Illness in Returned Canadian Travelers

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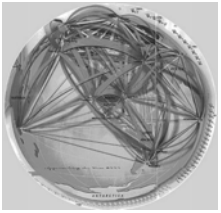
Objectives

- To understand the utility and limitations of large sentinel surveillance databases
- To appreciate the spectrum of illness among ill returned Canadian travelers and immigrants presenting for care at a CanTravNet site
- To recognize the demographic and travel-related associations between particular travelers and diagnoses

Outline

- GeoSentinel Surveillance Network
- CanTravNet
- First Surveillance Summary of CTN
  - Methods
  - Results
  - Limitations
  - Conclusions
- Questions / Discussion

GeoSentinel: The Global Surveillance Network of the ISTM and CDC



A worldwide communications and data collection network of travel/tropical medicine clinics

www.geosentinel.org

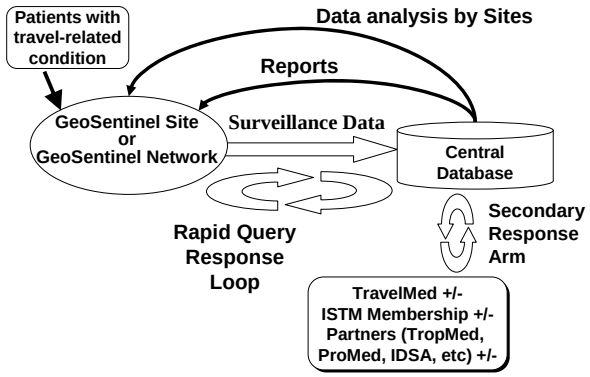
What is GeoSentinel?

• Provider-based Surveillance of international travelers and migrants.
Does not cover endemic diseases in local populations
- 54 travel/tropical medicine clinics globally (since 1996)
& 233 Network Members on all 6 continents (since 2002)

Provider-based Sentinel Surveillance The 3 Functions of GeoSentinel

1. Surveillance – Response
   - Alarming sentinel events
2. Surveillance – ongoing trends
3. Analysis of morbidity and estimating risk
   - Diagnosing the ill-returnee; the clinician perspective
   - Advising the Prospective Traveler; the traveler perspective
   - Defining associations between patient characteristics and disease

How does GeoSentinel Work?

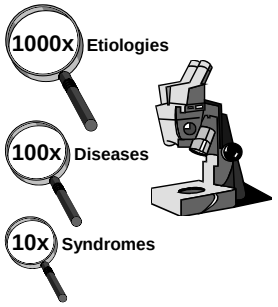


Diagnoses: Comprehensive & Flexible

Comprehensive

- 521 available diagnosis codes in table
- New codes added as needed
- 214,212 final diagnoses for 167,060 patients

Flexible

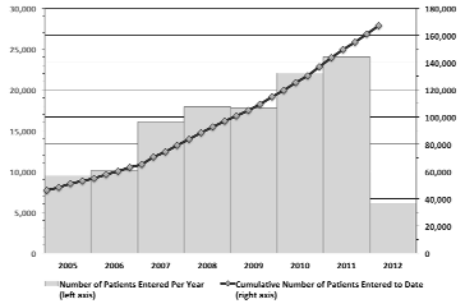


GeoSentinel data collection

- Data from patient (anonymous)
  - Travel itinerary
- Data from provider
  - Presenting symptoms
  - Patient classification
  - Diagnosis
- Data entry on secure web site

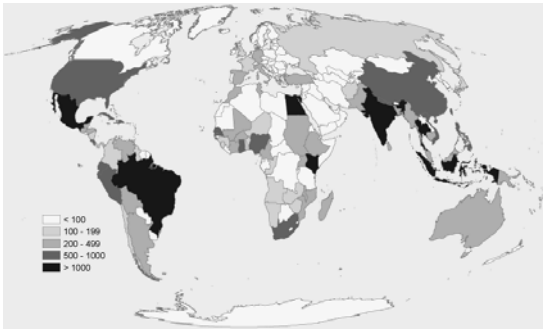
GeoSentinel Dataset, Mar 2012

Number of Patients in GeoSentinel (*n* = 167,060)



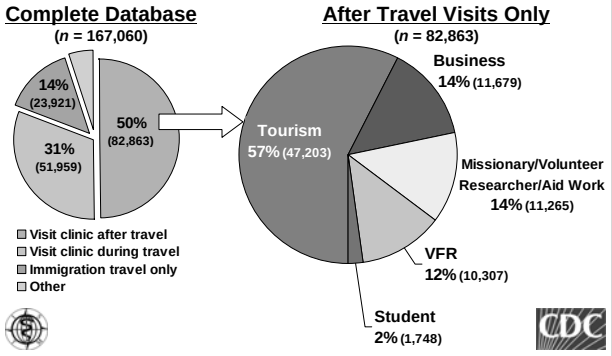
GeoSentinel Dataset, Mar 2012

Place of Likely Exposure in Patients Seen After Travel



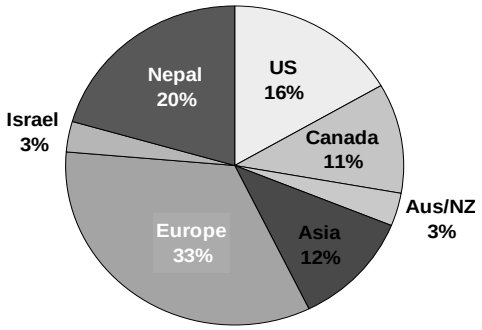
Who are GeoSentinel patients?

(as of March 2012)



Contribution by Treating Site

***n* = 167,060 patients as of March 2012**



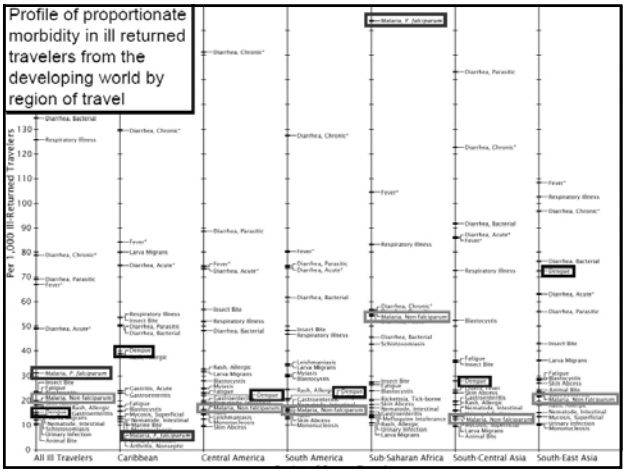
1.9% from Latin America/Africa/Caribbean

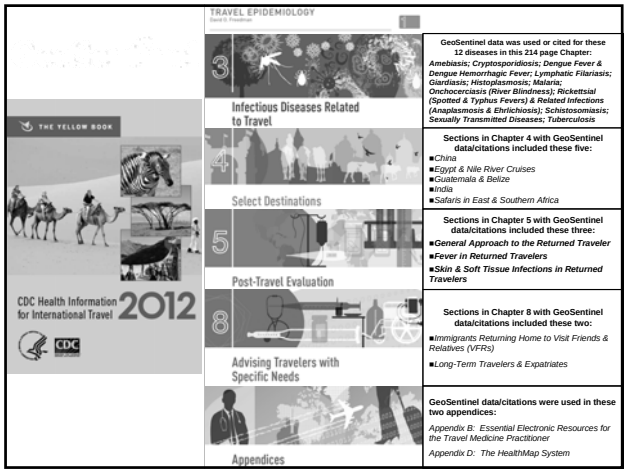
GeoSentinel

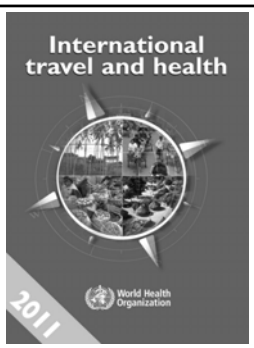
Rich Database of Travel Morbidity

- Benefits
  - Guide diagnostic approach
  - Guide empiric therapy
  - Prioritize pre-travel prevention strategies

Profile of proportionate morbidity in ill returned travelers from the developing world by region of travel







CHAPTER 9

Special groups of travellers

9.1 Travel to visit friends and relatives

According to the United Nations, international migration rose from 120 million in 1990 to more than 200 million in 2006. In many countries immigrants now constitute more than 20% of the population. Immigrants increasingly travel to their place of origin to visit friends and relatives (VFR), and VFR travel is now a major component of the international journeys that take place annually. The term "VFRs" generally refers to immigrants from a developing country to an industrialized country who subsequently return to their home countries for the purpose of visiting friends and relatives.

Compared with tourists to the same destinations, VFRs are at increased risk of travel-related diseases. These include – but are not limited to – malaria, hepatitis A and B, typhoid fever, rabies, tuberculosis, and the diseases normally preventable by routine childhood immunization. For example, the global surveillance data of GeoSentinel (an international network of travel medicine providers) on returned travel patients show that eight times more VFR travellers than tourists present with malaria as their diagnosed illness. It is estimated that VFRs account for more than half the total imported malaria cases in Europe and North America.

Further reading

Ahmed QA, Arabi YM, Memish ZA. Health risks at the Hajj. *Lancet*, 2006, 367:1008–1015.

Behrens RH, Barnett ED. Visiting friends and relatives. In: Keystone JS et al. eds. *Travel medicine*, 2nd ed. Edinburgh, Mosby, 2008, 295–298.

Geretti AM et al. British HIV Association guidelines for immunization of HIV-infected adults 2008. *HIV Medicine*, 2008, 9:795–848.

Guidelines for the treatment of malaria, 2nd edition. Geneva, World Health Organization, 2010.

Information on GeoSentinel: http://www.istm.org/geosentinel/main.html

International migration and development. Report of the Secretary General. New York, United Nations, 2006 (A/60/871).

Leder K et al. Illness in travelers visiting friends and relatives: a review of the GeoSentinel Surveillance Network. *Clinical Infectious Diseases*, 2006, 43(9):1185–1193.

Tourism highlights: 2006 edition. Madrid, World Tourism Organization, 2006 (available at http://www.unwto.org/facts/menu.html).

Freedman et al. N Engl J Med 2006; 354: 119-130.

Leder et al. Clin Infect Dis 2006; 43: 1185-1193.

Wilson et al. Clin Infect Dis 2007; 44: 1560-1568.

Hagmann et al. Pediatrics 2010; 125: e1072-e1080.

Boggild et al. J Travel Med 2007; 14(6): 361-368.

Gautret et al. Vaccine 2007; 25(14): 2656-2663.

Leder et al. Clin Infect Dis 2003; 36(4): 399-406.

Freedman et al. N Engl J Med 2006; 354: 119-130.

Boggild et al. Vaccine 2010; 28 (46): 7389-7395.

Freedman et al. N Engl J Med 2006; 354: 119-30.

What more do we need to know?

What more do we need to know?

- Our understanding of the range and frequency of infectious diseases in Canadian travelers is based on existing synthesized knowledge of travel acquired illness in other populations
- Expert references such as the WHO Green Book, CDC Yellow Book, and PHAC's CATMAT provide guidance to practitioners but whether these guidelines are appropriate in the Canadian context is unknown
- Many imported communicable diseases are nationally notifiable to PHAC, the quality of data accrued is hindered by delayed and under-reporting

What more do we need to know?

- A comprehensive multicentre comparison of the spectrum of illnesses acquired by a broad range of Canadian travelers returning from developing regions on all continents has been lacking

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CanTravNet GeoSentinel

- Consortium of Canadian GeoSentinel sites located in:
  - Vancouver / Victoria (1)
  - Calgary (1)
  - Toronto + satellite Mississauga (1)
  - Ottawa (1)
  - Montreal (2)

CanTravNet GeoSentinel

- Structure:
  - Kevin C. Kain, Director
  - Andrea K. Boggild, Associate Director
  - Site Directors and Co-directors:
    - Patrick Doyle and Wayne Ghesquiere
    - Susan Kuhn
    - Anne McCarthy
    - Michael Libman
    - Jean Vincelette
  - Collaboration with Travel and Migration Health Division of PHAC

CanTravNet GeoSentinel The Global Surveillance Network of the ISTM and CDC

- Contributions to the Network:
- 16,696 records between Jan. 1/00 – Jan. 1/12
  - 545 cases of intestinal nematode infections
  - 398 cases of malaria
  - 368 cases of TB
  - 237 cases of schistosomiasis
  - 169 cases of dengue
  - 131 cases of filariasis
  - 123 cases of echinococcosis
  - 54 cases of cysticercosis
  - 29 cases of rickettsioses

CanTravNet GeoSentinel The Global Surveillance Network of the ISTM and CDC

- Contributions to the Network:
- 16,696 records between Jan. 1/00 – Jan. 1/12
  - Tourists – 7847 (47%)
  - Immigrants – 3652 (22%)
  - VFRs – 1970 (12%)
  - Business travelers – 1549 (9.3%)
  - Missionaries / volunteers / researchers / aid workers – 1556 (9.3%)
  - Students – 282 (1.7%)
  - Medical tourists – 10 (0.06%)

First Major Initiative

- Collaboration between PHAC-CanTravNet modeled after that between ECDC-EuroTravNet
- Contracts between PHAC-CTN and PHAC-GeoSentinel for deliverables including:
  - On-screen report access
  - Annual "data deposit" for production of a surveillance report
  - Queries to the master database ad hoc
  - Canada-specific Healthmap

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Annual Surveillance Report

- To date, there are no specific, comprehensive, and large-scale published data on illness in Canadian travelers
- Descriptive analysis of Canadian data from September 2009-September 2011 for publication in a Canadian journal and internal use by PHAC
- Standard GeoSentinel methodology and analysis applied

Annual Surveillance Report

- Sub-categorical analyses relevant to the public health of Canadians
  - Blood-borne illness: HBV, HCV, HIV/AIDS, and HTLV-I/II
  - Vaccine preventable illness: HAV, HBV, influenza and ILI, enteric fever, varicella, measles, Japanese encephalitis, and cholera
  - Sexually transmitted infections: *Chlamydia trachomatis*, HSV, molluscum contagiosum, scabies, syphilis, and unspecified sexually transmitted disease

Proportionate Morbidity

$$\frac{\text{no. of patients with given diagnosis (or group of diagnoses)}}{\text{all } \textbf{\textit{ill}} \text{ travelers to a destination}}$$

Risk

$$\frac{\text{All incident cases}}{\text{All travelers to a destination}}$$

Estimation of Risk requires that true numerator and true denominator are ascertainable

Odds Ratio

Defines quantitative <u>associations</u> between patient related characteristics and diagnosis

– Does not define absolute incidence or risk of disease

Risk

$$\frac{\text{All incident cases}}{\text{All travelers to a destination}}$$

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Results

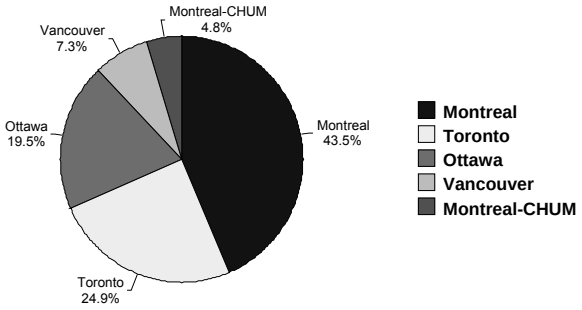
- 4365 travelers or immigrants seen at a CTN site between 09/2009 and 09/2011
- 4776 confirmed and 535 probable diagnoses
- 3943 (90.3%) had a travel-related diagnosis, 363 (8.3%) had a non-travel related diagnosis, and 59 (1.4%) had a diagnosis whose relatedness to travel could not be ascertained

Results

- **Sex**
  - Males 2026 (46.4%)
  - Females 2337 (53.5%)
  - Unknown 2 (0.1%)
- **Age** – Median 38 years, range 0 – 95 years (IQR 28 – 53 years)
- **Immigrant** (check-box)
  - Yes 1837 (42.1%)
  - No/Blank 2528 (57.9%)

Results

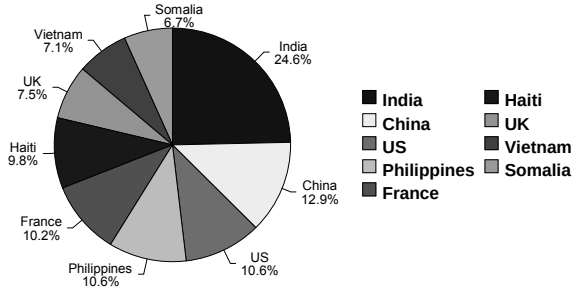
GeoSentinel Reporting Site



Results

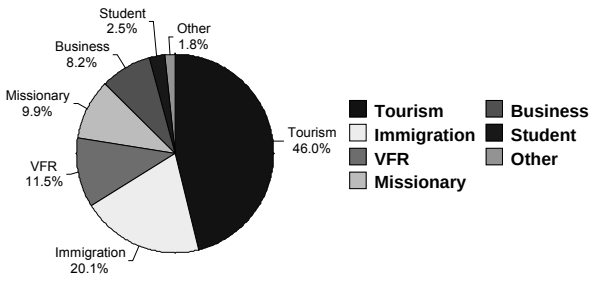
■ 55% born in Canada

Top 10 Birth Countries

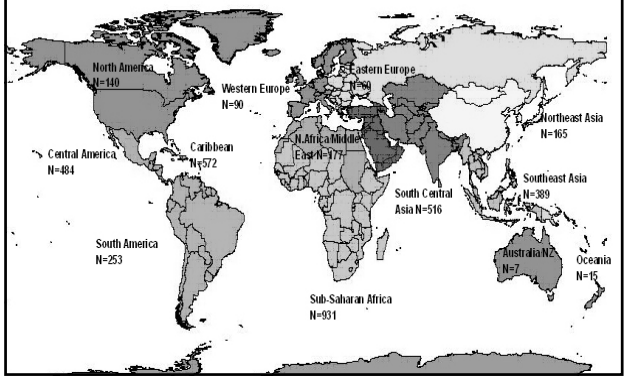


Results

Travel Reason

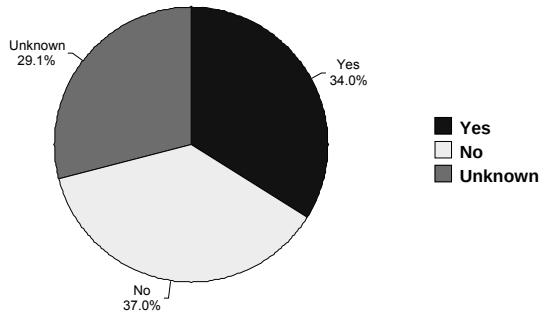


Results



Results

Pre-Travel Encounter



Diagnoses

Diagnosis: CHIEF COMPLAINT FEVER (N=675)	Number with CC	%	Total Number in Database	Top 3 Source Countries for Diagnosis
Malaria	80	11.9	94	Pf / complicated: Ghana, Burkina Faso, Guinea Pv: India, Honduras, Pakistan
Dengue fever	48	7.1	61	India, Indonesia, Nicaragua, Haiti
Active TB	48	7.1	128	India, China, Philippines
Enteric fever	29	4.3	36	India, Bolivia, Tanzania, Pakistan, Bangladesh
URTI	20	3.0	55	India, Mexico, Ghana
Pneumonia	18	2.7	31	Mexico, Canada, United States
ILI	15	2.2	18	Tanzania, Panama, Brazil
Acute UTI	12	1.8	30	Mexico, India, Cameroon
Rickettsioses, spotted fever*	5	0.7	6	South Africa, Swaziland

Diagnosis: CHIEF COMPLAINT GI (n=1950)	Number with CC	%	Total Number in Database	Top 3 Source Countries for Diagnosis
Chronic Diarrhea	268	13.7	268	Mexico, Cuba, India
Acute Diarrhea	246	12.6	253	India, Mexico, Cuba
Post-infectious Irritable Bowel Syndrome	241	12.4	248	India, Mexico, Cuba, Dominican Republic
Giardia	84	4.3	97	India, Mexico, Costa Rica
Dientamoeba fragilis	63	3.2	66	Mexico, India, Thailand
Campylobacter	23	1.2	25	Peru, India
Cryptosporidium / Cyclospora	16	0.8	17	Philippines, Mexico, India
Entamoeba histolytica†	12	0.6	14	India, Sri Lanka, Honduras

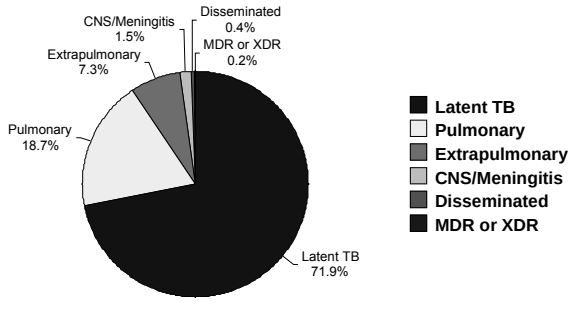
Diagnosis: CHIEF COMPLAINT DERM (N=865)	Number with CC	%	Total Number in Database	Top 3 Source Countries for Diagnosis
Rash	145	16.8	155	Mexico, Cuba, Peru
Arthropod Bite	129	14.9	135	United States, Cuba, Mexico
Skin and soft-tissue infection‡	103	11.9	107	India, Cuba, Costa Rica
Cutaneous larva migrans	61	7.1	62	Jamaica, Mexico, Barbados
Animal Bite**	27	3.1	30	Thailand, India, Honduras
Cutaneous leishmaniasis	21	2.4	21	Syria, Libya, Costa Rica, Belize, Afghanistan
Marine Envenomation	17	2.0	19	Cuba, United States, Mexico

Results - Top 10 Travel Related Diagnoses in 93 Children <13 years

Diagnosis	Number
Abdominal Pain	**8**
Malaria **P. falciparum**	**7** **(5)**
Cutaneous Larva Migrans	**5**
Skin and soft-tissue infection	**5**
Dientamoeba fragilis	**4**
Cutaneous leishmaniasis	**4**
Giardia	**4**
Febrile illness unspecified <3 wks	**4**
Acute Diarrhea	**3**
Superficial fungal infection	**3**

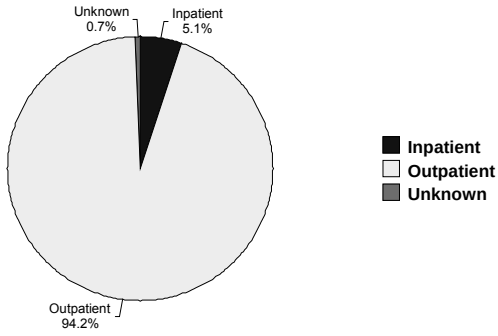
Results (N=455)

Mycobacterium tuberculosis



Results

Patient Type



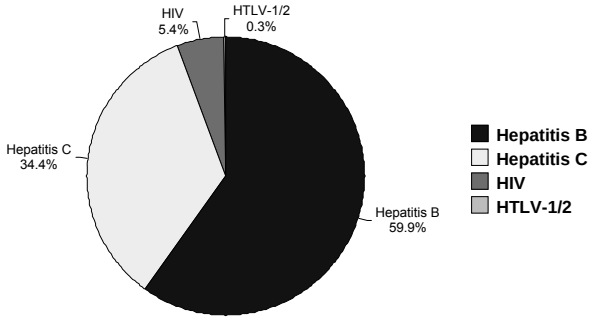
Results – Top 10 Inpatient Diagnoses

Diagnosis	N	%
M. tuberculosis (N=128 active)	66	51.6
Malaria (N=94)	40	42.5
Pneumonia (N=31)	20	64.5
Adverse drug reaction (N=26)	18	69.2
Enteric fever (N=36)	13	36.1
Bacteremia / Sepsis (N=11)	9	81.8
Dengue fever (N=61)	5	8.2
Acute UTI (N=30)	5	16.6
Acute Brucellosis (N=7)	4	57.1
Acute bacterial diarrhea (N=102)	4	3.9

Sub-Categorical Analysis

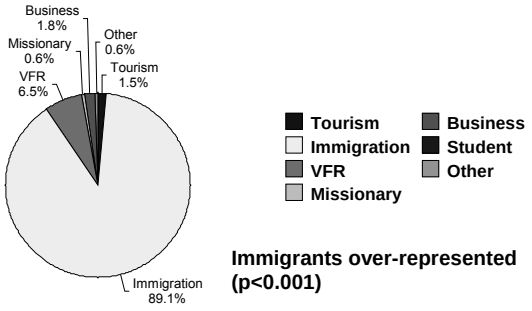
Results (N=349)

Blood-Borne Infections



Results

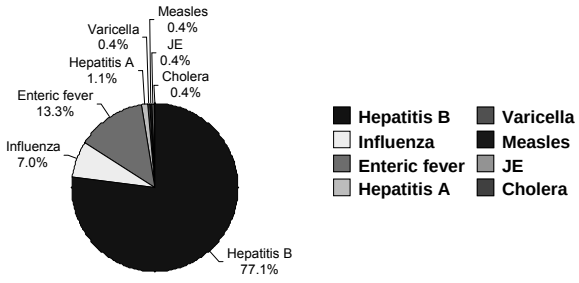
Travel Reason - Blood Borne Infections



Immigrants over-represented (p<0.001)

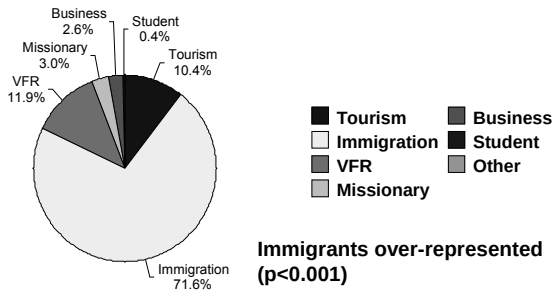
Results (N=271)

Vaccine Preventable Diseases



Results

Travel Reason - VPD



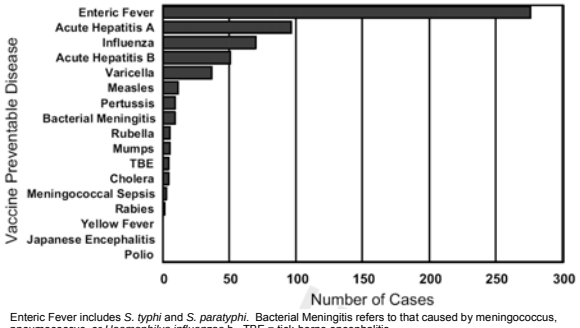
Immigrants over-represented (p<0.001)

Enteric Fever

- Most likely acquired in South Central Asia (p<0.0001)
- Over-represented among those traveling for the purpose of VFR (p<0.0001)
  - 52% of cases of *S.* Typhi or Paratyphi occurred in VFRs

Vaccine preventable diseases in ill returned travelers

n = 37,542 reported to GeoSentinel 1997-2007



Enteric Fever includes *S. typhi* and *S. paratyphi*. Bacterial Meningitis refers to that caused by meningococcus, pneumococcus, or *Haemophilus influenzae* b. TBE = tick-borne encephalitis.

Boggild AK, et al., for the GeoSentinel Surveillance Network. Vaccine preventable diseases in returned international travelers: Results from the GeoSentinel Surveillance Network. *Vaccine*. 2010 Oct 28;28(46):7389-95.

Demographic predictors of common specific VPDs

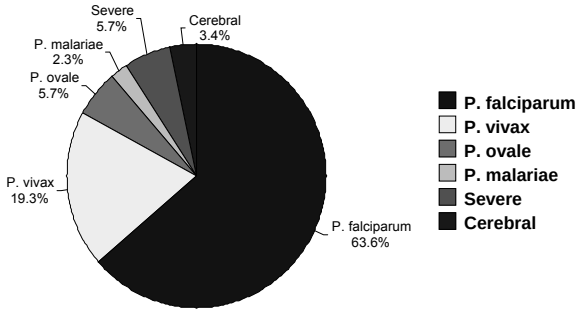
Vaccine preventable disease	Independent predictor	OR* (95% CI)
Enteric fever due to *S. typhi*	VFR travel	3.3 (2.3-4.6)
	Travel to South Central Asia	6.5 (4.8-8.9)
	Birth in India	9.8 (5.9-16.1)
Acute hepatitis A virus	Male gender	1.9 (1.3-3.0)
	Longer trip duration (>30 days)	5.6 (3.5-8.9)
Acute hepatitis B virus	Male gender	3.9 (2.0-7.8)
	Older age (>30 yrs)	2.3 (1.2-4.4)
Influenza	Male gender	1.5 (1.0-2.3)
	Business travel	3.1 (1.8-5.3)
	Travel to North Asia	9.9 (5.6-17.3)
	Travel to Southeast Asia	3.7 (2.3-5.9)
Varicella virus	Younger age (<25 yrs)	2.0 (1.0-4.0)

* All significant with $p \leq 0.05$.

Boggild AK, et al., for the GeoSentinel Surveillance Network. Vaccine preventable diseases in returned international travelers: Results from the GeoSentinel Surveillance Network. *Vaccine*. 2010 Oct 28;28(46):7389-95.

Results (N=94)

Malaria

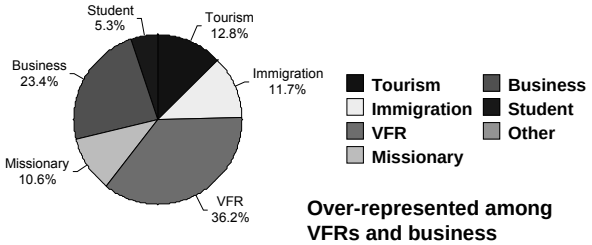


Results

- Malaria Demographic & Region of Exposure:
  - Over-represented among males (p=0.00019)
  - Over-represented among those traveling to Sub-Saharan Africa – 76.6% (p<0.0001)

Results

Travel Reason - Malaria



Over-represented among VFRs and business travelers (p<0.001)

MALARIA AND VFRS

Country of Exposure	Frequency
India	5
Cameroon	4
Congo	3
Guinea	3
Nigeria	3
Uganda	2
Ghana	2
Congo, The Democratic Republic Of The	2
Senegal	2
Mozambique	1
Kenya	1
Pakistan	1
Burundi	1
Gabon	1
Ethiopia	1
Togo	1
Guyana	1

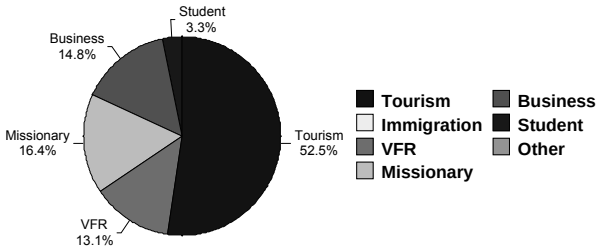
BUSINESS TRAVELERS AND MALARIA

Of 22 with malaria, 15 had received pre-travel advice

Country of Exposure	Frequency
Ghana	5
Guinea	4
Equatorial Guinea	2
Cote d'Ivoire	2
Congo	2
South Africa	1
Nigeria	1
Niger	1
Mali	1
Malawi	1
Indonesia	1
Burkina Faso	1

Results (N=61)

Travel Reason - Dengue

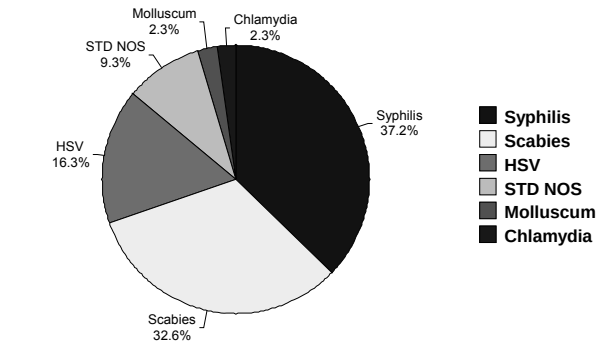


Results - Dengue

- Dengue Region of Exposure
  - Over-represented among those traveling to the Caribbean – 27.9% (p=0.00313)
  - Over-represented among those traveling to Southeast Asia – 21.3% (p=0.00335)

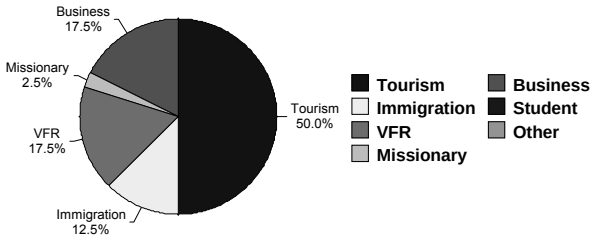
Results (N=43)

Sexually Transmitted Diseases (Excluding HIV and HBV)



Results

Travel Reason - STDs



VFRs

- Proportion of VFR travelers requiring inpatient management of their travel acquired illness was double that of non-VFR travelers ($p<0.0001$) [10.6% vs 5.1%]
- VFRs had the lowest proportionate uptake of pre-travel consult among all non-immigrant travelers ($p<0.0001$) [21% vs 34%]
- VFRs traveled for longer periods of time compared to non-VFR travelers (31 versus 19 days; $p<0.001$)

VFRs

- While VFRs constituted 11.4% of the entire cohort, they accounted for 36.2% of cases of malaria
- VFRs accounted for almost 52% of cases of enteric fever due to *S.* Typhi or *S.* Paratyphi
- The single case of measles in this cohort was imported by a VFR to India

Outline

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- Questions / Discussion

Limitations

- Population analyzed represents only ill returned travelers presenting to CTN sites → conclusions may not extend to all ill returned travelers
  - Top countries of exposure for ill returned non-immigrant travelers paralleled top countries visited by traveling Canadians in general, with Mexico, Cuba, Dominican Republic, and China as top 10 destinations for both this cohort and the general Canadian population
  - Top 3 source countries for new immigrants to Canada (Philippines, China, and India) were also represented among top 4 source countries for ill returned immigrant travelers in this cohort

Limitations

- Travellers with mild or self-limited illnesses or illnesses with short or long incubation periods may have sought care in different settings
- Study does not capture illnesses for which care was sought during travel
- Ill travellers returning from destinations perceived to be low-risk may be under-represented in the database

Limitations

- Data do not permit estimation of incidence rates or destination-specific numerical risks for particular diseases
- Inter-site variation in screening protocols for new immigrants and refugees may have led to over- or under-contributions of particular diagnoses from individual sites

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Conclusions

- Synthesized Canada-specific surveillance data will necessarily inform provincial and national level policy and strategic initiatives around defining, monitoring, and preventing travel-acquired illness
- Surveillance data constitute a Canada-specific epidemiologic roadmap of diseases and syndromes, which will inform clinical decision-making by front line Canadian practitioners

Conclusions

- Serious and potentially fatal infections common and demonstrate epidemiologic preponderances
  - Travelers with malaria proportionately more likely to require inpatient management vs those with alternate diagnoses (44% versus 5%)
  - Of 94 cases of malaria, 60% caused by *Pf*, and 8.5% severe or complicated
  - Malaria → SSA source region in 77%
  - Dengue → travel to Caribbean and SEAsia
  - Enteric fever → South Central Asia

Conclusions

- Highly feared travel-acquired illnesses (Ebola, Lassa, YF, meningococcal meningitis) not observed, but cosmopolitan and vaccine-preventable diseases present
  - Single case of measles in this cohort was imported by a VFR to India
  - Cases of highly communicable influenza (N=21) and varicella (N=1) reported
  - Case of JE occurred in tourist to Thailand

Conclusions

- VFRs constitute a particular high risk group of travelers
  - VFRs constituted 11.4% of cohort, but accounted for 36.2% of malaria and 52% of enteric fever
  - Double the proportion of VFRs required inpatient management of their illness and they traveled for a longer period of time compared to other non-VFR travelers

Conclusions

- An accurate knowledge of the health problems that are faced by international travelers in different geographical destinations provides a robust evidence base for physicians to deliver effective preventative advice, immunizations, and prophylactic medications to travellers
- This profile further informs post-travel diagnosis and therapy, as well as prioritization of pre-travel intervention strategies for the most significant illnesses

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