



Cervical cancer screening in Greece

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Abstract

The aim of this study was to describe the state of the art in cervical cancer screening in Greece by presenting the two regionally organised screening programmes that currently operate in the country. Both programmes were initiated in 1991 and are partly funded by the European Union. The Ormylia screening programme covers the population of Halkidiki (Northern Greece), a predominantly rural area. The second programme covers the regions of Messinia and Ilia (Southern Greece). Both programmes are targeted at women aged 25–64 years of age and a Papanicolaou (Pap) smear test is recommended every 2–3 years. Electoral and municipal registries are used to identify the target population and personal invitations are sent to the eligible women in the screening programme. The Ormylia programme is based at the Centre ‘Our Lady Who Loves Mankind’, whereas mobile units are used by the Messinia and Ilia programme. Slide reading for the Ormylia programme is performed in the cytology laboratory of Alexandra Hospital in Athens and epidemiological support is provided by the Department of Hygiene and Epidemiology (Medical School, University of Athens). A specifically designed database is used for data recording. Over 80% of the target population in the region have already been screened. Communication of results is by means of a personal letter upon a negative result and in person upon a suspicious result. Quality assurance in both programmes is based on the European protocol. These two programmes are the sole organised cervical cancer screening activities in Greece in the absence of a national programme. They employ well-trained personnel, they use modern equipment and have strict quality assurance procedures. © 2000 Elsevier Science Ltd. All rights reserved.

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1. Introduction

Cancer of the uterus is the fifth most frequent type of female cancer in Greece and corresponds to cancer of the cervix and cancer of the endometrium, two epidemiologically distinct types of female cancer [1].

Based on data from the 1991 census in Greece the total female population in the country was 5 204 000, of which 1 724 000 (33.1%) belonged to the 0–24 year age group, 2 694 000 (52.8%) to the 25–64 year age group and 786 000 (15.1%) women were 65 years or over. The mortality rate for cancer of the uterus was 7.24 (per

100 000) and the mortality of cervical cancer was 2.48 (per 100 000).

In August 1990 the Greek National Cancer Registry was set up, which recently released data on its first year of operation (August 1990–July 1991). According to these data, 497 new cervical cancer cases were recorded during this period, 554 new cases of cancer of the endometrium and 46 new cases of unspecified uterus location. According to the most recent data available, the incidence rate for cervical cancer for 1991 was 9.55 per 100 000 [2]. The 1995 estimate for the incidence of cervical cancer in Greece from the EUCAN database of 1998 [3] was 9.29 per 100 000 (age-standardised for the European population).

Cervical cancer mortality in Greece is relatively low when compared with the other European Member States, but it is difficult to determine its time trends

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because of differences in death certification, where a clear distinction on the cause of death between the cervix and endometrium is absent. During the period 1981–1985, only 33% of the total recorded deaths from cancer of the uterus specified the exact location of cancer while during the period of 1966–1970, the percentage was just 13% [4]. For this reason, the time trends are misleading, in that cause-specific mortality from cancers of the cervix and endometrium seem to have increased in recent years, whereas overall mortality from uterine cancers seems to have declined. Therefore, the increase in the site-specific uterine cancer categories most probably results from the corresponding increase in recording the exact cancer locations. Mortality data released by the National Statistical Service indicate that in Greece, cervical cancer was the cause of death in women above the age of 25 years for 113 women in 1990, 129 women in 1991, 117 women in 1992, 111 women in 1993, 69 women in 1994, 84 women in 1995 and 81 women in 1996.

At present, there are two organised regional screening programmes which are members of the European Network for Cervical Cancer Screening set up by the 'Europe Against Cancer' programme: the Ormylia Cervical Cancer Screening Programme which covers the female population of the regions of Halkidiki and partly (small portion) Thessaloniki in Northern Greece and the Oncological Society Programme which covers the regions of Messinia and Ilia in Southern Greece. There is no nationally organised cervical cancer screening programme in Greece.

In parallel with the regional cancer screening programmes, opportunistic cervical cancer screening facilities exist in all major hospitals and in private practices. State and university hospitals provide free smear tests for all women who wish to be examined, but no invitation system is available. Smear tests are also performed in health centres and family planning clinics [5]. Based on the most recent data available (for the year 1992) there were 29 cytology laboratories operating in Greece, 24 of which belong to the National Health System, four belong to University hospitals and one belongs to IKA (the major state social security provider). These laboratories employ over 100 cytologists and provide professional training leading to specialisation in cytology for approximately 50 residents. In addition, an unspecified number of private cytology laboratories are operating across the country. At present, 350 cytologists are members of the Greek Cytology Society.

Private hospitals and private practices charge a fee for the smear test which is refundable (either in full or as a percentage of the cost) by the woman's social/medical care provider. In some cases, justification of the costs for the insurance companies is very time-consuming due to the large amounts of paperwork required, so that women are discouraged to take the smear test. However, state hospitals are usually short-staffed, so that a

smear test appointment may be arranged only after several days' waiting time. There are no data for any proportion of the population covered by opportunistic screening.

2. Population and methods

2.1. The Ormylia Regional Cervical Cancer Screening Programme (Halkidiki)

The Ormylia Cervical Cancer Screening Programme has operated since 1991 and is partly funded by the European Union (programme 'Europe Against Cancer'-DG/V). It addresses all women who permanently reside in the region of Halkidiki (Northern Greece). The Ormylia Screening Programme, apart from some isolated grants from the Secretariat of Youth and Athletics and the Ministry of Health and Welfare, receives no other regular financial support from any organisation and its operation mostly relies on donations and initiatives from local enterprises.

2.2. Invitation to screening

The Ormylia Cervical Cancer Screening Programme is located at the Centre 'Our Lady Who Loves Mankind' a model cancer prevention unit in Northern Greece, which employs highly trained medical and para-medical health professionals. The region of Halkidiki covers an area of 2918 km² and consists of 70 municipalities with over 115 villages in total, many of which are isolated and difficult to access, especially during winter. It has a total population of 91 653 [6].

The majority of the local population (over 75%) live in rural areas, engaged in agricultural activities such as farming, cattle breeding, as well as fishing and mining, with only a minority engaged in white-collar occupations. Although hospitals and health centres exist in some remote areas of the region, they mostly cover emergencies, due to a lack of specialised staff. As a result, the population is forced to seek routine medical care in non-organised family or preventive medicine services or in the major urban centres located on average 150–200 km away from their villages. This fact, combined with the poor road network of the area, results in major health inequalities of the Halkidiki population compared with the rest of Greece and other countries of the European Union.

All women aged 25 years and above and who are permanent residents of Halkidiki are identified through the electoral and municipal registries. These names are cross-checked with all other locally available registries and population lists (e.g. church, social clubs) to define the target population of the screening programme. The target population of the cervical cancer screening

programme is a dynamic cohort, thus the number of eligible women, as well as their age distribution, changes over time and over screening round. Since the female population of Halkidiki lacks substantially in medical services, the vast majority of the permanent residents have never visited a gynaecologist before, thus women younger than 25 years (provided they are sexually active) or older than 64 years may still be screened at least once and the re-screening interval is decided according to the first smear test result.

Using information stored in a large computer database, personal invitations are printed and sent out to all eligible women in combination with repeated announcements in the local press, radio and TV stations throughout the region. Posters are also placed in all villages at central locations (municipal offices, hospitals, health centres, church, schools, registration offices, GP practices, pharmacies, etc.). Semi-personal invitations are also given to school children to pass them on to their mothers, grandmothers and other female relatives. Information pamphlets have been printed containing information on the natural course of cervical cancer, details on the Papanicolaou (Pap) smear examination and all information related to the operation of the regional screening programme (exact location, contact numbers, opening hours, transport). In addition, lectures on cancer prevention are regularly delivered by health specialists at the Centre and in several key villages of the region.

2.3. Target population

The target population of the Ormylia Cancer Screening Programme is just under 17 000 women (ages 25–64 years). When joining the programme each woman undergoes a personal interview with a trained interviewer where a questionnaire is completed giving detailed information on her personal, gynaecological, reproductive and family history. A unique personal identification number (ID) is given to each woman which is noted on her records, examination slides, correspondence and communication of results. Each woman is identified through this personal ID number.

2.4. Local organisation and screening practices

All information concerning each participating woman is stored in computerised form in a large database that uses a multi-link file system. Each file contains a set of information for each woman and with the use of a special programme, the data manager can choose any combination of information fields that is required.

In order to operate a successful and efficient screening programme, the co-operation of the Centre with other centres of excellence in the field of cytopathology, epidemiology and cancer prevention was imperative.

Therefore, the Centre has established a direct communication line with the Cytology Laboratory of the Alexandra General Hospital of Athens and the Department of Hygiene and Epidemiology of the University of Athens. Alexandra's Hospital Cytology Laboratory is a unit where over 78% of the total number of smear slides from different sources on the national level are read [5], with sound experienced and well-trained personnel. This laboratory employs seven trained cytologists and six residents. The Department of Hygiene and Epidemiology of the University of Athens is the largest epidemiology department in Greece and provides solid scientific and epidemiological support to the Ormylia cervical cancer screening programme.

Despite the fact that these centres are located in Athens which is more than 600 km away from the screening centre in Ormylia, the use of modern technology has enabled the establishment of a solid communication line. All collaborating centres are connected to the Internet and use high speed telecommunication lines for data transfer, data reporting and inter-centre communication. Thus, all examination slides from the Ormylia programme are sent to the Cytology Laboratory of Alexandra Hospital where they are read and the diagnosis is directly entered into the database [7]. From this point on, the data files can be extracted by the other two centres in order to print out the results which will be sent to each woman, update the call–recall lists by entering the date of the next examination, activate the further examination procedure for those women tested positive and open the follow-up record.

At present, each woman is advised to have a Pap smear test every 2 years following a negative result with a personal letter sent 1 month prior to the date of examination and two reminders at 1-monthly intervals after the due date. In cases where the woman does not show up for screening, she is telephoned to find out the reason for her non-attendance. In cases where the woman has moved away from the region, or is deceased, her name is taken off the computer records, otherwise efforts continue. After two reminders and three repeated phone calls, the woman is considered lost to follow-up. Upon a result suspicious for malignancy, great effort is taken to conduct the further examinations suggested within 2 weeks following the communication of the abnormal result. Each woman is free to choose the medical care provider to conduct these examinations, but the centre has established a direct referral system with the Theagenion Anti-Cancer Hospital of Thessaloniki, the largest cancer centre in Northern Greece and the Medical School of the University. In cases of suspicious findings, the follow-up file remains open until follow-up and treatment have been completed and the result of final treatment is entered. A copy of the hospital records and reports is kept in the woman's archive file.

Normally the time period between the smear test and communication of results ranges from 4 to 6 weeks depending on the number of smear slides sent for reading to the laboratory. The time period between recommendation of further examinations and completion is from 6 to 8 weeks and the indicated treatment is mostly completed within 5 weeks.

So far, over 80% of the target population have been screened (smear test and gynaecological examination) while the vast majority of those had never visited a gynaecologist before. Smears are taken using a brush and a spatula and are sent in batches of 300–600 tests to the Cytology Laboratory of Alexandra Hospital (using express mail), where they are read by the cytology screeners, who are trained specialists having received additional training on screening cytology. Upon a suspicious result, the responsible person (internist/general practitioner) of the screening programme is immediately notified and the woman is called at the Centre where everything will be explained to her in detail and an appointment will be made for her referral to the appropriate medical centre to have the further examinations (colposcopy, biopsy, etc.). While a letter is sent to all women with non-malignant findings, no written notification is sent out on suspicious smear test results purely for ethical reasons. It must be noted that the majority of the population of Halkidiki is rural and of low educational background, thus a plain letter stating the result of the smear test would create great anxiety and distress to the woman, without convincing her to visit a specialist and carry out the recommended examinations. Therefore, a discussion with the responsible person of the screening programme gives them the opportunity to find answers to all their questions and make arrangements for the examinations. In cases of inadequate smears, the screening centre is notified and the woman is called back for a repeat examination. The programme has recently initiated a biopsy register in computerised form, but there are some difficulties and a substantial delay in obtaining copies of the histology reports from the medical centres, so this registry is at present rather incomplete.

2.5. *Quality assurance*

Quality assurance of smear taking is ensured by keeping the same health professionals in the screening programme who have received special training and are all experienced gynaecologists. The cytology laboratory of Alexandra Hospital is conducting its internal quality control tests. The screening programme is currently organising a reliability study of smear reading, where a random sample of diagnosed smears will be re-read in order to assess observer variability. The quality assurance protocol used is the one set by the 'Europe Against Cancer' programme and is closely followed.

2.6. *The Messinia and Ilia screening programme*

The Hellenic Society of Oncology started in May 1991, a pilot cervical cancer screening programme, within the frame of the programme 'Europe Against Cancer' which was targeted at the rural female population in the counties of Ilia and Messinia (Peloponese) and used the Pap-smear method. The aim was to obtain the necessary experience, with a view to implementing a national screening programme.

The smears are taken with the use of a mobile unit by a gynaecologist or a trained rural doctor or midwife and are sent together with the medical history and the code number of each woman to the headquarters of the Hellenic Society of Oncology in Athens. The smears are distributed to three cytopathology laboratories of the Anti-Cancer Hospitals in Athens (Agi Anargiri Cancer Hospital, Agios Savas Anti-Cancer Hospital and Metaxas Anti-Cancer Hospital). Moreover, three private cytopathology laboratories are used. For the same purpose in the central office of the Hellenic Society of Oncology a cytopathology laboratory is also operating.

The programme is funded by the 'Europe Against Cancer' programme, the Ministry of Health from the Anti-cancer Fund Raise, the Hellenic Anti-Cancer Institute and other private sponsors.

2.7. *Invitation to screening*

A computerised call-recall system is in use, based on the National Census of 1981, and the electoral lists of the countries which have a reliability of 80%. There was no national death and migration registry in these counties. The women received a personal invitation letter, with a predetermined appointment (that they could modify with a telephone call). A reminder letter was sent to those who did not respond to the first invitation. The compliance to invitation in the first round was 53.49%.

In order to increase the participation rate, various methods were used 8 months prior to the beginning of the programme. The local television, radio stations and the Press, doctors of health centres, the church, schools and the local authorities have helped us to advertise the programme and mobilise the public. Informative seminars were held by experienced specialised doctors addressing both the women and the doctors of the district (rural doctors, gynaecologists, general doctors and midwives) explaining the nature and purpose of cervical cancer screening. Special lectures were given at social clubs. Leaflets, posters, banners were used to mobilise the female population. A mini-bus was used to carry the women from the remote and mountainous villages where access of the mobile unit was difficult. Social groups such as Red Cross annexes, cultural associations, social workers, etc. have co-operated and assisted our effort.

2.8. Target population

The screening programme was initiated in the counties of Ilia and Messinia. The choice of these counties was random since there is no screening programme at a national level. The target population referred to women aged 25–64 years, and who are permanent residents of these counties.

2.9. Local organisation and screening practices

The smears are taken in the mobile unit. The average number of women screened is 45–50 per day. The frequency of smear taking is every 2 years. The smears are taken by experienced doctors, gynaecologists and midwives. Gynaecological examination is *not* performed.

Three smears are taken from each woman: a vaginal smear with a cotton swab, an ectocervical smear with a wooden Ayer's spatula and an endocervical smear with a cytobrush, a most effective combination for achieving adequate samples [8–10]. Normal results or those with benign lesions are mailed to each woman within 4–6 weeks.

All women with squamous atypia, or a more severe lesion (human papilloma virus (HPV), cervical intra-epithelial neoplasia (CIN) I, II, III, invasive cancer) after a call invitation and a predetermined appointment are informed about the result and are invited for colposcopy assessment and biopsies which are performed by their own gynaecologist. The Hellenic Society of Oncology disposes of a biopsy database.

A repeat smear is suggested for the women who have inflammation, 3–6 months after the initial diagnosis and therapy by their own gynaecologist. The repeat smear ensures the reliability of the diagnosis. There is no treatment protocol in our programme which depends on the practices of each gynaecologist.

A gynaecologist is responsible for the follow-up and further investigation of women sent for biopsy. The gynaecologist communicates with them by telephone, or visits them at home. He also collects the copies of the histology reports and biopsies programme. Special forms are completed for the cases (HPV, CIN I, CIN II, CIN III and invasive cancer) for each round. Patients are informed about the kind of the performed treatment and the histological diagnosis.

2.10. Quality assurance

In Greece, there are no national or regional guidelines for cervical cancer screening. For this purpose, the European Guidelines for 'Quality Assurance in Cervical Cancer Screening' were used [10,11]. The smears are sent to the headquarters of the Hellenic Society of Oncology in Athens, with the request form, and are distributed to the three cytopathology laboratories of the Anti-Cancer Hospitals in Athens.

Private cytopathology laboratories and one in the central office of the Hellenic Society of Oncology are used. A common computerised programme for reporting according to the World Health Organization (WHO) classification and the European recommendations is used [10,11].

Initial reading is performed by cytopathologists with experience of more than 5 years on these topics. A review of atypical smears (HPV, CIN, invasive cancer) is conducted by the supervisor. Some of the atypical smears are circulated to the other laboratories and discussed [10,12,13].

For this cervical cancer screening programme the project leader is a surgeon, the project manager is a cytopathologist, a surgeon is the local responsible, and a gynaecologist is responsible for the follow-up of the women. Eight cytopathologists are used for smear reading, and four rural doctors and three midwives are responsible for smear taking. All of the above staff had a continuous training and participation in national and world congresses and seminars.

2.11. Data collection

In the absence of a Greek cancer registry up to 1991, it is not possible to have mortality data on the participants of the programme. The option of active follow-up has not been exercised since it was decided that it would have a negative impact upon the primary screening programme.

The data are collected in the screening forms and the data entry is done in the central office of the Hellenic Society of Oncology in Athens. The data are entered in a Paradox 4.5 database residing in a PC network (Novell), a collection of programmes checks on the data entered to discover possible data entry errors. The responsible person has a B.A. in mathematics, from the National Capodistrian University of Athens and a Ph.D. and M.A. in mathematics from the Northeastern University of Boston.

The statistical analyses planned include comparison of cancer incidence rates across prefectures, as well as, the relationship of cancer occurrence with the demographic information collected. Three types of letter forms are used for reporting: (a) all results normal; (b) invitation for re-examination due to inflammation; (c) invitation for re-examination due to unsatisfactory original sample. The participants with cancer or pre-cancerous conditions are called for a face-to-face appointment.

The programme is based on the scheme suggested by the European Guidelines for Quality Assurance in Cervical Cancer Screening [11,14]. In Messinia county, 11832 women were screened in total during the first round. In the first round of Ilia, 8129 women were examined.

3. Conclusions

3.1. The Ormylia programme

The Ormylia Cervical Cancer Screening Programme has been very well accepted by the local population and is now expanding to the adjacent region of Thessaloniki. The provision of high-quality services as a consequence of the trained personnel, the modern equipment and the adherence to strict quality assurance protocols has earned the programme the trust of the local population and has advanced cancer prevention efforts in Northern Greece. In the absence of a national screening programme, the present regional programme is an effort of utmost importance for the early detection and prevention of cervical cancer in Northern Greece. The experience gained since the beginning of the screening programme may and should be used by the appropriate Greek governmental bodies to establish secondary prevention activities at the national level.

3.2. The Messinia and Ilia programme

The use of the mobile units are better than a permanent location, because they make it easier for women living in remote areas far from medical centres to participate. The use of the mini-bus has also contributed greatly to the implementation of the programme. Another factor that determined the success of the programme was the support of the local authorities and the church [15]. The financing of the programme was, and still is, a major problem. We are not yet able to estimate the cost of the Greek screening programme for cervical cancer exactly, but believe that it must be lower than that of similar programmes.

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