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► To cite this version:

G. Gentile, G. Fréchar, A. Dia, A. Buzens, R. Vives, et al.. Incidence of acute respiratory tract infections (2006–2015) and influenza (2006–2013) among French armed forces. *Médecine et Maladies Infectieuses*, 2019, 10.1016/j.medmal.2019.10.015 . hal-02465906

HAL Id: hal-02465906

<https://amu.hal.science/hal-02465906>

Submitted on 7 Nov 2022

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Incidence des infections respiratoires aiguës fébriles (2006-2015) et de la grippe (2006-2013) dans les armées françaises

Incidence of acute respiratory tract infections (2006-2015) and influenza (2006-2013) among French armed forces

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Mots-clés : infections de l'appareil respiratoire, grippe, prévention, armées, militaire

Keywords: respiratory tract infections, flu, prevention, armies, military

Abstract

Objectives. We aimed to assess the incidence of respiratory tract infections in military settings between 2006 and 2015.

Patients and methods. We performed a retrospective epidemiological study of the entire military population from 2006 to 2015. Comprehensive data was collected from all medical centers, operational medical units, naval services, and army training hospitals and provided by the epidemiological surveillance of the armies.

Results. The annual average population of the study was 331,394 soldiers. For acute respiratory tract infections (2006-2015), 22,818 cases were reported in metropolitan France, 3,211 cases in French overseas territories, 1,595 cases in the French Navy, and 1,318 cases in external military operations for a total of 28,942 cases. For influenza (2006-2013), 934 cases were reported in metropolitan France, 101 cases in French overseas territories, and 23 cases in external operations, for a total of 1,058 cases. The mean incidence rate of acute respiratory tract infections expressed as case number per 1,000 person-years (PY) was 8.7 PY (95% CI [8.6-8.8]) with an exceptional increased incidence rate in 2009 (25.9 PY, 95% CI [25.4-26.4]). The mean incidence rate of influenza was 0.35 PY (95% CI [0.33-0.37]) with a peak incidence rate of 1.9 PY in 2009.

Conclusion. Acute respiratory tract infections are at the forefront of infectious episodes in the French armies. Although not necessarily severe, current prevention measures are not enough to reduce the incidence threshold of these infections and need to be improved.

INTRODUCTION

Acute febrile respiratory tract infections (AFRTIs) are the most frequent seasonal infections in industrialized countries [1,2]. They affect adults three times a year on average and are mainly due to poorly pathogenic viruses in healthy adults, but also to seasonal influenza or sometimes to pandemic influenza strains (A H1N1) [1]. Although most often mild, these viral infections may have a strong impact on health expenditure and organization of care [3]. Bacterial infections are less frequent in young adults but when observed, pneumococcal infections and infections caused by intracellular bacteria such as mycoplasma are predominant [4].

Members of the French armed forces are particularly affected by AFRTIs, as they are the second leading infectious episodes in terms of incidence [5]. This may be explained by the demographic profile of this population (young adults, community life) and by the related occupational specificities (missions in metropolitan France and French overseas territories, external operations, high exposure to stress of various origins and to a varied microbial environment) [6]. AFRTIs may rapidly disturb military missions because of the associated temporary incapacity, mainly in cases of outbreaks.

The management and prevention of AFRTIs are a daily challenge for the French army health service [7], which strives to limit their impact on the operational capacity of soldiers and on the military network for primary care services [8]. The French army health service thus mainly relies on the medical network of the French armed forces, made of military primary care physicians who directly support military units. Prevention measures have been implemented such as hand hygiene, but the most important measure is the three-year vaccination against influenza for members of the French armed forces [9]. Vaccination against influenza is included in the military immunization calendar. The vaccination is

performed at enrollment for all members of the armed forces and is renewed every three years. This vaccination strategy was implemented in 1994 and aims at maintaining collective immunity to prevent outbreaks that would impact the operational capacity of the armed forces. Influenza may occur in vaccinated subjects. These influenza cases are due to the inadequacy between viruses circulating during seasonal outbreaks and valences. No data has however been systematically collected on that matter (only a few clusters of cases notified through alert messages and then investigated). A 2005 study (unpublished data) performed among members of the armed forces confirmed that individuals could only be protected against influenza if vaccinated within the previous 12 months. However, no influenza outbreak with an impact on the operational capacity of the army has so far been reported. The three-year vaccination strategy is therefore not questioned. Annual vaccination of soldiers before deployment may be required for highly operational situations in an epidemiological context of influenza outbreak. Such strategy was for instance implemented in Afghanistan during the winter season. The French army health service must also anticipate and adapt its strategies depending on the progress of the mission and on local epidemiological contexts.

To better comprehend the impact of AFRTIs in a military context and implement adequate strategies, we performed a retrospective epidemiological study to measure the incidence of AFRTIs among members of the French armed forces between 2006 and 2015.

MATERIAL AND METHODS

Epidemiological surveillance of the French armed forces

The French center for epidemiology and public health of the armed forces (French acronym CESPA) performs an epidemiological surveillance of all soldiers in activity in France, abroad,

or at sea. The surveillance focuses on approximately 60 disorders or diseases declared by the Army medical centers, the inter-army medical centers, the operational medical units, the navy medical services, and the military hospitals. CESPA collects and analyzes data to improve knowledge of these disorders and diseases, to inform the stakeholders of the surveillance network, to identify outbreaks, and to perform epidemiological surveys.

The epidemiological surveillance strategy is exhaustive and focuses on all 60 disorders or diseases mentioned above. AFRTI and influenza cases may be notified through alert messages (for outbreaks) and through weekly epidemiological messages (number of clustered cases in each declaring unit).

Population and study period

The target population was all members of the French armed forces over the period 2006-2015. We grouped regions into six categories for better interpretation of regional risks (Europe: metropolitan France and Kosovo; Africa and Indian Ocean: Uganda, Cameroon, Djibouti, Senegal, Niger, Chad, Ivory Coast, Guinea, Mali, Central African Republic, Gabon, Mayotte, and Reunion; Atlantic: Antilles and French Guyana; Middle East: United Arab Emirates, Jordan, Lebanon, Iraq, Qatar; Central Asia: Afghanistan, Tajikistan; Pacific: New Caledonia, French Polynesia). Regions were further subdivided by hemisphere for further assessment of AFRTIs and influenza outcome (Northern Hemisphere: Uganda, Cameroon, Djibouti, Senegal, Niger, Chad, Ivory Coast, Guinea, Mali, Central African Republic, Atlantic, Europe, Middle East, and Central Asia; Southern Hemisphere: Gabon, Mayotte, and Reunion; Pacific).

Inclusion criteria

We included confirmed cases of AFRTIs and influenza notified through the epidemiological surveillance of members of the French armed forces during the study period. Criteria for

AFRTI notification were acute catarrh of the respiratory tract combined with fever $\geq 38.5^{\circ}\text{C}$ and cough. Notification criteria for confirmed influenza were clinical influenza with biological confirmation (rapid test and/or PCR and/or culture) by nasopharyngeal specimens. Specific surveillance of influenza among members of the armed forces was stopped in 2013 as AFRTIs are an adequate indirect indicator to monitor influenza during seasonal outbreaks among soldiers [10]. Only the 2006-2013 data is therefore presented for influenza.

Data analysis

Data was analyzed using Excel[®]. The incidence rates expressed as the number of cases notified per 1,000 persons and per year (PY for person-year) were calculated taking into account the mean number of soldiers deployed to each territory and the results expressed as the annual and weekly incidence. The mean incidence rates were calculated by area taking into account the duration of the French armed forces operations in that specific area.

RESULTS

The target population was all members of the French armed forces from 2006 to 2015, *i.e.* a mean annual population of 331,394 individuals.

Incidence and annual incidence rates

A total of 28,942 AFRTIs were notified as part of the epidemiological surveillance of members of the French armed forces from 2006 to 2015. A total of 22,818 cases were declared in metropolitan France, 3,211 in French overseas territories, 1,595 in the Navy (naval fleet in mission), and 1,318 in external operations (Table I).

From 2006 to 2013, 1,058 cases of influenza were declared including 934 cases in metropolitan France, 101 cases in French overseas territories, and 23 in external operations.

Incidence rate

The mean incidence rate of AFRTIs over the study period was 8.7 PY (95% CI [8.6-8.8]). The annual incidence rates of AFRTIs decreased over time, from 11.7 PY in 2006 to 4.3 PY in 2015 (2006=11.7 PY; 2007=11 PY; 2008=8 PY; 2009=25.9 PY; 2010=4.6 PY; 2011=5.4 PY; 2012=6.1 PY; 2013=6 PY; 2014=3 PY; 2015=4.3 PY).

An exceptional peak was observed in 2009, with 8,793 cases and an incidence rate of AFRTIs of 25.9 PY (95% CI [25.4-26.4]). The mean incidence rate of influenza from 2006 to 2013 was 0.35 PY (95% CI [0.33-0.37]). A major increase in the incidence rate of confirmed cases of influenza was observed during the 2009 influenza pandemic, with an incidence rate of 1.9 PY versus 0.1 to 0.2 PY the other years.

Mean incidence rates by area

AFRTI cases were declared in metropolitan France and in 24 other countries or areas where the French armed forces were deployed (Table I).

The mean incidence rate for the study period in metropolitan France was 8.2 PY (22,818 incident cases). Countries of deployment with the highest number of incident cases, in absolute value, were New Caledonia (954 cases) and Afghanistan (700 cases). The highest incidence rates were observed in Tajikistan (82.3 PY), Afghanistan (45.1 PY), and the United Arab Emirates (42.3 PY).

Epidemic peaks were identified by assessing the incidence rate per year and per area (Figure 1). Thus, in the United Arab Emirates the incidence rate exceeded 100 PY in 2008 (181.2 PY) and in 2009 (378.5 PY). This incidence rate was also exceeded in New Caledonia in 2006 (117.9 PY), Tajikistan in 2006 (203.8 PY) and 2009 (437.8 PY), with the highest annual incidence rate reported in the present study. Incidences and mean incidence rates by country over the study period are presented in Figure 2. Low incidence rates were mainly

observed in Sub-Saharan Africa (except for Uganda). Regions with high incidence rates were Central Asia, Middle East, and the Atlantic and Pacific islands.

Weekly incidence: the 2009 specific case

A first peak in the incidence rates was observed on Week 33 of 2009 in the Pacific region, in Africa, and in the Indian Ocean (Figure 3).

This was followed by another peak on Week 37 in the Atlantic (+4 weeks). The last peak was observed in Central Asia on Week 44 (+11 weeks). No increase in the incidence rates was observed in the Middle East. A first increase in the incidence rates was observed in Europe from Week 34 to Week 42 before the usual seasonal outbreak. The epidemic profile was similar for influenza cases over the same period, with a peak on Week 33 in the Pacific region, on Week 37 in the Atlantic, and with the highest peak observed in Central Asia on Week 45 (versus 44 for AFRTIs).

DISCUSSION

A military public health problem

The present study confirms the predominant role of AFRTIs among infectious episodes observed in members of the French armed forces. The epidemiological surveillance of these infections is therefore justified in this population. Performed over 10 years, *i.e.* for a longer duration than previously published studies [11-18], the present study confirms the constant occurrence of these infections over the years among members of the French armed forces, irrespective of their missions. With a mean annual incidence rate of 8.7 PY, AFRTIs are among the leading infectious episodes in this population in metropolitan France, French overseas territories, and external operations, following diarrhea but ahead of vector-borne diseases [5]. This incidence rate is however probably underestimated because members of

the armed forces do not seek medical advice for uncomplicated presentations or consult community physicians. Another reason may also be the underreporting of cases managed in military medical facilities or health facilities on the field. Underreporting is expected for the 2006-2013 period, during which influenza was specifically monitored, because of the obligation for microbiological confirmation. Comparing this incidence rate in young adults with data related to the French general population is difficult.

Excluding the 2009 epidemic peak, the study of the annual incidence rate highlights a progressive decline in the incidence of this syndrome over the 10 years under study. This trend may reflect poorer reporting and/or effective implementation of prevention measures. However, the comprehensive epidemiological surveillance of AFRTIs revealed outbreaks during external operations. The incidence rates observed in Tajikistan, Afghanistan, and the United Arab Emirates thus remain very high. The US army made the same observations with US soldiers based in Iraq and Afghanistan; this might be due to the continental climate and the significant drop in temperature, the winter season, and the constant exposure to dust, sand, and petrochemical fumes [19].

As observed in the French general population, the incidence rates (AFRTIs and influenza) among the French armed forces varied as expected by seasons in metropolitan France, with an excessive incidence in autumn and winter. However, such seasonality was not observed overseas and in external operations, where sporadic cases were reported all year long, sometimes with localized outbreaks. We did not observe the expected six-month shift due to the reversal of seasons when comparing changes in the incidence rates among the armed forces between both hemispheres. This may be explained by the localizations of the missions, as they mainly occur in intertropical areas (Africa and French departments of the Americas).

Because of changes to the criteria for epidemiological surveillance in the armed forces (distinction between AFRTIs and confirmed influenza until 2013, and then AFRTIs only), we could not properly compare these two periods. However, it provides insight into the influenza burden among AFRTIs. The isolated study performed for the year 2009 (A H1N1 influenza pandemic) helps in revealing the impact of this outbreak on the armed forces. The influenza pandemic affected the armed forces in and outside metropolitan France, with an exceptional peak of confirmed cases (approximately 19 times higher than the mean rate observed in non-epidemic periods). This may be explained by the increased daily surveillance implemented at that time among the armed forces personnel [20], but also by a more systematic biological confirmation of cases. An increased number of AFRTI cases was at the time observed in all areas of deployment, probably due to unconfirmed influenza cases or superinfections with other pathogens. As for the geographical distribution of influenza in 2009, we observed an initial spread of the infection in the Southern Hemisphere on week 33, followed by dissemination to the Northern Hemisphere in autumn. This distribution is typical of new influenza strains. Every year, the time interval is put to good use to synthesize influenza vaccines using the three predominant strains circulating in the Southern Hemisphere. Up to 2016, such time was not enough to have an adequate vaccine in time for members of the armed forces deployed in the Southern Hemisphere. In 2017 to immunize French soldiers deployed to the Southern Hemisphere, the army medical centers located in this region were authorized to locally buy vaccines ahead of this stage.

A daily challenge for the armed forces healthcare professionals

AFRTIs are a major medical problem in military operations because of the associated incidence rate, clinical impact, and the frequent need for care. AFRTIs are the leading infections in the US army. They require treatment initiation, are associated with poorer

operational capacity for soldiers (up to 33.8%), and account for 25% to 30% of hospitalizations of military personnel [21,22]. The epidemic nature of these infections may also rapidly saturate the primary care system, especially in operational missions.

This clinical situation is also associated with a diagnostic problem for the armed forces physicians, just like for any other community family physician. Poor specificity of the respiratory symptoms, limited access to microbiological diagnostic tools, and limited access to imaging techniques are major obstacles to clinical diagnosis. Physicians deployed with the armed forces to external operations or on small Navy vessels do not have access to rapid diagnostic tests for AFRTIs, and access to chest imaging techniques or routine microbiological tests is only possible in rear base medico-surgical facilities. Diagnostic means in metropolitan France are similar to those of family physicians. The French army health service is currently assessing several areas for improvement: maximization of biological diagnostic tools on the field, development of point-of-care facilities in areas with a high number of soldiers, and studies to determine the microbial ecology of AFRTIs.

Although frequent, AFRTIs are rarely severe or complicated in members of the French armed forces according to internal data of the French army health service on medical evacuations and hospitalization of soldiers (unpublished data). This is probably due to the rapid access to care on the field, with early empirical antibiotic treatment when indicated. Members of the armed forces are also younger and healthier than the general population. By way of comparison, AFRTIs were the leading non-traumatic cause of medical evacuation in Afghanistan from 2010 to 2011 (all nationalities) [23]. This clinical situation may however lead to evacuation within the theater of operations or to metropolitan France, mainly because of the associated operational incapacity. Specific to the army, physicians deployed to external operations must consider a wider range of causative agents when confronted

with severe pneumonia [24-26]. Alongside common pathogens (influenza virus, *Streptococcus pneumoniae*, etc.) that may be associated [27-30], specific endemic infections should be considered depending on the circumstances on the field: leptospirosis, melioidosis or schistosomiasis following exposure to fresh water, Q fever, or American histoplasmosis following a stay in the forest in Guyana, and anthrax in a context of bio-terrorism risk. Early detection and confirmation are essential for military public health and sometimes for national security.

Limitations of current prevention measures

With such a high incidence rate and a few outbreaks with operational impact, the incidence threshold of AFRTIs (influenza included) cannot be reduced despite current prevention measures. The same problem is observed for other community-acquired infections such as bacterial skin infections, diarrhea, and sexually transmitted infections [5]. Prevention of AFRTIs is currently based on operational readiness of members of the armed forces for each mission, hygiene measures, and vaccination against influenza.

The health of each soldier is monitored at medical visits every 24 months. Members of the armed forces must also attend a medical visit before each mission, where they receive targeted health education on the risks associated with the mission. If needed, they receive the required vaccines and are prescribed malaria prophylaxis. They are declared fit for duty if they do not present with any active disorder, even dental infections, and if their vaccinations are up to date. Health education on preventive measures against AFRTIs is given to soldiers on a regular basis as well as in cases of outbreaks: regular ventilation of living areas, strict hand hygiene following each contact with a sick person. Measures aimed at stopping secondary transmission from suspect cases are implemented as much as possible; physical means of prevention (masks, etc.) must therefore be available in all

facilities. These measures have proved effective, but their implementation may be difficult because of the living conditions of operational missions; thus explaining some outbreaks observed in armed conflicts [7]. Since 1994 the French army health service has been implementing a prevention strategy against influenza through the vaccination of non-medical armed forces personnel every three years to achieve collective immunity and maintain minimum operational capacity, and through annual vaccination of military health professionals. The effectiveness of the three-year strategy has yet to be proven [31].

Because of a lack of insight, we cannot assess the influence of antipneumococcal vaccination — mandatory for children since 2004 [32] — on the progressive decline in AFRTIs among the armed forces over the 2006-2015 period.

Besides, the French army has never documented any AFRTI outbreak caused by adenoviruses, unlike the US army. The US army has therefore implemented oral vaccination against adenoviruses in 2012, with a confirmed decrease in AFRTI cases over the initial training period of soldiers [33-36]. Such vaccination is not considered by the French army.

We also could not assess whether antimalarial chemoprophylaxis with doxycycline (100 mg/day) in endemic areas had an impact on the incidence of AFRTIs in these areas. Although doxycycline is active against most streptococci, some strains of *Staphylococcus aureus*, various Gram-negative bacilli, several anaerobes, *Mycoplasma pneumoniae*, *Coxiella burnetii*, and leptospirosis, no data suggests the reduced incidence of cosmopolitan or exotic bacterial pneumonia.

Limitations of the study

The case definition of AFRTI presented in the method complies with epidemiological surveillance criteria that do not make the distinction between lower and upper respiratory tract infections.

Non-biologically confirmed influenza cases are de facto included among AFRTIs. Confirmed cases of influenza are not included among AFRTIs, but they are included among influenza cases. However, as the influenza surveillance was stopped in 2013, cases are included among AFRTI cases reported in 2014 and 2015.

Exhaustiveness of confirmed cases (required in the army) by declaring units presented in the method does not seem possible.

CONCLUSION

The present study reports the high incidence of AFRTIs in military public health because of their morbidity and operational impact in cases of outbreaks. Although their severity is reduced because of an effective healthcare chain, prevention measures do not seem to significantly reduce the incidence threshold. This observation highlights several areas for improvement in the short- and mid-term: maximization of diagnosis on the field (*e.g.*, rapid diagnostic test for influenza), oseltamivir on the field to limit the epidemic spread of influenza, study of the respiratory microbial ecology among members of the armed forces, assessment of the three-year vaccination strategy against influenza, strengthening of the response capacity to future emerging infections.

Disclosure of interests

The authors report no conflict of interest.

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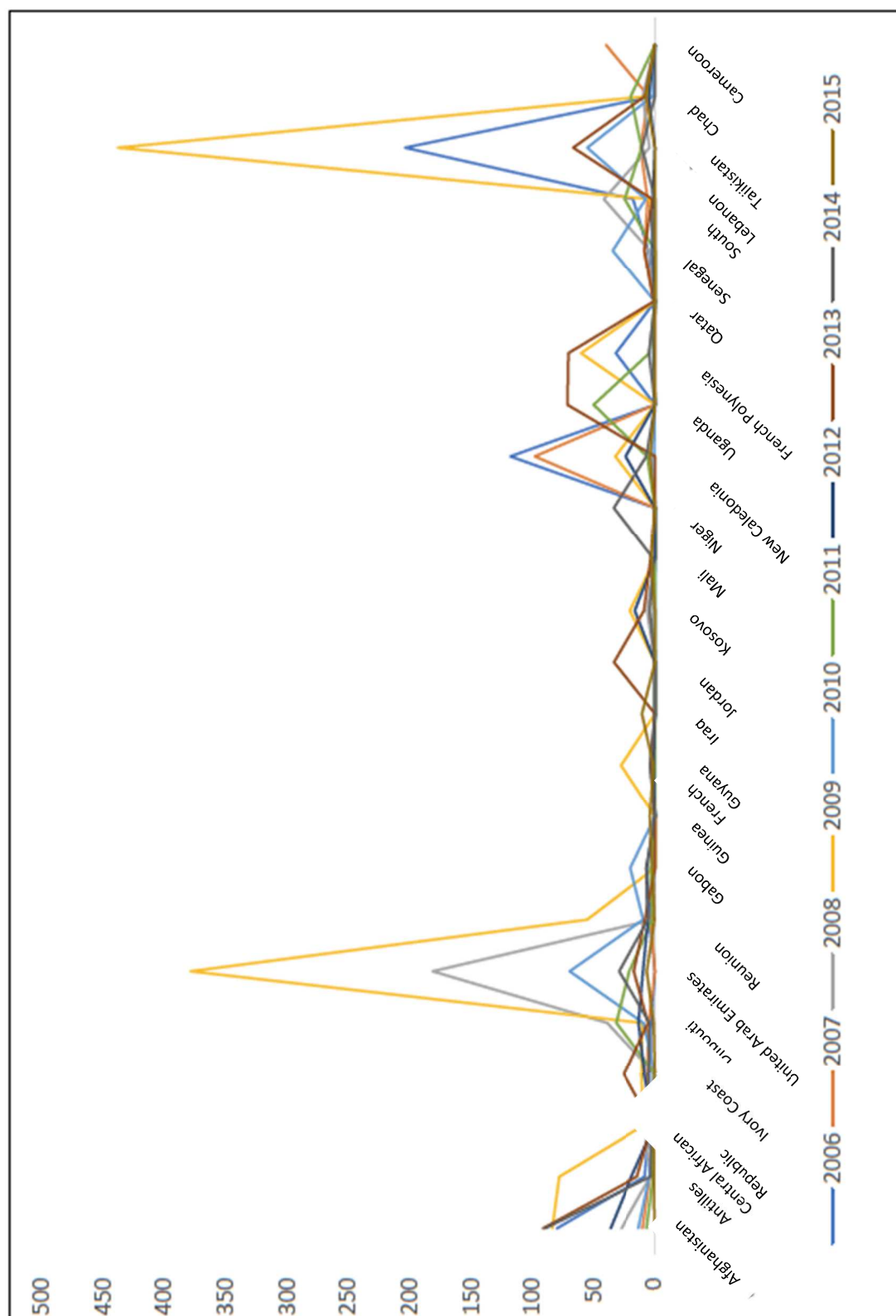
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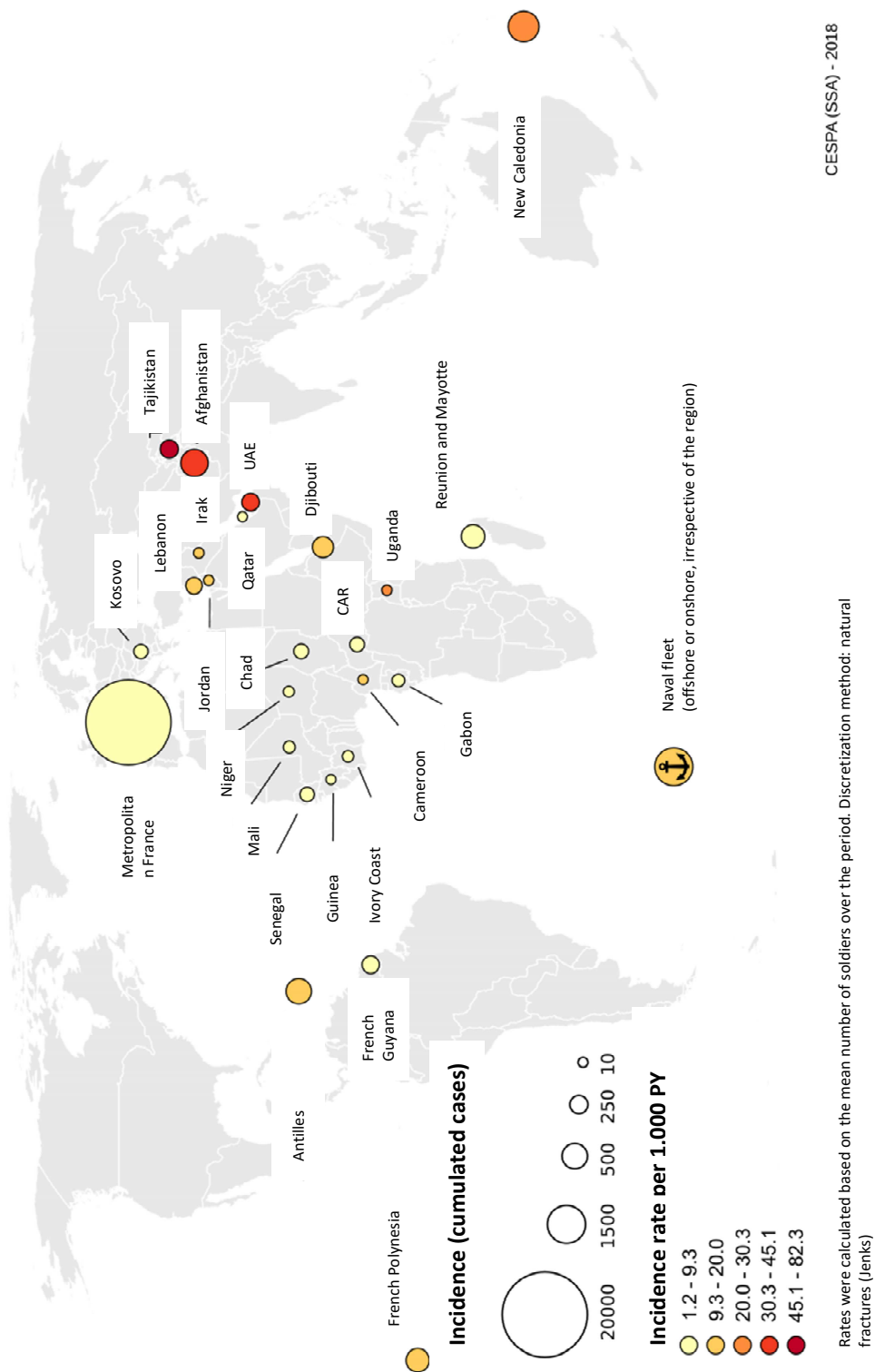
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Figure 1. Mean annual incidence rates from 2006 to 2015 (declared cases per 1,000 person-years) by territory

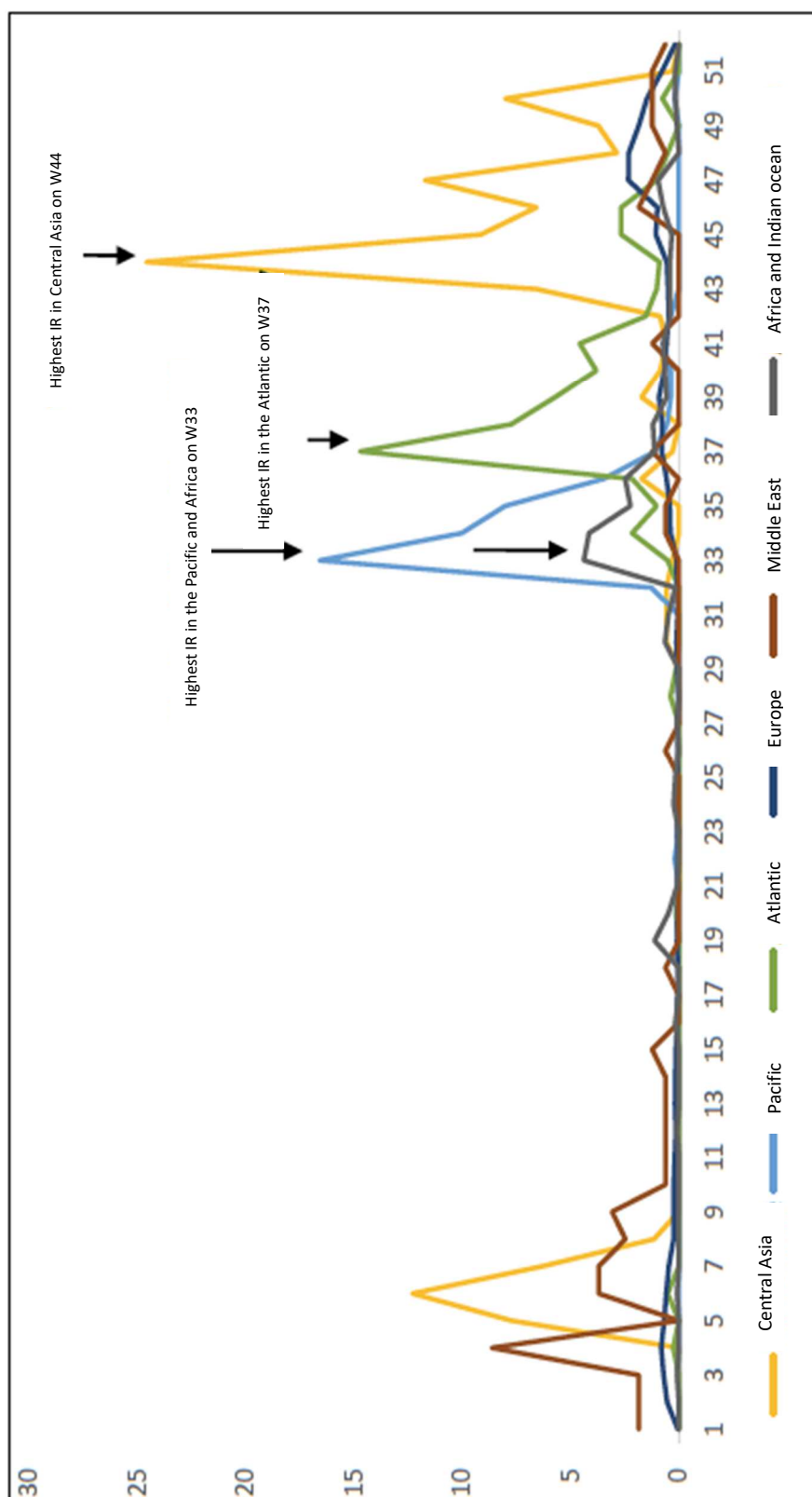




CESPA : Centre d'épidémiologie et de santé publique des armées (Center for Epidemiology and Public Health of the Armed Forces); UAE: United Arab Emirates; CAR: Central African Republic; SSA : Service de santé des armées (Army Health Service)

Figure 2. Incidence et taux d'incidence des IRAF (infections respiratoires aiguës fébriles) dans les Armées sur la période 2006-2015 pour 1 000 personnes année

Figure 2. Impact and incidence rates of respiratory tract infections in the armed forces over the 2006-2015 period per 1,000 person-years



W: week; IR: average incidence rate

Figure 3. Evolution des taux d'incidence par région sur l'année 2009 pour 1 000 personnes année

Figure 3. Changes in the incidence rate by region in 2009 per 1,000 person-years

Tableau I. Taux d'incidence moyens (TI) exprimés pour 1 000 personnes année (PA) des IRAF déclarées par territoire sur la période 2006-2015

Table I. Mean incidence rates per 1,000 person-years of respiratory tract infections reported by territory over the 2006-2015 period

Country	Number of cases	2006-2015 incidence rate as person year (PY)
Tajikistan	196	82.25
Afghanistan	700	45.11
United Arab Emirates	175	42.33
New Caledonia	954	30.26
Uganda	2	29.85
Cameroon	2	20
French Polynesia	448	17.48
Jordan	3	17.24
Antilles	577	13.16
Djibouti	329	13.14
Lebanon	132	11.78
Iraq	5	10.66
Mayotte - Reunion	457	9.35
Metropolitan France	22,818	7.94
Senegal	71	7.97
Niger	9	7.22
Chad	84	6.63
Kosovo	70	6.63
Ivory Coast	80	5.17
Guinea	1	4.22
French Guyana	165	4.19
Gabon	35	4.18
Mali	19	2.78
Central African Republic	14	2.34
Qatar	1	1.2
Naval fleet	1,595	13.29

PY: person year;

Naval fleet, offshore or onshore irrespective of the region