

Impact of implementing a nationwide cervical cancer screening program on female population coverage by Pap-tests in Estonia

Piret Veerus¹, Marc Arbyn², Camilla Amati³, and Paolo Baili³
on behalf of the EUROCHIP Working Group⁴

¹National Institute for Health Development, Tallinn, Estonia; ²Unit of Cancer Epidemiology, Scientific Institute of Public Health, Brussels, Belgium; ³Descriptive studies and health planning unit, Fondazione IRCCS "Istituto Nazionale dei Tumori", Milan, Italy; ⁴Listed in the Acknowledgments

ABSTRACT

Background. The objective of the EUROCHIP project in Estonia was to describe the organized cervical cancer screening program started in 2006 (after pilot studies in 2003-2005), to compare its performance with opportunistic screening, and to define priorities for improvement of the program.

Methods. Population data was retrieved from Statistics Estonia, data about performed Pap-smear tests within the screening program from the Estonian Cancer Society and from clinics and labs participating in the program, data about Pap-smear tests outside the screening program from the Estonian Health Insurance Fund, and data about cancer incidence and mortality from the Estonian Cancer Registry database.

Results. During the first year after implementing the nationwide cervical cancer screening program in Estonia, the number of tests outside the organized program remained high. Within the organized program, the number of Pap-tests in different age groups increased with age except for the oldest age group while population coverage with Pap-tests outside the organized screening program decreased with age. The number of cervical cancer cases at early stages increased after implementation of organized screening. The time-frame does not permit to draw any definitive conclusions.

Conclusions. Implementation of organized cervical cancer screening did not decrease the volume of opportunistic screening. The factors influencing attendance in the organized cervical cancer screening program in different age groups should be studied further. Moreover, a central cancer screening registry without restrictive data protection legislation would improve data collection and enable to evaluate performance of the program on a regular basis. Free full text available at www.tumorionline.it

Introduction

Estonia has a population of about 1.3 million¹. In the year 2004, the world age standardized incidence rate of cervical cancer was estimated at 17.1² per 100,000 women-years in Estonia with 162 new cervical cancer cases being detected. Incidence and mortality from cervical cancer are about four-fold higher in Estonia than in other Nordic countries^{3,4}. The way to reduce cervical cancer incidence and mortality is the implementation of an organized cervical screening program⁵.

A pilot study of organized cervical cancer screening in Estonia was started in 2003. The Estonian Health Insurance Fund mailed 12,960 invitations to randomly selected women in the age group of 30 to 40 years with health insurance. Only 2,808 of the invited women (21.7%) had a Pap-smear taken (Table 1), and in 6.7% of all Pap-tests the results were abnormal. Five clinics and one lab participated in the project. Midwives

Key words: EUROCHIP, cervical cancer, Estonia, cervical screening program barriers.

Correspondence to: Piret Veerus, National Institute for Health Development, Hiiu 42
11619 Tallinn, Estonia.
Tel +3726593946;
fax: +3726593901;
e-mail piret.veerus@tai.ee

participating in the program were specially trained to take and fix the test, and to inform women about the test result by phone⁶.

In 2004, all Estonian regions were included in the organized screening program. Due to the lack of resources, no personal invitations were used. Women in the age group from 35 to 40 years were invited to cervical screening tests via media. Altogether 5,264 women attended (Table 1), and for 5.6% the Pap-test was abnormal.

In 2005, a similar policy was continued. In addition, personal invitations to 35- and 40-years-old women were mailed in six Estonian districts. Altogether, 6,552 women participated in the program (Table 1), from among them 1,239 were those who had received the invitation to participate. For 6.7% the result was abnormal⁶.

In 2005, National Cancer Strategy was prepared by a group of experts and presented to the Estonian Government early in 2006. According to the National Cancer Strategy, personal invitations to the organized cervical cancer screening program have to be mailed to all insured women in the age group of 30 to 59 years with a 5-year interval after a negative test. Women diagnosed with cervical cancer, women without health insurance and women having had a Pap-smear in past 12 months are excluded from the list of invitees.

In 2006, a nation-wide organized cervical cancer screening program was started and 30,123 invitations were mailed to insured women from birth cohorts 1956, 1958, 1961, 1966, and 1971 (the cohorts together being as big as 49,385). Altogether, 6,249 women had their Pap-smears taken (Table 1) with a cytobrush at 19 clinics by specially educated midwives. The samples spread on glass and fixed in alcohol were stained according to Papanicolaou and interpreted by cytotechnologists according to the Bethesda system in seven labs.

Outside the organized cervical cancer screening program, the Pap-tests are taken by gynecologists, stained according to Papanicolaou or by Giemsa and interpreted by cytotechnologists in 14 labs. No information is available about the results of the Pap-tests taken outside organized screening.

Table 1 - Pap-smear tests in different age groups in Estonia from 2003 to 2006 within the screening program

Year/target group	Population	Invited	Screened	Proportion screened
2003				
30 to 40 yrs	92770	12960	2808	3.0%
2004				
35 to 40 yrs	45213	not sent	5264	11.6%
2005				
35 to 40 yrs	45462	not applicable	6552	14.4%
2006				
35, 40, 45, 48, 50 yrs	49385	30123	6249	12.7%

Source: Statistics Estonia, Estonian Cancer Society, Estonian Health Insurance Fund.

Within the Health Information framework of the European Commission, the EUROCHIP project performed descriptive studies on cancer indicators in order to define specific cancer control priorities and problems in various European countries⁷. The present article shows activities in Estonia related to cervical cancer screening performance. The paper aims to describe the organized cervical cancer screening program started in 2006, to compare its performance with the opportunistic screening and to define requirements for the improvement of national implementation in the future.

Material and Methods

Numbers of women in different age groups per year were obtained from Statistics Estonia.

Individual data about women whose Pap-smear test was taken in each birth cohort in the year 2006 within organized cervical cancer screening program were obtained from the clinics participating in the program and the results of the tests from the labs involved. The aggregated data resulting from the pilot studies of organized screening in the years 2003 to 2005 was obtained from the Estonian Cancer Society.

The database of the Estonian Health Insurance Fund was used to obtain numbers of women in different age groups who had a Pap-smear taken in the period from 2004 to 2006, and numbers of women who had undergone a Pap-smear in the year 2004, 2005, or 2006 outside the organized cervical cancer screening program. No data prior to 2004 were available. Pap-tests repeated for the same woman were not included in the analysis.

No identifying individual data from screening outside the organized program were available. Consequently we have no information about the test results of the women who had the smear outside the organized program.

Average annual incidence per 100,000 women, numbers of primarily detected cervical cancer cases in each age group and data on staging were obtained from the Estonian Cancer Registry database. The last follow-up date for the Estonian Cancer Registry database was December 31, 2006.

The evolution in population coverage with Pap-smears tests was analyzed. Moreover the incidence of cervical cancer and the proportion of early stages before and after start of the organized program were compared.

Results

Between 2003 and 2005 the female population who had been screened with Pap-smear tests within the target groups increased per year from 3.0% to 14.4%. These data are not completely comparable as the invitational mode as well as the target groups were different. The total number of women screened within the organized

screening program rose from 2,808 to 6,552 (Table 1). As the screening program changed repeatedly during the pilot study, it was not possible to analyze the population coverage by Pap-smear tests over this three-year period and thus the proportion of women screened per year was calculated only for the exact year indicated in the table.

The year 2006 was the first when invitations to attend organized cervical cancer screening program were mailed to predefined age groups all over Estonia. Only 30,123 women among the 49,385 included in targeted population were invited because of lack of health insurance, or an "opportunistic" Pap-smear in past 12 months, and women diagnosed with cervical cancer were excluded from the list of invitees.

The number of women screened in 2006 within the organized program according to the report from the clinics was 9,116, but the results of tests are known only for 6,249 of them. Based on the data from clinics, the proportion of women screened within the program in 2006 was 18.5%. According to the calculations based on the data from labs, the proportion of screened women in the target population in 2006 was 12.7%.

In the year 2006, the population screened with Pap-smear tests within the program was 8.4% in women 35 years of age, 10.7% for women 40 years of age, 13.7% for 45 years old and 18.6% for 48 years old. For women of 50 years of age, the proportion was lowest (11.3%) (Table 2).

The overall number of women (for all ages) having had a Pap-test outside the cervical cancer screening program was 111,252 in 2004, 116,908 in 2005 and 127,097 in 2006. The total number of women tested outside the organized program at least once between 2004 and 2006, was 251,884. The population coverage with Pap-tests outside the screening program, defined as the proportion of the female population with at least one Pap-smear in last three years, decreased by age: from 60% in the age group 30-34 years to 30% in the age group 55-59 years (Table 3).

The number of cervical cancer cases did not change significantly during the period from 2000 to 2005 (Table 4). There was no difference in the proportion of cervical cancer cases diagnosed at an early (localized) stage after

Table 2 - Pap-smear tests in different age groups in Estonia within organized screening program in 2006

Age	Size of cohort	Invited women	Screened women	Proportion screened
35 yrs	9633	4993	813	8.4%
40 yrs	8914	4678	955	10.7%
45 yrs	10462	5666	1438	13.7%
48 yrs	10137	9240	1887	18.6%
50 yrs	10239	5546	1156	11.3%
Total	49385	30123	6249	12.7%

Source: Statistics Estonia, Estonian Cancer Society, Estonian Health Insurance Fund.

the start of the organized cervical cancer screening program (Table 5). Most carcinomas discovered within the program are diagnosed at an early stage (Table 6).

Table 3 - Population coverage with Pap-smear tests from 2004 to 2006 outside the organized cervical cancer screening program

Age group	Average size of cohort	Number screened in last 3 yrs*	Coverage in last 3 yrs*
30 to 34 yrs	46484	27814	59.8%
35 to 39 yrs	46130	26904	58.3%
40 to 44 yrs	47426	25042	52.8%
45 to 49 yrs	51342	27472	53.5%
50 to 54 yrs	49981	24038	48.1%
55 to 59 yrs	47233	14294	30.3%
Total	288596	145564	50.4%

*Estimation of coverage was based on counting women screened at least once outside the program during the three calendar years studied. Source: Estonian Health Insurance Fund.

Table 4 - Numbers of primarily diagnosed cervical cancer cases in Estonia from 2000 to 2006

Year	All ages	30 to 34 yrs	35 to 39 yrs	40 to 44 yrs	45 to 49 yrs	50 to 54 yrs	55 to 59 yrs	Crude rate*	ASR [§]
2000	164	8	14	10	24	20	22	22.1	15.6
2001	151	7	9	20	21	15	15	20.5	14.3
2002	154	6	15	21	18	13	18	21.0	15.0
2003	143	13	8	20	21	14	11	19.6	14.1
2004	181	14	13	24	31	18	13	24.9	17.5
2005	157	9	14	16	28	23	16	21.6	15.5
2006	159	8	16	23	21	15	19	21.9	15.4

*Average annual incidence of cervical cancer per 100,000.

§World age-standardized incidence rate per 100,000.

Source: Estonian Cancer Registry.

Table 5 - Number and incidence* of primarily diagnosed cervical cancer cases by stage from 2000 to 2006 in Estonia

Year	Localized	Regional, nodes only	Neighboring tissues	Meta-static	Disseminated	Unstaged	Total
2000	82 11.1	31 4.2	17 2.3	17 2.3	11 1.5	5 0.7	163 22.1
2001	98 13.3	16 2.2	20 2.7	12 1.6	1 0.1	4 0.5	151 20.5
2002	93 12.7	19 2.6	21 2.9	14 1.9	5 0.7	2 0.3	154 21.0
2003	86 11.8	20 2.7	20 2.7	13 1.8	3 0.4	1 0.1	143 19.6
2004	114 15.7	21 2.9	21 2.9	13 1.8	4 0.5	8 1.1	181 24.9
2005	103 14.2	20 2.8	14 1.9	11 1.5	7 1.0	2 0.3	157 21.6
2006	102 14.1	16 2.2	25 3.5	5 0.7	5 0.7	6 0.8	159 21.9

*Average annual incidence rate of cervical cancer per 100,000.

Source: Estonian Cancer Registry.

Table 6 - Primarily detected cervical cancer cases within the screening program from 2003 to 2006 in Estonia

Year	Invasive cervical cancer	<i>In situ</i> carcinomas	Total number of diagnosed cancers
2003	7 (100%)	-	7
2004	1 (25%)	3 (75%)	4
2005	3 (43%)	4 (57%)	7
2006	4 (27%)	11 (73%)	15

Source: Estonian Cancer Society.

Discussion

On the 2nd December, 2003 the Health Ministers of the European Union unanimously adopted a recommendation on cancer screening⁸. This Recommendation of the Council of the European Union⁹ spells out fundamental principles of best practice in early detection of cancer and invites EU Member States to implement national organized cancer screening programs for three cancer sites (cervical, female breast and colorectal cancers) with a well-informed population-based approach and with appropriate monitoring, evaluation and quality assurance at all levels, taking into account European quality assurance guidelines for cancer screening^{10,11}.

Cancer screening can be opportunistic (spontaneous and unorganized) or organized (mass screening and population based screening programs). The major differences lie in the level of organization, planning, the systematic nature and scope of the activity, and in the use of validated and quality-assured action models and methods⁵. Organized cancer screening using evidence-based tests has considerable potential to improve the health of the population, provided that programs are implemented cost-effectively and with high quality. Its population-based approach ensures that screening also reaches the less fortunate who may be in greatest need of secondary prevention of cancer, and it also stimulates continuous improvement in the quality of diagnostic and therapeutic services wherever they are provided⁸.

Regarding cervical cancer the objective of organized screening is to reduce both cervical cancer incidence and mortality. The value of the high-quality Papanicolaou (Pap) smear in reducing the risk of invasive cancer and mortality has been firmly established, and it is estimated that regular screening can reduce the incidence of cancer by 80%^{5,12}; it is likely however that use of non-validated methods do not bring a similar impact. Organized screening programs for cervical cancer using standard validated Pap smears have been shown to be more effective than opportunistic or non-organized screening, also because opportunistic screening tends to miss the women at the greatest risk^{5,13}. It is a worrying phenomenon, that even though so big proportion of women have given smears compensated outside the program and without any quality assurance, almost no

or only a very small historical impact on cancer burden can be seen.

Cervical cancer incidence and mortality rates in Estonia are higher than those of the other Nordic countries^{3,4}. The EUROCHIP in Estonia was a study on cervical cancer screening indicators for the identification of major problems and needs for the Estonian organized screening program.

During the period from 2003 to 2005, a pilot study of cervical cancer screening was started in Estonia. Nationwide organized cervical cancer screening in Estonia was started in 2006 after the National Cancer Strategy was launched by the Estonian Parliament.

The analysis on the first year of organized cervical cancer screening program shows that participation in organized screening seemed to increase the population coverage with Pap-tests by age while in opportunistic screening it decreases with age. However, the increasing number of Pap-smears outside the program is worrying.

The present analysis incurred in the unfavorable climate for epidemiological research characterized by the aftermath of two data protection laws¹⁴, and by administrative restrictions on the use of data from registries hinders such studies in Estonia. The restrictive data protection law did not permit to perform a linkage study between the data from the screening program, from the Estonian Health Insurance Fund and from the Estonian Cancer Registry in order to evaluate the effectiveness of the program and the non-program activities. For the same reasons, compliance to treatment in cases of a pathological test could not be estimated.

In the future the impact of the invitational mode and other factors influencing population coverage with Pap-smear tests in different age groups within the organized screening program need to be studied in detail in order to evaluate the reasons for participation in the opportunistic screening and not in the organized one. More time is needed to observe the impact of screening on cervical cancer mortality.

In order to make cervical cancer screening an effective prevention measure, cancer cases resulting from non-participation in screening and from failures in detection have to be audited¹⁵. As there is no data about the test result and further follow-up of the women participating in opportunistic screening, the decision not to include women with a previous Pap-smear in past 12 months in organized screening should be questioned. The decision not to include women without health insurance into the national cancer screening program is also debated.

Moreover, according to the experience from the present study it is evident that there is an urgent need for establishing a central electronic screening registry to collect data on mailed invitations, reminders, test results, diagnostic and treatment procedures, etc. The legal basis and the necessary personnel and financial resources should be organized for this. For example, in 2006 the number of screened women within the organized

screening program was 9,116 according to the report from the clinics, but only 6,249 according to the report from labs. In addition, there was a large number of smears done outside the program. The screening registry would facilitate the data collection from different clinics and labs participating in the screening program as well as outside the program, improvement of the coverage of the program as well as validation of overall cost-effectiveness of the program.

Acknowledgments

The study was supported by: European Commission, Health and Consumer Protection Directorate-General (projects "EUROCHIP-2: European Cancer Health Indicator Project – The Action" and "EUROCHIP-3: European Cancer Health Indicator Project – Common Actions").

The authors thank Dr Andrea Micheli and Dr Ahti Anttila for their valuable and professional support, and the Estonian Health Insurance Fund, the Estonian Cancer Registry, the Estonian Cancer Society, and all clinics and labs participating in the program for pleasant collaboration.

Acknowledgments to the EUROCHIP Working Group: *Austria* W. Oberaigner (Cancer Registry of Tyrol); *Belgium* E. Van Eycken (Belgian Cancer Registry), H. Sundseth (European Cancer Patient Coalition); M. Arbyn (Scientific Institute of Public Health); *Bulgaria* Z. Valerianova (Bulgarian National Cancer Registry), V. Zlatkov (Sofia Medical University), P. Kostova (Sofia National Oncology Hospital), Y. Panayotova (Health Psychology Research Centre); *Czech Republic* J. Holub (Institute Of Health Information and Statistics of the Czech Republic); *Cyprus* P. Pavlou, C. Papageorgiou (Ministry of Health); *Denmark* M. Von Euler (University of Copenhagen); *Estonia* P. Veerus (National Institute Health Development); *Finland* R. Sankila, A. Anttila (Finnish Cancer Registry), K. Holli (Tampere University); *France* P. Grosclaude, A. Danzon (FRANCIM); *Greece* L. Tzala (Centre for Disease Control & Prevention), K.V. Kampouras (Ioannina University Hospital), G. Ferentinos (General Hospital of Halkida), D. Mauri (Papageorgiu Hospital); *Ireland* H. Comber (Irish National Cancer Registry); *Italy* A. Micheli, P. Baili, C. Amati, I. Casella, A. Cifalà, M. Esposito, S. Saltarelli, F. Di Salvo, R. Ciampichini, F. Berrino, G. Gatta, M. Sant, L. Ciccolallo, C. Allemani (Fondazione IRCCS Istituto Nazionale dei Tumori), R. Capocaccia, A. Verdecchia (Istituto Superiore di Sanità), F. Merzagora (Osservatorio Salute Donna), A. Costa (European School of Oncology); *Latvia* I. Viberiga (Riga Stradins University), L. Engele (Riga East hospital Cancer Center); *Lithuania* J. Kurtinaitis (Lithuanian Cancer Registry), R. Kurtinaitiene (Vilnius University); *Luxembourg* S. Couffignal (Centre de Recherche Public Santé); *Malta* M. Dalmás (Ministry of Health), R. Busuttil (Pathology Dept, St.Luke Hospital); *Poland* M. Bielska Lasota (National Institute of Public Health); *Portugal* A.

Miranda (South-Regional Cancer Registry); *Romania* I. Apostol (Victor Babes Foundation), A. Baban (Babes-Bolyai University); *Slovakia* I. Plesko, M. Ondrusova (Slovakia national cancer registry); *Slovenia* M. Zakeli, V. Zadnik (Slovenian National Cancer Registry); *Spain* C. Martinez (Escuela Andaluza de Salud Publica), C. Navarro (Consejería de Sanidad Murcia); *Switzerland* J.M. Lutz (Suisse Association of Cancer Registration), C. Quinto (ISPM Basel); *The Netherlands* R. Otter, M. Schaapveld (Comprehensive Cancer Centre North); *United Kingdom* M. Coleman (London School of Hygiene & Tropical Medicine), I. Kunkler (Western General Hospital Edinburgh), A. Gavin, F. Bannon (Northern Ireland Cancer Registry).

References

1. Statistics Estonia. Available at <http://www.stat.ee/statistics> (accessed 21 March 2010).
2. Arbyn M, Autier P, Ferlay J: Burden of cervical cancer in the 27 member states of the European Union: estimates for 2004. *Ann Oncol*, 18: 1425-1427, 2007.
3. Aareleid T, Pukkala E, Thomson H, Hakama M: Cervical cancer incidence and mortality trends in Finland and Estonia: a screened vs. an unscreened population. *Eur J Cancer*, 29A: 745-749, 1993.
4. Nygård M, Aareleid T, Härmaorg P, Mägi M, Nygård JF, Skare GB, Thoresen SØ: Changes in occurrence of cervical cancer in Estonia and Norway during 31 years. In: IACR 2002: 24th Annual meeting of the International Association of Cancer Registries, Tampere, Finland, 25-27 June 2002. Abstracts: P23. 2002.
5. Hakama M, Coleman MP, Alexe DM, Auvinen A: Cancer screening: Evidence and practice in Europe. *Eur J Cancer*; 44(10): 1404-1413, 2008.
6. Raud T, Klaar U: Pilot project of cervical cancer in Estonia (article in Estonian). *Eesti Arst*, 85(12): 834-848, 2006.
7. EUROCHIP: European Cancer Health Indicator Project. Available at www.tumori.net/eurochip (accessed 21 March 2010).
8. European Commission: Cancer screening in the European Union. Report on the Implementation of the Council Recommendation on cancer screening – First Report, 2008.
9. Council of the European Union: Council Recommendation of 2 December 2003 on Cancer Screening. *Off J Eur Union*, 878: 34-38, 2003.
10. WHO: Screening for cancer of the uterine cervix. Geneva, Switzerland, 1986.
11. Arbyn M, Anttila A, Jordan J, Ronco G, Schenck U, Segnan N, Wiener H, Herbert A, von Karsa L: European Guidelines for Quality Assurance in Cervical Cancer Screening. Second Edition - Summary Document. *Ann Oncol*, 21: 448-458, 2010.
12. Laara E, Day NE, Hakama M: Trends in mortality from cervical cancer in the Nordic countries. *Lancet*, 1: 1247-1249, 1987.
13. Anttila A, Ronco G, Clifford G, Bray F, Hakama M, Arbyn M, Weiderpass E: Cervical cancer screening programmes and policies in 18 European countries. *Br J Cancer*, 91: 935-941, 2004.
14. Rahu M, McKee M: Epidemiological research labelled as a violation of privacy: the case of Estonia. *Int J Epidemiol*, 37: 678-682, 2008.
15. Spayne J, Ackerman I, Milosevic M, Seidenfeld A, Covens A, Paszat L: Invasive cervical cancer: a failure of screening. *Eur J Publ Health*, 18: 162-165, 2008.