Article

What We Know About Sting-Related Deaths? Human Fatalities Caused by Hornet, Wasp and Bee Stings in Europe (1994-2016)

Xesús Feás [1,2*], Carmen Vidal [3,4] and Susana Remesar [5]

[1] Academy of Veterinary Sciences of Galicia, Edificio EGAP, Rúa Madrid, No. 2-4, 15707 Santiago de Compostela, Spain; xesusfeas@gmail.com
[2] Fundación Instituto de Investigación Sanitaria de Santiago de Compostela (IDIS), Hospital Clínico, Edificio D, 1ª Planta, Travesía da Choupana S/N, 15706 Santiago de Compostela, (A Coruña), Spain; Xesus.Feas.Sanchez@sergas.es
[3] Servizo de Alergoloxía, Área Sanitaria de Santiago de Compostela e Barbanza, Hospital de Conxo, Rúa de Ramón Baltar S/N, 15706 Santiago de Compostela, (A Coruña), Spain; carmen.vidal.pan@sergas.es
[4] Área de Medicina, Departamento de Psiquiatría, Radioloxía, Saúde Pública, Enfermaría e Medicina, Facultade de Medicina e Odontoloxía, Rúa San Francisco S/N, 15782 Santiago de Compostela, (A Coruña), Spain; mdelcarmen.vidal@usc.es
[4] INVESAGA Group, Departamento de Patoloxía Animal, Universidade de Santiago de Compostela, Avda. Carvalho Calero s/n, 27002 Lugo, Spain; susana.remesar@usc.es

* Correspondence: xesusfeas@gmail.com

Simple Summary: Fatalities due to stinging insects are poorly documented. Epidemiology of Hymenopteran-related deaths in 32 European countries based on official registers over a 23-year period (1994-2016) is described. The incidence of insect-sting mortality in Europe is statistically low, but not negligible. The countries with the highest and lowest fatalities per million inhabitants per year were: Estonia (0.61), Austria (0.6) and Slovenia (0.55); and Ireland (0.05), United Kingdom (0.06) and the Netherlands (0.06), respectively. The majority of deaths (n=1,691) occurred in males (78.1%), within the age group of 25-64 years (66.7%), and in an "unspecified place" (44.2%). The frequency of stings, and thus of subsequent reactions, is dependent on geographic, environmental, and ecological factors. With the expansion of new non-native Hymenopteran species across Europe, allergists should be aware that their community's exposures may continue changing. It is necessary to produce, assemble and interpret information and knowledge using diverse sources and in an interdisciplinary way. As part of the One Health philosophy, people and hornets, wasps and bees, as well as the environment that they share are closely connected.

Abstract: Epidemiology of Hymenopteran-related deaths in Europe due to bee, wasp and hornet stings (Cause Code of Death: X23) based on official registers from WHO Mortality Database is described. Over a 23-year period (1994-2016), a total of 1,691 fatalities were officially recorded, mostly occurring in Western (42.8%) and Eastern (31.9%) Europe. The victims tended to concentrate in: Germany (n=327; 1998-2015), France (n=211; 2000-2014) and Romania (n=149; 1999-2016). The majority of deaths occurred in males (78.1%), within the age group of 25-64 years (66.7%), and in an "unspecified place" (44.2%). The X23 gender ratio (X23GR) of mortality varied from a minimum of 1.4 for Norway to a maximum of 20 for Slovenia. The highest X23MR, expressed in terms of annual rates and per million inhabitants, were recorded in countries from Eastern Europe (0.35) followed by Western (0.28), Northern (0.23) and Southern Europe (0.2). The countries with the highest and lowest mean X23MR were Estonia (0.61), Austria (0.6) and Slovenia (0.55); and Ireland (0.05), United Kingdom (0.06) and the Netherlands (0.06), respectively. Country-by-country data show that the incidence of insect-sting mortality is statistically low, but not negligible.

Keywords: Hymenoptera; insect; bee; wasp; hornet; epidemiology; fatalities; venomous animals; public health

 doi:10.20944/preprints202112.0483.v1

1. Introduction

Anaphylaxis is an acute, life-threatening reaction that occurs shortly after contacting with a trigger. It is classically defined as the most severe form of an allergic reaction, but it could also be induced by non-IgE mediated pathways through the activation of mast cells and basophils through different mechanisms. Common triggers of anaphylaxis include: foods, drugs, venoms from insects, general anaesthetic, radiocontrast agents, and latex, among others, and their prevalence vary from region to region and depending on the patient group [1].

The medically important groups of the Hymenoptera order in Europe are those of the genus *Apis* (honey bees) and *Bombus* (bumble bees) in the family Apidae; *Vespula* (yellowjackets), *Dolichovespula* and *Vespa* (hornets) and *Polistes* (paper wasps) of the family Vespidae [2]. Social Apidae and Vespidae possess a large and comprehensive array of venom components [3]. Hymenoptera venoms are complex mixtures of biologically active proteins and peptides, some of them common to different species such as phospholipases, hyaluronidase, phosphatase, α-glucosidase, serotonin, histamine, dopamine, noradrenaline, and adrenaline. Besides, melittin, apamin, and mast cell degranulating peptide are exclusive to bees, while mastoparan and bradykinin are only found in wasps [4-9]. As a rule, Hymenoptera species are not especially predisposed to attack and sting humans; however, social hornets, wasps, and bees have developed a protecting response to whatever risk the colony faces through stings.

With each sting, Hymenopterans inject a small amount of venom that can cause reactions of varying intensity: (i) normal local reactions (NLR), (ii) large local reactions (LLR), (iii) systemic anaphylactic reactions (SAR), (iv) systemic toxic reactions (STR) and (v) unusual reactions (UR) [10]. The local reaction is limited to the area of the sting and is usually small in size, with redness, swelling, itching, and intense pain. If a person has a large reaction in the area of the sting, greater than 10 cm, it may mean that he or she has been sensitized but, as a rule, it does not need any special action. SAR reactions are those that cause symptoms beyond the point of the sting and can range from skin lesions to respiratory problems, digestive symptoms or anaphylaxis. The prevalence of SAR in Europe due to Hymenoptera stings ranged between 0.3 and 7.5% in adults and 0.15–3.4% in children [11]. STR are commonly due to multiple Hymenoptera stings because of the well-known toxic properties of their venoms. UR occur in a temporal relationship to hornet, wasp and bee stings, differ from typical allergic symptomatology and in some cases follow-up is required over many months [12].

At some point of their lifetime, 94.5% of humans are stung by wasps, honey bees, hornets or bumble bees [13]. Although most of these stings are not reported, general practitioners attend a large number of patients with Hymenoptera stings, and a few of them required rapid assistant at emergency departments. Thus, in USA, it was estimated 220,000 annual visits to the emergency department and nearly 60 deaths per year due to Hymenopteran stings. In addition, an analysis of 4,000 cases of anaphylaxis from Germany, Austria and Switzerland, show insect venom (n = 2074; 50.1%) as a common trigger of anaphylaxis [1]. For these reasons, researchers highlight that an effective and affordable treatment for anaphylaxis caused by these arthropods is critical [14].

In the last years, health risks and deaths caused by Hymenopteran stings have become a worldwide public health concern [15,16]. Despite the number of cases presented, this health problem can be underestimated. The lack of realistic mortality epidemiological data still is missing in some countries [17]. Information on the incidence of fatalities due Hymenoptera stings is crucial for an assessment of the problem, as well as for enhancing medical assistance for patients and creating public policies aimed to decrease the incidence of these events [18,19]. Around 40–85% of the people with sting fatal reactions had no documented records of preceding anaphylactic episodes [20,21].

Under the current International Classification of Diseases and Related Health Problems 10th Revision (ICD-11), Chapter XX permits the classification of environmental events and circumstances as the cause of injury, poisoning and other adverse effects.

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 30 December 2021 doi:10.20944/preprints202112.0483.v1

Fatalities due to hornet, wasp and bee stings (including yellow jackets) are coded as single category, the X23 [22]. The incidence of insect-sting mortality around the world ranged from 0.03 to 0.48 fatalities per 1,000,000 inhabitants per year being statistically low but not negligible [20].

Fatalities due to stinging insects are poorly documented. There is a need to improve the epidemiology of Hymenopteran related deaths in order to get more accurate, informative and contemporary figures. Therefore, to fill this gap, the aim of the present study was to document and characterize the European deaths due to hornet, wasp and bee stings over a 23 year period (1994-2016).

2. Materials and Methods

The number of deaths related to hornet, wasp and bee stings (including yellow jackets) were obtained from the World Health Organisation (WHO). The WHO Mortality Database (MDB) is a compilation of mortality data as reported annually by Member States from their civil registration systems. Based on the classification of environmental events and circumstances as the cause of injury, poisoning and other adverse effects [International Classification of Diseases and Related Health Problems 10th Revision (ICD-11), Chapter XX], fatalities due to hornet, wasp and bee stings (including yellow jackets) are coded as single three digit category, the X23 [22].

By using X23 as diagnosis code, the MDB returned a file, comprising individual data for all X23-related fatalities registered between 1994 and 2016, both included. For each observation, the following particular variables were obtained and grouped:

- Country in which the fatality happened (n=32) (**Figure 1**).

Figure 1. Map of Europe comprising the countries (n=32) included in the study: Austria (AT), Belgium (BE), Bosnia and Herzegovina (BA), Bulgaria (BG), Croatia (HR), Czechia (CZ), Estonia (EE), Finland (FI), France (FR), Germany (DE), Greece (EL), Hungary (HU), Iceland (IS), Ireland (IE), Italy (IT), Latvia (LV), Lithuania (LT), Luxembourg (LU), Malta (MT), Montenegro (ME), Netherlands (NL), Norway (NO), Poland (PL), Portugal (PT), Romania (RO), Serbia (RS), Slovakia (SK), Slovenia (SI), Spain (ES), Sweden (SE), Switzerland (CH) and United Kingdom (UK). Countries on the map are labeled by their ISO 3166-1 alpha-2 codes [23].

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 30 December 2021 doi:10.20944/preprints202112.0483.v1

Countries were grouped in four regions , based on the "Standard Country or Area Codes for Statistical Use" (M49) [24], from United Nations geographic scheme for the continent of Europe (numerical code 150), created by the United Nations Statistics Division (UNSD) (**Figure 2**).

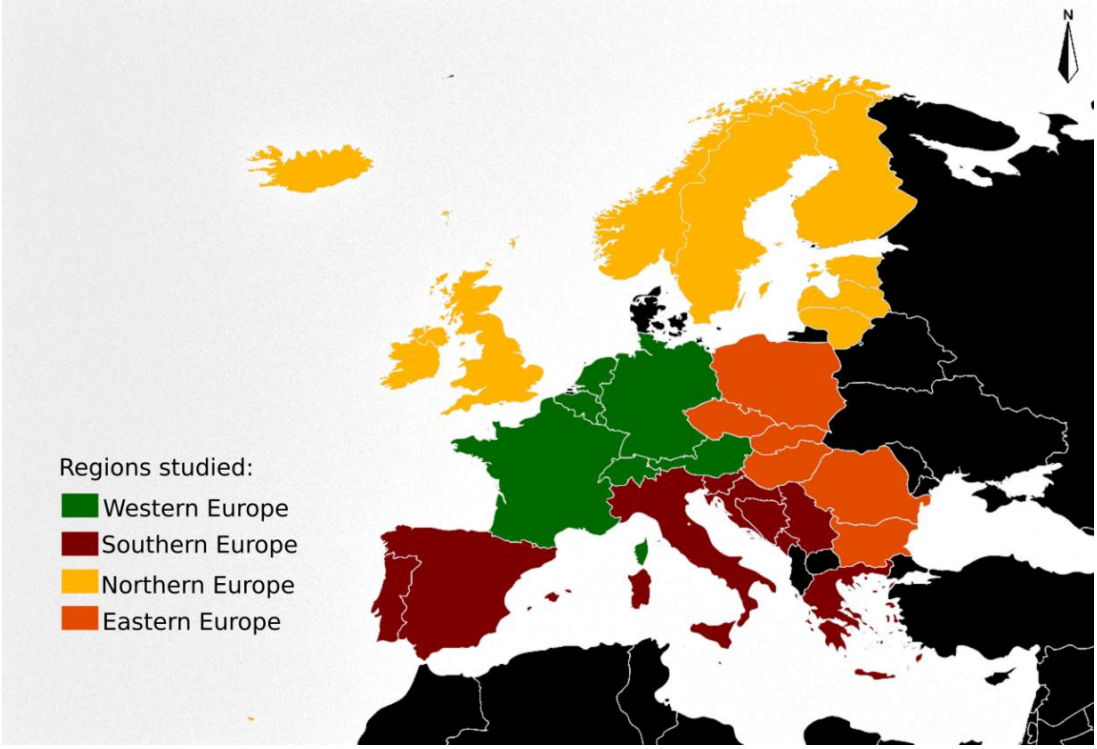

Figure 2. Map of Europe with the four regions assignment. ***Eastern Europe*** (in orange): (n=6), (numerical code 151): Bulgaria (BG), Czech Republic (CZ), Hungary (HU), Poland (PL), Romania (RO) and Slovakia (SK). ***Northern Europe*** (in green):(n=9), (numerical code 154): Estonia (EE), Finland (FI), Iceland (IS), Ireland (IE), Latvia (LV), Lithuania (LT), Norway (NO), Sweden (SE) and United Kingdom (UK). ***Southern Europe*** (in red): (n=10), (numerical code 039): Bosnia and Herzegovina (BA), Croatia (HR), Greece (EL), Italy (IT), Malta (MT), Montenegro (ME), Portugal (PT), Serbia (RS), Slovenia (SI) and Spain (ES). ***Western Europe*** (in green): (n=7), (numerical code 155): Austria (AT), Belgium (BE), France (FR), Germany (DE), Luxembourg (LU), Netherlands (NL), and Switzerland (CH).

- Year of occurrence, from 1994 to 2016.

- X23 code extension to four-digit. Comprising nine categories relative to the place of occurrence: X23.0 (home), X23.1 (residential institution), X23.2 (school, other institution and public administrative area), X23.3 (sports and athletics area), X23.4 (street and highway), X23.5 (trade and service area), X23.6 (industrial and construction area, X23.7 (farm), X23.8 (other specified places) and X23.9 (unspecified place). **Supplementary Table S1** lists the included and excluded places in each category.

- Gender, males (♂X23) and females (♀X23) who died from a X23 cause.

- Age categories, comprising four ranges: children (0-14 years), youth (15-24 years), adults (25-64) and seniors (65 years and older).

For each country set of data, calculations included: (a) mean, median and mode (central tendency of X23 deaths) and (b) range, variance and standard deviation (variability of X23 deaths).

The X23 gender ratio (X23GR) of mortality, was obtained by dividing the number of male who died from a X23 cause (♂X23), by the number of female who died from a X23 cause (♀X23):

$$X23GR = ♂X23 / ♀X23 \quad (1)$$

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 30 December 2021 doi:10.20944/preprints202112.0483.v1

The X23 gender differential (X23GD) in mortality is the absolute difference of the male (♂X23) and female (♀X23) who died from a X23 cause:

$$X23GD = ♂X23 - ♀X23 \quad (2)$$

The X23 mortality rates (X23MR) were on the basis of the yearly number of X23 deaths and the population size in each country as reported on the census, as of 1 January of each year:

$$X23MR = X23deaths/census \quad (3)$$

The X23MR were expressed in terms of annual rates (i.e., per year) and per 1,000,000 inhabitants. The X23GR, X23GD and X23MR were obtained both for countries and regions, as well as for each year and for the total years of the studied period. Countries censuses were obtained from the the European Statistical System (ESS), produced by the statistical office of the European Union (EU) (Eurostat) in partnership with National Statistical Institutes and other national authorities in the EU Member States. The software Gimp, was used to elaborate a map showing the spatial distribution of the average Hymenopteran sting-related deaths per 1,000,000 inhabitants (X23MR).

3. Results

3.1. Countries and study period

The countries for which data are available, as well as the year period to which they correspond, are presented in **Table 1**. Information is achievable for a total of 32 countries, although it varies from 1 year for Bosnia and Herzegovina to 23 years for Czechia. Eight out the 32 countries provided data during less than ten years; 15 countries report data ranged from eleven to 19 years; and nine countries reported data during 20 years or more:

< 10 years (n=8): BA, BG, EL, IE, LV, LT, LU and ME.

≥ 10 years and < 20 years (n= 15): AT, BE, HR, EE, FR, DE, IT, MT, PL, PT, RO, RS, SI, ES and UK.

≥ 20 years (n=9): CZ, FI, HU, IS, NL, NO, SK, SE and CH.

In the whole study period there is an annual variation in the data available and provided by each country. Thus, values varied from a minimum of 2, 5 and 9 countries reporting data in 1994, 1995 and 2016 respectively; to a maximum of 28 countries in 2003 and 2004, and 27 countries in 2002. Between the period 1998-2015, a total of 18-yr, there are data reported by more than 15 countries for each year.

Table 1. List of all European countries (n=32) analyzed in the present study with their country code, dataset range and number of datasets.

Country	Country code[1]	Dataset range (year), first–last	Number of datasets
Austria	AT	2002-2016	15
Belgium	BE	1998-2015	18
Bosnia and Herzegovina	BA	2011	1
Bulgaria	BG	2005-2013	9
Croatia	HR	1995-2013	19
Czechia	CZ	1994-2016	23
Estonia	EE	1997-2013	17
Finland	FI	1996-2015	20
France	FR	2000-2014	15
Germany	DE	1998-2015	18
Greece	EL	2014-2015	2
Hungary	HU	1996-2016	21
Iceland	IS	1996-2016	21
Ireland	IE	2007-2013	8

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 30 December 2021 doi:10.20944/preprints202112.0483.v1

Italy	IT	2003-2015	13
Latvia	LV	1996-2004	9
Lithuania	LT	1998-2004	7
Luxembourg	LU	1998-2004	7
Malta	MT	1995-2004	10
Montenegro	ME	1999-2004	5
Netherlands	NL	1996-2016	21
Norway	NO	1996-2015	20
Poland	PL	1999-2015	17
Portugal	PT	2002-2014	13
Romania	RO	1999-2016	18
Serbia	RS	1998-2015	18
Slovakia	SK	1994-2014	21
Slovenia	SI	1997-2015	19
Spain	ES	1999-2015	17
Sweden	SE	1997-2016	20
Switzerland	CH	1995-2015	21
United Kingdom	UK	2001-2015	15

[1] Based on the ISO 3166-1 alpha-2 code [23].

3.2. Hymenopteran Sting-Related Deaths

During the years 1994-2016, a total of 1,691 deaths have been officially registered in Europe with the external cause of injury code X23, i.e. deaths related to contact with hornets, wasps and bees. Fatalities were confirmed in 28 countries, with Germany (n = 327, 19.3%), France (n = 211, 12.5%) and Romania (n = 149, 8.8%) reporting the highest numbers for the period of study 1994-2016 (**Table 2**). A total of eleven countries (BG, FR, DE, EL, IT, PL, RO, RS, ES, CH and UK) report deaths due to hornets, wasps and bees stings every year. FR, DE, EL, PL and RO, lead the minimum number of annual deaths due to hornet, wasp and bee stings. At least one sting-related death is present yearly in six countries: BG, IT, RS, ES, CH and UK. In the rest of the countries (n=17), deaths due to stings of Hymenoptera insects are not always present as cause of death annually, showing years with zero deaths.

The maximum values of the number of annual deaths for the different countries, varied, ranking as: DE (32), FR (23), RO (16), CZ (14), HU (13); and AT, IT and FL (12).

The range of deaths due to hornet, wasp and bee stings found in the investigated period (1994-2016) varies from country to country, highlighting: DE (range=26); CZ, FR and RO (range=14); HU (range=13); AT (range=12) and IT (range=11).

Table 2. Descriptive statistics of fatalities due to hornet, wasp and bee stings by country (1994-2016).

Country[1]	Size	Sum	Minimum	Maximum	Range	Mode	Mean	Median	Standard deviation	Variance
AT	15	73	0	12	12	5	4.87	5	3.27	10.7
BE	18	27	0	5	5	1	1.5	1	1.42	2.03
BG	9	26	1	6	5	2	2.89	2	1.62	2.61
HR	19	35	0	6	6	1	1.84	1	1.71	2.92
CZ	23	111	0	14	14	4	4.83	4	3.04	9.24
EE	17	14	0	3	3	0	0.82	1	1.01	1.03
FI	20	25	0	4	4	0	1.25	1	1.25	1.57

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 30 December 2021 doi:10.20944/preprints202112.0483.v1

FR	15	211	9	23	14	14	14.07	14	4.15	17.21
DE	18	327	6	32	26	18	18.17	18	6.97	48.62
EL	2	9	4	5	1	4 & 5	4.5	4.5	0.71	0.5
HU	21	112	0	13	13	4	5.33	4	3.54	12.53
IE	8	2	0	1	1	0	0.25	0	0.46	0.21
IT	13	69	1	12	11	5 & 3	5.31	5	3.4	11.56
LV	9	9	0	2	2	2	1	1	1	1
LT	7	7	0	4	4	1 & 0	1	1	1.41	2
LU	7	1	0	1	1	0	0.14	0	0.38	0.14
NL	21	20	0	5	5	0	0.95	1	1.2	1.45
NO	20	19	0	3	3	1	0.95	1	0.76	0.58
PL	17	125	3	12	9	7&8&9	7.35	8	2.67	7.12
PT	13	9	0	4	4	0	0.69	0	1.32	1.73
RO	18	149	2	16	14	10	8.28	9	3.44	11.86
RS	18	53	1	6	5	3	2.94	3	1.43	2.06
SK	21	17	0	2	2	0	0.81	1	0.81	0.66
SI	19	21	0	4	4	0	1.11	1	1.37	1.88
ES	17	60	1	8	7	4 & 3	3.53	3	1.81	3.26
SE	20	44	0	6	6	1	2.2	2	1.61	2.59
CH	21	65	1	8	7	4	3.1	3	1.61	2.59
UK	15	51	1	7	6	2	3.4	4	1.84	3.4

[1] There are not registered deaths due to hornet, wasp and bee stings in: Iceland (1996-2016), Malta (1995-2004), Montenegro (1999-2004) and Bosnia and Herzegovina (2011).

3.2. Specific locations where Hymenopteran sting-related deaths occurred

The X23 code extension to four-digit is fully available for most of the countries, with a total of 18 reporting case details. In the opposite, three countries (FI, LV and SI) report all deaths without the four-digit extension. In seven countries (BE, BG, EE, LT, RS, SK and SE) both X23 code with and without extension to four-digit are used (**Suplemmentary Table 2**).

All countries register the highest number of deaths due to hornet, wasp and bee stings with the code X23.9 (unspecified place), except for Hungary, and Austria, where the code X23.0 (home) harbours the highest number of Hymenopteran sting-related death events. In general, the pattern observed for most countries, with the few exceptions is: X23.9 > X23.0 > X23.8 >X23.4 > X23.7; with no recorded deaths label led as X23.5 (trade and service area).

Very little used codes are: (i) 1 death coded as X23.3 (sports and athletics area) and 1 death coded as X23.6 (industrial and construction area), both having place in Romania; and (ii) 7 deaths coded as X23.2 (school, other institution and public administrative area) in Belgium (1), Czechia (1), Hungary (3), Poland (1) and Spain (1); and 8 deaths coded as X23.1 (residential institution) in Austria (1), Belgium (1), Czechia (3), Norway (1) and Poland (2).

3.3. Age distribution of Hymenopteran sting-related deaths

The most common age group to be fatally injured by hornet, wasp and bee stings was adults (25-64 years). Lithuania is the only exception, with equal adults and seniors (65 years and older) Hymenopteran sting-related deaths, a total of 3 (**Supplementary Table**

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 30 December 2021 doi:10.20944/preprints202112.0483.v1

3). Only adult deaths were found in two countries: Ireland and Luxembourg. Children (0-14 years) fatalities were recorded in 6 countries: FR (2), RO (2), AT (1), HR (1), PT (1), and SK (1). A total of 22 victims in the youth group (15-24 years) were recorded in 12 countries with the follow distribution: RO (6), AT (3), HU (2) and CH (2), and CZ, FR, DE, IT, LT, PL, RS and SI with only one death.

3.4. Hymenopteran sting-related deaths by gender.

The majority of deaths (n=1,691) in Europe during the studied period occurred in males (**Supplementary Table 4**). In fact, there are 4 countries with only male deaths: Greece and Portugal with 9 male victims each one; and Ireland and Luxembourg with 2 and 1 male victims respectively.

The X23 gender ratio (X23GR) of mortality varied from a min value of 1.4 for Norway to a maximum value of 20 for Slovenia, with a range of 18.6 for the whole dataset of countries. Obtained quartiles for X23GR were: Q1 = 2.8, Q2 = 3.85, Q3 = 7.2 and IQR (Q3-Q1) = 4.4.

Obtained values for the calculated X23 gender differential (X23GD) varied between countries, being over 100 in Germany, France and Romania, with values of 157, 113 and 111 respectively.

3.5. Hymenopteran sting-related deaths features by region: Eastern, Northern, Southern and Western Europe.

Fatalities mostly occurred in Western (42.8%), Eastern (31.9%), Southern (15.1%) and Northern Europe (10.1%). X23GR and X23GD varied for the four regions, as follow: X23GD [Western Europe (366), Eastern Europe (310), Southern Europe (190) and Northern Europe (83)] and X23GR [Southern Europe (6.8), Eastern Europe (3.7), Western Europe (3.0) and Northern Europe (2.9)] (**Table 3**).

Results show that eight and twenty one fatalities due to hornet, wasp and bee stings were recorded in children (0-14 years) and youth group (15-24 years), respectively. The most common age group to be fatally injured was adults (25-64 years) with 1,128 victims (66.7%) and seniors (65 years and older) with a total of 520 victims (30.8%) (**Table 3**).

Related to the place of occurrence, in Europe fatal stings occurred in a wide of situations, including: 29.4% at home; 11.2% at other specified places; 3.2% at street and highway and 1.5 at farm. However, the 44.2% of the fatalities, a total of 748 are recorded at "unspecified place". The ranked order of the place of occurrence was: X23.9 (unspecified place) > X23.0 (home) > X23.8 (other specified places) for Europe and Northern Europe; : X23.0 (home) > X23.9 (unspecified place) > X23.8 (other specified places) for Eastern Europe; and X23.9 (unspecified place) > X23.8 (other specified places) > X23.0 (home) for Southern Europe.

Table 3. Absolute and relative frequency of the deaths due to hornet, wasp and bee stings in Europe and by European region: counts, X23 gender ratio of mortality (X23GR), X23 gender differential in mortality (X23GD), by age distribution and by place of occurrence.

		Eastern Europe[1] 1994-2016	Northern Europe[2] 1996-2016	Southern Europe[3] 1995-2015	Western Europe[4] 1995-2016	Europe 1994-2016
Deaths	Total	540	171	256	724	1691
	Men	425 (78.7%)	127 (74.3%)	223 (87.1%)	545 (75.3%)	1320 (78.1%)
	Woman	115 (21.3%)	44 (25.7%)	33 (12.9%)	179 (24.7%)	371 (21.9%)
Ratio	X23GR	3.7	2.9	6.8	3	3.6
	X23GD	310	83	190	366	949
Age	≤ 14 years	3 (0.6%)	-	2 (0.8%)	3 (0.4%)	8 (0.5%)

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 30 December 2021 doi:10.20944/preprints202112.0483.v1

	15-24 years	10 (1.9%)	1 (0.6%)	3 (1.2%)	7 (1%)	21 (1.2%)
	25-64 years	418 (77.4%)	101 (59.1%)	169 (66%)	440 (60.8%)	1128 (66.7%)
	≥ 65 years	109 (20.2%)	55 (32.2%)	82 (32%)	274 (37.8%)	520 (30.8%)
Place	Not reported	33 (6.1%)	52 (30.4%)	73 (28.5%)	1 (0.1%)	159 (9.4%)
	X23 code extension to four-digit reported[5]	507 (93.9%)	119 (69.6%)	183 (71.5%)	723 (99.9%)	1532 (90.6%)
	X23.0 (home)	241 (44.6%)	35 (20.5%)	19 (7.4%)	202 (27.9%)	497 (29.4%)
	X23.1 (residential institution)	5 (0.9%)	1 (0.6%)	-	2 (0.3%)	8 (0.5%)
	X23.2 (school, other institution and public administrative area)	5 (0.9%)	-	1 (0.4%)	1 (0.1%)	7 (0.4%)
	X23.3 (sports and athletics area)	1 (0.2%)	-	-	-	1 (0.1%)
	X23.4 (street and highway)	17 (3.1%)	1 (0.6%)	6 (2.3%)	30 (4.1%)	54 (3.2%)
	X23.5 (trade and service area)	-	-	-	-	-
	X23.6 (industrial and construction area)	1 (0.2%)	-	-	-	1 (0.1%)
	X23.7 (farm)	18 (3.3%)	1 (0.6%)	6 (2.3%)	1 (0.1%)	26 (1.5%)
	X23.8 (other specified place)	48 (8.9%)	9 (5.3%)	21 (8.2%)	112 (15.5%)	190 (11.2%)
	X23.9 (unspecified place)	171 (31.7%)	72 (42.1%)	130 (50.8%)	375 (51.8%)	748 (44.2%)

[1] Eastern Europe (n=6): BG, CZ, HU, PL, RO and SK.[2] Northern Europe (n=9): EE, FI, IS, IE, LV, LT, NO, SE and UK. [3] Southern Europe (n=10): BA, HR, EL, IT, MT, ME, PT, RS, SI and ES.[4] Western Europe (n=7): AT, BE, FR, DE, LU, NL, and CH.[5] **Supplementary Table S1** lists the included and excluded places in each category.

3.6. Hymenopteran sting-related deaths, X23 mortality rates (X23MR).

The mortality rates (X23MR) were calculated based on the population size of each country, the obtained results ranged from 0 to 2.24 with an average of 0.26 (**Supplementary Table 5**). The country with the highest mean X23MR was Estonia (0.61) followed by Austria and Slovenia (0.6 and 0.55, respectively). The countries with the lowest X23MR values were Ireland (0.05), United Kingdom (0.06) and the Netherlands (0.06). The highest rates were recorded in countries from Eastern Europe (X23MR=0.35) followed by Western (X23MR=0.28), Northern (X23MR=0.23) and Southern (X23MR=0.2) Europe (**Figure 3**).

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 30 December 2021 doi:10.20944/preprints202112.0483.v1

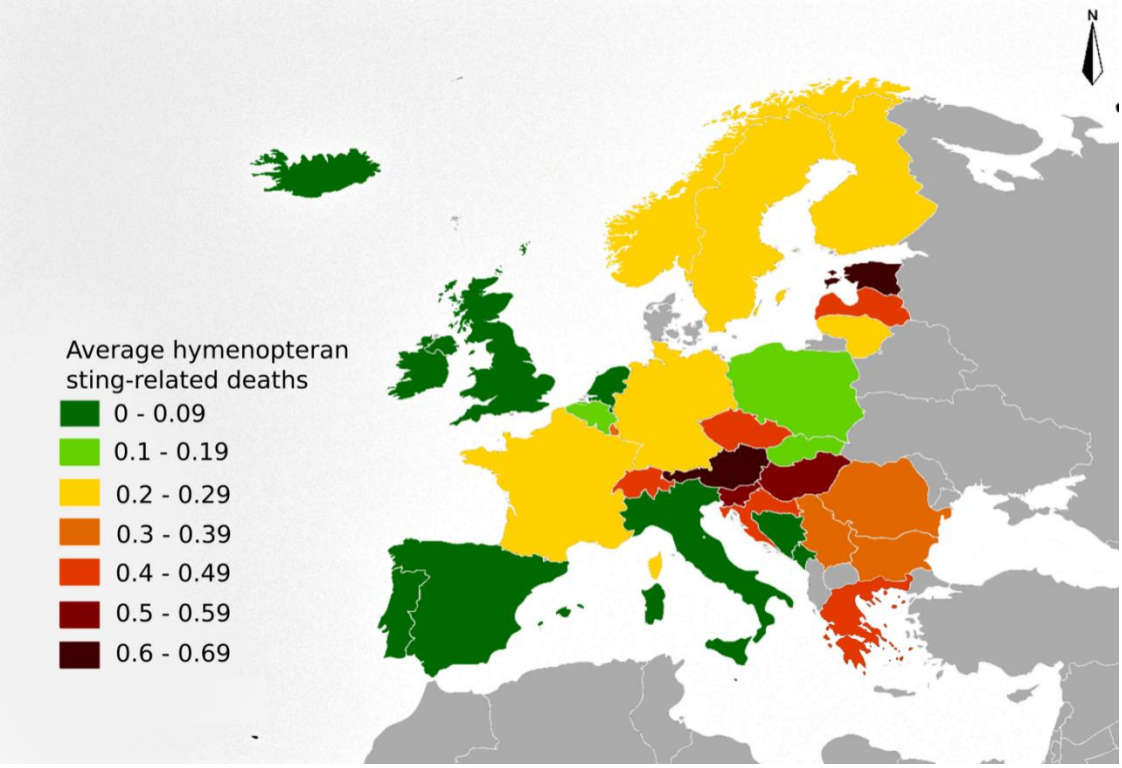

Figure 3. Map of Europe showing the average Hymenopteran sting-related mortality rates (X23MR) during the studied period (1994-2016). The X23MR are expressed in terms of annual rates (i.e., per year) and per 1,000,000 inhabitants, based in the dataset range for each country.

4. Discussion

Very little was found in the contemporary literature on the question of human fatalities caused by hornet, wasp and bee stings. The present study succeeded in gathering new and recent epidemiological information on Hymenopteran sting-related deaths in Europe. Country-by-country data show that the incidence of insect-sting mortality is statistically low, but not negligible. The majority of deaths (n = 1,691) in Europe over the 23-year period (1994–2016) can be described as occurring in males, in the age group of 65 years and older and at "unspecified places".

The higher incidence of anaphylaxis to venom in men may be related to different occupational roles and exposure degrees. Occupational anaphylaxis has been reported especially for beekeepers, electrical facility field workers, farming activities and forestry workers [25-27] being an activity mainly carried out by men. Moreover, males are more likely to suffer from mastocytosis, a risk factor for venom allergy [28]. Researchers highlight that woman should be monitored more closely for allergy-associated anxiety symptoms, while men need more encouragement to carry the emergency medication [29].

Related to the place of occurrence, fatal stings took place in an array of situations, however, almost half of the fatalities are recorded at "unspecified places". The frequent use of the above imprecise category gives little insight into the circumstances and the contexts in which such events occur, limiting the development of prevention initiatives. Increased specificity in the place coding of deaths would help public health professionals target prevention interventions.

Hymenopteran-induced fatalities differ by age. The number of deaths clearly indicates that adult (1128 = 66.7%) and elderly (570 = 30.8%) people are at a higher risk. Similar observations were described in Costa Rica, where the 50-year-and-older group accounted for the 73% of the fatalities [30], in South Korea, where deaths occurred in those over the age of 50 [31] and in UK where fatalities caused by insect stings affected mostly

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 30 December 2021 doi:10.20944/preprints202112.0483.v1

in those 60 years of age and older [32]. In contrast to insect allergy adults, the proportion of children who are anaphylactic to insect stings is lower [33]. In children, LLR to Hymenopteran stings is the most common presentation [34,35].

Historical available X23MR values for European countries were found at 0.09 in England & Wales, 13-yr period (1959-1971) [36]; 0.2 in Sweden, 10-yr period (1975–1984) [37]; 0.18 in Germany, 5-yr period (1979–1983) [38]; 0.25 in Denmark, 21-yr period (1960–1980) [39]; 0.43 in France, 12-yr period (1981–1991) [40] and 0.45 in Switzerland, 3-yr period (1961–1963) [41].

Between 1998 and 2012, there were 2688 admissions to the England and Wales hospitals because of anaphylaxis caused by insect stings, which is equivalent to an increase of 410% over the study period. A total of 93 deaths caused by sting-induced anaphylaxis between 1992 and 2012 were recorded. There was an increase in anaphylactic hospitalizations in UK, but no increase in anaphylactic deaths [32]. An analysis of 2,074 cases of anaphylaxis caused by insect stings from Germany, Austria and Switzerland, between 2006 to 2013, showed wasps (1,460=70.4%) as the most frequently reported trigger of anaphylaxis, followed by honey bees (412 = 19.9%) [1].

On the basis of population studies conducted in the United States of America (USA), it was estimated that 0.5% to 5% of the general population experience anaphylaxis after being stung by a Hymenopteran [42]. Considering the 1999 USA census of 272 million, the population at risk for anaphylaxis from insect stings is 1.36 to 13.6 million, being more common in adults than in children. The reported incidence of Hymenopteran sting-related deaths in USA is between 40 and 100 per year, nevertheless, this figure is believed to be severely underestimated [42]. More recently, during 2000-2017, hornet, wasp, and bee stings caused 1,109 deaths in the USA, which averaged 62 deaths each year. Deaths ranged from a low of 43 in 2001 to a high of 89 in 2017, and males accounted for about 80% of deaths [43].

The raw number of Hymenopteran-related deaths gives at the country level medical authorities quantitative information of interest, but it is less comparable across countries due to large differences in population. Equally important, detailed studies of the incidence of deaths from stings at the regional level within each country are desirable. As evidenced recently, sting-related deaths regional epidemiological data differ considerably from the average country rate [44]. For example, in Spain annual mortality rates during 1999-2018 varied from 0.02 to 0.19 per 1 million inhabitants. However, a more detailed and specific breakdown across Spanish communities reveals that some areas showed statistically higher X23MR values reaching 2.22 per million inhabitants [44].

Honey bees and the business of apiculture have economic importance for agricultural production. Moreover, beehive products (honey, pollen, propolis, bee bread, wax, royal jelly, and venom) have been useful since ancient times as food and for the treatment of medical conditions. However, farming honey bees brings with it health risks for beekeepers and those living in proximity to hives [27]. The estimated total number of honey bee colonies in the European Union in 2010 was 13.845.070, with a high heterogeneity distribution [45]. Out of the total European beehive stock, 18% (4.9 hives/km^2 ; 5.4 hives/100 inhabitants), 10.8% (11.4 hives/km^2 ; 13.5 hives/100 inhabitants), and 9.7% (2.5 hives/km^2 ; 2.1 hives/100 inhabitants) are distributed in Spain, Greece, and France, respectively. Greece and Hungary possess the highest density of colonies (about 10 colonies/ km^2). The lowest density (1 colony/km^2 or less) is found in the countries located in the extreme north of Europe (Estonia, Finland, Ireland, Latvia, Norway and Sweden). The country with the highest mean X23MR was Estonia (0.61) followed by Austria and Slovenia (0.6 and 0.55, respectively). Estonia had a total of 42,000 hives in 2010, corresponding to 0.3% of the total in Europe, with a density of 1 and 3.2 hives per km^2 and per 100 inhabitants. Austria had a total of 367,583 beehives in 2010, corresponding to 2.7% of the total in Europe, with a density of 4.4 hives per km^2 and per 100 inhabitants. Slovenia had a total of 48,990 beehives in 2010, corresponding to 2.1% of the total in Europe, with a density of 17.2 and 7.6 hives per km^2 and per 100 inhabitants

respectively. There is not a high presence of beehives in either country with the highest X23MR.

Although wasps are indeed universally disliked by the public [46] there is evidence and reasons to consider the regulatory, provisioning, supporting and cultural ecosystem services value of wasps on a par with other insects as bees [47]. There are marked biogeographical differences in terms of vespid species, populations, and ecosystems throughout Europe. In this way, while the genera *Dolichovespula*, *Vespa* and *Vespula* are distributed all over Europe; the genus *Polistes* is present in central Europe, is resident in the Channel Islands and seemingly just a transient visitor on the British mainland [48]. Although there are significant differences in distribution of hymenoptera, the genus *Vespula* predominates over *Polistes* and *Vespa* throughout Europe, except in Mediterranean areas and in the northwest of the Spanish peninsula. In geographic regions near the Mediterranean Sea, *Polistes* represents a particular clinical problem [49].

It is necessary to point out that within the past two decades, not-native species have been detected in Europe: (i) the yellow-legged Asian hornet (*Vespa velutina* Lepeletier 1836), found in southwestern France in 2004 [50]; (ii) the black shield hornet (*Vespa bicolor* Fabricius, 1787) found in 2013 in the community of Andalucía in Spain [51] and the (iii) American paper wasp *Polistes major major* Palisot de Beauvois found in 2008 in Asturias in northern Spain [52]. In addition, some vespids have been translocated from certain European countries to others, such as: (i) the Oriental hornet (*Vespa orientalis* Linnaeus 1771) naturally distributed in the south-eastern Europe was found in eastern Spain (Community of Valencia) in 2012 [53], in southern Spain in Algeciras in 2018 [54], in the Northern part of Bucharest in Romania in 2019 [55], in southern France in 2021 [56], and in the central-northern of Italy in the city of Florence in 2021 [57]; and (ii) *Vespula* and *Dolichovespula* species were confirmed in Iceland, Shetland, Orkney and the Faroe Islands [58]. In the entrance areas, the species have maintained stable populations, but they differ in their ability to propagate, highlighting the fact that the *Vespa velutina* is a high invasive alien species (IAS).

With the expansion of the above mentioned non-native Hymenopteran species across Europe, allergists should be aware that their community's exposures may continue to change. Health risks and deaths caused by the IAS *Vespa velutina* stings have become a public health concern. In this way *Vespa velutina* was identified as responsible of three-quarters of the Hymenoptera anaphylaxis patients reported during the last years in north-western Spain [59,60,61].

Invasive species are a far-reaching, interdisciplinary topic given their broad impacts on human health, biodiversity and economics [62]. Worldwide, there have been over one hundred examples of IAS affecting human health, sometimes with devastating consequences on livelihoods [63]. As part of the One Health philosophy, people and animals as well as the environment that they share are closely connected. One Health's importance has also been recognized by opinion leaders within the European Academy of Allergy and Clinical Immunology (EAACI). Such recognition led to the establishment of an independent Working Group (WG) within the EAACI solely dedicated to One Health in 2021 [64]. Because of the highly interdisciplinary nature of this WG, it is desirable that EAACI members work together with colleagues from a variety of fields. Based on their expertise, veterinarians should play an important role in this labour [65] and work closely with the beekeepers and recognizing the insects involved in the attacks. Lastly, description of the stings have an important value in this study since, it has been reported that the identification of these insects performed by general population and allergy specialists is poor [35,66-69].

5. Conclusions

The incidence of insect-sting mortality in Europe is statistically low, but not negligible. Over a 23-year period (1994-2016), a total of 1,691 human fatalities caused by hornet, wasp and bee stings were officially recorded in Europe, mostly occurring in Western and Southern areas and in males. The countries with the highest and lowest fatalities per million inhabitants per year (X23MR) were: Estonia, Austria and Slovenia; and Ireland, United Kingdom and the Netherlands, respectively.

The most obvious shortcoming of the present investigation is that the hymenoptera species involved were not individually identified, with data provided by ICD code. Knowledge of the different stinging insects found in various parts of Europe is important for diagnostic and therapeutic purposes. Our study has the advantage of using a large country-based data set, which allow us to analyze time trends and age / gender distributions of hymenoptera sting-related deaths. However epidemiological data at the regional level is needed to improve our understanding of Hymenoptera sting incidence.

The frequency of stings and allergic reactions depends on different variables such as geographic, environmental, and ecological factors. When dealing with complicated challenges, such as the health risks caused by native and not-native species of bee and wasp stings, it is necessary to produce, assemble and interpret information and knowledge using diverse sources and in a interdisciplinary way. As part of the One Health philosophy, people and animals as well as the environment that they share are closely connected. With the expansion of not-native Hymenopteran species across Europe, allergists should be aware that their community's exposures may continue to change and include these insects as causes of sting related allergic reactions.

Supplementary Materials: The following are available online at www.mdpi.com/xxx/s1 Supplementary Table 1. Place of occurrence code. The following categories are provided to to be used as separate variables in addition to ICD categories W00-Y34 to identify the place of occurrence of the external cause where relevant. Supplementary Table 2. Absolute and relative frequency of the deaths due to hornet, wasp and bee stings by place of occurrence. Supplementary Table 3. Absolute and relative frequency of the deaths due to hornet, wasp and bee stings by age. Supplementary Table 4. Absolute and relative frequency of the deaths due to hornet, wasp and bee stings by gender; and the X23 gender ratio (X23GR) of mortality and the X23 gender differential (X23GD) in mortality. Supplementary Table 5. Hymenopteran sting-related mortality rates (X23MR) during the studied period (1994-2016) calculated on the basis of the yearly population size of each country as reported on the census, as of 1 January of each year. The X23MR are expressed per year and per 1,000,000 inhabitants.

Author Contributions: Conceptualization, X.F.; methodology, X.F., C.V. and S.R.; writing—original draft preparation, X.F.; writing—review and editing, X.F., C.V. and S.R.; supervision and funding acquisition, C.V. All authors have read and agreed to the published version of the manuscript.

Funding: The authors thank the Instituto de Salud Carlos III (Fondo de Investigaciones Sanitarias, Spanish Ministry of Health, PI19/01023) (Co-funded by the European Regional Development Fund "A way to make Europe") for the financial support. X.F. thanks Instituto de Salud Carlos III for a research contract (program number: RD16/0017/001).

Institutional Review Board Statement: Institutional review board review was not needed because the data are publicly available and contain no personal identifiers.

.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Acknowledgments: We thank Christopher Rosario (Guam Department of Agriculture, Biosecurity Division) for critically reading the manuscript. Thank you to Ramón Rodríguez Dean (Occupational Risk Prevention Management Office, University of Santiago de Compostela) for inserting energy and encouragement into this research.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Worm, M.; Eckermann, O.; Dölle, S.; Aberer, W.; Beyer, K.; Hawranek, T.; Hompes, S.; Koehli, A.; Mahler, V.; Nemat, K.; Niggemann, B.; Pföhler, C.; Rabe, U.; Reissig, A.; Rietschel, E.; Scherer, K.; Treudler, R.; Ruëff, F. Triggers and treatment of anaphylaxis: an analysis of 4,000 cases from Germany, Austria and Switzerland. *Dtsch. Arztebl. Int*. **2014**, *111*, 367–375, doi:10.3238/arztebl.2014.0367.
2. Demain, J.G.; Minaei, A.A.; Tracy, J.M. Anaphylaxis and insect allergy. *Curr. Opin. Allergy Clin. Immunol*. **2010**, *10*, 318–322, doi:10.1097/ACI.0b013e32833a6c72.
3. Yoon, K.A.; Kim, K.; Kim, W.-J.; Bang, W.Y.; Ahn, N.-H.; Bae, C.-H.; Yeo, J.-H.; Lee, S.H. Characterization of venom components and their phylogenetic properties in some Aculeate bumblebees and wasps. *Toxins* **2020**, *12*, 47, doi:10.3390/toxins12010047.
4. Pucca, M.B.; Cerni, F.A.; Oliveira, I.S.; Jenkins, T.P.; Argemí, L.; Sørensen, C.V.; Ahmadi, S.; Barbosa, J.E.; Laustsen, A.H. Bee Updated: Current Knowledge on Bee Venom and Bee Envenoming Therapy. *Front. Immunol*. **2019**, *10*, 2090, doi:10.3389/fifimmu.2019.02090.
5. Pak, S.C. An Introduction to the Toxins Special Issue on "Bee and Wasp Venoms: Biological Characteristics and Therapeutic Application". *Toxins* **2016**, *8*, 315, doi:10.3390/toxins8110315.
6. Feindor, M.; Heath, M.D.; Hewings, S.J.; Carreno Velazquez, T.L.; Blank, S.; Grosch, J.; Jakob, T.; Schmid-Grendelmeier, P.; Klimek, L.; Golden, D.B.K.; Skinner, M.A.; Kramer, M.F. Venom Immunotherapy: From Proteins to Product to Patient Protection. *Toxins* **2021**, *13*, 616, doi:10.3390/toxins13090616.
7. Perez-Riverol, A.; Justo-Jacomini, D.L.; Zollner, R.D.L.; Brochetto-Braga, M.R. Facing Hymenoptera Venom Allergy: From Natural to Recombinant Allergens. *Toxins* **2015**, *7*, 2551–2570, doi:10.3390/toxins7072551.
8. Pascoal, A.; Estevinho, M.M.; Choupina, A.B.; Sousa-Pimenta, M.; Estevinho, L.M. An overview of the bioactive compounds, therapeutic properties and toxic effects of apitoxin. *Food Chem. Toxicol*. **2019**, *134*, 110864, doi:10.1016/j.fct.2019.110864.
9. Abd El-Wahed, A.; Yosri, N.; Sakr, H.H.; Du, M.; Algethami, A.F.M.; Zhao, C.; Abdelazeem, A.H.; Tahir, H.E.; Masry, S.H.D.; Abdel-Daim, M.M.; Musharraf, S.G.; El-Garawani, I.; Kai, G.; Al Naggar, Y.; Khalifa, S.A.M.; El-Seedi, H.R. Wasp Venom Biochemical Components and Their Potential in Biological Applications and Nanotechnological Interventions. *Toxins* **2021**, *13*, 206, doi: 10.3390/toxins13030206
10. Elieh Ali Komi, D.; Shafaghat, F.; Zwiener, R.D. Immunology of bee venom. *Clin. Rev. Allergy Immunol*. **2018**, *54*, 386–396, doi:10.1007/s12016-017-8597-4.
11. Sahiner, U.M.; Durham, S.R. Hymenoptera Venom Allergy: How Does Venom Immunotherapy Prevent Anaphylaxis From Bee and Wasp Stings?. *Front. Immunol*. **2019**, *10*, 1959, doi: 10.3389/fimmu.2019.01959.
12. Mingomataj, E.Ç.; Bakiri, A.H.; Ibranji, A.; Sturm, G.J. Unusual reactions to hymenoptera stings: what should we keep in mind?. *Clin. Rev. Allergy Immunol*. **2014** , *47*, 91–99, doi: 10.1007/s12016-014-8434-y.
13. Nittner-Marszalska, M.; Cichocka-Jarosz, E. Insect sting allergy in adults: key messages for clinicians. *Pol. Arch. Med. Wewn*. **2015**, *125*, 929–937, doi: 10.20452/pamw.3216.
14. Forrester, J.A.; Weiser, T.G.; Forrester, J.D. An Update on Fatalities Due to Venomous and Nonvenomous Animals in the United States (2008-2015). *Wilderness Environ. Med.* **2018**, *29*, 36–44, doi:10.1016/j.wem.2017.10.004.
15. Ferreira, R.S.Jr.; Almeida, R.A.; Barraviera, S.R.; Barraviera, B. Historical perspective and human consequences of Africanized bee stings in the Americas. *J. Toxicol. Environ. Health B Crit. Rev*. **2012**, *15*, 97–108, doi: 10.1080/10937404.2012.645141.
16. Herrera, C.; Leza, M.; Martínez-López, E. Diversity of compounds in Vespa spp. venom and the epidemiology of its sting: a global appraisal. *Arch Toxicol*. **2020**, *94*, 3609–3627, doi: 10.1007/s00204-020-02859-3.
17. Tanno, L.K.; Calderon, M.A.; Smith, HE, Sanchez-Borges, M.; Sheikh, A.; Demoly, P.; Joint Allergy Academies. Dissemination of definitions and concepts of allergic and hypersensitivity conditions. *World Allergy Organ J*. **2016**, *9*, 24, doi:10.1186/s40413-016-0115-2.
18. Linard, A.T.S.; Barros, R.M.; Sousa, J.A.; Leite, R.S. Epidemiology of bee stings in Campina Grande, Paraíba state, Northeastern Brazil. *J. Venom Anim. Toxins Incl. Trop. Dis.* **2014**, *20*, 13, doi:10.1186/1678-9199-20-13.
19. Golden, D.B.; Demain, J.; Freeman, T.; Graft, D.; Tankersley, M.; Tracy, J.; Blessing-Moore, J.; Bernstein, D.; Dinakar, C.; Greenhawt, M.; Khan, D.; Lang, D.; Nicklas, R.; Oppenheimer, J.; Portnoy, J.; Randolph, C.; Schuller, D.; Wallace, D. Stinging insect hypersensitivity: A practice parameter update 2016. *Ann. Allergy Asthma Immunol.* **2017**, *118*, 28–54, doi:10.1016/j.anai.2016.10.031.
20. Bilò, M.B.; Bonifazi, F. The natural history and epidemiology of insect venom allergy: clinical implications. *Clin. Exp. Allergy* **2009**, *39*, 1467–1476, doi: 10.1111/j.1365-2222.2009.03324.x.

21. Biló, B.M.; Rueff, F.; Mosbech, H.; Bonifazi, F.; Oude-Elberink, J.N.; EAACI Interest Group on Insect Venom Hypersensitivity. Diagnosis of Hymenoptera venom allergy. *Allergy* **2005**, *60*, 1339–1349, doi:10.1111/j.1398-9995.2005.00963.x.
22. International Statistical Classification of Diseases and Related Health Problems (ICD). Available on line: http://www.who.int/classifications/icd/en/ (accessed on 11 May 2021).
23. International Standard ISO 3166-1, Codes for the representation of names of countries and their subdivisions--Part 1: Country codes, ISO 3166-1: 2006 (E/F), International Organization on Standardization (Geneva, 2006). Available on line: https://www.iso.org/iso-3166-country-codes.html (accessed on 11 May 2021)
24. Standard country or area codes for statistical use, Series M, No. 49 (M49), United Nations, Statistics Division, New York. Available on line: https://unstats.un.org/unsd/methodology/m49/ (accessed on 11 May 2021)
25. Hayashi, Y.; Hirata, H.; Watanabe, M.; Yoshida, N.; Yokoyama, T.; Murayama, Y.; Sugiyama, K.; Arima, M.; Fukushima, Y.; Fukuda, T.; Ishii, Y. Epidemiologic investigation of hornet and paper wasp stings in forest workers and electrical facility field workers in Japan. *Allergol. Int.* **2014**; *63*, 21–26, doi: 10.2332/allergolint.13-OA-0556.
26. Arcangeli, G.; Traversini, V.; Tomasini, E.; Baldassarre, A.; Lecca, L.I.; Galea, R.P.; Mucci, N. Allergic Anaphylactic Risk in Farming Activities: A Systematic Review. *Int. J. Environ. Res. Public Health* **2020**, *17*, 4921, doi: 10.3390/ijerph17144921.
27. Stanhope, J.; Carver, S.; Weinstein, P. Health outcomes of beekeeping: a systematic review. *J. Apic. Res.* **2017**, *56*, 100–111, doi: 10.1080/00218839.2017.1291208.
28. Salvati, L.; Vitiello, G.; Parronchi, P. Gender differences in anaphylaxis. *Curr. Opin. Allergy Clin. Immunol.* **2019**, *19*, 417–424, doi: 10.1097/ACI.0000000000000568.
29. Schoeben, L.S.; Bubak, C.; Schaarschmidt, M.L.; Schmieder, A. Sex Differences in Adults with Insect Venom Allergy regarding Psychological Distress, Attitudes toward the Emergency Medication, and Factual Knowledge about the Disease. *Int. Arch. Allergy Immunol.* **2020**, *181*, 529–535, doi: 10.1159/000507625.
30. Prado, M.; Quirós, D.; Lomonte, B. Mortality due to Hymenoptera stings in Costa Rica, 1985–2006. *Rev. Panam. Salud Publica* **2009**, *25*, 389–393, doi: 10.1590/s1020-49892009000500002.
31. Choi, M.B.; Kim, T.G.; Kwon, O. Recent Trends in Wasp Nest Removal and Hymenoptera Stings in South Korea. *J. Med. Entomol.* **2018**, *56*, 254–260, 10.1093/jme/tjy144.
32. Turner, P.J.; Gowland, M.H.; Sharma, V.; Ierodiakonou, D.; Harper, N.; Garcez, T.; Pumphrey, R.; Boyle, R.J. Increase in anaphylaxis-related hospitalizations but no increase in fatalities: an analysis of United Kingdom national anaphylaxis data, 1992-2012. *J. Allergy Clin Immunol.* **2015**, 135, 956–963, doi: 10.1016/j.jaci.2014.10.021.
33. Tan, J.W.; Campbell, D.E. Insect allergy in children. *J. Paediatr. Child Health* **2013**, *49*, 381–387. doi: 10.1111/jpc.12178.
34. Golden, D.B.; Kagey-Sobotka, A.; Norman, P.S.; Hamilton, R.G.; Lichtenstein, L.M. Outcomes of allergy to insect stings in children, with and without venom immunotherapy. *N. Engl. J. Med.* **2004**, *12*, 668–674, doi: 10.1056/NEJMoa022952.
35. Giovannini, M.; Castagnoli, R.; Mori, F.; Arasi, S.; Barni, S.; Saretta, F.; Mastrorilli, C.; Pecoraro, L.; Liotti, L.; Caminiti, L.; Marseglia, G.L.; Novembre, E.; from the Rare Allergic Diseases Commission of the Italian Society of Pediatric Allergy and Immunology. Hymenoptera venom allergy among children in Italy: time for pediatricians to take action. *Allergol. Immunopathol. (Madr).* **2020**, *48*, 804–809, doi: 10.1016/j.aller.2020.04.003.
36. Somerville, R.; Till, D.; Leclerq, M.; Lecomte, J. Les morts par piqûre d'hyménoptères aculéates en Angleterre et au Pays de Galles (statistique pour la periode 1959-1971). *Rev. Med. Liege* **1975**, *30*, 76–78.
37. Johansson, B.; Eriksson, A.; Ornehult, L. Human fatalities caused by wasp and bee stings in Sweden. *Int. J. Legal Med.* **1991**, *104*, 99–103, doi: 10.1007/BF01626039.
38. Przybilla, B.; Ring, J. Diagnostik und therapie der Allergic vom Sofort-Typ gegenuber Bienen-und Wespengift. *Allergologie* **1985**, 8, 31–39.
39. Mosbech, H. Death caused by wasp and bee stings in Denmark 1960-1980. *Allergy* **1983**, *38*, 195–200, doi: 10.1111/j.1398-9995.1983.tb01606.x.
40. Charpin, D.; Birnbaum, J.; Vervl oet, D. Epidemiology of hymenoptera allergy. *Clin. Exp. Allergy* **1994**, *24*, 1010–1015, doi: 10.1111/j.1365-2222.1994.tb02736.x.
41. Muller, U. Prophylaxe und Therapie der Insektenstichallergic. *Pharma-Klinik* **1985**, *7*, 25–28.
42. Neugut, A.I.; Ghatak, A.T.; Miller, R.L. Anaphylaxis in the United States: An Investigation Into Its Epidemiology. *Arch. Intern. Med.* **2001**, *161*, 15–21, doi:10.1001/archinte.161.1.15.

43. QuickStats: Number of Deaths from Hornet, Wasp, and Bee Stings, Among Males and Females — National Vital Statistics System, United States, 2000–2017. MMWR *Morb. Mortal. Wkly. Rep*. **2019**, *68*, 649, doi: 10.15585/mmwr.mm6829a5external icon..

44. Feás, X. Human Fatalities Caused by Hornet, Wasp and Bee Stings in Spain: Epidemiology at State and Sub-State Level from 1999 to 2018. *Biology* **2021**, *10*, 73, doi: 10.3390/biology10020073.

45. Chauzat, M.P.; Cauquil, L.; Roy, L.; Franco, S.; Hendrikx, P.; Ribière-Chabert, M. Demographics of the European apicultural industry. *PLoS One* **2013**, *8*, e79018, doi: 10.1371/journal.pone.0079018.

46. Sumner, S.; Law, G.; Cini, A. Why we love bees and hate wasps. *Ecol. Entomol*. **2018**, *43*, 836–845, doi: 10.1111/een.12676.

47. Brock, R.E.; Cini, A.; Sumner, S. Ecosystem services provided by aculeate wasps. *Biol. Rev. Camb. Philos. Soc.* **2021**, *96*, 1645–1675, doi: 10.1111/brv.12719.

48. NBN Atlas website at http://www.nbnatlas.org Accessed 01 November 2021.

49. Fernández, J. Distribution of vespid species in Europe. *Curr. Opin. Allergy Clin. Immunol*. **2004**, *4*, 319–324, doi: 10.1097/01.all.0000136760.43571.f2.

50. Haxaire, J.; Bouguet, J.-P.; Tamisier, J.-P. *Vespa velutina* Lepeletier, 1836, une redoutable nouveauté pour la faune de France (Hymenoptera, Vespidae). *Bull. Soc. Entomol. France* **2006**, *111*, 194, doi: 10.3406/bsef.2006.16309.

51. Castro, L. Una nueva introducción accidental en el género *Vespa* Linnaeus, 1758: *Vespa bicolor* Fabricius, 1787 en la provincia de Málaga (España). *Revta. Gad. Entom*. **2019**, *10*, 47–56.

52. Castro, L.; Arias, A.; Torralba-Burrial, A. First European records of an alien paper wasp: *Polistes* (*Aphanilopterus*) *major* Palisot de Beauvois, 1818 (Hymenoptera: Vespidae) in northern Spain. Zootaxa **2013**, *3681*, 89–92, doi: 10.11646/zootaxa.3681.1.7.

53. Hernández, R.; García-Gans, F.J.; Selfa, J.; Rueda, J. Primera cita de la avispa oriental invasora *Vespa orientalis* Linnaeus 1771 (Hymenoptera: Vespidae) en la Península Ibérica. *Bol. SEA* **2013**, *52*, 299–300.

54. Sánchez, I.; Fajardo, M.C.; Castro, M. Primeras citas del avispón oriental *Vespa orientalis* Linnaeus 1771 (Hymenoptera: Vespidae) para Andalucía (España). *Rev. Soc. Gad. Hist. Nat.* **2019**, *13*, 11–14.

55. Zachi, M.; Ruicănescu, A. *Vespa orientalis*, a new alien species in Romania. *Travaux du Muséum National d'Histoire Naturelle "Grigore Antipa"* **2021**, *64*, 67–72, doi: 10.3897/travaux.64.e61954.

56. Gereys, B;, Coache, A.; Filippi, G. Présence en France métropolitaine d'un frelon allochtone: *Vespa orientalis* Linnaeus, 1771 (Le Frelon oriental) (Hymenoptera, Vespidae, Vespinae). *Faunitaxys* **2021**, *9*, 1–5.

57. Graziani, F.; Cianferoni, F. The northernmost record of *Vespa orientalis* Linnaeus, 1771 (Hymenoptera: Vespidae) in peninsular Italy. 179 – 182.

58. Hammer, S.; Jensen, J-K. The invasion of two species of social wasps (Hymenoptera, Vespidae) to the Faroe Islands. *Bioinvasions Rec.* 2019, 8, 558–567, doi: 10.3391/bir.2019.8.3.11.

59. Vidal, C.; Armisén, M.; Monsalve, R.; González-Vidal, T.; Lojo, S.; López-Freire, S.; Méndez, P.; Rodríguez, V.; Romero, L.; Galán, A.; González-Quintela, A. Anaphylaxis to *Vespa velutina nigrithorax*: pattern of sensitization for an emerging problem in Western countries. *J. Investig. Allergol. Clin. Immunol*. **2021**, *31*, 228–235, doi: 10.18176/jiaci.0474.

60. Vidal, C. The Asian wasp Vespa velutina nigrithorax: entomological and allergological characteristics. *Clin. Exp. Allergy* **2021**, *00*, 1–10, doi: 10.1111/cea.14063.

61. Feás, X.; Vidal, C.; Vázquez-Tato, M.P.; Seijas, J.A. Asian Hornet, *Vespa velutina* Lepeletier 1836 (Hym.: Vespidae), Venom Obtention Based on an Electric Stimulation Protocol. *Molecules* **2022**, 27, 138, doi: 10.3390/molecules27010138

62. Neill, P.E.; Arim, M. Human Health Link to Invasive Species. *Encyclopedia of Environmental Health*. 2011, 116–123, doi:10.1016/B978-0-444-52272-6.00528-6.

63. Mazza, G.; Tricarico, E.; Genovesi, P.; Gherardi, F. Biological invaders are threats to human health: an overview. *Ethol. Ecol. Evol*. **2014**, *26*, 112–129, doi: 10.1080/03949370.2013.863225.

64. Pali-Schöll, I.; Roth-Walter, F.; Jensen-Jarolim, E. One Health in allergology: A concept that connects humans, animals, plants, and the environment. Allergy. **2021**, *76*, 2630–2633, doi: 10.1111/all.14804.

65. van Herten, J.; Meijboom, F.L.B.; Veterinary Responsibilities within the One Health Framework. *Food ethics* **2019**, *3*, 109–123, doi: 10.1007/s41055-019-00034-8.

66. Baker, T.W.; Forester, J.P.; Johnson, M.; Stolfi, A.; Stahl, M.C. The HIT study: Hymenoptera Identification Test--how accurate are people at identifying stinging insects? *Ann. Allergy Asthma Immunol*. **2014**, *113*, 267–270, doi: 10.1016/j.anai.2014.05.029.

67. Baker, T.W, Forester, J.P.; Johnson, M.L.; Sikora, J.M.; Stolfi, A.; Stahl, M.C. Stinging insect identification: Are the allergy specialists any better than their patients? *Ann. Allergy Asthma Immunol*. **2016**, *116*, 431–434, doi: 10.1016/j.anai.2016.01.025.

68. Feás Sánchez, X.; Charles, R.J. Notes on the Nest Architecture and Colony Composition in Winter of the Yellow-Legged Asian Hornet, Vespa velutina Lepeletier 1836 (Hym.: Vespidae), in Its Introduced Habitat in Galicia (NW Spain). *Insects* **2019**, *10*, 237. doi: 10.3390/insects10080237.

69. Feás, X.; Vázquez-Tato, M.P.; Seijas, J.A.; Pratima, G. Nikalje, A.; Fraga-López, F. Extraction and Physicochemical Characterization of Chitin Derived from the Asian Hornet, Vespa velutina Lepeletier 1836 (Hym.: Vespidae). *Molecules* **2020**, *25*, 384, doi: 10.3390/molecules25020384.