

**Socioeconomic environment and disparities in cancer survival for 19 solid tumor sites.
An analysis of the French Network of Cancer Registries (FRANCIM) data.**

Short title: Socioeconomic environment and cancer survival

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French Network of Cancer Registries (FRANCIM)*

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Abbreviations:

ASNS: Age-Standardized Net Survival

CCTIRS: Comité Consultatif sur le Traitement de l'Information en matière de Recherche dans le domaine de la Santé

CER: Comité d'Évaluation des Registres

CI: Confidence Interval

CNIL: Commission Nationale de l'Informatique et des Libertés

CNS: Central Nervous System

DG: Deprivation Gap

EDI: European Deprivation Index

EU-SILC: European Union Statistics on Income and Living Conditions

FRANCIM: French network of cancer registries

IARC: International Agency for Research on Cancer

ICD-O-3: 3rd edition of the International Classification of Diseases for Oncology

ICSS: International Cancer Survival Standards

INSEE: Institut National de la Statistique et des Etudes Economiques

IRIS: Ilots Regroupés pour l'Information Statistique

Q1-Q5: quintile 1-quintile 5 of the national distribution of the European Deprivation Index

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What's new:

Social inequalities in cancer survival are significant worldwide. However, no previous study has investigated the influence of social environment on cancer survival for various cancers in the French Network of Cancer Registries. Our findings show, for the first time in France, that cancer survival was lower for patients living in the most deprived areas compared to those living in the least deprived ones, for almost all solid tumors, with variable magnitudes across the cancer sites.

Abstract:

Social inequalities are concerning along the cancer continuum. In France, social gradient in health is particularly marked but little is known about social gradient in cancer survival. We aimed to investigate the influence of socioeconomic environment on cancer survival, for all cancers reported in the French Network of Cancer Registries. We analyzed 189,657 solid tumors diagnosed between 2006 and 2009, recorded in 18 registries. The European Deprivation Index (EDI), an ecological index measuring relative poverty in small geographic areas, assessed social environment. The EDI was categorized into quintiles of the national distribution. One- and five-year age-standardized net survival (ASNS) were estimated for each solid tumor site and deprivation quintile, among men and among women. We found that 5-year ASNS was lower among patients living in the most deprived areas compared to those living in the least deprived ones for 14/16 cancers among men and 16/18 cancers among women. The extent of cancer survival disparities according to deprivation varied substantially across the cancer sites. The reduction in ASNS between the least and the most deprived quintile reached 34% for liver cancer among men and 59% for bile duct cancer among women. For pancreas, stomach and esophagus cancer (among men), and ovary and stomach cancer (among women), deprivation gaps were larger at 1-year than 5-year survival. In conclusion, survival was worse in the most deprived areas for almost all cancers. Our results from population-based cancer registries data highlight the need for implementing actions to reduce social inequalities in cancer survival in France.

Introduction

Social inequalities along the cancer continuum are of major concern, resulting in social disparities in cancer survival.¹⁻⁸ According to many studies, patients with a low socioeconomic status experienced a 30 to 50% lower cancer survival compared to those with a high socioeconomic status.¹⁻⁴

The mechanisms explaining disparities in cancer survival according to social deprivation are complex and not fully understood. Underlying hypotheses have been proposed by previous research and comprise a more advanced stage at diagnosis, worse access to healthcare services, less optimized choices of treatment, as well as higher prevalence of comorbid illnesses and more frequent unhealthy lifestyle among the more socially disadvantaged.^{1-5,7,9} Individual socioeconomic characteristics are known to be strong predictors of cancer survival as revealed in many studies worldwide.¹⁰⁻¹⁷ However, some of the potential explanations mentioned above as well as previous research^{14,18,19} suggest that not only individual but also contextual and environmental factors might contribute to social inequalities in cancer survival. Indeed, several population-based studies from different countries have shown that patients living in the most deprived areas experienced lower survival rates than those living in the most affluent ones, for most of the cancer sites.^{14,18,20-27}

Health indicators in France are among the best in the world, especially with regard to cancer.^{28,29} Although France has a universal health coverage system, it is not free of charge and do not impede health inequalities. As a matter of fact, social inequalities in cancer screening,^{30,31} incidence³² and mortality³³ are substantial and relatively high in France considering the European context.^{34,35} Thus, one can expect social inequalities in cancer survival to be important as well. Tackling socio-spatial inequalities in France is therefore one of the priorities of the 2014-2019 National Cancer Plan. However, although such data is essential to guide public health policies, little is known about social inequalities in cancer survival in France and specifically for each cancer site, since the few existing studies were restricted to a specific region, only one cancer site and/or small samples.³⁶⁻⁴⁰

The French Network of Cancer Registries are a resourceful tool to investigate cancer survival because they provide a large coverage of the French population, completeness of cases in the considered areas, and certified high quality data. Moreover, life tables are available in France in order to estimate *net survival* (that is the probability of surviving a specific cancer in the absence of other causes of death)⁴¹ based on cancer registries data and in the absence of cause of death information. To study social deprivation and cancer survival (or incidence) in the absence of individual socioeconomic information available in those registries and in order to account for the contextual part of social environment, an ecological index of social deprivation –the European Deprivation Index (EDI)⁴²– has been developed in France and assigned to each cancer case in the cancer registries.

Thus, the aim of the present study was to investigate, for the first time in France, the disparities in net survival according to the social environment (assessed by the EDI) for a wide range of solid tumor sites, and based on the French Network of Cancer Registries data.

Materials and Methods

Data - French Network of Cancer Registries (FRANCIM)

The study population comprised 189,657 primary invasive solid tumors diagnosed between 1 January 2006 and 31 December 2009, in patients over 15 years old, and recorded in 18 population-

based cancer registries (members of the French Network of Cancer Registries (FRANCIM)). Follow-up ended on 30 June 2013, i.e. patients alive at that date had their survival time censored.

The areas covered by the French Network of Cancer registries and by the registries included in this study are described on the map presented in supplementary figure 1. A brief description of the cancer registries included in the present study is provided in table 1. Each registry covered the entire corresponding French *Département*, except for the 'Lille area cancer registry', which encompassed only the city of Lille and its suburban area. The area covered by the registries included in the present study represented 20% of the French population and 20% of the French territory. Cancer diagnoses were available only from 1 January 2008 for the 'Gironde registry of Central nervous system (CNS) tumors' and the 'Lille area cancer registry' and from 1 January 2009 in the 'Haute-Vienne cancer registry'. Quality controls of the FRANCIM registries have been regularly completed by the *National Committee of Registries (CER)* at the national level, and the *International Agency for Research on Cancer (IARC)* at the international level. The study was approved by the *Consultative Committee for the Processing of Health Research Data (CCTIRS)* and the *French Data Protection Authority (CNIL)*.

Information available in the registries databases were date of birth, sex, date of cancer diagnosis, topographical and morphological codes of the 3rd edition of the *International Classification of Diseases for Oncology (ICD-O-3)*, vital status and date of last information (on vital status). The information on vital status was collected through an active standardized search procedure by the French Network of Cancer Registries, based on requests to the Repertoire National d'Identification des Personnes Physiques and, if necessary, other sources of information (medical records or birthplace public services).⁴³ Survival time was defined as the difference between the date of last information and the date of cancer diagnosis. Information on the day or month of the date of last information was missing in 54 cases (<0.1%) (table 1). Missing days were then replaced by 15 and missing months by July. The date of death was the same as the date of cancer diagnosis in 222 cases (0.1%). Those cases were included in the analyses with a survival time equals to 0.5 day. Lost to follow-up accounted for 2.1% overall. Cancer sites were classified according to the ICD-0-3. Only the 19 most common solid tumor sites were included in the study (table 2).

Social Deprivation

Social environment was assessed by the EDI, an ecological index measuring relative poverty in small geographic areas, based on information from the *European Union Statistics on Income and Living Conditions survey (EU-SILC)* and on census information.⁴² In France, the EDI has been developed at the 'Ilots Regroupés pour l'Information Statistique' (IRIS) level, the smallest geographic area for which data from the 2007 census were available. IRIS have been defined by the 'Institut National de la Statistique et des Etudes Economiques' (INSEE) and comprised approximately 2,000 inhabitants. In each IRIS, the continuous value of the EDI has been calculated and categorized into quintiles of the EDI national distribution – 'Quintile 1' (Q1) being the most affluent one and 'Quintile 5' (Q5) the most deprived one.

For each cancer diagnosed in FRANCIM registries, patient's address at the time of diagnosis, has been collected, geolocalized using *Geographic Information Systems (ArcGIS 10.2, ESRI, Redlands, California, USA)*, and assigned to an IRIS. Hence, a deprivation quintile has been attributed to each cancer case recorded in the registries.

Statistical analyses

Net survival was estimated using the consistent estimator proposed by Pohar-Perme⁴¹ for estimating cancer-specific survival in the absence of cause of death information (not available in FRANCIM registries). This method provides cancer-specific survival probabilities, which are not impacted by other causes of death, assuming patients could only die from their cancer. Net survival is based on the *excess mortality* hazard estimation for the studied cancer. This excess mortality is obtained by subtracting from the observed mortality in the registry for this cancer the *expected mortality*, as derived from general population life tables (produced by INSEE). These life table data contain mortality rates detailed by age, sex, year (1975 to 2017) and French *Département* of residence. Furthermore, net survival estimate relies on the assumption that the studied cancer represents a small part of the overall mortality.

Net survival probabilities were age-standardized according to the *International Cancer Survival Standards* (ICSS)⁴⁴ with age strata and weights depending on the cancer site. We computed 95% confidence intervals (95% CI) of age-standardized net survival (ASNS) probabilities using Greenwood's formula and the delta-method, assuming normality of the log of the cumulative excess hazard. When the standardization stratum included less than 10 cases, we merged adjacent age categories and assigned the sum of their respective weights to the combined age category to estimate ASNS. We could not compute standardized estimates for breast cancer survival among men because of the limited sample size (N=275). ASNS are survival probabilities (ranging from 0 to 1) but will be presented throughout the results section as percentages (ranging from 0 to 100).

For each tumor site, 1-year and 5-year ASNS were assessed overall and for each deprivation quintile (separately among men and women). Then, based on these results, we calculated the *deprivation gap* (DG), that is the difference in ASNS between the least (Q1) and the most (Q5) deprived quintiles ($DG = ASNS_{Q1} - ASNS_{Q5}$). The 95% CI of deprivation gap was derived using the variance of the ASNS of the least deprived quintile ($var(ASNS_{Q1})$) and the variance of the ASNS of the most deprived quintile ($var(ASNS_{Q5})$), previously obtained when calculating the 95% CI of the ASNS probabilities. Since $ASNS_{Q1}$ and $ASNS_{Q5}$ were independently estimated, we used the following formulas to estimate the variance of the DG: $Var(DG(t)) = Var(ASNS_{Q1}(t) - ASNS_{Q5}(t)) = Var(ASNS_{Q1}(t)) + Var(ASNS_{Q5}(t))$. Then, we derived the 95% CI of the DG, assuming the DG follows approximately a normal distribution. We considered that the difference in ASNS between the least and the most deprived quintile was statistically significant when the 95% confidence interval of the corresponding deprivation gap did not include zero. Furthermore, the percentage of variation of ASNS between the least (Q1) and the most (Q5) deprived quintiles was derived ($\Delta ASNS_{Q1 \rightarrow Q5} = (ASNS_{Q5} - ASNS_{Q1}) / ASNS_{Q1} * 100$).

Cases with missing values regarding the EDI (less than 1%) were excluded from the analyses (complete cases analyses).

Analyses were performed using R software (version 3.3.2) and the 'relSurv' (2.1-2) package for the estimation of net survival.

Results

A total of 109,071 cancer cases allocated over 16 solid tumor sites were analyzed among men, and 80,586 cancer cases allocated over 18 solid tumor sites were analyzed among women (table 2). For all solid tumor sites and for both sexes, 5-year ASNS were comparable to the latest reference data relative to cancer survival in France.⁴³

Distribution of patients into the five quintiles of deprivation was very variable across the cancer sites. In particular, patients living in the most deprived quintile (Q5) were overrepresented for

cervical cancer, lung cancer, head & neck cancers, bladder cancer, liver cancer (among women only), and to a lesser extent sarcoma, stomach cancer, bile duct cancer, esophagus cancer, corpus uteri cancer, CNS cancer and pancreas cancer (among women only). On the opposite, patients living in the most affluent quintile (Q1) were overrepresented for melanoma and CNS cancer (among men only).

Tables 3 and 4 provide 1- and 5-year ASNS in each deprivation quintile and the deprivation gaps (DG) for each cancer site, respectively among men and among women. One-year ASNS was lower among patients living in the most deprived quintile (Q5) than among patients living in the least deprived one (Q1) for all cancer sites except thyroid cancer among men, and except sarcoma and thyroid cancer among women. Among men, the deprivation gap regarding 1-year ASNS, was statistically significant for colon-rectum cancer ($ASNS_{Q1}= 85.6$, $ASNS_{Q5}= 82.7$, $DG= 2.9$ [1.0;4.8]), head and neck cancers ($ASNS_{Q1}= 75.7$, $ASNS_{Q5}= 68.9$, $DG= 6.8$ [3.1;10.5]), stomach cancer ($ASNS_{Q1}= 58.8$, $ASNS_{Q5}= 52.4$, $DG= 6.4$ [1.1;11.7]), bladder cancer ($ASNS_{Q1}= 81.7$, $ASNS_{Q5}= 76.9$, $DG= 4.8$ [0.8;8.7]), esophagus cancer ($ASNS_{Q1}= 51.1$, $ASNS_{Q5}= 43.5$, $DG= 7.5$ [1.9;13.2]), liver cancer ($ASNS_{Q1}= 49.0$, $ASNS_{Q5}= 42.2$, $DG= 6.8$ [2.1;11.4]) and pancreas cancer ($ASNS_{Q1}= 36.3$, $ASNS_{Q5}= 29.5$, $DG= 6.7$ [1.7;11.8]). Among women, the deprivation gap regarding 1-year ASNS, was statistically significant for colon-rectum cancer ($ASNS_{Q1}= 85.9$, $ASNS_{Q5}= 82.0$, $DG= 3.9$ [1.9;6.0]), corpus uteri cancer ($ASNS_{Q1}= 91.8$, $ASNS_{Q5}= 88.3$, $DG= 3.5$ [0.5;6.5]), breast cancer ($ASNS_{Q1}= 97.6$, $ASNS_{Q5}= 96.0$, $DG= 1.6$ [0.6;2.5]), bladder cancer ($ASNS_{Q1}= 77.4$, $ASNS_{Q5}= 67.9$, $DG= 9.5$ [1.3;17.8]), esophagus cancer ($ASNS_{Q1}= 56.4$, $ASNS_{Q5}= 40.8$, $DG= 15.7$ [3.3;28.1]) and pancreas cancer ($ASNS_{Q1}= 37.5$, $ASNS_{Q5}= 30.2$, $DG= 7.2$ [1.6;12.8]).

Five-year ASNS was lower in Q5 than in Q1 for all cancer sites except sarcoma and bile duct cancer among men and except sarcoma and CNS cancer among women (tables 3 and 4). Among men, the deprivation gap regarding 5-year ASNS was statistically significant for lung cancer ($ASNS_{Q1}= 17.2$, $ASNS_{Q5}= 14.3$, $DG= 2.9$ [0.7;5.0]), colon-rectum cancer ($ASNS_{Q1}= 64.2$, $ASNS_{Q5}= 57.9$, $DG= 6.4$ [3.3;9.5]), head and neck cancers ($ASNS_{Q1}= 49.7$, $ASNS_{Q5}= 38.1$, $DG= 11.6$ [6.8;16.5]), prostate cancer ($ASNS_{Q1}= 93.8$, $ASNS_{Q5}= 90.7$, $DG= 3.0$ [1.1;5.0]), bladder cancer ($ASNS_{Q1}= 57.7$, $ASNS_{Q5}= 51.2$, $DG= 6.4$ [0.9;12.0]) as well as liver cancer ($ASNS_{Q1}= 18.4$, $ASNS_{Q5}= 12.2$, $DG= 6.2$ [2.5;10.0]). Among women, the deprivation gap regarding 5-year ASNS was statistically significant for colon-rectum cancer ($ASNS_{Q1}= 66.0$, $ASNS_{Q5}= 60.6$, $DG= 5.5$ [2.2;8.7]), head and neck cancers ($ASNS_{Q1}= 56.4$, $ASNS_{Q5}= 41.6$, $DG= 14.9$ [6.2;23.5]), breast cancer ($ASNS_{Q1}= 88.8$, $ASNS_{Q5}= 83.7$, $DG= 5.1$ [2.9;7.3]), cervical cancer ($ASNS_{Q1}= 68.2$, $ASNS_{Q5}= 56.9$, $DG= 11.3$ [3.4;19.3]), bile duct cancer ($ASNS_{Q1}= 23.1$, $ASNS_{Q5}= 9.5$, $DG= 13.6$ [4.0;23.3]) and esophagus cancer ($ASNS_{Q1}= 23.0$, $ASNS_{Q5}= 10.9$, $DG= 12.1$ [1.9;22.4]).

Various patterns emerged regarding fluctuation of ASNS according to deprivation quintile (tables 3 and 4). There was a negative gradient in ASNS with increasing deprivation for example for prostate cancer, breast cancer, colon-rectum cancer, corpus uteri cancer. For some cancer sites such as ovarian cancer, head and neck cancers, lung cancer or kidney cancer, we could not observe such a clear relation but ASNS in the most deprived quintiles was overall lower than ASNS in the least deprived ones. In addition, for some cancer sites, ASNS in the most deprived quintile (Q5) was lower than ASNS in the least deprived one (Q1) but ASNS varied inconsistently between Q2 and Q4 (e.g. pancreas cancer, stomach cancer, cervical cancer).

Figures 1 and 2 show the variation of 1-year and 5-year ASNS between Q1 and Q5, for each cancer site among men and women, respectively. A decrease of at least 5% in 1-year ASNS between Q1 and Q5 was observed in 11/16 cancer sites among men and 8/18 cancer sites among women. The decline in 1-year ASNS between Q1 and Q5 reached 19% for pancreas cancer, 15% for esophagus

cancer, 14% for liver cancer among men and 28% for esophagus cancer, 19% for pancreas cancer, 19% for bile duct cancer among women. Furthermore, there was a decrease of at least 5% in 5-year ASNS between Q1 and Q5 in 11/16 cancer sites among men and 11/18 cancer sites among women. The reduction in 5-year ASNS between Q1 and Q5 reached 34% for liver cancer, 23% for head and neck cancers, 20% for breast cancer among men and 59% for bile duct cancer, 53% for esophagus cancer, 29% for pancreas cancer among women.

For most of the cancer sites, the decline in ASNS between Q1 and Q5 widened from 1 year of follow-up to 5 years of follow up (figures 1 and 2). However, this decline was larger at 1 year of follow-up than at 5 years of follow up for pancreas cancer ($\Delta 1$ -year $ASNS_{Q1 \rightarrow Q5} = 19\%$ vs. $\Delta 5$ -year $ASNS_{Q1 \rightarrow Q5} = 8\%$), stomach cancer ($\Delta 1$ -year $ASNS_{Q1 \rightarrow Q5} = 11\%$ vs. $\Delta 5$ -year $ASNS_{Q1 \rightarrow Q5} = 7\%$), esophagus cancer ($\Delta 1$ -year $ASNS_{Q1 \rightarrow Q5} = 15\%$ vs. $\Delta 5$ -year $ASNS_{Q1 \rightarrow Q5} = 2\%$) and CNS cancer ($\Delta 1$ -year $ASNS_{Q1 \rightarrow Q5} = 6\%$ vs. $\Delta 5$ -year $ASNS_{Q1 \rightarrow Q5} = 3\%$) in men and for stomach cancer ($\Delta 1$ -year $ASNS_{Q1 \rightarrow Q5} = 7\%$ vs. $\Delta 5$ -year $ASNS_{Q1 \rightarrow Q5} = 2\%$) and ovary cancer ($\Delta 1$ -year $ASNS_{Q1 \rightarrow Q5} = 5\%$ vs. $\Delta 5$ -year $ASNS_{Q1 \rightarrow Q5} = 2\%$) in women.

Supplementary analyses revealed consistent results when stratifying on the year of diagnosis, the French *Département*, the registry or the type of registry (i.e. general or specialized) (data not shown).

Discussion

We found that cancer survival was (or tended to be) lower among patients living in the most deprived areas compared to those living in the least deprived ones, for almost all cancer sites (14/16 among men and 16/18 among women at 5 years of follow-up) while no significant inverse association was observed for the remaining cancer sites. The extent of the impact of social environment on cancer survival varied a lot across the cancer sites. The decline in ASNS between the least and the most deprived quintiles generally widened during follow-up, but for some cancer sites (e.g. ovary cancer, stomach cancer), this decline was wider at 1 year than at 5 years of follow-up. Moreover, patterns were different between men and women, since larger variations of survival between the least and the most deprived quintile were observed in women compared to men (the maximum variation of survival between Q1 and Q5 was 59% in women vs. 34% in men). In addition, the impact of social deprivation could differ between men and women for a given cancer site (e.g. significant difference in survival from bile duct cancer according to deprivation among women vs. no effect among men).

Previous studies investigating the influence of social environment on cancer survival for several solid tumor sites with comparable methodology (i.e. population-based registries data, ecological deprivation index, net survival) also showed lower survival among patients living in the most deprived environments compared to those living in the least deprived ones, for most cancer sites.^{18,20-25} More broadly, all studies investigating social inequalities in cancer survival worldwide have reported lower survival among the most deprived for a large majority of cancer sites, with no significant inverse association.^{10-17,26,27} Our findings are therefore supported by those from the literature, and bring new information about the situation in France and the impact of social deprivation on cancer survival for cancer sites with mitigated results in the literature (such as stomach, ovary, melanoma, thyroid, CNS or pancreas). The deprivation gaps were broadly similar to those reported by studies with comparable methodology, conducted in the UK,²⁰ in Germany,²² in Japan,²¹ in Australia²⁴ and in New Zealand.²³ Compared to those previous studies, we found slightly smaller deprivation gaps for colon-rectum cancer, prostate cancer and esophagus cancer (in men)

and slightly wider deprivation gaps for esophagus cancer (in women), head and neck cancers, breast cancer and cervical cancer. However, differences in methodology across studies investigating the influence of social environment on cancer survival make it difficult to precisely compare their results. It would be very useful to have access to cancer registries data, with the same deprivation index estimated at a comparable geographical level, for all countries in Europe, to place disparities in cancer survival according to the social environment observed in France with regard to the European context.

The lower survival found among patients living in the most deprived areas compared to those living in the least deprived ones regarding colon-rectum cancer, breast cancer and cervical cancer might result from inequalities in cancer screening uptake,^{1-4,7} which have been identified in several French studies.^{30,31,45} Additionally, disparities in stage at diagnosis and therapeutic management according to deprivation have been related to cancer survival inequalities in previous research.^{1-4,7,11,12,15,16,26,27,46} However, neither stage at diagnosis nor patients' treatment history were available in the cancer registries data used for the present study. Collection of data on stage at cancer diagnosis by the French network of cancer registries has been initiated in a pilot study for breast and colon-rectum cancers diagnosed after 2009.⁴⁷ It would be very much valuable to reproduce the present study, accounting for data on stage at cancer diagnosis, for all cancers reported in the Francim registries after 2009, in order to better explain the disparities in cancer survival according to social environment. In the present study, we found substantial variations in survival between patients living in the least versus the most deprived environment regarding lung cancer, head and neck cancers or digestive cancers, whose incidence and survival are (independently) strongly related to behavioral risk factors (such as tobacco smoking, alcohol intake, unhealthy diet). A potential explanation to this may be that these risk factors are more frequent among the most socially disadvantaged, resulting in higher risk of cancer incidence on the one hand, and lower chances of cancer survival on the other hand among them.⁴⁸ It would be interesting in further research to investigate whether the lower survival among the most deprived could be due to higher occurrence of risk factors-related cancer histological types among them. Some studies also suggest that the higher occurrence of risk factors among the most deprived might be responsible for higher comorbidities prevalence, preventing from using optimal cancer treatments or masking cancer symptoms and delaying its diagnosis, thus reducing survival among them.^{1-4,7,9}

Overall, our results confirm the existence of a social gradient regarding cancer survival in France, which is part of the 'social gradient in health' described by the World Health Organization.⁴⁹ Furthermore, we highlighted a different impact of social environment on cancer survival across the cancer sites, according to the time of follow-up or between men and women, suggesting different underlying mechanisms and the need for implementing specific actions to reduce social inequalities in cancer survival in each situation.

The social gradient in cancer survival observed in the present study widened between one year and five years of follow-up for a majority of the cancer sites, except pancreas cancer, stomach cancer, esophagus cancer and CNS cancer among men, and stomach cancer and ovary cancer among women. This suggests that disparities in cancer survival may not uniquely result from differences in stage at diagnosis or initial therapeutic management according to deprivation, but could build up throughout every step of the follow-up and relapse. From a methodological point of view, such results also point out a potential non-proportional effect of deprivation, which will be addressed (as well as possible non-linearity of EDI) in a next step using flexible excess-hazard regression models.⁵⁰

A previous study,³² that used the same data from the French Network of Cancer registries (diagnoses 2006-2009) has investigated the influence of the EDI on cancer incidence. It is worth noting that, while a more deprived environment was (or tended to be) systematically associated with lower survival for all cancer sites in the present study, either positive or negative social gradients could be observed regarding cancer incidence in that previous study. As a matter of fact, Bryere *et al.* have found that individuals living in the most deprived environment experienced higher incidence rates for head and neck cancers, lung cancer, digestive cancers and cervical cancer but lower incidence rates for melanoma, prostate cancer, breast cancer and ovary cancer as compared to those living in the least deprived environment. It is important to better understand and distinguish the social gradients regarding cancer incidence and cancer survival respectively, since actions to reduce them must be considerably different.

This is the first study, to our knowledge, that investigates disparities in cancer survival according to social environment for several solid tumor sites, through population-based cancer registries in France. The French Network of Cancer Registries represent a powerful tool to monitor cancer survival (and disparities in survival according to social deprivation) since they are based on large population-based data and offer high quality and validated data. Using net survival allowed us to observe cancer survival independently of mortality from other causes than the cancer of interest, and independently of the national general population mortality.⁴¹ Moreover, we used a validated indicator for social deprivation, developed and used in several European countries.⁵¹ The EDI offers an acceptable approximation of social deprivation at the individual level when used in small geographic units such as IRIS,⁵² while also providing information on the social environment, known to have a proper effect on cancer survival for some cancer sites.^{14,18} The measure of the variation of survival between the least and the most deprived quintiles brought new information on the extent of survival disparities according to social deprivation that can be compared across cancer sites or different times of follow-up since it is a relative measure of the deprivation gap.

Our study presents some limitations. In the absence of reliable data on cause of death, we used life tables from INSEE to estimate expected survival. However, those life tables did not provide deprivation-specific expected mortality rates even though it is highly possible that the most deprived individuals have higher mortality in the general population. Therefore, it is likely that expected mortality was underestimated among the most deprived patients and that excess mortality among them was overestimated (and thus the deprivation gaps). It would be more accurate to estimate net survival based on deprivation-specific life tables but such life tables do not exist in France yet. A possible way to comprehend the maximal extent of the bias induced by the absence of deprivation-specific life tables would be to use, in sensitivity analyses, those from another country with known substantial difference in general population mortality according to deprivation (“worst case scenario”). This has been done by Ito and colleagues²¹ who used England and Wales deprivation-specific life tables to analyze net survival of Osaka population (Japan). The authors have shown (assuming similar inequalities in general population mortality in Osaka and in England and Wales) that overestimation of the deprivation gap was small at one-year survival but non-negligible at five-year survival. However, sensitivity analyses using this type of modelling approach cannot fully compensate the absence of deprivation-specific lifetables. Building such deprivation-specific life tables remains a major step forward that needs to be undertaken in France for studying socioeconomic inequalities in cancer survival. Another important point to note is that the French Network of Cancer Registries used in this study do not entirely cover France but around 20% of the

population, preventing us from generalizing our results to the whole French population diagnosed with cancer. As it turns out, the area covered by the French Network of Cancer Registries comprises more rural zones than the whole French territory and excludes major metropolis (Paris, Marseille, Lyon). Therefore, the whole French population diagnosed with cancer may somewhat differ from our study population. However, while this might influence cancer incidence or general mortality, it is not sure whether it would modify the impact of deprivation on cancer survival in the whole French population diagnosed with cancer as compared to our study population. Moreover, data regarding stage at cancer diagnosis, access to healthcare services, treatment or comorbid illnesses were not available. Therefore, we could not investigate the influence of deprivation on cancer survival according to those parameters.

In conclusion, this study provides reference data on disparities in cancer survival according to social environment, for several solid tumor sites in France, and confirms the existence of important and recurring social inequalities in cancer survival. These results thereby suggest that the French health coverage and social security system may not be sufficient to eliminate the social gradient in health. It would be of great interest to reproduce this study on a regular basis in order to monitor social inequalities in cancer survival over time, which could help public health policies implementing actions to reduce social deprivation-related disparities in cancer survival. In order to improve cancer survival among patients living in the most deprived environment, it is important to implement actions along the whole cancer continuum and to focus on both incidence-related (cancer screening, prevalence of cancer risk factors etc.) and survival-related (stage at diagnosis, access to healthcare services, treatment modalities etc.) factors. To that end, further research about the relative part of social inequalities in cancer incidence and cancer lethality in the overall cancer mortality-related disparities would be relevant.

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Tables Legends

Table 1. Description of records from the FRANCIM registries used in the study

Table 2. Characteristics of the population by cancer site and by sex (FRANCIM registries, cancer cases diagnosed between 2006-2009)

* 1- Topography codes for sarcoma: C381, C382, C383, C47, C480, C49, C696, C76, C809, morphology codes for sarcoma : 8900-05, 8910, 8912, 8920, 8991, 8810, 8811, 8813-15, 8821, 8823, 8834-35, 8820, 8822, 8824-27, 9150, 9160, 9491, 9540-971, 9580, 9140, 8587, 8710-13, 8806, 8831-33, 8836, 8840-42, 8850-58, 8860-62, 8870, 8880, 8881, 8890-98, 8921, 8982, 8990, 9040-44, 9120-25, 9130-33, 9135, 9136, 9141, 9142, 9161, 9170-75, 9231, 9251, 9252, 9373, 9581, 8830, 8963, 9180, 9210, 9220, 240, 9260, 9364, 9365, 8800-05
ASNS: age-standardized net survival

Table 3. One- and five-year age-standardized net survival (ASNS) in each deprivation quintile and deprivation gap (DG), by cancer site, among men

ASNS: Age-standardized net survival
DG : Deprivation Gap= ASNS_{Q1} - ASNS_{Q5}
CI95% : 95% confidence interval
* age-standardization was not possible for breast cancer in men due to small sample size

Table 4. One- and five-year age-standardized net survival (ASNS) in each deprivation quintile and deprivation gap (DG), by cancer site, among women

ASNS: Age-standardized net survival
DG : Deprivation Gap= ASNS_{Q1} - ASNS_{Q5}
CI95% : 95% confidence interval

Table 1. Description of records from the FRANCIM registries used in the study

	N	Inclusion period for dates of diagnosis	Incomplete date of last information		Date of diagnosis= date of death		Lost to follow-up	
			N	%	N	%	N	%
Calvados registry of digestive tumors	3,051	2006-2009	0	0	3	0.1	35	1.1
Calvados cancer registry	9,385	2006-2009	0	0	3	<0.1	25	0.3
Côte d'Or/Saône et Loire registry of digestive tumors (data relative to Côte d'Or)	2,401	2006-2009	0	0	2	0.1	17	0.7
Côte d'Or registry of gynecological tumors	1,552	2006-2009	0	0	0	0	34	2.2
Doubs cancer registry	9,632	2006-2009	0	0	6	0.1	126	1.3
Finistère registry of digestive tumors	4,724	2006-2009	14	0.3	11	0.2	83	1.8
Gironde cancer registry	11,924	2008-2009	30	0.3	6	0.1	579	4.9
Gironde registry of CNS tumors	385	2006-2009	3	0.8	0	0	13	3.4
Hérault cancer registry	18,775	2006-2009	0	0	18	0.1	429	2.3
Isère cancer registry	21,152	2006-2009	0	0	11	0.1	422	2.0
Loire-Atlantique/Vendée cancer registry (data relative to Loire-Atlantique)	23,094	2006-2009	5	<0.1	27	0.1	490	2.1
Manche cancer registry	9,537	2006-2009	0	0	19	0.2	129	1.4

Kidney	C64/all	3,704	1,404	4.28	65	19	20	19	20	19	68.	1,933	659	4.32	69	18	21	19	19	21	72.
Bladder	C67/all	5,331	3,121	3.12	73	16	19	20	20	23	53.	1,280	811	1.74	78	16	17	18	21	25	49.
Central nervous system	C70-72/all	1,681	1,374	1.06	61	22	19	19	19	19	22.	1,318	1,027	0.97	65	17	20	19	20	22	28.
Thyroid	C739/all	1,081	134	4.88	55	21	20	18	18	20	90.	3,407	161	5.05	51	22	20	19	18	20	96.

* 1- Topography codes for sarcoma: C381, C382, C383, C47, C480, C49, C696, C76, C809, morphology codes for sarcoma: 8900-05, 8910, 8912, 8920, 8991, 8810, 8811, 8813-15, 8821, 8823, 8834-35, 8820, 8822, 8824-27, 9150, 9160, 9491, 9540-971, 9580, 9140, 8587, 8710-13, 8806, 8831-33, 8836, 8840-42, 8850-58, 8860-62, 8870, 8880, 8881, 8890-98, 8921, 8982, 8990, 9040-44, 9120-25, 9130-33, 9135, 9136, 9141, 9142, 9161, 9170-75, 9231, 9251, 9252, 9373, 9581, 8830, 8963, 9180, 9210, 9220, 240, 9260, 9364, 9365, 8800-05
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	1-year age-standardized net survival					1-year DG [CI95%]	5-year age-standardized net survival					5-year DG [CI95%]
	Q1 (Least deprived)	Q2	Q3	Q4	Q5 (Most deprived)		Q1 (Least deprived)	Q2	Q3	Q4	Q5 (Most deprived)	
Solid tumor sites												
Head & neck	75.7	75.9	70.8	72.1	68.9	6.8 [3.1;10.5]	49.7	45.6	39.6	40.7	38.1	11.6 [6.8;16.5]
Esophagus	51.1	51.9	47.8	46.0	43.5	7.5 [1.9;13.2]	16.4	15.9	11.7	12.4	16.0	0.4 [-4.2;5.0]
Stomach	58.8	52.2	54.8	56.5	52.4	6.4 [1.1;11.7]	28.1	22.2	25.1	23.9	26.1	2.0 [-3.3;7.3]
Colon-rectum	85.6	84.5	84.7	81.7	82.7	2.9 [1.0;4.8]	64.2	63.7	61.0	60.1	57.9	6.4 [3.3;9.5]
Liver	49.0	49.5	42.9	48.2	42.2	6.8 [2.1;11.4]	18.4	15.6	16.2	14.5	12.2	6.2 [2.5;10.0]
Bile duct	55.4	46.4	57.1	51.5	50.2	5.2 [-5.5;15.8]	17.9	20.8	21.1	18.1	21.6	-3.7 [-13.6;6.2]
Pancreas	36.3	33.4	29.4	31.7	29.5	6.7 [1.7;11.8]	9.9	8.5	7.5	8.7	9.2	0.8 [-2.7;4.2]
Lung	45.6	44.5	43.2	43.6	43.0	2.6 [-0.1;5.2]	17.2	15.2	15.0	15.4	14.3	2.9 [0.7;5.0]
Sarcoma	88.2	84.2	81.8	78.9	81.8	6.4 [-1.1;13.9]	58.7	58.1	53.9	59.9	61.0	-2.3 [-14.6;9.9]
Melanoma	98.9	98.9	95.8	95.8	97.5	1.4 [-0.8;3.7]	92.3	87.8	85.6	84.6	87.3	5.0 [-0.5;10.6]
Breast*	100.0	97.5	95.6	98.2	94.9	5.2 [-3.3;13.6]	89.3	74.4	87.5	76.6	71.1	18.2 [-2.7;39.2]
Prostate	98.2	98.3	97.9	97.5	97.7	0.5 [-0.3;1.3]	93.8	93.1	91.8	91.7	90.7	3.0 [1.1;5.0]
Kidney	85.8	86.0	82.4	81.2	81.7	4.2 [0.0;8.4]	72.2	71.0	65.9	67.0	67.2	5.0 [-1.2;11.3]
Bladder	81.7	81.2	78.5	77.9	76.9	4.8 [0.8;8.7]	57.7	55.6	53.7	50.1	51.2	6.4 [0.9;12.0]
Central nervous system	58.4	62.8	56.4	54.5	55.1	3.2 [-3.8;10.2]	23.9	20.6	21.9	22.9	23.2	0.6 [-5.7;6.9]
Thyroid	95.6	93.3	95.3	95.5	96.6	-1.1 [-5.7;3.6]	98.0	86.8	88.5	90.6	90.9	7.1 [-0.6;14.8]

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	1-year age-standardized net survival					1-year DG [CI95%]	5-year age-standardized net survival					5-year DG [CI95%]
	Q1 (Least deprived)	Q2	Q3	Q4	Q5 (Most deprived)		Q1 (Least deprived)	Q2	Q3	Q4	Q5 (Most deprived)	
Solid tumor sites												
Head & neck	77.0	76.5	79.4	77.7	73.1	3.9 [-2.9;10.7]	56.4	56.8	55.0	55.1	41.6	14.9 [6.2;23.5]
Esophagus	56.4	41.8	45.1	43.5	40.8	15.7 [3.3;28.1]	23.0	20.2	10.9	13.8	10.9	12.1 [1.9;22.4]
Stomach	61.9	53.8	59.6	59.9	57.6	4.3 [-3.5;12.0]	31.4	30.3	31.8	35.0	30.7	0.8 [-7.4;8.9]
Colon-rectum	85.9	85.0	83.6	83.5	82.0	3.9 [1.9;6.0]	66.0	64.0	63.4	63.7	60.6	5.5 [2.2;8.7]
Liver	48.9	48.7	50.1	44.2	42.0	6.9 [-2.9;16.7]	17.3	21.0	16.9	18.7	13.9	3.4 [-4.4;11.1]
Bile duct	49.4	53.6	51.6	42.0	40.0	9.3 [-1.3;19.9]	23.1	22.7	22.9	16.5	9.5	13.6 [4.0;23.3]
Pancreas	37.5	35.2	33.8	35.1	30.2	7.2 [1.6;12.8]	11.7	7.4	6.2	10.1	8.4	3.4 [-0.6;7.4]

Lung	51.9	51.1	48.5	47.4	49.0	2.9 [-1.6;7.4]	20.9	20.8	18.3	19.1	17.3	3.6 [-0.2;7.4]
Sarcoma	76.4	85.3	91.1	84.5	82.1	-5.7 [-16.4;4.9]	57.4	61.2	72.1	57.0	59.3	-1.9 [-15.6;11.8]
Melanoma	98.9	98.6	99.2	98.7	98.1	0.8 [-1.0;2.6]	92.9	94.4	90.4	91.6	89.8	3.1 [-1.3;7.4]
Breast	97.6	97.2	97.0	96.5	96.0	1.6 [0.6;2.5]	88.8	87.6	87.3	86.3	83.7	5.1 [2.9;7.3]
Cervix uteri	88.0	88.2	85.9	86.9	87.2	0.8 [-4.8;6.4]	68.2	64.4	61.2	62.6	56.9	11.3 [3.4;19.3]
Corpus uteri	91.8	90.6	90.3	88.7	88.3	3.5 [0.5;6.5]	77.7	75.5	73.6	72.3	72.8	4.9 [-0.2;9.9]
Ovary	79.1	78.3	74.7	75.4	75.4	3.8 [-1.0;8.6]	41.7	46.1	40.5	40.6	40.8	1.0 [-5.1;7.0]
Kidney	89.4	85.2	84.6	83.0	85.4	4 [-0.8;8.8]	77.0	74.0	68.9	70.9	73.3	3.6 [-3.6;10.9]
Bladder	77.4	70.9	69.9	71.9	67.9	9.5 [1.3;17.8]	54.2	45.6	53.4	50.3	45.3	8.9 [-2.0;19.8]
Central nervous system	57.9	63.4	57.3	56.4	56.2	1.6 [-6.1;9.4]	25.1	31.8	29.2	26.8	27.5	-2.4 [-10.4;5.6]
Thyroid	96.2	97.5	98.0	96.7	97.3	-1.2 [-4.1;1.7]	97.4	96.2	96.5	96.6	96.5	0.9 [-3.2;4.9]

ASNS: Age-standardized net survival

DG : Deprivation Gap= ASNS_{Q1} - ASNS_{Q5}

CI95% : 95% confidence interval

Figures Legends

Figure 1. Variation of 1- and 5-year age-standardized net survival (ASNS) between the least (Q1) and the most (Q5) deprived quintile, by cancer site, among men

ASNS: Age-standardized net survival

* age-standardization was not possible for breast cancer in men due to small sample size

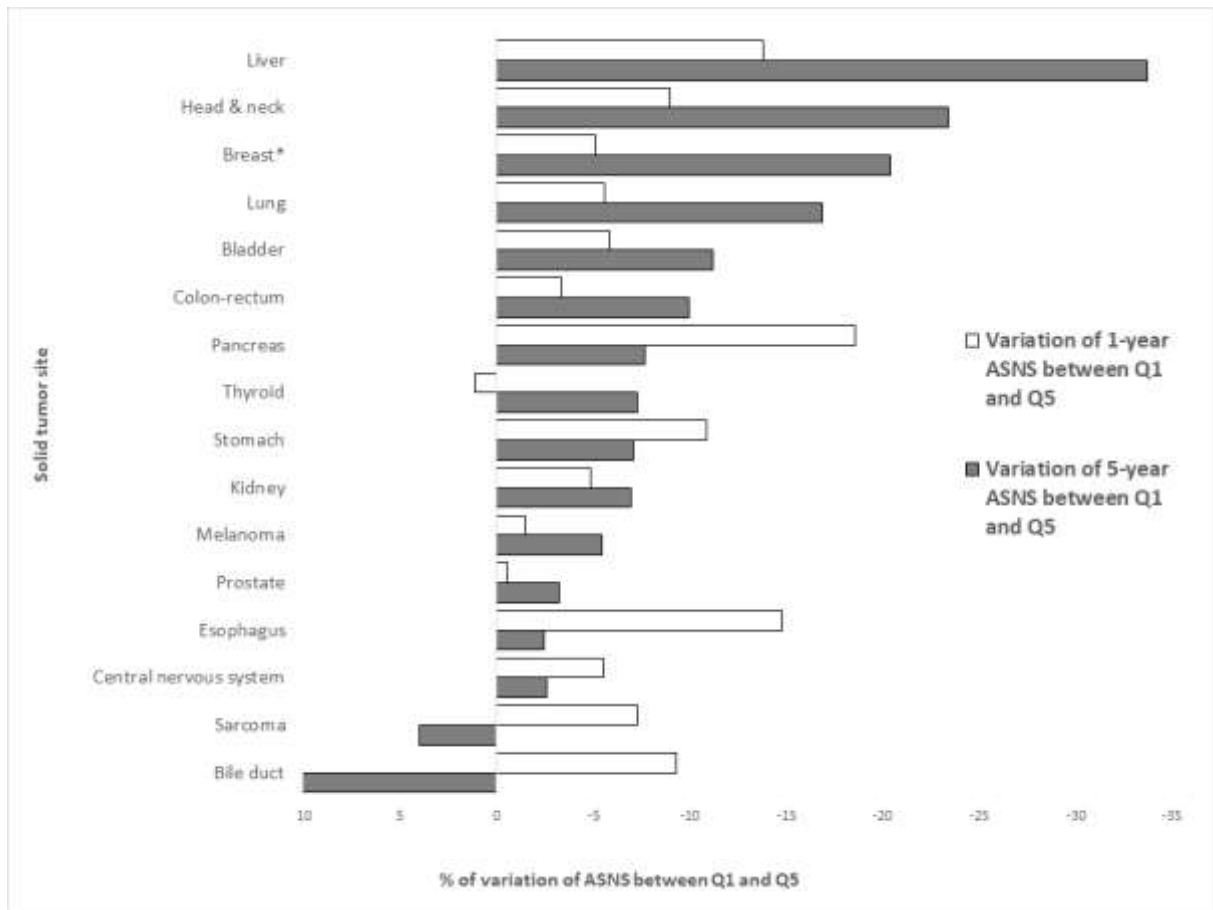
Figure 2. Variation of 1- and 5-year age-standardized net survival (ASNS) between the least (Q1) and the most (Q5) deprived quintile, by cancer site, among women

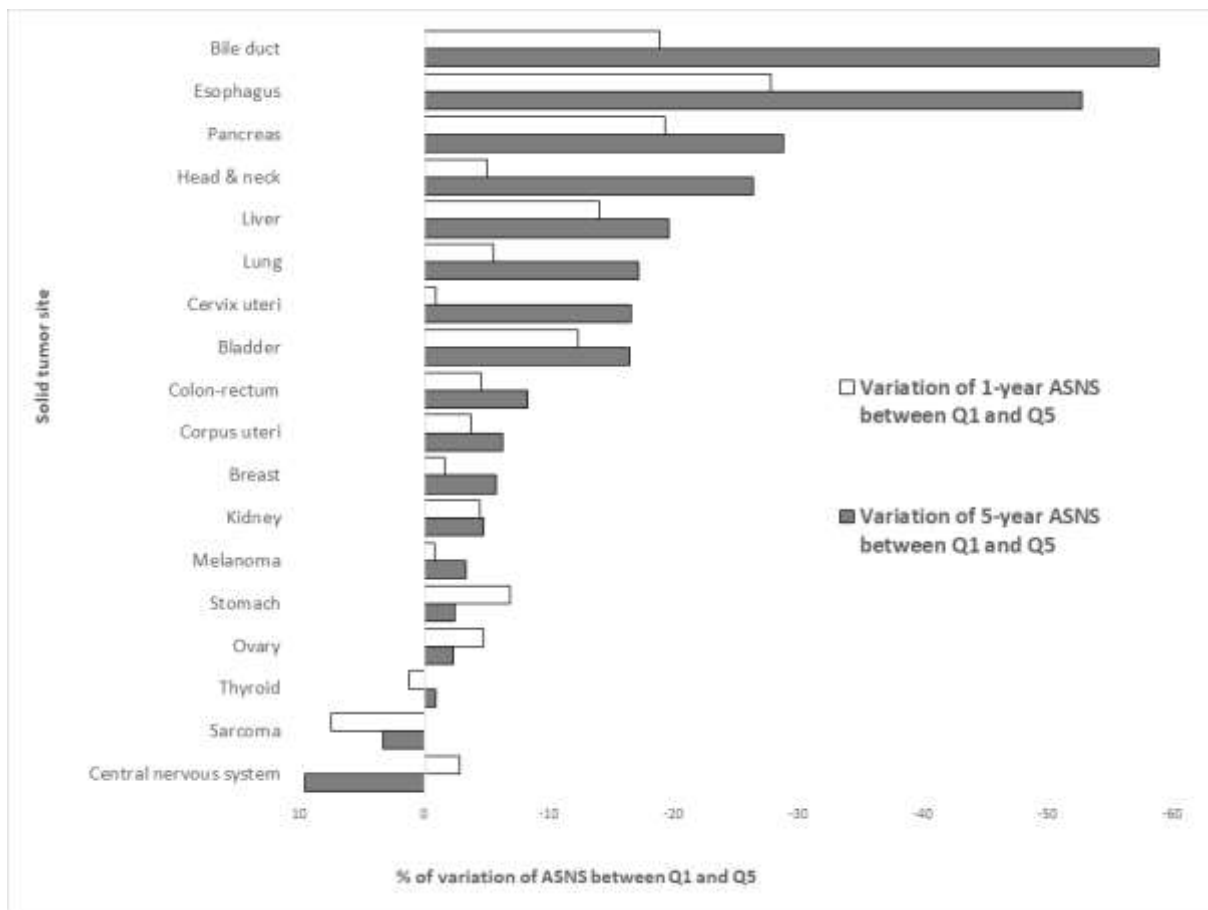
ASNS: Age-standardized net survival

Supplementary figure 1. Map of the French Network of Cancer Registries coverage and the study population coverage.

Appendix

Members of the French Network of Cancer Registries (FRANCIM): Françoise GALATEAU-SALLE (Registre multicentrique du mésothéliome à vocation nationale (Mesonat)), Anne-Marie BOUVIER (Registre Bourguignon des cancers digestifs), Simona BARA (Registre des cancers de la Manche), Clarisse JOACHIM-CONTARET (Registre des cancers de la Martinique), Olivier GANRY (Registre général des cancers de la Somme), Claire SCHVARTZ (Registre des cancers de la thyroïde Marne Ardennes), Sandrine PLOUVIER (Registre des cancers de Lille et de sa région), Guy LAUNOY (Registre des cancers digestifs du Calvados), Emilie MARRER (Registre des cancers du Haut-Rhin), Patrick ARVEUX (Registre des cancers du sein et des cancers gynécologiques de Côte d'Or), Pascale GROSCLAUDE (Registre des cancers généraux du Tarn), Xavier TROUSSARD (Registre des hémopathies malignes de Basse-Normandie), Marc MAYNADIE (Registre des hémopathies malignes de Côte d'Or), Alain MONNEREAU (Registre des hémopathies malignes de la Gironde), Jean Pierre DAURES (Registre général des tumeurs de l'Hérault), Florence MOLINIE (Registre des tumeurs de Loire-Atlantique/Vendée), Anne-Sophie WORONOFF (Registre des tumeurs du Doubs et du Territoire de Belfort), Isabelle BALDI (Registre des tumeurs primitives du système nerveux en Gironde), Jean-Baptiste NOUSBBAUM (Registre Finistérien des tumeurs digestives), Gaëlle COUREAU (Registre général des cancers de la Gironde), Jacqueline DELOUMEAUX (Registre général des cancers de la Guadeloupe), Marc COLONNA (Registre général des cancers de l'Isère), Michel VELTEN (Registre général des cancers du Bas-Rhin), Tania D'ALMEIDA (Registre général des cancers en région Limousin), Anne-Valérie GUIZARD (Registre général des tumeurs du Calvados), Jacqueline CLAVEL (Registre national des hémopathies malignes de l'enfant (RNHME)), Brigitte LACOUR (Registre national des tumeurs solides de l'enfant (RNTSE)), Borson-Chazot (Registre Rhône Alpin des cancers thyroïdiens), Pierre INGRAND (Registre des cancers de Poitou-Charentes), Sylvie Laumod (Cancers généraux - Nouvelle Calédonie), Emmanuel CHIRPAZ (Registre des Cancers de la Réunion), Laure-Manuella DESROZIERES-IMOUNGA (Registre des cancers généraux de Guyane).





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