A Comparative Dataset of Six Cancers in the European Union

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INTRODUCTION

Cancer causes one-quarter of all deaths in Ireland and is the largest single cause of death for the Irish population. In Ireland in 1999 patients with cancer accounted for over 300,000 in-patient days in hospital, thus making the disease a major drain on the economy.[1] A similar situation exists throughout the European Union (EU). In order to fight what has become the biggest health concern in Europe, it is necessary to examine all the available data.

Cancer registries are becoming more common and extremely valuable in the information that they provide. The European Network of Cancer Registries produces EUCAN a database which pools all the cancer statistics from the EU countries.[2] EUCAN is a unique source of the most up to date information on cancer incidence, mortality, prevalence and survival in the EU and its member states. A database such as this allows for comparisons with other pooled data sources, such as those held by the Organisation for Economic Co-operation and Development (OECD), enabling us to gain a comparative view of cancer costs. While the information provided is invaluable, there is still a need for standardisation of recording methods. For example, Italy has 14 registries each with its own separate standard of measurement. In spite of this, pooled databases cast light on discrepancies and similarities between people that would be considered to have similar genetic and cultural backgrounds.

In terms of focus, the current study looks at six cancers listed in the database, which are diverse in their treatment, screening and aetiology: oesophageal cancer, colorectal cancer, lung cancer, prostate cancer, breast cancer, and cancer of the cervix.

Oesophageal Cancer

The aetiology of oesophageal cancer is very complex. Smoking and excessive alcohol consumption, especially of spirits, are thought to be major risk factors. While they are independently significant, the risk of developing oesophageal cancer is more than 100 times greater when the two are combined.[3] A higher incidence is also associated with diets low in vegetables and fruit and deficient in vitamins or trace elements.[4] Plummer-Vinson syndrome, long-standing achalasia and Barrett's oesophagus all increase an individual's risk. The only hereditary transmission of oesophageal cancer is in patients with a genetic condition known as tylosis.[8] Incidence increases with advancing age. Oesophageal cancer is rare below the age of 40 and peak incidence is between 60 and 70 years of age.[4]

Oesophageal cancer can exist *in situ* for up to three or four years. The disease is largely asymptomatic in its early stages, and thus usually presents at an advanced stage. At the moment, the only way to screen for oesophageal cancer is endoscopy with biopsy.[5] Screening for oesophageal cancer is not widely available as there are high risks associated with these procedures such as perforation of the oesophagus. Screening is only recommended for high-risk individuals to provide early diagnosis in the asymptomatic patient.

Colorectal Cancer

Colorectal cancer is one of the major malignancies affecting western societies in terms of both incidence and mortality. Globally, risk seems to be correlated with economic development, with the highest rates in the western world and the lowest rates in Africa, South America and Asia.[6] This may be in large part due to dietary factors. Experimental evidence suggests that high dietary levels of meats, fats and refined carbohydrates promote colorectal cancer.[7] As most of the countries included in our study are considerably industrialised and have a high *per capita* income, a high incidence of colorectal cancer might be expected. A positive family history for colorectal cancer is another important risk factor.[7] A number of conditions such as ulcerative colitis and familial adenomatous polyposis coli predispose to the development of the disease.[8]

The incidence of colorectal cancer in the European Union, and the western world in general, is sufficiently high for screening to be a realistic proposition. There are three methods: faecal occult blood testing (FOB testing), digital rectal examination (DRE) and sigmoidoscopy. These investigations are relatively inexpensive; however FOB testing has a high level of false positives and DRE lacks sensitivity. Most cases of colorectal cancer occur in patients over 50 years

old, so a high-risk group is easy to identify.[8] A new technique known as virtual colonoscopy is proving to be the way forward in screening for this disease. This technique uses a reconstructed image based on Computed Tomography (CT) data.

Lung Cancer

The majority of cases of this disease are attributed to exposure of the bronchial epithelia to inhaled carcinogens.[9,10] There is a strong causal relationship between cigarette smoking and lung cancer with approximately 95% of cases associated with tobacco.[6] Risk is related to duration and intensity of smoking.[9] Other factors include exposure to asbestos, radon gas, air pollution and passive smoking.[10] Lung cancer had always been more common in men than in women, though recently the incidence in women has been increasing due to the increase in smoking among women.[11]

There are two different forms of lung cancer: small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). SCLC grows rapidly and is likely to spread to other organs. Patients can die two to four months after development if not treated. NSCLC is a silent disease and grows very slowly, sometimes going unnoticed for years.[3] In the past, screening was shown to be ineffective, with no improvement in patient care or survival rates.[10] However recently at an International Lung Cancer Conference recommendations were made for spiral CT screening of the chest for high-risk patients to improve survival rates. The normal survival rate for lung cancer is 10% but with this screening test survival jumps to 70% for very early stage lung cancer.[12]

Prostate Cancer

Carcinoma of the prostate is a disease of ageing men, with a peak incidence and mortality of approximately 70 years of age.[13] The disease is rare under the age of 45 years, and is almost universal at post-mortem in men over 80 years of age.[14] Even taking into consideration the limited population affected by this disease, it is one of the most common forms of cancer in men.[8] The disease is more common in married men and is thought to be related to the number of sexual partners, frequency of sexual activity and a history of a sexually transmitted disease.[14]

The main methods available for prostate cancer screening are digital rectal examination and prostate-specific antigen (PSA) testing. Both of these are problematic as there is a chance of obtaining false negatives with PSA tests and digital rectal examination lacks sensitivity.[13] At present there is much debate over the value of

prostate screening and whether it is ethically correct. Although prostate cancer is extremely prevalent in men over 80 it is mostly asymptomatic, which means that many men may never realise that they have the cancer and die from other causes.[15] If a screening program were introduced to identify prostate cancer, it would result in many more men living with the diagnosis of cancer, and undergoing treatment which may not be of benefit in terms of reducing disease-related morbidity or mortality. Treatment-related morbidity would be increased with no benefit. Prostate screening would therefore not fulfil Wilson and Junger's criteria for implementation of a screening program: that the chance of harm is less than the chance of benefit.[15] Quoted from Health Technology Assessment, "evidence concerning effectiveness of screening in reducing the number of prostate cancer deaths is very poor. There is no justification for the introduction of population screening."[15] This is a serious ethical issue and further studies must be taken before population screening for prostate cancer could be implemented.

Breast Cancer

Breast cancer is the most common malignant disease in women.[8] Up to 8% may be due to inherited genetic abnormalities.[16] Relative risk is increased three-fold when primary relatives have been affected.[8] History of benign breast disease, early menarche, late menopause, use of oral contraceptives, hormone replacement therapy and obesity increase an individual's risk of developing the disease.[17]

There is sufficient evidence to suggest that screening women aged 50 to 69 years is effective. A one-third reduction in mortality from breast cancer among these women has been demonstrated. There is also limited evidence showing some efficacy in women aged 40 to 49 years. Screening is carried out by means of mammography with or without physical examination of the breasts, and follow up of positive suspicious findings is by biopsy. National screening programmes have expanded rapidly in Western Europe.[18] Women are also advised to carry out 'self-checking' as this is often how the malignancy is first detected.

Cancer of the Cervix

Cervical cancer is strongly associated with the human papilloma virus. Young age at first sexual intercourse, multiple sexual partners, promiscuous male partners, cervical dysplasia and smoking increase the risk of developing the disease.[8] Risk decreases with the use of the contraceptive pill and number of full-term pregnancies.[19]

Cervical cancer has a long developmental phase with a detectable pre-clinical phase, which makes it ideal for screening. Screening for cervical cancer has been shown to reduce mortality. It is carried out by means of a Papanicolaou (Pap) smear test. This cytological test is far more effective in reducing mortality from cervical cancer than mammography screening in breast cancer. This test is widely available to women over 25 years of age in many European countries and it is recommended that the test be repeated every 3 to 5 years, although a screening program with an interval of 10 years can reduce the incidence of invasive cervical carcinoma.

METHODS

The data used in this paper was obtained from the EUCAN Database.[20] This website contains a breakdown of the incidences (including crude rate and age specific rate for Europe), mortality (including crude rate and age specific rate for Europe), 1-year prevalence and 5-year prevalence for various different sites of cancer in different European populations. The data on this website represented cancer statistics for all European Union Countries for the year 1998.

STATISTICS

Incidence is the number of new cancer cases arising in a given period of time in a specific population. Mortality is the number of cancer deaths occurring in a given period of time in a specific population. The age-standardised rate (ASR) is a summary measure of a rate that a population would have if it had a standard age structure. The figure used is per 100,000 people in the population. The ASR is important when comparing several populations that differ with respect to age, as one is comparing like with like and removing a bias, so making the comparison more accurate. This is especially important when investigating the incidence of cancer, as it is an age-related disease.

The mortality:incidence (M:I) ratio is the expression of newly reported cases to reported deaths, giving an indication of survival. As part of our calculations, we took the incidence as 1 and expressed the mortality as a fraction of that.

RESULTS

Table 1 demonstrates mortality:incidence ratios for the six selected cancer sites in 15 EU countries compared to the EU average. The figures below are calculated as the mortality if the incidence is taken as 1.

Table 2 shows the rank order of incidence of the six selected cancer sites in 15 EU countries with comparison to the EU average. The figures that are used in the table below are age standardised rates. They are taken per 100,000

Table 1: Mortality:Incidence for the Six Selected Cancer Sites in 15 EU Countries

Country	Oesophagus Both*	Colorectal Both*	Lung Both*	Breast Female*	Cervix Female*	Prostate Male*
EU	**0.90**	**0.49**	**0.91**	**0.31**	**0.39**	**0.38**
Austria	0.84	0.47	0.93	0.32	0.36	0.30
Belgium	0.92	0.48	0.91	0.32	0.43	0.32
Denmark	1.07	0.56	0.95	0.33	0.40	0.55
Finland	0.84	0.45	0.94	0.23	0.32	0.25
France	0.86	0.46	0.92	0.26	0.35	0.31
Germany	0.86	0.52	0.91	0.32	0.40	0.38
Greece	0.89	0.47	0.89	0.31	0.39	0.42
Ireland	0.89	0.46	0.99	0.35	0.40	0.44
Italy	0.96	0.45	0.89	0.30	0.34	0.36
Luxembourg	0.92	0.52	0.93	0.24	0.42	0.31
Netherlands	0.92	0.46	0.94	0.32	0.36	0.35
Portugal	0.95	0.47	0.90	0.33	0.41	0.51
Spain	0.94	0.49	0.88	0.33	0.41	0.53
Sweden	0.91	0.45	1.01	0.22	0.36	0.33
United Kingdom	0.93	0.51	0.90	0.35	0.44	0.43

people in the affected population and adjusted for age.

Table 2: Rank Order of Incidence of the Six Selected Cancer Sites in 15 EU Countries.

Country	Oesophagus	Country	Colorectal	Country	Lung
Greece	1.4	Greece	24.19	Sweden	23.69
Italy	2.8	Finland	32.46	Portugal	25.68
Sweden	3.09	Sweden	39.71	Finland	32.22
Finland	3.23	UK	41.74	Austria	36.66
Austria	3.55	Spain	41.77	Germany	39.03
Spain	4.2	Italy	43.53	Spain	39.57
Portugal	4.31	France	43.68	France	39.68
Germany	4.53	*EU*	*44.04*	*EU*	*42.16*
Belgium	4.86	Portugal	44.37	Ireland	43
Denmark	5.15	Belgium	45.74	Italy	43.79
EU	*5.38*	Luxembourg	48.73	Greece	44
Netherlands	6.29	Germany	48.74	Luxembourg	46.03
Luxembourg	6.6	Austria	49.19	UK	50.56
France	7.61	Netherlands	49.85	Netherlands	51.96
Ireland	9.04	Ireland	50.86	Denmark	52.75
UK	9.43	Denmark	51.8	Belgium	55.15
Country	*Breast*	*Country*	*Cervix*	*Country*	*Prostate*
Spain	66.81	Finland	5.6	Greece	41
Greece	67.97	Luxembourg	7.53	Spain	45.33
Portugal	70.46	Spain	7.55	Italy	52.78
Austria	86.14	Greece	8.14	Denmark	53.89
Italy	87.87	Netherlands	8.22	Portugal	55.23
Luxembourg	89.24	Italy	8.43	UK	60.97
Germany	89.43	Sweden	9.23	*EU*	*67.55*
Ireland	91.01	UK	9.45	Ireland	69.57
EU	*92.04*	*EU*	*10.3*	Germany	70.21
UK	94.66	Belgium	10.66	Luxembourg	78.53
Finland	102.02	Ireland	11.75	Netherlands	85.74
France	107.7	Germany	12.07	France	87.1
Netherlands	112.04	France	12.41	Austria	89.49
Sweden	113.98	Portugal	12.89	Belgium	95.34
Belgium	114.27	Austria	13.25	Sweden	114.95
Denmark	115.45	Denmark	14.47	Finland	121.84

The incidence of oesophageal cancer in selected EU countries is shown in figure 1. The error bars represent 1 standard error of the mean values within the EU.
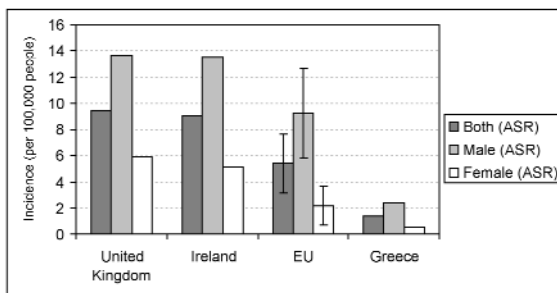

Figure 1: Incidence of Oesophageal Cancer in Selected EU Countries.

The United Kingdom presents with the highest incidence of oesophageal cancer for both sexes combined as well as males and females alone. In comparison, Greece presents with the lowest incidence in all three categories. The incidence in Ireland is also quite high, almost equaling that of the UK.
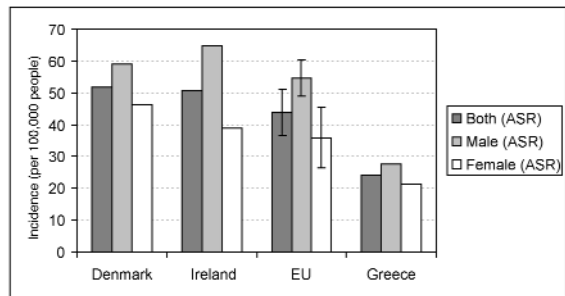

Figure 2: Incidence of Colorectal Cancer in Selected EU Countries.

As seen in figure 2, Denmark has the highest incidence in colorectal cancer overall with Ireland following closely behind. However, Ireland has the highest incidence in males. Greece has the lowest incidence in all three categories. The error bars represent 1 standard error of the mean values within the EU.
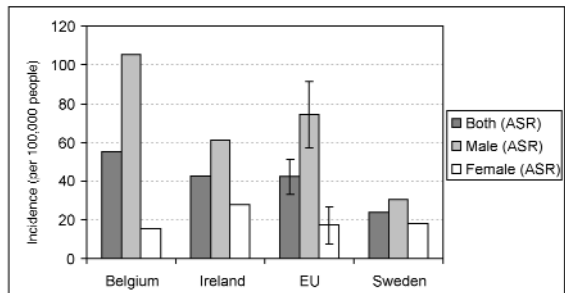

Figure 3: Incidence of Lung Cancer in Selected EU Countries.

Figure 3 shows that Belgium has the highest overall incidence of lung cancer, but it has the lowest incidence of lung cancer in females. Sweden has the lowest overall incidence. The error bars represent 1 standard error of the mean values within the EU.
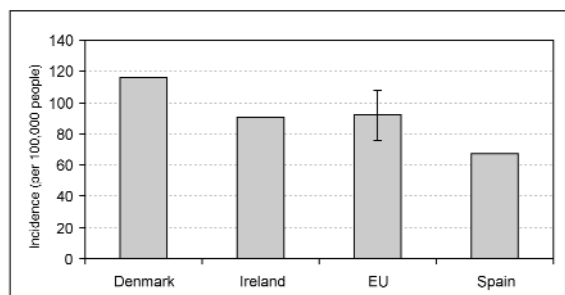

Figure 4: Incidence of Breast Cancer (Female only) in Selected EU Countries.

Figure 4 clearly demonstrates that Denmark has the highest incidence of breast cancer whereas Spain has the lowest incidence. The error bar represents 1 standard error of the mean values within the EU.

As seen in figure 5, Denmark has the highest incidence of cancer of the cervix whereas Finland has the lowest incidence. The error bar represents 1 standard error of the mean values within the EU.
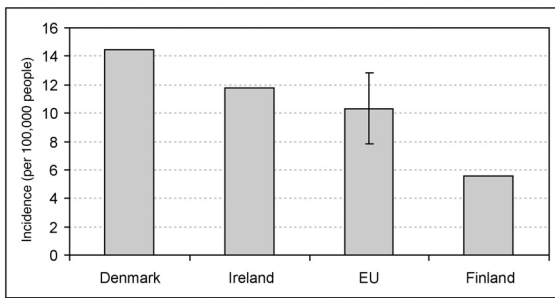
Figure 5: Incidence of Cancer of the Cervix(Female only) in Selected EU Countries.
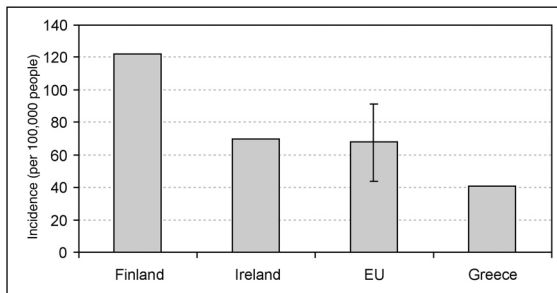

Figure 6: Incidence of Prostate Cancer (Male only) in Selected EU Countries.

Figure 6 clearly shows that the highest incidence of prostate cancer is in Finland and is almost double that of the EU average. The Irish incidence is very close to the EU average. Greece has the lowest incidence. The error bar represents 1 standard error of the mean values within the EU.

DISCUSSION
Oesophageal Cancer
The countries which presented with the highest incidence of oesophageal cancer were Ireland and the UK, while Greece had the lowest incidence rates (table 2). The differences between male and female incidence rates for oesophageal cancer are significant for all populations studied. This is likely to be due to the social culture present in the UK and Ireland, which expose the male population to regular alcohol intake and tobacco smoke, the two main risk factors in oesophageal cancer. In the aetiology of oesophageal cancer, tobacco smoke and alcohol act synergistically. The relative risk of an individual who both smokes and drinks is much greater than that of the individual who either smokes or drinks.[3]

In relation to the M:I for oesophageal cancer, the proportion of those who die from this form of cancer is high. Denmark and Italy have the highest M:I ratio for both sexes. Finland has the lowest M:I ratio. The M:I ratio for both sexes is large. There is quite a difference between this ratio in Belgium with a male M:I ratio of 0.91 and a much lower female M:I ratio of 0.46 (table 1). In contrast however, the male and female M:I ratios of Denmark are both similar and higher than the

European average.

Oesophageal cancer has the highest M:I ratio in Denmark and this may be directly related to the number of cigarettes smoked and the high amount of alcohol consumed. For example, during the seventies and eighties a dynamic change in drinking habits and beverage choice took place in Denmark. *Per capita*, wine consumption rose from 5.91 litres in 1970 to 21.31 litres in 1990, an increase of 260%. In the same time, the absolute consumption of alcohol also rose.[21]

Colorectal Cancer
Ireland has one of the highest incidences of colorectal cancer (table 2). Ireland's M:I ratio of 0.46 is lower than that of the EU so although the incidence is high, people are surviving the disease (table 1). However, the Irish diet contains too much fat and too little carbohydrate and this is a factor in the high incidence of the disease.[22] Greece has the lowest incidence, which is likely to be related to their Mediterranean diet of low saturated fat.

It is also very interesting to see that Denmark has the highest M:I ratio and incidence (above the EU average). The Danish diet is high in fat and this could contribute to the incidence.[23] This may suggest a need for public health campaigns and the high incidence may make screening a viable option. The treatment techniques should also be reviewed in view of the M:I ratio. Non-starch polysaccharides (fibre) and vegetables are established factors that reduce risk largely owing to the effect of non-starch polysaccharides in regulating bowel function. An intake of 18g per day of non-starch polysaccharides is recommended. This increases stool weight and reduces constipation thus reducing the risk of bowel cancer. Eating greater amounts of red meat also increases an individual's risk, as there is an association between metabolism of meat and the risk of developing polyps, which can become cancerous. Meat also increases the amount and type of residue entering the bowel, thus affecting the by-products formed by the colonic flora. These by-products, which include N-nitroso compounds, may be carcinogenic.[24]

Lung Cancer
Belgium presents with the highest incidence of lung cancer in Europe, whereas Sweden has the lowest incidence of lung cancer (table 2). Similar to oesophageal cancer, there are visible differences between the incidences in males and females. An example of this is in Ireland where the ratio of male to female lung

cancer incidence is almost 2:1 (figure 3). The M:I ratio in Ireland is also high for lung cancer (table 1).

Sweden has the highest M:I ratio at 1.01 (table 1) which means that more people died from lung cancer than were diagnosed in those years. Once again the M:I in Denmark is well above the EU average. Of note also is that Ireland is 2nd only to Sweden in terms of the worst survival from lung cancer. Spain has the lowest M:I ratio for both sexes. There is not much variation between the male and female incidence for this country.

There is a clear dose-response relationship between lung cancer risk and the number of cigarettes smoked per day, the degree of inhalation and the age of initiation of smoking.[9] The rate of smoking in Ireland, Denmark and the UK are high and therefore these countries present with high incidence rates. One of the most remarkable finding from Denmark is that it presents with the highest pre-standardised rates for female lung cancer in the world. In the beginning of the 1950's, the prevalence of smoking among Danish females was as high as 40% and in the 1980's; the proportion of females who smoked was almost the same as males.[25] This in turn explains the substantial number of females presenting with and dying from lung cancer in Denmark.

Another reason for the high rates of cancer in Denmark is the fact that radon gas is related to 10% of all lung cancers, accounting for 300 deaths per year.[26] The high level of radon gas is due to geographical and geological reasons. The European average for radon-caused cancers is five per cent, while in Denmark, this is doubled.

Breast Cancer

Our results show that Denmark has the highest incidence of breast cancer in the EU. A high incidence of breast cancer may indirectly reflect a good national screening programme. High incidence of breast cancer is due to genetic factors, and long-term levels of hormones in the blood.[17] It is very hard to attribute breast cancer to a single risk factor, as it is known that multiple factors are to blame. One contributing factor could be that Danish women have a poor diet that is high in fat. They have the highest rate of smoking amongst women in Europe and this could attribute to the high incidence. Incidence of breast cancer in Ireland is similar to the EU average, at an ASR of 92.04.

With regard to the M:I ratio, Ireland ranked the highest in Europe (table 1). The figures show that over 35% of women diagnosed with breast cancer in Ireland die from the disease. This suggests that screening in Ireland at this time was insufficient and the need for a national screening programme was extremely important. Also treatment techniques and waiting times for treatment may need to be examined. However these results were taken from 1998 which is the same year that the first phase of the programme was set up. Screening did not actually begin until 2000 and therefore any results yielded from this programme would not be reflected in statistics until subsequent studies were carried out post 2000. However, it must be noted that although the highest in the EU, the average figure is over 30%. Sweden has the lowest M:I ratio, which may suggest that many women are diagnosed at an early stage.

Cervical Cancer

As demonstrated in table 2, there is an approximate three-fold increase in incidence of cervical cancer between the countries that ranked the lowest and highest. Even though the absolute values are relatively low, this is quite a large gap.

Finland has the lowest incidence (table 2) and M:I ratio (table 1). Since the 1960s, Finland has had a national cervical cancer-screening programme in place, which would decrease the incidence.[27] Normally screening would increase the incidence but as the test detects the disease in a pre-malignant stage, the progression of cells to full malignancy is reduced. Figure 5 demonstrates that there is a large variation in the incidence of cervical cancer and this may be attributed to screening. Another reason for the low incidence of cervical cancer in Finnish women may be that they have one of the lowest smoking rates among women in Europe.[28] As smoking is seen as one of the risk factors for cervical cancer, this may be a supplementary factor.

Denmark has the highest ASR incidence (table 2). Public awareness campaigns may be necessary. As smoking plays a part in the aetiology of this disease and alcohol consumption is very high in Denmark, a partial explanation could lie here. Although Denmark has the highest incidence of cervical cancer it ranks sixth highest in Europe for M:I ratio. The U.K has the highest M:I ratio in Europe (table 1), which indicates that they must take a closer look at their treatment practices and the use of Pap smear tests in a screening programme to detect the disease at an earlier stage to decrease the mortality rate. Ireland also has a larger M:I ratio than the EU average and the same recommendations must be made here. A new national screening programme is due to be in place in Ireland in the near future.

Prostate Cancer

Finland has the highest incidence of prostate cancer while Greece has the lowest (table 2). The high incidence in Finland is possibly due to screening. In Finland in 1996/97, a nationwide study was carried out on prostate cancer. More men were screened and more made aware of their condition. Greece does not have well developed screening implying that patients are not diagnosed, even though the condition may be present. Finland's M:I ratio is the lowest ratio in the EU at 0.25 (table 1). This shows that although there is a high incidence, there is a very low death rate. This can be interpreted as proof that screening programs can be effective. By comparison, in Greece the M:I is above the EU average. However in the case of prostate cancer which is often asymptomatic and may not be the cause of death, we would suggest caution at comparing M:I data between countries that have screening programs and those that do not.

Although Greece had very low figures in incidence and M:I ratio for all the selected cancer sites, the results come from the southern Italy registry. Therefore the registries are insufficient and may not provide a true reflection of the cancer situation in Greece.

CONCLUSION

Throughout all the cancer sites that were studied in this paper, Denmark produced alarmingly high results in both incidence and M:I ratio for specific cancers. The figures for the latter are more worrying as they reflect the number of people who are dying from cancer. With cancer, no one factor can be pinpointed as the cause of disease. During research for this paper factors were found that may be a cause for this high incidence and mortality in Denmark. These include the high saturated fat in their diet, high alcohol consumption and high level of tobacco intake.[21] What is most striking is that Denmark departs from the Nordic countries in its incidence and outcomes of cancer. This illustrates that the genetic and cultural similarities are outweighed by lifestyle choices at a national level. Furthermore, the public awareness of cancer in Denmark is arguably lower than that of their Nordic neighbours. This is surprising, given that the educational systems of all four countries are reasonably similar. The divergence would appear to be at a governmental level, where health services planning and health promotion activities are coordinated.

Incidence of cancer in Ireland is above the EU average in every site studied except for breast cancer. The most worrying cases are those of oesophageal and colorectal cancer which have a much higher incidence in Ireland compared to the EU average. This shows that cancer is a major concern to Irish health services and that both public health campaigns and research are vital.

It is likely that there will be further refinements in cancer registries as clinicians, governments, and health insurers will want to have more information on cost effectiveness in order to better shape cancer strategy. As governments are establishing their cancer management plans, they need to have an overall view of the epidemiological state of their country in order to effectively distribute available funding. For example, if the government had to pay to treat a Stage IV lung cancer it would cost the state approximately 7,500.[29] However, if the government invests in cancer awareness campaigns, the future cost may decrease as the incidence decreases.

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