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Process performance of cervical screening programmes in Europe

Guglielmo Ronco[a,*], *Marjolein van Ballegooijen*[b], *Nikolaus Becker*[c], *Arkadiusz Chil*[d], *Muriel Fender*[e], *Pamela Giubilato*[a], *Juozas Kurtinaitis*[f,†], *Lesz Lancucki*[g], *Elsebeth Lynge*[h], *Antonio Morais*[i], *Marian O'Reilly*[j], *Pär Sparen*[k], *Ofelia Suteu*[l], *Matejka Rebolj*[b], *Piret Veerus*[m], *Maja Primic Žakelj*[n], *Ahti Anttila*[o]

[a]*Unit of Cancer Epidemiology, Centre for Cancer Prevention (CPO), Via San Francesco da Paola 31, 1023 Torino, Italy*
[b]*Department of Public Health, Erasmus MC Medical Centre, Rotterdam, The Netherlands*
[c]*Division of Cancer Epidemiology, German Cancer Research Centre, Heidelberg, Germany*
[d]*Regional Coordinating Office for Cervical Cancer Screening, Holycross Cancer Centre, Kielce, Poland*
[e]*Association EVE, Strasbourg, France*
[f]*Institute of Oncology, Vilnius University, Lithuania*
[g]*NHS Cancer Screening Programmes, Sheffield, UK*
[h]*Institute of Public Health, University of Copenhagen, Denmark*
[i]*Oncology Committee Coordination, Regional Health Administration of Central Portugal, Coimbra, Portugal*
[j]*CervicalCheck, The National Cervical Screening Programme, Limerick, Ireland*
[k]*Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden*
[l]*"Prof. Dr. I. Chiricuţă" Cancer Institute, Cluj-Napoca, Romania*
[m]*Department of Epidemiology and Biostatistics, National Institute for Health Development, Tallinn, Estonia*
[n]*Epidemiology and Cancer Registry, Institute of Oncology, Ljubljana, Slovenia*
[o]*Finnish Cancer Registry, Helsinki, Finland*

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ABSTRACT

Standardised tables of aggregated data were collected from 15 European national or regional cervical screening programmes and key performance indicators computed as reported in European Union (EU) Guidelines, 2nd edition.

Cytological results varied widely between countries both for the total proportion of abnormal tests (from 1.2% in Germany (Mecklenburg-Vorpommern) to 11.7% in Ireland-Midwest Region) and for their distribution by grade. Referral rates for repeat cytology (ranging from 2.9% of screened women in the Netherlands to 16.6% in Slovenia) or for colposcopy (ranging from 0.8% in Finland to 4.4% in Romania-Cluj) and the Positive Predictive Value (PPV) of colposcopic attendance (ranging from 8% in Romania-Cluj to 52% in Lithuania) were strongly influenced by management protocols, in particular for atypical squamous cells of undetermined significance (ASCUS) and low-grade squamous intraepithelial lesion (LSIL) cytology. However, cytology-specific PPV also showed remarkable variability. The detection rate of CIN2+ histology ranged from <0.1% of screened women in Poland to >1% in England and Denmark. Low attendance for colposcopy after referral was observed in some east-European countries.

These comparisons may be useful for improving the performance of cervical screening in general and more so if new screening technologies and vaccination for Human Papillomavi-

* *Corresponding author:* Tel.: +39 0116333850; fax: +39 016333861.
E-mail address: guglielmo.ronco@cpo.it (G. Ronco).
† Deceased.
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rus are introduced. Overall, quality was better in countries that have operated organised programmes for a longer time, plausibly as a result of long-lasting monitoring and quality assurance activities. Therefore, the availability of these data, the first comparing European countries, and the increased number of countries that can provide such data (only five in 2004) represent progress. Nevertheless, there is a clear need to standardise the cytological and histological classifications used in screening, as well as data registration systems across Europe.

1. Introduction

Cervical cancer screening is a complex activity involving different coordinated steps. It also involves a vulnerable balance between positive and negative effects and costs. These include anxiety and costs for unneeded diagnostic work-up and treatments, possible obstetric complications of treatment, and false reassurance by false negative tests. Direct evaluation of the impact of screening activities in terms of their final outcome – reduction of the incidence of and mortality from cervical cancer – is needed, such as auditing of the screening histories of women who developed cancer.[1] However, a continuous, ongoing evaluation of whether a programme is achieving its intermediate objectives is relevant in order to improve quality and reduce undesired effects, mainly those due to too high a referral for further actions. Monitoring screening process performance and making comparisons within countries provides feedback to help identify problems and is recommended by the recently published European Guidelines for Quality Assurance in Cervical Cancer Screening.[1,2]

Statistics for cervical screening have been regularly produced by a few European countries including England from 1989[3] (which also developed a set of indicators[4]), Scotland[5] from 1999, Wales from 2000,[6] Italy from 2002,[7] Slovenia from 2003,[8] the Netherlands from 2004[9] and Finland from 2005.[10] Performance data has also been published by the Estonian pilot[11] and French regional Alsace[12] programmes, as well as the distribution of cytology results for the Flemish region of Belgium.[13]

Comparing performance parameters between European screening programmes can provide important knowledge in order to improve their quality. However, the format of published data differs and comparisons are difficult. Some parameters from a few European countries were previously reported but comparisons could only be made between the recommended policies.[14,15] The new edition of the European Guidelines for Quality Assurance in Cervical Cancer Screening provides a set of standard tables[1] and parameters[2] for screening monitoring. In this paper we present the results of the EUNICE project, supported by the European Commission. In this framework we aimed at providing data as comparable as possible and to evaluate the applicability of the proposed tables and parameters.

2. Materials and methods

The members of EUNICE submitted tables of aggregated data based on those recommended by the European Guidelines for Quality Assurance in Cervical Cancer Screening.[1]

National data were reported whenever possible. If national data were not available we collected data for specific regions. The latter were, as a rule, from one single region in each country, except in Italy where data refer to organised programmes covering some 70% of the female population (further denoted as 'Italy – organised programmes'). Tables were completed on the basis of routine screening registration systems, except for the German Mecklenburg-Vorpommern region where they were based on cytology monitoring activity ([16] and Büttner HH, personal communication to NB).

Tables were checked for internal consistency and providers were contacted for clarifications. A single centre in Italy was responsible for computing some of the 'key performance indicators' reported by the European guidelines.[2] With the exceptions specified below, the instructions reported in the guidelines themselves were followed. In Italy not all data were available for all local screening programmes. Therefore, for each indicator the appropriate denominator, based on the programmes that had provided data for the numerator, was used. In Finland, 16,294 women who had had Human Papillomavirus (HPV) testing as primary screening were excluded.

Distribution of cytology results – for most countries cytological tests were the unit of information and all cytological results for a woman were considered. However, in England, Estonia, Finland, Germany, the Netherlands and Poland, women were the units of information and the worst result in case of repeated testing was considered. Smears taken during colposcopies were not considered. Usually we obtained data according to the Bethesda 2001 classification.[17] Abnormal results (i.e. $\geqslant$atypical squamous cells of undetermined significance (ASCUS)) were grouped as: (1) malignant cells, (2) high-grade squamous intraepithelial lesions (HSIL), (3) low-grade squamous intraepithelial lesions (LSIL) and (4) ASCUS + ASC-H + AGC. Here, AGC = atypical glandular cells and ASC-H = atypical squamous cells where high grade lesions cannot be excluded. Cytology results were provided already converted to the Bethesda system from England and Ireland (where they were originally reported according to the UK system) and from Denmark (where SNOMED codes are registered).

Finland, Germany and the Netherlands provided cytology reported using different (modified Pap) classifications, pregrouped as follows:

- The Netherlands (CISOE-A classification): Unsatisfactory, Pap1 (translated as Normal), Pap2/3a1 (which corresponds

to ASCUS, ASC-H, AGC and LSIL but was translated as LSIL for the purpose of this work) and ⩾Pap3a2 (translated as HSIL).[18]
- Finland (Papanicolaou Classification): Pap 1 (translated as Normal), Pap2 (which corresponds to ASCUS, ASC-H, AGC and LSIL but was translated as ASCUS for the purpose of this work), Pap3/4 (translated as HSIL).
- Germany, Mecklenburg-Vorpommern (Munich classification[19]): Group I/II (translated as Normal), Groups III and IIID (together translated as LSIL), Group IVa/IVb (translated as HSIL), Group V (translated as Malignant).

Referral rate for repeat cytology was computed as the number of screened women referred for repeat cytology at a shorter interval than routine in a given time period divided by the number of women screened in the same period.

In most countries the actual recommendation was not registered. Therefore, the number of women who should have repeated cytology according to local guidelines was the numerator. The actual recommendation was considered in Italy and England. Slovenia reported the number of women who were either registered as referred to repeat or should have repeated according to local guidelines. This was done because of the incompleteness of registration of recommendations.

Referral rate for colposcopy was computed as the number of screened women referred to colposcopy in a given time period divided by the number of women screened in the same period. We considered the actual recommendation in Italy, Portugal and Finland. Slovenia considered both the actual recommendation and the guidelines, similar to the criterion used for cytology repeat analysis. In the other countries the number of women who, given their cytology result, should have been referred to colposcopy according to local guidelines was noted. In Finland some referrals following borderline cytology may have been recommended outside the organised programme and may not have been recorded in the present data. Results were stratified by the last cytological diagnosis before referral.

The positive predictive value (PPV) for Cervical Intraepithelial Neoplasia grade 2 or more severe lesion (CIN2+) was calculated as the number of screened women with CIN2+ histology divided by the number of screened women who had attended for colposcopy. In Finland, Slovenia and Romania (Cluj county) the denominator was the number of women referred for colposcopy. In Denmark, Germany (Mecklenburg-Vorpommern) and the Netherlands the denominator was the number of women who should have had colposcopy according to the local protocol. In Lithuania only an audit sample of women who had both cytology and histology was available.

The *detection rate (DR) of CIN2* or more was calculated as the number of screened women with CIN2+ histology divided by the number of screened women. As the detection rate (DR) depends on the interval between screening rounds, for countries with a 3-year interval a rough estimate of the detection rates with a 5-year interval was obtained by multiplying the observed value by 5/3. This estimate was not calculated for Germany because of the high variability of the personal screening interval. In England a 5-year interval was assumed.

3. Results

Data from 15 countries could be obtained: national data from nine countries and regional cervical screening programme data from the other six countries. Details on the organisation and screening policies of the participating programmes are described in this special issue for each country[20] and in a summary report[21] which also reports coverage data. However, some information relevant for data interpretation, together with the list of parameters available for each country, is summarised in Table 1.

The proportion of women with cytology ⩾ASCUS (Table 2 and Fig. 1) was below 4% in Mecklenburg-Vorpommern (lowest at 1.2%), the Netherlands, Poland, and in Italian organised programmes while it was over 6% in Finland, England, Slovenia and Ireland-Midwest region (highest at 11.7%). Also, the distribution between the different grades of abnormality varied remarkably between countries. For example, women with HSIL represented less than 10% of all abnormal cytology in France-Alsace and in Italian organised programmes versus more than 25% in the Netherlands and in Ireland-Midwest region. However, there was not a clear relation between this distribution and the total percentage of abnormal cytology. In addition, the proportion of all screened women that was classified as HSIL ranged from values below 0.3% in Mecklenburg-Vorpommern, in Italian organised programmes and in France-Alsace to values above 1% in England, Slovenia, Denmark and Ireland-Midwest region (highest at 3.29%).

The proportion of women referred for repeat cytology (Fig. 2) varied from 2.9% in the Netherlands and 3.1% in France-Alsace to 16.6% in Slovenia. When considering the reasons for these referrals:

- The proportion of screened women advised to repeat cytology because of an unsatisfactory primary smear result was below 1% in Slovenia, France-Alsace and in the Netherlands while it reached 8.0% in England. The referral for a repeat cytology because of an unsatisfactory test could not be reported in Finland but is estimated to be very low.
- The proportion of screened women advised to have a repeat cytology because of a LSIL or ASC result was only 0.6% in Italian organised programmes and 1.1% in Poland while it was 5.9% in Ireland-Midwest Region and 7.9% in Slovenia.
- No woman was advised to repeat cytology for other reasons in England and the Netherlands while the 'other' component was very large in some countries (over 8% of screened women in Poland and Slovenia). These cases were not registered in France-Alsace.

The referral rate for colposcopy (Fig. 3) was below 1.5 % in Finland, Poland and the Netherlands while it was close to 4% in Ireland-Midwest Region and in Romania-Cluj. The referral rate because of HSIL or more severe cytology was below 0.5% in Italy, France-Alsace and Poland, between 0.5% and 1% in Portugal, Finland, the Netherlands, Romania-Cluj and England and over 1% in Slovenia and Ireland-Midwest region. Women with cytology less severe than HSIL represented only

Table 1 – Available data and selected features of the screening programmes included in the analysis.

Country	N screened women[a]	Period considered	Prevalence/incidence screening round	Target age[b]	Screening interval form (years)	Management of LSIL and ASCUS	Cervical cancer incidence[c]	Available parameters					
								Cytology distribution	Referral to repeat cytology	Referral to colposcopy	Compliance to colposcopy	PPV of colposcopy	Detection rate of CIN2+
Denmark	417,602	2006	Incidence	23–59	3	Repeat cytology or Colposcopy[e]	15.2					X	X
England	3,638,900	2004–2005	Incidence		3 or 5[d]	Repeat cytology	9.8	X	X	X	X	X	X
Estonia	6,249	2006	Prevalence	30–59	5	Colposcopy	20.3	X					X
Finland	176,507	2005	Incidence	30–60	5	Repeat cytology	4.9	X	X	X	X	X	X
Franlce Alsace	178,170	2004	Incidence	25–65	3	Colposcopy or repeat cytology or HPV triage[g]	11.7	X	X	X	X	X	X
Germany Mecklenburg-Vorpommern	378,291	2003–2005	Incidence	20+	1	Repeat cytology[h]	12.3	X				X	X
Ireland-Midwest Region	20,278	2006	Incidence	25–60	5	Repeat cytology	8.6	X	X	X	X	X	X
Italy Organised programmes	1,299,932	2006	Mixed, majority incidence		3	Mostly colposcopy	9.5	X	X	X	X	X	X
Lithuania	84,974	2006	Prevalence	30–60	3	Repeat cytology	20.1	X				X	X
The Netherlands	426,108	1999 and follow-up	Incidence	30–60	5	Repeat cytology	8.0		X	X	(X)[f]	X	X
Poland	682,805	2007	Prevalence	25–59	3	Mostly Colposcopy	19.2		X	X	X	X	X
Portugal, Central Region	110,516	2007	Prevalence	25–64	3	Repeat cytology, HPV triage	17.2		X	X			
Romania, Cluj County	7759	2005	Mainly Prevalence	25–65	5	Repeat cytology	24.5		X	X		X	X
Slovenia	205,036	2006	Prevalence	20–64	3 yrs (1 after first smear)	Repeat cytology	19.6		X	X		X	X
Sweden		2002	Prevalence	23–60	3 for age <50, 5 over 50	Repeat cytology	9.7						

a These numbers were used as denominators for computing the referral rate to cytology repeat (Fig. 2), referral rate to colposcopy (Fig. 3) and detection rate of CIN2+ (Fig. 4) except for Italy where the number of programmes that provided relevant data changes for different parameters (denominator reported in each figure).

b Most common, see Ref. [20] for details.

c Estimated national European age-standardised cervical cancer incidence rate per 100,000 women year in 2004. Source: Ref. [38].

d In England intervals are currently of 3 years up to age 49 and of 5 years over such an age. However, at the time of data collection these changes had not yet been implemented; instead, local programmes had a 3- or 5-year interval across all ages.

e Changes by administrative area.

f A minimum estimate, based on women who had biopsy available.

g The three options were possible on judgement of the gynaecologist for ASCUS. Only either colposcopy or repeat cytology was possible for LSIL.

h The gynaecologist could choose either colposcopy or repeat cytology. However, in most cases repeat cytology was recommended at the first ASCUS/LSIL test.

Table 2 – Distribution of abnormal cytological results in screening programmes from 15 European countries.

Country	N cytological exams	Total exams[a] with non-normal cytology (⩾ASCUS)		High grade intraepithelial lesion (HSIL) or invasive			Low grade intraepithelial lesion (LSIL)			ASCUS/ASC-H/AGC		
		N	% of all cytological exams	N	% of all cytological exams	% of exams with cytology ⩾ASCUS	N	% of all cytological exams	% of exams with cytology ⩾ASCUS	N	% of all cytological exams	% of exams with cytology ⩾ASCUS
Denmark	451,083	25,547	5.7	7765	1.72	30.4	6122	1.36	24.0	11,660	2.58	45.6
England	3,638,900	240,100	6.6	44600	1.23	18.6	71800	1.97	29.9	123,700	3.40	51.5
Estonia[b]	6153	346	5.6	77	1.25	22.3	47	0.76	13.6	222	3.61	64.2
Finland[c]	176,507	11,165	6.3	1244	0.70	11.1				9921	5.62	88.9
France-Alsace	187,484	8,719	4.7	563	0.30	6.5	2503	1.34	28.7	5653	3.02	64.8
Germany Mecklenburg-Vorpommern	378,291	4,439	1.2	615	0.16	13.9	3824	1.01	86.1			
Ireland-Midwest Region	20,995	2,452	11.7	690	3.29	28.1	945	4.50	38.5	817	3.89	33.3
Italy Organised programmes	1,384,034	37,824	2.7	2996	0.22	7.9	11,109	0.77	29.4	23,719	1.71	62.7
Lithuania	145,214	6927	4.8	1621	1.12	23.4	960	0.66	13.9	4346	2.99	62.7
The Netherlands[d]	426,108	11,779	2.8	3157	0.74	26.8	8622	2.02	73.2			
Poland	682,805	16,434	2.4	1934	0.28	11.8	4482	0.66	27.3	10,018	1.47	61.0
Portugal, Central Region	110,516	5819	5.3	663	0.60	11.4	1419	1.28	24.4	3737	3.38	64.2
Romania, Cluj County[e]	39,633	2362	6.0	447	1.13	18.9	902	2.28	38.2	1013	2.56	42.9
Slovenia	228,593	23,531	10.3	3167	1.40	13.5	7919	3.5	33.7	12,445	5.4	52.9
Sweden	702 716	32,120	4.6	6928	0.99	21.6	9762	1 39	30 4	15,430	2.20	48.0

a Units are women for England, Estonia, Finland, Germany, the Netherlands and Poland (see Materials and methods).
b Result unknown for 96 women.
c The The Pap2 category that corresponds to ASCUS, ASC-H, AGC and LSIL was translated as ASCUS for the purpose of this work.
d The Pap2/a1 category, that corresponds to ASCUS, ASC-H, AGC and LSIL was translated as LSIL for the purpose of this work.
e Results of tests performed in the years 2002–5 are considered.

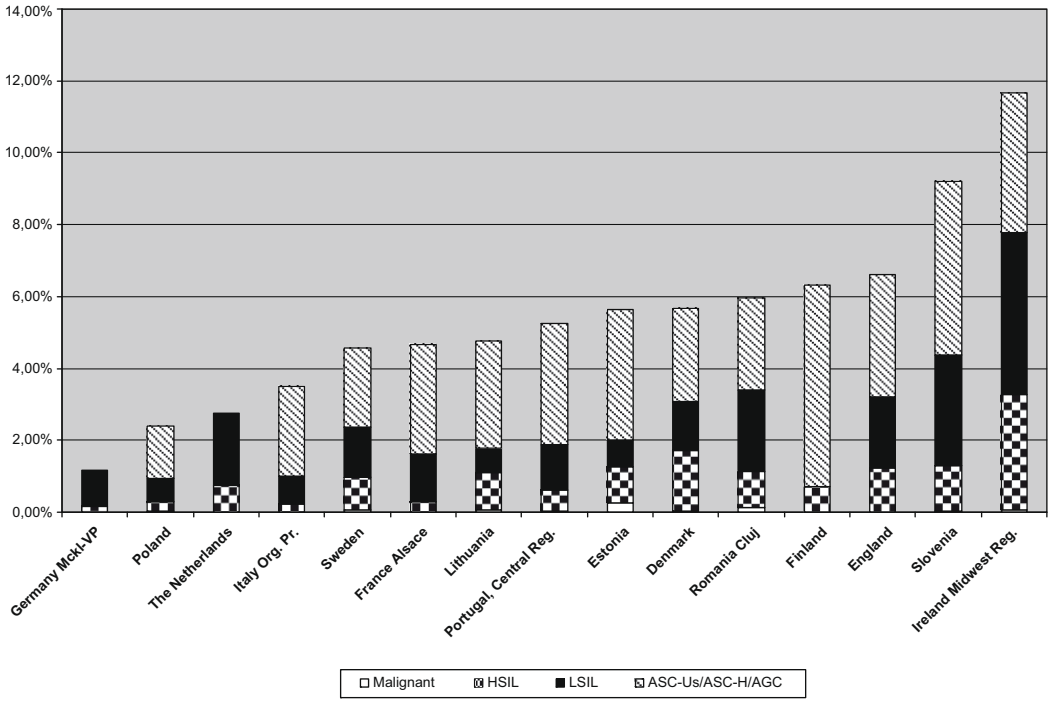
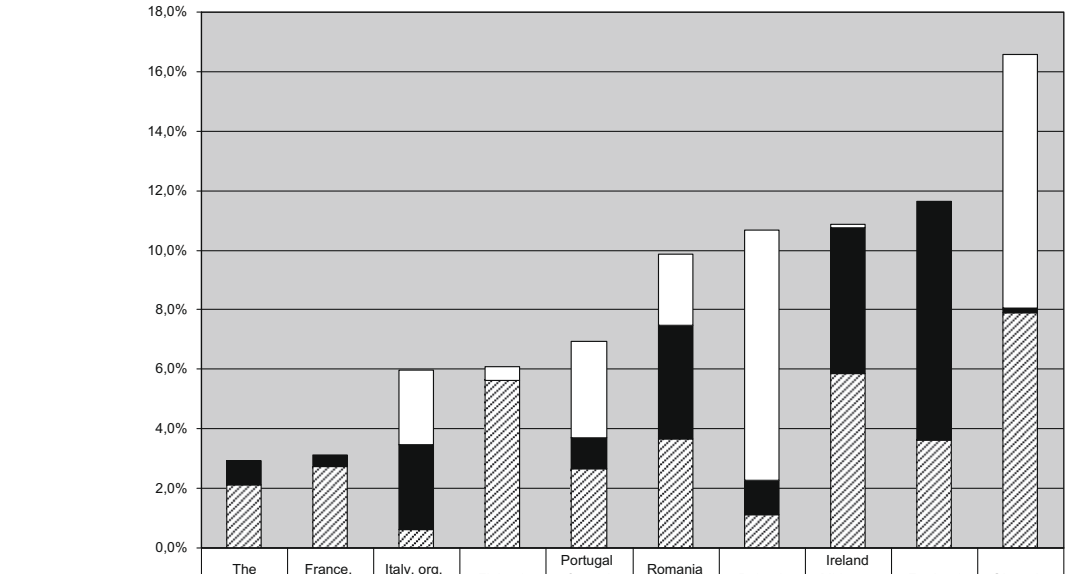


Fig. 1 – Proportion of screened women with abnormal cytology.



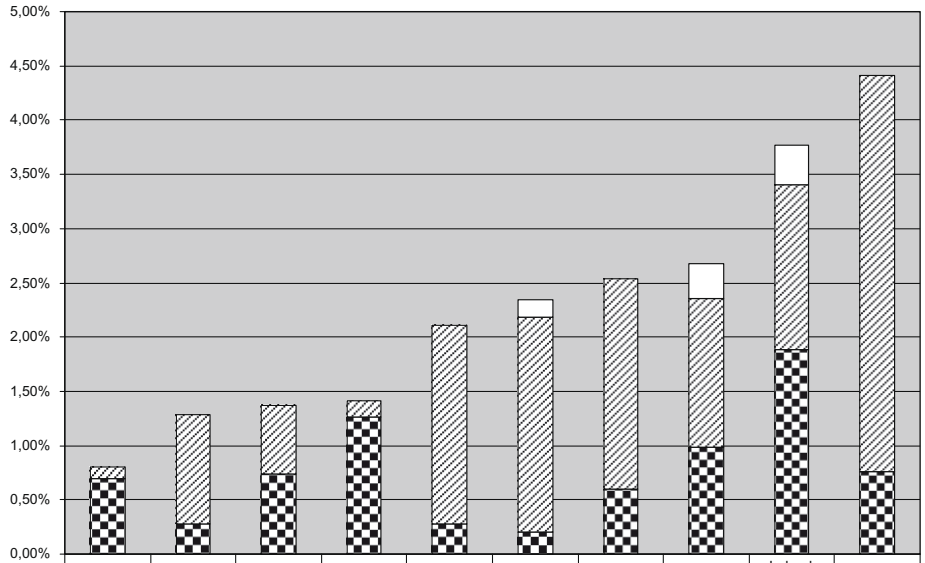
	The Netherlands	France, Alsace	Italy, org. progr.	Finland	Portugal Central Reg.	Romania Cluj	Poland	Ireland Midwest Reg.	England	Slovenia
other	0,0%	0,0%	2,5%	0,5%	3,3%	2,4%	8,4%	0,1%	0,0%	8,5%
unsatisfactory	0,8%	0,4%	2,9%		1,0%	3,8%	1,1%	4,9%	8,0%	0,2%
ASCUS/LSIL/AGC/ASC-H	2,1%	2,7%	0,6%	5,6%	2,7%	3,6%	1,1%	5,9%	3,6%	7,9%

Referrals for "other" are not registered in France-Alsace

Fig. 2 – Referral rate to repeat cytology by reason.

a small proportion of those referred to colposcopy in Slovenia (10%) and Finland (13%) while they were about half in the Netherlands (46%), Ireland (50%) and England (63%) and the large majority in Portugal-Central region (76%), Poland (78%), Romania-Cluj (83%), France-Alsace (87%) and Italy (91%).

The actual attendance to colposcopy after referral was available in only a few countries. It was over 80% in Finland (>99%), France-Alsace (84.5%), England (83.7%) and Italy (81.6%) and was 70.6% in Ireland-Midwest Region. It was at least 77% in the Netherlands and 72% in Slovenia (based on



	Finland	Poland	The Netherlands	Slovenia	France Alsace	Italy org. Prog.	Portugal Central reg.	England	Ireland Midwest Reg.	Romania Cluj
☐ Other	0,00%	0,00%	0,00%	0,00%	0,00%	0,16%	0,00%	0,32%	0,36%	0,00%
▨ ASC-US/ASC-H/AGC/LSIL	0,10%	1,00%	0,63%	0,15%	1,83%	1,98%	1,94%	1,37%	1,52%	3,65%
◧ HSIL+	0,70%	0,28%	0,74%	1,27%	0,28%	0,21%	0,60%	0,99%	1,89%	0,76%

Fig. 3 – Referral rate to colposcopy by reason.

the women with a histology report following referral). However, the registered attendance to colposcopy following referral was only 30.3% in Poland. Very low attendance was anecdotally reported, although it was impossible to measure it, in Romania-Cluj.

The overall positive predictive value (PPV) of referral to colposcopy for histologically confirmed CIN2+ varied widely between the observed programmes (Table 3), from values below 10% in Romania-Cluj to values close to 50% in the Netherlands, Slovenia and Lithuania. This overall PPV of referral to colposcopy was mainly related, with few exceptions, to the proportion of women with HSIL+ cytology among those referred to colposcopy. Variability was more reduced but still relevant when considering the specific PPV by cytology that caused the referral (Table 3).

The observed detection rate of CIN2+ histology per 1000 screened women (Fig. 4) was below 3 in Mecklenburg-Vorpommern, Finland, Poland and Italy, 3 to 4.5 in France-Alsace and Lithuania. On the other hand it was 6 to 7 in the Netherlands, Estonia and Romania-Cluj and approximately 10 in Ireland-Midwest Region, England, Slovenia and Denmark. When projecting the detection rate to 5 years, six out of 12 programmes had a DR between 4.5 and 7.5 per 1000 but outliers were still observed.

4. Discussion

Information on screening performance – either national or regional data – could be collected from 15 countries out of 27 European Union (EU) member states. Registration is however increasing: in a previous study, information on screening performance was available from only five member states.[15]

Due to the different registration systems, not all programmes could provide all the data required and there were clear differences in how the parameters were calculated for the different countries. A further difficulty was due to the use of different classifications for cytology. All classifications were converted to the Bethesda 2001 system but some classifications were only partly translatable. In addition, cytological results were received in pre-defined aggregations, which made it impossible to apply the existing tables of conversion.[22] Data required for calculating age-adjusted parameters were not available. Finally, some programmes were still at the prevalence screening phase while most of them conducted incidence screening rounds (see Table 1). As a result, great care is needed in the interpretation. On the other hand, the parameters calculated here are the most comparable produced so far.

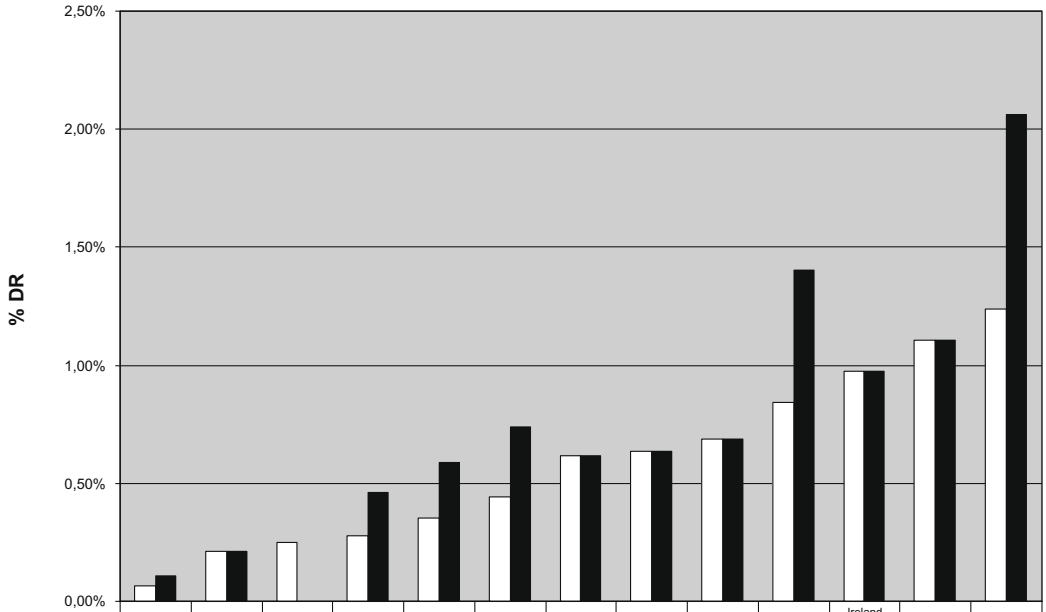
Differences in the proportion of women with abnormal cytology depend both on variations in the true frequency of abnormalities (that in turn is also affected by screening intervals and by either considering prevalence or incidence screening) and on differences in criteria for reporting cytology. The latter have as a result variability in the mix of different cytological grades among women with abnormalities. Remarkable variability in the interpretation of cytology was reported in the literature between centres in the same country, especially for lower grade abnormalities.[23–27] Additional differences between countries were previously observed in one study[26] but not in another study.[27]

Both referral rates for repeat cytology and for colposcopy were mainly determined by management protocols. Particularly, the fact that women with LSIL and ASC/AGC cytology were either referred for repeat cytology or directly for colposcopy was determinant. Women with LSIL/ASC/AGC cytology were a highly variable component of the referral rates for colposcopy and for repeat cytology and there was, in general, a balance between the two (referral for colposcopy increased

Table 3 – Positive predictive value (PPV) for CIN2 or more severe histology of referral to colposcopy and of cytology-specific PPV in different European cervical screening programmes.

Country	Reason for referral to colposcopy									
	All referrals				ASCUS, AGC, ASC-H or LSIL			HSIL+		
	With positive Histology	Denominator[a]	PPV (95% CI)	% with HSIL+ in denominator	With positive Histology	Denominator[a]	PPV (95% CI)	With positive Histology	Denominator[a]	PPV (95% CI)
Romania-Cluj	167	2197	7.6% (6.5–8.7)		ND	ND	ND	ND	ND	ND
Italy Organised programmes	3398	22414	15.2% (14.7–15.6)	19	1717	18071	9.5% (9.1–9.9)	1588	2230	71.2% (69.3–73.1)
Poland	441	2636	16.7% (15.3–18.2)	17	182	2179	8.4% (7.2–9.5)	259	457	56.7% (52.1–61.2)
France-Alsace	629	3163	19.9% (18.5–21.3)	14	304	2725	11.2% (10.0–12.3)	325	438	74.2% (70.1–78.3)
Denmark	5166	24750	20.9% (20.4–21.4)	78	1249	5531	22.6% (21.5–23.7)	3472	6063	57.3% (56.0–58.5)
Germany Mecklenburg-Vorpommern	946	4439	21.3% (20.1–22.5)	14	419	3824	11.0% (10.0–11.9)	557	615	90.6% (88.3–92.9)
Finland	374	1356	27.6% (25.2–30.0)	96	4	109	3.7% (0.1–7.2)	370	1244	29.7% (27.2–32.3)
Ireland-Midwest Region	198	540	36.7% (32.6–40.7)	62	26	207	12.6% (8.0–17.1)	171	293	58.4% (52.7–64.0)
England	40,200	95,400	42.1% (41.8–42.5)	42	9700	55,200	17.6% (17.3–17.9)	30,500	40,200	75.9% (75.5–76.3)
The Netherlands	2838	5829	48.7% (47.4–50.0)	54	483	2677	18.0% (16.6–19.5)	2355	3152	74.7% (73.2–76.2)
Slovenia	1462	2957	49.4% (47.6–51.2)	90	78	304	25.7% (20.7–30.6)	1384	2599	53.3% (51.3–55.2)
Lithuania	376	721	52.1% (48.5–55.8)	67	93	235	39.6% (33.3–45.8)	256	280	91.4% (88.1–94.7)

a See Materials and methods. The denominator is the number of women who had colposcopy (for England, France-Alsace, Ireland, Italy and Poland), who were referred to colposcopy (for Finland, Slovenia and Romania), and who should have had colposcopy according to the local protocol (for Denmark, Germany and the Netherlands). For Lithuania, data are based on an audit sample of women who had both cytology and histology.



	Poland	Finland	Germany, Mckl-VP	Italy Org. Progr.	France Alsace	Lithuania	Romania Cluj	The Netherlands	Estonia	Slovenia	Ireland Midwest Reg.	England	Denmark
□ Actual DR	0,06%	0,21%	0,25%	0,28%	0,35%	0,44%	0,61%	0,64%	0,69%	0,84%	0,98%	1,10%	1,24%
■ projected 5 years	0,11%	0,21%		0,46%	0,59%	0,74%	0,61%	0,64%	0,69%	1,40%	0,98%	1,10%	2,06%

Fig. 4 – Detection Rate of histologically confirmed CIN2 or more.

when referral to repeat cytology decreased). The overall proportion of women referred to either was quite stable, between 12% and 18% with the exception of Finland and the Netherlands, where it was below 8%.

Concerning repeat cytology, there was also a strong variability in criteria used to define a satisfactory smear. These were clearly stricter in England than in the other countries. Unfortunately, we had no data concerning the use of liquid-based cytology (LBC), which is associated with a lower proportion of unsatisfactory cytology.[28,29] In the UK, the switch to LBC has indeed resulted in a strong reduction of unsatisfactory rates. In most countries repeat cytology was also advised for other reasons, particularly so in Poland and Slovenia. These reasons include dystrophic or inflammatory changes in some Italian programmes, Slovenia and Poland.

The overall PPV of referral to colposcopy was mainly related to the cytology mix among referred women, and therefore, again, to referral criteria. Cytology-specific PPV also showed, however, variation between countries. The PPV of HSIL was low in Ireland and in Denmark where the proportion of screened women classified to have HSIL was high (which could reflect broader criteria in reporting) but also in Poland where this proportion was low. Part of this variability reflects problems in conversion of cytological classifications. This is plausibly the case for PPV of HSIL that was very high in Germany, low in Denmark and very low in Finland, where part of the Pap3 cytology included among HSIL is likely to correspond to LSIL. High values in Lithuania are plausibly due to selection, as only women who had a biopsy were considered in the denominator. Variations in PPV of LSIL/ASC/AGC cytology may partly depend on differences in the CIN2+ prevalence, as approximated by the corresponding DR (low in Germany, Italy, France-Alsace, Finland and Poland, high in Denmark and Slovenia). Another reason is that in some countries these women were directly referred to colposcopy following the first cytology result (e.g. in most Italian organised programmes). Instead, in other countries, they were referred only if this diagnosis was confirmed by a repeat cytology result. However, it is also possible that differences in criteria for reporting played a role. Indeed, the proportion of women with LSIL/ASC/AGC cytology among all those with abnormal cytology was very high in Italy, France-Alsace and Poland and PPV for the same category was low in these countries.

Detecting cytological abnormalities is clearly useless without treatment of intraepithelial lesions, based on assessment by colposcopy and biopsy. Therefore, high attendance at recommended colposcopies is crucial for screening to be effective in reducing incidence and mortality. Incomplete follow-up was shown to be the reason for a remarkable proportion of invasive cancers in some programmes.[30–34] Incompleteness of colposcopic assessment and of its registration seems to be a major problem in some east-European countries. Reasons are discussed elsewhere in this special issue.[35,20]

The DRs of histologically confirmed CIN2+ showed high variability. The DR depends on screening frequency. Indeed, most programmes with a low DR had a short recommended screening interval. However, remarkable exceptions are the low DR in Finland (5-year interval) and the high DR in Denmark and Slovenia (both with 3-year intervals). The projection to 5 years is, however, a very crude estimation that does not take into account regression of high grade lesions. The background risk is another obvious determinant of DR. For example, the population prevalence of HPV infection – the necessary cause of high grade CIN – was found to be high in England (although with heterogeneity between areas), Ireland and Denmark that also have high DRs of CIN2+.[36] Incidence of cervical cancer is reported in Table 1 for comparison, although it must be remembered that it re-

flects both the baseline risk and the effect of screening. In any case cervical cancer incidence was already high before screening in Denmark.[37] The population that participates in registered screening could also be selected differently regarding their baseline risk in different countries. DR was also expected to be higher in programmes that had just started their activity and where most women had not been screened previously. This was not always observed. Remarkably, low or intermediate DR was observed in some eastern European countries where screening had just started and where incidence and mortality from cervical cancer was high.[38,39] In Poland, Romania-Cluj and possibly in other countries the DR may have been greatly reduced by the reported low completeness of diagnostic follow-up. Unregistered opportunistic screening also possibly played a role. Indeed, the DR may have been reduced by unregistered CIN detection and treatment following opportunistic cytological tests performed between regular intervals. In fact, this is equivalent to reducing the screening interval. In Finland, when including the lesions treated outside the organised programme, the DR would be about double the observed one. The current recommendation is to include all screening tests and services in the registration systems.[1,2]

Finally, it is known from the literature that the reproducibility of interpretation of cervical histology is far from perfect, especially for CIN2.[25,40–43] Different criteria between countries could have been relevant in determining the observed differences in DR.

In conclusion, large differences in process performances were observed between European cervical cancer screening programmes. Some of these differences can have a remarkable impact on effectiveness, for example, the low attendance at recommended colposcopies observed in some east-European programmes. The observed large differences in referral rates for repeat cytology, colposcopy and in PPV have major consequences on costs, both economic and for women (e.g. loss of time and anxiety). Differences in cost-effectiveness would be even larger when cumulated over a long time period, considering that the lifetime recommended number of tests varies from seven to more than 50 in EU member states.[21] Referral rates to repeat cytology or to colposcopy are partly reciprocally balanced and result from different protocols, partly justified by different local costs and availability of colposcopy. Nevertheless, different quality in cytology interpretation and in organisation plays a relevant role. It is quite clear that the programmes that have been running for a longer period of time have better overall quality. This is plausibly the result of many years of monitoring and feedback and of quality assurance activities. The presence of a strong coordination also seems to be relevant. On the other hand, many East-European countries show problems. Most of these only started recently and have limited resources.

Reporting comparable monitoring data in EU countries is essential in order to improve quality. There is a clear need to standardise the cytological and histological classifications used in screening, as well as data registration systems across Europe. The data produced by current registration systems need to be improved and these data should be produced and compared on a regular basis. This will also help in providing reference values for the measured parameters, to be used as a benchmark. The relevance of monitoring would be even greater if HPV testing and vaccination were introduced, as discussed elsewhere in this special issue.[44,45]

Conflict of interest statement

- Guglielmo Ronco – Minor payment for participating in two internal scientific advisory meetings for GenProbe, a firm developing a test for HPV RNA. No conflict of interest since March 2008.
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