

RESEARCH ARTICLE

2 Predicting the cancer burden in Catalonia between 2015 and 2025:

the challenge of cancer management in the elderly

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- 8 Received: 17 July 2017 / Accepted: 5 October 2017
- 9 © Federación de Sociedades Españolas de Oncología (FESEO) 2017

10 Abstract

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11 Background Developing effective cancer control pro-12 or grammes requires information on the future cancer burden 13 in an ageing population. In our study we predicted the

- burden of cancer in Catalonia from 2015 to 2025.
- 15 Methods Bayesian age-period-cohort models were used to
- 16 predict to predict the burden of cancer from 2015 to 2025
- 17 using incidence data from the Girona and Tarragona cancer
- 18 registries and cancer mortality data from the Catalan
- 19 mortality registry. Using the Bashir-Estève method, we
- 20 divided the net change in the number of cases between
- 21 2015 and 2025 into changes due to population size (S),
- 22 cancer risk (R) and age (A) distribution.
- 23 Results By 2025, there will be 21,743 new cancer cases in
- 24 men (40% aged > 74 years) and 17,268 in women (37%
- 25 aged > 74 years). More than 40% of the new cases will be

diagnosed among population aged 74 and older in prostate,	26
colorectal, lung, bladder, pancreatic and stomach cancers	Q2 27
in men, and in colorectal, pancreatic and bladder cancers	28
and leukaemia in women. During 2015-2025, the number	29
of new diagnoses will increase by 5.5% in men $(A + R)$	30
+ S = 18.1% - 13.3% + 0.7% = 5.5%) and 11.9% in	31
women $(A + R + S = 12.4\% - 1.1\% + 0.6\% = 11.9\%)$.	32
Overall cancer mortality rates will continue to decrease	33
during 2015-2025. Lung cancer will be the most lethal	34
cancer among men $(N = 2705)$ and women $(N = 1174)$.	35
Conclusions The increase in the number of cancer cases in	36
Catalonia from 2015 to 2025 will mostly affect the elderly,	37
prompting the need for increased collaboration between	38
geriatricians and oncologists.	39

Keywords Cancer · Incidence · Mortality · Projections · Ageing · Burden

A1	Electronic supplementary material The online version of this
A2	article (doi:10.1007/s12094-017-1764-5) contains supplementary
A3	material, which is available to authorized users.

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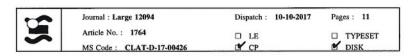
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Introduction

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Predicting the future burden of cancer in a given population is of interest to the institutions responsible for cancer control, as this information is required for planning future services and allocating resources [1].

Changes in exposure to cancer risks and protective factors help determine the future burden of cancer in a population [1], as do changes in population demography. As life expectancy increases, so too does the lifetime risk of developing cancer [2]. Since a large proportion of cancers in Catalonia are diagnosed in older adults [3, 4], population ageing leads to an increase in the absolute number of cancer cases [5]. By 2050, 40% of Spain's population is set to be aged 60 years or older (Population Ageing and Development 2009: http://www.unpopulation. org), so it is crucial to take into account the effect of ageing when assessing the cancer burden [6]. At the same time, treating elderly patients is challenging due to agerelated metabolic changes and comorbidities as well as the lack of guidelines, posing a huge problem for policy makers [7, 8]. These factors increase the demand for healthcare resources, particularly for controlling chronic diseases such as cancer.

This paper quantifies the changes in Catalonia's cancer burden between 2015 and 2025, with particular focus on the changes associated with population ageing.

Materials and methods 69

We aggregated cancer incidence data from the Tarragona and Girona population-based cancer registries for the period between 1994 and 2012 and used them to estimate cancer incidence in Catalonia. We obtained cancer mortality data for the period between 1994 and 2013 from the Catalan mortality registry. These cancer incidence and mortality data were stratified by sex and cancer type according to the IXth and Xth edition of the International classification of diseases depending on the period of mortality data (See Classification of cancer cases/deaths section and supplementary Table S1 included in the supplementary material). Incidence and mortality data were arranged in annual intervals in 18 5-year age groups, from 0-4 years to 85 and older.

The Catalan Institute of Statistics (http://www.idescat. cat) provided data on the Catalan population and its age 8 distribution in both sexes for the study period. We used the predicted population by 5-year age groups for 2015 to 2025 to project cancer incidence and mortality.

Modelling projections

We derived cancer incidence in Catalonia from 1994 to 2012 by applying the age-specific cancer rates in Girona and Tarragona, accounting for 20% of the Catalan population [3], as a whole to the age-specific population counts in Catalonia. We assumed homogeneous rates for the whole autonomous community.

Based on these estimates, Bayesian autoregressive ageperiod-cohort models [9] were fitted to data from the period between 1994 and 2012, and these models were used to predict incidence and mortality for 2015-2025, assuming Poisson distribution for the number of cases [10]. We describe extensive details of the prior distributions, models used and the model choice in the Supplementary material file. Tables 1, 2, 3, 4 present crude and age-standardised (world population) incidence (ASIR) and mortality rates (ASMR), the number of new cancer cases and deaths in the 35-64 and \geq 65 age groups and the proportion of cases diagnosed in people aged over 74 years for the years 2015 and 2025.

To assess the percentage change in incident cases between 2015 and 2025, we used the Bashir-Estève method through the web tool RiskDiff [11], which enabled us to split the net change (NC) in the number of cases into changes in demography and changes in cancer risk (R). Since demographic changes can be divided into changes in population size (S) and population structure (ageing: A), the NC can be partitioned into three additive quantities NC = A + RIA + SIA, where changes in risk and population size are conditioned by changes in population structure (RIA and SIA) [6]. Based on this method let $\frac{N_{2025}-N_{2015}}{N_{2015}} \times 100 = NC(\%)$, assuming that the predicted number of cases in 2025, could be partitioned into the number of cases due to changes in risk N_{2025}^R and the number of cases due to changes in population size and age structure, known as changes in demography, N_{2025}^D , then $N_{2025} = N_{2025}^R + N_{2025}^D$. Note that changes in demography can be obtained through $N_{2025}^D = \sum_i \lambda_{i2015} \times P_{i2025}$, where λ_{i2015} is the age-specific incidence rate for a specific cancer that was observed during the period 2015, and P_{i2025} is the age-specific population at risk predicted for the year 2025. If we let $P_{2015} = \sum_{i} P_{i2015}$ and $P_{2025} = \sum_{i} P_{i2025}$ as the total population counts in 2015 and 2025, respectively,

 $P_{2025} imes rac{\sum_i N_{i2015}}{P_{2015}}$ is the total expected number of cases in 2025 due to changes in population size. Since N_{i2015} = $\lambda_{i2015}P_{i2015}$ and $N_{2025}^R = N_{2025} - N_{2025}^D$ all these quantities are related to changes in population structure, ageing. We carried out a factorial analysis to assess the most likely contribution of risk, ageing and population size to the percentage changes in incidence between periods.



Table 1 Projected number of incident cancer cases in Catalonia for the years 2015 and 2025 according to sex and age group

Cancer type	Men										Women									
	2015					2025					2015					2025				
1200	35-64 ^a (N)	× 64 ^b	Total ^c (N)	8	ASIR	35-64 ^a (N)	> 64 ^b	Total ^c (N)	8	ASIR	35-64 ^a (N)	> 64 ^b	Total ^c (N)	8	ASIR	35-64 ^a (N)	× 64°	Total ^c (N)	2	ASIR
Oral cavity and pharynx	373	354	733	20.2	11.5	356	368	729	20.0	7.6	71	134	217	5.8	2.9	19	128	224	5.9	3.1
Oesophagus	119	186	305	8.4	4.6	89	195	263	7.2	3.0	21	42	63	1.7	0.7	25	48	73	1.9	0.7
Stomach	178	431	612	16.9	8.3	168	401	573	15.7	6.5	68	321	416	Ξ	4.1	81	326	413	10.9	3.8
Colorectal	1027	2461	3508	9.96	47.9	1064	2916	4015	6.601	45.8	919	1800	2493	66.3	27.2	792	2143	2966	78.4	28.4
Gallbladder and biliary tract	27	87	114	3.1	1.5	18	82	103	2.8	::	39	173	212	5.6	1.9	30	194	224	5.9	1.8
Liver	236	332	579	16.0	8.8	264	353	627	17.2	8.5	62	206	268	7.1	2.5	78	228	306	8.1	2.7
Pancreas	195	395	591	16.3	8.2	215	481	169	1.61	8.1	93	376	470	12.5	4.4	107	438	546	14.4	4.5
Larynx	206	206	413	11.4	6.5	136	199	335	9.2	4.3	32	18	50	1.3	8.0	36	22	28	1.5	8.0
Lung	951	2192	3150	8.98	44.5	655	2271	2928	80.2	32.2	353	414	770	20.5	10.5	368	884	1253	33.1	13.6
Bone	18	14	52	1.4	1.4	18	15	50	1.4	1.2	6	9	23	9.0	9.0	7	9	18	0.5	0.4
Skin melanoma	189	188	399	11.0	6.5	222	252	497	13.6	7.2	197	178	416	11.1	6.7	203	208	447	11.8	6.7
Breast	13	25	38	1.0	0.5	13	25	38	1.0	0.5	2556	1811	4462	118.6	61.9	2679	2107	4877	129.0	0.79
Prostate	886	3269	4258	117.3	57.7	1037	3614	4652	127.4	51.6	1	1	1	1	1	1	1	1	1	1
Testis	06	=	211	5.8	5.6	94	17	247	8.9	7.3	1	1	1	1	1	1	1	1	1	1
Cervix uteri	1	1	1	1	1	1	1	1	1	1	195	85	314	8.3	5.5	175	86	293	7.7	4.9
Corpus uteri	1	1	1	1	1	I	1	ı	1	1	334	479	815	21.7	10.9	285	550	840	22.2	9.2
Ovary	1	1	1	1	1	1	1	1	1	k	221	207	445	11.8	9.9	176	193	377	10.0	5.0
Kidney	276	448	736	20.3	11.0	285	490	786	21.5	10.1	142	233	380	10.1	5.1	162	358	521	13.8	5.5
Bladder	478	1315	1797	49.5	24.0	491	1438	1931	52.9	20.6	80	325	407	10.8	3.8	68	381	472	12.5	3.8
Brain and other CNS	114	152	303	8.3	5.5	114	153	300	8.2	5.0	104	149	276	7.3	4.3	107	162	287	9.7	3.9
Thyroid	99	21	68	2.5	1.7	53	21	85	2.3	9.1	293	83	458	12.2	9.1	355	123	534	14.1	6.6
Hodgkin's lymphoma	42	15	88	2.4	2.1	43	17	87	2.4	2.0	45	22	85	2.3	1.7	19	27	93	2.5	4.1
Non Hodgkin's lymphoma	297	347	692	19.1	11.7	295	418	757	20.7	11.2	187	310	530	14.1	7.6	192	296	533	14.1	7.5
Myeloma	54	156	210	5.8	2.8	47	163	210	5.7	2.3	58	172	230	6.1	2.5	99	210	276	7.3	2.6
Leukaemia	140	302	487	13.4	8.0	140	331	509	13.9	7.2	122	251	411	10.9	6.1	141	273	452	12.0	6.3
Total except non- melanoma skin	6418	13,755	20,611	567.8	297.8	6129	15,169	21,743	595.2	262.4	6247	8714	15,437	410.4	206.3	6554	10,289	17,268	456.7	204.6

Lung includes trachea, CNS central nervous system, Myeloma includes multiple myeloma and immunoproliferative disease, CR crude rate per 100,000 person-years, ASIR age-standardised incidence rate (World Standard Population) per 100,000 person-years

^aDiagnosed in people aged 35-64 years

^bDiagnosed in people aged over 64 years

^cAll ages considered

Table 2 Ten leading incident cancer types and percentage of cases diagnosed in people aged over 74 years, in men and women in Catalonia in 2015 and 2025

2015			2025		
Cancer type	Na	> 74 (%) ^b	Cancer type	Na	> 74 (%) ^b
(a) Men					
Prostate	4258	1605 (37.7)	Prostate	4652	1893 (40.7)
Colorectal	3508	1386 (39.5)	Colorectal	4015	1702 (42.4)
Lung	3150	1062 (33.7)	Lung	2928	1282 (43.8)
Bladder	1797	740 (41.2)	Bladder	1931	913 (47.3)
Kidney	736	228 (31.0)	Kidney	786	267 (34.0)
Oral cavity and pharynx	733	185 (25.2)	Non-Hodgkin's lymphoma	757	216 (28.5)
Non-Hodgkin's lymphoma	692	173 (25.0)	Oral cavity and pharynx	729	202 (27.7)
Stomach	612	243 (39.7)	Pancreas	697	282 (40.5)
Pancreas	591	221 (37.4)	Liver	627	175 (27.9)
Liver	579	171 (29.5)	Stomach	573	253 (44.2)
2015			2025		
Cancer type	N	>74 (%)	Cancer type	N	>74 (%)
(b) Women					
Breast	4462	991 (22.2)	Breast	4877	1156 (23.7)
Colorectal	2493	1207 (48.4)	Colorectal	2966	1459 (49.2)
Corpus uteri	815	239 (29.3)	Lung	1253	400 (31.9)
Lung	770	220 (28.6)	Corpus uteri	840	290 (34.5)
Non-Hodgkin's lymphoma	530	194 (36.6)	Pancreas	546	315 (57.7)
Pancreas	470	269 (57.2)	Thyroid	534	42 (7.9)
Thyroid	458	26 (5.7)	Non-Hodgkin's lymphoma	533	184 (34.5)
Ovary	445	115 (25.8)	Kidney	521	192 (36.9)
Stomach	416	227 (54.6)	Bladder	472	286 (60.6)
Skin melanoma	416	101 (24.3)	Leukaemia	452	199 (44.0)

^aTotal number of cases diagnosed

Results

The burden of cancer incidence

Table 1 presents the projected incidence of the selected cancer types in Catalonia in 2015 and 2025 by age group in both sexes. The total number of new cancer cases in 2015 was predicted to be 36,048 (N=20,611 in men and N=15,437 in women). Between 2015 and 2025, we predicted an increase of 5.5% in men (N=21,743) and 11.9% in women (N=17,268). Our results show a 4.7% decrease in new diagnoses among men aged between 35 and 64 years over the 10-year study period ($N_{2015}=6418$; $N_{2025}=6129$) and a 10.3% increase among those aged 65 and older ($N_{2015}=13,755$; $N_{2025}=15,169$). In women, the pattern is slightly different, with an increase predicted in both age groups (35–64 years: 4.9%; > 64 years: 18.1%).

Figure 1 shows the time trend of the overall age-standardised incidence and mortality rates from 1995 to 2025. The age-standardised incidence rate (ASIR) is expected to decrease in men and stabilise in women. When we examine the time trends for each cancer type, we see that there are few exceptions to the general trend (Figures S1 and S2, Supplementary Material). Figure S1 shows a stabilisation of pancreatic cancer and a slight rise in melanoma and testicular cancer in men, while Figure S2 shows an expected rise in lung, kidney and thyroid cancer in women.

Table 2 shows the most common cancer types predicted for 2015 and 2025. In men, the three most common types for both years are prostate ($N_{2015} = 4258$; $N_{2025} = 4652$), colorectal ($N_{2015} = 3508$; $N_{2025} = 4015$) and lung ($N_{2015} = 3150$; $N_{2025} = 2928$). Incidence of the latter cancer is expected to decrease by 7% over the 10-year study period. In women, the three most common cancer types in 2015 are breast (N = 4462), colorectal (N = 2493) and corpus uteri (N = 815). In 2025, however,



^bPercentage of cases diagnosed in people aged over 74 years

Table 3 Differences in the number of incident cases in Catalonia between 2015 and 2025 due to changes in the risk of developing cancer and changes in population demographics (age distribution and population size)

Cancer funo	Mon							W						
cancel type	INICII							women						
)	2015 (N)	2025 (N)	Difference ^a (N)	Net change ^b (%)	Risk° (%)	Structure ^d (%)	Size° (%)	2015 (N)	2025 (N)	Difference ^a (N)	Net change ^b (%)	Risk° (%)	Structure ^d (%)	Size ^e (%)
Oral cavity and pharynx	733	729	4 -	- 0.5	- 17.6	16.4	0.7	217	224	7	3.2	- 10.0	12.6	9.0
Oesophagus	305	263	- 42	- 13.8	- 32.1	17.8	0.5	63	73	10	15.9	0.2	15.1	9.0
Stomach	612	573	- 39	- 6.4	-25.8	18.8	9.0	416	413	- 3	- 0.7	- 15.0	13.7	9.0
Colorectal	3508	4015	507	14.5	- 5.4	19.1	8.0	2493	2966	473	19.0	3.6	14.8	9.0
Gallbladder	114	103	- 11	9.6 -	-30.3	20.1	9.0	212	224	12	5.7	-10.7	15.8	9.0
Liver	579	627	48	8.3	-10.3	17.9	0.7	268	306	38	14.2	- 2.3	15.8	0.7
Pancreas	591	L69	106	6.71	- 1.6	18.7	8.0	470	546	76	16.2	0.2	15.4	9.0
Larynx	413	335	- 78	- 18.9	- 36.8	17.4	0.5	20	58	∞	16.0	2.2	13.2	9.0
Lung	3150	2928	- 222	- 7.0	- 26.8	19.1	0.7	770	1253	483	62.7	46.6	15.3	8.0
Bone	52	20	- 2	- 3.8	- 12.5	8.0	0.7	23	18	- 5	- 21.7	-27.2	5.1	0.4
Skin melanoma	399	497	86	24.6	11.1	12.7	8.0	416	447	31	7.5	- 0.3	7.2	9.0
Breast	38	38	0	0.0	-20.0	19.4	9.0	4462	4877	415	9.3	- 2.1	10.8	9.0
Prostate	4258	4652	394	9.3	- 12.0	20.5	8.0	1	1	1	1	1	1	,
Testis	211	247	36	17.1	26.1	8.6 -	8.0	1	1	1	1	ı	1	,
Cervix uteri	1	1	1	1	1	1	1	314	293	- 21	- 6.7	- 11.8	4.6	0.5
Corpus uteri	1	1	1	1	1	1	1	815	840	25	3.1	-12.7	15.2	9.0
Ovary	ï	ī	ı	ı	1	ı	1	445	377	- 68	- 15.3	- 27.5	11.8	0.4
Kidney	736	786	50	8.9	-10.5	16.7	9.0	380	521	141	37.1	22.2	14.2	0.7
Bladder	1797	1931	134	7.5	-12.8	9.61	0.7	407	472	65	16.0	0.3	15.0	0.7
Brain and other CNS	303	300	- 3	- 1.0	- 14.0	12.4	9.0	276	287	=	4.0	9.8 –	12.0	9.0
Thyroid	68	85	4 -	- 4.5	- 9.5	4.4	9.0	458	534	76	16.6	14.2	1.8	9.0
Hodgkin's lymphoma	88	87	1-	- 1.1	- 3.3	1.6	9.0	82	93	8	9.4	4.1	4.8	0.5
Non Hodgkin's lymphoma	692	757	92	9.4	- 4.0	12.7	0.7	530	533	3	9.0	- 11.4	11.5	0.5
Myeloma	210	210	0	0.0	-20.3	19.7	9.0	230	276	46	20.0	4.0	15.4	9.0
Leukaemia	487	806	22	4.5	- 11.5	15.3	0.7	411	452	41	10.0	- 3.1	12.5	9.0
Total except non- melanoma skin	20,611	21,743	1132	5.5	- 13.3	18.1	0.7	15,437	17,268	1831	11.9	- 1.1	12.4	9.0

Lung includes trachea, CNS central nervous system, Myeloma includes multiple myeloma and immunoproliferative disease

*In the number of incident cases between 2025 and 2015

⁵In incident cases between 2015 and 2025

Percentage change attributable to changes in the risk of developing cancer between 2015 and 2025

Percentage change attributable to changes in population structure (age distribution) between 2015 and 2025 (note: these changes are related to ageing of the population)

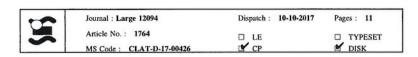
Percentage change attributable to changes in population size between 2015 and 2025



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Table

Cancer	Men										Women									
type	2015					2025					2015					2025				
	35-64 ^a (N)	> 64 ^b	Total ^c (N)	8	ASMR	35-64 ^a (N)	> 64 ^b	Total ^c (N)	8	ASMR	35-64 ^a (N)	> 64 ^b	Total ^c (N)	R	ASMR	35-64 ^a (N)	> 64 ^b	Total ^c (N)	8	ASMR
Oral cavity and pharynx	Ξ	165	77.2	7.6	4.1	27	194	270	7.4	3.1	26	69	96	2.6	1.0	24	11	101	2.7	6.0
Oesophagus	91	154	245	6.7	3.5	49	991	230	6.3	2.6	7	36	43	1.1	0.4	7	42	49	1.3	0.4
Stomach	125	367	493	13.6	6.3	93	380	475	13.0	4.9	89	249	318	8.5	2.9	71	263	335	6.8	2.8
Colorectal	310	1179	1492	41.1	17.9	310	1247	1559	42.7	15.4	183	826	1012	56.9	8.7	158	870	1031	27.3	9.7
Gallbladder and biliary tract	6	49	73	2.0	8.0	7	61	89	1.9	9.0	13	87	100	2.7	8.0	4	08	94	2.5	0.7
Liver	177	395	574	15.8	7.7	218	440	662	18.1	8.0	35	255	290	7.7	2.3	38	250	288	7.6	2.1
Pancreas	152	382	535	14.7	7.1	161	491	653	17.9	7.0	9/	362	438	11.6	4.0	75	408	483	12.8	3.7
Larynx	51	115	166	4.6	2.3	27	133	160	4.4	1.6	4	7	=	0.3	0.1	S	10	15	0.4	0.1
Lung	191	1978	2748	75.7	37.3	505	2196	2705	74.1	28.3	296	425	722	19.2	9.1	330	843	1174	31.0	12.0
Bone	7	13	25	0.7	0.5	00	15	28	8.0	0.5	3	=	61	0.5	0.3	3	12	17	0.4	0.2
Skin melanoma	30	99	26	2.7	1.3	29	68	611	3.3	1.3	18	37	55	1.5	9.0	12	44	26	1.5	0.5
Breast	2	8	10	0.3	0.1	1	10	Ξ	0.3	0.1	346	199	1013	26.9	11.3	321	999	066	26.2	9.6
Prostate	42	765	807	22.2	7.6	34	098	894	24.5	6.5	1	Ţ	1	1	1	ï	1	1	Ţ	1
Testis	0	0	0	0.0	0.0	2	0	5	0.1	0.0	ı	į.	ı	ı	1	į.	1	ĵ	1	L
Cervix uteri	ı	1	ı	1	1	1	1	1	1	1	46	47	26	5.6	1.3	43	54	86	5.6	1.2
Corpus uteri	Ţ	1	1	1	1	1	1	1	1	1	28	137	165	4.4	1.6	31	185	216	5.7	1.7
Ovary	ı	ı	ı	I	1	1	ī	1	ı	1	83	182	566	7.1	3.0	89	176	245	6.5	2.4
Kidney	82	276	329	6.6	4.4	87	367	458	12.5	4.6	25	127	153	4.1	1.3	24	145	170	4.5	1.3
Bladder	9/	513	589	16.2	6.4	28	504	295	15.4	8.4	12	121	133	3.5	6.0	10	127	137	3.6	8.0
Brain and other CNS	100	149	260	7.2	4.1	94	174	279	7.6	3.7	09	136	204	5.4	2.6	28	141	211	5.6	2.5
MDS and MPS	12	139	151	4.2	1.4	41	154	168	4.6	1.3	4	132	136	3.6	0.7	9	137	143	3.8	0.7
Thyroid	9	14	20	9.0	0.3	∞	91	24	0.7	0.3	5	56	31	8.0	0.3	4	27	31	8.0	0.2
Hodgkin's Lymphoma	∞	10	19	0.5	0.3	6	10	19	0.5	0.3	2	15	22	9.0	0.3	9	16	24	9.0	0.3
Non Hodgkin's Lymphoma	19	164	230	6.3	3.0	26	181	241	9.9	2.6	35	179	216	5.7	1.9	32	175	209	5.5	1.6
Myeloma	27	134	161	4.4	1.9	22	143	165	4.5	1.5	12	129	141	3.7	1.0	80	107	115	3.0	0.7
Leukaemia	20	258	318	8.8	3.9	38	268	311	8.5	2.9	36	210	254	8.9	2.3	32	215	254	6.7	2.0





Cancer type	Men										Women									
	2015					2025					2015					2025				
io,	35-64° (N)	> 64 ^b Total ^c CR ASMR (N) (N)	Total ^c (N)	CR	ASMR	35-64 ^a (N)	> 64 ^b	Total ^c (N)	CR	ASMR	35-64 ^a (N)	> 64 ^b	Total° (N)	S	CR ASMR	35–64 ^a (N)	> 64 ^b	Total ^c (N)	CR	ASMR
Total except non- melanoma skin	2442	9777	10,272	283.0 129.9	129.9	2038	8601	169'01	292.7	108.2	1552	5017	9199	175.9	64.9	1492	5619	7156	189.3	61.2

Fable 4 continued

Lung includes trachea, CNS central nervous system, MDS and MPS myelodysplastic and myeloproliferative syndromes, Myeloma includes multiple myeloma and immunoproliferative disease,

mortality rate (World Standard Population) per 100,000 person-years

CR crude rate per 100,000 person-years, ASMR age-standardised

Diagnosed in people aged over 64 years

ages considered

Diagnosed in people aged 35-64 years

lung cancer (N = 1253) will surpass corpus uteri cancer (N = 840). Our predictions showed that in men, more than 40% of the new cases of prostate, colorectal, lung, bladder, pancreas and stomach cancer will be diagnosed in people aged over 74 years. In women, this age group will account for more than 40% of new cases of colorectal cancer and leukaemia, and more than 50% of new cases of pancreatic and bladder cancer. The change in the burden of these cancers by age group from 1995 to 2025 is depicted in Figure S3 (Supplementary Material). Here, we can see a rising number of new cancer cases among people aged over 64 years, with a large proportion of cases diagnosed in those aged over 74 years. Overall, we predict that between 35 and 40% of new cases diagnosed in 2025 will affect people over 74 years (men: 8681 of 21,743; women: 6330 of 17,268; see Figure S3 d and h).

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Comparing cancer incidence between 2015 and 2025: changes in demography and risk in the 35-64 and > 64 age groups

Table 3 shows the percentage difference in the number of cases from 2015 to 2025 due to changes in the risk of developing cancer and changes in population structure (ageing) and size. In men, the 5.5% increase is chiefly attributable to changes in population structure (18.1%) and size (0.7%) since risk of developing cancer is expected to decrease by 13.3%. We observed this pattern for all cancer types except melanoma and testicular cancer, for which an increase in risk is expected (11.1 and 26.1%, respectively). In women, we find a similar pattern, with the decline in gynaecological and breast cancer mainly due to the decrease in risk. In contrast, our results predict a rise in the risk of thyroid (14.2%), kidney (22.2%) and lung cancers (46.6%), with respective net increases in incidence of 16.6, 37.1 and 62.7%, respectively. As with men, population demographics contribute the most (ageing: 12.4%; size: 0.6%) between 2015 and 2025, although to a markedly lesser extent than among men due to the more modest reduction in risk.

Figure 2 depicts the changes in the number of incident cases from 2015 to 2025 by sex and by age group (35–64 and > 64 years). The supplementary material file presents tables with the corresponding percentage differences in these age groupings (Tables S3–S6). The increase in number of cases in the 35–64 age group is relatively small; the tumour types with the largest increases were prostate cancer in men (49 cases) and breast cancer in women (123 cases) in women. It follows that the overall rise in the number of cases over the 10-year study period is primarily due to the considerable increased number of cases among people aged over 64 years. The increase in population size of this age group (light blue bar) is the main driver of

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-	Journal : Large 12094	Dispatch: 10-10-2017	Pages: 11
	Article No.: 1764	□ LE	□ TYPESET
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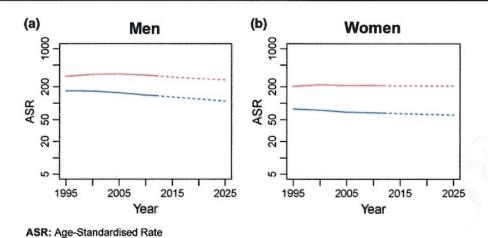


Fig. 1 Observed and projected rates of cancer incidence (red) and mortality (blue) in Catalonia from 1995 to 2025 accounting for all cancer types except non-melanoma skin cancer. ASR age-standardised rate

change. Note that changes in population size in a subgroup of older population shows that ageing is a major contributing factor to the burden of the total population. The types of cancer expected to increase by more than 40 cases between 2015 and 2025 are: in men (Fig. 2a, b), colorectal, prostate, bladder, pancreas, lung, non-Hodgkin's lymphoma, melanoma and kidney; in women (Fig. 2c, d), lung (74% of cases attributable to changes in risk) followed by colorectal, breast, kidney, corpus uteri, pancreas, bladder and thyroid. For these cancer types, the increase is proportional to the change in population size whereas changes in risk may drive the expected increase for kidney and thyroid. To assess these results, a principal components analysis (See Supplementary material) making use of the count variables estimated using these differences has shown that changes in population structure, and, therefore ageing, are the main contributors to the increase in the burden of cancer in Catalonia by 2025 (See supplementary material for details).

Burden of cancer mortality

ASMRs are expected to decrease in men (2015: 129.9 per 10^5 person-years (py), 2025: 108.2 per 10^5 py) and level off in women (2015: 64.9 per 10^5 py, 2025: 61.2 per 10^5 py) (Table 4; Fig. 1). However, according to our predictions, the number of deaths will increase in men (2015: N = 10,272, 2025: N = 10,691) and in women (2015: N = 6616; 2025: N = 7156) mainly due to the rise in the number of deaths among people aged over 64.

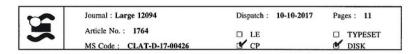
In this age group, the types of cancer for which the greatest increase in number of deaths is expected are lung [Difference (D) = 218 deaths, 11%], pancreas (D = 109 deaths, 28.5%), prostate (D = 95 deaths, 12.4%), kidney

(D=91 deaths, 33%), colorectal (D=68 deaths, 5.8%) and liver (D=45, 11.4%) in men, and lung (D=418; 98.4%), corpus uteri (D=48; 35%), pancreas (D=46, 12.7%) and colorectal (D=44, 5.3%) in women. Our results show a stabilisation followed by a decrease in breast cancer mortality. By 2025, lung cancer is expected to be the leading cause of cancer mortality among women in Catalonia (N=1174), followed by colorectal cancer (N=1031) and breast cancer (N=990).

Discussion

According to the results of our study, from 2015 to 2025, cancer incidence rates in Catalonia will decrease in men and level off in women, mainly due to decreasing incidence rates in the younger population. On the other hand, we predicted a slight increase in the absolute number of new cases between 2015 and 2025, due for the most part to population ageing. Our predictions show that in 2025, 35–40% of new cancer cases will be diagnosed in patients over 74 years of age.

As life expectancy increases, the number of new cancer cases is expected to do the same [2]. However, projections need to focus not only on demographic changes [12], but also on the time lags between changes in risk factors and their effect on the burden of cancer [6] (e.g., smoking prevalence and lung cancer [13]). Our study predicts a significant rise in lung cancer incidence and mortality rates in women in Catalonia, reaching levels similar to those described in the female population of other European countries [14]. Despite this result, the recent stabilisation of the most common cancer types in men (prostate) and



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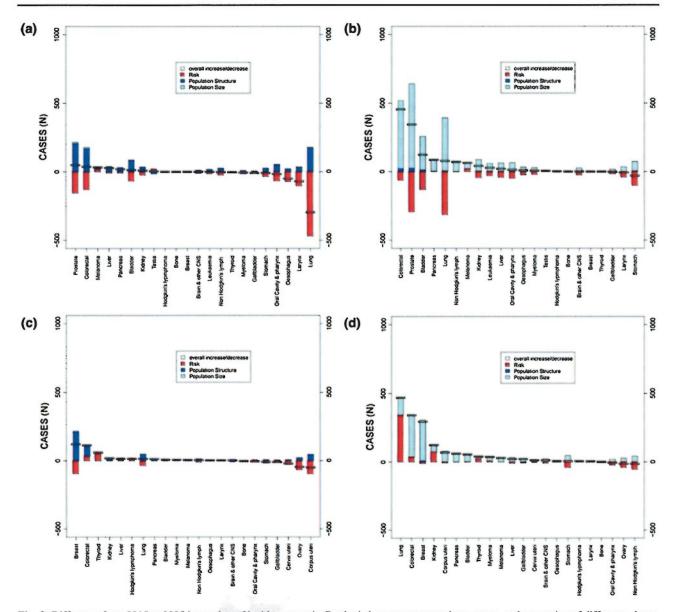


Fig. 2 Difference from 2015 to 2025 in number of incident cases in Catalonia by cancer type and age group, and proportion of difference due to changes in risk, population structure and population size. Men: a 35-64 years, $b \ge 65$ years; Women: c 35-64 years, $d \ge 65$ years

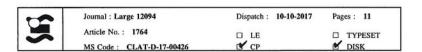
women (breast) is the trend with the greatest effect on predicted burden of cancer incidence by 2025.

There are some limitations in the interpretation of our results. The most important limitation is related to the estimation of cancer incidence in Catalonia during the base period. Since cancer incidence data for the whole region are not available, we assumed that the aggregated cancer incidence rates from Girona and Tarragona could be used as an estimate. This assumption may lead to an underestimate of the cancer burden (total number of cases/deaths) for the whole region although it may affect less the time trend effect [10]. Second, the method we used is based on projecting the most recent trends into the future through

future population estimates. Changes in the most recent trends as well as in future population counts and age distribution can affect predictions to a considerable degree [1]. Third, we note that the burden of cancer in Catalonia presented here is smaller than that predicted using with the same data in a previous study [4], since the base period was different and the future population counts were 10% higher than currently estimated.

Prostate cancer has been the most widely diagnosed cancer in Spanish men since the mid 1990 s [15] due to the

Cancer sites selected 313





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introduction and widespread use of the prostate-specific antigen (PSA) test [3]. Figure S3.1 shows a stable trend in new diagnoses in Catalonia since 2010, while Figure S1 shows a stabilisation followed by a decrease in ASIR. However, we also predicted an increase in the number of cases observed in men aged over 64 years, with 40.7% of new cases expected to be diagnosed in men aged over 74 years by 2025. A similar pattern was previously observed in other countries [16]. Nevertheless, we detected a marked decrease in prostate cancer mortality, possibly as a result of improved treatment and screening [16].

By 2025, colorectal cancer will continue to be the second most common cancer type in both sexes. The predicted increase in crude rates in Catalonia from 2015 to 2025 is mainly due to the ageing of the population (more than 40% of new cases will be diagnosed in people aged over 74 years: 42.4% in men; 49.2% in women). Alcohol and tobacco consumption have been associated with colorectal cancer risk, with studies showing that 70% of new colorectal cancers could be avoided through a healthy lifestyle [17]. The development of screening programmes has also been important for colorectal cancer control. The faecal occult blood test in particular has been shown to reduce cancer incidence and cause-specific mortality by up to 10% through the detection of adenomatous polyps [18]. In 2018, a specific screening programme covering the whole population aged 50-69 years is expected to be fully implemented in Catalonia, and our incidence and mortality predictions may need to be modified depending on the results.

Since 2001, breast cancer incidence in Spain has stabilised [3, 15], with a downturn attributed to routine screening among women aged 45–64 [19]. The slight increase in the number of incident cases from 2015 to 2025 in Catalonia chiefly affects women aged 65 and older. Our mortality predictions show a decrease in the number of breast cancer deaths among women under 65 years, mainly as a result of access to mammography screening and more effective breast cancer management and treatment [6]. As Table 4 shows, lung cancer could soon surpass breast cancer as the most lethal cancer among women in Catalonia.

Lung cancer and other tobacco-related cancers

By 2025, lung cancer will be the third most common cancer in Catalonia and the most lethal cancer in both sexes. The increased burden in women is primarily due to changes in the risk of developing this cancer (46.6%), although the highest increase between 2015 and 2025 is expected to affect women aged 65 years and older $(N_{2015} = 414; N_{2025} = 884; Table 1)$. The most important risk factor for lung cancer is smoking [20], so the increased

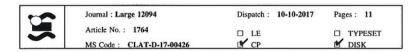
prevalence of smoking among Catalan women can explain the rising lung cancer incidence and mortality rates in this population since the late 1990s. This trend stands in contrast to that observed among men in Spain [3, 21, 22], who have increasingly given up the habit since the mid 1980s [21]. It would, therefore, be reasonable to expect a continued rise in lung cancer burden in women [6, 15, 21, 22]. According to our predictions, the male-female ratio of lung cancer incidence and mortality will decrease from fourfold to threefold between 2015 and 2025. This narrowing of the gender gap may also extend to other tobacco-related cancers such as oral cavity, pharyngeal and laryngeal cancer [15]. These types of cancer share common risk factors, such as tobacco and alcohol consumption [20, 23] and, to a lesser extent, human papillomavirus (HPV) infection [24, 25], which is more specifically associated with cancer of the tonsils, base of the tongue and other parts of the oropharynx [24].

A further two types of tobacco-related cancer are urinary bladder (population attributable fraction 50%) [26] and pancreatic cancer ($\sim 30\%$) [27]. Our predictions show that in women, more than 55% of new cases in these cancers will be diagnosed in people aged over 74 years.

Other cancer types

Other cancers diagnosed to a large extent in people older than 74 years are stomach cancer (44.2% in men) and leukaemia (44% in women). We also predicted a non-significant difference in the number of cases of corpus uteri, ovary and cervix uteri cancer in women between 2015 and 2025. However, with the parallel introduction of the HPV vaccine and opportunistic screening for HPV in Spain, cervical cancer incidence and mortality are expected to decrease in the coming years [15]. The incidence of non-Hodgkin's lymphoma has also stabilised and is expected to decrease, possibly due to the decreased incidence of AIDS-related lymphomas among young adults and the efficacy of available treatment in recent years [28].

In Catalonia, skin melanoma incidence may rise slightly among men and level off among women, resulting in similar incidences in both sexes, as observed in other Spanish regions [15]. Our results also show an expected rise in the number of cases of kidney cancer (37.1%) and thyroid cancer (14.2%) in women between 2015 and 2025. Evidence suggests that the increase in kidney cancer may be due to variations in risk factors as well as increased use of imaging techniques, resulting in better detection of small tumours [29], while the stable prevalence of established risk factors for thyroid cancer in the last few decades suggests that rising incidence is associated with improved detection and diagnosis, and largely or totally reflects



417 overdiagnosis of small papillary carcinomas [30]. This 418 could also be the situation in Catalonia.

419 Conclusion

- 420 The increase in the number of new cancer cases from 2015 to 2025 will affect the elderly in particular. These findings 421 422 can inform planning and resource allocation for future 423 services, having implications for enhancing and expanding 424 existing geriatricians and oncologists' collaboration [8]. In 425 addition, targeting risk factors such as obesity, physical
- 426 inactivity and tobacco use may help to reduce cancer risk 427 in younger populations.
- 428 Acknowledgements This work was supported by the Agència 429 d'Avaluació d'Universitats i Recerca (2014SGR0635), and partially 430 supported by Instituto de Salud Carlos III through the Project PI14/ 431 01041, co-funded by European Regional Development fund/European
- 432 Social fund: "investing in your future".

433 Compliance with ethical standards

- 434 Conflict of interest The funders had no role in the design of the 435 study, the collection, analysis, or interpretation of the data, the writing 436 of the manuscript, or the decision to submit the manuscript for pub-437 lication. The authors state that there are no conflicts of interest con-438
- 439 Research involving human participants and/or animals This 440 article does not contain any studies with human participants or ani-441 mals performed by any of the authors.

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