



# MICI et voyages, conseils pratiques

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# OBJECTIFS PEDAGOGIQUES

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- Savoir anticiper et mettre à jour les vaccinations
- Connaître les délais d'interruption et de reprise de traitement IS ou par biothérapie en cas d'utilisation d'un vaccin vivant
- Savoir gérer le traitement et anticiper ses contraintes
- Connaître les principes de prévention et de traitement de la diarrhée aiguë

# CONFLITS D'INTERET

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- Speaker fee: Abbvie, MSD, Takeda, Pfizer, Ferring, Falk, Galapagos, Celltrion, Alphasigma
- Consultancy: Abbvie, Takeda, Hospira, Mundipharma, MSD, Pfizer, GlaxoSK, Amgen, Galapagos, Celltrion, Alphasigma
- Research grant: Takeda, Abbvie

# PLAN

- Voyage: Etat des lieux, type de voyage et de voyageur
- Voyage et MICI: besoins patients et connaissance médecins
- Conseils pre travel, IBD passport et Vaccination
- Malade sur place ? Risque associé a l'immunodepression ? Tous égaux devant diarrhée du voyageur et autres pathologies ?
- Traveling in hypoxic conditions
- Sex and traveling, sun exposure
- The returning traveler

Prepare and prevent,  
don't repair and repent!

# H1n1 influenza

WHO 2010:17000  
H1N1 related deaths



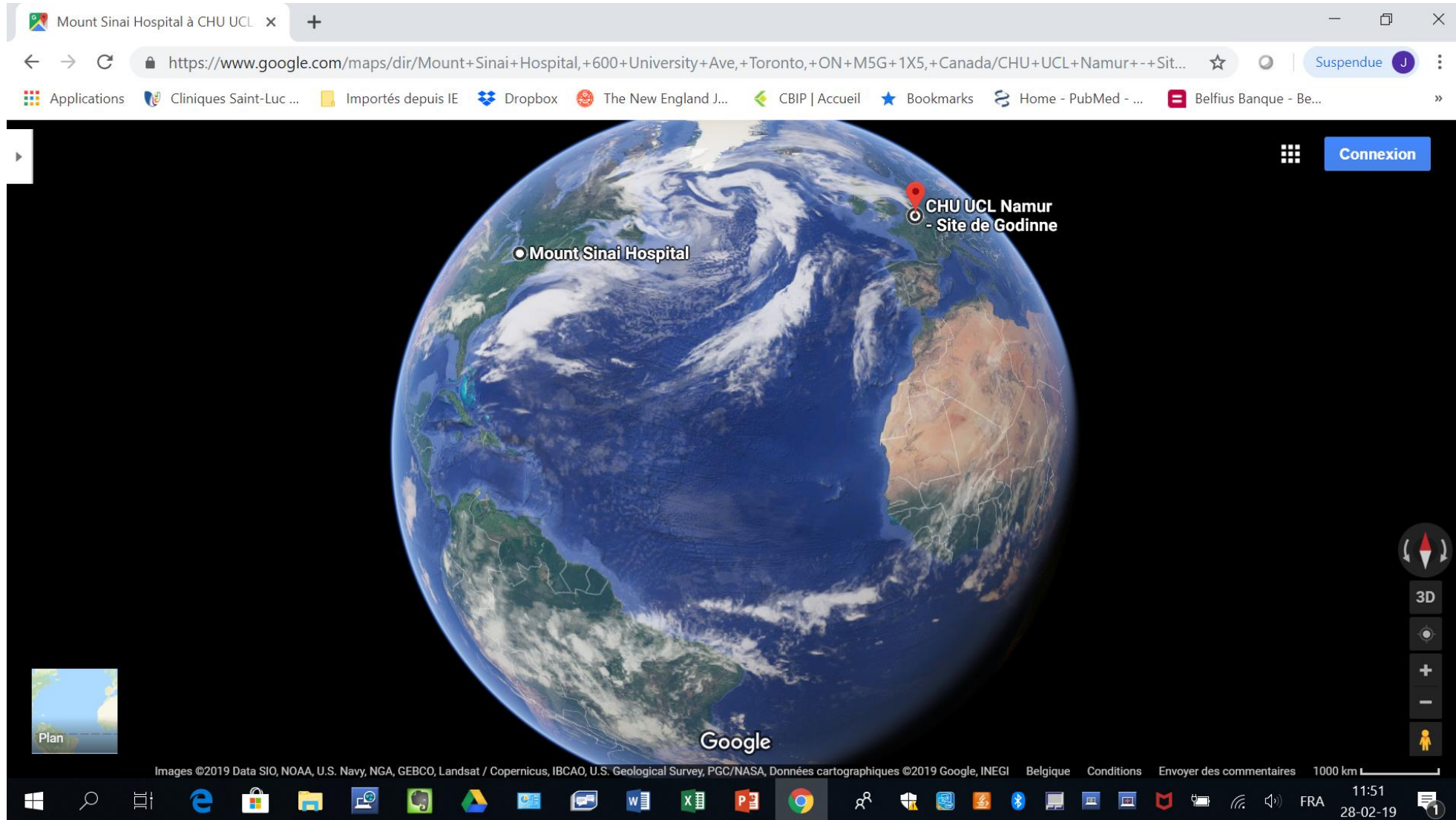
**Table 1** | Demographic, clinical characteristics, treatment of 25 patients with inflammatory bowel disease and flu-like illnesses

Demographic characteristics	
Male, <i>n</i> (%)	8 (32)
Median age, years (IQR)	33 [27-45]
Median BMI, kg/m <sup>2</sup> (IQR)	22 [20-28]
Current smoker, <i>n</i> (%)	4 (16)
IBD phenotype	
CD, <i>n</i> (%)	14 (56)
UC, <i>n</i> (%)	11 (44)
Treatment	
Corticosteroid, <i>n</i> (%)	6 (24)
Azathioprine, <i>n</i> (%)	16 (64)
Anti-TNF, <i>n</i> (%)	8 (32)
Combined therapy, <i>n</i> (%)	8 (32)
No use of immuno-modulators and/or biologics	3 (12)
Presence of underlying medical conditions	7 (28)
Receipt of vaccines	
H1N1v vaccine	0 (0)
Seasonal influenza vaccine	8 (32)
Pneumococcal vaccine	4 (16)

*Receipt H1N1 vaccine: 0%*  
*88% on IM/biologics*  
*12% ICU stay*  
*4% death*

Rahier JF et al, APT 2010

# Voyage: Etat des lieux, type de voyage et de voyageur



# Voyages voyages ...

## WORLDWIDE

- 1950 - 25 million international tourist arrivals
- 2000 - 664 million international tourist arrivals
- 2010 - 940 million international tourist arrivals (growth rate 7% from 2009)
- 2030 – forecast 1.8 billion

World Tourism Organisation

## Importance of travel medicine

Of 100,000 travellers to the [developing world](#) for 1 month

- 50.000 will develop some sort of health problem during their trip
- 8000 will see a physician
- 5000 will have to stay in bed
- 300 will have to be admitted to hospital either during their trip or on return
- 50 will need to be air evacuated
- 1 will die

# Types of travelers

- Tourists
- VFRs (visiting friends and relations)
- Business travellers
- Migrant workers
- Military
- Aid and Development workers
- Students
- Gap Year travel
- Refugees
- Pilgrims

# Special populations

**IBD**

Elderly travellers

Infants and children

Pregnant women

Travellers with chronic diseases

Travellers with disability

Immunocompromised traveller

# Special journeys

- Cruise ship travel
- Diving
- Extended stay
- Extreme travel
- Mass gatherings (eg. The Hajj)
- Wilderness/remote regions travel

❖ Risk depends on destination

# Voyage et MICI: besoins des patients et connaissance des médecins

- **Statement 7.1\***
- Given the lack of data, it is currently not possible to advise against travelling to countries with increased infection rates. However, pre-travel counselling regarding safety measures is strongly recommended for patients under immunosuppression travelling to endemic areas [EL4].
- Specific travel recommendations from national authorities and the World Health Organization should be consulted [EL5]

# Travelling & IBD

- Over one billion people travel outside their country annually
- Only few studies assessed risks of travelling in IBD patients
- IBD societies' guidelines acknowledge the existence of severe obstacles for IBD patients who travel for leisure or business

UNWTO World tourism barometer 2008; 6:5-8  
Rahier JF, JCC 2014; Vavricka SR et al, J Crohn Colitis 2014;  
Ben-Horin S et al, Clin Gastroenterol Hepatol, 2012

# Adherence to Anti-TNF Therapy in Inflammatory Bowel Diseases: A Systematic Review

Anthony Lopez, MD,\* Vincent Billioud, MD,\* Carina Peyrin-Biroulet, MD,<sup>†</sup>  
and Laurent Peyrin-Biroulet, MD, PhD\*

**Background:** Nonadherence to medications may affect disease outcomes. The aim of this article was to review methods of assessment, prevalence, and predictors of nonadherence to anti-tumor necrosis factor therapy in inflammatory bowel diseases (IBD).

**Methods:** Studies were identified through the electronic database of MEDLINE (up to January 2012) and the annual meetings of Digestive Disease Week, the American College of Gastroenterology, the United European Gastroenterology Week, and the European Crohn's and Colitis Organization.

**Results:** Among 1783 citations identified, 13 studies evaluated adherence to biologics in IBD. Several methods were used to assess adherence to anti-tumor necrosis factor, including the medication possession ratio, the medication refill adherence, and the Morisky Medication Adherence Scale 8. Pooled adherence to anti-tumor necrosis factor therapy was 82.6%. Pooled adherence was 83.1% in adalimumab and 70.7% in infliximab-treated patients. Female gender, smoking, constraints related to treatment, anxiety, and moodiness were associated with nonadherence to both infliximab and adalimumab. Concomitant immunomodulator use and time since first infusion more than 18 weeks were predictors for nonadherence to infliximab. Regimen of 40 mg every other week, syringe use (versus pen), internal medicine center prescription (versus gastroenterology center prescription), retail pharmacy (versus speciality pharmacy) and new user (versus previous user) were predictors for adalimumab nonadherence.

**Conclusions:** More than three-quarters of patients with IBD adhere to biologics. Predictors of nonadherence include female gender, smoking, constraints related to treatment, anxiety, and moodiness. These data could be used to develop intervention studies aimed at improving adherence to biologics in IBD.

(*Inflamm Bowel Dis* 2013;19:1528–1533)

**Key Words:** anti-TNF, adherence, inflammatory bowel disease

An increased proportion of patients suffering from inflammatory bowel diseases (IBD) are receiving anti-tumor necrosis factor (TNF) agents. In a French referral center, 60% of patients with Crohn's disease (CD) received at least 1 anti-TNF agent in the era of biologics.<sup>1</sup> In the same referral center during the same period, the probability of receiving infliximab at 5 years from the time of diagnosis was 29% in patients with ulcerative colitis (UC).<sup>2</sup>

Adherence to treatment is recognized as a major therapeutic goal in chronic disorders, including diabetes,<sup>3</sup> hypertension,<sup>4</sup> or AIDS.<sup>5</sup> However, adherence rates to long-term therapies seem low, with an average rate of 50%.<sup>6</sup> Nonadherence with medication increases the risk of clinical relapse among patients with quiescent UC.<sup>7</sup> Poor adherence may undermine the potential therapeutic

benefits of biologics by contributing to treatment failure<sup>8</sup> and increasing the risk of developing immunogenicity to anti-TNF agents. Nonadherence has also been associated with increased health care costs.<sup>9,10</sup>

Numerous methods have been developed to assess adherence to oral medications, including patient surveys, pill counts, and prescription claims.<sup>11,12</sup> In IBD, several adherence scales have been used to assess drug adherence, such as the medication adherence reporting scale and the Modified Morisky Adherence Scale.<sup>8,13</sup> However, no validated scale or definitions of nonadherence have been validated for biological therapies requiring scheduled subcutaneous or intravenous injection. The aims of this article were to review (1) the methods used to measure adherence, (2) the rates of adherence, and (3) the predictors of nonadherence in patients with IBD receiving infliximab or adalimumab.

## METHODS

A literature search was conducted to identify studies that measured rates of adherence to biological treatments in patients with IBD in clinical practice. We conducted a computerized search of English language publications listed in the electronic databases of MEDLINE (source: PubMed 1990 to January 2012). Studies were identified using the following search terms: "Patient compliance" and "Medication adherence" as medical subject headings as

Travel is among leading causes for drug cessation or drug holiday (non-compliance)

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The authors have no conflicts of interest to disclose.

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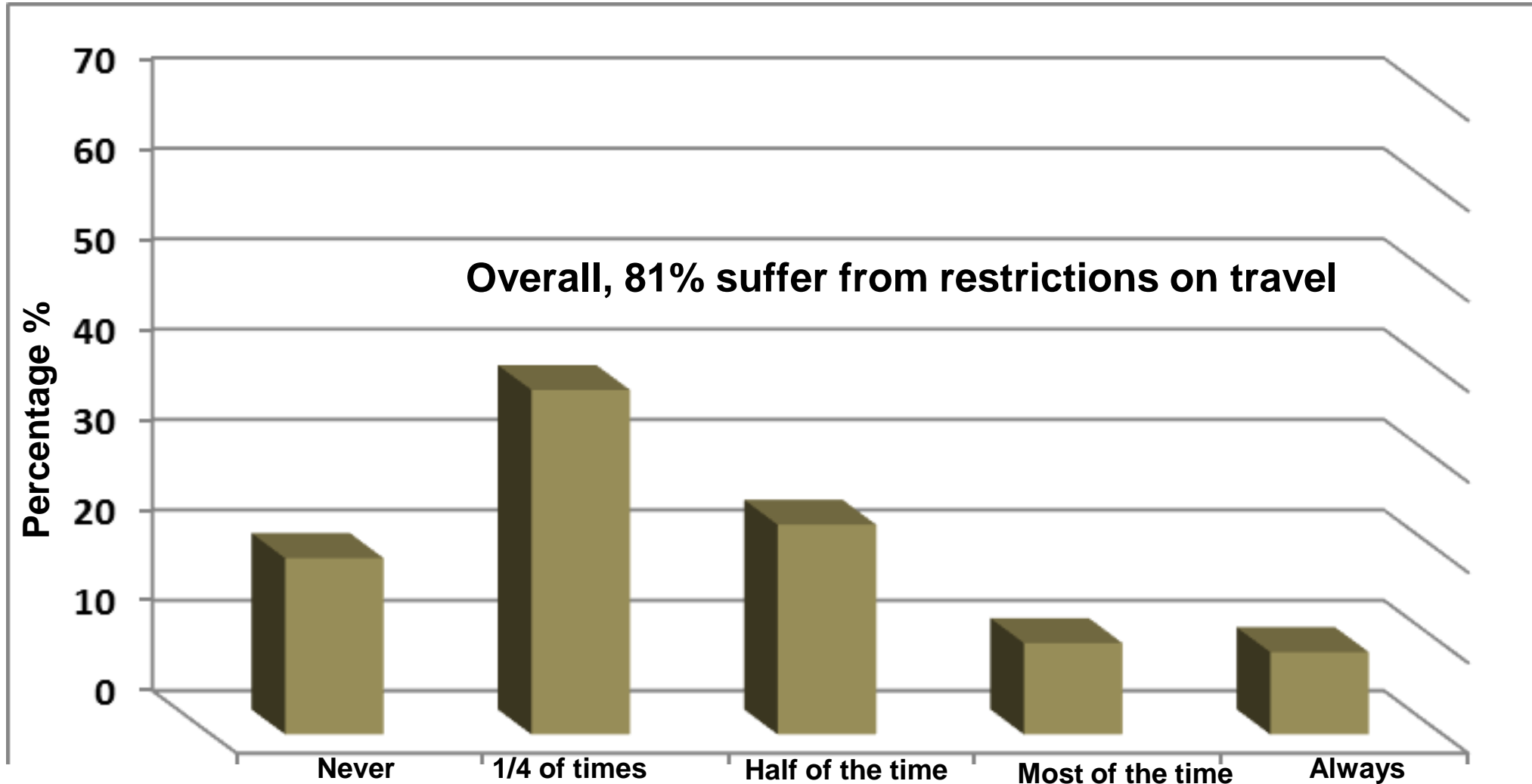
Published online 20 March 2013.

# What are the patients' needs ?

- Survey to map IBD patients, their needs and the gaps in care abroad
- Over 2500 answers: UK, Israel, Australia and New-Zealand

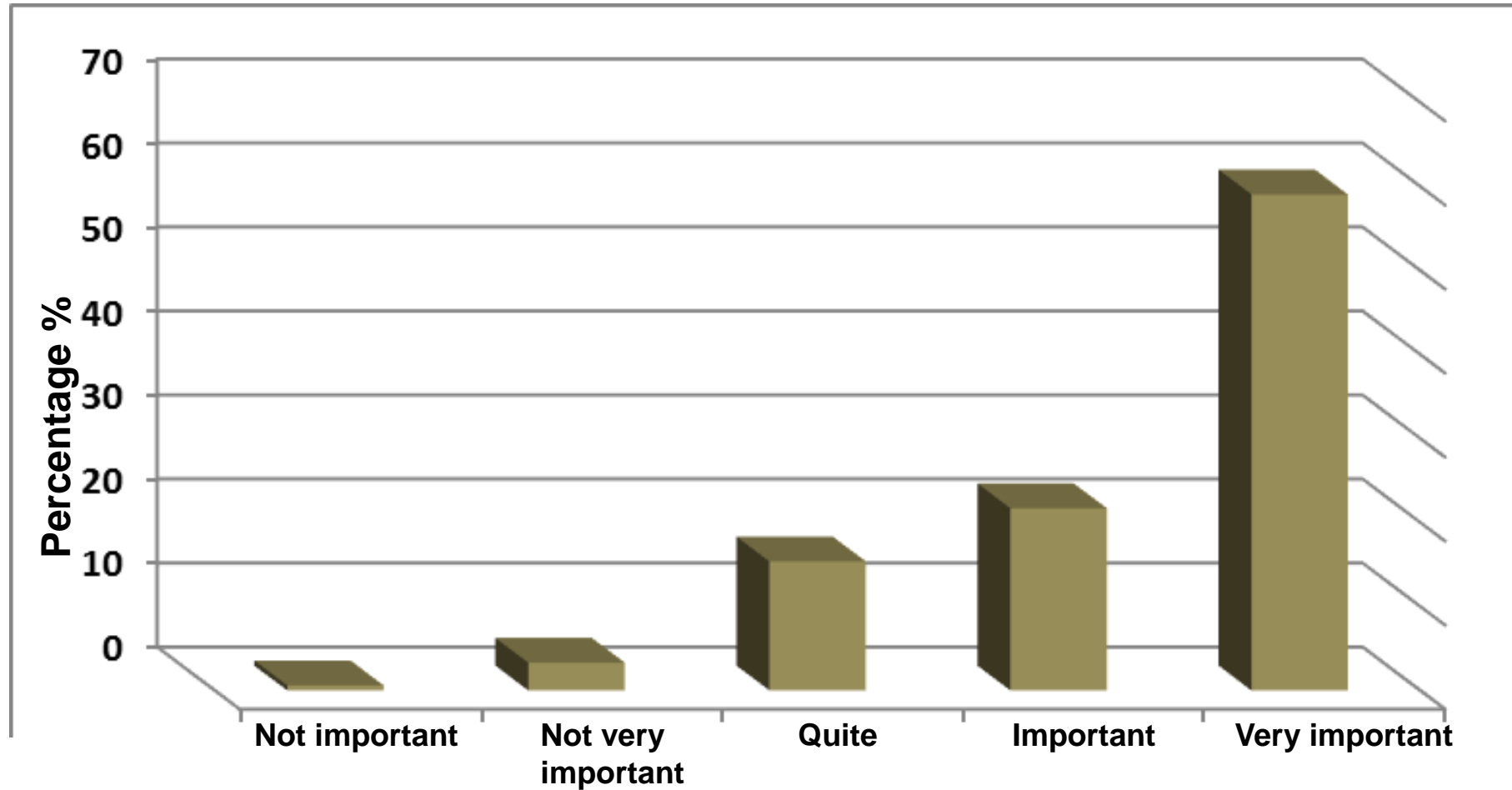
# Preliminary survey results (n=344)

How often do you feel IBD limits your ability to travel abroad ?



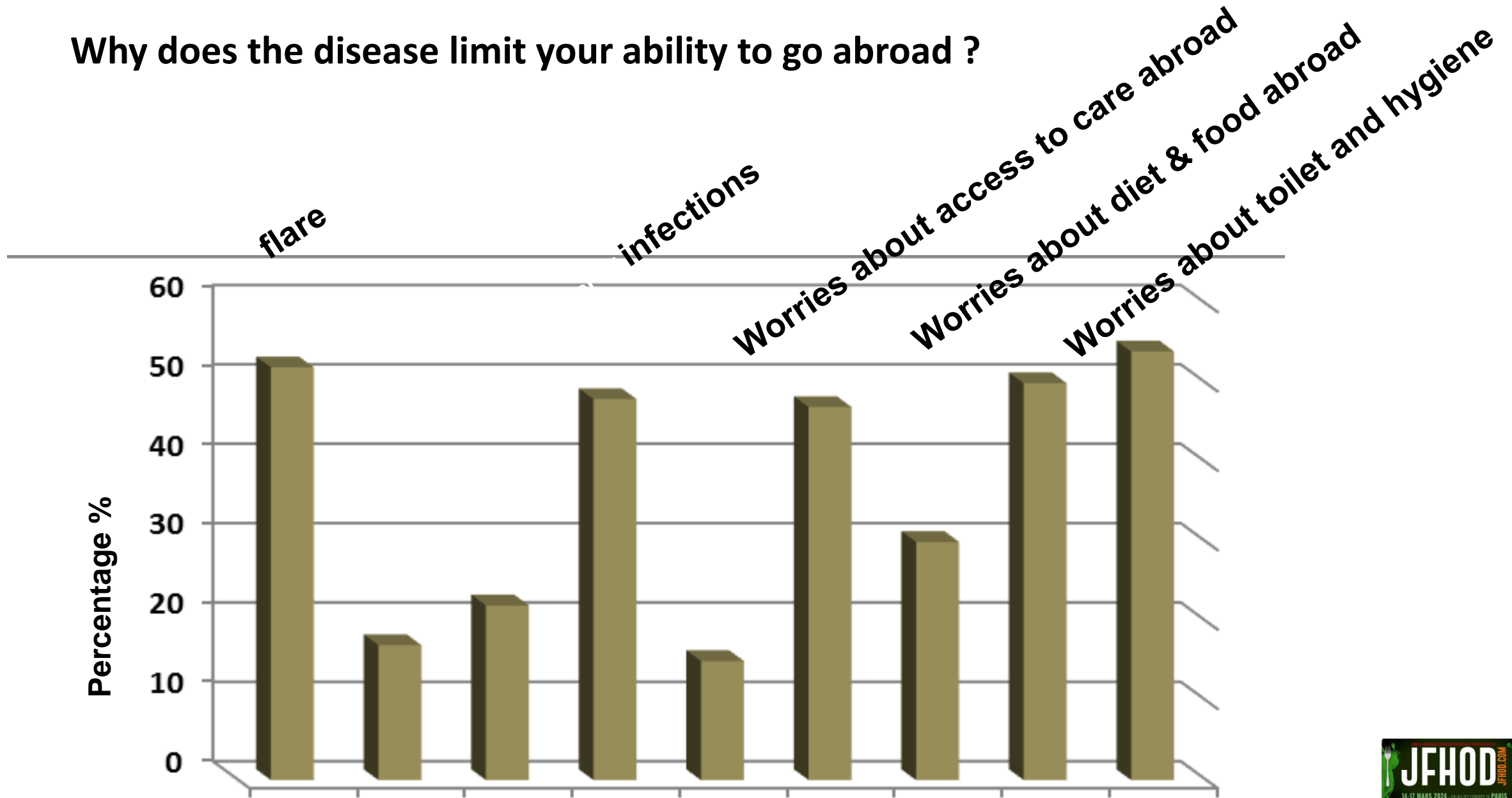
# Preliminary survey results (n=344)

How important is travel abroad for your general quality of life ?



# Preliminary survey results (n=344)

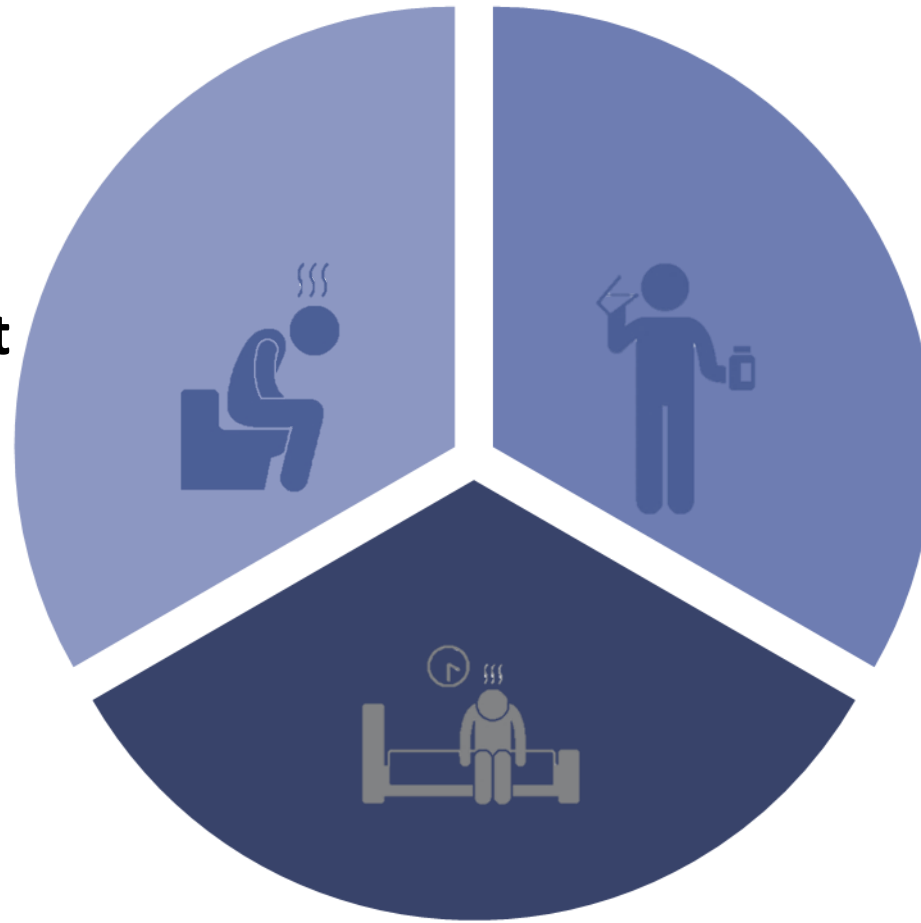
Why does the disease limit your ability to go abroad ?



# Challenges

## Disease specific

- Sanitary facilities at destination
- Fitness to travel
- Dietary concerns
- Stoma care
- Vaccination



## Medication concerns

- Availability
- Storage
- Customs

## Availability of healthcare

- Insurance concerns
- Seeking help overseas

Greveson et al, 2015; Aluzaitė et al, 2018, GastroNZ; Billioud V et al, Inflamm Bowel Dis 2011

# Challenges

- Increased travel-related morbidity in IBD
- Travel is among leading causes for drug cessation or drug holiday (non-compliance)
- Greater risk for immunosuppressed
  - Infections
  - Relapse
  - Destination specific
  - Vaccinations

Rahier et al European Crohns and colitis organisation 2014.  
Soonawala et al, Inflamm bowel Dis 2012.  
Lopez A et al, Inflamm Bowel dis 2013

# IBD treatments

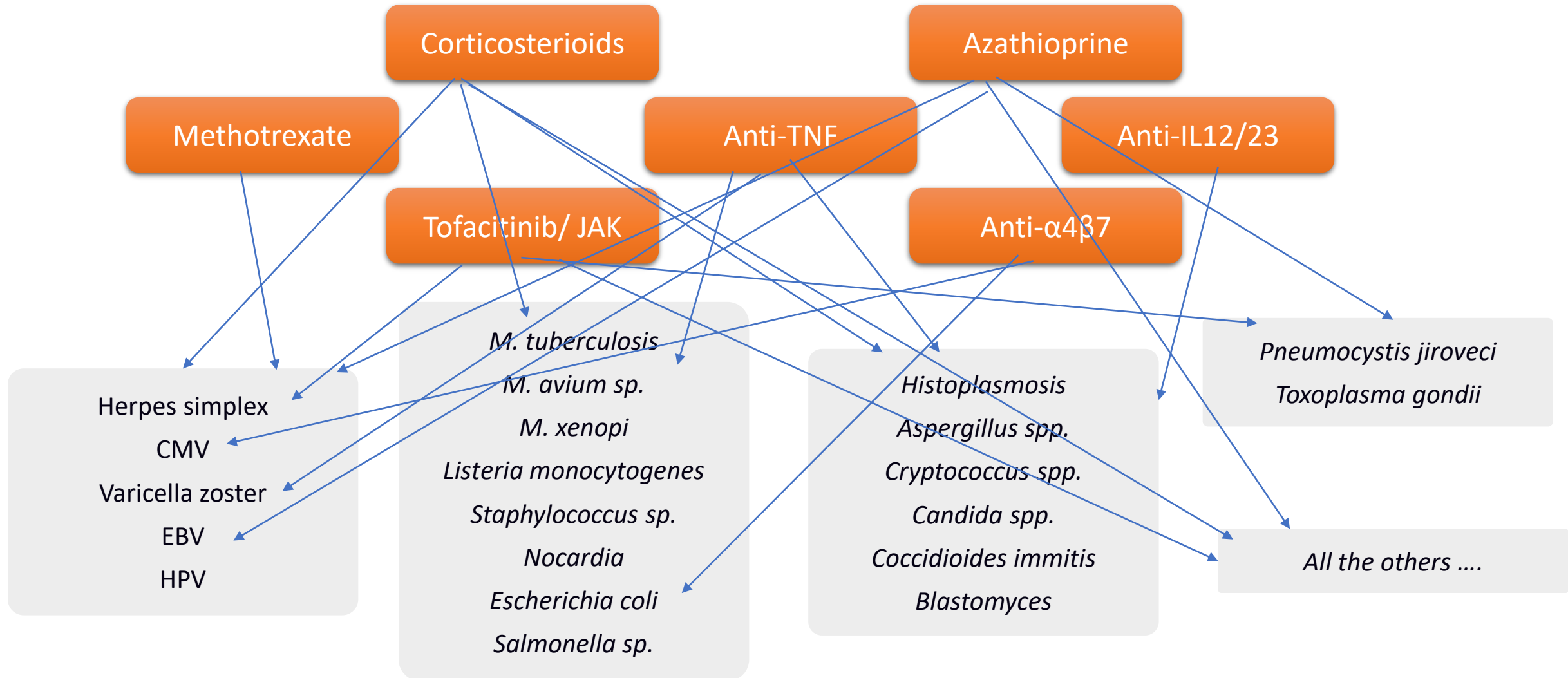
**“The good old days”**

Corticosteroids

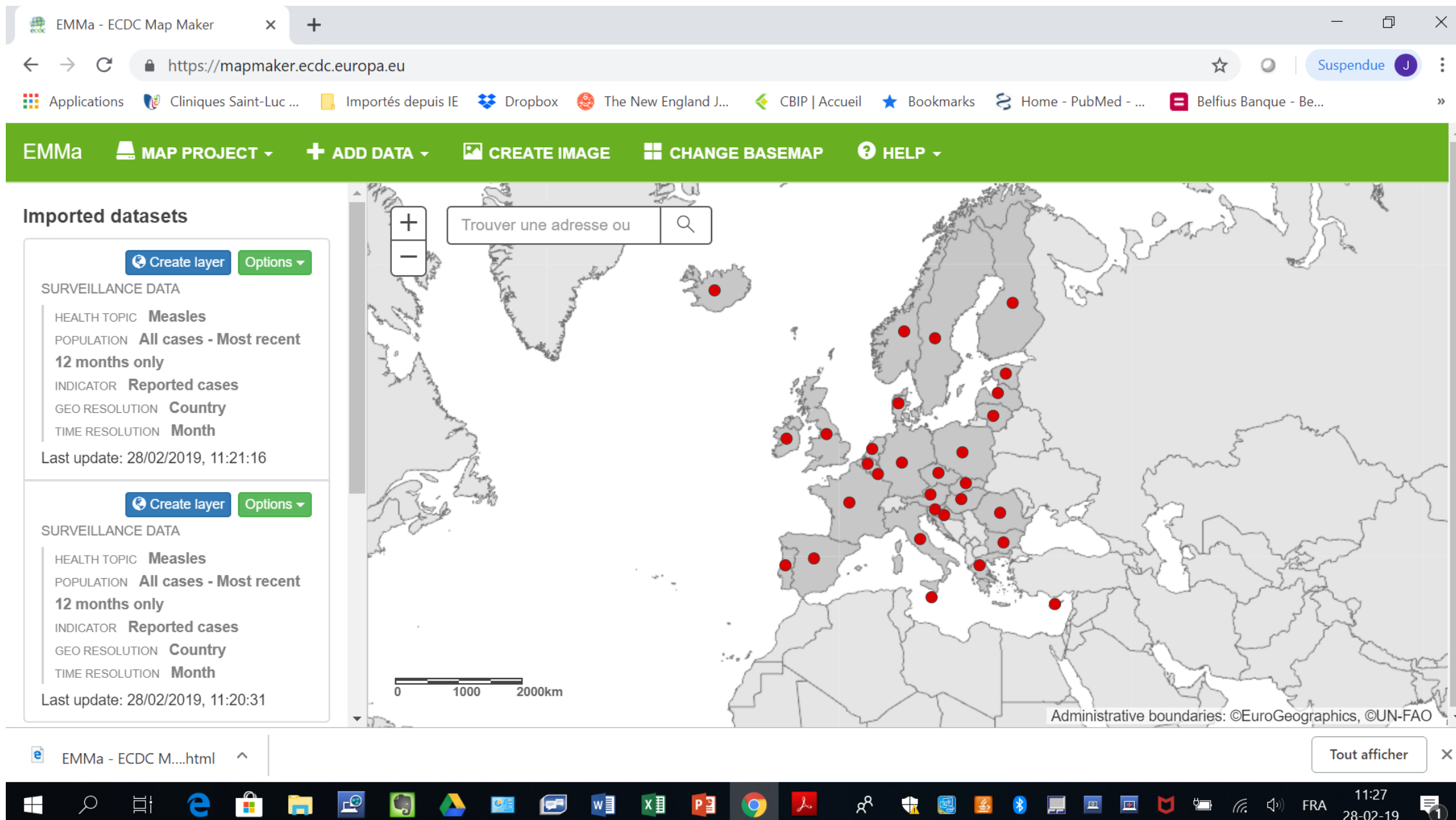
Azathioprine

Methotrexate

# IBD treatments and types of infection: one expert's view



# 12.500 incident cases of Measles in 2018

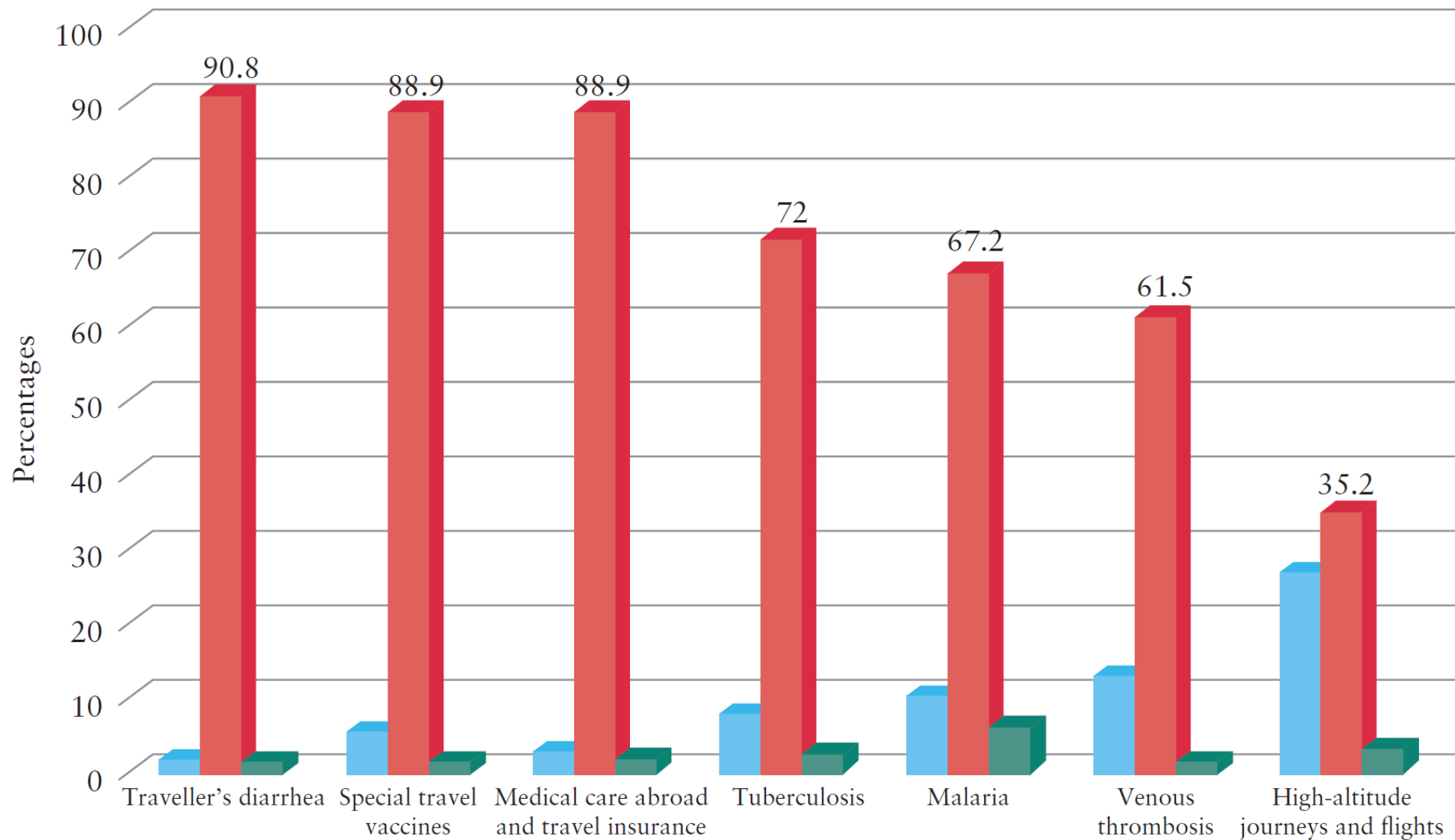


# Knowledge of GI specialists ?

- A 57-question survey was distributed to **305 IBD physicians in 23 countries** in Asia, Europe and USA.
- They were asked about:
  - Topics they would covered during a pre travel consultation ?
  - Are specific live vaccine contraindicated in CD patient treated with anti-TNF therapy and azathioprine ?

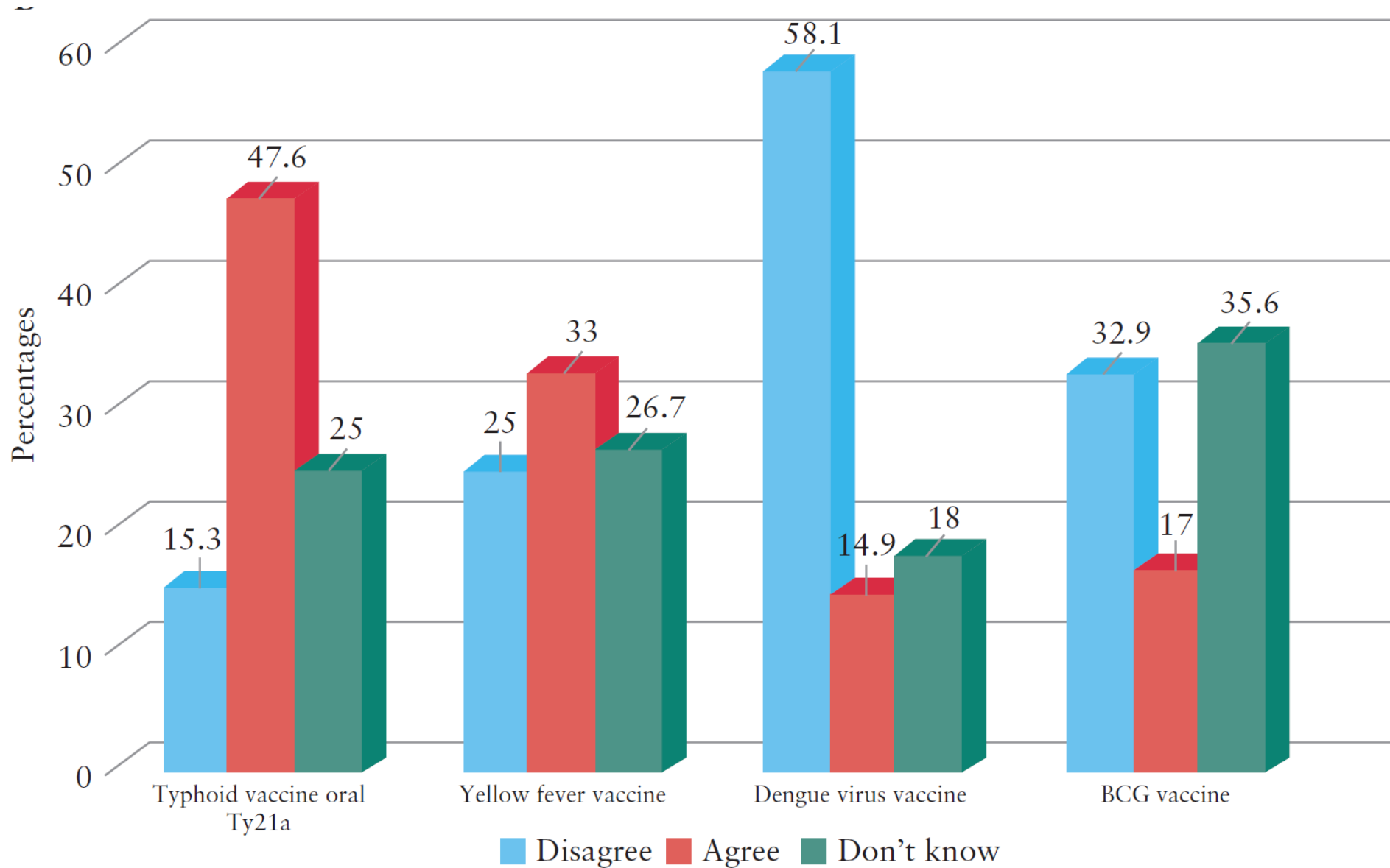
Chan W et al, JCC 2018, 1261–1269

# Topics covered during a pre travel consultation



Chan W et al, JCC 2018, 1261-1269

# Is live vaccine CI in CD patient anti-TNF therapy and AZA ?



Chan W et al, JCC 2018, 1261–1269



Senior gastroenterologists [ $> 20$  years since leaving their training programme] were more deficient in knowledge on vaccines than junior gastroenterologists [ $< 5$  years ]

# Conseils pre travel, IBD passport et vaccinations

**Pre-travel  
consultation  
(4-6 weeks before  
departure)**

Risk assessment (potential hazards)

Risk management (advice to reduce exposure to health risks)

Service delivery: immunization, prophylaxis or self-medications

Empower traveler to manage his health

# Risk assessment

## Information about travelers

- Age and sex
- Medical history
- Medications
- Allergies
- Immunization history
- Special health needs

## Information about trip

- Destination
- Length of stay
- Mode of transport
- Purpose of trip and planned activities
- Financial budget, accommodation, insurance
- Healthcare in destination

# Risk factors and health problems facing international travelers

## RISK

- Overcrowding
- Low sanitation
- Climatic change
- Vector of diseases
- Stray animals
- Unsafe roads
- Security problems

## HEALTH PROBLEMS

- Aggravation of existing problem
- Food and water borne infections
- Air borne infections
- Unintentional & Intentional Injuries
- Vector borne diseases
- Zoonotic diseases

# Common diseases associated with international travel

## Gastrointestinal

- Traveler's diarrhea
- Typhoid fever
- Hepatitis A
- Cholera
- Poliomyelitis

## Respiratory diseases

- Influenza
- Meningitis
- Mers-Cov
- Tuberculosis
- **Covid-19**

## Vector borne diseases

- Yellow fever
- Malaria
- Dengue fever
- Leishmaniosis
- Japanese encephalitis

## Behavior related

- Sexually transmitted diseases

## Zoonotic diseases

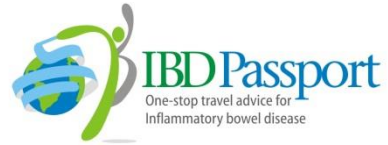
- Rabies

## Blood borne

- Hepatitis B

## Soil borne

- Tetanus



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IBD nurse specialist  
Gastroenterology Dept.  
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To create a comprehensive multi-level platform for supporting individuals with IBD who plan to travel, by providing a reputable source of information, orchestrating logistic resources and networking global IBD centers



# What advice can we give our patients?

[Home](#)[IBD Network](#)[Travelling with IBD](#)[Healthcare Professional Area](#)[About](#)[Contact](#)

## Travelling with IBD

Below you will find practical information containing advice on travelling with IBD.



[Travel and IBD](#)



[Vaccinations](#)



[Travelling with Medication](#)



[Diet](#)



[Travel after Surgery](#)



[Managing Travellers Diarrhoea](#)



[Travel Insurance](#)



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# IBD Network


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## IBD Network

Choose your destination from the map or menu below. To view the Physician listings you will need to be logged in.

Select your Destination 

Includes Vaccination & Healthcare arrangements for each country!




Africa	>
Asia (Central)	>
Asia (East)	>
Asia (South East)	>
Australasia & Pacific	>
Caribbean	>
Central America	>
Europe & Russia	>
Middle East	>
North America	>
South America	>



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# IBD Passport Global Programme



-  Content & translation complete
-  Content & translation in-progress
-  Content & translation planned in the next 6 months

# Pretravel Advice for IBD travelers

- Antibiotic for self-use in gastroenteritis
- Monitor immunity after vaccination
- No travel to yellow fever endemic areas if IS
- Sun exposure (increased susceptibility /drugs)
- Ask specialist advice

# Types de vaccin

**Table 2 Types of vaccines and examples**

Carbohydrate/polysaccharide antigens	Protein antigen: recombinant/inactivated/conjugated**	Live/attenuated organisms
Pneumococcal polysaccharide (PPSV-23, for example, Pneumovax®)	Tetanus, diphtheria, acellular pertussis (TD/DT, TDAP, DTAP)	Varicella (VZV, Varivax®, Varilrix®)
Meningococcal polysaccharide (MPSV-4)	Hepatitis A, hepatitis B	Shingles, zoster (for example, Zostavax®)
Typhoid polysaccharide (Vi injection)	Seasonal influenza A/B injection	Intranasal influenza (for example, Flu-mist®)
	Pandemic influenza (H1N1) injection	
	Human papilloma virus	Measles, mumps, rubella
	Anthrax (acellular)	Yellow fever
	Inactivated polio (IPV, Salk, IM/SQ)	Oral polio (OPV)
	Oral cholera (killed cells)	Typhoid (Ty21a oral)
	Pneumococcal conjugate** (PCV-7, PCV-13, for example, Prevnar®)	Vaccinia (smallpox)
	Meningococcal conjugate** (MCV-4, <55 years old)	Bacillus Calmette-Guérin
	Haemophilus influenza type B protein polysaccharide conjugate** (HiB, PRP)	Rotavirus
		Anthrax (live spore)
		Smallpox

Vaccinations may vary in terms of their constituents from country to country (for example, Japanese encephalitis virus, rabies, anthrax) and over time as new vaccines are developed. Providers are advised to consult product inserts of specific vaccines to confirm constituents before use. DTAP, diphtheria, tetanus, and pertussis; HiB, Haemophilus influenza type B; IM/SQ, intramuscular/subcutaneous; IPV, inactivated polio virus; MCV-4, quadrivalent meningococcal conjugate; MPSV-4, quadrivalent meningococcal polysaccharide vaccine; OPV, oral polio virus; PCV, pneumococcal conjugate vaccine; PPSV, pneumococcal polysaccharide vaccine; PRP, polyribosylribitol phosphate; TD/DT, Tetanus Diphtheria/Diphtheria Tetanus; TDAP, Tetanus diphtheria acellular pertussis; Vi, Vi capsular polysaccharide; VZV, varicella zoster vaccine. \*\*conjugated vaccines.

# Types de vaccin

**Table 2 Types of vaccines and examples**

Carbohydrate/polysaccharide antigens	Protein antigen: recombinant/inactivated/conjugate**	Live/attenuated organisms
<ul style="list-style-type: none"> <li>- inactivé</li> <li>- peu immunogène</li> <li>- protège moins lgts</li> <li>- ne protège pas du portage</li> <li>- pas d'effet booster</li> <li>- virtuellement aucune CI</li> </ul>	<ul style="list-style-type: none"> <li>- inactivé</li> <li>- immunogène et plus longtemps</li> <li>- protège du portage</li> <li>- virtuellement aucune CI</li> </ul>	<ul style="list-style-type: none"> <li>- vivant atténué</li> <li>- très immunogène</li> <li>- protège très longtemps</li> <li>- attention CI</li> </ul>
V-23, (IPV) SV-4 (IPV) h) (IPV)	Tetanus (IPV), DTA (IPV) Hepatitis A (IPV) Seasonal influenza (IPV) Polio (IPV) Human rabies (IPV) Anthrax (IPV) Inactivated polio virus (IPV) Oral polio virus (OPV)	Variola (smallpox) Shingles (live attenuated) Intranasal influenza (live attenuated) Measles (live attenuated) Yellow fever (live attenuated) Oral polio virus (OPV) Typhoid (live attenuated)
	Pneumococcal conjugate** (PCV-7, PCV-13, for example, Prevnar®) Meningococcal conjugate** (MCV-4, <55 years old) Haemophilus influenza type B protein polysaccharide conjugate** (HiB, PRP)	Vaccinia (smallpox) Bacillus Calmette-Guérin Rotavirus Anthrax (live spore) Smallpox

Vaccinations may vary in terms of their constituents from country to country (for example, Japanese encephalitis virus, rabies, anthrax) and over time as new vaccines are developed. Providers are advised to consult product inserts of specific vaccines to confirm constituents before use. DTAP, diphtheria, tetanus, and pertussis; HiB, Haemophilus influenza type B; IM/SQ, intramuscular/subcutaneous; IPV, inactivated polio virus; MCV-4, quadrivalent meningococcal conjugate; MPSV-4, quadrivalent meningococcal polysaccharide vaccine; OPV, oral polio virus; PCV, pneumococcal conjugate vaccine; PPSV, pneumococcal polysaccharide vaccine; PRP, polyribosylribitol phosphate; TD/DT, Tetanus Diphtheria/Diphtheria Tetanus; TDAP, Tetanus diphtheria acellular pertussis; Vi, Vi capsular polysaccharide; VZV, varicella zoster vaccine. \*\*conjugated vaccines.

# Attention aux vaccins vivants atténués!

## Vaccins vivants atténués

- Fièvre Jaune
- Rougeole Rubéole Oreillons (RRO)
- BCG
- VZV varicelle, zona
- Typhoïde oral
- (Polio oral)
- (Variole: military)
- (Influenza vivant nasal)

L'Immunosuppression est une contre-indication aux **vaccins vivants atténués** à cause du risque de **réplication non contrôlée de la souche vaccinale**  
Ex: Fièvre jaune vaccinale  
→ **Problème de SAFETY**

# Recommended vaccines in IMID patients?

## Basic vaccines

Tetanus	Every 10 years
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Diphtheria	Every 10 years
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Pertussis	Once
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Polio	Once
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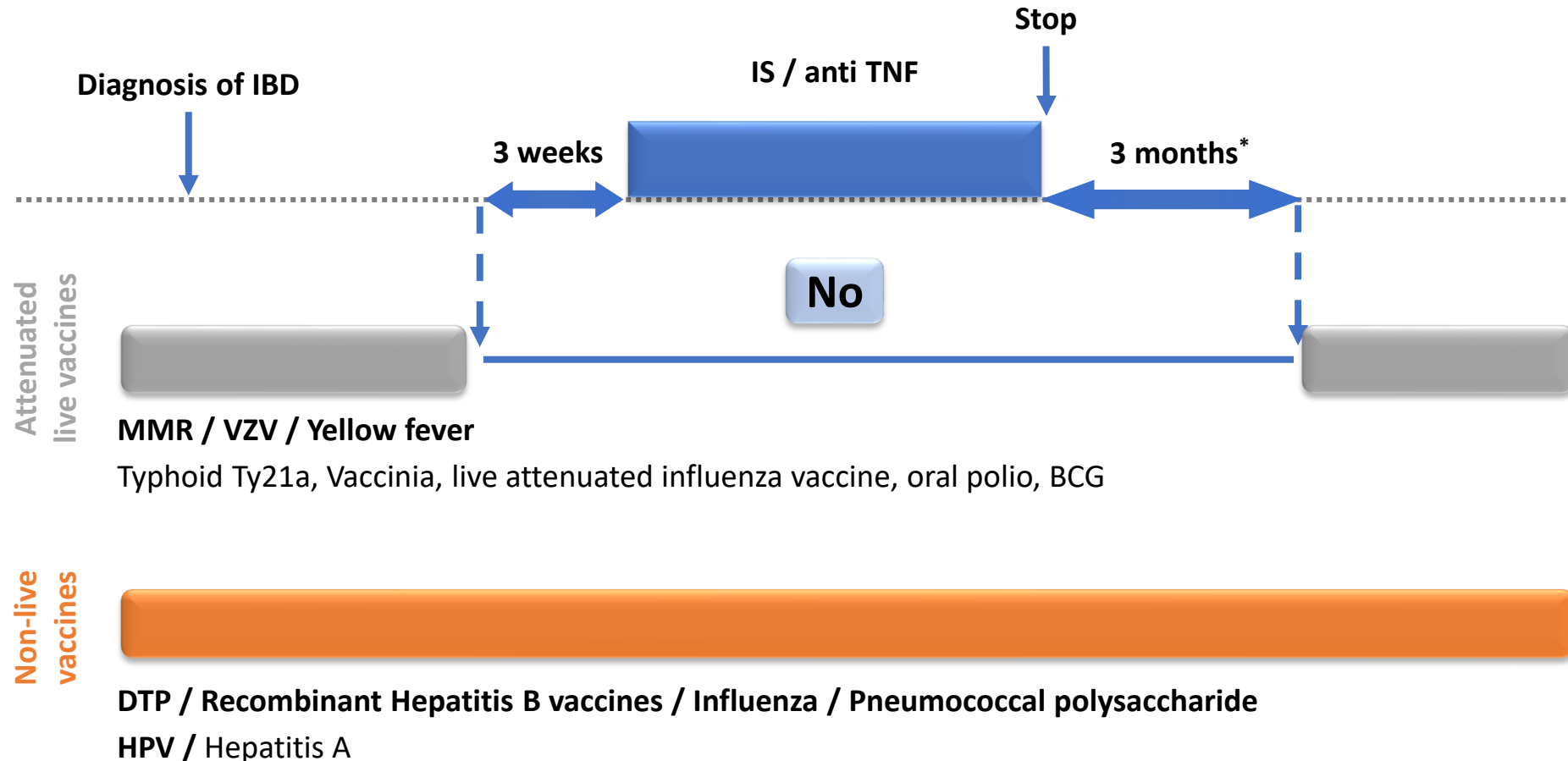
- Brezinschek HP, et al. *Curr Opin Rheumatol*. 2008;20:295–299; Sands B, et al. *Inflamm Bowel Dis*. 2004; 10: 677–92; Rahier JF, et al. *J Crohns Colitis*. 2014; 8: 443–68 ; Lebowhl M, et al. *J Am Acad Dermatol*. 2008; 58: 94–105; British Society for Rheumatology: [http://rheumatology.org.uk/guidelines/guidelines\\_other/vaccinations/view](http://rheumatology.org.uk/guidelines/guidelines_other/vaccinations/view); Van Assen S, et al. *Ann Rheum Dis*. 2011; 70: 414–22; Superior Health Council: [www.health.fgov.be/CSS\\_HGR](http://www.health.fgov.be/CSS_HGR); 8. CDC: [www.cdc.gov/mmwr/preview/mmwrhtml/rr5515a1.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5515a1.htm); Wasan SK, et al. *Am J Gastroenterol*. 2010; 105: 1231–1238

# Recommended vaccines in IMID patients?

Vaccine	Impact of disease in IC patients?	Belgian Superior Health Council	CDC	IMID Patients		
				RA Assoc.	European Crohn's & Colitis Org.	American Psoriasis Foundation
Influenza	Increased mortality	YES	YES	YES	YES	YES
Pneumonia	Increased mortality	subgroups	YES	YES	YES	
HPV	Increased morbidity	subgroups		(yes) Selected	YES	
Varicella/ Zoster	Increased mortality		YES	YES	YES	
HBV	Increased morbidity	subgroups	subgroups	(yes) At risk	YES	

- Brezinschek HP, et al. *Curr Opin Rheumatol*. 2008;20:295–299; Sands B, et al. *Inflamm Bowel Dis*. 2004; 10: 677–92; Rahier JF, et al. *J Crohns Colitis*. 2014; 8: 443–68 ; Lebwohl M, et al. *J Am Acad Dermatol*. 2008; 58: 94–105; British Society for Rheumatology: [http://rheumatology.org.uk/guidelines/guidelines\\_other/vaccinations/view](http://rheumatology.org.uk/guidelines/guidelines_other/vaccinations/view); Van Assen S, et al. *Ann Rheum Dis*. 2011; 70: 414–22; Superior Health Council: [www.health.fgov.be/CSS\\_HGR](http://www.health.fgov.be/CSS_HGR); 8. CDC: [www.cdc.gov/mmwr/preview/mmwrhtml/rr5515a1.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5515a1.htm); Wasan SK, et al. *Am J Gastroenterol*. 2010; 105: 1231–1238

# Vaccines in IBD patients



\* This delay may be reduced to 1 month in case of use of corticosteroids alone.  
IS: Immunosuppressed; MMR: Measles, mumps, rubella; VZV: Varicella zoster virus; BCG: Bacillus Calmette–Guérin; DTP: Diphtheria, pertussis, tetanus; HPV: Human papilloma virus

**Table 4.** Suggested time frame between stopping immunosuppressants and live vaccination, considering drug elimination half-life.[2,218,429-432](#)

<b>Drug</b>	<b>Elimination half-life</b>	<b>Stopping before live vaccines</b>	<b>Restart after live vaccines</b>
Steroids [prednisone] >1 mg/kg, >14 days [children] >20 mg/day, >14 days [adults]	2–3 h	1 month	1 month
Thiopurines <sup>a</sup> [azathioprine and 6-MPb: approximately 2 h]	Several days [6-TGNc]	3 months	1 month
Methotrexate, low dose [adults]	3–10 h	1 month	1 month
Tofacitinib	3 h	1 month	1 month
Infliximab	7–12 days	3 months	1 month
Adalimumab	Approximately 2 weeks	3 months	1 month
Golimumab	Approximately 2 weeks	3 months	1 month
Certolizumab	Approximately 2 weeks	3 months	1 month
Cyclosporine <sup>d,e</sup>	8.4 h [10–27]	1 month	1 month
Tacrolimus	23–46 h	1 month	1 month
Vedolizumab <sup>f</sup>	25 days	3–4 months	1 month
Ustekinumab	Approximately 19 days	3 months	1 month

<sup>a</sup>Zoster live vaccine [ZVL] administration is considered safe with low-dose methotrexate [ $\leq 0.4$  mg/kg/week] and azathioprine [ $\leq 3.0$  mg/kg/day] or 6-mercaptopurine [ $\leq 1.5$  mg/kg/day].

<sup>b</sup>6-MP: 6-mercaptopurine.

<sup>c</sup>6-TGN: 6-thioguanine nucleotides.

<sup>d</sup>Cyclosporin modified.

<sup>e</sup>Immediate-release formulations

<sup>f</sup>Vedolizumab is gut selective. The period of 3–4 months for stopping the drug before administration of a live vaccine may be lengthy, but further information is currently unavailable. The stopping period should be discussed on a case-by-case basis.

# Vaccination: REFER your patient to a specialist !!!!!

## Non-live vaccines

Diphtheria and tetanus toxoids  
Acellular pertussis  
Inactivated parenteral poliovirus  
Influenza  
Pneumococcal polysaccharide  
Recombinant hepatitis A and B  
Parenteral typhoid (*Salmonella typhi* Vi polysaccharide)  
Meningococcal polysaccharide  
Oral killed-cholera  
Inactivated Japanese encephalitis  
Human papilloma virus  
Inactivated tick-borne encephalitis

## Live-attenuated vaccines

MMR (measles, mumps, and rubella)  
Typhoid Ty21a  
Vaccinia  
**Yellow fever**  
Live-attenuated influenza  
Varicella zoster  
Oral polio  
BCG (Bacillus Calmette–Guérin)



# Safety and Efficacy of Live Measles Vaccine Administered to a Crohn's Disease Patient Receiving Vedolizumab

Alana Wichmann, APN<sup>1</sup>,  
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David T. Rubin, MD, FACG<sup>1</sup>

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doi:10.1038/ajg.2016.21

the nation-wide measles resurgence, we assessed her measles titers in order to assess her risk for infection. Although she reported having received prior measles, mumps, and rubella (MMR) vaccination as a child, her measles antibody index (AI) was 0.7 (negative). We instructed her to stop MTX and to continue the vedolizumab. Two weeks after stopping MTX, we administered the MMR vaccine. The MTX was restarted 4 weeks after the MMR vaccination was administered. Measles AI 8 weeks after the MMR vaccine was 2.06 (positive). In 3-month follow-up after she received the vaccine, there have been no adverse sequelae.

**Financial support:** None.

**Potential competing interests:** Alana Wichmann is on a speaker's bureau with Abbvie. David T. Rubin is a consultant and has received grant support from Abbvie, Janssen, UCB, Pfizer, Amgen, and Takeda Pharmaceuticals. Informed consent was obtained for this case report.

## REFERENCES

1. Wasan SK, Baker SE, Skolnik PR *et al.* A practical guide to vaccinating the inflammatory bowel disease patient. *Am J Gastroenterol* 2010;105:1231–38.
2. Wyant T, Leach T, Sankoh S *et al.* Vedolizumab affects antibody responses to immunisation

# Problems with vaccination strategies

- Awareness of patients
- Awareness of physicians
- Fear of side effects (patients)
- Fear of inefficacy (physicians)
- Cost
- Timing of vaccination

# Tips and tricks

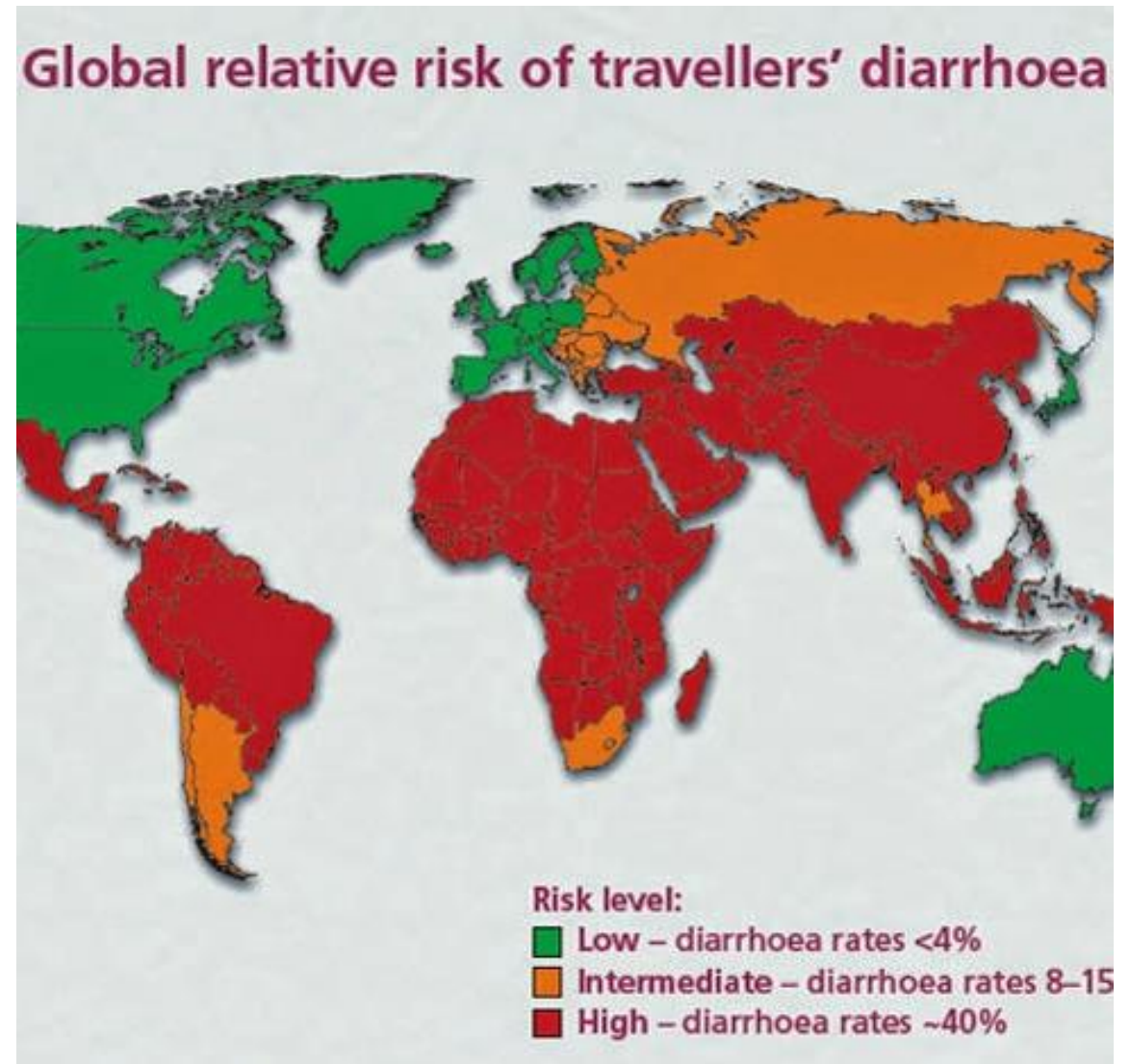
- Educate the patient
- Educate the gastroenterologist
- Educate the paediatrician!
- Windows of opportunity ( drug holidays ! )

**Malade sur place ? Risque associé a  
l'immunodepression ? Tous égaux devant  
diarrhée du voyageur et autres pathologies ?**

# Traveler's diarrhea

- **Cause:**

- Bacterial (60-80%)
- Viral (10-20%)
- Parasitic (5-10%)



# Traveler's diarrhea

Two case-control studies further indicate that IBD patients do not have an increased risk for traveller's diarrhoea. Nevertheless, traveller's diarrhoea is the most common health problem reported during travel to developing countries and can have a severe course.

## Prevention:

- Wash It, Peel It, Cook It, or Forget It
- Only Drink Bottled Water
- Wash hands frequently



# Food and Water Precautions

- Bottled water
- Selection of foods
  - well-cooked and hot
- Avoidance of
  - salads, raw vegetables
  - unpasteurized dairy products
  - street vendors
  - ice

While fluoroquinolones and metronidazole are mostly prescribed, azithromycin should be considered in case of patients already on fluoroquinolones for IBD or in case of high resistance, lack of response to fluoroquinolones after 36–48 hours, or contraindications to fluoroquinolones [such as allergy, pregnancy, young age].

Increasing rates of fluoroquinolone resistance [particularly in Southeast Asia] limit their use.

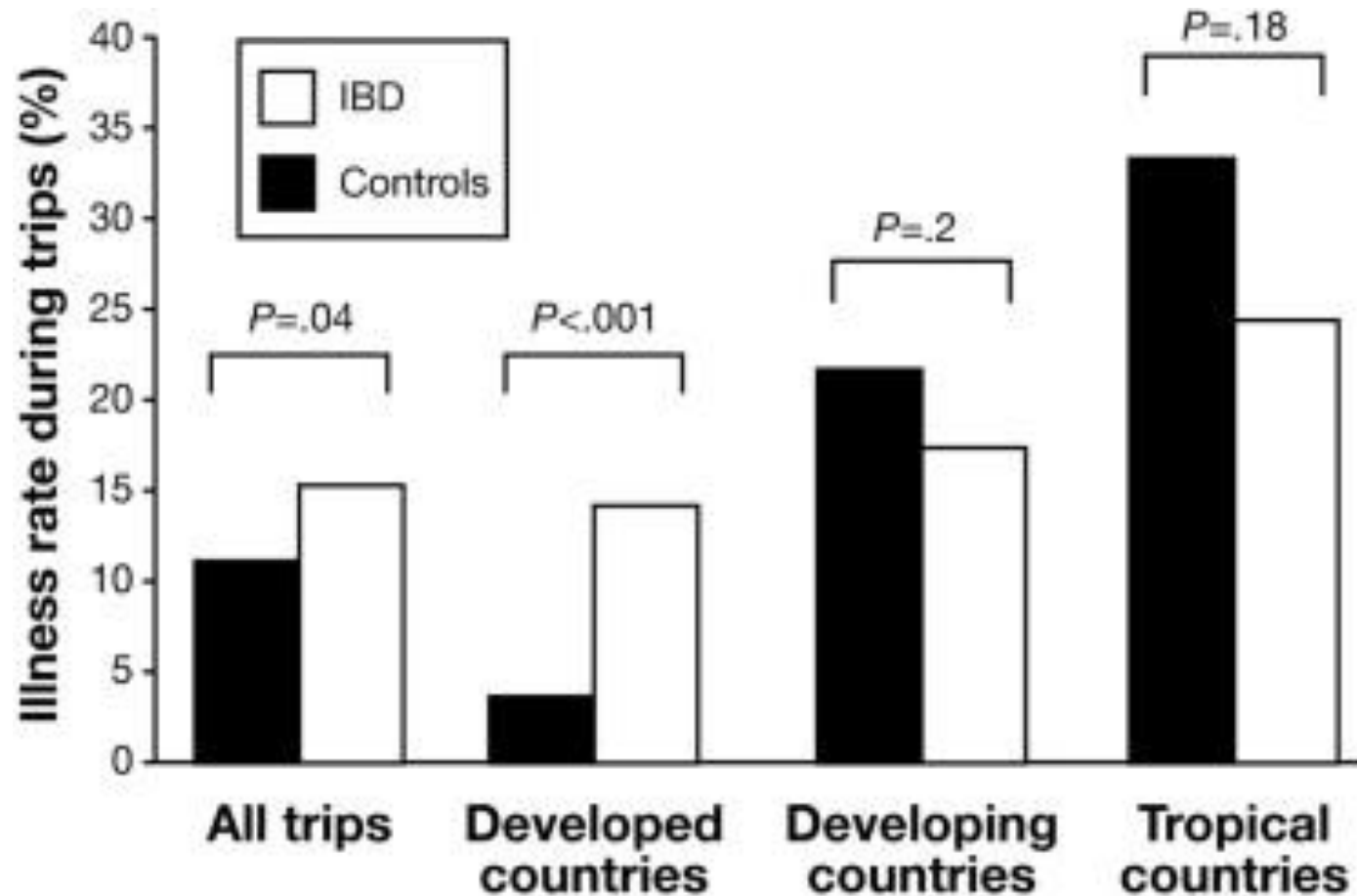
Rifaximin is not recommended

*T. Kucharzik et al. JCC 2021*

# Illness in IC and NIC patients, all the same ?

- Retrospective study on **429 individuals** enrolled:
  - 221 controls, 208 IBD (127 Crohn's, 81 UC)
  -
- **1061 trips** analyzed:
  - 496 trips of IBD patients
  - 565 trips of control individuals
- Severe illness was defined as one that required any of :
  - Staying at the hotel for more than 24 hours
  - Consulting a physician
  - Being admitted to a medical facility
  - Un-planned return home for medical care
- All other disease episodes were classified as mild

# Rate of illness during trips in IBD and healthy C



Participants had 142 episodes of illness during the trips; 92% were related to abdominal symptoms and considered as mild to moderate

Ben-Horin S et al., CGH 2012

# Rate of illness during trips in IBD and healthy C

**Table 4.** Multivariate Analysis of Risk Factors for Illness During Traveling Among the IBD Population

Parameter	Odds ratio	Confidence interval	<i>P</i> value
Age (quartiles)	1.62	0.9–2.8	.1
BMI (quartiles)	1.3	0.7–2.5	.3
Developed country	0.8	0.5–1.5	.6
Ever treated with IM	1.2	0.5–3.1	.7
Number of flares (quartiles)	1.9	1.1–3.4	.02
Ever hospitalized	3.5	1.3–9.3	.01
IM during the trip	1.1	0.8–1.6	.5
Remission for >3 mo before traveling	0.3	0.16–0.5	<.001

# Illness during trips in IBD and healthy C

## Symptoms of Infectious Diseases in Immunocompromised Travelers: A Prospective Study With Matched Controls

Gijs G. Baaten, MD, PhD,<sup>\*†‡</sup> Ronald B. Geskus, PhD,<sup>\*§</sup> Joan A. Kint, RN,<sup>\*</sup> Anna H.E. Roukens, MD, PhD,<sup>||</sup> Gerard J. Sonder, MD, PhD,<sup>\*†‡</sup> and Anneke van den Hoek, MD, PhD<sup>\*†</sup>

<sup>\*</sup>Department of Infectious Diseases, Public Health Service (GGD) Amsterdam, Amsterdam, The Netherlands; <sup>†</sup>Department of Internal Medicine, Division of Infectious Diseases, Tropical Medicine and AIDS, Academic Medical Centre, Amsterdam, The Netherlands; <sup>‡</sup>National Coordination Centre for Traveler's Health Advice (LCR), Amsterdam, The Netherlands; <sup>§</sup>Department of Clinical Epidemiology, Biostatistics and Bioinformatics, Academic Medical Centre, University of Amsterdam, Amsterdam, The Netherlands; <sup>||</sup>Department of Infectious Diseases, Leiden University Medical Centre, Leiden, The Netherlands

**Conclusions: The incidence of travel related diarrhea in IC and IBD (30% IC) was not more often or longer than non-immunocompromised travelers ( companions)**

Baaten Gg, et al, J Travel Med 2011

Increased rate of IBD flares after travelling has not been observed.  
Neither recent antibiotic use nor recent travel was associated with exacerbation of IBD in a case-control study.

T. Kucharzik et al. JCC 2021



# Other infections

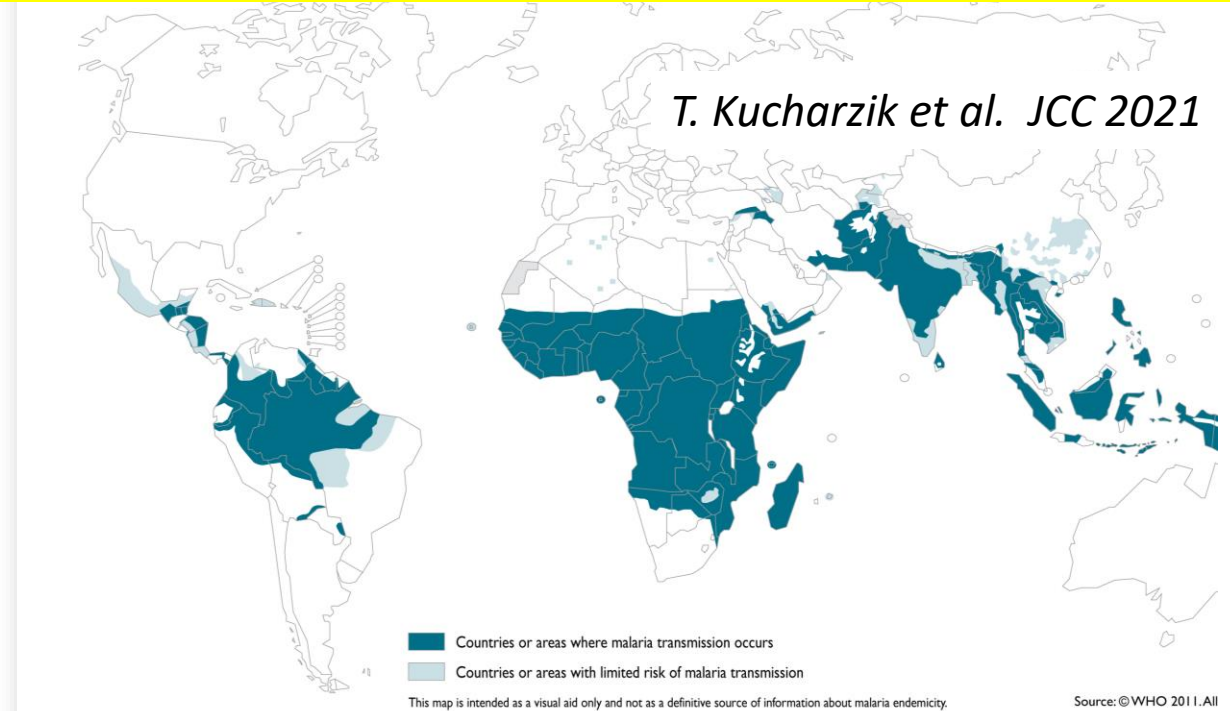


# Malaria

- Transmission by mosquito bite
- Prevention:
  - Awareness
  - Bite avoidance
  - Chemoprophylaxis
  - Diagnosis of febrile illness
- Fever in returned traveler is a medical emergency considered malaria until proven otherwise

## Statement 7.2

Patients with IBD, including those on immunosuppressive therapy, do not appear to be at increased risk for acquiring malaria or for a more severe disease course and should follow standard guidelines for prevention [EL5].



While there are no known interactions between IBD-specific drugs and malaria chemoprophylaxis, an interaction check should be performed before treatment initiation, particularly for novel biologics and small molecule therapies



# Tchad

Zones d'endémie du paludisme

- Risque élevé  
voyages au sud du Sahara
- Risque moyen  
voyages uniquement au Sahara

**Limit of our knowledge !**

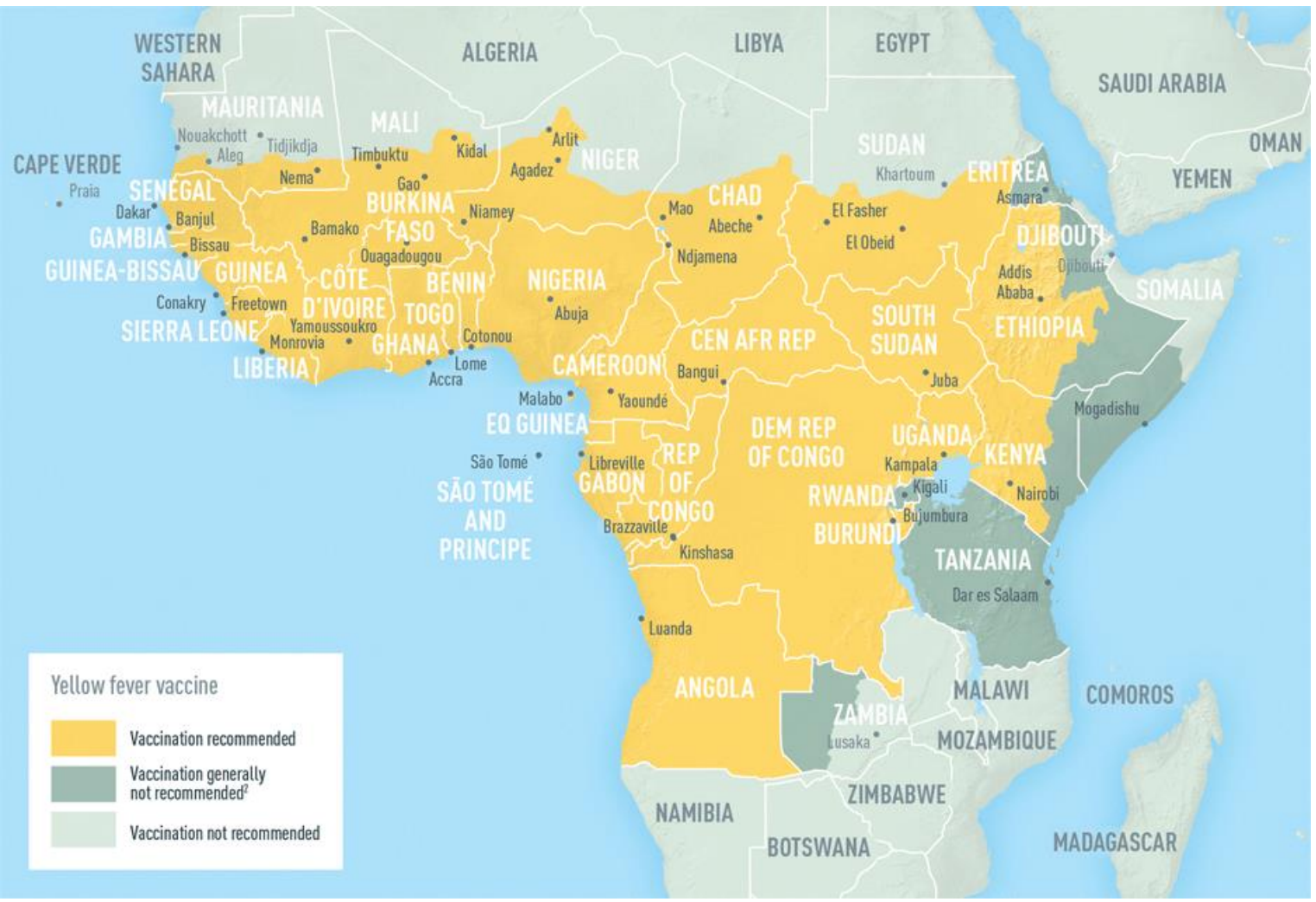


If yellow fever vaccination is required and not feasible, it is recommended to issue a letter of medical exemption.

## Yellow fever vaccine

- Live attenuated virus vaccine
- Single subcutaneous injection
- Immunity starts after 10 days
- Valid for 10 years
  
- **Not recommended for**
- Infants < 9 months
- Immune compromised patients
- Pregnant women
- Egg allergies
- HIV-positive individuals

# Yellow fever vaccine recommendations



# Tick-borne encephalitis

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## Prevention:

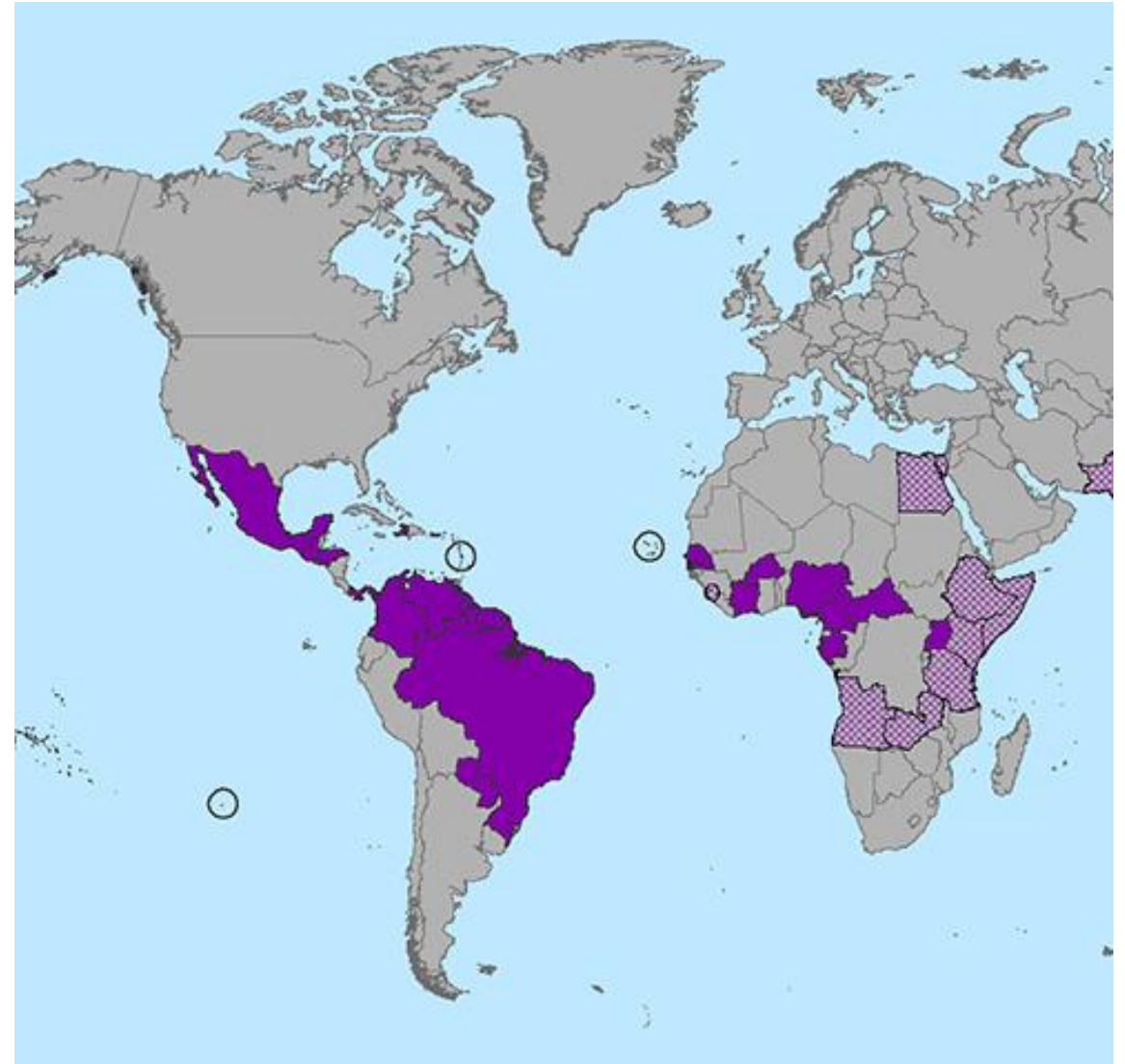
- Tick prevention
- Avoidance of unpasteurized dairy products
- Vaccination
- Self check and removal ASAP (tweezers)

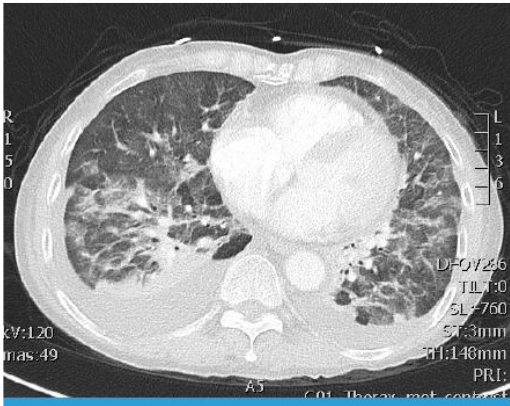


# Zika virus

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- Transmission by mosquito bite
- Risk to pregnant women → microcephaly and other brain abnormalities
- Prevention: preventing mosquito bites





# *Pneumocystis jirovecii* pneumonia in IBD patients treated with immunomodulator(s)

Immunosuppressive treatment exposure in IBD patients	n=14
<b>Monotherapy</b>	<b>n=3</b>
Steroid monotherapy	n=2
Thiopurine monotherapy	n=1
<b>Double immunosuppression</b>	<b>n=9</b>
Steroid + thiopurine	n=4
Steroid + infliximab	n=1
Steroid + methotrexate	n=1
Steroid + tacrolimus	n=1
Infliximab + thiopurine	n=2
<b>Triple immunosuppression</b>	<b>n=2</b>
Steroid + thiopurine + cyclosporin	n=2

*14% death*

# Traveling in hypoxic conditions

# Traveling in hypoxic conditions

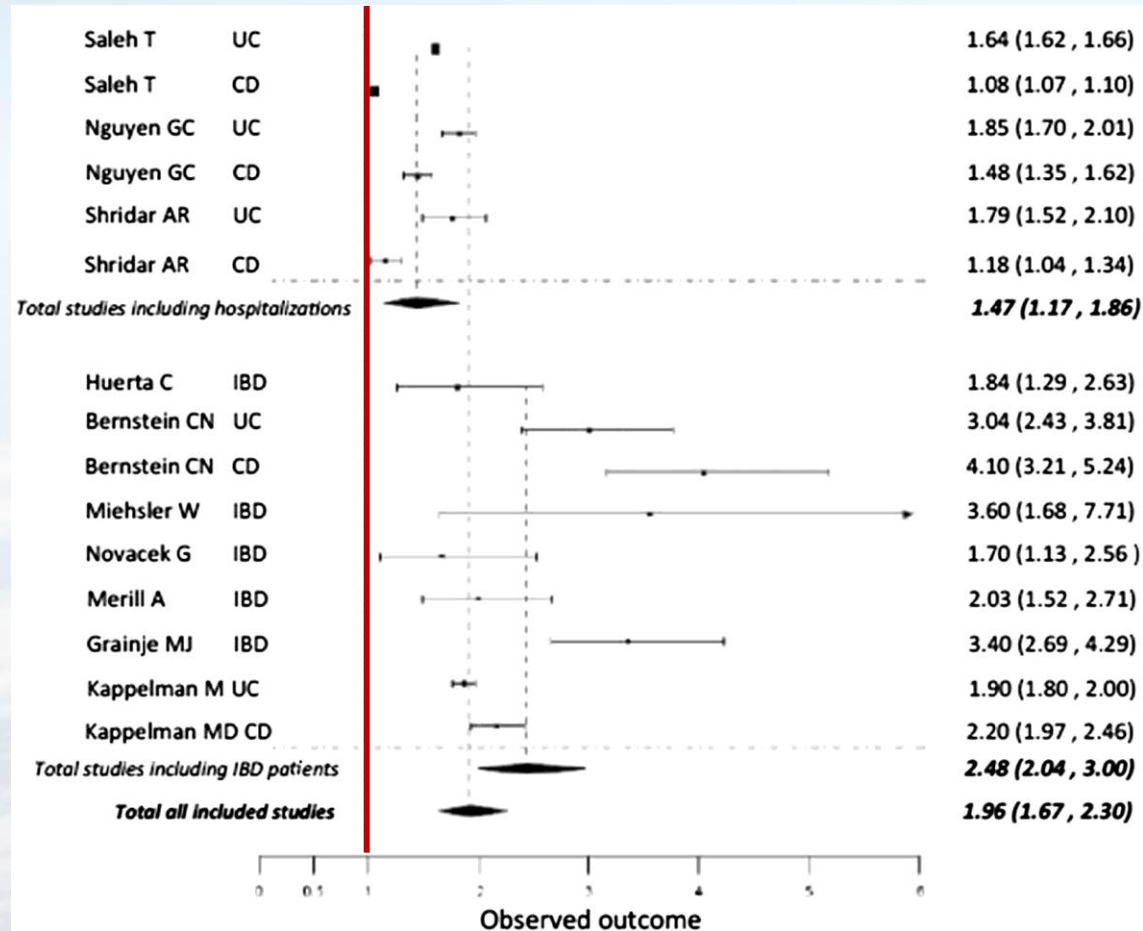
## Absolute Risk of Venous Thrombosis after Air Travel: A Cohort Study of 8,755 passengers

Case/N° flight: 1/1264 if >16 hours

Duration	Cases	Person-Years	IR/1,000 PY (95% CI)	IRR (95% CI) <sup>a</sup>	Flights	Risk/flight <sup>b</sup>	Case/number of flight <sup>c</sup>
No flight	29	27,772	1.0 (0.7–1.5)	1 <sup>d</sup>	—	—	—
0–4 hrs	2	4,267	0.5 (0–1.4)	0.4 (0.1–1.9)	213,333	0.9	1/106,667
4–8 hrs	5	2,180	2.3 (0.7–4.8)	2.3 (0.9–5.9)	46,272	10.8	1/9,254
8–12 hrs	6	2,676	2.2 (0.8–4.4)	2.2 (0.9–5.4)	37,903	15.8	1/6,317
12–16 hrs	7	1,344	5.2 (2.0–9.9)	5.3 (2.3–12.4)	13,209	53.0	1/1,887
>16 hrs	4	672	5.9 (1.5–13.4)	5.7 (2.0–16.5)	5,045	79.3	1/1,264

Kuipers S et al. PLoS Med 2007

# Meta-analysis of studies on venous thromboembolic events in IBD patients



## 2.75 billion passengers fly worldwide/year

Peterson DC et al. N Engl J Med 2013

**Table 1. In-Flight Medical Emergencies According to Medical-Problem Category and Outcome.**

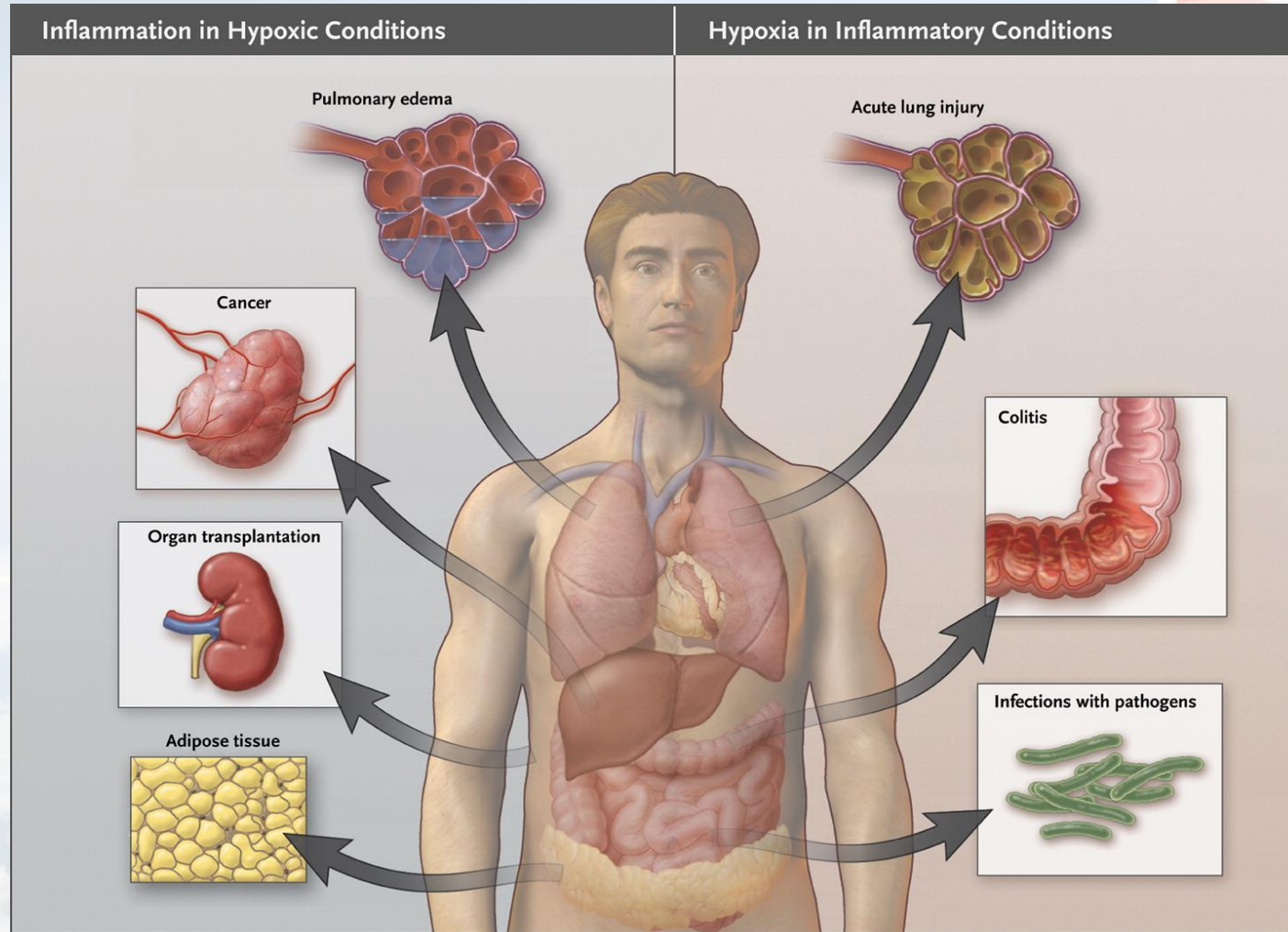
Category	All Emergencies	Aircraft Diversion	Transport to a Hospital*	Hospital Admission	Death
	<i>no./total no. (%)</i>				<i>no.</i>
All categories	11,920/11,920 (100)	875/11,920 (7.3)	2804/10,877 (25.8)	2229/10,877 (20.5)	36
Syncope or presyncope	4463/11,920 (37.4)	221/4463 (5.0)	938/4463 (21.0)	706/4463 (15.8)	4
Respiratory symptoms	1447/11,920 (12.1)	81/1447 (5.6)	477/1447 (33.0)	279/1447 (19.3)	1
Nausea or vomiting	1137/11,920 (9.5)	56/1137 (4.9)	317/1137 (27.9)	164/1137 (14.4)	0
Cardiac symptoms	920/11,920 (7.7)	169/920 (18.4)	422/920 (45.9)	222/770 (28.7)	0
Seizures	689/11,920 (5.8)	8/689 (1.2)	339/689 (49.2)	75/602 (12.5)	0
Abdominal pain	488/11,920 (4.1)	8/488 (1.6)	239/488 (48.8)	41/391 (10.5)	0
Infectious disease	330/11,920 (2.8)	0/330 (0.0)	159/330 (48.2)	8/232 (3.4)	0
Agitation or psychiatric symptoms	287/11,920 (2.4)	0/287 (0.0)	38/249 (15.3)	17/244 (7.0)	0
Allergic reaction	235/11,920 (2.0)	0/235 (0.0)	40/233 (17.2)	8/229 (3.5)	0
Possible stroke	214/11,920 (1.8)	7/238 (2.9)	92/214 (43.0)	46/196 (23.5)	0
Trauma, not otherwise specified	216/11,920 (1.8)	14/216 (6.5)	34/185 (18.4)	5/180 (2.8)	0
Diabetic symptoms	193/11,920 (1.6)	15/193 (7.8)	45/181 (24.9)	13/172 (7.6)	0
Headache	123/11,920 (1.0)	10/123 (8.1)	23/108 (21.3)	4/107 (3.7)	0
Arm or hand symptoms	114/11,920 (1.0)	6/114 (5.3)	27/100 (27.0)	4/98 (4.1)	0
Obstetrical symptoms	61/11,920 (0.5)	11/61 (18.0)	29/53 (54.7)	11/47 (23.4)	0
Ear pain	49/11,920 (0.4)	1/49 (2.0)	2/43 (4.7)	1/43 (2.3)	0
Cardiac arrest	38/11,920 (0.3)	22/38 (57.9)	14/34 (41.2)	1/6 (16.7)	31
Laceration	33/11,920 (0.3)	1/33 (3.0)	3/26 (11.5)	0/25	0
Other	821/11,920 (6.9)	62/821 (7.6)	162/705 (23.0)	36/679 (5.3)	0
Unknown	8/11,920 (0.1)	0/8 (0.0)	0/8 (0.0)	0/8 (0.0)	0

**Recent survey by major airline:  
There is at least one physician on 85% of all flights!!!**



# Hypoxia and inflammation

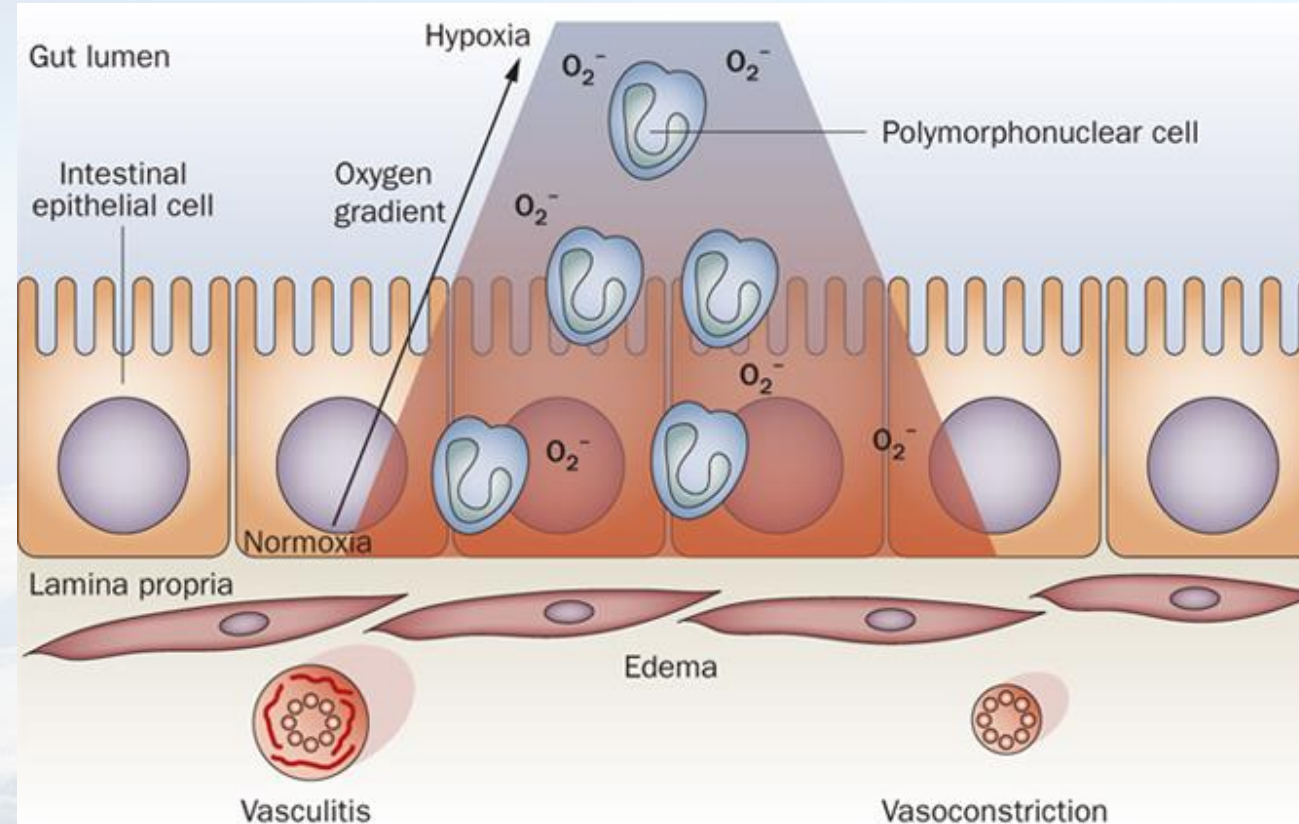
Eltzschig HK, Carmeliet P. N Engl J Med 2011;364:656-665.



The NEW ENGLAND  
JOURNAL of MEDICINE

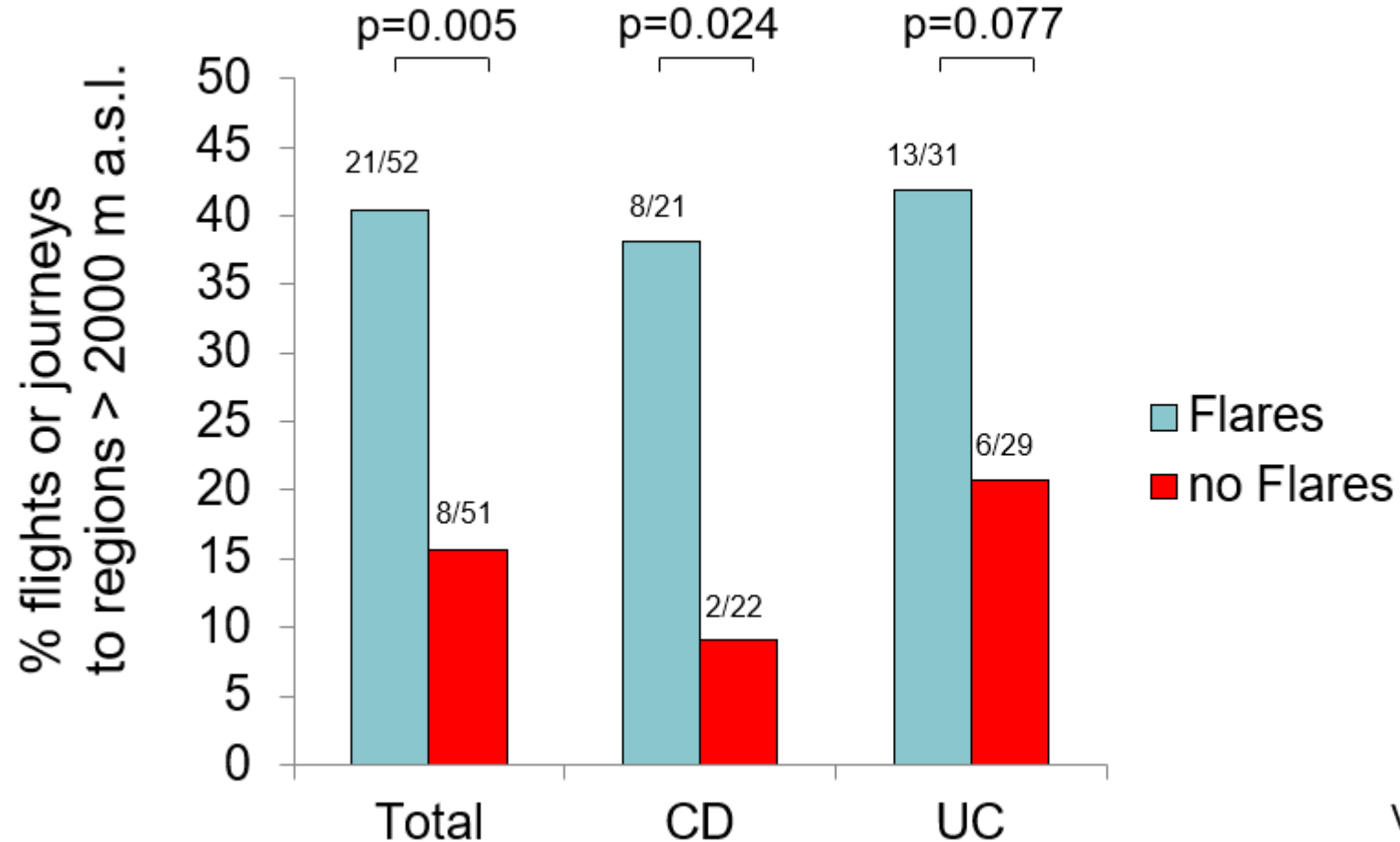


# Potential sources of hypoxia in mucosal inflammation



Colgan, S. P. & Taylor, C. T. *Nat. Rev. Gastroenterol. Hepatol* 2010

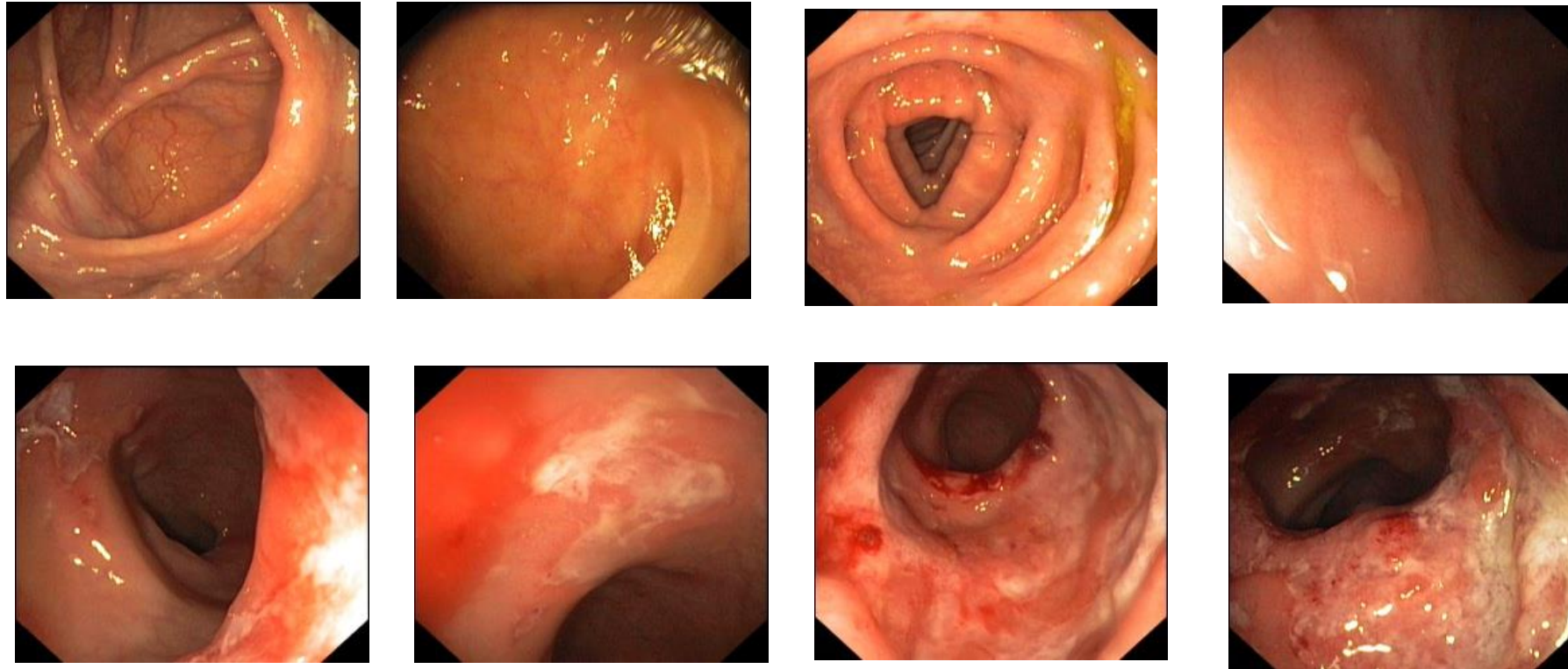
# High Altitude Journeys and Flights are associated with increased risk of flares in IBD Patients



Vavricka et al, JCC 2012

# Sex and travelling ( Sea , sex and sun)

male 43 years, UC for 4 years in remission (5-ASA rectal foam)  
coming back from Thailand



PCR for Chlamydia trachomatis positive

# Sun exposure

- Some drugs increase susceptibility to sun light:
  - Methotrexat (Metoject®)
  - Ciclosporin (Sandimmun®)
  - Azathioprin, 6-MP (Imurek® und Purinethol®)
  - Sulfasalazin (Salazopyrin®)



*Sun protection at least 30,  
If above mentioned drugs, 50*

# The returning traveler

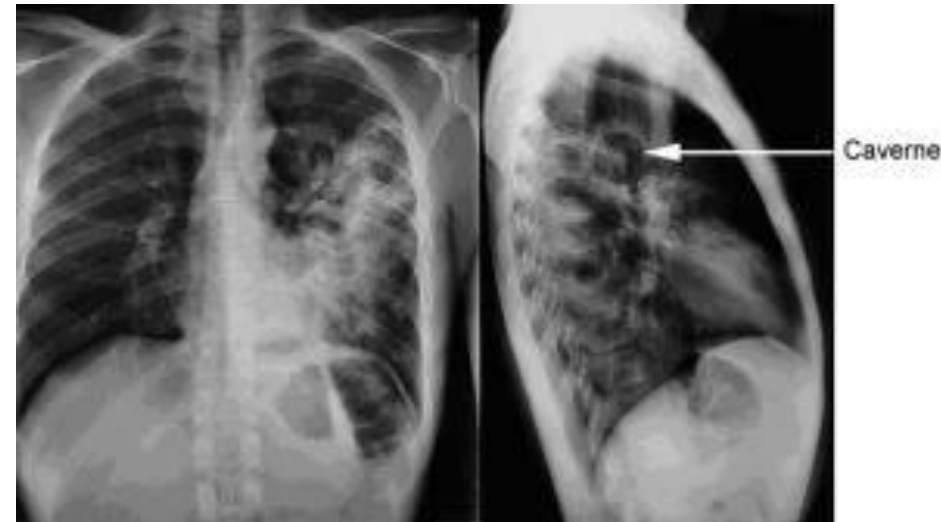
## A targeted on demand check up

**Table 3 Preventive measures for inflammatory bowel disease patients coming from developing countries (mainly while taking immunosuppressants or before starting)**

	<b>South America</b>	<b>Maghreb and Western Orient</b>	<b>Sub-Saharan Africa</b>	<b>Southeast Asia and India</b>	<b>Other</b>
Thick drop	Consider	No	Always	Consider	No
Stool parasite	Always	Consider	Always	Always	No
Urine parasite	No	No	Always		No
Strongyloides (culture, serology)	Always	Consider	Always	Always	No <sup>1</sup>
Trypanosoma (serology)	Always	No	No	No	No
Histoplasma (serology)	Always	No	Always	No	No
HBV and HCV (serology)	Always	Always	Always	Always	Always
Tuberculin skin test or IGRA	Always	Always	Always	Always	Always

# Dépistage de Tbc latente

- Anamnèse détaillée (atcd, épidémio, contagé, symptômes, tout séjour dans pays endémique)
- Ex clinique
- RXTX- si anomalie : scanner thoracique
- Intradermo *et* IGRA



**At the outpatient visit, the next question to  
your patient is NOT:**

“Will you travel ?”

BUT

**WHEN WILL YOU TRAVEL ?**

# POINTS FORTS

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Un diagnostic de MICI limite les possibilités de voyage pour certains patients.

- Les vaccins vivants sont contre indiqués chez les patients sous immunosuppresseurs, biothérapies ou corticothérapie.
- Le gastroentérologue doit s'impliquer dans l'aide à la préparation au voyage chez un patient porteur d'une MICI.
- Un voyage en pays à risques nécessite d'être anticipée sur les conseils du gastroentérologue et d'un professionnel de médecine tropicale.
- Les complications médicales au retour de voyage sont souvent indépendantes de la MICI et de son traitement.