**Cancer incidence in France over the 1980-2012 period: Haematological malignancies.**

S. Le Guyader-Peyrou \* a b, A. Belot c d e f g,M. Maynadié h, F. Binder-Foucard i j, L. Remontet c d e f X. Troussard  k l, N. Bossard c d e f, A. Monnereau b m, the French network of cancer registries (Francim)

a Réseau français des registres des cancers, Francim, 31073 Toulouse, France

b Registre des Hémopathies malignes de la Gironde, Institut Bergonié, 33076 Bordeaux, France

c Service de biostatistique, Hospices Civils de Lyon, centre hospitalier Lyon-Sud, 69424 Lyon, France

d Université de Lyon, F-69000, Lyon, France

e Université Lyon-I, 69622 Villeurbanne, France

f CNRS, UMR5558, Laboratoire de Biométrie et Biologie Evolutive, Equipe Biostatistique-Santé, F-69100, Villeurbanne, France

g Institut de veille sanitaire, Département des maladies chroniques et traumatismes, 94410 Saint-Maurice, France

h Registre des Hémopathies Malignes de Côte d’Or, EA4184, Université de Bourgogne, Dijon,

i Registre des cancers du Bas-Rhin, Laboratoire d’épidémiologie et de santé publique, EA 3430, Faculté de médecine, Université de Strasbourg, 67085 Strasbourg cedex, France

j Service de santé publique, Hôpitaux universitaires de Strasbourg, 67000 Strasbourg, France

k Registre des Hémopathies malignes de Basse Normandie, Caen, France

l Laboratoire d’Hématologie, CHU de Caen, France

m Centre INSERM U897, CIC 1401, Bordeaux, France

\*corresponding author

Le Guyader-Peyrou Sandra

Registre des Hémopathies malignes de la Gironde

228 cours de l’Argonne

33076 Bordeaux cedex

05 56 33 32 55

05 47 30 60 72

[*S.LeGuyaderPeyrou@bordeaux.unicancer.fr*](mailto:S.LeGuyaderPeyrou@bordeaux.unicancer.fr)

**Abstract:**

**Background**

The classification of haematological malignancies (HMs) has changed in recent decades. For the first time, the French network of cancer registries (Francim) provides estimates for incidence and trends of HM in France between 1980 and 2012 for major HM subtypes.

**Methods**

Incidence is directly estimated by modelling the incidence rates measured in the cancer registry area. For each HM subtype, a “usable incidence period” was *a priori* defined, corresponding to the years for which all the registries collected them in a homogeneous way. For each sex and HM subtypes, age-period-cohort models were used to estimate national incidence trends.

**Results**

Overall in France, there were an estimated 35,000 new HMs in 2012 (19,400 in men and 15,600 in women). Lymphoid malignancies represent more than two-thirds of HM incident cases (n=25,136). Incidence sex ratio (M/F) varied from 1.1 for classical Hodgkin lymphoma to 4.0 for mantle cell lymphoma. The median age at diagnosis ranged from 62 to 81 years according to the major HMs subtypes. Overall in both sexes, the top five most frequent HMs in 2012 were plasma cell neoplasm (about 4,900 estimated cases), chronic lymphocytic leukaemia/small lymphocytic lymphoma (4,500 cases), diffuse large B-cell lymphoma and myelodysplastic syndromes (4,100 cases) and acute myeloid leukaemia (2,800 cases), respectively.

The incidence rates increased for follicular lymphoma and plasma cell neoplasm during the study period in both sexes. Classical Hodgkin lymphoma was relatively stable in men between 1980 and 2012 and increased in both sexes during the most recent period. Chronic myeloproliferative neoplasms, other than chronic myelogenous leukaemia, are the only subtype that showed a slightly downward trend in incidence between 2003 and 2012 in both sexes.

**Conclusion**

The striking differences in the incidence patterns by histologic subtype strongly suggest a certain level of etiologic heterogeneity among haematological malignancies and support the pursuit of epidemiologic analysis by subtype for HM in international studies. Age-standardised incidence rates are essential to analyse trends in risk, whereas the number of incident cases is necessary to make provisions for healthcare resources and to evaluate the overall burden of HM.

Keywords: Haematological malignancies. Incidence. Trends. Registry.

**Résumé**

**Position du problème**

La classification des hémopathies malignes a considérablement évolué ces dernières années. Pour la première fois en France, les registres publient l’incidence et les tendances des principaux sous types d’hémopathies malignes en population entre 1980 et 2012.

### Méthodes

L’incidence est estimée directement à partir de la modélisation de l’incidence de la zone registre. Pour chacune des entités, une « période d’incidence utilisable » a été préalablement définie : cette période correspond aux années pour lesquelles l’ensemble des registres du réseau Francim a recueilli de façon homogène l’entité correspondante. En fonction des entités, l’estimation porte donc sur des périodes de longueur différente.

### Résultats

35000 hémopathies malignes (HM) diagnostiquées entre 1975 et 2009 en France ont été analysées (19400 chez l’homme et 15600 chez la femme). Les hémopathies lymphoïdes représentent plus de deux tiers de cas incidents (n=25136). Le sex ratio varie de 1,1 pour le lymphome de Hodgkin classique à 4 pour le lymphome du manteau.

L’âge médian au diagnostic s’échelonne de 62 à 81 ans pour les principales hémopathies. Considérant les deux sexes, les cinq plus fréquents sous types d’HM en 2012 sont : le myélome/plasmocytome (4900 cas incidents), la leucémie lymphoïde chronique (4500 cas), le lymphome diffus à grandes cellules B et les syndromes myélodysplasiques (4100 cas) et les leucémies aigues myéloïdes (2800 cas).

Les taux standardisés d’incidence (population Monde) varient selon le type d’hémopathie maligne considérée et le sexe : l’incidence augmente dans les deux sexes pour le lymphome folliculaire et les myélomes, le lymphome de Hodgkin classique reste relativement stable chez l’homme entre 1980 et 2012 alors qu’il augmente dans les deux sexes durant la période la plus récente. Au contraire, l’incidence diminue entre 2003 et 2012 uniquement pour les syndromes myéloprolifératifs (hors LMC).

### Conclusion

Les fortes disparités d’incidence par sous-type histologique suggèrent un certain degré d’hétérogénéité étiologique entre les différentes hémopathies malignes et justifient la poursuite d’études étiologiques par sous type, en particulier au sein de collaborations internationales.

L’estimation de l’incidence et des tendances sont nécessaires pour la planification des soins et l’évaluation de la charge globale des hémopathies malignes.

**Mots clés : Hémopathies malignes, Incidence, Tendances, Registre de population.**

**1. Introduction**

In 2012, 14.1 million new cancer cases were diagnosed worldwide including more than 900,000 individuals with haematological malignancies (HMs). This makes it one of the most common cancers, particularly in more economically developed regions of the world [1]. HMs are composed of numerous diseases with distinctive morphologic, immunophenotypic, genetic, and clinical features, some of which are closely related yet heterogeneous. The availability of updated cancer incidence is of paramount importance for decision-making and public health policy implementation. Trends of incidence allow accurate description of the epidemiological features of cancers and their progression over time. These data are used to develop and assess programmes for primary prevention, screening and care. They also provide public healthcare policy-makers with the necessary information to assess the needs of the population in terms of cancer management, prioritise prevention strategies, and evaluate therapeutic progress.

The last report on cancer incidence and mortality in France was published in 2008, on the period 1980-2005 [2, 3].

Updating these results was an integral part of the national cancer programme (Plan Cancer 2009–2013) related to cancer epidemiology [4]. Following the National cancer programme, a scientific working programme was defined in a partnership that involves the French networks of cancer registries (Francim), the biostatistics department of the Hospices Civils de Lyon (HCL), the Institut de Veille Sanitaire (InVS) and the Institut National du Cancer (INCa). This work is performed in the context of that partnership and these results for HM supplement those published for solid tumors [5].

Cancer registries provide continuous and exhaustive records on all cancer cases in a pre-defined geographical area, and registry data are fundamental in order to estimate incidence at a national level. The Francim network has created a common database that brings together all the cancer data from participating registries, some dating back as far as 1975. The database is regularly updated and is administrated by the biostatistics department of the HCL as well as the Francim network, in collaboration with the InVS and INCa.

The aim of this study is to present the estimates for incidence and trends of HMs in France between 1980 and 2012.

**2. Methods**

# *Incident cases*

Data on incidence were extracted from the joint database of all the Francim network registries. For the purpose of this study, we used data from 14 French registries with at least 5 years of recorded data (table 1). We classified incident cases according to the International Classification of Diseases-Oncology 3rd edition (ICD-O-3) [6] grouped according to WHO indications [7]. Major HM subtypes were analysed (table 2) and lymphoid malignancies were presented according to the InterLymph recommendations [8, 9], leading to the study of 16 HM subtypes (including NHL NOS). Due to rarity, less frequent mature B-cell NHL subtypes, counted for less than 4% of new lymphoid cases, are not discussed in this paper.

For each HM, a period of “usable incidence period” was *a priori* defined. This period corresponds to the years for which all the registries collected the HMs in a homogeneous way. Consequently, according to the HM type, the estimation of the trends was based on different periods of observed incidence (see table 2). Taking into consideration the changes in HM classification overtime, we defined four different periods of observed incidence that ended in 2009. The first year considered was either 1975 (or the year of beginning of the registry) for HMs without any change in their classification; 1995, that corresponds to the year after the publication of the REAL classification [10]; 2003, that corresponds to the following year after ICD-O-3 publication. Finally, for one subtype (precursor lymphoblastic leukemia /lymphoma (B, T or NOS) (PLL/L)), we choose 1990 as the first year considered to obtain reliable data for trends analyses.

# *Population data and rate calculation*

The Institut National de la Statistique et des Etudes Economiques (Insee) provided population data for each “*département”* and for each year from 1975 to 2013. We used the same principle as those detailed in a previous report on solid tumours for the rate calculation [5].

***Estimation methods***

We used age-period-cohort models to estimate incidence trends for each sex and HM subtype, including observed incidence data from the area covered by registries up to 2009. Estimated incidence rates were then applied to the person-years (PY) of France to obtain national incidence estimates, assuming that the area covered by the registries is representative of France.

Because the last year for which incidence was observed is 2009, short term projections were necessary to reach our aim to provide estimates up to 2012.

Depending on the “usable incidence period” available, two different models were utilised. When the “usable incidence period” is 1975-2009, 1990-2009 or 1995-2009, the following model was fitted:

Log(Ka,c,d/ PYa,c,d)= Id+ s1(a)+ s2(c)+p2

where Ka,c,d is the number of cases diagnosed at age a [11] from cohort c in the département d, PYa,c,d is the corresponding person-years, p is the period of diagnosis (year), and Id indicates the *département* d (i.e. equal to 1 if *département* =d, 0 otherwise). This prevented from confusion between time and space, registries having available data on heterogeneous periods. Effects of age a and cohort c were modelled using smoothing splines, denoted by s1 and s2. The second-order period term p2 (where p=a+c) allowing linear interaction between age and cohort was introduced in the model only when it was statistically significant (likelihood ratio test, α = 1%).

When the “usable incidence period” is 2003-2009, a simpler model without the second-order period term p2 was used because a shorter period was studied. No indicator for *département* Id was included as all registries covered the entire period. We partitioned the difference in the total number of cases between 1980 and 2012 into three components using the Bashir method: (1) differences due to change in the population size; (2) differences due to change in the population structure (age distribution); and (3) differences due to the change in cancer incidence [12]. These results are presented in table 5.

## 3. Results

## Overall in France, there were an estimated 35,000 new HMs in 2012 (19,400 in men and 15,600 in women). For the major HM subtypes classified according to the ICD-O-3 and for each sex, we present in table 3, the number of cases, median of age at diagnosis, crude and estimated age-standardized incidence rates (world standard) and incidence *sex ratio*, estimated in 2012 in France. Major subtypes of lymphoid malignancies are presented in the table 3, and represent more than two-thirds of HM incident cases (n=25,136). This large group of HMs comprises non-Hodgkin lymphomas (NHL) detailed into ten different histological subtypes (92% of new lymphoid malignancies) and classical Hodgkin lymphoma (CHL). Incidence of myeloid malignancies totalled an estimated 9,622 new cases in France, in 2012. They are divided into three groups of diseases (described in table 3): Myelodysplastic syndromes (MDS), that were the most frequent myeloid malignancies (42.2%), acute myeloid leukaemias (AML) (29%) and myeloproliferative neoplasms (28.8%). We delineated two relatively rare but well-recognised myeloid subtypes (e.g. myelogenous chronic leukemia – CML and acute promyelocytic leukemia) representing 8.4% and 2% of myeloid malignancies, respectively. Figure 1 shows the numbers of new cases by HM subtype in 2012, in men and women sorted by decreasing frequency. A detailed report describing each HM is available to download elsewhere in pdf format [13] and paper format [14].

***Incidence estimates in 2012 in France detailed by sex and HM’s subtypes***

Overall, in both sexes, the top five most frequent HMs in 2012 were as follows: plasma cell neoplasm (PCN) with 4,888 new cases, chronic lymphocytic leukaemia/small lymphocytic lymphoma(CLL/SLL) with 4,464 new cases, diffuse large B-cell lymphoma (DLBCL) with 4,096 cases, MDS with 4,059 and AML with 2791 cases. All together, these top five more frequent HMs represent nearly 60% of all new cases in France in 2012 (figure 1).

Within lymphoid malignancies, we report the incidence rates for different NHL subtypes that showed a great heterogeneity in crude incidence ranking from 0.7 to 8.7 per 100,000 PY in men and 0.7 to 7.1 per 100,000 PY in women (table 3). The gap was smaller for estimated world age-standardised incidences (WASR) ranking from 0.3 to 4.5 per 100,000 PY in men and 0.3 to 2.9 per 100,000 PY in women.

Two recently described entities, mantle cell lymphoma (MCL) and marginal zone lymphoma (MZL) had a crude incidence rate of 1.6 and 2.8, respectively per 100,000 PY in men and 0.5 and 2.8, respectively per 100,000 PY in women. The proportion of incident NHL cases with a non-specific code (NHL NOS) in 2012 totalled to less than 2% of all lymphoid incident cases (n=465, crude incidence 0.7 per 100,000 PY and WASR 0.3 in both sexes).

Regarding myeloid malignancies, MDS and chronic myeloproliferative neoplasms other than CML (MPN), both conditions that were previously classified as neoplasms of uncertain or unknown behaviour in past classifications, are now categorised as malignant (table 3). These two HMs are chronic diseases that group several different disease entities that occur in elderly and represent nearly two-thirds of myeloid malignancies (i.e. more than 6,000 cases estimated in 2012, in France).

Incidence rates and number of estimated new HM cases in 2012, in France are higher in males in most HM subtypes. The highest *sex ratio* was observed for MCL (M/F=4.0) (table 3). Only CHL and AML didn’t show any difference in incidence by sex.

Overall, HM cases are more frequently diagnosed in elderly, but sporadic cases arise in younger ages. The median age at diagnosis was above 70 years for both sexes in ten HMs (CLL/SLL, DLBCL, MCL, MZL, PCN, LL/WM, NHL NOS, MDS, AML, and MPN (i.e. CML excluded)) (table 3). In two lymphoid malignancies, new cases occurred at younger age with a median age lower than 45 years (i.e. CHL: 42 in men and 32 in women, precursor lymphoblastic leukemia /lymphoma (B.T or NOS): 17 in men and 22 in women). Two myeloid malignancies have a median age below 65 years of age (i.e. CML: 62 in men and 64 in women and promyelocytic AML: 57 in both sexes). The highest median age was observed in MDS (78 in men and 81 in women). In most of the HMs studied, the median age was greater in females but may be similar in both sexes in MCL, AML and promyelocytic AML, or lower in women for CHL and mature T-cell NHL (table 3).

***Time trends in incidence over the study period***

The annual rate of change in incidence during the study period is reported in table 4. We identified three different groups of HMs according to their distinct incidence trends patterns showing increased, decreased or stable annual rates of change.

The incidence rates increased during the study period in both sexes for FL and PCN. The annual rate of change in incidence was +3% and +2.2% in men and women, respectively for FL and +2.0% and +1.8% for PCN. In the most recent period (2005-2012), the annual rates were slightly lower (table 4). CHL was relatively stable in men during 1980-2012 and increased in both sexes during the most recent period (2005-2012) (table 4). The annual rate of change in AML was different in men and women showing positive trends during 1980-2012 in women (+1.4%) and an upward trend in incidence during 1980-2005 followed by a downward trend in the most recent period (2005-2012) for men (-1.0%). The same pattern was observed for DLBCL with a positive trend in incidence during 1995-2012 for men (+1.4%) and a slight rise until 2005 followed by a downward trend in incidence in the most recent period (2005-2012) for women (-3.3%). Finally, the annual rate of change CLL/SLL in both sexes showed positive trends during 1980-2005 followed by a downward trend in the most recent period (-1.3% in men and -2.4% women).

Lymphoplasmacytic lymphoma/Waldenström macroglobulinemia (LL/WM) showed decreased annual rates of change in incidence during 1995-2012 in both sexes (-1.2% in men and -1.8% in women). CML annual rates of change in incidence decreased slightly during 1980-2012 in both sexes (-1.0% in men and -0.6% in women) and stabilised in the most recent period of time. Lastly, NHL NOS showed a constant decrease of incidence rates during 1980-2012 in both sexes,particularly in the most recent period of time (-14.7% in men and -12.2% in women during 2005-2012).

PLL/L was the only HM subtype to show relatively stable incidence trends during 1980-2012, although incidence decreased during the most recent period of time in women (-3.5%).

For 6 subtypes, analyses of trends were performed on the most recent period (2003-2012). Among these, MZL showed the highest positive trend in incidence during 2003-2012, in both sexes, with an annual rate of change in incidence of +4.4% in men and +3.6% women. On the contrary, Chronic MPN other than CML were recently reported (from 2001) and showed decreasing trends in incidence during 2003-2012 (-6.4% in men and -4.8% in women).

***The role of demographic change in the evolution of the number of HM cases diagnosed during the study period by subtypes in France, by sex***

Demographic and/or incidence changes may impact the evolution of numbers of new HM cases during the study period. Table 5 describes the global change in number of new HM cases during the study period and the attributable portion due to demographic changes (population changes and ageing) or risk (incidence) change, by sex and HM subtypes.

The number of incident HM cases diagnosed during 1980-2012 tripled for PCN and doubled for AML and CLL/SLL in both sexes: +229.6% in men and +197.2% in women for PCN, +159.1% in men and +146.9% in women for AML, + 129.3% in men and +133.2% in CLL/SLL. For these three HMs, demographic changes explained 87.7%, 67.4% and 71.9% of these increases in men, respectively (table 5). These proportions were slightly lower in women (table 5). Consequently, the increase in the number of cases due to ‘risk’ during the study period was 141.9%, 91.7% and 57.4% in men, respectively. This represents +4,321 new cases in 2012 compared to 1980 that were due to ‘risk’ (e.g. PCN: +2,096, AML: +1,002 and CLL/SLL: +1,223) (data not shown).

Other HM subtypes studied over a shorter period of time such as FL (1995-2009), showed positive trends (+125.8% for men and +82.3% for women) with a relatively low portion due to demographic change in contrast with a high portion due to ‘risk’: +90.2% for men and +50.4% for women).

Interestingly, we also observed sex-specific results for CHL, MDS and MCL. The attributable portion of the global change in number of CHL cases during the study period due to risk was -2.3% in men compared to +33.5% in women (table 5). We observed the same pattern for MDS. Inversely, with the demographic changes in the population during 2003-2012, we expected a +18.7% increase of number of MCL cases in men and +14.3% in women but we observed +38.7% and +2.4% increase in men and women, respectively. Therefore, the portion of the increase due to ‘risk’ was +20% in men and -11.9% in women.

Lastly, for CML and LL/WM in both sexes, we observed a pattern where the demographic changes, if alone, would have led to a greater increase of incident cases than observed in our analysis. Due to population change and ageing, we would expect +41.1% CML male cases in 2012 compared to 1980. However, the global rate of change in the number of CML during the period slightly changed in male (+3.5%). Consequently, the portion due to risk was -37.6% in men (i.e. decrease of risk), leading to a relative stable number of new cases during the study period. The same pattern was observed for LL/WM (table 5).

## 4. Discussion

In this article, we report the first estimations of incidence of haematological malignancies in France according to major subtypes, using newest classification and HMs grouping that is mostly useful for clinicians [8]. These results were based on data from a large number of cancer registries, and a long time period (1980-2012).

We report a low percentage of cases coded as lymphoma NOS (e.g. 5% on average and 2% in 2012), which is an indicator of good quality of diagnosis and coding, that allowed us to calculate the incidence for major NHL subtypes. The US SEER program recently reported a similar proportion of NOS lymphoma cases (e.g. 4.9 %) during 2001-2009 [15], whereas an older study in Europe showed a higher percentage (17.6%) [16]. However, the downward trend in the incidence for lymphoma NOS maybe either due to a better diagnosis by pathologists and/or a more precise coding in the most recent period of time. This recent decrease in the number of cases of lymphoma NOS may have had an impact on upward trends observed in some NHL subtypes, if more cases were diagnosed as a specific HM subtype. In France, we started a training program to improve HM coding in 2005 which may also have led to over coding NHL subtypes [17]. Nevertheless, the annual number of Lymphoma NOS cases is quite low and a putative transfer from NOS codes toward any specific NHL code may only explain a small portion of the rise in incidence for various NHL subtypes.

Overall, the age-standardised incidence rates of HMs in France in 2012 are globally comparable to other industrialised countries. For example, the age-adjusted incidence rate of PCN in 2012 in France is comparable to those of the United Kingdom, [18] and Scandinavia [19]. Another example is the incidence rate in whites in the US [15] which is lower than blacks [20] (although these rates were standardized based on the US population). AML age-adjusted incidence rates are equivalent to the average of the central and southern European countries [16, 21]. The modifications provided by the international classification in 2000 had no major effect on the incidence rates, despite the reduction of the threshold of blast cells that define these proliferations [22]. The consideration of the new classification over a long period could maybe show changes between AML's subcategories, particularly an increase of the incidence of those age-related or in cytotoxic treatments [23]. The incidence rates of FL, published by the registries of the US SEER program, are slightly higher (rates in men and women were 4.0 and 3.4 per 100,000 PY, respectively). One likely explanation could be that these rates were standardized on the US population (close to the European population, yet not similar) and have been calculated on a different period of time (2001-2009), although relatively close to our study [15]. Furthermore, the observed differences could perhaps be attributed to the choice of study methods.

The only European study published to date on HMs incidence by subtype reported a lower incidence rate of DLBCL during 2000-2002 than those estimated in France in 2012, with strong regional variations in Europe [16]. Yet again, a different period of time and a higher percentage of NOS cases might partly explain these discrepancies. A more recent study from the UK reported higher incidence rates of DLBCL and lower incidence rates of FL. These combined variations could be explained by differences in coding rules of these HMs which are characterized based on histological transformations from follicular lymphoma towards DLBCL [18]. However, this does not completely explain the differences observed with the US SEER program where both histological subcategories have a higher incidence than in France.

In our study, we also show that the age-adjusted incidence rates (world standard) for HMs were generally lower in women than men, which is a well-known finding [15-17]. The *sex ratio* (M/F) varied from 1.1 for classical Hodgkin lymphoma to 4 for mantle cell lymphoma. Our results are comparable to previous studies performed by The Haematological Malignancy Research Network, UK [18]. This could be the result of lower exposure to environmental and occupational risk factors as well as hormonal factors in women than men [24]. Uncovering the reason for the difference in the sexes for lymphoma should be a priority for future etiologic research [25].

One of the major interests of this study is to report trends for the major subtypes of HMs and the difference in the total number of cases for a period time due to risk and demographic factors. We have shown upward trends in incidence for PCN and that most of the incidence was due to risk. This positive trend in incidence was not reported in the United States [15] and to a lesser extent in Scandinavia [19]. Changes in definitions, diagnostic criteria or coding rules could explain some of these positive trends. However, it also shows the impact of recent changes in the prevalence of environmental risk factors that may be particularly associated with PCN occurrence. The aetiology of PCN (mostly represented by multiple myeloma) remains largely unknown apart from a family history of a first degree lymphoid haematological or myeloma, a history of monoclonal gammopathy of undetermined origin or black origins [26]. Some evidence suggests that unlike acute leukaemia, PCN can occur after an extremely long latency following exposure to ionising radiation [27]. An association with pesticides was also observed [28]. More recently, an association with a genetic polymorphism on chromosome 8 has been highlighted in a Caucasian population, a locus involved in the occurrence of other cancers [29].

As for FL, the upward trends observed in our data are partially linked to demographic modifications among which the attributable part corresponds to about a third of the increase in the number of new FL cases in both sexes during 1995-2012. These trends are perhaps due to modifications in the way new FL cases are coded. However, this is unlikely to explain the observed increase as it would only concern a small proportion of cases. Indeed, the rule states that a new case of FL histologically transformed into DLBCL at diagnosis should be coded as FL. Furthermore, this increase should have been concomitant with the decrease of the incidence of DLBCL in both sexes (which is not the case).

The sex-specific results regarding the attributable portion of the global change in number of new cases during the study period, due to risk for CHL, MDS and MCL are of valuable interest because this information may provide hypothesis for the causes. For example in CHL, it is interesting to note that the attributable portion of the global change in number of cases during the study period due to risk was -2.3% in men compared to +33.5% in women. This observation could correspond to what has been reported in Northern Europe [30] and Asia [31] with a trend of increased CHL, especially in young female adults with nodular sclerosis histological subtype. These results should be confirmed by a systematic analysis of trends by gender and histologic CHL subtypes in France. If confirmed, this trend would suggest according to the late infection model, that the variation in age-specific CHL incidence patterns is due to the association between socio-economic affluence and infectious disease pressure in childhood [32].

Incidence rates are essential to analyse trends in risk, whereas the number of incident cases is necessary to make provisions for healthcare resources and to evaluate the overall burden of haematological malignancies. Recently, a report focusing on the net survival in France based on a similar method of grouping haematological malignancies was published [33] and should be jointly analysed with the present data on incidence and trends. As the classification of HMs continues to evolve [34-35], detailed investigations of the incidence of HM subtypes should continue to provide clues to the causes of HMs [36]. Our analyses emphasise the striking differences in incidence patterns by histologic subtype strongly suggesting etiologic heterogeneity among haematological malignancies. We advocate the pursuit of epidemiological analysis by subtype such as the InterLymph Consortium initiative on lymphoid neoplasm at international level.

**Note:**

## More detailed results for each haematological site are available from:

http://www.invs.sante.fr/Dossiers-thematiques/Maladies-chroniques-et-traumatismes/Cancers/Surveillance-epidemiologique-des-cancers/Estimations-de-l-incidence-et-de-la-mortalite

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## Conflict of interest:

No author has any conflict of interest to declare.

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**Table 1:** Data used to estimate the incidence of haematological malignancies

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Registry** | *Département* | **Type of registry** | **Years with available data** | **Population (2012)** |
| 1 | Calvados | General a | 1978-2009 | 692049 |
| 2 | Côte-d’Or | Haematopoietic | 1980-2009 | 529967 |
| 3 | Doubs | General | 1978-2009 | 533494 |
| 4 | Gironde | Haematopoietic | 2002-2009 | 1476927 |
| 5 | Hérault | General | 1987-2009 | 1062393 |
| 6 | Isère | General | 1979-2009 | 1237946 |
| 7 | Loire-Atlantique | General | 1998-2009 | 1315880 |
| 8 | Manche | General a | 1994-2009 | 502092 |
| 9 | Orne | Haematopoietic a | 2002-2009 | 293256 |
| 10 | Bas-Rhin | General | 1975-2009 | 1117803 |
| 11 | Haut-Rhin | General | 1988-2009 | 756230 |
| 12 | Somme | General | 1982-2009 | 575153 |
| 13 | Tarn | General | 1982-2009 | 385356 |
| 14 | Vendée | General | 1997-2009 | 650594 |
|  |  |  |  |  |

a The registry of haematopoietic cancers of Basse-Normandie covers the following ”*départements”*: Calvados, Manche and Orne for the period 2002-2009.

**Table 2** : Incidence of haematological malignancies - ICD-O-3 codes eligible for the present study and corresponsing periods of inclusion

|  |  |  |  |
| --- | --- | --- | --- |
| **HMs** | **ICD-O-3 codes** |  | **Usable period: Begin - End** |
|  |  |  |  |
| **Classical Hodgkin lymphoma (CHL)** | *(>=96503 & <=96553 or >=96613 & <= 96673)* |  | 1975-2009 |
|  |  |  |  |
| **Non Hodgkin lymphoma (NHL)** |  |  |  |
| Chronic lymphocytic leukaemia  /small lymphocytic lymphoma (CLL/SLL) | *96703, 98233* |  | 1975-2009 |
| Follicular lymphoma (FL) | *(>=96903 & <=96983)* |  | 1995-2009 |
| Diffuse large B cell lymphoma (DLBCL) | *96783, 96793, 96803, 96843* |  | 1995-2009 |
| Mantle-cell lymphoma (MCL) | *96733* |  | 2003-2009 |
| Marginal zone lymphomas (MZL) | *96893, 96993, 97643* |  | 2003-2009 |
| Plasma cell myeloma (PCN) | *(>=97313 & <=97343)* |  | 1975-2009 |
| LPL/Waldenstrom (LL/WM) | *97613, 96713* |  | 1995-2009 |
| Mature T-cell NHL (MTCL) | *(>=97003 & <=97193) or {97683 ,98273, 98313, 98323, 98343, 99483}* |  | 2003-2009 |
| Precursor lymphoblastic leukaemia   /lymphoma (B,Tor NOS) (PLL/L) | *97273, 97283, 97293, 98353, 98363, 98373* |  | 1990-2009 |
| Lymphoma NOS | 95903,95913 |  | 1975-2009 |
| **Acute myeloid leukaemia (AML)** | *98403, 98603, 98613, 98663, 98673, 98703, 98713, 98723, 98733, 98743, 98913, 98953, 98963,98973, 99103, 99203, 99303, 99313, 98053, 99843* |  | 1975-2009 |
| Acute promyelocytic leukaemia | *98663* |  | 2003-2009 |
| **Myeloproliferative neoplasms** |  |  |  |
| Chronic myelogenous leukaemia (CML) | *98633, 98753, 98763* |  | 1975-2009 |
| Others myeloproliferative neoplasms (MPN) | *99503, 99603, 99613, 99623, 99633, 99643* |  | 2003-2009 |
| **Myelodysplatic syndromes (MDS)** | *99803, 99823, 99833, 99853, 99863, 99873, 99893* |  | 2003-2009 |

**Table 3:** Estimates of incidence rates of haematological malignancies by sex in 2012

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **HMs** |  | **Number of incident cases estimated in France in 2012** | | |  | **Median age at diagnosis** | |  | **Crude incidence rate in 2012\*** | |  | **World age-standardized incidence rate in 2012a** | |  | **Incidence**  **sex ratio** |
|  | **Total** | **M** | **F** |  | **M** | **F** |  | **M** | **F** |  | **M** | **F** |  | **M/F** |
| **Classical Hodgkin lymphoma (CHL)** |  | 1880 | 1033 | 847 |  | 42 | 32 |  | 3.3 | 2.6 |  | 3 | 2.7 |  | 1.1 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Non Hodgkin lymphoma (NHL)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Chronic lymphocytic leukaemia/  small lymphocytic lymphoma (CLL/SLL) |  | 4464 | 2696 | 1768 |  | 71 | 74 |  | 8.7 | 5.4 |  | 4.4 | 2.2 |  | 2.0 |
| Follicular lymphoma (FL) |  | 2530 | 1303 | 1227 |  | 64 | 66 |  | 4.2 | 3.7 |  | 2.5 | 2.1 |  | 1.2 |
| Diffuse large B cell lymphoma (DLBCL) |  | 4096 | 2463 | 1633 |  | 69 | 74 |  | 8 | 5 |  | 4.5 | 2.2 |  | 2.0 |
| Mantle-cell lymphoma (MCL) |  | 659 | 491 | 168 |  | 74 | 74 |  | 1.6 | 0.5 |  | 0.8 | 0.2 |  | 4.0 |
| Marginal zone lymphomas (MZL) |  | 1772 | 866 | 906 |  | 70 | 74 |  | 2.8 | 2.8 |  | 1.5 | 1.2 |  | 1.3 |
| Plasma cell myeloma (PCN) |  | 4888 | 2561 | 2327 |  | 72 | 75 |  | 8.3 | 7.1 |  | 4.2 | 2.9 |  | 1.4 |
| LPL/Waldenstrom (LL/WM) |  | 1247 | 800 | 447 |  | 73 | 74 |  | 2.6 | 1.4 |  | 1.3 | 0.6 |  | 2.2 |
| Mature T-cell NHL (MTCL) |  | 1419 | 870 | 549 |  | 67 | 66 |  | 2.8 | 1.7 |  | 1.7 | 1 |  | 1.7 |
| Precursor lymphoblastic leukaemia /  lymphoma (B, T or NOS) (PLL/L) |  | 810 | 487 | 323 |  | 17 | 22 |  | 1.6 | 1 |  | 1.9 | 1.2 |  | 1.6 |
| Lymphoma NOS |  | 465 | 221 | 244 |  | 76 | 77 |  | 0.7 | 0.7 |  | 0.3 | 0.3 |  | 1.1 |
| **Acute myeloid leukaemia (AML)** |  | 2791 | 1381 | 1410 |  | 71 | 71 |  | 4.5 | 4.3 |  | 2.6 | 2.3 |  | 1.1 |
| Acute promyelocytic leukaemia |  | 193 | 89 | 104 |  | 57 | 57 |  | 0.3 | 0.3 |  | 0.2 | 0.2 |  | 1.0 |
| **Myeloproliferative neoplasms** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Chronic myelogenous leukaemia (CML) |  | 807 | 476 | 331 |  | 62 | 64 |  | 1.5 | 1 |  | 1 | 0.6 |  | 1.7 |
| Others myeloproliferative neoplasms (MPN) |  | 1965 | 988 | 977 |  | 69 | 73 |  | 3.2 | 3 |  | 1.8 | 1.4 |  | 1.3 |
| **Myelodysplatic syndromes (MDS)** |  | 4059 | 2056 | 2003 |  | 78 | 81 |  | 6.7 | 6.1 |  | 2.8 | 1.9 |  | 1.5 |

*a per 100,000. M=male F=female*

**Table 4**: Annual rate of change by subtypes of haematological malignancies by study period.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Annual rate of change in incidence (%)  for a period time  ≥18 yeara** | | |  | **Annual rate of change in incidence (%) for the most recent periodb** | | |
| **Type of HMs** | **Covered period** | **M** | **F** |  | **Covered period** | **M** | **F** |
| **Classical Hodgkin lymphoma (CHL)** | 1980-2012 | -0.1 | 1.2 |  | 2005-2012 | 1.5 | 1.8 |
|  |  |  |  |  |  |  |  |
| **Non Hodgkin lymphoma (NHL)** |  |  |  |  |  |  |  |
| Chronic lymphocytic leukaemia  /small lymphocytic lymphoma (CLL/SLL) | 1980-2012 | 0.9 | 1.1 |  | 2005-2012 | -1.3 | -2.4 |
| Follicular lymphoma (FL) | 1995-2012 | 3 | 2.2 |  | 2005-2012 | 2.6 | 1.9 |
| Diffuse large B cell lymphoma (DLBCL) | 1995-2012 | 1.4 | 0.9 |  | 2005-2012 | 1.2 | -3.3 |
| Mantle-cell lymphoma (MCL) | NA |  |  |  | 2003-2012 | 0.4 | -1.4 |
| Marginal zone lymphomas (MZL) | NA |  |  |  | 2003-2012 | 4.4 | 3.6 |
| Plasma cell myeloma (PCN) | 1980-2012 | 2 | 1.8 |  | 2005-2012 | 1.6 | 1.3 |
| LPL/Waldenstrom (LL/WM) | 1995-2012 | -1.2 | -1.8 |  | 2005-2012 | -1.3 | -1.8 |
| Mature T-cell NHL (MTCL) | NA |  |  |  | 2003-2012 | -1 | -0.4 |
| Precursor lymphoblastic leukaemia   /lymphoma (B.T or NOS) (PLL/L) | 1990-2012 | 0.1 | -0.5 |  | 2005-2012 | 0.1 | -3.5 |
| Lymphoma NOS | 1980-2012 | -7.1 | -6.4 |  | 2005-2012 | -14.7 | -12.2 |
| **Acute myeloid leukaemia (AML)** | 1980-2012 | 1.5 | 1.4 |  | 2005-2012 | -1 | 1.1 |
| Acute promyelocytic leukaemia | NA |  |  |  | 2003-2012 | 0.5 | 4.6 |
| **Myeloproliferative neoplasms** |  |  |  |  |  |  |  |
| Chronic myelogenous leukaemia (CML) | 1980-2012 | -1 | -0.6 |  | 2005-2012 | -0.7 | 0 |
| Others myeloproliferative neoplasms (MPN) | NA |  |  |  | 2003-2012 | -6.4 | -4.8 |
| **Myelodysplatic syndromes (MDS)** | NA |  |  |  | 2003-2012 | -1.1 | 1.9 |

a *The period varies from 18 to 32 years according to the available data and “Largest available period for incidence” for each subtype ; bThe most recent period varies according to the HMs subtype. CLL : Chronic lymphocytic leukaemia/small lymphocytic lymphoma ; M : Male ; F : Female ; NA : Not applicable.*

**Table 5**: Difference in the total number of cases due to risk and demographic factors by subtypes of haematological malignancies and by study period.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Usable period: Begin - End** | **Men** | | | | | |  | **Women** | | | | | |
|  | **Number of cases** | | **Global rate of change (%) for a period time** | **% of variation in the total number of cases into three components:  (%) for a period timeb & for men** | | |  | **Number of cases** | | **Global rate of change (%) for**  **a period time** | **% of variation e in the total number of cases into three components:  (%) for a period timeb & for women** | | |
| **Type of HMs** | **year begina** | **2012** | **due to population size** | **due to age distributionc** | **due to risk (HM’s incidence)** |  | **year begina** | **2012** | **due to population size** | **due to age distributionc** | **due to risk (HM’s incidence)** |
| **Classical Hodgkin lymphoma (CHL)** | 1980-2009 | 882 | 1033 | 17.1 | 17.4 | 2,0 | -2.3 |  | 539 | 847 | 57.1 | 25.2 | -1.6 | 33.5 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Non Hodgkin lymphoma (NHL)** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Chronic lymphocytic leukaemia /small lymphocytic lymphoma (CLL/SLL) | 1980-2009 | 1176 | 2696 | 129.3 | 34.1 | 37.8 | 57.4 |  | 758 | 1768 | 133.2 | 37.3 | 22.9 | 73.0 |
| Follicular lymphoma (FL) | 1995-2009 | 577 | 1303 | 125.8 | 20.3 | 15.3 | 90.2 |  | 673 | 1227 | 82.3 | 17.2 | 14.7 | 50.4 |
| Diffuse large B cell lymphoma (DLBCL) | 1995-2009 | 1409 | 2463 | 74.8 | 15.8 | 18.5 | 40.5 |  | 1057 | 1633 | 54.5 | 14.6 | 14.8 | 25.1 |
| Mantle-cell lymphoma (MCL) | 2003-2009 | 354 | 491 | 38.7 | 7.5 | 11.2 | 20.0 |  | 164 | 168 | 2.4 | 5.4 | 8.9 | -11.9 |
| Marginal zone lymphomas (MZL) | 2003-2009 | 506 | 866 | 71.1 | 9.2 | 10.2 | 51.7 |  | 483 | 906 | 87.6 | 10.0 | 6.6 | 71.0 |
| Plasma cell myeloma (PCN) | 1980-2009 | 777 | 2561 | 229.6 | 48.9 | 38.8 | 141.9 |  | 783 | 2327 | 197.2 | 47.6 | 22.7 | 126.9 |
| LPL/Waldenstrom (LL/WM) | 1995-2009 | 716 | 800 | 11.7 | 10.0 | 25.8 | -24.1 |  | 471 | 447 | -5.1 | 8.9 | 17.0 | -31.0 |
| Mature T-cell NHL (MTCL) | 2003-2009 | 790 | 870 | 10.1 | 5.9 | 9.4 | -5.2 |  | 507 | 549 | 8.3 | 5.8 | 5.8 | -3.3 |
| Precursor lymphoblastic leukaemia   /lymphoma (B.Tor NO) (PLL/L) | 1990-2009 | 436 | 487 | 11.7 | 11.9 | -2.4 | 2.2 |  | 321 | 323 | 0.6 | 11.4 | -2.2 | -8.6 |
| **Acute myeloid leukaemia (AML)** | 1980-2009 | 533 | 1381 | 159.1 | 38.4 | 29.0 | 91.7 |  | 571 | 1410 | 146.9 | 39.5 | 17.7 | 89.7 |
| Acute promyelocytic leukaemia | 2003-2009 | 76 | 89 | 17.1 | 6.3 | 4.5 | 6.3 |  | 58 | 104 | 79.3 | 9.5 | 2.6 | 67.2 |
| **Myeloproliferative neoplasms** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Chronic myelogenous leukaemia (CML) | 1980-2009 | 460 | 476 | 3.5 | 15.4 | 25.7 | -37.6 |  | 289 | 331 | 14.5 | 18.4 | 14.9 | -18.8 |
| Others myeloproliferative neoplasms (MPN) | 2003-2009 | 1532 | 988 | -35.5 | 3.5 | 10.7 | -49.7 |  | 1325 | 977 | -26.3 | 3.9 | 8.5 | -38.7 |
| **Myelodysplatic syndromes (MDS)** | 2003-2009 | 1823 | 2056 | 12.8 | 6.1 | 17.6 | -10.9 |  | 1391 | 2003 | 44.0 | 7.6 | 14.0 | 22.4 |

**a** *First year of the usable period, b The period varies from 18 to 29 years according to the available data and “usable incidence period” for each subtype ; c differences due to the population structure (age distribution)*

**Figure 1:** Number of incident haematological malignancies cases in men and women in France: estimates for 2012.

**Figure Legends: (**AML) Acute myeloid leukaemia (CHL) Classical Hodgkin lymphoma (CLL/SLL) Chronic lymphocytic leukaemia/Small lymphocytic leukaemia (CML) Chronic myelogenous leukaemia (DLBCL)  
Diffuse large B cell lymphoma (FL) Follicular lymphoma (LL/WM) LPL/Waldenstrom (MCL) Mantle-cell lymphoma (MTCL) Mature T-cell NHL (MZL) Marginal zone lymphomas (MDS) Myelodysplatic syndromes(MPN)Others myeloproliferative neoplasms (PCN) Plasma cell neoplasms (PLL/L) Precursor lymphoblastic leukaemia /lymphoma (B.Tor NOS)

fig1