



Estimates and Projections of Incidence, Prevalence and Mortality of Pancreas Cancer in, Spain, for the Period 1998 and 2022

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ABSTRACT

Objective: Estimate pancreas cancer incidence and prevalence in , Spain, based on mortality and survival data from the period 1998-2007, and provide projections of incidence, prevalence and mortality until the year 2022. **Methodology:** General and pancreas cancer mortality rates were obtained from the National Statistics Institute and survival data was obtained from the EURO-CARE study. Estimations were carried out through the program MIAMOD. The joinpoint program was used to quantify the annual change expected in the projections. **Results:** In men, an increase in prevalence is expected, from 110.36 (Adjusted Rate - AR=96.54) to 190.4 (AR=130.19) per 100.000 inhabitants/year. Incidence rates would increase from 19.73 (AR=17.65) in 1998 to 32.98 (AR=23.02), and mortality would increase from 9.65 (AR=8.53) to 15.87 (AR=10.95) when comparing 1998 and 2022. In women, the increase in prevalence is from 87.09 (AR=61.46) to 155.41 (AR=91.95) cases per 100.000 inhabitants/year. Incidence would change from 15.54 (AR=11) in 1998 to 26.48 (AR=15.84), and for mortality there is also an expected increase, from 7.29 (AR=4.92) to 12.14 (AR=6.9). **Conclusion:** The projections indicate that pancreas cancer in Spain follows an increasing trend in incidence, mortality and prevalence in men - women. These projections must be considered in order to plan more effective prevention and treatment measures.

Keywords : Pancreas cancer, projections, incidence, mortality, prevalence.

Introduction

Pancreatic cancer is not one of the most common types of cancer in developed countries, but it has seen a significant increase in recent years. Between 1968 and 2000, the incidence of pancreatic cancer rose at an annual rate of 3.07% in men and 3.63% in women (1). It is a disease with increasingly low survival rates.

The pancreatic cancer mortality rate in Spain, according to the National Institute of Statistics (INE, from the Spanish acronym) (2), increased from 4,000 individuals in the year 2000 to 5,714 in 2010.

Information gathered about the cancer's fatalities and incidence is the primary resource, not only for epidemiological and clinical research about the causes of the cancer, but also for quantifying the magnitude of the disease and planning/evaluating health services. Knowledge of past trends in incidence, mortality rates and prevalence can be used to project the number of cases and deaths in the future, as well as to predict treatment needs.

Statistics concerning the pancreatic cancer mortality rate are generated at the national level, while other information, such as the incidence and survival rates, are compiled and analyzed by the Population-Based Cancer Registries (RCBP, from the Spanish acronym), which cover only a part of the country (3). In these situations, when it is not possible to obtain incidence or survival information at the national level or for a given region, cancer estimates and projections are an important tool for quantifying care needs and, consequently, for planning prevention and control measures.

The objective of this article was to estimate pancreatic cancer incidence and prevalence rates in Spain based on mortality and survival data from the period 1998-2007, and to provide

projections of rates of incidence, prevalence and death until 2022.

Methods

Pancreatic cancer mortality data were taken into account (*International Classification of Diseases, 10th revisión - ICD-10: C25*), as were data about the population's sex and age and the year for the 1998-2007 period. The data were obtained from the Spanish National Institute of Statistics (INE). The INE makes estimations and projections for the Spanish population. These data have been used for the 2008-2022 period. The relative survival data have been taken from the EURO-CARE study, which includes data from six Spanish RCBPs (5).

The incidence, prevalence and mortality estimates and projections were calculated using the *Mortality-Incidence Analysis Model (MIAMOD)* statistical software (6) by applying a "backward" calculation using mortality and survival data. This method is based on mathematical relationships between mortality and prevalence, as well as on incidence and survival rates, and can be used for other chronic diseases. Incidence is calculated using a Poisson regression model, which provides the most accurate estimates of mortality. The model calculates the raw and adjusted incidence rates (per 100,000 inhabitants/year), using the European population as a reference. Incidence is projected beginning after the last year of observed data and is based on changes in age-period-cohort during the observed period. The software uses a Weibull parametric model and the relative survival data. The model was chosen because it offered the best likelihood. The model was validated by verifying that the mortality estimates that it obtains retrospectively are similar to those observed. The "backward" calculation model of the *MIAMOD* software recalculates the mortality data necessary to begin the program, in such a way that a correlation between the observed and esti-

mated data can be performed in order to evaluate the validity and reliability of the estimates.

The data estimated using the *MIAMOD* software have been used to conduct a trend study using the regression program *Joinpoint* (7). The objective was to determine whether the estimated trends are statistically significant or not, using the adjusted rates (AR). The joinpoint analysis identifies the moment in which changes in the trend occur and calculated the Annual Percentage Change (APC) in each segment. The analysis begins with a minimum number of joinpoints and checks to see if one or more of these are significant enough to add to the model.

Results

The projections until the year 2022, based on the data from 1998 to 2007, reveal different results between the pancreatic cancer incidence, prevalence and mortality rates depending on gender, although the general trend predicts an increase until the year 2022.

In men, an increase in prevalence from 110.36 (AR (adjusted rate) = 96.54) to 190.4 (AR 130.19) cases per 100,000 inhabitants/year in the year 2022. The incidence rate would increase from 19.73 (AR=17.66) in 1998 to 32.98 (AR=23.02), and the mortality rate from 9.65 (AR= 8.53) to 15.87 (AR=10.95), when comparing the years 1998 and 2022 (Table 1), (Figure 1)

In women, an increase in prevalence from 87.09 (AR=61.46) to 155.41 (AR=91.95) cases per 100,000 inhabitants/year is predicted. The incidence rate would rise from 15.54 (AR=11) in 1998 to 26.48 (AR=15.84), and the mortality rate is also expected to increase, from 7.29 (AR=4.92) to 12.14 (AR=6.9) between the years 1998 and 2022 (Table 2), (Figure 2)

In men, the APCs found for prevalence, incidence, and mortality were 4.51 (CI 95%: -1.34; 10.71); 1.10 (CI 95%:1.8/1.11), and 0.72 (-1.95; 3.47), respectively, between the years 1998 and 2022. However, it is necessary to mention the notable increases that are produced when the changes studied are analyzed in different lengths of time. Thus, for example, prevalence would increase by 9.07% (CI 95%:4.61; 13.73) between the years 2003 and 2022, while the incidence rate would increase slightly between 2009 and 2022, with a APC of 1.12% (CI 95%:1.1/1.13, and mortality would drastically increase between 2012 and 2022, with a APC of 6.58 (CI 95%:6.50/6.65) (Table 3)

In women, for the entire 1998-2011 period, the APC for prevalence was 2.21 (CI 95%:-1.52/6.10). For incidence, the APC was 6.25 (CI 95%:0.97; 11.8). The mortality trend in women had an APC of 0.90 (CI 95%:-3.50/5.50). Just as was done with the men, it is necessary to point out different periods in which all of the rates were markedly increasing. Thus, between the years 2007 and 2022 an increase of 7.44% (CI95%:1.29/14) is predicted; the incidence rates would remain stable over any period of time considered, and with respect to mortality, an increase of 6.13% (CI95%:0.32/12.28) is predicted for the 2002-2020 period.

Discussion

Different trends in the incidence of pancreatic cancer can be observed all over the world. Some results (8) reveal that the highest incidence rates in Europe can be found in Italy (19.8, 8.8 adjusted), followed by central European countries such as the Czech Republic (15.1, 6.7 adjusted), with the rates in Finland and Denmark slightly lower.

In the USA (9), the rate during the 2004-2008 period was 13.6 per 100,000 people in men and 10.7 in women. Mortality was 12.5 in men and 9.4 in women, and the trend in increases between 2000 and 2008 was 1.6% in men and 1.2% in women; as we can see, the trend of this type of cancer to increase is a constant in developed countries.

Mortality rates for pancreatic cancer are parallel to morbidity rates. This, together with the shortage of screening methods, worsens the panorama of the disease. However, prevention by controlling several risk factors could play an important role in reducing the disease (10).

This cancer has remained stable over a long period of time in developed countries and was rarely detected in developing countries. Currently, numerous publications express a trend in which the incidence and mortality rates are increasing, especially in some industrialized countries in which it appears to have now occupied fourth place on the list of different types of cancer. In the US, pancreas cancer among African-Americans reaches the highest rates in the world. (11)

Different risk factors have allowed this disease to develop, especially those associated with other risk factors like belonging to certain blood groups, such as ABO (12) and variant rs505922. (13)

The genes responsible for inherited pancreatic cancer explain around 5-10% of cases and have been well documented. (14)

The American report for monitoring cancer between 1975 and 2008 shows the increase in pancreatic cancer in recent decades, while at the same time citing risk factors such as inactivity, lack of exercise and obesity. (15)

Environmental factors (16), such as occupational exposure, pesticides and tobacco smoke are also cited as potential risk factors for the development of pancreatic cancer. (17).

The data of this investigation have revealed a trend of increasing mortality caused by pancreatic cancer in men and women that is repeated in the projected incidence and prevalence rates; this makes the situation in the population worrisome and warns of the importance of more knowledge about risk factors.

At the international level, the choice of a certain screening method for pancreatic cancer depends on the cost and availability of diagnostic resources. Pancreatoscopies (18) continue to be the gold standard; however, this option requires a qualified examiner and entails higher costs. For these reasons, pancreatoscopies as a screening method for the general population is the least recommended method in countries with few resources.

In Spain, despite the high incidence rates, early detection programs are rare. Therefore, no relationship between the observed trends and the implementation of screening programs can be found. Moreover, these trends could be related with changes in risk factors.

Among the mentioned risk factors linked to pancreatic cancer are diet (19), obesity (20), little physical activity, and tobacco (21) and alcohol consumption (22). An increase of 50% in the risk of suffering pancreatic cancer was observed in men and women that smoked more than one pack of cigarettes per day. The individuals that stopped smoking, even more than 10 years later, presented a high risk compared with non-smokers. The quantity of tobacco smoked was more important than the number of years the individual smoked (23).

The new tobacco consumption control law in Spain took effect on January 1, 2011. The smoking ban in bars and restaurants was the most controversial measure. The primary objective of this law is to reduce the prevalence of tobacco consumption and, consequently, reduce the incidence of diseases related to smoking, such as pancreatic cancer.

The projections presented in this study are based on past trends and were made in the short term, which makes it impossible to reflect the results of this new law.

With regard to alcohol consumption among Spaniards, the

data show that it increased until the end of the 1970s and then decreased until the late 1990s (24). Currently, according to the Ministry of Health and Consumer Affairs, alcohol consumption among Spaniards is high and remains stable. Approximately 64.6% of the Spanish population routinely consumes alcohol and 14.9% consumes it daily (25). Spanish laws regarding alcohol consumption are still not in agreement with the measures recommended by the scientific community with respect to restrictions on sales hours and licenses, covert advertising and other topics. (26)

The increase of incidence rates of pancreatic cancer in Asia and Eastern Europe reflect changes in diet and lifestyle caused by "westernization", such as smoking and obesity. In the Czech Republic, for example, approximately 60% of men smoke and the prevalence of obesity in adults exceeds 35%. (27, 28).

The prevalence of obesity in Spain is high. According to the National Health Survey for the 1993-2006 period, an increase in morbid obesity from 1.8 cases per 1,000 inhabitants/year to 6.1 cases per 1000 was reported. The prevalence was higher in women, after adjusting for age, and an annual increase of 12% in men and 4% in women was observed. (29).

The link between incidence of pancreatic cancer and factors associated with lifestyle, such as diet, obesity, little physical activity, and tobacco and alcohol consumption, has been well documented and needs to be considered when deciding which strategies to use to make prevention effective.

The projected incidence, mortality and prevalence rates of pancreatic cancer in this study reveal important information about the organization of health services. It is critical to point out that the projections found here are based on the risks found in the current populations, and therefore any change in the population will need to be evaluated at later periods.

Table 1. Projections the prevalence rates, incidence and mortality from pancreatic cancer in men

Year	Prev	Std.prev	Inc
Std Inc	Mor	Std Mort	
1998	110,36	96,54	19,73
17,66	9,65	8,53	
1999	114,77	98,18	20,4
17,89	9,93	8,59	
2000	117	99,77	20,73
18,11	10,01	8,63	
2001	119,44	100,77	21,07
18,23	10,16	8,67	
2002	122,52	102,53	21,52
18,48	10,36	8,78	
2003	125	104	21,88
18,68	10,53	8,87	
2004	127,34	105,38	22,24
18,88	10,69	8,97	
2005	129,62	106,81	22,59
19,09	10,86	9,07	
2006	131,69	108,1	22,93
19,29	11,02	9,17	
2007	133,45	109,44	23,22
19,51	11,15	9,27	
2008	136,77	110,81	23,78
19,72	11,42	9,38	
2009	140,09	112,17	24,34
19,94	11,69	9,49	
2010	143,42	113,54	24,92
20,16	11,96	9,59	
2011	146,78	114,89	25,51
20,39	12,23	9,69	
2012	150,19	116,23	26,1
20,61	12,51	9,80	

2013	153,63	117,59	26,71
20,84	12,79	9,91	
2014	157,11	118,98	27,32
21,07	13,08	10,01	
2015	160,65	120,36	27,93
21,31	13,37	10,12	
2016	164,27	121,73	28,57
21,54	13,68	10,24	
2017	168,02	123,07	29,22
21,78	14	10,36	
2018	171,94	124,44	29,89
22,03	14,33	10,47	
2019	176,04	125,83	30,59
22,27	14,68	10,59	
2020	180,4	127,23	31,33
22,52	15,05	10,71	
2021	185,16	128,69	32,12
22,77	15,44	10,83	
2022	190,42	130,19	32,98
23,02	15,87	10,95	

Prev: Pevalence; Std: Standart; Inc: Incidence; Mort: Mortality

Table 2. Projections the prevalence rates, incidence and mortality from pancreatic cancer in women

year	Prev	Std.prev	Inc
Std Inc	Mort	Std Mort	
1998	87,09	61,46	15,54
11	7,29	4,92	
1999	90,17	62,45	16
11,13	7,54	4,98	
2000	91,96	63,58	16,25
11,28	7,61	5,01	
2001	94,01	64,57	16,54
11,41	7,72	5,05	
2002	96,14	65,65	16,85
11,55	7,84	5,1	
2003	98,26	66,77	17,15
11,7	7,96	5,15	
2004	100,34	67,89	17,45
11,86	8,1	5,22	
2005	102,43	69,04	17,76
12,02	8,24	5,29	
2006	104,4	70,16	18,06
12,19	8,37	5,36	
2007	106,14	71,3	18,32
12,36	8,49	5,44	
2008	108,99	72,47	18,77
12,55	8,7	5,51	
2009	111,8	73,68	19,23
12,73	8,9	5,6	
2010	114,61	74,9	19,68
12,93	9,11	5,68	
2011	117,45	76,13	20,15
13,13	9,31	5,76	
2012	120,35	77,38	20,63
13,34	9,52	5,85	
2013	123,28	78,66	21,12
13,55	9,72	5,93	
2014	126,24	79,99	21,61
13,77	9,93	6,03	
2015	129,26	81,34	22,12
14	10,15	6,12	
2016	132,34	82,73	22,63
14,24	10,37	6,22	
2017	135,56	84,12	23,17
14,49	10,61	6,33	
2018	138,96	85,57	23,74
14,74	10,86	6,43	
2019	142,54	87,07	24,34

15	11,13	6,54	
2020	146,36	88,62	24,97
15,27	11,43	6,66	
2021	150,61	90,25	25,68
15,56	11,76	6,78	
2022	155,41	91,95	26,48
15,84	12,14	6,9	

Prev: Pevalence; Std: Standart; Inc: Incidence; Mort: Mortality

Table 3

Trend the projections of the prevalence rates, Incidence and Mortality

Men

Year	PAC Prevalence	PAC Incidence	PAC Mortality
1998-2022	4.51(IC 95%: -1.34; 10.71)		1,10 (IC
95%:1.8/1,11).	0.72 (IC 95% -1.95; 3.47)		
2003-2022	9.07 (IC 95%:4.61;13.73)		1.12 (IC
95%:1.1/1,13).	6.58 (IC 95%:6.50/6.65)		

Women

Year	PAC Prevalence	PAC Incidence	PAC Mortality
1998-2022	2.21(IC 95%:-1.52/6.10)		6.25 (IC
95% :0.97;11.8)	0.90(IC 95%:- 3.50/5.50).		
2007-2022	7,44 % (IC 95%:1,29/14		6.25 (IC
95% :0.97;11.8)	6.13 % (IC 95%:0.32/12.28)		

PAC: Annual Percent Change (APC)

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