

# Effectiveness of opportunistic screening for cancer of the cervix uteri

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## Abstract

The incidence and mortality of uterine cervical cancer in the Maltese Islands has remained relatively constant in medical records of the last few decades. The aim of this study was to determine the cervical cancer screening history and other characteristics of the invasive cervical cancer cases diagnosed in Malta between 1992 and 2002, from a review of their medical records. Only 5% of the cases reviewed had had regular cervical smears prior to the diagnosis of the invasive lesion.

Well organised national cancer screening programmes overseas indicate that if less than 70% of the target population (ages 20 to 65 for cervix) is regularly screened, the incidence and mortality will not decrease.<sup>1</sup> In Malta, cervical screening is opportunistic and the percentage and sectors of the target population being screened is unknown. A national study is needed to quantify the number of women undergoing cervical screening and to assess how much of the relevant target population is being screened.

## Introduction

Following breast cancer, invasive cancer of the uterine cervix is the second most common type of cancer in women worldwide.<sup>2</sup> Annually, about 471,000 new cases and 190,000 deaths are reported globally.<sup>2</sup> It is estimated that more than 12,800 women in the European Union die each year from the disease.<sup>3</sup> In Malta, between 1992 and 2002, 132 new cases of cervical cancer and 49 deaths from this cancer were reported.<sup>4</sup> In many countries cervical cancer is the commonest pelvic gynaecological organ cancer. In Malta, however, cancer of the uterine cervix is the third most common cancer of the female genital organs. It is preceded by cancers of the body of the uterus and ovaries.

## Overview of Cervical Cancer Screening

Cervical cancer was the first malignancy world-wide for which an effective method of screening was introduced. Direct evidence from randomized clinical trials to support the value of the cervical smear in reducing mortality from cervical cancer is scarce. However, a huge body of indirect evidence suggests that this inexpensive test may be among the most effective screening techniques available.<sup>5</sup>

Quantitative studies have shown an 84% reduction in cancer incidence by screening women aged 35-64 years every 5 years, which increases to 91% if screening is undertaken every 3 years. Screening more frequently (every 1-2 years) did not appreciably reduce incidence further (93%).<sup>6</sup>

A national screening programme would entail testing invited women, in pre-defined age groups, at pre-defined intervals, in contrast to opportunistic screening done only on the initiative of the subjects themselves, or of their private doctors. The EU recommendations on cancer screening<sup>7</sup> declare that for optimization of a screening programme (in terms of cost effectiveness), high level of coverage with regular tests at defined intervals in the age group at greatest risk, is needed.

Efficient national screening programmes exist in various countries, including Scandinavian/Nordic countries such as Finland, Sweden and Iceland. The programmes were started between 1963 and the mid-1970s. Soon after the introduction of these programmes, there were large decreases in cervical cancer incidence and later mortality rates. The decrease was confined largely to the age groups 30-59 years, i.e. to those groups targeted in the programmes.<sup>8</sup>

A similar national screening programme was started in the UK in the early 1960s. However, after about two decades (1960-1986) of British NHS cervical screening service, the mortality

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from cervical cancer, although not rising, was not decreasing.<sup>9</sup> The reason for this less effective UK cervical screening was tracked down to the fact that only a small proportion of the women at risk were being screened.

The British screening programme was remodeled in 1988, by introducing a computerized call and recall system for invitations, new quality standards, and the adoption of a 3 year screening interval rather than the previous 5 year interval. Subsequently, the effectiveness of this screening programme with regards to cervical cancer incidence and mortality improved markedly<sup>10</sup>. In England and Wales, there are approximately 2700 cases of invasive cervical cancer per year, and approximately 19000 *in situ* cancers registered per year, with approximately 1200 deaths per annum. The incidence had fallen from 16 per 100 000 in 1986 to 9.3 per 100 000 in 1997. Moreover mortality rates have fallen at about 7% per annum.<sup>3</sup>

Since 1978, the public primary health care centres in Malta and St. Luke's Hospital have offered a free cervical cytology screening service. Also, most of the private laboratories also provide a similar service against payment. To date, there is still not an organized national cervical screening programme in place, and hence all the cancer screening activity in Malta is opportunistic in nature.

The number of women availing themselves of these services is not known. A question focused on the screening attitudes of Maltese women from the National Health Interview Survey (NHIS), held in 2002, revealed that 41% of the women interviewed reported that they had never had a cervical smear test.<sup>11</sup>

In view of the rate of cervical cancer incidence and mortality in recent years, it is thought that only a small proportion of the female population at risk is actually being screened.

## Aim

The aim of this study was to determine the cervical cancer screening experience of the cases diagnosed with invasive cancer of the uterine cervix in Malta during the time period 1992-2002.

## Materials and Methods

The St. Luke's hospital (SLH) files of the patients diagnosed with invasive cervical cancer between 1992-2002 (n=132) were reviewed. These cancer cases were extracted from the Malta National Cancer Register. This cancer registry collects and analyses information on cancer diagnoses performed on all residents of the Maltese Islands. The registry utilizes a number of both passive and active methods for data collection such that multiple sources of data are employed for any registration of cancer. Information sought and extracted included any information related to the patient's sexual lifestyle habits and their smear history. Any documented cervical smears performed prior to the diagnosis of the invasive lesion (if any), their frequency and their results were noted. Other information collected included the locality of residence at the time of presentation and the tumour histological type, differentiation and stage at diagnosis.

Ninety two patient files out of the 132 in the study population were viewed. Out of the files viewed, 77 were of patients still alive whilst 15 were of patients who had subsequently died. Forty files could not be retrieved, 6 of these were of patients still alive and the remaining 34 were of deceased cases.

Apart from the file review, the results of the National Health Information Survey (NHIS) will be cited in this study. This is being done in order to serve as a comparison with the results of this study.

The NHIS was performed in 2002 by the Department of Health Information. It was conducted at a national level involving a randomly selected sample of 5510 individuals, of which 2213 were women, aged 16 years and over currently residing in the Maltese Islands. The sample has been drawn from a population register and has been stratified by age, gender, and locality to ensure as representative a sample as possible to the general adult population. The design of the questionnaires involved the use of survey instruments already used in several surveys performed in other European countries with due consideration to the local context. This has been facilitated by collaboration with WHO/ EUROHIS project. The questions focused on various health topics, including one question focusing on cervical screening.<sup>10</sup>

**Table 1:** Cases of invasive cervical cancer 1992-2002, by age groups

Age	Number of Cases
<24	0
25-34	9
35-44	36
45-54	32
55-64	26
65-74	16
75-84	8
>85	5
Total	132

**Table 2:** Cases of invasive cervical cancer 1992-2002, by parity

Parity	Number of Cases
Nulliparous	11
1	13
2	19
3	15
4	4
5	3
6	3
>6	7
No information	18

**Table 3: Cases of Invasive Cervical Cancer by Region**

Number	Region	Number of Cases
1	Inner Harbour Region	44
2	Outer Harbour Region	40
3	South Eastern Region	17
4	Western Region	10
5	Northern Region	11
6	Gozo and Comino	10
<b>Malta, Gozo and Comino</b>		<b>132</b>

## Results

### *Age distribution and sexual lifestyle*

Table 1 shows the cases of cervical cancer patients investigated in this research by age groups. Diagnosis of this condition was commonest in the peri-menopausal age groups. However, cases continue to present even later in life and in old age. About 7% of cases presented at or before the age of 34 years.

The median age at diagnosis was 52 years, while the median age at death was 55 years. The underlying cause of death of 83% of the deceased cases was invasive cancer of the uterine cervix.

The information available in the hospital files of these cases related to the sexual lifestyles of these cases was practically non-existent. The only data that was often documented was related to their parity. Eighty (80%) percent of the files reviewed recorded this variable. Table 2 illustrates the findings with regards to parity.

### *Smear History*

Only 54% (50/92) of files of patients with invasive cervical cancer had information about the patients' smear history. Smear results found in these files were those performed at St. Luke's Hospital and did not include those which could have been performed in private laboratories. However in some of the cases there were notes which indicated that the patient had performed smears in private laboratories.

Of the 50 files which had information regarding smear history, 44% (22/50) did not have any reported smears prior to the diagnosis of the invasive lesion, 46% (23/50) had rare smears (1 or 2 smears found) and only 10% (5/50) had regular smears (once every 3 years). In the 5 cases with regular smears, no pre-cancerous lesions were detected in the smears prior to the detection of the invasive lesion.

### *Regional differences of incidence of Invasive Cervical Cancer*

The cases in this study were divided into the 6 census regions used in 1995.<sup>11</sup> Table 3 shows the cases reviewed in this study by the region corresponding to their locality of residence at the time of presentation with invasive cervical cancer.

**Table 4: Standardised incidence ratios of cases by region related to locality of residence at time of diagnosis**

Region	Observed	SIR	Exp UCL*	Exp LCL**
1	44	1.27	1.28	1.27
2	40	1.04	1.04	1.03
3	17	1	1.01	1
4	10	0.56	0.57	0.56
5	11	0.82	0.82	0.82
6	10	0.83	0.84	0.83

\* Exponential Upper Confidence Limit

\*\* Exponential Lower Confidence Limit

Statistical analysis was performed to compare cervical cancer incidence in the 6 regions. Standardised incidence ratios (SIR) were constructed; using the indirect standardization method and STATA statistical software and confidence interval (95%) was calculated around them using the following formula:

$$\text{Var} = \sum w_j^2 \left[ \frac{\text{cases}_j}{\text{pap}^2_j} \right]$$

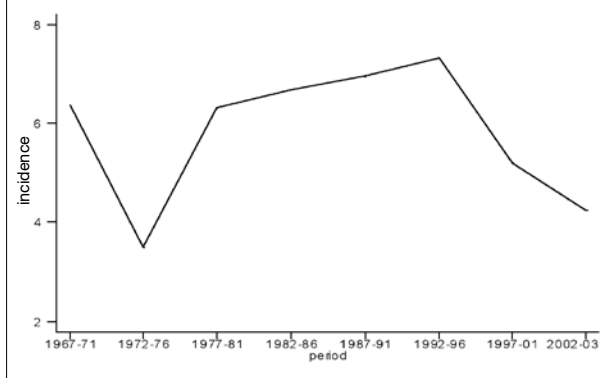
Regions 1 and 2 which include the most densely populated, urbanised and industrialized regions of the Maltese Islands showed significantly higher incidence than the national incidence rate. On the other hand, regions 4, 5 and 6 which are the northern and the more predominantly rural areas showed significantly lower incidences.

### *Tumour morphology and stage at diagnosis*

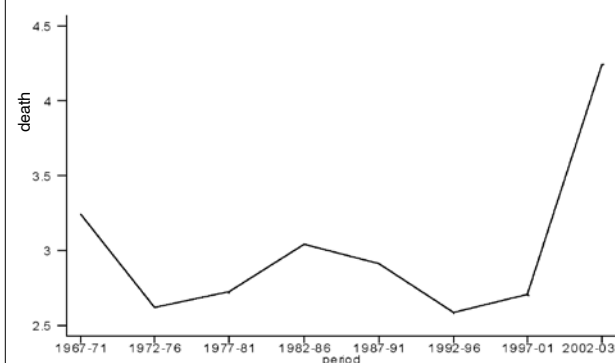
Squamous-cell carcinoma and adenocarcinoma are the most commonly occurring histological types of cervical cancer, and account for approximately 80% and 15% of all cases, respectively.<sup>12</sup> In our series, 78% had squamous-cell carcinomas, 11% had adenocarcinomas, and there was a case each of small cell carcinoma, adenosarcoma, rhabdomyosarcoma (arising in the cervix of an adolescent girl) and malignant mesonephroma. These last 2 cases were excluded from the study. For ten of the cases (7.6%), the diagnosis established that there was a carcinoma but the type of malignancy was not further identified in the histological reports. All but 2 of the cases in this series had microscopical verification of their tumour. These two cases were older than 85 years at diagnosis and they were registered on the basis of a clinical diagnosis only.

Tumour stage has long been recognized as the most important determinant of outcome in patients with cancer of the cervix.<sup>12</sup> Reviewing the histologies, operative reports and radiological examinations available in the patients' files the researchers endeavored to stage the cancers at diagnosis. From the information available, the staging exercise was possible only in 52.3% (69/132) of cases. Of these, 40 cases were at FIGO Stage I at diagnosis, 17 cases were at Stage II, 7 at Stage III and 5 at Stage IV.

**Figure 1: Incidence of Invasive Cervical Cancer by year (using Total Crude Rates)**



**Figure 2: Mortality of Invasive Cervical Cancer by year (using Total Crude Rates)**



## Discussion

Mortality and incidence rates of invasive cervical cancer in the last 36 years in Malta maintained a steady trend, with minor fluctuations.<sup>13</sup> Evaluation of these rates did not reveal any statistically significant changes in the incidence of ( $p=0.88$ ), and mortality from ( $p=0.38$ ), cervical cancer. Figures 1 and 2 show graphical illustrations of these temporal trends over the last four decades.

The information obtained in this review, regarding the smear history of the women diagnosed with invasive cervical cancer between 1992-2002, compares well with the findings on the reported smear history of women that were interviewed in the NHIS conducted in 2002. In this survey, 2213 women at and above the age of 16 years, were interviewed and asked about "when was the last time you had a cervical smear?". Only 45.2% reported having had a smear test in the 3 years prior to the survey. The remaining respondents included 41% who reported never having had a smear test, and 13.8% reporting that their most recent smear was performed more than 3 years prior to the survey. The EU recommendations on cervical cancer screening, as well as the practices followed in most organized

screening programmes, advise that cervical smear testing should be performed every 3 years. The findings of our study, together with the results of the NHIS, indicate that this practice is not being adhered to in Malta.

Table 5 illustrates the results from the NHIS on cervical smear activity by age groups. Women in the age group 25-44, followed by the 45-64 age group, are those who are being screened most. Reported screening activity in women over the age of 65 and below the age of 25 years was very low.

The regional analysis of the cases reviewed in this study showed that incidence was higher in regions 1 and 2 of the Maltese Islands. Table 6 shows information extracted from the NHIS corresponding to reported smear history of the interviewed women by regions that include their locality of residence.

NHIS showed that more women from regions 4 and 5 had a smear in the last 3 years, than women from regions 1, 2, 3 and 6. The percentage of women who never had a smear was greatest in regions 1 and 6. This is reinforced by adding those women who never had a smear test with those who never had

**Table 5: Cervical Screening by Age Groups (NHIS, 2002)**

Age	16-24	25-44	45-64	65-74	75+	All ages
<3 yrs	22.10%	68.60%	51.00%	11.60%	5.80%	45.10
>3yrs	0.70%	13.30%	19.40%	17.60%	9.10%	13.80
Never	77.20%	18.10%	29.60%	70.80%	85.10%	41.10
No Screening*	77.90%	31.40%	49.00%	88.40%	94.20%	54.90

\* > 3 yrs and never screened

**Table 6: Cervical Screening by Regions (Source: NHIS, 2002)**

Region	1	2	3	4	5	6	All regions
<3 yrs	35.73%	47.17%	46.33%	50.33%	53.39%	35.34%	44.98
>3yrs	15.90%	13.94%	11.18%	12.75%	15.30%	10.78%	13.78
Never	48.37%	38.90%	42.49%	36.91%	31.32%	53.89%	41.24
No Screening*	64.27%	52.84%	53.67%	49.66%	46.62%	64.67%	55.02

\* > 3 yrs and never screened

a smear test in the last 3 years. This review showed that the cases of invasive cervical cancer in Malta tend to reside most commonly in regions 1 and 2 (see Table 3). Interpreting this finding together with the lower rates of smear activity reported by women in the NHIS residing in the same regions, suggests that women at higher risk for the invasive condition are not being effectively reached by the current screening activity in the Maltese Islands.

Interestingly, women residing in region 6 reported the lowest level of cervical screening activity. Contrastingly, this review also showed that the incidence rate for invasive cervical cancer in Gozo is statistically significantly lower than the national rate. These anomalous findings may be tentatively and partially explained by possible different attitudes of Gozitan women regarding sexual practice. The NHIS data shows that Gozitan women report very low rates of multiple sexual partners (0% of women reported having multiple sexual partners, while 35% declined to answer the relevant question).

Just over half the cases of cervical cancer had a smear history in their files. Improving the smear history documentation of all gynaecological referrals, and especially of patients presenting with cervical-related symptoms and pathology, will help towards more accurate evaluation of the effect of screening activity. In 2004, a new cervical smear request form was introduced for the Primary Health Care Centres. This includes appropriate fields for the gynaecologist to document the number and regularity/pattern of cervical smears undertaken by women attending these clinics. However, request forms from the hospital facilities in both Malta and Gozo have retained the old format. Updating of similar forms used by private laboratories should be encouraged. This is important since the majority of the cervical smear tests in Malta are performed by the private sector.

Although an opportunistic cervical screening programme in the public sector has been in place since 1978, no national studies have been performed to quantify the amount and characteristics of women who are being attracted to do routine cervical smear tests. This is also true in the case of private laboratories where a considerable amount of smears are done every year. Till now there are no relevant statistics about the amount of smears done yearly in the private sector.

EU recommendations state that when screening is to be undertaken, it should only be offered in organized programmes with quality assurance at all levels, and good information about the benefits and risks. The benefits of a screening programme are only achievable if the target population coverage is high. Opportunistic screening activities are usually not acceptable as they may not achieve the potential benefits and may cause unnecessary negative side-effects.<sup>7</sup>

The major aim of cervical screening is to decrease incidence and mortality of invasive cervical cancer. The audit information presented shows that there was no significant decrease in incidence and mortality of cervical cancer in Malta over time, in spite that cervical screening services have become more available and accessible in the last 2-3 decades. The percentage

of the female target population being screened is unknown, and the effectiveness of this Maltese opportunistic cervical cancer screening is therefore questionable.

The mortality rate also maintained a steady trend with minor fluctuations, reinforcing doubts about the effectiveness of the screening activity since it is not detecting the precancerous lesions or the invasive lesions at curable stages to increase survival.

Women at higher risk for cervical cancer due to their lifestyles, especially sexual practices, are known to be more likely not to present for cervical screening.<sup>14,15</sup> Screening that concentrates solely on a high-risk group is rarely justified, as identified risk groups usually represent only a small proportion of the cancer burden. In planning the coverage (target population) of screening programmes, however, steps must be taken to ensure that all those at high risk are included. This is often a difficult requirement to fulfill.<sup>16</sup> Health promotion directed at women's health should focus on increasing the frequency and scope of campaigns promoting the advantages of cervical screening in prevention of cervical cancer.

The situation in Malta is analogous to that in the UK before 1988. After more than two decades (1960–1986) of British NHS cervical screening service, the mortality from cervical cancer, although not rising, was not decreasing. It was established that this screening service was largely opportunistic and that the percentage of the target female population (ages 20 to 65) being regularly screened was unknown. It was also established that regular screening of more than 70% of the target population was needed to decrease invasive cervical incidence and mortality. Remodeling of the programme in 1988 resulted in a 34% decrease in the incidence of cervical cancer and the age standardized mortality decreased from 6.1 per 100,000 in 1987 to 3.7 in 1997.<sup>1</sup> The crucial remodeling feature was introduction of an incentive for family doctors to screen at least 90% of the target female population (ages 20 to 65).

Also until now there is no standardized system in the reporting of smears in Malta. The dyskaryosis/cervical intraepithelial neoplasia (CIN) classification is still very much in use. The Bethesda system was developed by the United States National Cancer Institute (NCI) to provide more detailed information about cervical smear results. Apart from giving information regards descriptive diagnosis when there is an abnormality in a smear, it also provides information about the quality of the cell sample and criteria for smear suitability. The Bethesda system has been introduced in many European countries, and has become the most popular classification in the reporting of cervical smears. Standardization of cervical smear reporting by choosing one system by which all smears are reported both in the public and private sector can result in less confusion and facilitate research audits about the subject.<sup>17</sup>

In conclusion, we suggest a national study to quantify the number of women undergoing regular cervical screening so that the percentage of the target population being screened is established. This study should include all the public and private



clinics/hospitals that offer cervical screening in Malta and Gozo, so that an accurate estimation can be obtained. The researchers have to collect information about the cervical smears submitted to the laboratories for a specified time period. It is important that all private laboratories/clinics will support this study to increase its accuracy. The results of such a study can show a clear picture of the situation of cervical screening activity in Malta. It can be used to assess the situation, identify problems of attendance in specific age groups and any regional discrepancies, if present and finally to propose changes to improve the uptake of cervical screening on the Islands.

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