Coll. Antropol. **31** (2007) Suppl. 2: 17–22
Professional paper

Cervical Cancer Screening Programme in Finland with an Example on Implementing Alternative Screening Methods

Ahti Anttila[1] and Pekka Nieminen[2]

[1] Mass Screening Registry, Finnish Cancer Registry, Helsinki, Finland
[2] Department of Obstetrics and Gynaecology, Helsinki University Central Hospital, Helsinki, Finland

A B S T R A C T

In Finland (population 5 million) the organised Pap screening programme for preventing cervical cancer has been in action already for 45 years. Women aged 30 to 64 are targeted (N 1.25 million) and the screening interval is five years. The programme invites women seven times in a lifetime; the attendance rate per one screening invitational round is 73%. The programme has affected markedly the cervical cancer rates in our country. During the decennia of its action there has been about 80% decrease in the age-adjusted cervical cancer incidence and mortality rates. The current age-standardised incidence rate is 4 and mortality rate 1 per 100,000 woman-years. In the current article we describe the organisational aspects of the programme; and pay attention to renovation of the programme taken place during the last decade when novel technological alternatives have been started to be used as the screening tests. By expanding the coverage and compliance of screening we still expect to increase the impact of the programme. Same time, efforts are needed to avoid overuse of services due to spontaneous screening, in order to decrease potential adverse effects and improve overall cost-effectiveness. A large-scale public health policy trial on Human papillomavirus (HPV) screening is on-going. Cross-sectional information available thus far suggests promising results. Follow-up of cancer rates after screening episodes are still required to evaluate optimal screening policies (e.g., screening intervals by age groups, and starting and stopping ages). We propose speeding up the use of modern technological alternatives in organised screening programmes.

***Key words**: Cervical cancer, incidence, mortality, organised screening, effectiveness, cytological screening, HPV-DNA screening*

Introduction

In Finland (population 5 million) organised cervical screening was introduced in the early 1960s; piloting first within the area of three municipalities in 1963 and extending within a few years time to most parts of the country. From the early 1970s onwards, the registered screening invitational coverage has been almost complete within the centrally targeted screening ages.

During 1955–1964 the incidence of invasive cervical cancer in Finland was at a level of 15 cases per 100,000 woman-years; age-adjusted to the world standard population, with a slight increasing trend within the period. Mortality from cervical cancer was around 7 cases per 100,000 woman-years, respectively. Subsequent to implementation of organised screening, there was a rapid decrease in the invasive cervical cancer incidence and mortality rates. Currently the age-adjusted rates are 4 and 1 per 100,000 woman-years (Figure 1). Most of the reduction has occurred in the incidence of squamous cell carcinomas, whereas the incidence rate of cervical adenocarcinoma has been quite stable over the decades[1,2].

Effectiveness of Conventional Screening

Screening effectiveness in Finland was demonstrated first by a very large-scale cohort follow-up study among women invited in the implementation phase of the programme[3,4]. The study followed subsequent cervical cancer rates, based on about 425,000 invitations in 1963–

Received for publication January 31, 2007

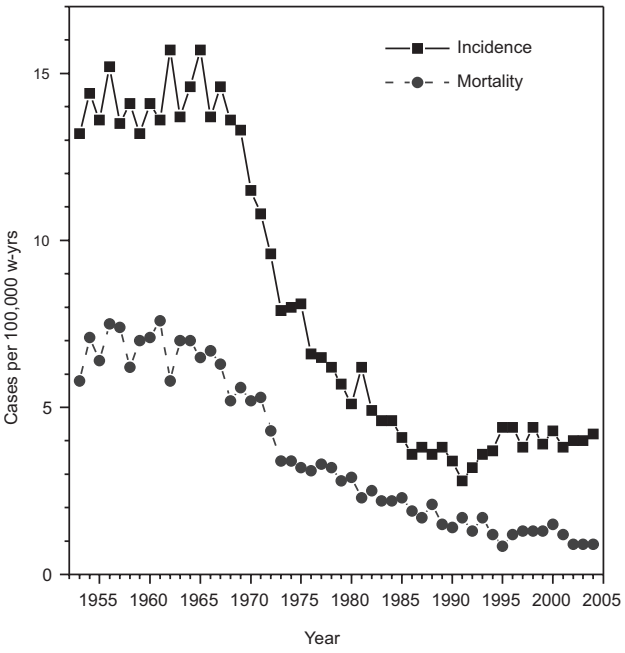

Fig. 1. Cervical cancer incidence and mortality rates in Finland in 1953–2004, adjusted for age to the World standard population (Finnish Cancer Registry).

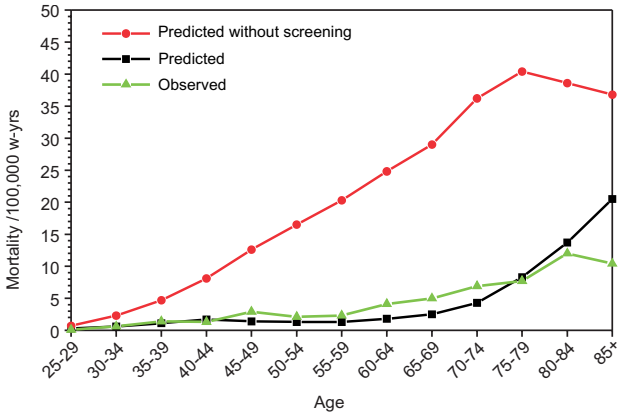

Fig. 2. Observed (Finnish Cancer Registry, 2007) and predicted (from Hristova & Hakama, 1997[6]) mortality rates from cervical cancer in Finland 1998–2002, by age.

1972. Most part of the women had been screened once during the study period. The efficacy estimate among screened was 80%. The attendance rate was 85% and the effectiveness of the programme was estimated at 60%. Among invited but not attended there was about 60% increase in the subsequent cervical cancers in comparison with the rates in the population before screening. It is likely that thereafter the effectiveness of the programme has increased, as more testing rounds have become available. However, there are mainly a number of ecological-level trend studies performed in the later years in our country (see IARC, 2005[4], for a recent synthesis on these). According to a cohort follow-up study among a

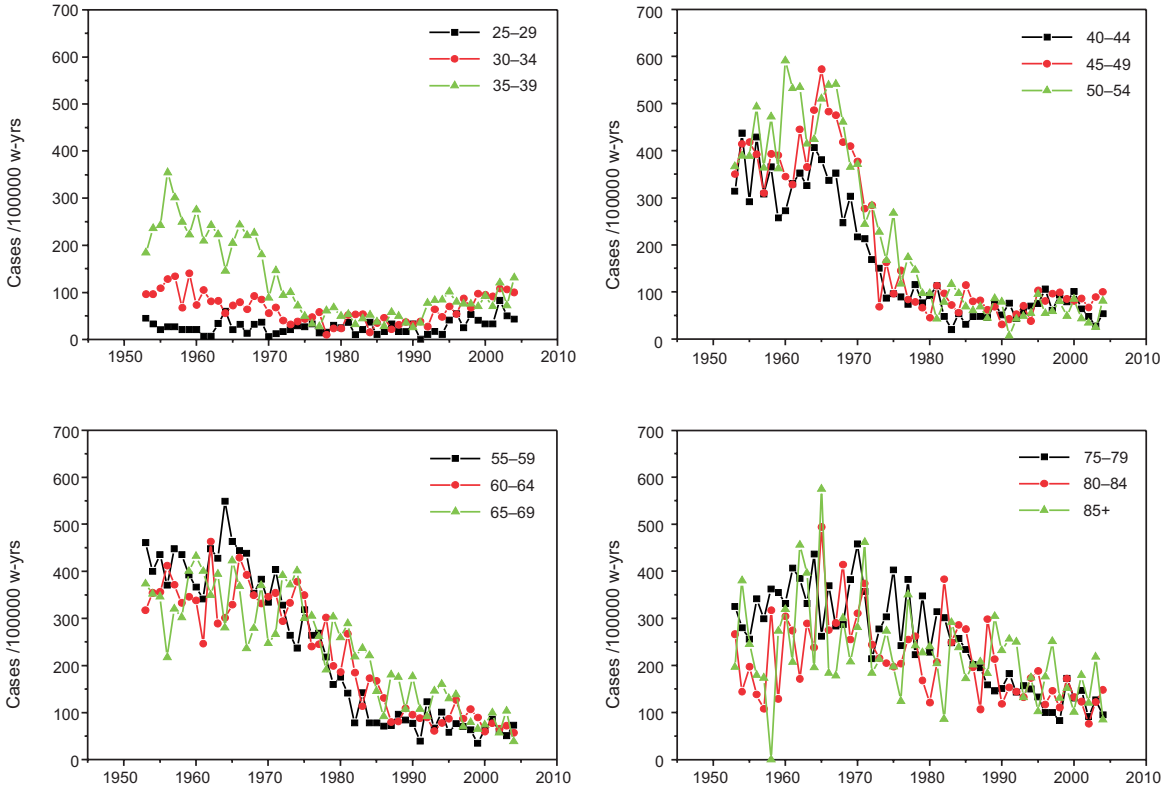

Fig. 3. Age-specific incidence rates of cervical cancer in Finland, 1953–2004 (Finnish Cancer Registry).

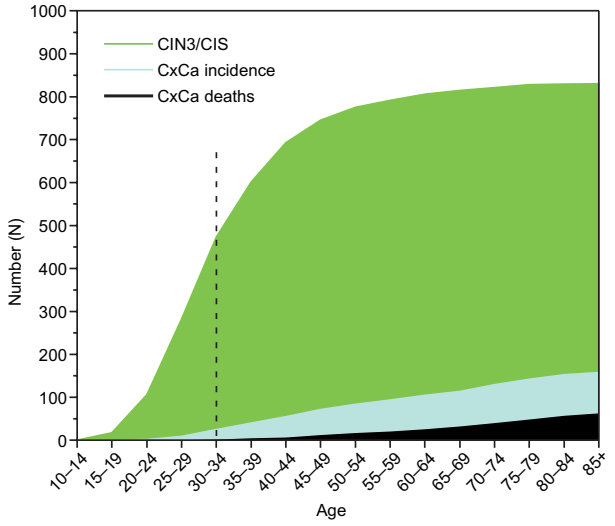

Fig. 4. Cumulative number of cases of severe dysplasia or carcinoma in situ (CIN3/CIS), cervical cancer incidence,0 and deaths from cervical cancer in Finland, annual averages in 1998 over age (Finnish Cancer Registry, 2007).

sample of women with a negative cytological result in the programme, the absolute rate of cervical cancer after screening negative is about 5 cases per 100,000 woman-years[5].

It is estimated based on the trends that each year almost 300 deaths are prevented due to Pap-screening; these deaths would have occurred at a broad set of ages from rather young (30 or 35 years) up to very old (more than 85 years) women (Figure 2)[6]. In the oldest age groups the incidence and mortality rates from cervical cancer are still expected to decrease due to ageing of female population screened previously in their life. There are still some 60 deaths per year, and the number of incidence cases is 160.

The incidence of cervical cancer has somewhat increased during the last decade in ages 25–39 (Figure 3) even though the number of cases in this age group is still small, below 30 cases annually (Figure 4). There are almost no deaths from this cancer type in ages below 50 years and the death rate among young women has not increased.

Growing Concerns on Opportunistic Screening

In the early days, opportunistic screening was not available in large-scale. Later on, use of such services has increased. There are no data to study the trends in the use of opportunistic screening. According to information from an annual population survey as available from late 1990s[7], any Pap smears (the estimate including also the opportunistic and diagnostic smears in addition to the programme smears) have been taken during a five-year period roughly for 93% of the women at target ages of the programme. The estimated coverage of any smears lifetime is 98%, respectively[8,9]. Trend studies[4] and a population-based case-control study using questionnaire-based self-reported information on the screening history (ever vs. never screened)[8] have suggested that the overall effect in decreasing cervical cancer incidence with spontaneous smears is up to 40%. In the latter study the effect among women participating in organised screening was about two-fold compared to those who had never participated (but given only spontaneous smears); spontaneous screening showed no additional impact among those subjected to organised screening.

One problem in the national screening policy is that there are apparently wide testing practices outside screening, also in rather young women – where almost all of the pre-cancerous lesions would regress naturally (see IARC, 2005[4] for estimates of regression probabilities). Figure 4 illustrates the numbers of CIN3/CIS incidence and treatments as available from cancer registry files: about 60% of these are diagnosed already in age before screening. More evaluation research, including also research on the potential adverse effects, on any screening is needed. There are yet no register-based data available on the spontaneous screening; such data is required in order to evaluate that activity and reduce the unnecessary actions. Recently, efforts have been started to include any smears in register-based evaluations.

Organisation of Cervical Cancer Screening

The screening activities have become an integral part of the health care system. Women in ages 30 to 60 years are invited with help of population registry, using a five-year interval when normal screening results. The two older age groups (55, 60) were added to the programme only in 1990s. There are nowadays thus seven invitations lifetime. Some municipalities invite also women in ages 25 and/or 65; women at a younger age than

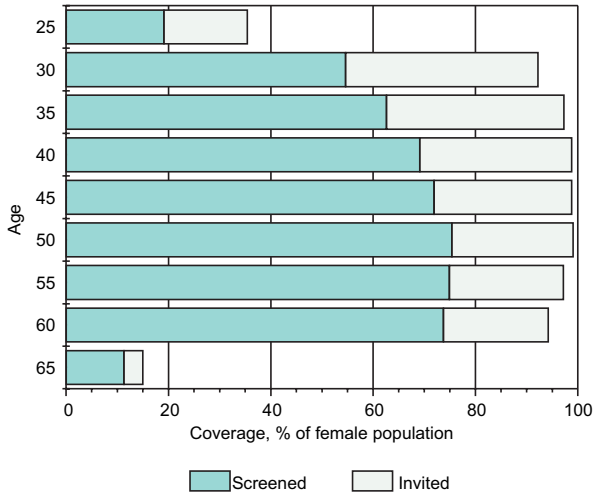

Fig. 5. Invitational and screening coverage within the Finnish cervical cancer screening programme in 2004 (Finnish Cancer Registry).

TABLE 1
CERVICAL CANCER SCREENING PROGRAMME IN FINLAND IN 2004: THE NUMBER AND PERCENTAGE DISTRIBUTION OF SCREENING TESTS IN THE ORGANISED SCREENING PROGRAMME, BY SCREENING TEST RESULTS, REFERRALS AND FINAL HISTOLOGICAL DIAGNOSIS (MASS SCREENING REGISTRY, 2007, PRELIMINARY INFORMATION BASED ON DATA FROM 437 MUNICIPALITIES OUT OF 444 IN THE WHOLE COUNTRY)

Screening test	Screened	Referred		Histological diagnosis									
				Cervix cancer		CIN3/CIS		CIN2		CIN1		Other or normal	
	N	N	%	N	%	N	%	N	%	N	%	N	%
Pap-test	170205	1290	0.8	18	0.01	178	0.1	192	0.1	175	0.1	727	0.4
I	158894	–	–	–	–	–	–	–	–	–	–	–	–
II	10022	132	0.1	1	0.0	4	0.0	6	0.0	10	0.01	111	0.07
III–V	1161	1158	0.7	17	0.01	174	0.1	186	0.1	165	0.1	616	0.4
Inadequate	128	–	–	–	–	–	–	–	–	–	–	–	–
HPV-test	14585	186	1.3	4	0.03	14	0.1	48	0.3	32	0.2	88	0.6
Negative	13433	7	0.05	–	–	1	0.01	–	–	1	0.01	5	0.03
Positive	1152	179	1.2	4	0.03	13	0.09	48	0.3	31	0.2	83	0.6
All	184790	1476	0.8	22	0.01	192	0.1	240	0.1	207	0.1	815	0.4

CIN – Cervical Intra-epithelial Neoplasia, CIS – Carcinoma *in situ*, Pap – Papanicolaou, HPV – Human papillomavirus, – magnitude nil, women with Papanicolaou group I or II or HPV test negative are not referred for further examinations unless repeated cytology or other results are suggestive of cancer or CIN, women with HPV test positive are referred for further examinations on the basis of cytology.

25 are not encouraged to be screened (http://www.kaypahoito.fi/). In the organised programme the present coverage of invitations is 95% of the target age (http://www.cancerregistry.fi/statistics). In one calendar year, there is about 250,000 invitations in the programme. The attendance rate is more than 70%.

Even though the attendance rate is satisfactory, close to 80%, in the older targeted ages, one main problem in the programme is the fact that among young targeted ages, particularly, in ages 25 to 35, the rate is very low, only slightly above 60%. This has lead to the situation that hardly half of the targeted population participates in those ages (Figure 5).

Attending organised screening for women is free of charge. Sample taking is done by trained nurses or midwives in the local primary health care centres or clinics. The sample quality is under continuous control done by the cytology laboratories, based on individual coding for sample-takers for a potential personal feed-back. The samples taken are VCE smears; i.e., samples from posterior vaginal fornix, cervix, and from endocervical canal are taken separately, using Ayre's spatula and endocervical brush, and are placed on the same slide. The samples are stained with modified Papanicolaou staining. The samples are screened by cytotechnicians, and the cytologist checks every abnormal smear and a proportion of normal smears. More recently, also the Human papillomavirus (HPV)-DNA samples are taken in contracted municipalities (see below).

There are some 15 cytology laboratories contracted by the municipalities to the programme. Confirmation and treatment is integrated into the normal health care routines. Treatment is provided for women with relatively mild lesions (CIN1) or with a more severe finding. All the data on the confirmation are included on the personal screening cards kept for every woman in the cytology laboratory; they are registered and the compliance and adequacy of treatment followed by the cytology laboratory and also by the mass screening registry.

The average referral rate is constantly about 1%, and the detection rate for an CIN+ (cervical intraepithelial neoplasia, or a worse histologically confirmed finding) about 0.3–0.5%. In addition, about 6% of the screened women get a re-invitation within a shorter interval, usually one year, based on borderline cytology (Table 1). There is still some variation in the detection rates and performance parameters which appear not to reflect directly the effectiveness aspects but, rather, some variation in the local cost-effectiveness[10].

Data collection infrastructures

Screening laboratories are responsible for recording screening visit and confirmation and treatment information within the programme. The invitational and screening data of the programme, including cytological and histological screening findings, are filed centrally at the Mass Screening Registry that it a subunit within the national Finnish Cancer Registry. This makes an efficient tool for evaluation and monitoring of the programme. The Finnish Cancer Registry provides complete data on cancer incidence and mortality, arranged individually with the help of the unique personal identifier. The mor-

tality records are obtained from the files of the Cause-of-Death Registry at the Statistics Finland. The cancer registry notifies also carcinoma *in situ* cases of the cervix uteri (CIS, including both squamous and adenocarcinoma *in situ* cases), as well as cases of severe intraepithelial neoplasia (dysplasia gravis, or CIN3 not specified in more detail).

Quality assurance

In the normal screening practice of the organised programme there is a number of quality control activities, such as control of sample quality that takes place mainly within the cytological laboratories within the programme[9]; and re-reading, consultation and training meetings; even though there have been no systematic publications on their results. Important for developing the screening specificity criteria, there are, normally, weekly sessions between cytology and pathology units/laboratories. Since 1999 a systematic re-reading programme of potentially false negative smears have been in action; including re-reading of these smears together with control slides both in a reference laboratory and in the original screening laboratory. This material is based on linkages between the screening and cancer registry files.

Novel Screening Methods

The main aim of the evaluation of alternative screening techniques is to assess screening effectiveness, i.e., comparing incidence of subsequent cervical cancers as the outcome and screen-detected pre-cancers as surrogates. Also performance e.g. in form of screen-detected findings will be monitored and compared. It is important to verify that, if the treatment rates would increase, it reflects, respectively, to better efficacy and effectiveness. Modifications on the screening policy need also to be considered, e.g. the need of lifetime number of tests in the programme. For the time being, approximately 860,000 women have been allocated to automation-assisted cytology, HPV DNA testing, or to conventional cytology within the organised screening programme[11,12,13]. In the HPV-DNA screening arm, run within a restricted area, the plan is to invite about 100,000 women in 2003–2008. In numerical terms, almost 10% of the whole national target population will be subjected to HPV screening. Follow-up results on subsequent cervical cancers will become available during 2007– 2015.

First reports on screening detection rates are available[12,13]. Screening detection rates as well as specificity estimates in automation-assisted screening are very similar to conventional screening. Based on early results from HPV screening, the detection rate of mild pre-cancerous lesions was in excess in the HPV screening protocol[12]; see also Table 1 on the routine statistics on 2004. CIN3+ detection rates were about the same as in conventional screening. There is a cytological triage protocol after a positive primary HPV test. Noteworthy, when considering the referral to colposcopy, based on the cytology triage, the cross-sectional specificity and positive predictive value estimates were closely resembling those of the conventional screening.

Discussion

Historically, the overall incidence of invasive cervical cancer, as well as that of *in situ* carcinoma of the cervix uteri, has drastically decreased in those ages subject to organised screening activities. Organised screening is effective. There is no similar decrease in the CIN detection frequencies, however. On the contrary, the detection rates of CIN grades 2 and 3 have even slightly increased[2], indicating that the biologic background risk has been likely increased. Also invasive cervical cancer incidence has increased in ages 25–39 years, even though based on a small number of cases registered annually. This still warrants improvements in the rather poor attendance rate in the programme in the above young targeted ages. Interventions testing written reminder or, preferably, reminding by phone, are required[14]. Self-sampling could also be tested in order to check whether one can increase compliance meaningfully.

On the other hand, based on the finding that a very large proportion of registered CIN3/CIS cases have been detected and treated outside the organised programme, e.g. in opportunistic screening, in parallel with improving the population-based coverage and access to the services, also decrease and stopping of unnecessary actions should take place.

Concluding Remarks

Following from the 45-year period of its action the cervical cancer screening programme in Finland has contributed to a large decrease in cervical cancer incidence and mortality rates. The purpose of cervical cancer screening is to prevent mortality and incidence from the disease. One can conclude that organised screening is effective in combating cervical cancers. With introducing modern screening technologies and more systematic quality control activities in the programme, and moderately expanding the coverage and as well as compliance – particularly, at the young target ages of the programme – we still aim to increase the effectiveness of the programme. Alternative methods in screening, such as automation-assisted screening and HPV testing, have shown promising cross-sectional findings. We propose speeding up the use of modern technological alternatives in organised screening programmes. Follow-up information of cervical cancers in still required, to acquire evidence for possible modifications on the screening policies.

REFERENCES

1. NIEMINEN P, KALLIO M, HAKAMA M, Obst & Gynecol, 85 (1995) 1017. — 2. ANTTILA A, PUKKALA E, SÖDERMAN B, KALLIO M, NIEMINEN P, HAKAMA M, Int J Cancer, 83 (1999) 59. — 3. RÄSÄNEN-VIRTANEN U, HAKAMA M, Am J Epidemiology, 103 (1976) 512. — 4. International Agency for Research on Cancer (IARC). IARC Handbooks of cancer prevention, Volume 10. Cervix cancer screening (IARC Press, Lyon, 2005). — 5. VIIKKI M, PUKKALA E, HAKAMA M, J Med Screen, 6 (1999) 103. — 6. HRISTOVA L, HAKAMA M, Acta Oncologica, 36 (1997) 1. — 7. National Public Health Institute (NPHI). Health behaviour among Finnish adult population (NPHI, Helsinki Finland 1997). — 8. NIEMINEN P, KALLIO M, ANTTILA A, HAKAMA M, Int J Cancer 83, (1999) 55. — 9. ANTTILA A, NIEMINEN P, Eur J Cancer, 36 (2000) 2209. — 10. KOTANIEMI-TALONEN L, NIEMINEN P, HAKAMA M, SEPPÄNEN J, IKKALA J, MARTIKAINEN J, TARKKANEN J, TOIVONEN T, ANTTILA A, Eur J Cancer, 43 (2007) 169. — 11. ANTTILA A, HAKAMA M, KOTANIEMI-TALONEN L, NIEMINEN P, BMC Public Health, 6 (2006) 252. — 12. KOTANIEMI-TALONEN L, NIEMINEN P, ANTTILA A, HAKAMA M, Br J Cancer, 93 (2005) 862. — 13. NIEMINEN P, KOTANIEMI L, HAKAMA M, TARKKANEN J, MARTIKAINEN J, TOIVONEN T, IKKALA J, LUOSTARINEN T, ANTTILA A, Int J Cancer, 115 (2005) 307. — 14. EAKER S, ADAMI H-O, GRANATH F, WILANDER E, SPARÉN P, Cancer Epidemiol Biomarkers Prev, 13 (2004) 346.

A. Anttila

Finnish Cancer Registry, Liisankatu 21 B, FIN-00170 Helsinki, Finland
e-mail: ahti.anttila@cancer.fi

PROGRAM PROBIRA RAKA VRATA MATERNICE U FINSKOJ S PRIMJEROM UVOĐENJA ALTERNATIVNIH METODA PROBIRA

SAŽETAK

U Finskoj (5 milijuna stanovnika) je organizirani program Papa-testiranja u prevenciji raka vrata maternice u upotrebi već 45 godina. Testiranje obuhvaća žene u dobi od 30 do 64 godine (1,25 milijuna), a period između dva testiranja je pet godina. Prema programu, žene se poziva sedam puta tijekom života; odaziv jednoj rundi poziva na testiranje je 73%. Ovaj program je značajno utjecao na stopu pojave raka vrata maternice u našoj zemlji. Tijekom desetljeća njegove primjene zabilježen je pad od oko 80% u dobno-standardiziranim stopama pojavnosti i smrtnosti od raka vrata maternice. Trenutna stopa pojavnosti, obzirom na dob je 4, a stopa smrtnosti 1 na 100.000 žena godišnje. U ovom članku opisujemo organizacijske značajke programa; sva pažnja je usmjerena na obnovu programa tijekom zadnjeg desetljeća s novim, alternativnim metodama koje su se počele koristiti u sklopu testova probira. Povećanjem pokrivenosti i suglasnosti s programom, očekujemo povećanje utjecaja programa. Istovremeno, potreban je napor kako bi se izbjegla pretjerana upotreba službi zahvaljujući spontanom probiru, sa svrhom smanjenja mogućih štetnih učinaka te smanjenja troškova. Trenutno se pokušava uvesti pokrivanje troškova testiranja na HPV kroz zdravstveno osiguranje. Očekujemo povoljne rezultate. Praćenje stope raka nakon testova probira je potrebno i dalje kako bi se procijenila najbolja strategija probira (vremenski razmaci između testiranja po dobnim skupinama te početna i završna dob). Predlažemo brže uvođenje novih, modernih metoda u organiziranim programima probira.