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 **ESCMID** EUROPEAN SOCIETY  
OF CLINICAL MICROBIOLOGY  
AND INFECTIOUS DISEASES



*Refugees, migrants and infections 27 Apr 2015, 09:00 - 11:00 h, Hall E*

## **Immigrants returning home to visit friends and relatives (VFRs) and imported infectious diseases: Travelers, immigrants or both?**

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## Visiting Friends and Relatives (VFRs): Definition

- **VFRs: Immigrants** settled in the host country traveling back to their countries of origin **to visit friends and relatives**
- **A new definition has been proposed:** VFRs should be those whose primary purpose of travel is to visit friends and relatives and for whom there is a gradient of epidemiologic risk between home and destination.

[-] Barnett ED, MacPherson DW, Stauffer WM, Loutan L, Hatz CF, Matteelli A, et al. The visiting friends or relatives traveler in the 21st century: time for a new definition. *J Travel Med* 2010;17:163e70.

# Visiting Friends and Relatives (VFRs): Increasing travelers

## Tourism in the world: key figures

**9%** of GDP- direct, indirect and induced impact

**1 in 11** jobs

US\$ **1.4** trillion in exports

**6%** of the world's exports

from **25** million international tourists in 1950

to **1087** million in 2013

**5 to 6** billion domestic tourists

**1.8** billion international tourists forecast for 2030

UNWTO Tourism Highlights, 2014 Edition

## Inbound tourism by purpose of visit, 2013\*

(share)

Leisure, recreation and holidays  
52%

VFR, health, religion, other  
27%

Business and professional  
14%

Not specified 7%

Source: World Tourism Organization (UNWTO) ©

# Visiting Friends and Relatives (VFRs): Increasing patients

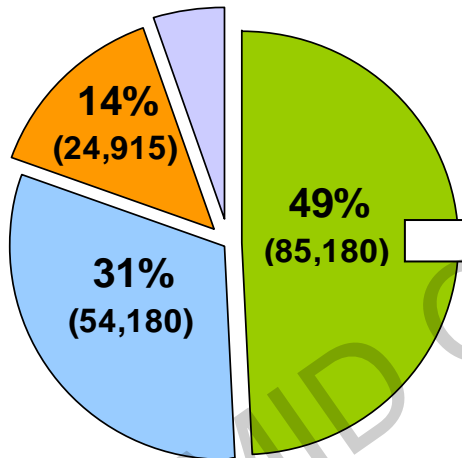


## Who are GeoSentinel patients? (as of June 2012)



### Complete Database

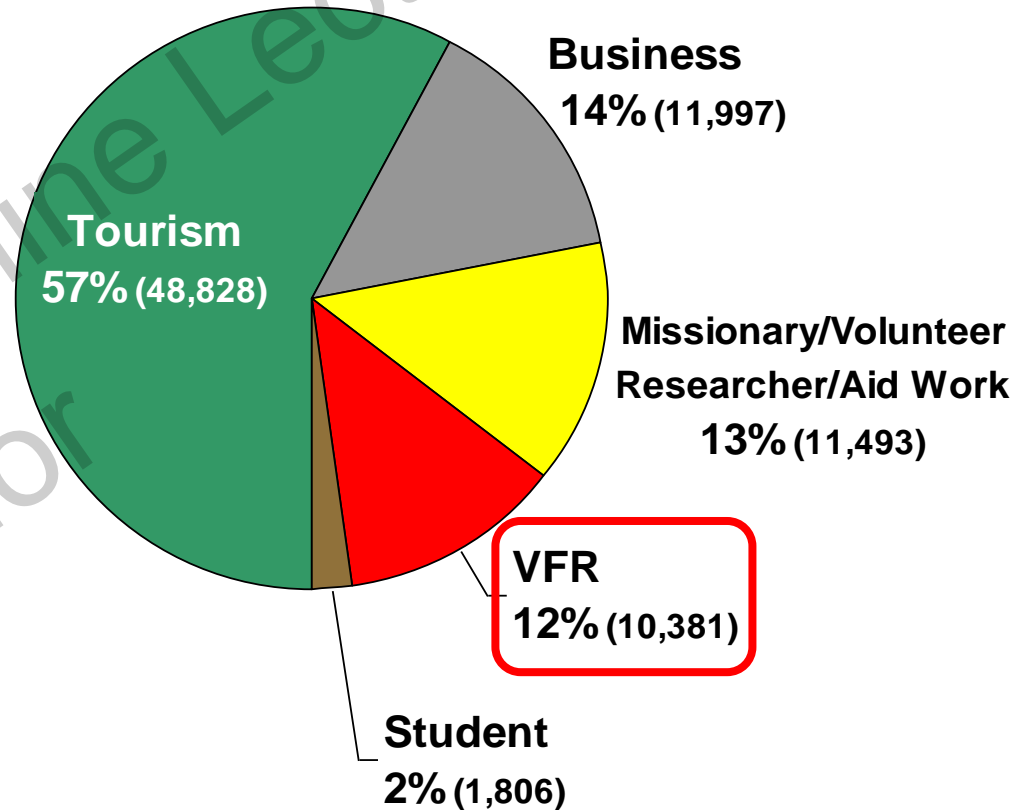
(n = 173,205)



- Visit clinic after travel
- Visit clinic during travel
- Immigration travel only
- Other

### After Travel Visits Only

(n = 85,180)



**VFR**  
12% (10,381)

## VFRs: How should be approached?

- They have been described as a **special risk group for certain travel-related illnesses**, specially infectious diseases, when compared to other kinds of travelers.
- **They are also immigrants whose countries of origin frequently have higher prevalences of certain infectious diseases** when compared to the host country. This confers a higher risk for infections acquired before migration which may persist in an asymptomatic form for long periods of time
- **How VFRs should be approached: as travelers or as immigrants or as both?**

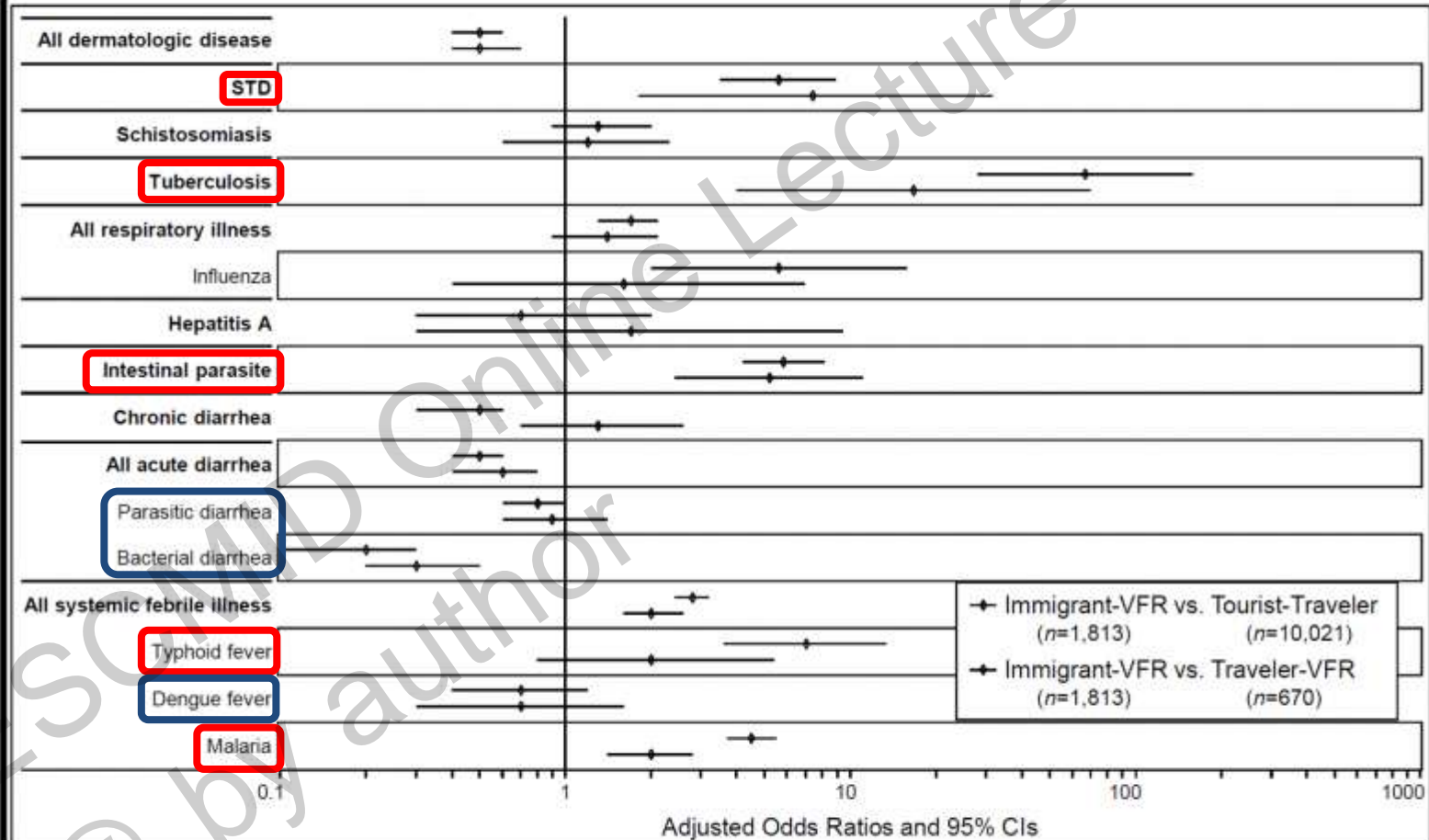
*[-] Bacaner N, Stauffer B, Boulware DR, Walker PF, Keystone JS. Travel medicine considerations for North American immigrants visiting friends and relatives. J Am Med Assoc 2004;291:2856e64.*

*[-] Angell SY, Cetron MS. Health disparities among travelers visiting friends and relatives abroad. Ann Intern Med 2005;142:67e72.*

*[-] Angell SY, Behrens RH. Risk assessment and disease prevention in travelers visiting friends and relatives. Infect Dis Clin North Am 2005;19:49e65.*



## Differing Disease Diagnosis Profiles in immigrant-VFRs, traveler-VFRs and tourist travelers



- Retrospective, descriptive study of demographic variables and infectious diseases diagnosed amongst VFRs attended from April 1989 to June 2010 at the Tropical Medicine National Referral Centre (TMC) of the Ramon y Cajal Hospital in Madrid, Spain
- Description of the spectrum of infectious diseases diagnosed in VFRs (N=351) and comparison with two previously published cohorts: of immigrants (N=2198) and travelers (N=2462) attended at our centre
- **The most frequent diagnoses observed among VFRs were typical travel-associated infections** such as malaria [21.4%], traveler's diarrhea [4.8%], intestinal parasites [4.6%] and dengue [3.1%]
- **Asymptomatic chronic infectious diseases**, such as latent tuberculosis [16%], chronic viral hepatitis [5.1%] and filariasis [5.1%], probably acquired before migration, were also observed.

## SIGNIFICANTLY MORE FREQUENT

- among immigrants: filariasis, Chagas dis, cysticercosis, TB, LTI, chronic viral hepatitis, STI and HIV
- among VFRs: malaria, dengue and enteric fever
- among travelers: traveler's diarrhea and intestinal parasites

**Table 3** Comparative study of infectious diseases among VFRs, immigrants and travelers seen at the TMC.

Diagnostic categories		IMM (N = 2198) (N %)	VFRs (N = 351) (N %)	TR (N = 2426) (N %)	p
Tropical infectious diseases	Malaria	212 (9.6%)	75 (21.4%)	269 (11.1%)	<0.001
	Filariasis	421 (19.2%)	18 (5.1%)	49 (2%)	<0.001
	Intestinal parasites	242 (11%)	16 (4.5%)	298 (12.3%)	<0.001
	Chagas diseases	101 (4.6%)	12 (3.4%)	0 (0%)	<0.001
	Dengue	0	11(3.1%)	34 (1.4%)	<0.001
	Schistosomiasis	39 (1.8%)	2 (0.6%)	44 (1.8%)	0.231
	Cysticercosis	31 (1.4%)	0	0	
Transmissible infectious diseases	LTI	716 (32.6%)	56 (16%)	189 (9.4%)	<0.001
	TB	107 (4.9%)	3 (0.9%)	6 (0.2%)	<0.001
	Chronic viral hepatitis	262 (11.9%)	18 (5.1%)	0 (0%)	<0.001
	Acute viral hepatitis	31 (1.4%)	3 (0.8%)	25 (1%)	0.225
	Enteric fever	7 (0.3%)	4 (1.1%)	10 (0.4%)	0.644
	STI	107 (4.9%)	11 (3.1%)	49 (2%)	<0.001
	HIV	97 (4.4%)	10 (2.8%)	15 (0.6%)	<0.001
Common infectious diseases	Traveler's diarrhea	0	17(4.8%)	284 (11.7%)	<0.001

IMM: immigrants, VFRs: visiting friends and relatives, TR: travelers, LTI: latent tuberculosis infection, TB: tuberculosis, STI: sexually transmitted infections, HIV: human immunodeficiency virus infection.



## VFRs and malaria

- High prevalence of malaria. Mainly due to *P. falciparum* and mostly from SSA
- Due to several risk factors such as traveling to highly endemic areas, for longer periods of time and with poorer adherence to anti-malarial prophylaxis
- **In our experience**
  - median length of VFRs travel is 1 month
  - only 5% take malaria chemoprophylaxis correctly
  - 96% from SSA
  - 11% are children
  - 80% caused by *P. falciparum*
  - 3% are asymptomatic

[–] Zamarron Fuertes P, Perez-Ayala A, Perez Molina JA, Norman FF, Monge-Maillo B, Navarro M, et al. Clinical and epidemiological characteristics of imported infectious diseases in Spanish travelers. *J Travel Med* 2010;17:303e9.

[–] Leder K, Tong S, Weld L, Kain KC, Wilder-Smith A, von Sonnenburg F, et al. Illness in travelers visiting friends and relatives: a review of the GeoSentinel Surveillance Network. *Clin Infect Dis* 2006;43:1185e93.

[–] Smith AD, Bradley DJ, Smith V, Blaze M, Behrens RH, Chiodini PL, et al. Imported malaria and high risk groups: observational study using UK surveillance data 1987e2006. *BMJ* 2008;337:a120.

## VFRs and arboviriais: Dengue & Chikungunya

- Most first-generation immigrants have evidence of past DENV infection, probably comparable to inhabitants of their country of origin
- Same acute DENV infection rate as in travelers
- CHIKV described in VFRs
- Potential for introducing these emerging viral infections into new areas
- **In our experience**
  - Dengue: 3%, all cases from LA, no severe cases

*[-] Overbosch FW, van den Hoek A, Schinkel J, Sonder GJ. High prevalence of previous dengue virus infection among first-generation Surinamese immigrants in the Netherlands. BMC Infect Dis. 2014 Sep 10;14:493*

*[-] Leder K, Tong S, Weld L, Kain KC, Wilder-Smith A, von Sonnenburg F, et al. Illness in travelers visiting friends and relatives: a review of the GeoSentinel Surveillance Network. Clin Infect Dis 2006;43:1185e93.*

*[-] Lim PL, Oh HM, Ooi EE. Chikungunya in Singapore: imported cases among travelers visiting friends and relatives. J Travel Med. 2009 Jul-Aug;16(4):289-91*

## VFRs and gastro-intestinal infections

- **Traveler's diarrhea** seems to be less frequent among VFRs than among travelers (They preserve a degree of immunity from their previous residence in less developed countries).
- **Enteric fever** is more frequent when compared with other types of travelers. Occurs mostly among those coming from Asia (mainly Pakistan, Cambodia, Nepal, India and Sri Lanka)
- **Intestinal parasites** described in a wide range.
- **In our experience**
  - Traveler's diarrhea in only 5%: *Salmonella spp*, *Shigella spp*
  - Intestinal parasites in 5%: *Giardia intestinalis* in children, *Strongyloides stercoralis* in LA

[–] Steinberg EB, Bishop R, Haber P, Dempsey AF, Hoekstra RM, Nelson JM, et al. Typhoid fever in travelers: who should be targeted for prevention? *Clin Infect Dis* 2004;39:186e91.

[–] Keller A, Frey M, Schmid H, Steffen R, Walker T, Schlagenhauf P. Imported typhoid fever in Switzerland, 1993 to 2004. *J Travel Med* 2008;15:248e51.

# VFRs and viral hepatitis A

- Pediatric patients have a higher risk.
- Adults have a higher rate of natural immunization (more significant among those who migrate when they were over 20 years of age).
- However, the gradual improvement in socioeconomic conditions in certain areas of the world is reducing the rates of natural immunization and thus increasing the population who may be susceptible to infection during travel and that should be vaccinated.
- **In our experience**
  - rare cases of acute HAV and HEV

[–] Weinberg M, Hopkins J, Farrington L, Gresham L, Ginsberg M, Bell BP. Hepatitis A in Hispanic children who live along the United States-Mexico border: the role of international travel and food-borne exposures. *Pediatrics* 2004;114:e68e73.

[–] Barnett ED, Holmes AH, Geltman P, Phillips SL, Harrison TS. Immunity to hepatitis A in people born and raised in endemic areas. *J Travel Med* 2003;10:11e4.

[–] Jacobsen KH, Koopman JS. Declining hepatitis A seroprevalence: a global review and analysis. *Epidemiol Infect* 2004;132:1005e22.

## VFRs and chronic viral hepatitis: HBV & HCV

- In the majority of cases such infections will have probably been acquired in their countries before migration
- A higher frequency of HBV infection among VFRs could be linked to certain risk factors such as tattooing, acupuncture or dental procedures.
- **In our experience**
  - Chronic viral hepatitis: 8% prevalence in SSA, but only 1.4% in LA
  - 61% due to HBV and 39% due to HCV
  - Rare HBV/HDV co-infection
  - In 50% of cases diagnosis resulted from screening when the patient attended for other reasons after arrival.

*[-] Boggild AK, Castelli F, Gautret P, Torresi J, von Sonnenburg F, Barnett ED, et al. Vaccine preventable diseases in returned international travelers: results from the GeoSentinel Surveillance Network. Vaccine 2010;28:7389e95.*

*[-] Lavanchy D. Hepatitis B virus epidemiology, disease burden, treatment, and current and emerging prevention and control measures. J Viral Hepat 2004;11:97e107.*

*[-] McCarthy AE, Weld LH, Barnett ED, So H, Coyle C, Greenaway C, et al. Spectrum of illness in international migrants seen at GeoSentinel clinics in 1997e2009, part 2: migrants resettled internationally and evaluated for specific health concerns. Clin Infect Dis 2013;56:925e33.*



# VFRS and Sexually transmitted infections (STI) & HIV

- VFRs may have higher risk sexual contacts during travel resulting in a prevalence of STI and HIV in VFRs significantly higher than in travelers.
- **In our experience**
  - STI in 3%
  - Diagnoses: genital herpes, latent syphilis infection, gonorrhoea, non-gonococcal-urethritis
  - Cases of latent syphilis were diagnosed as a result of general screening performed in VFRs after arrival.
  - HIV infection in 4.3% SSA, 0.7% in LA
  - HIV infection was already known in 70% cases, the other 30% were diagnosed as a result of screening.

*[-] Fenton KA, Chinouya M, Davidson O, Copas A., MAYISHA Research Team. HIV transmission risk among sub-Saharan Africans in London travelling to their countries of origin. AIDS 2001;15:1442e5.*

*[-] Fenner L, Weber R, Steffen R, Schlegelhauf P. Imported infectious disease and purpose of travel, Switzerland. Emerg Infect Dis 2007;13:217e22.*

## VFRs and tuberculosis

- Travel for long periods of time to highly endemic areas for TB increases the risk of infection both in travelers and in VFRs. There are scarce studies in which TT conversion after travel has been documented.
- Active TB cases diagnosed in VFRs after travel may be acquired during travel or be the consequence of reactivation of infection acquired before migration, or may even represent new acquisition in the host country.
- **In our experience**
  - Active tuberculosis in 0.9%. None were co-infected with HIV.
  - 16% with latent tuberculosis infection: 73% from SSA.
  - Only 5% had a negative TT documented prior to travel. For all other cases, the time of infection could not be determined.
  - Treatment for LTI with Isoniazid (300 mg/day for 6-9 months) was prescribed in 54%: only 50% of them completed the treatment correctly

*[-] Cobelens FG, van Deutekom H, Draayer-Jansen IW, ScheppBeelen AC, van Gerven PJ, van Kessel RP, et al. Risk of infection with Mycobacterium tuberculosis in travellers to areas of high tuberculosis endemicity. Lancet 2000;356:461e5.*

*[-] Cobelens FG, van Deutekom H, Draayer-Jansen IW, ScheppBeelen AC, van Gerven PJ, van Kessel RP, et al. Association of tuberculin sensitivity in Dutch adults with history of travel to areas of with a high incidence of tuberculosis. Clin Infect Dis 2001;33:300e4.*

*[-] Kik SV, Mensen M, Beltman M, Gijsberts M, van Ameijden EJ, Cobelens FG, et al. Risk of travelling to the country of origin for tuberculosis among immigrants living in a low-incidence country. Int J Tuberc Lung Dis 2011;15:38e43.*

*[-] Abubakar I, Matthews T, Harmer D, Okereke E, Crawford K, Hall T, et al. Assessing the effect of foreign travel and protection by BCG vaccination on the spread of tuberculosis in a low incidence country, United Kingdom, October 2008 to December 2009. Euro Surveill 2011;16:19826.*

## VFRs and “Tropical Parasitic Diseases”

- For some tropical diseases determining time of acquisition may be difficult. Such infections are most probably acquired prior to migration having no association with the recent travel episode
- **Strongyloidiasis** is common among immigrants from endemic areas
- **Filariasis** is common among immigrants from endemic areas
- **Chagas disease** is exceptional among travelers. Most imported cases outside endemic areas are described in immigrants from LA, mainly those from rural areas of Bolivia, who may be asymptomatic
- **In our experience**
  - Filariasis: in 9% from SSA. Non from LA. *Onchocerca volvulus*, *Loa loa*, *Mansonella perstans*. For 2/18 cases the infection was probably acquired during travel
  - Chagas disease: 22% prevalence in Bolivians. Organ involvement in 25%. All cases were diagnosed as a result of systematic screening
  - Other infections: Strongyloidiasis, Amoebic liver abscess, Schistosomiasis, Cutaneous leishmaniasis, Fascioliasis, Cysticercosis, etc

[–] Norman FF, Perez de Ayala A, Perez-Molina JA, Monge-Maillo B, Zamarron P, Lopez-Velez R. Neglected tropical diseases outside the tropics. *PLoS Negl Trop Dis* 2010;4:e762.

[–] Perez-Ayala A, Perez-Molina JA, Norman F, Navarro M, Monge-Maillo B, Diaz-Menendez M, et al. Chagas disease in Latin American migrants: a Spanish challenge. *Clin Microbiol Infect* 2010;17:1108e13.

## VFRs approach

- VFRs have a higher risk for certain infectious diseases **related to travel**
- VFRs also seem to have a higher prevalence of certain infectious diseases which could be **acquired before migration**. Immigrant status and area of origin seem to be relevant and should be taken in to account with regards to the prevalence of those infectious diseases that could have been acquired before migration.
- This justifies **screening for certain infectious diseases** when seen after arrival that would probably not be considered in other types of travelers. So, when VFRs consult for other reasons after travel systematic screening for other infectious disease should probably be performed.

## VFRs screening recommendations

- Due to the prevalence and impact on individual and public health of these chronic infections, and because they may have a long asymptomatic course, screening for HIV, HBV, HCV and TB, should be considerate.
- Based on the published data about **HIV, HBV, HCV and TB** screening recommendations in immigrants:
  - HIV, HBV & TB systematic screening for VFRs coming from SSA; Asia and LA.
  - HCV systematic screening for SSA, but in LA or Asia only if there are other risks factors

*[-] Branson BM, Handsfield HH, Lampe MA, Janssen RS, Taylor AW, Lyss SB, et al. Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. MMWR Recomm Rep 2006;55:1e17.*

*[-] Eckman MH, Kaiser TE, Sherman KE. The cost-effectiveness of screening for chronic hepatitis B infection in the United States. Clin Infect Dis 2011;52:1294e306.*

*[-] Dasgupta K, Menzies D. Cost-effectiveness of tuberculosis control strategies among immigrants and refugees. Eur Respir J 2005;25:1107e16*

*[-] Almasio PL, Babudieri S, Barbarini G, Brunetto M, Conte D, Dentico P, et al. Recommendations for the prevention, diagnosis, and treatment of chronic hepatitis B and C in special population groups (migrants, intravenous drug users and prison inmates). Dig Liver Dis 2011;43:589e95.*



## VFRs screening recommendations

- Based on epidemiological risk or on analysis results (such as eosinophilia or hematuria), even if asymptomatic, screening for **strongyloidiasis, filariasis and schistosomiasis** could probably be recommended for VFRs who have traveled to SSA.
- Screening for **Chagas disease** should probably be recommended for VFRs from LA, especially among those from Bolivia

[*-*] Bacaner N, Stauffer B, Boulware DR, Walker PF, Keystone JS. Travel medicine considerations for North American immigrants visiting friends and relatives. *J Am Med Assoc* 2004;291:2856e64.

[*-*] Angell SY, Cetron MS. Health disparities among travelers visiting friends and relatives abroad. *Ann Intern Med* 2005;142:67e72.

[*-*] Leder K, Tong S, Weld L, Kain KC, Wilder-Smith A, von Sonnenburg F, et al. Illness in travelers visiting friends and relatives: a review of the GeoSentinel Surveillance Network. *Clin Infect Dis* 2006;43:1185e93.

# VFRs travel diseases preventive measures

## Strategic change is needed

- Lack of risk perception when travelling to their countries of origin
- Poor seeking for pre-travel health advice
- Their level of knowledge about travel health tends to be poor.
- Heterogeneous group including different generations of immigrants, of different origins and with cultural differences
- Intercultural mediation and culturally adapted health promotion campaigns for pre-travel advice addressed to specific immigrant groups should be considered

[-] Pistone T, Guibert P, Gay F, Malvy D, Ezzedine K, Receveur MC, et al. Malaria risk perception, knowledge and prophylaxis practices among travellers of African ethnicity living in Paris and visiting their country of origin in sub-Saharan Africa. *Trans R Soc Trop Med Hyg* 2007;101:990e5.

[-] Fenner L, Weber R, Steffen R, Schlagenhauf P. Imported infectious disease and purpose of travel, Switzerland. *Emerg Infect Dis* 2007;13:217e22.

[-] Schlagenhauf P, Steffen R, Loutan L. Migrants as a major risk group for imported malaria in European countries. *J Travel Med* 2003;10:106e7.

[-] Leder K, Lau S, Leggat P. Innovative community-based initiatives to engage VFR travelers. *Travel Med Infect Dis* 2011;9:258e61.

**Navarro M, Navaza B, Guionnet A, López-Vélez R.**

**A multidisciplinary approach to engage VFR migrants in Madrid, Spain.**

**Travel Med Infect Dis. 2012 May;10(3):152-6.**

- The Tropical Medicine Unit of the Ramón y Cajal Hospital in Madrid, Spain, holds a pioneering health education programme adapted to migrants which also embraces activities aimed at VFRs.
- In this programme, called **‘New citizens, new patients’**, activities are community-based and culturally-sensitive.
- It is aimed at migrants living in Spain and run by a multidisciplinary team of physicians, translators, intercultural mediators and a psychologist.
- Distribution of **multilingual and culturally tailored leaflets** and delivering of information about travel health by trained intercultural mediators in: -TMU waiting room, - NGOs devoted to migrants, - Health care centres, etc.
- ***www: saludentreculturas.es***

## HEALTH AND TRAVEL

Why to protect myself when travelling to my own country?



Because there are diseases that do not exist here and against which your body has no natural protection or has lost it over time, it is especially important to protect children.

### What Risks Do I Run if I Travel to the Tropics?



Travellers are at risk of acquiring certain infections, such as those transmitted through water, food or insect bites.



Malaria, transmitted through a mosquito bite, is a disease that can have very serious consequences, particularly in children and pregnant women.



You must protect yourself against this disease if you are travelling to Africa or certain areas of Latin America and Asia.

### What to Do while Travelling?



Take malaria pills if the doctor has recommended this.



Use a mosquito net when sleeping. Use insect repellent.



Eat food that has been prepared recently and avoid food that has been at room temperature for some time. Take precautions if you are in contact with people with diseases.



Drink potable water. It is better to use bottled water for children and for preparing babies' food bottles.



Minimize your contact with sharp objects and health instruments. Remember that there is a risk of transmitting diseases through injections and dental extractions if the material is not sterile, as well as blood transfusions if the blood is not analysed.



Use a condom if you have sexual relations.



Remember that a condom can protect you against many infections.



 **SALUD ENTRE CULTURAS**



### What Should I Do before Travelling?



At least one month before travelling, you should go to your doctor or paediatrician to receive health advice.



Children should be up to date with vaccinations, and some of these must be given earlier. Depending on the trip, some are compulsory (yellow fever, meningitis) and others recommended (Hepatitis A, Typhoid).



International Vaccination Centres can give these vaccines, as well as medication to prevent against malaria.

### What Should I Bear in Mind after Travelling?



You must continue taking the malaria pills according to the instructions.



If you or your children show symptoms such as diarrhoea or skin problems when returning from your trip, you should go to a health centre. If you have a fever, you should go to the doctor urgently, since it could be due to malaria.



Malaria in children can also cause diarrhoea or coughing.

