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Survival of cancer patients in France: A population-based study from The Association of the French Cancer Registries (FRANCIM)

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ABSTRACT

We present the main results of the first population-based cancers survival study gathering all French registry data. Survival data on 205,562 cancer cases diagnosed between 01/01/1989 and 31/12/1997 were analysed. Relative survival was estimated using an excess rate model. The evolution of the excess mortality rate over the follow-up period was graphed. The analysis emphasised the effect of age at diagnosis and its variation with time after diagnosis. For breast and prostate cancers, the age-standardised five-year relative survivals were 84% and 77%, respectively. The corresponding results in men and women were 56% *versus* 58% for colorectal cancer and 12% *versus* 16% for lung cancer. For some cancer sites, the excess mortality rate decreased to low values by five years after diagnosis. For most cancer sites, age at diagnosis was a negative prognostic factor but this effect was often limited to the first year after diagnosis.

1. Introduction

In France, population-based cancer registration is carried out on a Departmental level, a *Département* or Department being the territorial and administrative division of the country. This registration provides information on cancer incidence regarding approximately 13% of the French population. In 2000, the Association of the French Cancer Registries (FRANCIM) and the Biostatistics Unit of Lyon University Hospital joined 20 different registries to create a common database that counts nearly 520,000 patients diagnosed between 1975 and 2002. This centralised approach has facilitated the emergence of several collaborative projects.

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One of the epidemiological goals of FRANCIM is to provide estimates of incidence, survival and prevalence of cancer in France. The first objective was achieved in 2003 with the publication of national incidence estimates.[1] A second objective, reported here, was to obtain survival estimates to assess globally the performance of the health care system. Population-based survival data for cancer have been already published for France and for several European countries (for example, see references [2–8]) separately or within the collaborative European project EUROCARE.[9–11] EUROCARE provides regularly net survival estimates; *i.e.* survival of cancer patients after elimination of all other causes of death than cancer. The project uses a database on more than 6.5 million cancer patients and a complete methodology for analysis of survival data including data collection, standardisation, quality control and statistical analysis. As mentioned above, population-based survival data have been published for several French Departments and these have been partially included in EUROCARE. However, no clear picture of the survival data for France using all French available data of the FRANCIM network has been given yet.

The aim of the present study was to produce estimates of crude and relative survivals at 1, 3 and 5 years with their corresponding age-standardised relative survivals, for 47 cancer sites, by sex, different age classes and different periods of diagnosis. It focused also on the analysis of the proper effects of gender, age at diagnosis, and year of diagnosis on survival. The study emphasised the effect of age at diagnosis and its variation with time after diagnosis. The evolution of the excess mortality rate over the follow-up period could be graphed. This analysis used a single and consistent approach based on an excess rate model[12] and optimised the advantages of the modelling strategy in each of these objectives.[13]

2. Material

All neoplasms registered between 01/01/1989 and 31/12/1997 by the French registries were included in the present survival analysis (Table 1). The quality and the completeness of the participant registries are assessed every four years via an audit by the *Institut de Veille Sanitaire* (InVS) and the *Institut National de la Santé et de la Recherche Médicale* (INSERM). Some quality controls were made at registry level and others at the common database level. For this purpose, the tools provided by the International Agency for Research on Cancer were used. All cancers diagnosed in patients over 15 were included in the analysis. Forty-seven cancer sites were defined according to the codes of the International Classification of Diseases-Oncology 2 (ICD-O 2); they mainly corresponded to the ICD-9-defined EUROCARE sites (Table 2).

An active search for the vital status of all 205,562 cases at 01/01/2002 was carried out using a standardised administrative procedure. The information was collected 'at first line' via birthplace public services or via an electronic request to the *Répertoire National d'Identification des Personnes Physiques (RNIPP)*. Both procedures required the knowledge of the birthplace. As this could not be obtained for some cases, other sources of information for vital status were used (medical records or public services of the place of residence). Nevertheless, priority was given to the first line standardised strategy. The general principle was to minimise the number of lost to follow-up patients (alive at some date before 01/01/2002) without compromising the quality of the information or introducing bias. At last, the proportion of lost to follow-up patients was 4% (Table 1).

Table 1 – Description of the data provided by the French Registries

Department	Number of cases	Lost to follow-up[a] (%)	Median follow-up in alive patients (months)
Calvados[b]	21,632	2.1	87.2
Côte d'Or[c]	5822	1.6	84.9
Doubs	15,900	1.0	89.9
Hérault	10,381	6.4	61.7
Isère	34,131	5.8	82.3
Manche	8115	0.5	69.3
Bas-Rhin	36,908	2.0	87.3
Haut-Rhin	25,613	6.8	81.9
Somme	18,240	4.7	86.6
Tarn	13,828	3.0	86.7
Loire Atlantique[d]	8,219	7.8	78.0
Saône et Loire[e]	6,301	4.3	81.9
Ardennes[f]	151	8.0	97.9
Marne[f]	321	5.6	94.5
Total	205,562	4.0	81.0

The diagnosis period was [1989–1997] for all Departments but for Hérault [1995–1997] and Manche [1994–1997].
a Alive and lost before the end of December 2001.
b Two registries for digestive tract cancers and all cancers.
c Two registries for haematological and digestive tract cancers.
d One registry for breast and colorectal cancers.
e One registry for digestive tract cancers.
f One registry for thyroid cancers.

3. Method

Relative survival was estimated using an excess rate model.[12] For each subject, the observed mortality rate λ at time t is considered to have two components: one due to cancer – hereafter referred to as λ_c, the excess mortality rate – and another due to other causes – referred to as λ_{exp}, the expected mortality rate. The latter component can be viewed as the mortality rate if the subject had no cancer. It was obtained from published vital statistics provided by the *Institut National de la Statistique et des Etudes Economiques (INSEE)*. The time t is the duration of follow-up defined as the time elapsed from the date of diagnosis to the date of death or to the date of last observation. The excess mortality rate λ_c was modelled as a smoothed parametric function of time chosen among several candidate functions according to the Akaike Information Criterion (AIC).[14] Data until 10 years follow-up were used in order to take into account all available information. Relative survival probabilities at different times were calculated by exponentiation of the corresponding cumulative rates. This model-based approach enabled to deal with sparse data met in some subgroups and to describe the evolution of the excess mortality rate λ_c along

Table 2 – International classification of diseases-oncology 2, number of cases and deaths, and five-year relative survival [95% confidence intervals] for each cancer site

Cancer site	ICD-O 2 code[a]	Cases/deaths	Five-year relative survival	
			Non-standardised	Age-standardised
Lip	C00	460/125	95 [90–97]	NA
Tongue	C01–C02	1947/1322	35 [33–37]	35 [33–38]
Oral cavity	C03–C06	2579/1606	41 [39–42]	39 [37–41]
Salivary glands	C07–C08	377/179	61 [56–67]	NA
Oropharynx	C09–C10	2815/1940	33 [32–35]	33 [31–35]
Nasopharynx	C11	235/132	47 [41–53]	NA
Hypopharynx	C12–C13	2726/2030	27 [26–29]	26 [24–28]
Head and neck	C01–C06/C09–C13	10302/7030	34 [33–35]	34 [32–35]
Oesophagus	C15	5303/4689	12 [11–12]	10 [9–11]
Stomach	C16	7718/6007	25 [24–26]	25 [24–26]
Small intestine	C17	665/409	44 [40–49]	41 [37–45]
Colon	C18	21806/11647	56 [55–57]	56 [56–57]
Rectum	C19/C20/C21	13821/7360	56 [55–57]	55 [54–56]
Colon and rectum	C18–C21	35627/19007	56 [56–57]	56 [55–57]
Liver	C22	4513/4155	8 [7–8]	7 [7–8]
Biliary tract	C23–C24	2041/1740	16 [14–17]	15 [14–17]
Pancreas	C25	4517/4201	6 [5–6]	6 [5–6]
Nasal cavities	C30–C31	460/268	47 [42–52]	NA
Larynx	C32	3216/1641	55 [53–56]	54 [52–56]
Lung	C33–C34	19507/16817	14 [13–14]	13 [12–13]
Pleural mesothelioma	C384	422/390	7 [5–10]	7 [5–10]
Bone	C40–C41	394/172	60 [55–65]	54 [49–60]
Skin melanoma	C44	4271/972	87 [86–88]	84 [83–86]
Soft tissues	C47 and C49	905/406	60 [56–63]	60 [56–63]
Breast	C50	30923/7033	85 [84–85]	84 [83–84]
Vagina and vulva	C51–C52	648/378	52 [47–56]	49 [45–54]
Cervix uteri	C53	2932/1013	70 [69–72]	70 [68–71]
Corpus uteri	C54	4236/1424	76 [74–77]	74 [72–75]
Ovary	⩾'C569' and ⩽'C574'	3570/2213	40 [39–42]	40 [38–41]
Prostate	C61	19448/8059	80 [79–80]	77 [76–78]
Penis	C60	222/97	67 [58–74]	68 [60–78]
Testis	C62	1321/90	95 [93–96]	95 [93–96]
Kidney	C64	4810/2171	63 [62–65]	62 [60–63]
Bladder	C67	7288/3958	58 [56–59]	56 [55–58]
Choroidal melanoma	C692–C694/C696/C698/C699	282/87	78 [73–82]	NA
Brain	C71	2381/1885	20 [18–21]	18 [17–20]
Thyroid gland	C739	2694/346	94 [92–95]	88 [84–92]
Non-Hodgkin's lymphomas	(⩾'95903' and ⩽'95953') or (⩾'96703' and ⩽'97233')	6375/3383	55 [53–56]	53 [51–54]
Hodgkin's lymphomas	⩾'96503' and ⩽'96673'	1175/225	88 [86–90]	83 [81–85]
Multiple myeloma	⩾'97313' and ⩽'97323'	2273/1462	42 [40–45]	40 [38–42]
Acute lymphocytic leukaemia	'98213' or '98263' or '98273'	341/251	26 [22–31]	26 [21–31]
Chronic lymphocytic leukaemia	'98233'	2077/739	81 [78–83]	77 [75–80]
Acute myeloid leukaemia	'98613' or '98403' or '98663' or '98673' or '98913' or '99103'	1333/1089	19 [17–21]	18 [16–20]
Chronic myeloid leukaemia	'98633'	666/380	49 [45–53]	44 [40–48]
Leukaemia	⩾'98003' and ⩽'99413'	5042/2856	51 [49–52]	49 [48–51]

a Topography codes for solid tumours and morphology codes for haematological neoplasms. In all neoplasm codes, the final '3' is for 'malignant'. For solid tumours, all morphology codes are included but haematological codes. For ovary, {'84423', '84513', '84613', '84623', '84723', '84733'} are excluded. For pleural mesothelioma, only 90503–90533 are included. For skin melanoma, only 87203–87803 are included. For choroidal melanoma, only 87203–87803 are included. NA, not available.

time. Crude survival was estimated using the same approach with λ_{exp} fixed to zero. Age-standardised relative survival was calculated using the same age structure as that of the EUROCARE 3 cancer patient population (http://www.eurocare.it) to allow direct comparisons of our results with those of this reference work.

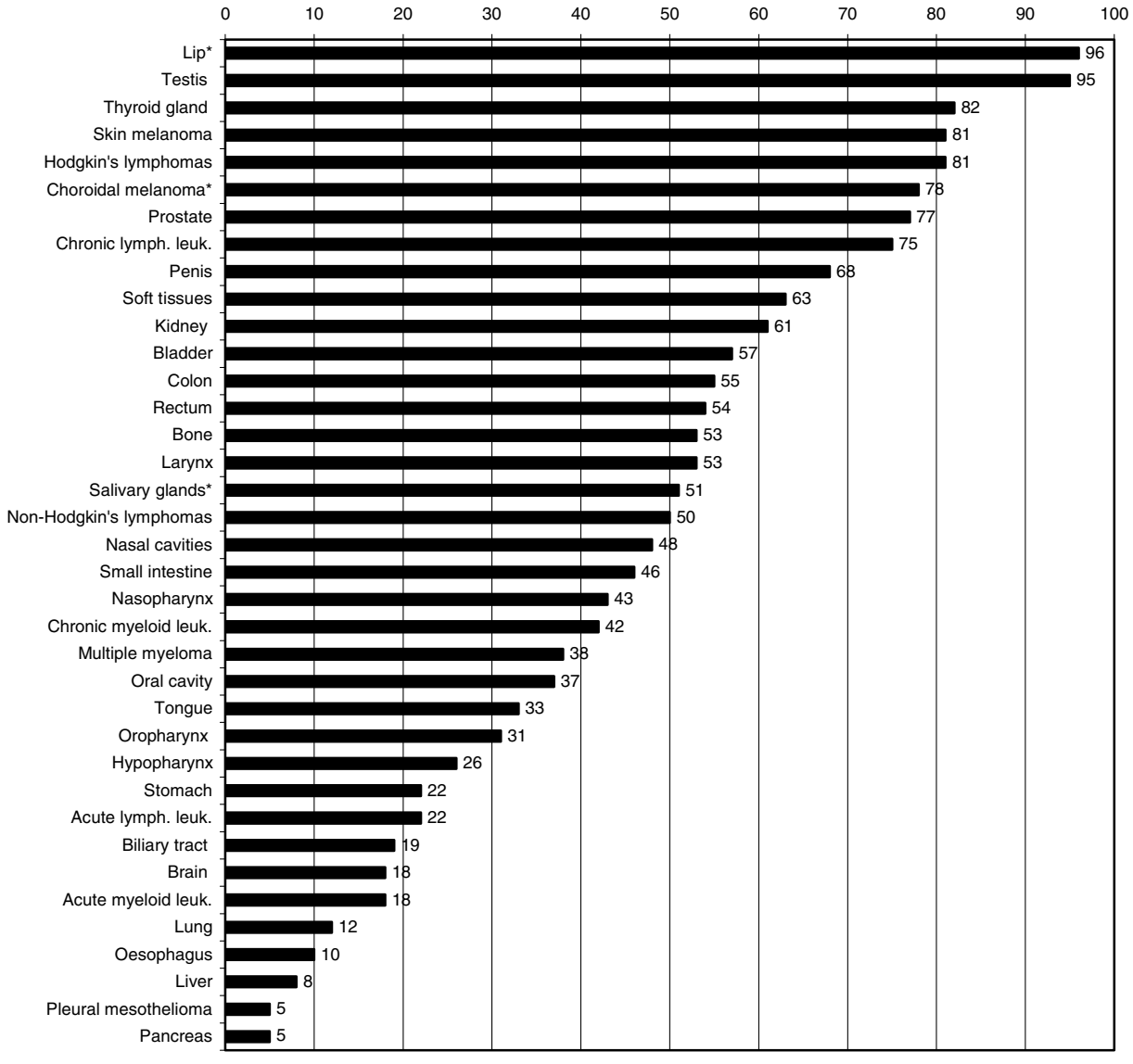
The proper effects of sex, year of diagnosis and age at diagnosis were estimated by including simultaneously these covariates – with Department – in the same model. Cubic regression splines, with a knot at mean age, were used to estimate the effect of age while the effect of year of diagnosis was considered linear. The reference categories for relative rates

were 'men' for sex, and 'subjects of mean age' for age at diagnosis. The statistical significance of the covariate effects was calculated using a Wald test for 'sex' and 'year of diagnosis' and the likelihood ratio test (LRT) for 'age'. In this multivariate analysis, we only used the information provided by the first five years to avoid the noise due to frequent non-proportional effects beyond five years follow-up. The non-proportional effect of age was explored by introducing an interaction term into the model.[13]

To estimate the model parameters, we used the framework of the generalised linear models (GLM): as noted by Dickman, when λ_c is a step function, the likelihood of the corresponding model may be considered as deriving from a GLM (Poisson model) with a specific outcome and an adequate link function so that standard algorithms for GLM can be used.[13,15] In our model, we have adapted Dickman's approach to let λ_c be a continuous function; with this adaptation, the estimators stemming from the GLM approach become nearly identical to the maximum likelihood estimators. Actually, continuous functions produce clinically convincing patterns of excess mortality rate and reduce considerably the number of parameters. The functions were written using S-Plus software package (version 6). The whole procedure has been detailed elsewhere.[13]

4. Results

The definition of each site according to the ICD-O 2, the corresponding number of cases and deaths, and the five-year relative survival estimates are reported in Table 2. Age-standardised five-year relative survivals in men and women are given in Fig. 1. Crude and relative survivals at 1 and 5 years are presented by sex for a selection of cancer sites in Table 3. For some sites, the evolution of the excess mortality rate over the period of follow-up is reported in Fig. 2. When it is numerically low (<0.1), the excess mortality rate is very close to the annual probability of death from the disease. The relative rates



* Non-standardized (too few cases and/or events to yield reliable estimates)

Fig. 1a – Age-standardised five-year relative survival (%) in men.

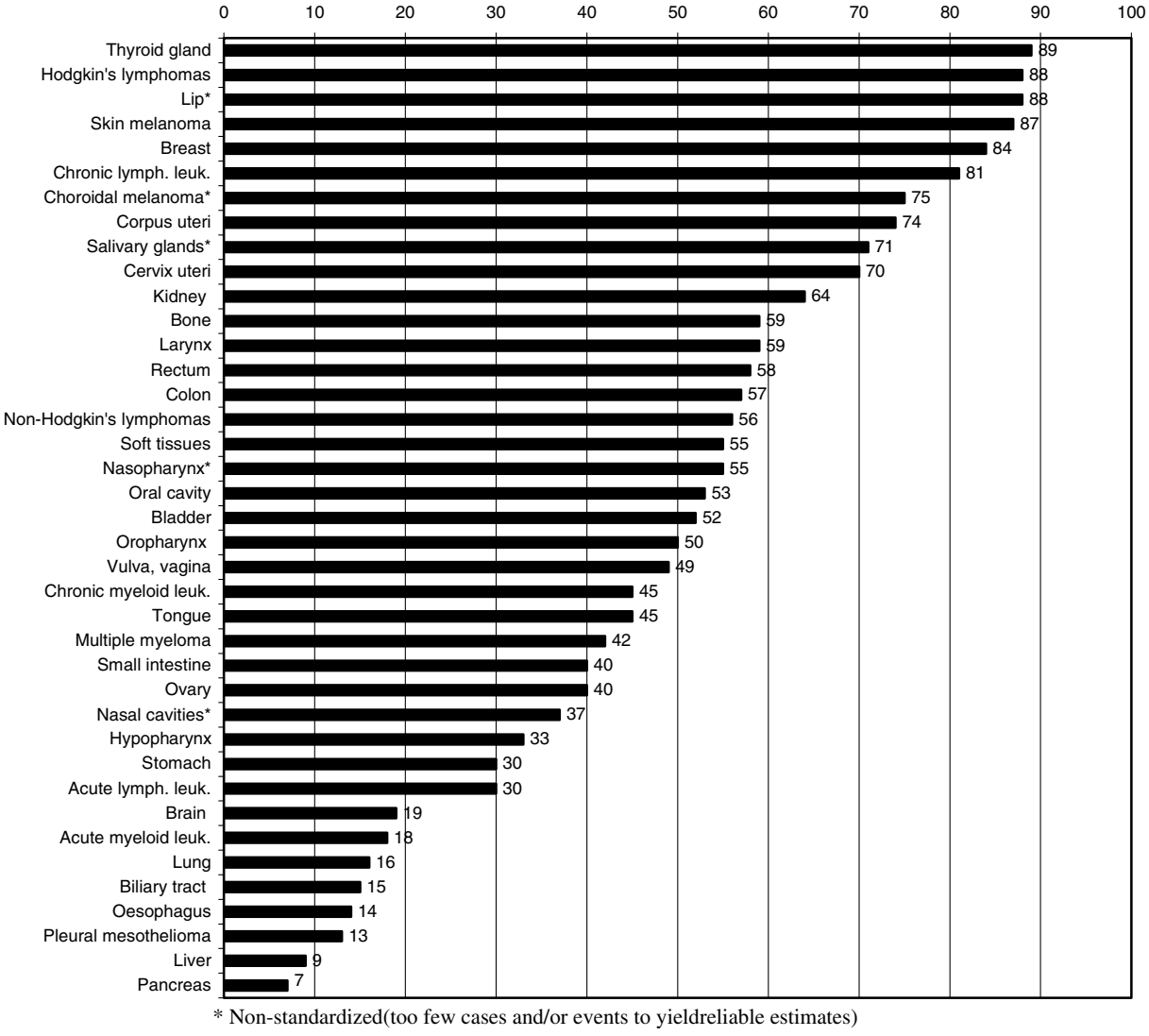


Fig. 1b – Age-standardised five-year relative survival (%) in women.

associated with sex and period of diagnosis – and their statistical significance – are reported in Table 4. The relative rate for age and its potential change with time since diagnosis is shown for selected cancer sites in Fig. 3. Some comments concerning selected cancers are given below.

4.1. *Breast*

The age-standardised five-year relative survival for the most frequent cancer among women was 84% (Table 2 and Fig. 1). Globally, the excess mortality rate never exceeded 5%, even during the first years after diagnosis. However, in contrast with that of many other cancer sites, this excess mortality rate did not show a trend towards the null value (Fig. 2). There was a significant improvement due to the year of diagnosis with a 4% decrease in mortality per year (Table 4). This has to be interpreted considering earlier stages at tumour diagnosis due to mammographic screening that became widely prevalent in France since the nineties. The mean effect of age on the relative rate was not linear; very young women were at higher risk than middle-aged ones. Nevertheless, that effect varied with the time elapsed since diagnosis. During the first year after diagnosis, older women were at higher risk of mortality in comparison with both very young and middle-aged women. The effect of age was almost inversed 5 years after diagnosis with a higher relative rate in younger women in comparison with both middle-aged and old women (Fig. 3). The excess mortality rate pattern as well as the time-dependent effect of age should be explored considering other prognostic factors.

4.2. *Uterus and ovaries*

Age-standardised five-year relative survival estimates for corpus uteri, cervix uteri and ovarian cancers were 74%, 70% and 40%, respectively (Table 2 and Fig. 1). The excess mortality rate for corpus and cervix uteri decreased progressively from about 10% to nearly 2% at five years. Ovarian cancer showed a very different pattern with a much higher excess mortality rate during the first year after diagnosis and a regular decrease thereafter (Fig. 2). For all these sites,

Table 3 – Crude and relative survivals [95% confidence intervals] at 1 and 5 years in women and men

	Crude and relative survival (%)							
	Women				Men			
	One year		Five year		One year		Five year	
	Crude	Relative	Crude	Relative	Crude	Relative	Crude	Relative
Head and neck	73 [70–75]	76 [73–78]	43 [40–46]	48 [45–51]	69 [68–70]	70 [70–71]	29 [28–30]	32 [31–33]
Oesophagus	38 [34–41]	39 [36–43]	12 [9–14]	14 [12–18]	41 [40–43]	43 [42–44]	10 [9–10]	11 [10–12]
Stomach	46 [44–48]	49 [47–51]	22 [20–23]	28 [26–30]	45 [43–46]	47 [46–49]	18 [17–19]	23 [22–24]
Colon and rectum	75 [74–75]	79 [78–79]	46 [46–47]	57 [56–58]	74 [74–75]	79 [78–79]	43 [42–44]	55 [54–56]
Liver	30 [27–33]	31 [28–35]	8 [6–10]	9 [7–12]	31 [29–32]	32 [30–33]	6 [5–7]	7 [6–8]
Lung	45 [43–47]	46 [45–48]	16 [15–17]	18 [16–19]	41 [40–41]	42 [42–43]	11 [11–12]	13 [13–14]
Skin melanoma	95 [94–96]	97 [96–98]	80 [78–81]	89 [88–91]	92 [91–93]	95 [94–96]	71 [69–73]	83 [81–85]
Breast	95 [94–95]	97 [97–97]	76 [76–77]	85 [84–85]	–	–	–	–
Cervix uteri	87 [86–88]	89 [88–90]	64 [62–66]	70 [69–72]	–	–	–	–
Corpus uteri	87 [86–88]	90 [89–91]	65 [64–67]	76 [74–77]	–	–	–	–
Ovary	72 [70–73]	74 [72–75]	37 [35–38]	40 [39–42]	–	–	–	–
Prostate	–	–	–	–	88 [88–88]	94 [94–95]	57 [56–58]	80 [79–80]
Bladder	67 [64–69]	72 [70–74]	38 [36–41]	50 [47–53]	77 [76–78]	82 [80–83]	46 [44–47]	60 [58–61]
Kidney	77 [75–79]	80 [78–81]	56 [54–58]	64 [61–66]	77 [75–78]	80 [78–81]	52 [50–54]	63 [60–65]
Thyroid gland	93 [92–94]	96 [95–97]	89 [87–90]	95 [94–96]	88 [85–90]	91 [88–93]	78 [75–82]	88 [85–91]
Non-Hodgkin's lymphomas	71 [69–72]	74 [72–75]	47 [45–49]	56 [54–58]	70 [69–72]	74 [72–75]	44 [43–46]	54 [52–55]
Hodgkin's lymphomas	94 [91–95]	97 [96–98]	85 [82–88]	92 [90–94]	90 [87–92]	93 [91–95]	77 [74–80]	85 [81–87]
Multiple myeloma	76 [73–78]	79 [77–81]	35 [32–38]	43 [40–46]	75 [73–78]	80 [77–82]	33 [30–36]	42 [39–45]
Acute lymphocytic leukaemia	56 [49–63]	58 [50–65]	27 [20–34]	29 [22–36]	57 [50–62]	57 [51–63]	22 [17–28]	24 [18–30]
Chronic lymphocytic leukaemia	89 [87–91]	94 [92–95]	67 [64–70]	85 [81–87]	89 [87–90]	94 [92–95]	60 [57–63]	77 [74–80]
Acute myeloid leukaemia	40 [36–43]	41 [37–44]	18 [15–21]	19 [16–22]	40 [37–44]	42 [38–45]	16 [13–19]	18 [16–22]
Chronic myeloid leukaemia	84 [82–86]	87 [84–89]	42 [37–47]	49 [43–54]	77 [73–81]	81 [77–85]	40 [35–45]	48 [43–54]

more advanced ages at diagnosis were associated with poorer survivals. For ovarian and cervix uteri cancers, the youngest women had a very favourable excess risk pattern in comparison with the oldest ones (shown for ovary). The effect of age at diagnosis varied with time and was more pronounced at the beginning of the follow-up in the case of ovarian cancer (Fig. 3). For corpus uteri cancer, a slight but not statistically significant survival improvement with more recent years of diagnosis could be observed (Table 4).

4.3. *Kidney and bladder*

In our study, only renal parenchyma cancers were considered as kidney cancers. This excluded better prognosis cancers that develop from the transitional epithelium (*e.g.* pelvis and urethra). The age-standardised five-year relative survival was 61% in men and 64% in women (Fig. 1). The pattern of excess mortality rate showed a rather high excess risk during the first year (Fig. 2). The multivariate analysis confirmed that prognosis was significantly better in women than in men. A slight but significant improvement of prognosis with more recent years of diagnosis was observed; 2% decrease in mortality per year (Table 4). Advanced age at diagnosis was associated with a worse prognosis, essentially at the very beginning of follow-up (Fig. 3). The excess mortality rate in the rare patients under 45 appeared particularly low (not shown).

Age-standardised five-year relative survival for bladder cancer was 57% in men and 52% in women; this difference was statistically significant (Fig. 1 and Table 4). In comparison with kidney cancer, the pattern of excess mortality rate showed a lower excess risk during the first year (Fig. 2). No significant improvement with the advance of the year of diagnosis could be shown when a common trend for men and women was tested (Table 4). However, it should be mentioned that survival trends for men and women were different (not shown).

4.4. *Prostate*

Age-standardised five-year relative survival for prostate cancer was 77% (Table 2 and Fig. 1). An important improvement of prognosis with the year of diagnosis was observed; 7% decrease in mortality per year (Table 4). This should be interpreted taking into account the increasingly efficient diagnostic tools and the wide use in France of individual screening with Prostate Specific Antigen; both influence the distribution of cancer stage over time. At 5 years, the excess mortality rate remained at a non-null value (Fig. 2), but this pattern should be explored allowing for stage. The prognostic impact of age at diagnosis was not linear; a slightly higher excess risk was observed in young *versus* middle-aged patients. Old patients were however at a much higher risk than young ones, especially during the first year after diagnosis (Fig. 3).

4.5. *Testis*

Our data confirmed the excellent prognosis of testis cancer. The age-standardised five-year relative survival was 95% (Table 2 and Fig. 1) suggesting a null excess risk for the most favourable cases. No period of diagnosis effect was found. The great majority of patients were young adults. The excess mortality rate was weak and occurred mainly during the first year after diagnosis (Fig. 2).

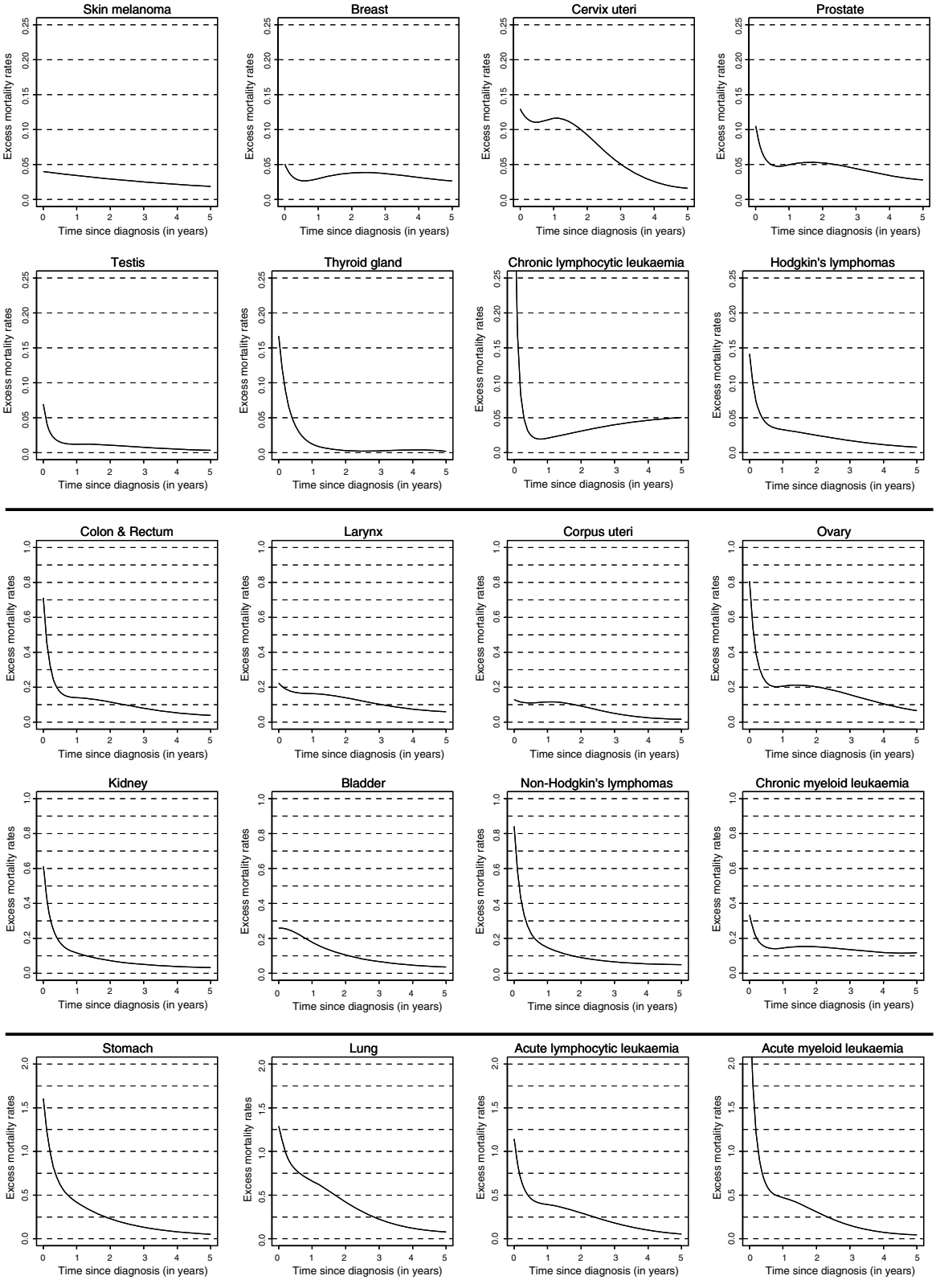


Fig. 2 – Evolution of the excess mortality rate with time elapsed since diagnosis for 20 cancer sites. The extents of the *X* scales for the mortality rates are different.

4.6. *Digestive tract*

Age-standardised five-year relative survivals for colon and rectum cancers were 55% and 54% in men, 57% and 58% in women (Fig. 1), respectively. The estimates that corresponded to the other digestive sites in men and women were, respectively, 46% and 40% for small bowel cancer, 22% and 30% for gastric cancer, 19% and 15% for biliary tract cancer, 10% and 14% for

Table 4 – Relative rates [95% confidence intervals] associated with sex and year of diagnosis

Cancer site	Sex RR[a] [95% CI]	Year of diagnosis RR[b] [95% CI]
Head and neck	0.65 [0.60–0.72]**	0.99 [0.98–1.00]
Oesophagus	0.91 [0.82–1.00]	0.98 [0.97–0.99]**
Stomach	0.82 [0.78–0.88]**	1.00 [0.99–1.00]
Colon and rectum	0.90 [0.87–0.93]**	0.99 [0.98–0.99]**
Liver	0.99 [0.91–1.08]	0.96 [0.95–0.98]**
Lung	0.87 [0.83–0.91]**	1.00 [0.99–1.01]
Skin melanoma	0.60 [0.50–0.73]**	0.97 [0.93–1.00]
Breast	–	0.96 [0.95–0.97]**
Cervix uteri	–	1.01 [0.98–1.04]
Corpus uteri	–	0.98 [0.95–1.01]
Ovary	–	0.99 [0.98–1.01]
Prostate	–	0.93 [0.91–0.95]**
Bladder	1.22 [1.10–1.34]**	1.01 [0.99–1.03]
Kidney	0.90 [0.81–1.00]*	0.98 [0.96–1.00]*
Thyroid gland	0.60 [0.45–0.82]**	0.92 [0.87–0.97]*
Non-Hodgkin's lymphomas	0.83 [0.77–0.90]**	0.98 [0.97–1.00]*
Hodgkin's lymphomas	0.70 [0.51–0.98]*	1.04 [0.97–1.11]
Multiple myeloma	0.88 [0.78–1.00]*	1.00 [0.97–1.02]
Acute lymphocytic leukaemia	0.75 [0.57–0.99]*	0.98 [0.93–1.03]
Chronic lymphocytic leukaemia	0.69 [0.53–0.89]*	1.02 [0.97–1.07]
Acute myeloid leukaemia	0.96 [0.84–1.08]	0.98 [0.96–1.01]
Chronic myeloid leukaemia	0.86 [0.68–1.10]	1.01 [0.96–1.06]

a Relative rate – women *versus* men.
b Relative rate – yearly increase or decrease relative to 1989.
* *p*-Value <0.05.
** *p*-Value <0.001.

oesophageal cancer, 8% and 9% for liver cancer, and 5% and 7% for pancreatic cancer. For colorectal cancer, the excess mortality rate was mainly seen over the first months after diagnosis; it regularly decreased afterwards (Fig. 2). The initial levels of the excess mortality rate as well as its evolution over the follow-up period were very different according to the cancer site and, globally, the prognosis of colorectal cancer appeared more favourable than that of other digestive tract cancers.

Survival was longer in women *versus* men for colorectal (Fig. 1 and Table 4), gastric, pancreatic and oesophageal cancers, whereas it was longer in men *versus* women for biliary tract cancer (Fig. 1). Our results showed an improvement of survival in recently diagnosed colorectal, liver and oesophageal cancers (Table 4). For colorectal cancer, the effect of age was far from linearity and was essentially observed in patients over 70 (Fig. 3). A similar pattern was observed for oesophageal cancer. For all sites but small bowel and liver, the effect of age at diagnosis was essentially observed at the beginning of the follow-up period. This is illustrated in Fig. 3 for colorectal cancer.

4.7. *Malignant melanoma of the skin*

Age-standardised five-year relative survival was 81% in men and 87% in women (Fig. 1). The multivariate analysis showed that the difference between men and women was statistically significant with a relative rate of 0.60. A slight improvement, close to significance ($p = 0.07$), was shown with the year of diagnosis (Table 4). The worst prognoses were observed in the oldest patients and this effect of age was constant over the follow-up period. Combining all these considerations, an excellent prognosis was observed in young women (>90% survival).

4.8. *Lung*

Our data confirmed the well-known bad prognosis of lung cancer, with age-standardised five-year relative survival of 12% in men and 16% in women (Fig. 1). A high level of excess risk was observed, even at the end of the follow-up period. It is partially due to an important comorbidity linked to smoking and exposure to other toxic agents (Fig. 2). The difference between men and women was statistically significant in the multivariate analysis (Table 4). No improvement with the year of diagnosis could be demonstrated (Table 4). However, young age was a factor of better prognosis (Fig. 3), especially in women: the five-year relative survivals in people aged 15–44 and more than 75 were 31% and 10% in women *versus* 17% and 9% in men, respectively. Further analyses that explore survival differences between small-cell and non-small-cell lung cancer should be conducted.

4.9. *Pleural mesothelioma*

Age-standardised five-year relative survival was 5% in men and 13% in women (Fig. 1). No period of diagnosis effect could be found over the study period.

4.10. *Lip, tongue, oral cavity, pharynx and larynx*

These cancers, occurring mainly in men, have very different prognoses (Table 2 and Fig. 1). Lip cancer had an excellent well-known prognosis: a (non-standardised) five-year relative survival of 95%. At the opposite, oropharynx and hypopharynx cancers had poor survivals: age-standardised five-year estimates being 33% and 26%, respectively (Table 2). For larynx cancer, the age-standardised five-year relative survival was 54%. Prognosis appeared generally much better in women than in men (except lip).

4.11. *Thyroid gland*

Age-standardised five-year relative survival was 82% in men and 89% in women (Fig. 1). This difference in survival between sexes was significant and the associated relative rate was 0.6 in the multivariate analysis (Table 4). An 8% annual decrease of the excess mortality rate with the year of diagnosis was shown (Table 4) and non-standardised five-year survival for the more recent period (1995–1997) reached 96%. Young age was a very strong protective factor. We observed that the excess mortality was wholly supported by old patients, whereas it was near zero in young ones (not shown).

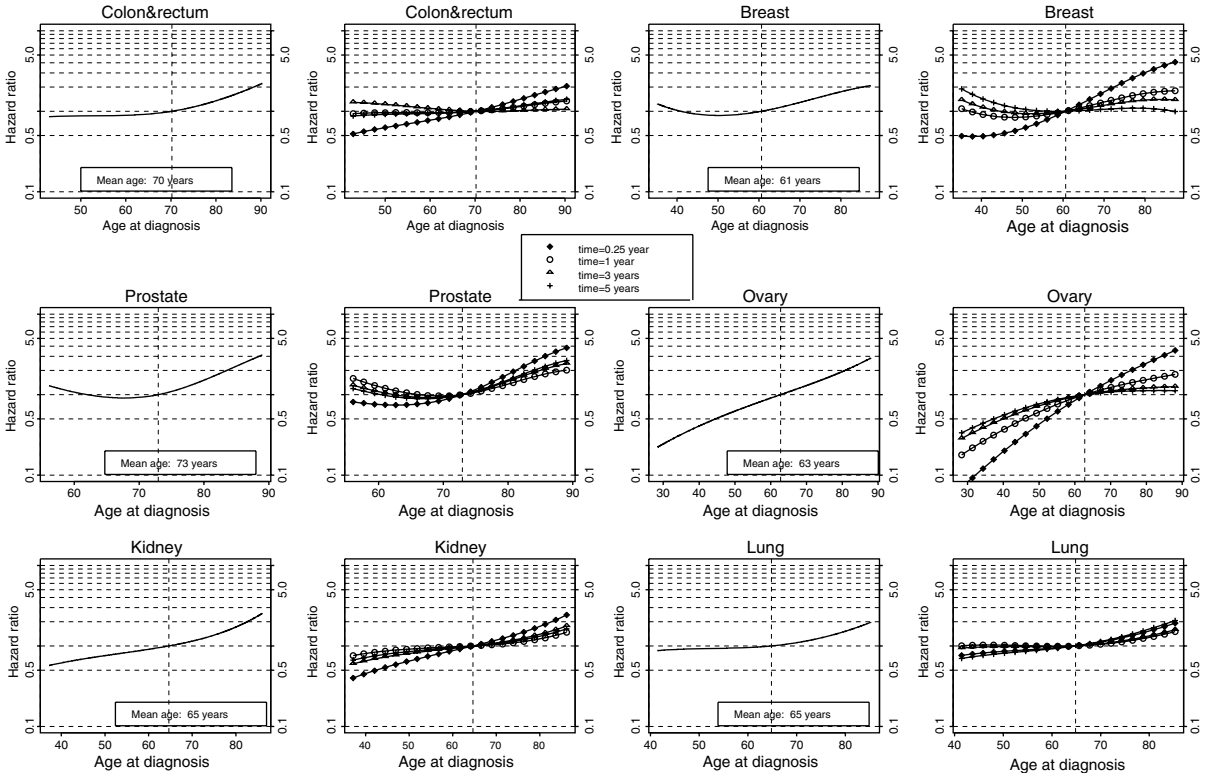


Fig. 3 – Effect of age at diagnosis for 6 cancer sites. Two diagrams for each cancer site. Left diagrams: relative rates according to age at diagnosis (adjusted for sex, Department and year of diagnosis). Right diagrams: relative rates at 3 months, 1, 3 and 5 years follow-up (non-adjusted).

4.12. *Haematology*

4.12.1. *Hodgkin's lymphomas*

Age-standardised five-year relative survival for Hodgkin's lymphomas was 81% in men and 88% in women (Fig. 1). The difference between sexes was significant (Table 4). The excess mortality rate was under 5% by 6 months after diagnosis and dropped to a very low value by 5 years (Fig. 2). The effect of age at diagnosis was important and constant over the entire follow-up period with an excellent prognosis in patients aged 15–44. The combined effects of age and sex resulted in a five-year relative survival of 98% in young women and 92% in young men (aged 15–45). No favourable period of diagnosis effect could be detected over the study period (Table 4).

4.12.2. *Non-Hodgkin's lymphomas*

Age-standardised five-year relative survival for non-Hodgkin's lymphomas was 50% in men and 56% in women (Fig. 1 and Table 4). The excess mortality rate decreased to values under 5% only by 5 years after diagnosis. The effect of age was significant but less important than the one observed for Hodgkin's lymphomas in very young patients. In contrast with Hodgkin's lymphomas, a modest period of diagnosis effect could be shown (Table 4).

4.12.3. *Multiple myeloma*

The age-standardised five-year survival for multiple myeloma was 38% in men and 42% in women. No period of diagnosis effect could be shown.

4.12.4. *Leukaemia*

Acute lymphocytic leukaemia occurs mainly in children and young adults. The analysis was carried out on subjects aged over 15. The age-standardised five-year survival was 22% in men and 30% in women (Fig. 1). It is important to mention here that, for this type of leukaemia, 17% of the patients were aged 15–20. The excess mortality rate was very high during the first year (especially in old patients, not shown) but it decreased slowly and regularly thereafter (Fig. 2).

For acute myeloid leukaemia, age-standardised five-year relative survival was 18% in men as in women (mean age 63 years). The excess mortality rate was dramatically high during the first months after diagnosis (Fig. 2).

For chronic lymphocytic leukaemia, the five-year relative survival reached 75% in men and 81% in women (Fig. 1). The excess mortality rate decreased during the first year after diagnosis, but it increased regularly afterwards (Fig. 2).

For chronic myeloid leukaemia, the age-standardised five-year survival was 42% in men and 45% in women, but this difference was not significant. The excess mortality rate did not decrease with time after diagnosis (Fig. 2). For all leukaemia cases studied here, no statistically significant linear trend for better survival along the entire period of diagnosis could be shown (Table 4). Nevertheless, improvements in the more recent periods were observed for acute leukaemia (not shown).

5. Discussion

This article reports the main results of the first French population-based cancer survival study, gathering all the available data in the French cancer registries. The highest age-standardised five-year relative survival estimates reached 95% for testis cancer that accounted for 1% of all cancers though it remains the most frequent cancer in young men. High survival estimates, greater than 80%, were found for breast cancer – the first incident cancer in France – thyroid cancer, skin melanoma – both among the top ten cancers in women – and Hodgkin's lymphomas. Several sites had a good prognosis (five-year relative survival estimates between 60% and 79%) such as prostate cancer – the second incident cancer in France – corpus uteri and cervix uteri cancers in women, kidney cancer, choroidal melanoma and chronic lymphocytic leukaemia. Cancers with a moderate prognosis (40–59% five-year relative survival) included colorectal cancer (58%) – second and third incident cancer in women and men, respectively – bladder cancer, ovarian cancer, larynx and nasopharynx cancers and chronic myeloid leukaemia. The poor survival category (20–39% five-year relative survival) included the other otorhinolaryngologic cancers in men, and acute lymphocytic leukaemia. As expected, the prognosis at 5 years of lung cancer – the second incident cancer in men – was found in the very poor survival category (five-year relative survival under 20%). A dramatic increase in its incidence among French women – three times more cases in 2000 than in 1980[1] – should reinforce the current preventive strategies and therapeutic researches because this cancer is, theoretically, the most preventable one while it remains among the most difficult to treat. The lowest survival was observed for acute myeloid leukaemia, pleural mesothelioma, oesophagus, biliary tract, liver and pancreas cancers. Ongoing analyses will soon provide information about the prognostic impact of the histological type that is routinely collected in general cancer registries.

The stage at diagnosis, an important prognostic factor, could not be considered in this study because this information is routinely available only in some specialised registries and in some general registries for specific studies on a sample of cases. 'High-resolution' studies that explore specifically the impact of clinical prognostic factors – such as the stage at diagnosis, the grade, or the therapeutic management – have been already planned using the methodology of the present study on well-documented samples of cases.

The statistical analysis allowed a deep exploration of the impact of age at diagnosis considering it as a continuous covariate instead of a categorical one and optimizing then all the available information. Age was found to be a strong prognostic factor in the majority of the herein analysed cancer sites. Its effect presented increasing patterns, linear or non-linear. However, this effect varied according to the period of follow-up and, in many cancer sites, it affected essentially early follow-up. The particular pattern observed for breast cancer and its variation over time are consistent with previous results from European or North-American population-based data[5,16,17] The adverse effect of age beyond menopause may reveal interactions between histological and biological characteristics of the tumour and some hormone-related processes; this needs further exploration taking into account the stage at diagnosis.

It is well known that, all cancers combined, survival is better in women than in men. Differences in cancer site distributions are one explanation. However, considering cancer sites separately, this study showed a better prognosis in women for most cancer sites. As in EUROCARE 3, an important survival advantage at 5 years was found in head and neck cancers, thyroid cancer and skin melanoma. Our analysis detected also a modest but significant difference regarding lung cancer. That difference has been already reported in some population-based studies[18] but not in EUROCARE 3. Differences between sexes as to the distribution of histological types with various prognoses should be considered.[19] A histology-specific effect in women has been also suggested.[20] The relative survival estimation method takes already into account differences in background mortality; thus, disparities between sexes in terms of excess mortality rate may be generally attributed to different biological phenomena, health behaviours, and probably earlier detection in women. It should be mentioned here that relative survival methods lead to include as 'deaths due to the disease' some deaths caused by the risk factors of the cancer under study. This observation is especially relevant for cancers associated with tobacco and alcohol consumption. These exposures are responsible for deaths from other causes over the follow-up period, not directly due to cancer, but due to the risk-factors-associated morbidity. The large difference in relative survivals between sexes for head and neck cancers might be explained by a less frequently associated morbidity in women. For thyroid cancer, the distribution of the histological subtypes, associated with different prognoses, differs according to age, sex and period of diagnosis.[21]

Unfortunately, the most recently diagnosed tumours were not always those of better prognosis. This could be due to the shortness of the study period. However, in the cancer of cervix uteri, the absence of improvement in survival with the period of diagnosis has been already documented.[22] Its interpretation was that large screenings remove from analysis the most favourable stages that account no more for cancers. An important 'period' effect was demonstrated in breast cancer as well as in prostate, thyroid gland and liver cancers. The widespread use of screening tests (mass or individual screenings) in most of these cancers may lead to overoptimistic conclusions about the related therapeutic advances. Indeed, it is recognised that length bias, lead-time bias, and over-diagnosis have to be taken into account here. The shift in the spectrum of stages at diagnosis towards more favourable patterns has to be considered when discussing potential advances in therapeutic management of cancer or cancer-related diseases. Thus, improvement in survival has to be analysed considering incidence and mortality data. For thyroid cancer, the period effect may also be explained by a shift in the spectrum of histological types towards more favourable patterns, as suggested above. A slight improvement in survival from colon cancer was observed over the study period. However, large advances in management and survival of colon cancer have been observed before the nineties[4] and a more steady situation may have been reached.

To update the vital status, we have used a standardised procedure using administrative data at first attempt. When this attempt failed, other methods were used if deemed reliable by the registry researchers. Some patients born abroad may have been wrongly censored at 01/01/2002 whereas they would be in fact already lost to follow-up or dead. Indeed, the RNIPP was able to insure a good information quality regarding patients born in France but not a good one regarding patients born abroad. This may hypothetically bias our estimations and overestimate survival. However, these patients accounted for only 9% of the censored patients.

The statistical method we adopted was based on a modelling approach. It differed from the method used in EUROCARE [23] but was similar to that of the English study by Coleman and colleagues.[7] Relative survival estimates were not calculated from the ratio of observed survival/expected survival[24] but were obtained through an excess mortality rate model,[12,13] with a parametric continuous function for the excess rate.[13] This modelling approach allowed for a multivariate analysis and resulted in the estimation of relative rates associated with some covariates of interest. It could be argued that comparisons with EUROCARE 3 results are somewhat hazardous because the statistical methods to estimate survival in each age stratum are different. However, this difference is expected to affect long-term survival but not five-year relative survival. Our results with this French dataset are globally more favourable than those of the European average five-year survival estimates given by EUROCARE 3 but they are close to those observed in comparable Western European countries considered in EUROCARE 3 (except for bladder cancer because of different invasiveness criteria). Our results are also close (less than 3% difference regarding the main cancer sites) to the 'French' results in EUROCARE 3 despite the fact that the latter were based on only 5% of the French population. However, the present study provides more accurate estimates and consistent additional information on the proper impact of each prognostic factor. The EUROCARE project covered a larger period of diagnosis than ours (1983–1994 *versus* 1989–1997) and we failed to detect improvements of prognosis over time for some cancers. For example, survival from malignant melanoma of the skin, Hodgkin's lymphomas, and testis cancer was already high at the beginning of our study period and no period of diagnosis effect could be observed. We used the age structure of the EUROCARE 3 population: however, Corazziari and colleagues[25] have proposed three standard cancer populations characterizing three incidence patterns in both broad and five-year age classes. These standard populations are simple to use in comparison with the site-specific standards we used in our study and may be adopted in future analyses.

Our results were obtained with data collected from 14 French registries that cover only 13% of the French population. Thus, there is no reason to consider that survival data obtained from these registries are representative of the entire French population. Nevertheless, our study presents the first and the clearest picture of survival of cancer patients in France. Besides, this study offers many perspectives in terms of public health. Indeed, for the first time in France, survival data of all cancer registries were centralised to form a single database that can be updated anytime through a standardised procedure. The burden of cancer as well as its evolution over time can be estimated now. Relative survival at 5 years is an important indicator usually reported in such population-based studies. However, the statistical analysis performed in the present study provided some interesting additional and original information, such as the evolution of the excess mortality rate with time since diagnosis. For some cancer sites, the excess mortality rates decreased to low values by 5 years, sometimes well before. For other sites, the excess mortality rates decreased regularly but then flattened at non-null values. This should be explored on the long term and/or considering prognostic covariates such as stage at diagnosis or therapeutic management. This kind of information is important because some patients are often erroneously stigmatised or penalised, on a socio-professional level, long after cancer diagnosis. The use of cure rate models[26] to estimate the proportion of cured patients and the excess mortality rate in the others may also yield interesting information on long-term outcome.

Cancer-related excess mortality rates can now be estimated using the whole available French population-based data. The methodological and statistical procedures for their regular update are operational. High-resolution studies to explore the impact of additional prognostic factors may be planned as well as studies to evaluate clinical practices. An interesting tool for epidemiologic surveillance, health system performance evaluation, preventive and therapeutic research is now available in France.

Conflict of interest statement

None.

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