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HEALTH TECHNOLOGY ASSESSMENT IN THE AREA OF PREVENTION

Selected Screening Cases in Greece

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Abstract

Objective: To explore the impact of health technology assessment (HTA) on health policy and practice in Greece through selected screening case studies in the prevention area. The three cases studied were mammography screening, PSA screening, and routine ultrasonography in normal pregnancy.
Methods: Official policy recommendations or reports, a literature review of Greek published research as well as gray literature from various sources, and interviews with specialists and medical associations were performed, and their impact on health policy formulation was examined.
Results: The implementation of the screening tests does not take the form of structured mass screening programs. Almost all physicians (urologists-pathologists, gynecologists) apply PSA and routine ultrasonography in normal pregnancy respectively with the purpose of either prevention or diagnosis. Mammography is applied generally for prevention or diagnosis, but there are some mass screening programs at a local level. In addition, the results show no evidence that the efficacy and the cost-effectiveness of the three screening programs have been a matter of serious concern and investigation for the purposes of policy formulation in Greece.
Conclusion: The results point to a need for the implementation of HTA methods on mass screening preventive programs in which real value and cost remain unclear and whose use is based on empirical and personal assessments.

Keywords: Health technology assessment, Prevention, Mass screening, Mammography, Ultrasonography in pregnancy, Prostate-specific antigen

Health technology assessment (HTA) systematically examines the short- and long-term consequences of the application of a health technology, a set of related technologies, or a technology-related issue. In this broad context, prevention programs are a specific case of

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health technology (36). As the practice, provision, and management of health care undergo rapid technological and organizational change, HTA has increasingly become a valuable tool to examine effectiveness, quality of care, patient outcomes, and cost-effectiveness. In Europe, several researchers have touched upon the questions of the effectiveness and efficacy of prevention programs, and there is scientific evidence available that can be used in decision making and setting policies (28;52).

A brief description of the Greek healthcare system with emphasis on available preventive services was considered essential for the understanding and interpretation of the situation as regards the implementation of principles of HTA, which progresses rather slowly, although promising steps are being made toward this direction. The strength of governmental regulations, combined with the necessary expert guidance and the experience gained, will determine the rate at which HTA will expand in the increasing number of fields in the healthcare sector.

This paper focuses on prevention policies and the extent and manner of use of scientific evidence on three specific prevention programs in Greece. The objective of the research was to explore the influence of HTA on policy and practice in Greece through selected case studies in the prevention area. The cases studied were mammography screening, prostate-specific antigen (PSA) screening, and routine ultrasonography in normal pregnancy.

In order to identify policy recommendations or reports on the assessment of prevention programs and their interface with health policy formulation, we performed a thorough literature review of Greek and foreign bibliography, as well as gray literature from various sources. Greek databases were investigated, several specialists were interviewed, including officials from the Ministry of Health, and the relevant medical associations were contacted. In the event that some unpublished research on the three screening programs has gone unnoticed, the chance that it has actually influenced policy or attitudes in the area of prevention and screening is slim.

As this report will show, the issues of efficacy and cost-effectiveness or HTA in general play a small role in health policy formulation in Greece. Public consciousness of the value of HTA is now being developed through institutional initiatives. Furthermore, recent legislation offers a hope that assessment and evaluation procedures may play an increasing role in the decision-making process in the not-so-distant future.

DESCRIPTION OF THE HEALTHCARE SYSTEM

A Historical Perspective

Health care became a major political issue in Greece after the fall of the dictatorship in 1974. The health sector, historically underfinanced and without a coherent health policy, lagged behind pensions, which consumed the major part of public social expenditures (47). Health was highly privatized, with private payments exceeding public expenditures and 700 small private hospitals, mostly owned by doctors working part-time in public hospitals.

A working party set up in 1976 found inequity and inefficiency, large geographical inequalities in the distribution of resources and services, problems of hospital infrastructure, and lack of coordination between the Ministry of Health, other government departments, and social security funds. The alternative proposals were: a) the establishment of a National Health Service; b) the unification of major social security funds or their cooperation; and c) coordination in the financing and delivery of services (13). A progressive health bill proposed in 1980 by Minister of Health Doxiades adopted many of these proposals, but charges of "covert socialization" by conservative doctor-MPs, did not allow the bill to reach Parliament (37). As a result, the socialist party came to power in 1981 with major health reform high on its agenda and established the national health system with Law 1397 in 1983 (1).

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The 1983 reform aimed at universal coverage and equity in the distribution of services. It was, however, outdated in relation to health reform in other European countries at the time, since many of the principles and policy objectives then prevailing in Europe were ignored (11). The guiding principle was the de-commercialization of health, with the state responsible for the financing and delivery of services, and a reduction of the role of the private sector. Efficiency through cost containment was not a concern, as the major objective was an increase in public expenditure to 4.5% to 5% of the gross domestic product (GDP) in order to limit private expenditure.

The Healthcare System Today

The Greek healthcare system evolved along the lines of the social insurance (Bismarck) model, with a strong element of government control and publicly provided services as a mixture of the public contract model and the public integrated model (45;46). At the same time, there is a significant "parallel" health economy financed by out-of-pocket payments, which some estimates put as high as 3% of the GDP (34). This economy, including private health insurance, financed an explosion in "big-ticket" technology in the last ten years (35).

Healthcare delivery is fragmented and uncoordinated. Ambulatory care is offered through the Social Security Institution (IKA) polyclinics, hospital outpatient departments, and by 10,000 private physicians on contract with government and social security on a fee-for-service basis. Access to basic care is easy, but solo practitioners are cut off from the rest of the system, since there is no referral system to other specialties, and admission to the hospital is usually through the outpatient department with no follow-up by the primary care physician. Public hospitals account for 70% of the beds and 60% of public health expenditure. Queuing problems exist in Athens, where 30% to 40% of patients from other areas seek specialized hospital care and there are shortages in intensive care units and other specialized clinical facilities. The private sector plays a strong role in outpatient and diagnostic services, and private hospitals, especially in Athens, are highly fashionable (and profitable), financed by private health insurance and private payments (12).

Despite considerable increase in health expenditures during the last 10 years, health care in Greece suffers from low credibility and consumer dissatisfaction (21). There are problems in health services management, since the system is centrally controlled by the Ministry of Health and Welfare, where even minor staffing decisions are made. On the demand side, the lack of the institution of the family doctor as gatekeeper leads to doctor-shopping and uncontrolled access to specialists, usually in private practice. On the supply side, Greece has one of the highest numbers of doctors and four times the pharmacists and drugstores per 1,000 population in the European Union (EU). This may explain the high pharmaceutical expenditure at 1.9% of the GDP, the proliferation and overutilization of high-technology diagnostic facilities, and the increased health expenditure, which, according to recent data, was 8.6% of the GDP in 1997 (49). Although the key aim of the 1983 reform was to increase public spending and provision of services, on an ideological commitment to increase equity, the shift in financing has hardly occurred (39). Despite the substantial increase in absolute terms, public spending as a proportion of total spending declined from 62.7% in 1990 to 57.7% in 1997 (49).

In 1994 the Greek government commissioned a team of foreign experts, led by Brian Abel-Smith, to study the major problems facing the health sector. The main problems detected were weaknesses in public health personnel, programs, and policy measures, unethical practices causing cost-shifting from the public sector to private payments, public dissatisfaction and distrust, geographical inequalities in resource distribution and in the quantity and quality of services, overcentralization, bureaucratic management at all levels, and high administrative costs due to the multiple sources of financing. The lack of HTA and

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evaluation activities was also implicitly recognized as lack of cost-effectiveness, inefficient use of hospital beds, and the excessive use of drugs and diagnostic tests (42).

HTA IN GREECE

Until a few years ago, there was almost no activity in the area of HTA and evaluation of health services (60). The first HTA efforts appeared after 1995, aided by know-how and stimulus offered by international activities and projects without, however, official support. At this time, there are good prospects for the establishment of a formal HTA organization after enabling legislation (Law 2519), passed in 1997, provided for a new public organization assigned quality assurance, HTA, and evaluation functions.

National Agencies or Committees and Educational Programs

- The Biomedical Technology Division: Created in 1990 by the Ministry of Health, responsible for planning, preparing specifications, and allocating funds for the procurement of biomedical equipment in the public sector at a national level (50);
- The National Health Council: Created in 1982 as an advisory agency to the government on a variety of public health and other health matters;
- The National Drug Organization (EOF): A governmental agency responsible for the licensing of pharmaceuticals;
- The Central Committee on Hospital Infections: An advisory body to the Ministry of Health charged with issuing guidelines on the prevention, surveillance, and control of hospital infections, the proper use of antibiotics, etc;
- The Center for the Control of Special Infections (KEEL): Created in 1992, mainly as a response to the growing need for dealing with AIDS. It is a state-owned corporation charged with epidemiologic research, the issuance of guidelines, and the approval of new and experimental treatment;
- The Center for Quality Assurance in Biochemistry in the Evangelismos Hospital in Athens: A research and accreditation center with a mission to perform quality control and quality assurance functions on biochemistry-measuring instruments and methods or technologies; and
- The Committee on Safety and Biohazards of genetically modified products from animals, plants, and other biological sources: Established in 1997 by the Ministries of Health, the Environment, and Agriculture in the form of a quasi-government organization charged with the study and assessment of biotechnology and genetic modification.

The aims of all these groups, committees, and agencies are not necessarily directly related to HTA but rather to aspects of HTA referring to specific objectives such as licensing, performance monitoring, and purchasing of equipment. The concepts of assessment or evaluation in general are rather undeveloped, and, as a consequence, all relevant activity lacks focus and direction.

Educational Programs in Greece

HTA is a multidisciplinary area involving medicine, epidemiology, biostatistics, health economics, medical physics, informatics, and systems science. The main problem is that health economics and evaluation of health services are not taught in Greek universities, with the exception of a three-course curriculum at the Nursing Department of the University of Athens. The Athens School of Public Health shows some HTA activity from the sociologic point of view through a newly founded scientific society and some pharmaco-economic research.

Some educational programs with some relevance to HTA are listed below:

- In 1986, the Institute of Technical Education in Athens established a 3-year course for biomedical equipment technicians;

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- A postgraduate course leading to a Master's degree in medical physics and biomedical engineering was established in 1989 at the University of Patras under the Erasmus Program;
- Almost at the same time, the National Technical University of Athens established a Department of Biomedical Technology, offering courses on health technology and bioengineering at undergraduate and graduate levels; and
- A postgraduate program in organization and management of healthcare services was established in 1993 in the School of Nursing at the University of Athens, aiming to educate students in the areas of health economics, economic evaluation, HTA, and health services management.

These programs, which are expected to expand in effect and increase in number in the future, prepare the groundwork for the formulation and implementation of formal HTA policy as required.

PREVENTION POLICY IN GREECE

The Greek government has been active in providing preventive health services, but there are several reasons for questioning the effectiveness and cost of the services provided. The basic legislation concerning prevention policy in Greece is Law 1397 of 1983, which established the new National Health System. Among other things, the law provided for the establishment of health centers as decentralized hospital units in each of the 52 prefectures. The health centers, established in rural and semi-urban areas, were to provide primary healthcare services to a population of approximately 10,000 people. These services included pre-hospital and follow-up services, emergency care, transport to the hospital, and dental care.

Preventive activities were to be an integral part of the health centers' operation. Besides the provision of first aid, the doctors and nurses were to practice preventive medicine, develop and offer health education seminars, conduct epidemiologic research, and offer school hygiene services. Finally, there were educational and training activities for health employees and the provision of other social care services. The health centers also dispensed drugs to beneficiaries of the Farmers Social Security Fund.

Another important law dealing with primary health care and prevention is Law 2071/1992, for the modernization and organization of the health sector in Greece. Besides the creation of mobile primary healthcare units, this law established the Center for Research, Prevention, and Treatment for Diabetes Mellitus and the Center for the Control of Special Infections. It also established home care services for the frail and elderly and created a directorate of home care services in the Ministry of Health. Finally, the establishment of a Committee for the Planning of Health Education created the preconditions for charting a long-term strategy in the area.

Despite the existence of adequate legislation, preventive healthcare services in Greece seem to fall short of their stated goals. The 200 health centers operating in 1999 face a number of problems, with the largest being the lack of sufficient and well-trained medical and other staff. According to a Ministry of Health study, the present number of occupied doctor posts is 50% lower than the required number. The main problem, however, is with the organization of the entire ambulatory or outpatient care sector, especially in the urban areas. Law 2519 of 1997 established the primary healthcare networks, based on the family doctor, which could offer the necessary administrative and scientific support for the promotion of primary prevention activities.

The fact that such networks have not yet been established, perhaps because of the lack of the institution of the family doctor, makes the effective implementation of preventive policy difficult. The number of trained general practitioners (GPs), who constitute the first link between the patient and primary health care, is approximately 750, compared with the

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5,000 to 6,500 GPs needed according to international standards (44). Recently instituted incentives, together with rising doctor unemployment, may increase the production of GPs. For the time being, however, the structure of the medical profession is not amenable to the promotion of preventive activities. The two prevailing models of physician practice are that of the salaried doctor working for a public social security fund or the doctor on solo private practice. None of these two models allows the active integration of the doctor into an organized health system where the dissemination of information on prevention or health education, and all health services provision, including referral to hospital, takes place on the framework of a coherent health policy. The doctor is actually cut off from the rest of the healthcare system, and primary prevention is mainly left to the Public Health Services.

THE CASE STUDIES

Breast Cancer Screening

According to 1995 OECD data, mortality from breast cancer in Greece is 22.9 deaths per 100,000 women (48), a figure still fairly low compared with most European countries. The incidence of the disease, however, increased at a rate of 2% each year during the last decade (57), and mortality increased at the highest rate in Europe, almost doubling from 13,6 deaths per 100,000 women in 1970 to 22.9 in 1995. In this decade, more than 1,200 Greek women died of breast cancer every year (4% of total deaths).

Mammography is currently used in all breast cancer screening programs because it can detect small-size lesions (of less than 5 mm in diameter). It is a simple and specific test, easily accepted by the female population, and has high sensitivity and low risk in relation to its benefit (24). It has been shown that mammography screening for women over 50 years of age leads to a mortality reduction of 25% to 35% (41). However, the efficacy of such a screening program in younger women is controversial (19).

Breast Cancer Prevention in Greece. Although Greek women are increasingly concerned about breast cancer, their sensitization to its prevention remains fairly low, according to the opinion of Greek gynecologists and heads of mammography departments in public hospitals of Athens, who recognize the diagnostic value of mammography. According to a recent study, a mean of 11.2 months delay in seeking medical advice was observed in 100 breast cancer patients admitted to the Evangelismos Hospital with their first manifestations of the disease. The delay was shorter in women with higher IQ and educational level and in women with T1–2 and N0–1 stages compared to women with T3–4 and N2–3 stages (14). Women in rural areas are usually poorly informed about the possibilities and the benefits from early detection of breast cancer signs by monthly breast self-examination, and many Greek doctors, even surgeons and gynecologists, are not fully aware of the value of regular mammography examinations for the early detection of breast lesions. Furthermore, there are accessibility problems due to the poor distribution of mammography centers throughout the country.

A woman needing a mammography must either obtain a referral from her personal gynecologist or have a preliminary clinical breast examination (CBE) at a hospital outpatient department. The cost is partially covered by health insurance, with IKA, the largest social security fund, reimbursing the amount of US $10 for every two-viewed mammography. The rate of mammography use in Greece has not been formally estimated. Some specific rates from the mass screening program conducted by the Hellenic Society of Oncology (HSO) will soon be released. We found only one study reporting 4,000 mammographies performed during 1984–88 at the breast diagnostic imaging department of Theagenion Hospital in Thessaloniki (27).

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Medical Practice Guidelines: Indications for Mammography in Greece. The First Surgical Clinic of the University of Athens has formulated the following indications for mammography screening (10):

1. Women with suspicious findings in CBE.
2. Every year for women over age 50 exposed to a risk factor (e.g., fibrocystic change).
3. For screening reasons:
   (a) In women under age 40 with breast cancer history (mastectomy);
   (b) In women between ages 40 to 49 years:
   - With a history of cancer; or
   - Whose mother or sister(s) had breast cancer (high-risk group).

According to these indications, breast cancer screening is a selective form of screening. Until a few years ago, mass screening in all asymptomatic women over 50 was considered to be extremely costly and difficult to apply (15). The initiative taken by the HSO suggests that breast cancer mass screening is feasible and effective.

With respect to cost-effectiveness, no formal assessments have been carried out in Greece. However, the views of physicians in mammography centers, obtained during interviews for the purposes of this paper, can be summarized as follows:

- Mammography is considered an excellent diagnostic method with reliability higher than 90% in women over 50 years of age;
- Mammography results are decisive for the surgical excision of an abnormality, irrespective of CBE or cytological examinations; and
- The cost of mammography, as expressed by the official reimbursement rate, is low and has to be adjusted to reflect the true cost.

The Hellenic Society of Oncology Screening Program. The HSO is a private, nonprofit medical association founded in 1967 to promote the fight against cancer (25). In 1988 the EU funded the implementation of a 10-year screening program for early breast cancer detection using mobile mammography units under the direction and supervision of the HSO. This program started in 1989 and is still operating under the Europe Against Cancer program. The objective of this program is to investigate the feasibility of developing a breast cancer screening program in Greece and to indicate that screening programs for early breast cancer detection can and should be applied throughout Greece. A pilot study was conducted in the Prefecture of Ilia in Western Peloponnese covering the period from September 1989 to July 1990. The results were submitted to the European Network of Reference Centres for Breast Cancer Screening (EUREF) and the Greek Ministry of Health and were found significant. On the basis of these results, the program was extended to the neighboring Prefecture of Messinia. The two prefectures were randomly selected.

According to the 1981 national census, the total population in the two prefectures was 320, 123, and the target population was 31,808 women, aged between 40–64 years, who were permanent inhabitants of the two prefectures. Although the recommendation of the Cancer Experts Committee was to screen females between 50 to 64 years old, it was decided to also include women in the 40 to 49 age bracket. For comparison reasons, however, only results for the age group of 50 to 64 years were evaluated. The average number of women screened (two-view mammography) was 45 per day and per unit. All mammograms were sent to the main HSO offices in Athens and evaluated according to the European Guidelines for Quality Assurance in Mammography Screening (20).

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Table 1. Breast Cancer Screening Outcomes from the Prefectures of Ilia and Messinia

	1st round	2nd round
Women (age 50–64) invited	20,444	22,655
Women screened	11,909	13,562
Result of screening		
Repeat mammography (due to technical reasons)	236	175
Negative	11,176	13,203
Intermediate mammography	–	–
Further assessment	733	359
Further assessment by additional imaging		
Repeat views for medical reasons	50	48
Ultrasound	–	–
MRI	–	–
Further assessment by invasive investigation		
FNA[a]		
Recommended	42	68
Performed	35	60
Biopsy		
Recommended	113	76
Performed	102	65
Malignant tumors detected		
DSIC[b]	2	5
Invasive cancers	44	36
Malignant tumors detected		
At routine screening	46	41
At intermediate mammography	–	–

[a]Fine needle aspiration.
[b]Ductal carcinoma in situ.

Table 2. Performance Parameters for the Two Rounds of the Screening Program

	1st round	2nd round
Participation rate	58%	59.86%
Further assessment rate	6.1%	2.6%
Biopsy rate (per 1,000 women)	8.5	4.8
Cancer detection rate (per 1,000 women)	3.86	3.02
Benign to malignant biopsy ratio	1.21/1	0.58/1

The results were processed electronically and sent in the form of a personal letter to the women who underwent the examination. The time between the day of examination and the day the woman received an answer was no longer than 4 weeks, while the time elapsed between examination and admission to the hospital did not exceed 8 weeks. Tables 1 and 2 present the main results of the HSO program. Table 3 shows that EUREF standards were to a large extent met by the HSO screening program (20). The HSO is convinced that "the development and implementation of a breast cancer screening program is the best way for saving thousands of Greek female lives" (25).

The enthusiastic acceptance of this screening program by the female population and the experience gained have led the HSO to develop its own screening program and call it Greece Against Cancer. The program was begun in 1992 (23;53), with funds coming from the Ministry of Health, the Hellenic Cancer Institute, and the private initiative of wealthy individuals. Women 40 to 64 years of age are being screened for breast cancer using mammography in 13 prefectures in Greece and two prefectures in Cyprus. In addition, a Pap smear is taken by all women aged 25 to 64 years, who reside in these prefectures.

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Table 3. Performance Parameters of the Breast Cancer Screening Program in the Prefectures of Ilia and Messinia as Compared to the European Guidelines

Performance parameter	Acceptable	Desirable	1st round	2nd round
Participation rate	60%	>75%	58%	59.86%
Additional imaging	NG	NG	2.7%	NA
Recall rate	<7%	<5%	6.1%	2.6%
FNA rate[a]	NG	NG	2.93%	NA
Biopsy rate[a]	NG	NG	8.5%	4.8%
Total cancer detection[a]	3IR[a]	>3IR[a]	3.86%[b]	3.02%
Invasive cancers 10 mm diameter[a]	>15	>20	5	NA
Benign open biopsy rate[a]	<90	<50	47	NA

Abbreviations: NG = none given; IR = expected incidence rate in absence of screening; NA = not available; FNA = fine-needle aspiration.
[a]Per 1,000 women screened.
[b]Incidence rate data for breast cancer are not available in Greece; however, these figures are considered unsatisfactory and need to be improved.

Since the initiation of this program, a total of 106,278 mammography examinations had been performed by summer 1998 (23). All procedures that have to be done in the event of a positive result (repeat mammography, biopsy, and surgical excision of tumor) are free of charge.

Other Programs. Another local breast cancer screening program is currently operating in the Prefecture of Halkidiki, also covering the rest of Northern Greece. The Monastery of Ormilia is coordinating a program, partly funded by the EU, although at a declining rate. The program has been in effect since September 1993, with the support of Theagenion Cancer Hospital in Thessaloniki. EU experts perform regular quality control. About 400 women over age 40 are undergoing a mammography examination every week. Apart from programmed screening performed in a region, provision is also made for examinations for all women who are residents of the region by appointment during a certain week every month, after the relevant information has been given and sensitization efforts have been made. The program has a data processing service, and there is also a scientific advisor in Athens. About 8,500 women were screened in the period from 1993–98, but no published data yet exist.

The Theagenion Hospital in Thessaloniki also runs a program using mobile mammography units, apart from the screening done in the Breast Department of the Centre for Preventive Screening of the hospital, which was begun 15 years ago and includes CBE and mammography by appointment. The mobile mammography unit program began in 1992 and covers the regions of Macedonia (excluding the Prefecture of Thessaloniki), Thrace, and Thessalia. The resources of the program come from the Prefecture of Thessaloniki and the HSO. Screened women undergo CBE, mammography examination, and Pap test. The program is operating in about the same way as the HSO program. Data from these programs are not, however, regularly kept or analyzed.

Conclusions. Research on the efficacy and cost-effectiveness of breast cancer screening has not been found in the Greek medical literature, but some reports on the positive predictive value (PPV) of mammography screening are cited. The PPV (the number of cancers detected as a proportion of the number of positive mammography results) is the most critical evaluation parameter of a screening test. However, some interesting parameters by which the effectiveness of a screening test is assessed are pointed out (56):

- The ultimate objective of every screening test is to impact favorably on the specific mortality of the disease, without affecting the health status of those who participate in the program;

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Table 4. Male Hospital Discharges for 1990 and 1993: Total Patients, Patients with Neoplasm, and Patients with Prostate Cancer

	1990	1993	% change[a]
Male patients discharged, total			
Absolute number	640,750	724,309	13
Per 1,000 males	126.74	143.2	
Male patients discharged with neoplasms			
Absolute number	61,265	83,878	36.1
Per 1,000 males	12.11	16.59	
Patients discharged with prostate cancer			
Absolute number	2,157	4,098	89.9
Per 1,000 males	0.42	0.81	

Source: National Statistic Service of Greece.
[a]% change = (number 1993 − number 1990) / number 1990.

- The improved 5-year survival rate of the detected cases is another criterion for the effectiveness of a screening test; and
- As for the methodology, randomized controlled trials and nonexperimental research designs are used in the evaluation of the effectiveness of a screening program. The population correlation is another relevant method.

As yet no formal policy concerning the use of mammography exists in Greece. However, Greek authorities have followed the European Guidelines for Quality Assurance in Mammography Screening (20). The main policy conclusion is that HTA is of great importance in breast cancer prevention, and that medical and political authorities have to take immediate action in order to improve the effectiveness of prevention programs in Greece.

Prostate Cancer Screening Using PSA

Prostate cancer screening using serum PSA determinations is becoming increasingly popular worldwide (40), and Greece is not an exception. The debate about the predictive value of a relatively high PSA level (2;32;33) accounts a great deal for the anxiety experienced by Greek men age 50 to 60, who feel they are approaching the "high-risk age." The mass media deliver partial information by overestimating the value of PSA screening with little mention of the high false-positive rate of the test and its implications, the ambiguous advantage of active treatment over surveillance, and all the other controversies related to secondary prevention of prostate cancer. Hence, while an increasing number of asymptomatic Greek men request a PSA measurement, Greek urologists are not at all convinced of its benefit.

Epidemiologic Data. There is no national record on the incidence rate of prostate cancer. According to Deliveliotis et al. (18), 1,207 new cases of prostate cancer were diagnosed in Greece in 1990. Some projections for the year 2020 show that the number of new cases per year will reach 1,752 (43). The National Statistical Service of Greece reports 4,098 hospital discharges or 0.81 per 1,000 males for 1993 (Table 4). Patients admitted for the first time and patients readmitted for prostate cancer are both included in these figures. The same source reports 1,095 deaths caused by prostate cancer in 1995 (Table 5).

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Table 5. Overall Greek Male Mortality for 1995: Total Deaths, Deaths Caused by Neoplasm, and Prostate Cancer

Mortality categories	1995	Per 1,000 population
Total deaths, males	52,850	10.45
Deaths, males with neoplasm	13,661	2.70
Deaths caused by malignant neoplasm of the urogenital organs	2,130	0.42
Deaths caused by prostate cancer	1,095	0.21

Source: National Statistic Service of Greece.

The Diffusion of PSA Measurements. The first PSA measurements in Greece were taken in the Laiko Regional General Hospital of Athens in 1988. This test was not applied within the context of a preventive program, but only for diagnosing and monitoring symptomatic patients. In the following years PSA measurements have mainly served as a method for diagnosing suspected cases of prostate cancer and monitoring them prior and after treatment. The Greek Urology Society has not formulated explicit screening guidelines, since the scientific evidence for mass serum PSA screening is inadequate. This conclusion does not derive from a formal assessment of the efficacy and cost-effectiveness of such a screening program, but it is rather the result of an implicit assessment process performed by each individual urologist and based on the present relevant literature.

On the other hand, it is not rare for a man 50-years-old or older to have his serum PSA level measured. Many private laboratories performing this test often give out high PSA levels which are not confirmed in a larger public hospital and cause a great deal of confusion. One must be cautious of results given out by private centers, since there is some evidence that these laboratories do not follow recommended calibration procedures, and the quality of reagents used is not properly assured. This may result in unnecessary healthcare costs, not mentioning the psychological and emotional implications of a false-positive test result for the patient.

Formal Assessments of PSA Screening. The majority of Greek physicians seem to agree that routine screening for prostate cancer using serum PSA is controversial because of the frequent false-positive results, the slow non-life-threatening growth of untreated cancer, the uncertainty of the impact the treatment has on life extension, and the potential for treatment complications. Deliveliotis et al. (18) conducted a study on the value of PSA in the early diagnosis of prostate cancer in Greece. The objective of this study was to assess whether it is worthwhile to screen asymptomatic men for prostate cancer using PSA and to determine the number of patients that could be cured of prostate cancer after detection by screening. The study included 1,400 asymptomatic men over 50 years old, all volunteers enlisted through an appeal in the Athens press. Prostate cancer was found in 23 of the 1,400 asymptomatic men screened. Of these, only eight had localized disease confirmed by pathological staging after surgery and were later considered cured. However, it is recognized in the paper that some of these eight men did not really need radical prostatectomy, and therefore were unnecessarily treated. The study concluded that screening for prostate cancer among asymptomatic men could not be justified until long-term randomized studies show that prostate cancer screening has a major impact on morbidity and mortality and until aggressive tumors, which need radical surgery, can be distinguished from those with a more benign course.

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This has been the largest prostate cancer screening program undertaken in Greece giving information on the effectiveness and efficacy of screening procedures in the general population. The study has made no effort to estimate the economic impact of the screening program. This also applies to all Greek literature on prostate cancer prevention, in which issues of cost-effectiveness for PSA measurements have not been addressed. HIPPOKRATES, a Greek medical database, as well as other bibliographic sources were thoroughly reviewed, but no articles were found regarding formal economic assessments of the serum PSA measurements in the early detection of prostate cancer.

Several studies have been conducted in Greece concerning the accuracy of PSA testing (3;29). All of these studies have enrolled subjects with indications for prostate cancer or with benign prostate hyperplasia (BPH). Depending on the study protocol, these patients underwent either radical prostatectomy or prostate biopsy. Given the results of the histologic examination and the initial serum PSA level, parameters such as the sensitivity, specificity, and PPV of the test were calculated.

In one of these studies by Karidis et al. (29), of 95 patients studied between 1992 and 1993, 87 had a negative digital rectal examination (DRE). Eight patients with a positive DRE had high PSA values, and biopsy was positive for malignancy in six of them (75%). Four of the 87 patients who underwent radical prostatectomy were found to have organ-confined cancer in the histologic examination and had a PSA value between 0. 6–4 ng/mL. In another study by Antoniou et al. (3), the serum PSA levels in patients with benign prostate hyperplasia and prostate cancer were compared with healthy control subjects. The study enrolled 200 men over 60 years old with BPH, 77 men over 60 years old with diagnosed prostate cancer, and 42 men assumed to be healthy aged between 40 to 60 years of age. All (100%) of the healthy control subjects had a PSA value less than or equal to 4 ng/mL with a mean value of $x = 0.83$ ng/mL. Eleven percent of the patients with BPH had a PSA value between 10 to 30 ng/mL and 33% of the patients with prostate cancer had a PSA value less than or equal to 4 ng/mL.

Accessibility of PSA Testing Procedure, Compliance Rate, and Rate of Use. As far as the accessibility of the procedure is concerned, there is practically no restriction on the performance of a serum PSA measurement. A pathologist or urologist decides on the advisability of this test, which may be performed either in a state hospital or in a private laboratory. Since early 1999, the cost of the test is reimbursed by all health funds, with IKA, the major social security institution, reimbursing the amount of 40 EURO. Patient compliance rate cannot be calculated, since there is no uniform record or database where test referrals or tests performed are entered, identifying tests performed on asymptomatic men. For the same reasons, the rate of use of PSA measurement as a preventive service cannot be estimated. At present, clinician compliance rate cannot be evaluated, since there are no recommended screening guidelines.

General Attitude and Public Involvement. The implementation of a mass screening program for prostate cancer would have significant public support in Greece, especially if the mass media disseminated information in favor of the value of prostate cancer prevention and treatment when detected at an early stage. However, no study has ever attempted to survey the attitude of Greek men toward prostate cancer screening or to assess how health education on PSA testing and its uncertain benefits would affect patients' desire for this procedure. Studies conducted in other countries indicate that preference regarding cancer screening and treatment would be greatly affected by information on medical uncertainties (22). At present, an increasing number of asymptomatic men over age 50 in Greece show a tendency to have their serum PSA measured to eliminate the possibility that prostate cancer will ever threaten their lives.

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Clinicians' Involvement. Systematic descriptive research of the attitude and practice of Greek urologists or primary care physicians was not found in the Greek literature. The general impression is that Greek physicians are ambivalent about the balance between the potential benefits and drawbacks of implementing PSA testing as a mass screening test. This ambivalence is mainly due to the fact that a great number of prostate cancer cases have a benign course, with the patient most likely to die of another cause. In addition, the false-positive rate and low specificity of PSA testing make its implementation as a screening procedure very difficult. Besides, it has not yet been firmly established that prostate cancer screening reduces mortality rates, since 50% to 60% of prostate cancer cases are at an advanced stage of the disease at the time of diagnosis.

For a great number of healthy patients, the distressing psychological and emotional consequences of a false-positive test result cannot be ignored. Regarding the psychological implications of PSA testing, joint research is currently in progress by the Department of Urology of Sismanoglion Hospital and the Department of Psychology of Middlesex Hospital in England. Patients enrolled in this study are asked to answer a questionnaire that measures their knowledge regarding prostate cancer and its early detection, their attitude toward prostate cancer tests before and after undergoing examination, and their way of dealing with health problems. No preliminary results have been reported.

The only attempt to assess clinicians' involvement is a study conducted by the Department of Urology of Agios Savas Hospital (55). Urologists were asked to answer a questionnaire in which most of the questions dealt with the way clinicians are kept up to date on cancer issues and surveyed their views on patient management procedures. Although there was a low response rate with only 14.3% of the questionnaires completed ($n = 58$), 86% of the urologists seemed to believe that Greek people did not seek medical consultation for cancer-related symptoms early enough. The paper concluded that physicians' knowledge on cancer-related issues should be improved and that the public should be properly informed on the importance of early diagnosis for the management of cancer.

Conclusions. A mass screening program for prostate cancer using serum PSA measurements has not been implemented in Greece. Serum PSA measurements are mainly performed in symptomatic patients consulting an urologist. Several studies have assessed the effectiveness of PSA testing on symptomatic patients measuring the sensitivity, specificity, and PPV of this test. No formal cost-effectiveness assessment of the procedure as a screening test has been performed. Research is continuing to improve the diagnostic potential of the test. Given the inadequacy of scientific evidence to either support or reject the implementation of a mass screening program for prostate cancer, no formal decision has been made on this issue, and neither governmental agencies nor the medical community has formulated relevant regulations. Serum PSA determination is therefore left to the discretion of the individual physician or the initiative of the individual patient. It is, however, a negative development that the test has been included in the three screening tests reimbursed by all Social Security Funds, as this might be taken to encourage its use as a mass screening program.

Ultrasonography Screening During Pregnancy

Ultrasonography in pregnancy is considered a simple, painless, and harmless examination used in everyday practice for the prenatal diagnosis of certain abnormalities. In this paper we present all relevant data from the Greek literature on this subject. Certain national services, such as the Central Health Council and the National Statistical Service of Greece, as well as interviews with specialized obstetricians served as data sources. Tables 6 and 7 present data on mortality by cause and age of death.

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Table 6. Infant Mortality in Greece by Age (<1 Year) and Cause of Death, 1995

Causes of death	Total	Age < 28 Days	28 Days to 1 Year
Bifurcate back with hydrocephaly	14	4	10
Bifurcate back without hydrocephaly	4	2	2
Microcephaly	1	0	1
Congenital hydrocephalous	1	0	1
Other specific abnormalities	1	0	1
Not defined heart abnormalities	111	57	54
Atresia and stenosis of small intestine	1	0	1
Atresia and stenosis of large intestine, rectum, and rectal duct	0	0	0
Renal agenesia and dysgenesia	3	1	2
Cystic renal disease	3	1	2
Osteodystrophies	2	0	2
Diaphragm abnormalities	10	10	0
Down syndrome[a]	30	3	27
Retardation of fetus development, not defined	1	1	0
Severe immaturity	131	131	0
Respiratory distress syndrome	34	34	0

[a]The incidence of Down syndrome in Greece is 1/800 births/year.

Table 7. Perinatal Deaths in Greece: Total Deaths Caused by Congenital Abnormalities and Other Perinatal Conditions, 1995

Cause of death	Total	Male	Female
Congenital abnormalities	389	224	165
Certain conditions originating in the perinatal period	411	230	181

Assessment of Ultrasonography in Pregnancy in Greece. The contribution and value of ultrasonography on the prenatal diagnosis of fetal abnormalities is controversial. In the Greek literature one can find studies that support its use as a screening test next to those that question it. One study reported that in a sample of 10,000 ultrasound examinations, nine cases of severe congenital malformations were diagnosed during pregnancy. These ultrasound diagnoses were confirmed after delivery and indicated that improvements of ultrasound equipment made in the last few years permit prenatal diagnosis of a significant number of fetal malformations (6).

Ultrasonography permits the control of gestation morphology and viability and the early detection of high-risk pregnancies. A study of 40 pregnant women has concluded that the use of ultrasonography is necessary for identifying disorders during the first months of gestation (58). Another contribution of ultrasonography in pregnancy is the determination of gestation age, which can prevent the development of respiratory distress syndrome, a real threat to the life of the infant. There are at least two studies in which gestation age and lung maturity have been evaluated by means of ultrasonography, and both have shown a reduction in the incidence of the syndrome (8;16). In general, real-time

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ultrasonography appears to be a safe and valid method for the determination of gestation age (17).

The method has been shown to be of high value for the localization and evaluation of the placenta, so that high-risk pregnancies are identified and conditions such as pre-eclampsia are prevented or diagnosed on a timely basis (9). It was also found that serial ultrasonographic evaluation of diabetic women in the third trimester of pregnancy provides a means for the early detection of a fetus that is large for its gestation age. This practice has been tested in a study of 47 pregnant women with diabetes and has been found to make the management of these pregnancies easier and more successful (30).

Another research team reported the use of ultrasonography in the case of a fetus carrying a large omphalocele, which was properly managed by terminating pregnancy without further complications. However, it must be pointed out that sonographic detection of front abdominal wall abnormalities such as omphalocele is possible only after the 12th week of pregnancy (5). Ultrasonography in pregnancy is also considered to be a reliable, quick, and harmless procedure that can provide crucial information in the event that there is suspicion of a missed abortion in order to confirm or exclude it (59), and in the detection of post-term pregnancies (54).

Down syndrome is the most common cause of severe mental retardation. During the second trimester of pregnancy, specific biometric indicators are measured using ultrasound to detect fetuses presenting with this syndrome. According to research findings, ultrasonography in the second trimester seems to be quite helpful, although it does not play the first role in the detection of Down syndrome. This derives from the fact that the false-positive rate of the examination is rather statistically significant, meaning that this method cannot be considered absolutely valid and reliable. A future improvement of the echographic equipment could improve the diagnostic potential of this method (4;51).

A more specialized echographic method is Doppler ultrasonography. It records the waveforms of the blood flow from the fetal umbilical arteries and the maternal uterine arteries. Doppler ultrasonography is applied for the medical attendance of high-risk pregnancies. The results of a study of 100 high-risk pregnancies show that the implementation of this method is very promising (7).

In Greece ultrasonography receives widespread use for prenatal diagnosis. Echographic equipment is found not only in all hospitals—public or private—but also in almost all private consulting rooms. It is a routine examination in provincial regions, and the rate of use of ultrasonography examinations varies from clinic to clinic, ranging from 10 to 40 per day, while in some private clinics it may reach 80 examinations per day. Echographic examinations are normally covered by public insurance funds, making the method easily accessible for the majority of the population. IKA, the largest public health insurance fund, reimburses the amount of 8 EURO for the examination, while the actual cost is around 28 EURO.

According to international guidelines, all the benefits a pregnant woman can receive are exhausted in three ultrasound examinations performed at defined intervals. In Greece the actual utilization rate is much higher, since many physicians often promote its use and defend the utility of this method as a simple, harmless, low-cost, and, most important, extremely useful means for the prenatal diagnosis of many congenital abnormalities. So they find no reason for restricting the number of ultrasonic examinations during pregnancy.

Research findings have not confirmed any of the potential risks that may be induced by ultrasonography in pregnancy. Under certain circumstances though, such as the long duration of the examination, transvaginal ultrasonography, and color Doppler, there is a risk of causing thermal damage to the fetus. Adequate expert knowledge and experience are necessary for the method to be reliable and beneficial. It is widely believed that the validity of these results and the effectiveness of ultrasonography depend mostly on the specialists ability to correctly interpret the findings of the examinations.

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Impact of HTA on Policy. A set of proposals for the implementation of ultrasonography during gestation was formulated by a scientific commission and was submitted to the Executive Committee of the Central Health Council in 1995. The Central Health Council finally accepted these proposals and in 1996 summarized them in the following regulations:

1. The use of ultrasound for diagnostic purposes during pregnancy has created a very difficult situation that has to be confronted with discretion and restricted by specified regulations.
2. The purpose of the imposed restrictions is to avoid the abuse of ultrasonography, particularly in low-risk pregnancies, and to establish its rational use during gestation.
3. For these reasons the Ministry of Health has taken a number of measures:
   (a) No more than three (3) ultrasonographic examinations are allowed in all gestations, without prejudice to any exceptions. These should be performed in the 10th, 20th, and 30th week of pregnancy. It has been shown that this scheme of ultrasound evaluation reduces perinatal mortality and morbidity.
   (b) In cases of high-risk pregnancies, the frequency of ultrasonography should be left to the discretion of the attending physician, in qualified medical centers. These centers must be departments of fetal and maternal medicine units or medical imaging centers, where experienced and licensed physicians should be members of the staff.
   (c) The official national service of the region of permanent residence of the user is responsible for attesting if a pregnancy needs systematic attendance.
   (d) If the prerequisites of paragraph (c) do not exist, Health Funds will not approve more than three ultrasonographic examinations.
   (e) The public should be informed about the potential risks of ultrasound during gestation.

The following institutions have been notified about the present regulations:

- Hospitals;
- The Ministry of Labor and Social Services, the General Secretariat of Social Services, the Administration of Illness and Maternity;
- The Greek Medical Association and all local medical associations;
- The Medical Society of Athens (through which all relevant scientific medical societies should be notified);
- The Greek Obstetrics and Gynecology Society; and
- The Midwives' Association.

Conclusions. While no specific effort to evaluate the cost-effectiveness of ultrasonography in pregnancy as a primary method of prenatal diagnosis in Greece was found, several studies have been conducted to prove its reliability in detecting a significant number of gestational disorders and fetal malformations, or to put it under question. It is obvious that there is some confusion in Greece about the real benefits and costs of routine ultrasonographic examinations in pregnancy. It seems that more than three echographic examinations, when not justified by some serious medical conditions, lead to no further reduction in perinatal mortality. However, both users of the method and many obstetricians appear unwilling to comply with the recommended guidelines, since the real value of the examination remains unclear and its use is based on empirical and personal assessments. This points to a need for formal HTA studies on the efficacy and cost-effectiveness of ultrasonography in pregnancy, so that specific policy measures can be taken to prevent or restrict its abuse.

DISCUSSION

In the last few years, there has been increased emphasis on the assessment of medical practice and health technology. However, most people involved in health care, especially

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policy makers, are still unfamiliar with the intent, the scope, and the role of HTA (26;31). This is especially true in Greece, where only a few decision makers are familiar with HTA and its role in health policy formulation (38).

Since Greece is one of the few European countries without an HTA agency, the assessment of prevention programs has not yet been attempted rigorously. This paper focuses on prevention policies and the extent and manner of use of scientific evidence on the implementation of three selected screening programs in Greece. One of our major findings was that the application of the screening tests does not take the form of structured mass screening programs. Almost all physicians (urologists-pathologists, gynecologists) apply PSA and routine ultrasonography in normal pregnancy accordingly with the purpose of either prevention or diagnosis. Mammography is applied generally for prevention or diagnosis, but there are some mass screening programs at a local level.

As a result, the use of these preventive methods is usually left to the discretion of the individual physician or the initiative of the individual patient. What is more disconcerting, however, is that the tests are not always used appropriately and that policy formulation is not made on the basis of the best available evidence on efficacy and cost-effectiveness. For example, given the inadequacy of scientific evidence to either support or reject the implementation of a mass screening program for prostate cancer, it is a negative development that the test has been included in the three screening tests reimbursed by all social security funds, since this might be taken to encourage its use as a mass screening program.

This points to a need for the implementation of HTA methods on mass screening preventive programs in which the real value and cost remain unclear and their use is based on empirical and personal assessments. The necessity of conducting formal assessments on the efficacy and cost-effectiveness of screening tests, so that specific policy measures can be taken to prevent or restrict their abuse, remains a priority issue.

The paucity of research on HTA, including cost-effectiveness research, in Greece can be partly explained by the fact that there are no systematic records or epidemiologic studies producing incidence rate data for chronic diseases. The National Statistical Service of Greece keeps data only on patients discharged from hospitals by sex, age group, disease category, average length of stay, and outcome, and it reports annual death rates by sex, age, and cause of death. Patients readmitted to a hospital are not distinguished from those admitted for the first time. The quality of the statistical information, therefore, does not permit the development of satisfactory outcome measures for health interventions.

It is encouraging that efforts toward this direction are being made, which allows us to believe that there may be better prospects for the future. It is our hope that the new agency to be established soon will promote the production and dissemination of HTA work and make it much more relevant to policy making than has been the case. In this respect, the work carried out at a European level in the framework of the projects EUR-ASSESS and HTA-EUROPE will be very helpful in providing much-needed information in terms of methodology, dissemination, and application of HTA to policy. It is for this reason that continuing support of research and policy implementation and assessment programs by the EU is essential, especially for countries in which the political and administrative decision-making process can gain experience through its participation in international collaborative efforts.

CONCLUSIONS

The need to acknowledge the value of HTA and promote its use is now being realized in Greece. In the last few years very promising steps have been made regarding education and training in the field, but also in the provision of legislative and institutional regulations supporting and facilitating the introduction of HTA in practice. A real problem that HTA work will face at first is the lack of appropriate data regarding incidence rate, prevalence,

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treatment outcomes, rates of use of specific tests, or interventions. The systematic records that were kept are very crude for the calculations involved in the processes of HTA and often incomplete. The problem is getting more complex since the private healthcare sector and out-of-pocket payments make a considerable contribution to health expenditure and to the rate of use of technology in some cases, which is rather difficult to estimate.

It is hoped the new agency to be established soon will promote the production and dissemination of HTA work. This is also needed to increase the awareness of the value of HTA in the medical profession, since the sense of control may cause negative and defensive reactions at first, which may hinder the HTA process. Healthcare professionals are not yet familiar with the intent of these assessments and may feel that their practice is being criticized.

The three case studies in the area of prevention presented in this paper give a rather representative picture of the Greek situation. The case of mammography, which is supported by the available evidence as a cost-effective screening test, shows that active measures are taken by formal organizations, and many screening programs have already been implemented at the local level. PSA has not yet been established as an appropriate test for mass screening for prostate cancer, because of the frequent false-positive results and the uncertainty about treatment benefits, although there is not enough evidence to reject this possibility. Hence, serum PSA determinations are left to the discretion of the individual patient or the initiative of the individual physician. Ultrasonography in pregnancy, on the other hand, is strongly favored by clinicians, since evidence underlining potential risks has not been confirmed. However, the widespread use of the method has led the Ministry of Health to formulate legislative regulations limiting the number of ultrasonography examinations performed in pregnancy to no more than three, without prejudice to any exceptions.

The cases reveal the lack of research on issues of efficacy and cost-effectiveness or HTA in general, which would influence public policy or attitudes in the health sector. These issues have played a small role in health policy formulation in Greece until now. Education, institutional and governmental activity, and legislation aim to change the scene in the near future.

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