ORIGINAL ARTICLE 10.1111/j.1469-0691.2011.03596.x

Travel-related imported infections in Europe, EuroTravNet 2009

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Abstract

The aim of this study was to investigate travel-associated morbidity in European travellers in 2009 in comparison with 2008, with a particular emphasis on emerging infectious diseases with the potential for introduction into Europe. Diagnoses with demographic, clinical and travel-related predictors of disease from ill returning travelers presenting to 12 core EuroTravNet sites from January to December 2009 were analysed. A total of 6392 patients were seen at EuroTravNet core sites in 2009, as compared with 6957 in 2008. As compared with 2008, there was a marked increase in the number of travellers exposed in North America and western Europe. Respiratory illnesses, in particular pandemic A(H1N1) influenza, influenza-like syndromes, and tuberculosis, were also observed more frequently. A significant increase in reported dengue cases in 2009 as compared with 2008 was observed (n = 172, 2.7% vs. n = 131, 1.90%) (p 0.002). The numbers of malaria and chikungunya cases were also increasing, although not significantly. Two deaths were recorded: visceral leishmaniasis and sepsis in a Sudanese migrant, and *Acinetobacter* sp. pneumonia in a patient who had visited Spain. This is the most comprehensive study of travel-related illness in Europe in 2009 as compared with 2008. A significant increase in travel-related respiratory and vector-borne infections was observed, highlighting the potential risk for introduction of these diseases into Europe, where competent vectors are present. The number of traveller deaths is probably underestimated. The possible role of the travellers in the emergence of infectious diseases of public health concern is highlighted.

Keywords: Europe, imported diseases, surveillance, travel, travel medicine
Original Submission: 11 March 2011; **Revised Submission:** 26 May 2011; **Accepted:** 1 June 2011
Editor: T. A. Zupanc

Clin Microbiol Infect

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Introduction

The international circulation of microorganisms, vectors and infected individuals and animals poses a global public health threat, and requires attention at the national and international levels. In 2009, 12 EuroTravNet sites from nine European countries, also belonging to the global GeoSentinel surveillance system (http://www.eurotravnet.eu), contributed to this study, whose aim was to describe demographic, epidemiological and clinical characteristics of ill travellers who presented in 2009 in order to assess the importance of infectious diseases that are non-endemic in Europe, but have the potential for re-introduction. Comparison with 2008 data [1] was performed when appropriate.

Patients and Methods

We included patients who presented from 1 January to 31 December 2009 at any of the participating EuroTravNet sites with a history of international travel and a travel-associated complaint as judged by the treating physician, as described previously [2]. Some patients were found to have no morbidity after examination. Reasons for travel were grouped into eight main categories (Table 1). Specific diagnoses from a list of 688 items were grouped into 22 broad syndromes, and countries of likely exposures were grouped into 13 regions (Table 1) [1]. Data were analysed with SPSS v16.0 (SPSS, Chicago, IL, USA). Owing to the absence of a true denominator, no incidence rates or risk estimates can be calculated. Rather, proportionate morbidity was used, comparing the number of cases of a specific diagnoses or syndrome with all cases of ill returned travellers seen during the same time period. Differences in proportionate morbidity between 2009 and 2008 in ill returned travellers seen at EuroTravNet core sites were tested with Pearson chi-square or Fisher exact tests. *t*-Tests were used for continuous variables. A p-value of <0.01 was chosen to adjust for the large number of statistical tests performed.

TABLE 1. Demographic characteristics of travellers

Site	2008	2009	p-value
Gender (%)			
Female	48.9	50.3	
Travel reason (%)			
Business	10.5	11.0	<0.001
Immigration	9.4	7.7	
Medical tourism	0.1	0.4	
Military	0.6	1.0	
M/V/AW/R	22.6	20.0	
Student	1.3	2.5	
Tourism	43.5	45.0	
VFR	11.9	12.5	
Risk level (%)			
Expatriate	6.9	8.6	<0.001
Pre-arranged or organized travel	22.6	26.6	
Risk travel[a]	69.8	63.7	
Missing	0.8	1.2	
Clinical setting (%)			
Immigration only	9.4	7.7	0.001
Seen after travel	82.0	84.4	
Seen during travel	8.5	7.9	
Inpatient	11.0	14.6	<0.001
Pre-travel advice (%)			
Yes	45.4	43.2	<0.001
No	22.4	26.1	
Do not know	32.2	30.7	
Born in Europe (%)			
Yes	76.0	77.5	0.035
Age (years)			
Mean	37.4	36.9	0.051
25th percentile	27.0	27.0	(*t*-test)
Median	36.0	35.0	
75th percentile	48.0	47.0	
Region of exposure, no. (%)			
Sub-Saharan Africa	1802 (25.90)	1641 (25.67)	
North Africa	330 (4.74)	248 (3.88)	
Carribean	115 (1.65)	126 (1.97)	
Central America	133 (1.91)	162 (2.53)	
South America	470 (6.76)	412 (6.45)	
North America	23 (0.33)	117 (1.83)	
Middle East	107 (1.54)	96 (1.50)	
Northeast Asia	78 (1.12)	52 (0.81)	
South Central Asia	676 (9.77)	550 (8.60)	
Southeast Asia	631 (9.07)	678 (10.61)	
Eastern Europe	114 (1.64)	55 (0.86)	
Western Europe	227 (3.26)	291 (4.55)	
Cannot be ascertained[b]	2201 (31.64)	1908 (29.85)	
Other	50 (0.72)	56 (0.88)	
Total	6957 (100)	6392 (100)	

M/V/AW/R, missionary/volunteer/Aid work/researcher; VFR, visiting friends and relatives.
[a]Risk travel: intended to identify travellers who will, by their behaviour, encounter a substantial number of the risks facing the local population. This classification would generally include no pre-booking of accommodation for most or all nights and/or use of accommodation specific to budget travellers or those staying in the house of local residents.
[b]Country of exposure is considered to be not ascertainable when: (i) no country/region was ascertainable by the physician; (ii) when possible exposure occurred in more than one country and/or in different regions; (iii) when the diagnosis could not be attributed to a single travel exposure; or (iv) the patient was found to be healthy.

Results

The same core sites contributed patients to the analysis in 2008 and 2009, although the proportionate contribution varied over time in some of the sites (Table 2).

Demographics and patient characteristics

In 2009, 6392 patients with travel-associated health complaints were seen at the participating institutions (n = 6957 in 2008). Information about demographics, reason for travel, risk level and clinical setting is given in Table 1.

Epidemiology and exposure region of ill travellers

The median times from travel to presentation at a clinic was 12 days (in 2008) and 13 days (in 2009) respectively in travellers and 2.4 years (2008 and 2009) in those whose reason for travel was immigration. In both 2008 and 2009, travellers were most likely exposed in sub-Saharan Africa (25.9% and 25.67%, respectively). In 2009, there was a remarkable

TABLE 2. Site contribution

Country	Site	2008, N = 6957 (%)	2009, N = 6392 (%)
Germany		43.5	35.1
	Hamburg	21.3	12.6
	Munich	22.2	22.5
France		12.9	16.9
	Marseilles	5.0	7.8
	Paris	7.9	9.1
UK		18.1	16.2
	Cambridge	1.8	2.0
	London	16.3	14.2
The Netherlands	Amsterdam	0.6	10.5
Norway	Oslo	7.2	7.4
Switzerland		9.2	6.7
	Geneva	6.0	4.6
	Zurich	3.2	2.1
Italy	Brescia	2.0	3.8
Spain	Madrid	6.5	3.4

increase in the proportion of travellers exposed in North America (0.33% in 2008 and 1.83% in 2009) and western Europe (3.26% in 2008 and 4.55% in 2009). The contrary was true for eastern Europe (1.64% in 2008 and 0.86% in 2009), North Africa (4.74% in 2008 and 3.88% in 2009) and South Central Asia (9.77% in 2008 and 8.6% in 2009). Country of exposure could not be ascertained in 31.64% and 29.85% of cases in 2008 and in 2009, respectively (Table 1). Region-specific proportionate morbidities are presented in Table 3.

Aetiology and clinical picture of travel-related diseases

Deaths. Two deaths were reported in 2009. The first was a 32-year-old male with chronic hepatitis B, born in Eritrea but of Sudanese nationality, who died after 6 days of visceral leishmaniasis and sepsis. The second was an 86-year-old male Norwegian with chronic obstructive pulmonary disease and Parkinson's disease, who died from *Acinetobacter* sp. pneumonia 4 days after returning from Spain. Three deaths were reported in 2008.

TABLE 3. Top diagnoses by region of exposure, 2008–2009

Top five diagnoses	2008, no. (%)	2009, no. (%)
Sub-Saharan Africa		
N = 1802, *N* = 1641		
Malaria	318 (18)	321 (20)
Viral syndrome, no rash	146 (8)	99 (6)
Diarrhoea, acute unspecified	113 (6)	118 (7)
Schistosomiasis	79 (4)	97 (6)
Diarrhoea, acute bacterial	52 (3)	40 (2)
Southeast Asia		
N = 631, *N* = 678		
Dengue	60 (10)	65 (10)
Diarrhoea, acute unspecified	58 (9)	52 (8)
Viral syndrome, no rash	64 (10)	43 (6)
Diarrhoea, chronic unknown	34 (5)	29 (4)
CLM, hookworm-related	24 (4)	38 (6)
South Central Asia		
N = 676, *N* = 550		
Giardia	74 (11)	62 (11)
Diarrhoea, acute unspecified	71 (11)	52 (9)
Diarrhoea, chronic unknown	40 (6)	36 (7)
Campylobacter	25 (4)	37 (7)
Viral syndrome, no rash	41 (6)	21 (4)
South America[a]		
N = 351, *N* = 374		
Diarrhoea, acute unspecified	23 (7)	30 (8)
Viral syndrome, no rash	26 (7)	12 (3)
Diarrhoea, chronic unknown	19 (5)	19 (5)
CLM, hookworm-related	17 (5)	20 (5)
Malaria	12 (3)	21 (6)
North Africa		
N = 330, *N* = 248		
Diarrhoea, acute unspecified	54 (16)	38 (15)
Diarrhoea, chronic unknown	25 (8)	16 (6)
Irritable bowel syndrome, post-infectious	21 (6)	18 (7)
Animal bite requiring rabies PEP	19 (6)	14 (6)
Gastroenteritis[b]	24 (7)	5 (2)
Europe		
N = 341, *N* = 346		
Gastroenteritis[b]	26 (8)	10 (3
Influenza-like illness[b]	1 (0)	34 (10)
Influenza, novel H1N1[b]	0 (0)	33 (10)
Pneumonia, bacterial (lobar)	21 (6)	11 (3)
Diarrhoea, acute unspecified	17 (5)	14 (4)
All regions[c]		
N = 6957, *N* = 6392		
No morbidity found	1056 (15)	977 (15)
Diarrhoea, acute unspecified	423 (6)	375 (6)
Malaria	365 (5)	374 (6)
Viral syndrome (no rash)	434 (6)	266 (4)
Diarrhoea, chronic unknown	265 (4)	226 (4)

CLM, cutaneous larva migrans; PEP, post-exposure prophylaxis.
[a]Bolivians screened for Chagas disease in Europe are excluded.
[b]Significant at p <0.01.
[c]Includes 1773 patients seen only for screening, with no morbidity found and region of exposure not ascertained.

Travel-related diseases in Europe. The proportion of patients suffering from respiratory illnesses increased from 7.8% in 2008 to 11% in 2009 (p <0.001). Most of this increase was attributable to cases in 2009 of pandemic A(H1N1) influenza.

Vector-borne disease with potential for re-introduction into Europe. . The number of malaria, dengue and chikungunya cases, considered all together, significantly increased from 507 (7.3%) to 564 (8.8%) (p <0.001), but most of the increase concerned dengue cases.

Malaria: The total number of imported malaria cases increased slightly from 365/6957 (5.2%) to 374/6392 (5.8%) (p 0.127), with a higher species identification rate (9.3% of unknown species in 2008, and 4.3% in 2009). *Plasmodium falciparum* was the most commonly reported species (68.2% in 2008, 74.3% in 2009). We observed a slight but non-significant increase in malaria from South America, particularly in military patients with *Plasmodium vivax* malaria coming from French Guyana and presenting at the Marseille clinic (3/7 in 2008 and 15/16 in 2009). The number of paediatric malaria cases rose from nine in 2008 to 28 in 2009, mainly in Italy (Brescia) and France. Pre-travel encounter was registered for 32% of all malaria patients observed in 2008 and 2009. Complicated malaria cases numbered 12 in 2008 and 14 in 2009 (20 adults and six children overall). Adult patients were European travellers (*n* = 12) or expatriates (*n* = 4) and migrants (*n* = 4). Six cases occurred in children: two immigrants and four children born in Europe who were visiting friends and relatives (VFR). They were mainly exposed in West Africa (Burkina Faso, Ghana, Guinea (two cases), and Nigeria) and Malawi.

Dengue: Dengue was the second most frequent cause of fever among ill returning travellers, with 172/6392 cases (2.7%) in 2009 (no dengue haemorrhagic fever/dengue shock syndrome), a significant increase as compared with 2008 (p 0.002). Of those, 115 cases (67%) were observed in tourists, a similar proportion to that recorded in 2008 (80/131; 61%). Most 2009 cases were imported from the Netherlands Antilles and Suriname or from Thailand and Vietnam.

Chikungunya: The total number of patients with imported chikungunya showed a non-significant increasing trend from 12/6957 (0.2%) in 2008 to 18/6392 (0.3%) in 2009 (p 0.184). Most patients were exposed in Southeast Asia (Thailand, Singapore, Malaysia, and Indonesia), South Central Asia (India and the Maldives), and the Indian Ocean Islands (La Reunion).

Emerging diseases. Pandemic A(H1N1) influenza: The pandemic A(H1N1) influenza was the main determinant of the increase in respiratory illnesses observed in 2009. As many as 171/6392 cases of influenza-like illness (2.3%) and 83/6392 cases of confirmed pandemic A(H1N1) influenza (1.1%) were observed, mainly in students and tourists returning from the USA, the UK, Spain, Argentina, and Mexico, in decreasing order. The first case of pandemic A(H1N1) influenza in the EuroTravNet network was reported on 28 April 2010 in a tourist from Mexico (Fig. 1). Influenza-like illnesses that were not confirmed as pandemic A(H1N1) influenza were seen in patients exposed in the USA, Spain, and the UK, although there were also cases from Thailand and India.

Chagas disease: The number of reported new Chagas cases, detected by serology, decreased from 94/6957 (1.4%) to 30/6392 (0.5%) (p ≤0.001).

Chronic diseases. There was a significant increase in the proportion of reported tuberculosis (TB) cases, from 1.5% in 2008 to 2.1% in 2009 (p 0.003), primarily from the clinic in Brescia. Human immunodeficiency virus (HIV)/AIDS represented the most frequent chronic diagnosis, followed by active TB and latent TB. Of the HIV/AIDS cases, 217 were migrants, and 76 were non-migrants. Arriving immigrants accounted for 163 cases, and the remaining cases were mainly VFR travellers.

Miscellaneous. In 2009, 19 cases of cutaneous leishmaniasis and four cases of visceral leishmaniasis were reported, as compared with 12 cases of cutaneous leishmaniasis and two cases of visceral leishmaniasis in 2008.

Diseases acquired in Europe. As many as 346 (5.4%) travel-related diseases were observed following travel within Europe in 2009, a similar number to that in 2008 (*n* = 341/5967, 4.9%). However, the exposure shifted slightly away from immigrants and VFR travellers from eastern Europe (4% and 9% in 2009, from 8% and 25% in 2008). The main European countries of exposure were Germany (*n* = 115), Spain (*n* = 64), the UK (*n* = 38), Italy (*n* = 25), and France (*n* = 12). Respiratory illness (p 0.003), including pandemic A (H1N1) influenza, and acute diarrhoea (p 0.010) were reported more often in 2009 than in 2008.

Discussion

Travel-related illnesses may have important public health consequences if conditions for re-introduction of diseases are met [3]. In our dataset, in 2008 and 2009, five deaths were reported. This is probably an underestimate of the mortality burden, as it does not include patients who died overseas, and patients who die may be more likely to be seen in other types of clinic.

During the last few years, the number of imported malaria cases in Europe has decreased, possibly reflecting malaria control activities in endemic countries [4,5]. However, malaria in Europe remains an important travel medicine issue, given the large number of imported cases [6]. Moreover, there is potential for the reappearance of malaria in countries where it was previously eradicated, and limited outbreaks do occur in Europe, where *Anopheles* mosquitoes are still present, mainly in the Mediterranean area [7], making the slight, although not statistically significant, increase observed in our dataset in 2009 a phenomenon that requires attention. In August 2006, one case of indigenous *P. vivax*

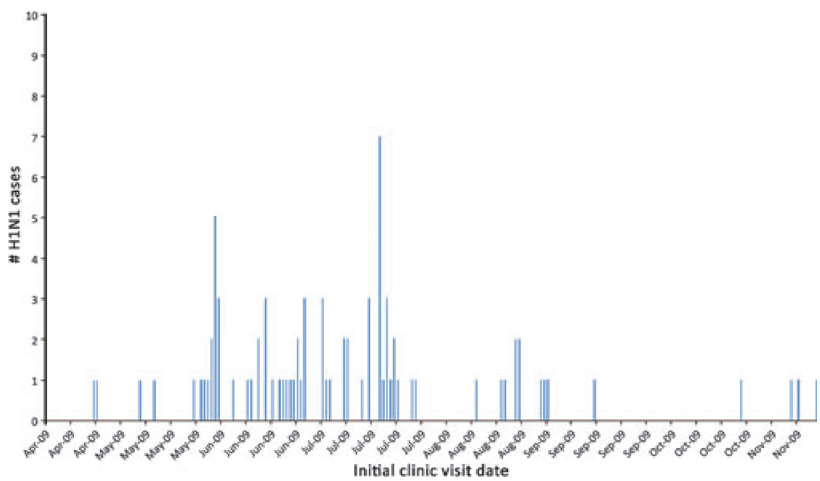

FIG. 1. Pandemic A(H1N1) incident cases.

malaria was diagnosed in Corsica [8], and in October 2010, another was diagnosed in Aragon, Spain, where the vector, *Anopheles atroparvus*, is present [9].

Dengue is the second most common cause of fever in returned ill travellers [10]. The increase in the number of dengue cases observed in 2009 is mainly attributable to the increased participation of the clinic in Amsterdam, with patients coming from the Netherlands Antilles and Suriname, and to an increase in the numbers of patients coming from Thailand and Vietnam, where dengue outbreaks in 2009 were reported [11,12]. In Mediterranean countries, the presence of *Aedes albopictus* can facilitate autochthonous cases [3]. In August 2010, a case of dengue fever acquired in southern Croatia in a traveller from Germany was reported [13], and in September 2010 two cases of autochthonous dengue fever were diagnosed in metropolitan France (Nice) for the first time. This strongly suggests that local transmission of dengue is ongoing [14]. Increased surveillance for dengue with mosquito control and increased vigilance by health professionals is needed [15].

Chikungunya remains an important global public health problem, with several outbreaks occurring worldwide, such as in Malaysia and Thailand in 2009. Chikungunya activity is ongoing in the French island of Reunion [16]. Since the 1980s, *A. albopictus* has spread worldwide, including to southern Europe [17]. After the Italian outbreak in 2007 [3], two autochthonous cases of chikungunya fever were reported in France, in September 2010 [18]. Climate changes, urbanization and international transport may facilitate the enlargement of areas endemic for chikungunya and other vector-transmitted infections, posing a threat to global public health even in areas previously considered to be safe, such as Europe. The presence of adequate vectors in Europe may favour the stable introduction of vector-borne diseases [19].

Chagas disease is a potentially life-threatening illness, affecting over 10 million people, originating mainly from Latin America. Although the vector (*Triatominae* spp.) is not present on the European continent, the chronic nature of the disease, together with the migration flow from endemic countries, can have a public health impact in Europe [20], as it is potentially transmissible to the autochthonous population through contaminated blood products, and also causes congenital and chronic diseases [21]. Owing to its historical links with Latin America, Spain reports the highest number of Chagas cases in Europe. A moderate decrease in the number of cases of Chagas infection detected by serology was observed in 2009. This is probably attributable to the 2009 economic crisis, which has forced many migrants to return to their country origin, or to a cohort effect, after much of the Bolivian migrant community in Madrid was screened in 2008. Efforts are needed to improve knowledge of Chagas disease among physicians [22] and to develop screening and control in blood banks, organ donation, and at-risk pregnant women.

Pandemic A(H1N1) influenza was first detected in the USA on 15 April 2009, and the WHO declared it a Public Health Emergency of International Concern on 25 April 2009. Recommendations to countries to intensify surveillance were soon issued [23]. In our dataset, after the first case, reported on 28 April in a European traveller returning from Mexico, the number of confirmed reported cases peaked in July 2009. Pandemic A(H1N1) influenza cases were primarily diagnosed, in decreasing order, in students and tourists exposed in the USA, the UK, Spain, Argentina, and Mexico. As pandemic A(H1N1) influenza became a global problem, we observed a progressive decrease in the number of cases reported in Europe, potentially reflecting the widespread management of these patients at various levels of the European health systems, as well as the possibility that new cases of pandemic A(H1N1) influenza were now more likely to be acquired locally rather than through travel. Our data underline the usefulness of surveillance networks to monitor an unexpected epidemic event in Europe. Pandemic A(H1N1) influenza greatly affected the profile of the patients observed in our network, with a shift to travellers and students returning from North America [24].

The small increase in the number of TB cases may reflect the changing composition of newly arriving migrant communities, particularly Pakistani and Indian migrants, in Brescia, Italy, a popular destination for migrants in Italy. The impact of imported TB on the local epidemiology may vary from country to country [25]. These numbers may change from year to year as migration patterns change, and could therefore be a marker for the possibility of other illnesses in migrants.

Most of the cases of HIV/AIDS in our study were in immigrants. The long incubation periods of HIV/AIDS and TB make it very difficult to ascribe these infections to a specific travel episode or to an infectious condition existing before travel in migrants [26,27]. Pre-travel and post-travel advice by infectious disease specialists will be important, as the prevalence of HIV infection is expected to rise as AIDS-related mortality is decreasing [28].

We recognize the following limitations that may possibly make time comparisons less accurate. (i) The relative contributions of participating centres varied from 2008 to 2009. This means that the 2009 proportionate morbidity presents a more legitimate baseline than counts. (ii) As EuroTravNet represents a sample of travellers who sought medical care, the incidence and risk of returning with any given diagnosis cannot be calculated. However, proportionate morbidity can be calculated to compare relative frequencies of illness in ill returned travellers. (iii) Our analysis could not capture all febrile illness in travellers, because infections that have short incubation periods may manifest during travel. The patient intake at each site reflects local or national differences in the composition of the travelling population, the distribution of the travel destinations, and access to medical care. However, we are confident that the large sample size, the European heterogeneous mix of sites and patients and the quality and consistency of the collected data compensated for biases and provide useful information.

Conclusions

The timely and accurate reporting of *ad hoc* surveillance networks such as EuroTravNet will supplement and reinforce regular routine disease reporting, and serve as a sentinel for emerging infectious diseases. Travellers played an important role in the spread of pandemic A(H1N1) influenza, as has already occurred in the past for other airborne infections (i.e. SARS). Vector-borne infections, such as malaria, chikungunya and dengue, need ongoing surveillance as global warming, urbanization and international transport may facilitate the enlargement of endemic areas. Secondary cases may be expected, and have already been reported in Europe. Increased surveillance for mosquito control and increased vigilance by health professionals are needed.

Acknowledgements

We are grateful to D. Freedman for helpful comments. In addition to the authors, members of the EuroTravNet/GeoSentinel Networks who contributed data are: P. Gautret and F. Simon, Hôpital Nord, Marseille, France; R. Weber, University of Zürich, Zürich, Switzerland; A. Pérignon, Paris, France; G. Carosi and A. Matteelli, University of Brescia, Brescia, Italy; and F. Chappuis, University of Geneva, Geneva, Switzerland.

Funding

EuroTravNet (http://www.eurotravnet.eu) is the European Centre for Disease Prevention and Control corresponding network for tropical and travel medicine, funded through the public tenders OJ/2008/07/08-PROC/2008/019 and OJ/2010/03/16-PROC/2010/011. It has been created by grouping the European sites of Geosentinel (http://www.geosentinel.org), the Global Surveillance Network of the International Society of Travel Medicine, supported by Cooperative Agreement U50 CI000359 from the US CDC.

Author Contributions

S. Odolini contributed to data collection, analysis, and interpretation, and first drafted the paper. F. Castelli contributed to the interpretation of the analyses, and drafting and reviewing of the paper; L. Weld performed the statistical analysis and reviewed the paper; E. Gkrania-Klotsas, E. Caumes, P. Schlagenhauf, R. López-Vélez, G.-D. Burchard, F. Santos-O'Connor, F. von Sonnenburg, P. de Vries, M. Jensenius and L. Loutan contributed to data collection and interpretation of the results, and reviewed the paper; P. Parola coordinated the work, contributed to study conception and design and the interpretation of the analysis, and reviewed the paper. All authors, external and internal, had full access to all of the data (including statistical reports and tables) in the study, and can take responsibility for the integrity of the data and the accuracy of the analysis. All authors read and approved the final manuscript.

Transparency Declaration

The paper is of epidemiological nature and no commercial interests are involved. However, the following conflicts of interest have been declared: PS has received research funding from GSK, Roche and Pfizer, speaking honoraria from GSK, Roche and Sigma-Tau and consultancy fees from Roche; EC has received speaking honoraria from Wyeth and Bristol-Myers Squibb and consultancy fees from Novartis and Aventis Pasteur; EGK has received speaking honoraria from Pfizer, Bristol-Myers Squibb and Gilead. All other authors declare no conflict of interest in relation to this paper.

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