Herpes zoster: Burden of disease in France.

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Abstract

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This work provides estimates of HZ incidence and HZ-related hospitalization and mortality rates in France, where no immunization programme has been implemented. Herpes zoster data was obtained from the Sentinelles surveillance general practitioners (GPs) network, the PMSI Data processing centre for hospital discharges and from the French National Mortality Database (INSERM CépiDC). The yearly HZ incidence rate averaged 382 cases per 100,000 inhabitants (95% CI 364–405) and exponentially increased with age. The annual rates of hospitalizations and mortality due to HZ varied from 4.14 ± 0.32 to 14.42 ± 0.39 and from 0.11 ± 0.03 to 0.29 ± 0.04 per 100,000 inhabitants, respectively, depending on whether HZ was coded in a 'primary' or 'primary or associated' diagnosis. One or more factors of immunodepression occurred in 43.4% of hospitalized cases and in 21.6% HZ-related deaths.

Keywords

Herpes zoster, hospitalization, mortality.

1. Introduction

There is a concern regarding herpes zoster (HZ) epidemiological trends since the prevalence of people with risk factors for HZ, such as older age or other immunodepression factors (malignancies or diabetes, for example) is increasing over time [1–4]. Also, an ageing population could result in an increase in the use of corticosteroid therapy, an important risk factor for HZ [5]. Moreover, the epidemiological impact of generalized vaccination against varicella on HZ is of concern, as this could result in an increase in HZ incidence due to fewer opportunities for varicella exposure, which is thought to boost specific immunity [6]. However, to date, varicella vaccination in France has only been available since 2007, and only then for a small proportion of the population, i.e. adolescents and child-bearing aged women with a negative or doubtful history of varicella. Consequently, varicella vaccine coverage remains very low and probably does not have an influence on HZ epidemiological trends. Regarding the herpes zoster vaccine, as for varicella, it is still not in use in France. In this context, current HZ epidemiological data are necessary to estimate the impact of this disease on public health and to guide future vaccination policies.

A national surveillance of HZ was set up in France in 2005, conducted by the French general practitioners' Sentinelles surveillance network [7], which also reports on another nine health indicators (flu, diarrhoea, male urethritis, chickenpox, Lyme disease, asthma, mumps, suicide attempts, hospitalizations). We report the results from the first years of this national HZ surveillance. We also retrieved data from national hospitalization and mortality statistics to estimate hospitalization and mortality rates due to HZ in France. Finally, the objective of this work was to assess the overall burden of HZ disease in France, in a pre-vaccination era.

2. Methods

2.1. Data source

2.1.1. Incidence and characteristics of herpes zoster cases

The members of the French general practitioners' Sentinelles electronic surveillance network, about 1200 voluntary, unpaid general practitioners (GPs), report cases of communicable diseases every week in a standardized and automated manner [7]. The characteristics of the GPs of the Sentinelles network are comparable to those of all French GPs regarding regional distribution, proportion in rural practice, type of practice and distribution of main clinical skills [8]. For surveillance purposes, a case of HZ is clinically defined as an acute and painful vesicular rash with a dermatomal distribution. For each patient with a diagnosis of HZ, GPs are asked to describe the age, gender, the need for hospitalization and the reason, the presence of immunodepression and its origin (drug induced or not) and the location of HZ (ophthalmic, disseminated or others). Data recovered for HZ were collected from January 1, 2005 (onset of HZ surveillance by the Sentinelles network) to December 31, 2008.

2.1.2. Herpes zoster hospitalizations

Hospitalization data were collected by reviewing all hospital discharge reports containing a HZ code from January 1, 2000 to December 31, 2006 (last available data at the time of writing this paper), obtained through the PMSI Data Processing Centre [9]. This database is a national register of all discharges from all short-stay/acute-care hospitals. It collects data described by the physicians who took care of the patients during their hospitalization, using the International Classification of

Diseases, Tenth Revision (ICD-10). Herpes zoster-related hospitalization was defined as either a hospital discharge report with a primary HZ diagnosis code (ICD-10 codes B02.0–B0.2.9), or a hospital discharge report with an associated HZ diagnosis code. Information on age, sex, length of hospital stay and the presence of underlying medical conditions known to increase the severity or risk of occurrence of HZ (human immunodeficiency virus/AIDS, blood dyscrasia and some immune deficiencies, malignancies, diabetes, malnutrition, rheumatoid arthritis and other connective tissue diseases and organ transplantation) was also obtained from the hospital discharge reports.

2.1.3. Herpes zoster deaths

Herpes zoster mortality was assessed through the French National Mortality Database (INSERM CepiDC) for deaths between January 1, 2000, and December 31, 2007 (the last available data at the time of writing this paper) [10]. This database includes all deaths in France. Herpes zoster death was defined as any death certificate with an International Classification of Disease code for HZ and its complications (ICD-10codes B02.0–B02.9) as primary or associated cause. Information on age, sex, and the presence of underlying medical conditions known to increase the severity or risk of occurrence of HZ was also obtained.

2.2. Analysis

To get the yearly national incidence rate, the mean number of cases per Sentinelles GP (standardized according to their participation and their geographical distribution) was multiplied by the total number of GPs in France and the result was then divided by the population of that year, using the French population included in national

censuses as a reference [2]. Age-specific incidences were estimated for the following age groups: 1–14, 15–24, 25–34, 35–44, 45–54, 55–64, 65–74, 75–84, 85–94 and ≥95 years. Calculation of the 95% confidence interval was based on the assumption that the number of reported cases followed a Poisson distribution. The lifetime risk of at least one occurrence of HZ was estimated by a crude calculation of [1 - (1 - overall annual incidence) $^{\text{life expectancy}}$] based on all individuals living to 80.35 years, which was the average life expectancy from 2004 to 2006 in France [11]. Hospitalization and mortality rates were calculated in a similar way, by dividing the mean annual number of cases obtained from the databases by the yearly French population. The results were expressed as means with their range, and percentages with their 95% confidence interval (95% CI). The Chi-2 analysis was used for comparison of HZ incidence rates with sex and age. All statistical tests were performed at the 0.05 alpha level.

3. Results

3.1. Incidence and characteristics of HZ

In the general population, during the period of 2005 to 2008, 2375 HZ cases were reported by GPs of the French Sentinelles network. The average yearly number of cases reported by each Sentinelles GP was 3.31 (95% CI 2.82–3.80).

The yearly HZ incidence rate averaged 382 cases per 100,000 inhabitants (95% CI 364–405) (Table1). The estimated lifetime risk of a person having one occurrence of HZ was 26.5%. Over the four years of surveillance, there was no particular temporal trend of incidences (Figure 1).

The mean age of HZ patients was 56 years ± 0.34 and the median age was 60 years old (range: 8 months to 102 years). A linear HZ incidence rate increase with age was observed ($p<0.001$) (Table 1).

Females represented 57.7% of HZ cases (95% CI 55.6–59.7). The age-adjusted relative risk of HZ for females vs. males was 1.15 (95% CI 1.12–1.18, $p<0.05$).

HZ ophthalmicus amounted to 6.5% of the reported cases (95% CI 5.2%–7.8%). This proportion peaked for cases occurring in persons ≥85 years old (13.1% $p<0.005$).

The overall percentage of reported HZ cases with an associated immunodepression condition was 4.7% (95% CI 3.8%–5.6%), mostly due to drug-induced immunodepression (67.3%).

The GPs declared that they hospitalized 25 subjects of the 2193 cases for whom information was available (1.13%, 95%CI 0.75%–1.65%). Their average age was 64.0 ± 9.1 years old and patients aged between 85 and 94 years were the most frequently hospitalized (3.7%, $p<0.005$). A higher rate of hospitalization was reported for immunodepressed people compared to non- immunodepressed people (11.0% and 0.8%, respectively) ($p<0.05$).

3.2. Herpes zoster hospitalizations

Over the seven-year study period, 61,429 hospital discharges with a primary or associated HZ code were identified, representing a mean of 8728 ± 237 hospitalizations per year (Table 2) and a mean annual HZ hospitalization rate of 14.21 ± 0.70 hospitalizations per 100,000 inhabitants (Table 1). Herpes zoster-related hospital discharges with a primary HZ code amounted to 17,661 (28.8% of all

hospitalizations) during the study period, representing a mean of 2523 ± 193 hospitalizations per year and a mean annual hospitalization rate of 4.14 ± 0.32 hospitalizations per 100,000 inhabitants.

According to gender, the annual hospitalization rate for HZ with a primary or associated diagnosis was 14.92 ± 0.43 per 100,000 females vs. 13.61 ± 0.42 per 100,000 males ($p<0.005$). For hospitalization with an HZ code as the primary diagnosis, the hospitalization rate was 4.44 ± 0.62 per 100,000 females vs. 3.61 ± 0.65 per 100,000 males ($p<0.001$). Stratified by age, for females and males, the relative risk for hospitalization with primary and associated HZ diagnoses amounted to 0.79 per 100,000 (95% CI 0.73–0.84) for the ≤ 64 years age group and 1.06 per 100,000 (95% CI 1.01– 1.12) for the ≥ 65 years age group ($p<0.001$). For HZ as a primary diagnosis, this relative risk amounted to 0.91 (95% CI 0.80– 1.02) for the ≤ 64 years age group and 1.20 (95% CI 1.08–1.34) for the ≥ 65 years age group ($p=0.800$).

For all hospitalizations, the mean age was 72 ± 0.43 years. Patients older than 55 years represented 64.1% of hospitalized cases. A linear increase in the HZ hospitalization rate with age was observed ($p<0.001$) (Tables 1 and 2).

The average length of stay for all hospitalizations was 9.18 ± 0.10 days. It was 8.1 ± 0.1 days for hospitalizations with HZ as the primary diagnosis and 10.0 ± 0.1 days for hospitalizations with HZ as an associated code.

Underlying conditions known to increase the severity of HZ were coded in at least 26,686 out of 61,429 hospital discharges (43.4%). Malignancies, human immunodeficiency virus infection and diabetes were the most prevalent conditions. Details of these underlying conditions are shown in Table 3.

For hospitalizations where HZ was coded as an associated diagnosis, the most frequently primary diagnosis codes were ‘Factors influencing health status and contact with health services’ (ICD-10 Z codes) in 28.7% of cases and ‘Diseases of the nervous system’ (G codes) in 11.1% of cases (Table 4). Among the Z codes, 39.7% was associated with malignancies.

For hospitalizations where HZ was coded as B02.9 (‘HZ without complications’), 27.6% corresponded to a primary code and 72.4% to an associated code. When the B02.9 code was used as an associated diagnosis, the most frequent primary diagnosis codes were ‘Factors influencing health status and contact with health services’ (ICD-10 Z codes) in 33.6% of cases and ‘Symptoms, signs and abnormal clinical and laboratory findings, not classified elsewhere’ (R codes) in 8.71% of cases (Table 4). Among the Z codes, 39.0% were most frequently associated with malignancies and 6.96% with dialysis. Among the R codes, 15.2% were most frequently associated with ‘malaise and fatigue’.

3.3. Herpes zoster mortality

For the period of 2000 to 2007, HZ as a primary or associated diagnosis was coded in 1405 death certificates, i.e. an average of 176 ± 13 HZ-related deaths per year. When HZ was coded as the primary diagnosis, it represented 39% of the overall death certificates with an HZ code. The average HZ mortality rate per year was 0.29 ± 0.04 per 100,000 inhabitants when considering all deaths including an HZ code, either as a primary or an associated diagnosis (Table 1). It was 0.11 ± 0.03 per 100,000 inhabitants when only considering death certificates with a primary HZ diagnosis.

For HZ as a primary diagnosis, the age-specific mortality rate was 0.03 ± 0.01 per 100,000 for the ≤64 years age group and 4.36 ± 0.20 per 100,000 for the ≥65 years age group, among whom 96.8% of deaths occurred. A linear increase of HZ death rate with age was observed ($p<0.001$). The highest mortality rate was observed in females of the ≥65 years' age group (5.76 HZ-related deaths per 100,000 female death certificates).

At least one underlying condition known to increase the severity of HZ was coded in 21.6% of deaths. Malignancies, blood dyscrasia and some immune deficiencies and diabetes were the most prevalent conditions. Details of these underlying conditions are shown in Table 3.

For deaths where HZ was coded as an associated diagnosis, the most frequent primary diagnosis codes were 'Diseases of the circulatory system' (ICD-10 I codes) in 30.1% of cases, 'Neoplasms' (C codes) in 25.6% of cases and 'Diseases of the respiratory system' (J codes) in 6.63% of cases (Table 4).

Herpes zoster-related deaths corresponded to a 'HZ cases without complication' code (B02.9) in 53.6% of HZ-related deaths. The primary diagnosis for deaths where B02.9 code was used as associated diagnosis was 'Diseases of the circulatory system' (ICD-10 I codes) in 31.7% of cases and 'Neoplasms' (C codes) in 28.0% of cases.

4. Discussion

This work provided estimates of HZ incidence and HZ-related hospitalization and mortality rates according to age in a country where no immunization has yet been implemented since unanswered questions regarding the epidemiological impact of a large-scale implementation of immunization remain to be answered [6]. The results

show that even though this disease involves all age groups, the incidence of HZ and the hospitalization and mortality rates increased exponentially with age, as expected.

The only epidemiological published data on HZ in France were issued from two surveys conducted in 1998, which permitted an estimate of annual incidence rate of 320 to 480 cases per 100,000 inhabitants, which is within the same range as the incidence estimated in the present study [12, 13]. Other HZ data in France, such as hospitalization and mortality related to HZ, have not yet been analyzed in other studies. The age-specific yearly HZ incidence rates observed in France in the general population and reported here correspond to those previously published for the USA [14] as do the French mortality and hospitalization rates per population [15]. In other countries, incidence rate estimates varied between 159 per 100,000 inhabitants in Italy [16] and 340 per 100,000 in the Netherlands [17]. Different survey designs, case recruitment, selected populations and lengths of assessment may explain the variations encountered. Time trends have shown that the incidence of HZ could be increasing in the USA as varicella vaccine coverage in children has increased and the incidence of varicella has decreased [18], resulting in a diminishing natural exposure to the varicella zoster virus and a consequent decrease in immunity against this virus in subjects with latent infection. This observation remains to be confirmed as others surveys found no change in HZ incidence rates [19, 20] or observe an increased incidence rate before the initiation of varicella vaccination [6]. The same increase has been shown regarding HZ-related hospitalizations [21]. The widespread vaccination of children against varicella would be only one of several possible explanations if the observed increase in HZ incidence and hospitalizations are confirmed in the future. Maintaining an operational surveillance system of HZ incidence is important in this context, such as the one reported in the present study.

The complications of HZ tend to be more severe in older adults than in children [1]. In previous studies, the risks of hospitalization and death were highest in the ≥65 year age group [16, 22 and 23]. For instance, the risk of hospitalization was 12 to 21 times greater in this age group compared to hospitalization rates in the ≤64 year age group in the Netherlands, the UK and Canada [24]. Our estimates showed a lower trend, where the risk of hospitalization was only eight times greater for the ≥65 years age group. However, our results showed that case fatality and hospitalization rates, far from being uniformly distributed in adults, are greatly dependent on age.

The topic of immune compromise is difficult as the relative importance of various diseases, drugs and other therapies is not truly known. However, some underlying conditions, most often immunodeficiencies, are related to an increased risk or severity of HZ incidence [5, 25]. This is in accordance with the higher frequency of underlying conditions among hospitalized cases vs. non-hospitalized cases as seen by the GPs in the present study. At least one underlying condition, most frequently malignancies, was found in 43.4% of hospitalizations with an HZ code, a higher proportion than previously reported in the USA or Spain [22, 26]. However, more than half of those who were hospitalized for HZ were also previously healthy individuals.

As observed for underlying conditions, malignancies were also frequent when analysing primary diagnosis for hospitalizations and deaths where HZ was coded as an associated diagnosis. Diseases of the nervous system were frequent primary diagnoses for hospitalizations with an associated HZ code, besides ‘HZ without complications’ code, as expected.

It is unclear whether, or why, the risk of herpes zoster disease is higher in females [1]. The predominance of HZ in females might be ascribed to a higher

proportion of females in the older population [13]. However, after age adjustment, the relative risk was still higher among females in the present study. A Dutch study confirmed that female gender independently increased the risk of HZ, but only in the 25 to 64 year age groups [27]. An increased incidence in women was also reported in the United Kingdom, and recently in Taiwan [11, 28].

Post-herpetic neuralgia (PHN) data is not included in the Sentinelles network questionnaire. It is invariably defined in the literature as the persistence of pain for more than one, three or six months after the onset of the HZ rash, with variable pain severity [13]. It is estimated to occur in 8% to 20% of cases at one month and 4.5% to 8% at 3 months [29]. Extrapolating this data to the national incidence gave about 18,000 to 55,000 annual cases of this HZ complication when considering the first definition and 10,000 to 22,000 annual cases with the second one.

This study had strength and limitations. It is estimated that HZ data from the Sentinelles surveillance is representative of HZ cases diagnosed by French GPs. However, there is a risk that the incidence of HZ was underestimated because this data is only reported by GPs. Hence, patients who consulted a paediatrician, a dermatologist, or who went to a hospital emergency unit were not accounted for. Other biases for incidence rate estimation may also appear as younger patients may not seek medical advice for an HZ case while older patients may have more severe and recurrent cases needing medical monitoring.

Herpes zoster cases are unlikely to be confused with other conditions causing vesicles with a dermatomal distribution. At the same time, we cannot completely rule out the possibility that certain cases of disseminated HZ in elderly adults might have been misclassified as primary varicella or other conditions, such as herpes simplex. However, previous studies conducted among general practitioners suggested that

the positive predictive value of a clinical diagnosis for serologically confirmed cases of HZ is over 90% [30].

There were several limitations associated with using hospitalization and death records: diagnostic errors, inadvertent omissions, the underreporting of pre-existing conditions, the unavailability of medical records to the certifying physician and difficulties in determining the underlying cause of death and hospitalization when several disease processes were involved [28]. Moreover, a HZ diagnosis code may be assigned to hospitalizations for another cause for a person with coincidental HZ [15]. There could be also repeated admissions of the same patient leading to an overestimated hospitalization rate [31]. The retrospective nature of the present study might then question the accuracy of the mortality and hospital discharge data. Notwithstanding, the hospitalization and mortality data were obtained from the full set of hospital discharge reports and death certificates, which certainly minimized under-diagnosis and deficiencies in reporting. The hospitalization rate for HZ coded as a primary diagnosis in the present study is, in fact, similar to those published by the Netherlands (3.1/100,000) [24] and England (4.4/100,000) [32]. Moreover, an outpatient study of HZ in which case finding was based in ICD diagnostic codes showed that the positive predictive value of a diagnostic code of HZ was 89-96% [26].

Regard a death certificate, quality assurance is maintained by trained nosologists who code conditions at the national level. We included separate estimates for hospitalizations and deaths with a primary diagnosis of HZ, which prevented overestimation of hospitalization and death rates. Regarding HZ-related deaths, the estimate reported here is probably an underestimation of the role of HZ in mortality. Indeed, reactivation of HZ infection has previously been associated with an

increased risk of death in the three years following an infection in immunocompetent older people, although the deaths were not directly correlated with such an infection, but occurred for various other reasons. This suggests that HZ infections may be a marker of early mortality, besides having a direct role in death, as shown here by the death statistics.

Data from the GPs' Sentinelles network and administrative hospitalization and death databases enabled an updated and ongoing description of the epidemiology of HZ in France. The estimates provided here confirm the strong dependence of HZ-related incidence, hospitalization and mortality rates on age, and the higher risk in women compared to men.

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Table 1. Average annual incidence rate (2005-2008), hospitalization rate (2001-2006) and mortality rate (2000-2006) for HZ in France, per 100,000 inhabitants.

Age group (years)	**Incidence** per 100,000 inhabitants (range)	**Hospitalization** per 100,000 inhabitants (95% CI)	**Mortality** per 100,000 inhabitants (95% CI)
0–14	184 (134–232)	2.45 (2.16–2.74)	0.003 (0–0.014)
15–24	157 (131–215)	2.50 (2.21–2.79)	0.005 (0–0.020)
25–34	174 (161–206)	5.04 (4.62–5.46)	0.009 (0–0.031)
35–44	169 (122–206)	8.41 (7.87–8.94)	0.029 (0–0.064)
45–54	416 (385–454)	10.48 (9.88–11.10)	0.031 (0–0.069)
55–64	577 (497–696)	14.39 (13.70–15.10)	0.072 (0.009–0.135)
65–74	868 (689–1051)	34.03 (32.96–35.11)	0.236 (0.102–0.370)
75–84	985 (862–1046)	57.30 (55.90–58.70)	1.25 (0.90–1.60)
85–94	1077 (895–1350)	105.9 (104.0–107.8)	7.24 (5.66–8.82)
≥95	1437 (0–2485)	84.07 (82.37–85.76)	19.48 (11.50–27.47)
Total	382 (341–444)	14.21 (13.52–14.91)	0.286 (0.244–0.328)

Table 2. Average annual number of HZ-related hospitalizations, by age-group, France, 2001-2006.

Age-group (years)	**HZ with meningitis, encephalitis or other nervous system involvement** (ICD-10 code B02.0-2)	**HZ ophtalmicus** (ICD-10 code B02.3)	**Disseminated HZ** (ICD-10 code B02.7)	**HZ with other complications** (ICD-10 code B02.8)	**HZ without complications** (ICD-10 code B02.9)	**Annual number of hospitalizations** (%)
0–14	20.4	26.9	13.3	23.7	191.1	275.4 (2.8%)
15–24	28.9	17.3	8.6	22.9	119.6	197.1 (2.0%)
25–34	43.1	34.6	18.9	32.9	271.6	400.9 (4.1%)
35–44	58.9	57.4	43.7	66.3	507.3	733.6 (7.5%)
45–54	79.9	70.1	38.9	88.3	605.9	883.0 (9.1%)
55–64	94.9	117.1	50.7	115.4	622.1	1000.3 (10.3%)
65–74	177.6	188.6	48.9	250.7	1064.7	1730.4 (17.8%)
75–84	285.0	276.0	46.6	293.7	1330.4	2231.7 (22.9%)
85–94	167.1	178.4	26.0	129.3	676.3	1177.1 (12.1%)
≥ 95	10.4	14.7	3.0	9.6	61.0	98.7 (1.0%)
All ages	966.1 (9.9%)	981.1 (10.1%)	298.4 (3.1%)	1032.7 (10.6%)	5440.0 (66.3%)	8728.2 (100.0%)

ICD-10: International Classification of Diseases, Tenth Revision

Table 3. Annual number of HZ hospitalized cases and HZ deaths in France with underlying conditions known to increase the severity or risk of occurrence of herpes zoster.

Underlying condition	International classification of diseases, tenth revision, codes used to determine underlying conditions	Number of hospitalizations with a primary or associated HZ diagnosis (%)	N° of deaths with a primary or associated HZ diagnosis (%)
Malignancies	C000-C970; D370-D480	10599 (34.3%)	449 (59.6%)
Human immunodeficiency virus/ AIDS	B200-B249	7277 (23.6%)	26 (3.45%)
Diabetes	E100-E140	5682 (18.4%)	94 (12.5%)
Blood dyscrasias and some immune deficiencies	D590-D890	2099 (6.8%)	82 (10.9%)
Rheumatoid arthritis and connectives tissues diseases	M05-M06; M30-M36	2160 (7.0%)	38 (5.04%)
Malnutrition	E400-E460; E500-E640	1033 (3.3%)	64 (8.49%)
Organ transplantation	Z94	2023 (6.6%)	1 (0.13%)

AIDS: acquired immune deficiency syndrome

Table 4. Primary diagnosis codes for hospitalizations and deaths where HZ was coded as an associated diagnosis.

Primary diagnosis codes (ICD-10)	**Hospitalizations where HZ was coded as an associated diagnosis** (n=43,768)		**Deaths where HZ was coded as an associated diagnosis** (n=860)	
	B02.9 codes (n=27,736)	**others HZ codes** (n=16,032)	**B02.9 codes** (n=558)	**others codes** (n=302)
'Factors influencing health status and contact with health services' (Z codes)	9,309 (33.6%)	3,273 (20.4%)	0	0
'Symptoms, signs and abnormal clinical and laboratory findings, not classified' elsewhere' (R codes)	2,415 (8.71%)	1,127 (7.02%)	0	0
'Diseases of the circulatory system' (I codes)	2,277 (8.20%)	960 (5.99%)	177 (31.7%)	82 (27.2%)
'Diseases of the respiratory system' (J codes)	1,886 (6.80%)	700 (4.37%)	35 (6.27%)	22 (7.28%)
'Diseases of the digestive system' (K codes)	1,565 (5.64%)	526 (3.28%)	17 (3.05%)	5 (1.66%)
'Malignancies' (C codes)	1,553 (5.60%)	610 (3.80%)	156 (28.0%)	64 (21.2%)
'Diseases of the nervous system' (G codes)	1,221 (4.40%)	3,634 (22.7%)	27 (4.84%)	22 (7.28%)
'Certain infections and parasitic disease' (A/B codes)	1,351 (4.87%)	674 (4.20%)	38 (6.81%)	16 (5.30%)
'Endocrine, nutritional and metabolic diseases' (E codes)	795 (2.87%)	347 (2.16%)	23 (4.12%)	18 (5.96%)
'Diseases of the eye, ear and mastoid process' (H codes)	567 (2.04%)	2,186 (13.6%)	35 (6.27%)	0
'Diseases of the genitourinary system' (N codes)	863 (3.11%)	292 (1.82%)	11 (1.97%)	7 (2.32%)
Others	3,934 (14.2%)	1,703 (10.6%)	67 (12.0%)	66 (21.9%)

Figure 1. Weekly incidence rate of HZ in France as estimated by the general practitioners' Sentinelles network during the HZ surveillance period.