e.	77	5	1037	24[f]	82	3692
Sweden	82	82	1.5	950	140	51	2300
UK (England)	61	76[h]	8	4408	90	93[f]	15 049
Average[e]	75		5		134		
(b) Regional data (regions with programme screening/pilot projects)							
Flanders (B)	82	82	3	750	203	74	1573
Copenhagen (DK)	75	75	5	70	174	70	165
Bas-Rhin (F)	69	69	5	104	178	77	255
Ormylia (GR)	71	71	5	4.6	117	50	13
Florence (I)	39	39	5	41	69	53	206
Turin (I)	70	70	10	90	99	42	271
Midregion (P)	37	37	5	61	86	69	292
C. y. León (E)	27	27	15	65	14	15	628

n.r.e., No reliable estimate. For France and Ireland, estimates are available for the coverage ever, 60% and 65%, respectively. For definitions of the outcome parameters, see the text.

[a] Of Greece, Portugal and Spain, no national data are available.

[b] E.g. for Germany: [17 000 000–(33 000 000×80% (3-year coverage)/3 years)]×1000/33 000 000=248.

[c] E.g. for Germany: 100×[17 000 000/(33 000 000×50% (interval coverage)/1 year (interval))]−100%=3%.

[d] For all countries or regions except Denmark, Finland and The Netherlands, the figure concerns the women in the age group corresponding to the target age range (e.g. 25–64 years), instead of the upper age increased with the length of the recommended screening interval minus 1 year (e.g. 25–66, see Materials and Methods). The resulting underestimation of the target population is probably less than 5%.

[e] Unweighted average.

[f] Calculated with 5-year coverage. For Finland, using the rough estimate for the 3-year coverage of 61% would result in 228 smears per 1000 women per year. For the UK, using the 3-year coverage of 61% would result in 44% relative excess smear use.

[g] Using the 60% (France) and 65% (Ireland) estimates for the ever-screened women as if they are 3-year coverages.

[h] 5-year coverage.

excluded, clinical smears e.g. because of symptoms included).

Germany

In Germany, statutory health insurers, issue yearly a voucher (computer-readable plastic card) to all persons and thus make free annual cervical screening available to $\geqslant$ 20-year old women, covering 90% of the population. In this 90% (and presumably also in the other 10%) the 1-year coverage is approximately 50%. The 3-year coverage is over 80% if only programme smears are accounted for (accounting for all smears it will be higher still). The total annual number of smears is estimated at 15 million programme smears plus at least 1.5 million of 'private' smears. The percentage of screen-positives is estimated at 7%, including roughly 5% ASCUS (data not shown).

Greece

In Greece, two regional programmes are running, one in Ormylia and one in Messina and Ilia. Data on the process parameters needed for this paper were only available for the Ormylia programme. Both the coverage and the total number of smears only take programme smears (including follow-up smears) into account. Data on other smears are not available.

Ireland

To date, opportunistic screening is occurring in Ireland. The age range of 25–60 years and an interval of 5 years or shorter was recommended in national guidelines in 1996. This results in a minimum of eight smears per women per lifetime. The percentage of women (aged 25–60 years) who ever had a smear on the basis of a survey was estimated to be 65%. The estimated 3% of screen-positives concerns one large laboratory (All smears are included (also follow-up smears), so 3% is an overestimate (data not shown).

Italy

National guidelines were decided in 1996. In 1997, 13% of the female target population was covered by programme screening, but this is rapidly increasing to probably approximately 50% in the year 2000. Local surveys on the 3-year coverage conducted in the late 1980s provided estimates of less than 50% in the absence of organised screening. In areas that had screening programmes in 1997 (covering 13% of the female target population) approximately two-thirds could report coverage. In these regions, the 3-year coverage rate was estimated at 66% of the invited women (not all the programmes have run for 3 years) [11]. In Turin, 3-year coverage was 43% before programme screening started in 1992, and was 74% in invited women in 1997. The total number of smears in Turin is estimated and subject to uncertainty. In Florence, where women without a smear in the last 3 years have been invited since 1980, the 3-year coverage in 1997 was 39% and the 4-year coverage 49%. In this latter measurement, 'private smears' were not included. These smears are also not included in the total number of smears (data not shown).

The percentage of screen-positives (including those requiring repeat smears) was not available for the programmes running in 1997. The average colposcopy referral rate was 2%. The percentage of positives (including those requiring repeat smears) in Florence was 5% (follow-up smears excluded, but clinical smears included) and 10% in Turin (programme smears only). The large majority of positive smears in the Turin programme only imply a single additional smear.

The Netherlands

In The Netherlands, the previous national 3-yearly screening policy between ages 35 and 53 years was changed into a 5-yearly policy between the ages 30 and 60 years in 1996. Coverage and the total number of smears are based on a nationwide registry including all smears in the country, irrespective of the reason for which they were taken. Not all 30–34-year olds and 55–64-year olds had at least one invitation in the last 5 years, because the first 5-year round with the extended age range was not completed by the end of 1997. The percentage of screen-positives accounted for primary programme smears only, and has decreased from over 10% in 1994 to 5% in 1997.

Portugal

In 1990, programme screening was launched in the Central Region of Portugal. Screening data are only available from this programme. Initially a 1-year interval is used before proceeding with a 3-year interval. The 5% of screen-positives probably refers to secondary (follow-up) smears as well, and thus might be too high.

Spain

No national cervical cancer screening data are available from Spain. The data presented concern a (pilot) programme in Castilla Y León. In this programme, a 1-year interval is recommended before proceeding with a 3-year interval. The 3-year coverage as defined here is estimated at 27%, not including women covered by 'private' smears. The estimated annual number of 65 000 smears also does not include 'private' smears. It does include follow-up smears after programme smears.

Fifteen per cent of the smears result in at least the recommendation of a cytological follow-up, of which 14% are classified as 'with infections, including viruses', and 0.8% as 'with morphological alterations'.

Sweden

Sweden has programme screening nationwide. According to the national guidelines a 3-year screening interval is recommended, but almost half of the counties use a 4-year interval. Women with a recent smear (within 18 months) are sorted out and not invited. The coverage is based on data for the city of Malmö: 76% of women had a recent smear, and a quarter of the other 24% attended the screening programme. In some rural areas coverage is lower, therefore the 82% may be too high an estimate for the total country.

Table A3
Predicted percentage reduction in incidence, mortality and life-years lost by policy (100% coverage)

Country policy[a]	NL/FIN 30(5)60 [#7]	IRL 25(5)60 [#8]	UK(5) 20(5)64 [#10]	DK 23(3)59 [#13]	S[b] 20(3)59 [#14]	B/F[c]/GR/I/E 25(3)64 [#14]	UK(3)/P 20(3)64 [#16]	G 20(1)72 [#53]
% incidence reduction	75	80	85	84	84	87	90	96
% mortality reduction	76	78	86	80	80	86	88	95
% life-years lost reduction	84	89	93	92	92	94	96	99.9

NL, The Netherlands; FIN, Finland; IRL, Ireland; DK, Denmark; S, Sweden; B, Belgium; F, France; GR, Greece; I, Italy; E, Spain; P, Portugal.

[a] Starting age (interval) ending age [number of smears per women in a lifetime], policies ranked by increasing number of smears in a lifetime.

[b] For Sweden, the new guidelines issued in 1998 recommend 23–60 years, with 3-year intervals in women 23–49 years and with 5-year intervals in women, 50–60 years. For this policy, the predicted figures are 84, 80 and 92%, respectively.

[c] For France the stopping age is 65 years.

Table A4
Life-years gained per 1000 women assuming a 1% cumulative risk[a], by policy and coverage.

Policy	NL/FIN 30(5)60[#7]		B/F[b]/GR/I/E 25(3)64[#14]		Germany 20(1)72[#53]	
Participants–participation Interval coverage (%)	Systematic	Random	Systematic	Random	Systematic	Random
	Life-years gained per 1000 women					
25	18	31	20	47	21	77
50	36	51	40	68	43	83
75	53	64	60	76	64	84
100	71	71	80	80	85	85

This risk is the cumulative incidence in the situation without any (previous or current) screening. For explanation of the participation pattern see Table 3. For abbreviations of countries see Table A3.

[a] The number of life-years gained is proportional to the cumulative risk for incidence: a 2-fold higher risk results in a 2-fold higher number of life-years gained. Therefore, the results can be adjusted to any specific percentage cumulative risk by multiplication.

[b] For France the stopping age is 65 years.

Table A5
Cost-effectiveness ratio (CER), expressed in number of smears per life-year gained, assuming a 1% cumulative risk[a] and no excess smear use[a]. The CER is given by policy and coverage

Policy	NL/FIN 30(5)60[#7]		B/F[b]/GR/I/E 25(3)64[#14]		Germany 20(1)72[#53]	
Participants–participation Interval coverage	Systematic	Random	Systematic	Random	Systematic	Random
25	88	53	152	68	516	146
50	88	63	152	92	516	266
75	88	74	152	120	516	392
100	88	88	152	152	516	516

For abbreviations of countries see Table A3. For explanation of the participation pattern see Table 3.

[a] The number of smears per life-year gained are proportional to the inverse of the cumulative risk for incidence and proportional to 1+ the interval related excess smear use (see Table A2): a 2-fold higher risk results in a 2-fold lower number of smears per life-years gained, and a 100% excess smear use results in a 2-fold higher number of smears per life-year gained. Therefore, the results can be adjusted to any specific cumulative risk and excess smear use.

[b] For France the stopping age is 65 years.

United Kingdom

In the UK a national screening programme is running. The data refer to screening in England. The target of the national programme is to screen women aged 20–64 years at least every 5 years. However, more than half of the health authorities invites women every 3 years. The 5-year coverage for the whole country is 76%, the 3-year coverage is 61%. Ideally, those parts of the country with a 3-yearly screening programme should be evaluated separately from those with a 5-yearly programme. The 8% screen-positives concerns all smears (including follow-up smears) instead of only primary programme smears, and may therefore be an overestimate (data not shown).

Acknowledgements

The project received financial support from the European Commission (Contract grant sponsor: European Union, Commission of the European Communities, Directorate-General for Employment, Industrial Relations and Social Affairs; Contract grant number: SOC 97 201143).

Neither the European Commission nor any person acting on its behalf is liable for any use made of this information.

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