Vaccine preventable travel health risks:

What is the evidence — what are the gaps?

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J Travel Med, 22 (2015), pp. 1-12

Conflict of interest declaration

I have or had within the past 3 years financial relationships

(grants for research or consultancy agreements, support to attend meetings, paid lectures, advisory boards) with:

Vaccine producers

Bavarian Nordic

Emergent BioSolutions

GlaxoSmithKline

Merck

Pfizer

Sanofi (-Aventis, -Pasteur)

Takeda

Valneva

Other paid lectures:

CRM

IFAK

pharmaSuisse

Outline

- **GRADE assessment + what we do NOT know**
- **Recent estimates on the incidence of vaccine-preventable infections (VPIs) in travellers**
- **Add 2nd dimension: Impact of VPIs in travellers**
- **Pre-travel consultation: Topic #1 — vaccines**
  - The 3 Rs: Required — Routine — Recommended
  - The 2 Cs: Concomitant — Cumulative future exposure
  - The 3rd C — cost: backpacker vs. 5* resort tourist
  - Implication: Europe vs. USA
- **Conclusions**

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Table 1 Methods by which data on vaccine-preventable diseases (VPD) in travelers resident in industrialized countries were generated (for references see text)

VPD	Design	Risk of bias	Consistency*, †	Recentness‡	Confidence as per GRADE
Travelers' diarrhea	Cohorts ($n = 3$)	Selection by recruitment in travel clinics	Yes for incidence rate	After 2000	From moderate to high
LT-ETEC	By-product of intervention studies	Few destinations only	Variations depending on destinations	After 2000	Moderate; older data unreliable for time frame after 2000
WC/rBS vaccine efficacy against TD	Nonrandomized, nonblinded studies, and expert opinions	Multiple, often inappropriate study design, lack of diagnostic tests, etc.	Broad variation	After 2000	Very low
Influenza	Cohorts ($n = 3$)	Selection by recruitment in travel clinics	Yes	After 2000	From moderate to high
Typhoid	Notification	Incomplete; missing cases§	On order of magnitude	Some after 2000	Moderate
Hepatitis A	Notification	Incomplete; missing cases§	On order of magnitude	Some after 2000	Moderate
Hepatitis B	Notification	Incomplete; missing cases§	On order of magnitude	Some after 2000	Moderate
Rabies	Anecdotal collection	Incomplete; missing cases; benefit PEP?	Only one review	After 2000	Very low for rabies infection
Tick-borne encephalitis	Expert opinion	Extrapolation from exposed locals	Only one statement	After 2000	Very low
Meningococcal disease	Notification	Incomplete; missing cases§	Only one review	Data 1986–1989	Very low
	Anecdotal reports	Incomplete, no systematic search	Only one review	After 2000	Very low
Japanese encephalitis	Anecdotal collection	Incomplete; missing cases§	Overlapping reviews	After 2000	Low
Poliomyelitis	Notification (WHO)	Migrants neglected	Probably reliable	After 2000	Moderate
Cholera	Notification (WHO)	Incomplete; missing cases§	Questionable	After 2000	Very low
Yellow fever	Expert opinion	Extrapolation from exposed locals	Repeated one statement	after 2000	Very low

GRADE = Grading of Recommendations, Assessment, Development and Evaluation; LT-ETEC = enterotoxigenic *Escherichia coli* producing heat-labile enterotoxin, WC/rBS = whole cell/B-subunit of cholera toxin, TD = travelers' diarrhea; WHO = World Health Organization; PEP = postexposure prophylaxis.

*Also considering imprecision, for example, because of lack of data on confidence intervals.

†Indirectness not listed, as no extrapolations from native populations were included.

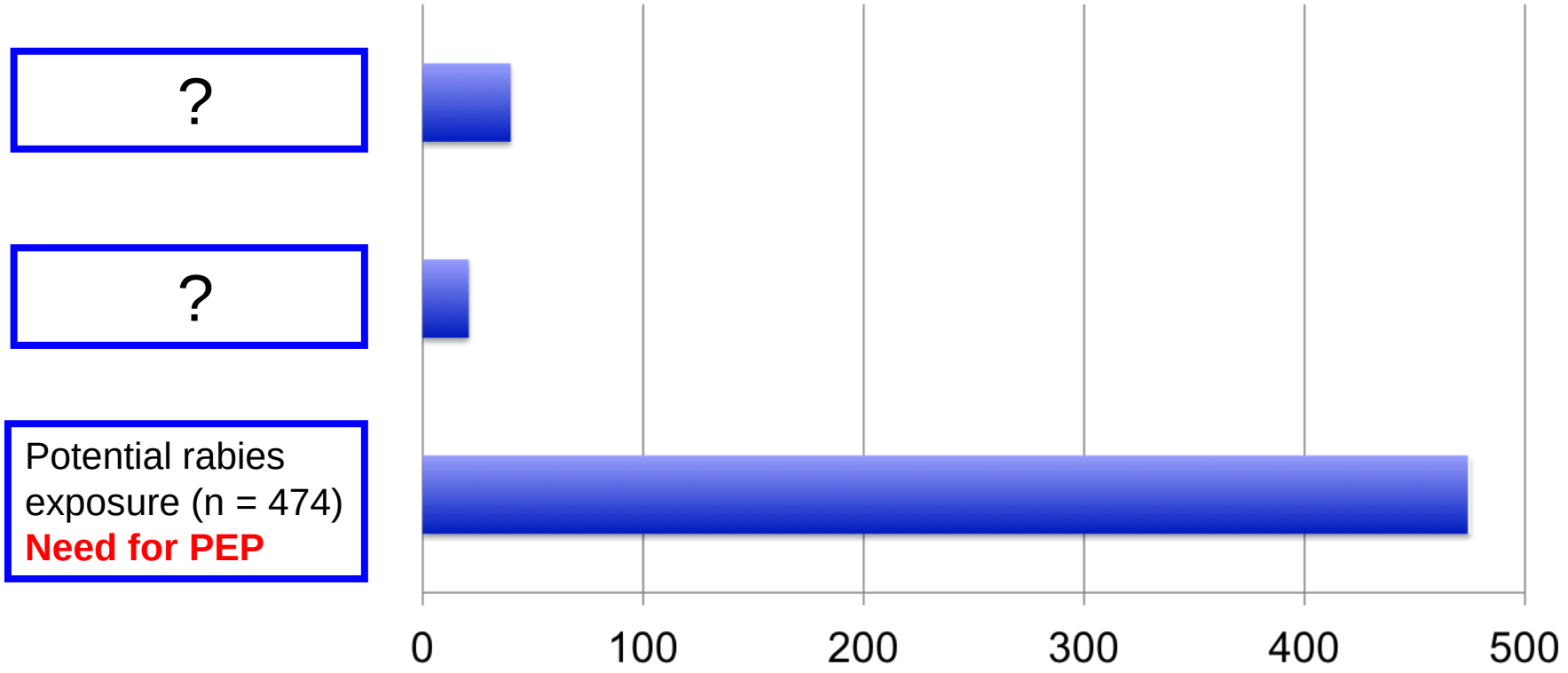
‡Year of data collection.

§Missing cases by lack of compliance with required notification, illness abroad, case not diagnosed, etc.

Lack of data

Criteria	Zero data (almost)	Limited data
Incidence	VPI **abroad** - Without medical consultatation - Diagnosed and treated	VPI imported to **home country** - Remained undiagnosed - No / incomplete reporting
Impact, CFR	No data on outcome while treated **abroad** (except from Nepal)	Usually no follow-up on outcome at **home**; e.g. hepatitis A
Immunity by infection, vaccine	No recent surveys. Possibly vaccination fatigue after COVID-19?	Airport surveys: estimation on proportion of unprotected travellers (few updates)
VPI by travel characteristics	No data from abroad	**GeoSentinel reports**
Rabies PEP	Lack of data on indication of PEP abroad and back home, no data on exposure to truly rabid animal	**GeoSentinel reports —** ***NO DENOMINATOR***
Asymptomatic VPI	Most VPI relating to travellers	Dengue

GeoSentinel cases per year (2007-18)



Incidence of exposure to rabies: 0.4% / month

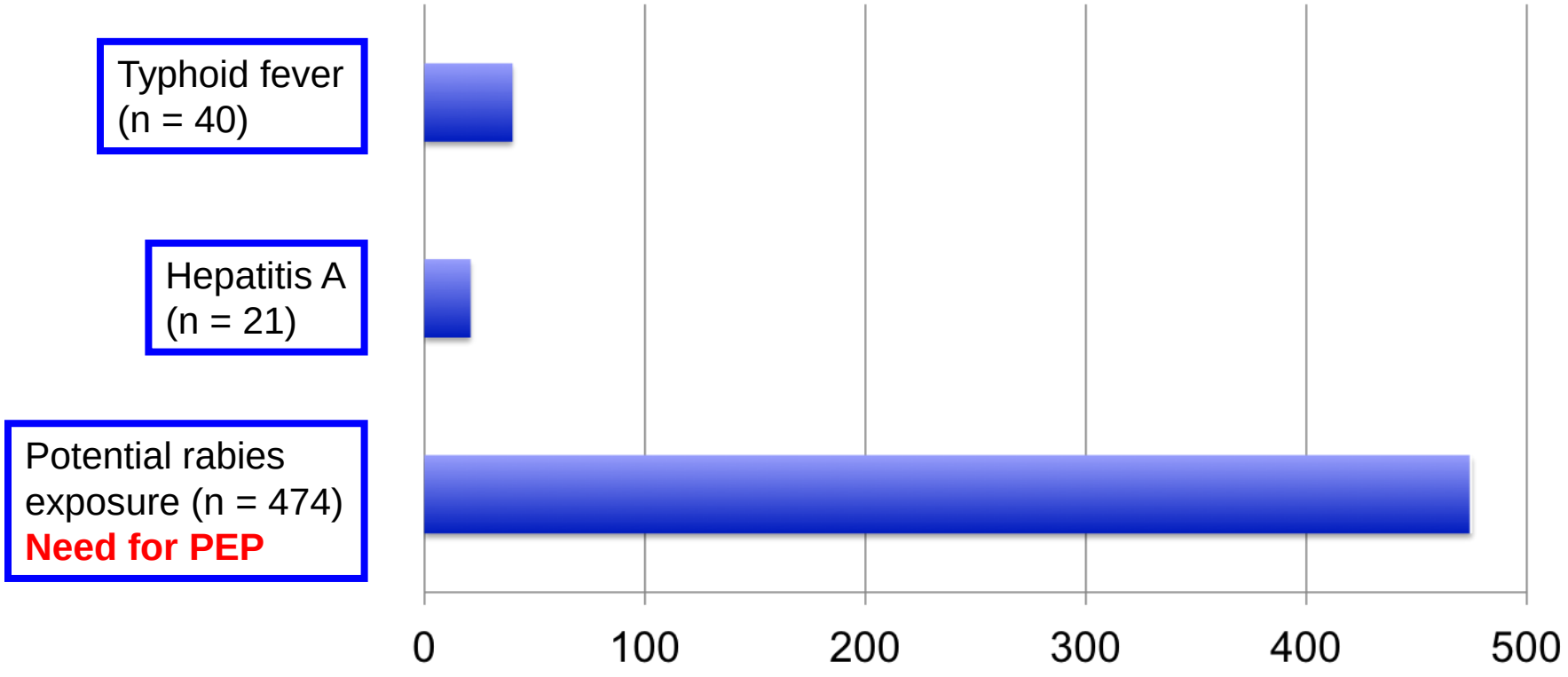
Gautret P & Parola P. Vaccine. 2012; 30:126-33.

„Only" 2.6 rabies victims / year: not decicive

Carrara P et al. PLoS Negl Trop Dis. 2013; 7:e2209.

Steffen R & Hamer DH. J Travel Med. 2020; 27:taaa173.

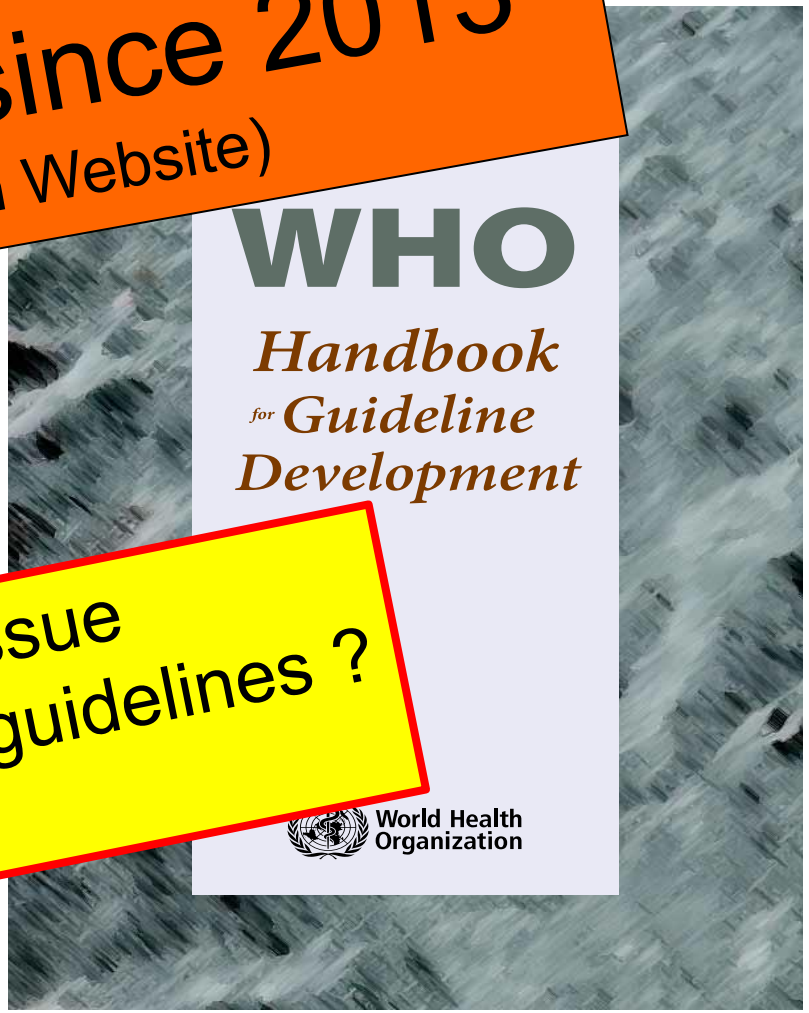
GeoSentinel cases per year (2007-18)



→ New priorities needed!?

Steffen R & Hamer DH. J Travel Med. 2020; 27:taaa173.

Guidance by the World Health Organization

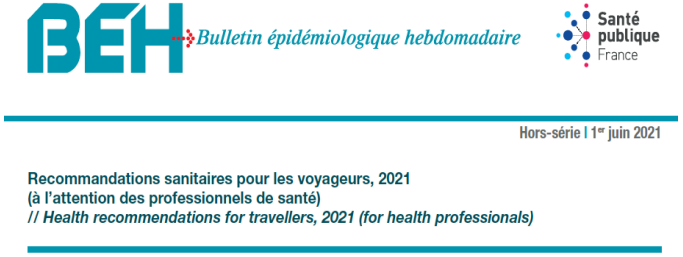


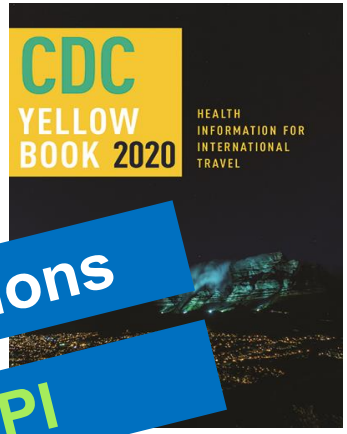
No publication since 2013
(except updates on Website)

Abandon to issue recommendations, guidelines ?
→ NO

Guidance by national authorities et al.

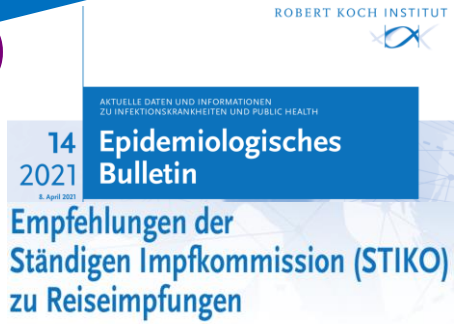
- CDC — United States
- CATMAT — Canada
- Australian Immunization Handbook
- NaTHNaC — United Kingdom
- Fit for Travel — Scotland (+Travax, professional)
- DTG → STIKO — Germany [vs. CRM Jelinek]
- Haut Conseil de la santé publ… …rance
- EKRM/ECTM … …end (+H… …ver.ch)
- C… …rcial: PassportHealth, Walgreens, etc.





Lack of uniform travel vaccine recommendations

Follow country recommendations, incl. EPI



What travel vaccine? For whom?

- Vaccines: **R**equired, **R**outine, **R**ecommended: **3 R**
- Vaccine preventable infections (VPI): 4 criteria
  - Incidence rate abroad:

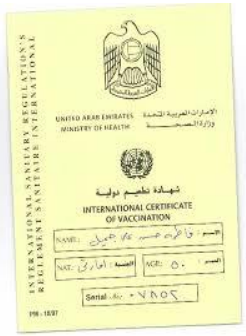
    Cumulative exposure!

    Consider incremental risk vs. exposure at home
  - Impact:

    Individual: death, sequelae
    Public health: outbreaks
  - Financial aspects
  - Legal aspects
- Special host factors:

  Risk profile!
  Possible contraindications

Required vaccines for travelers



- Yellow fever: based on Annex 7 IHR (2005) — Rationale:
  - Prevent international spread of disease
  - To protect individual travelers who may be exposed
  - Possible requirements:
    - Immigration from any country:
    - Only after transit through infected / endemic country:

The only ones of interest to the travel industry

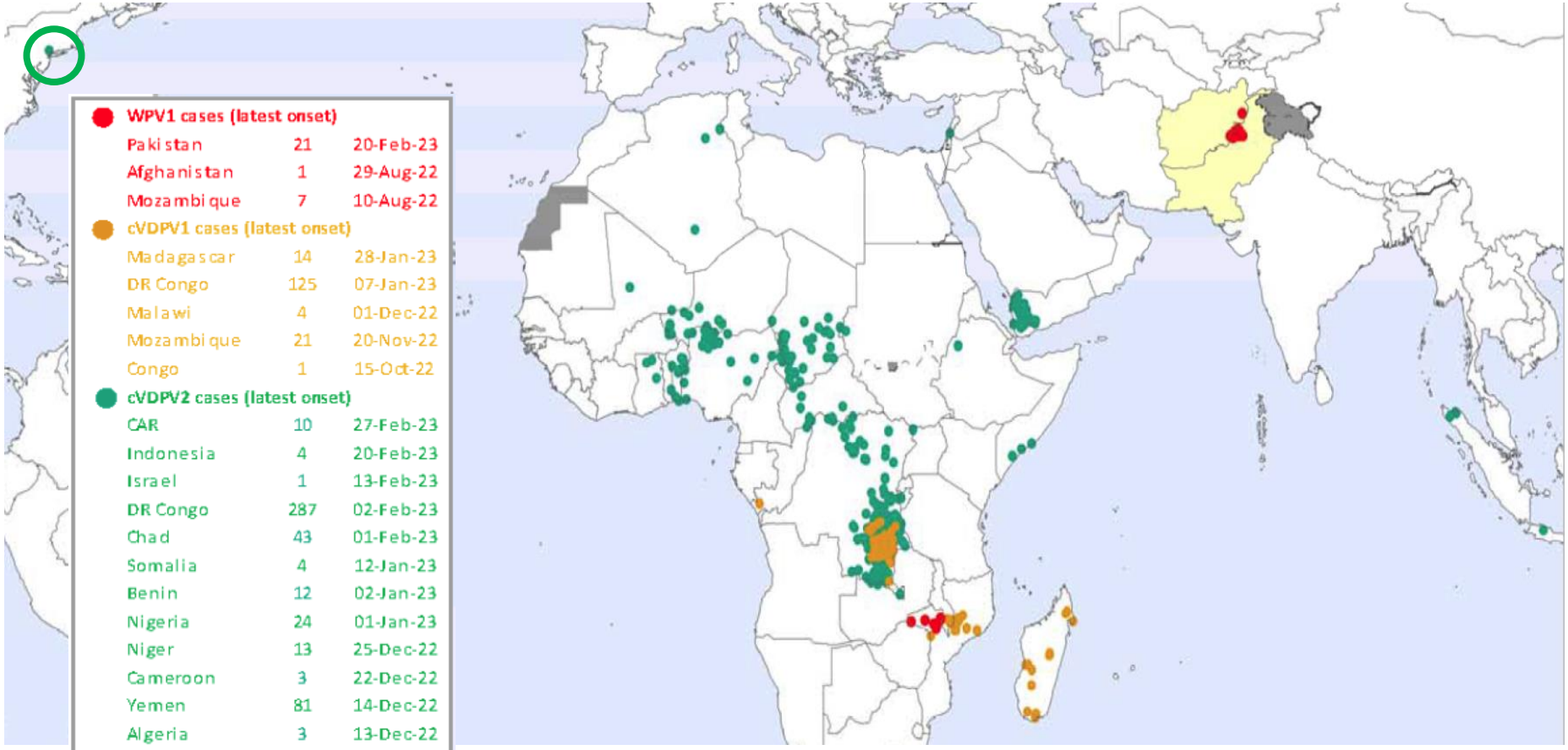
Info from embassy, airline

Info from airline

- COVID-19
- Poliomyelitis: based on Public Health Emergency of International Concern, all residents or long-term visitors to receive bOPV/IPV 4w to 12m pre-departure
- Hajj, Umrah
  - Yellow fever, IF arriving from … areas at risk of YF transmission
  - Meningococcal meningitis ACYW (MPV 3 y, MPV 5 y validity)
  - Poliomyelitis for travelers from areas with polio transmission, etc.

WHO, International Travel and Health: www.who.int/ITH (various pages)

Poliomyelitis previous 12 months, until 28 March 2023



WPV1 cases (latest onset)		
Pakistan	21	20-Feb-23
Afghanistan	1	29-Aug-22
Mozambique	7	10-Aug-22
cVDPV1 cases (latest onset)		
Madagascar	14	28-Jan-23
DR Congo	125	07-Jan-23
Malawi	4	01-Dec-22
Mozambique	21	20-Nov-22
Congo	1	15-Oct-22
cVDPV2 cases (latest onset)		
CAR	10	27-Feb-23
Indonesia	4	20-Feb-23
Israel	1	13-Feb-23
DR Congo	287	02-Feb-23
Chad	43	01-Feb-23
Somalia	4	12-Jan-23
Benin	12	02-Jan-23
Nigeria	24	01-Jan-23
Niger	13	25-Dec-22
Cameroon	3	22-Dec-22
Yemen	81	14-Dec-22
Algeria	3	13-Dec-22
Burundi	1	24-Nov-22
Sudan	1	31-Oct-22
Mali	2	26-Oct-22
Togo	1	30-Sep-22
Ghana	3	14-Sep-22
USA	1	20-Jun-22
Ethiopia	1	01-Apr-22

cVDPV = circulating Vaccine Derived Polio Virus

http://polioeradication.org/polio-today/polio-now/

Infections preventable by **Routine** vaccination in travelers

Vaccine	N =	Travel history	Reference
Diphtheria	Rare	Afghanistan > Finland (asylum), USSR	Sane J 2016
Tetanus	1	German in Spain	Werner GT 1985
Pertussis	Many	European, Americans	Dahl V 2017, Barbosa F 2017, Gomez-Junient J, 2015
Hepatitis B	Many	Immigrants, Scandinavians	Dahl V 2017, Daw MA 2017, Boggild AK 2015, Lachish 2013
Measles	Many	Europeans, Japanese in USA, etc.	Dahl V 2017, Barrett P 2016, Zhangzhu J 2016, Jost M 2015
Mumps	Some	N/A	Dahl V 2017, MMWR 2006
Rubella	Few	Yemen > US, various > Scandinavia	Robyn M 2017, Dahl V 2017
Poliomyelitis	1	Pakistan > Australia (student)	Stewardson AJ, Carnie JA 2009
Pneumococcal	Rare	Hajj pilgrimage	Memish ZA 2017, Boggild 2010
Rotavirus	1	India > Hungary	Laszlo B 2009
Tuberculosis	Many	Immigrants, VFR, Peace Cps, Expats	Lim PL 2012, Jung P 2008
Varicella	Many	Various, immigrants	Siikamäki H 2017, Boggild 2010

No data on *Haemophilus influenzae* B, Human Papilloma Virus

Routine immunizations recommended

COVID-19 vaccines — probably routine soon

Vaccine	Child	Adolescent	Adult	Senior
Dipht'ia/Tetanus/Pertussis	+++	++ §	++ §	++ø
Hepatitis B	Most: §	c/u — §	c/u	(risk)
Haemophilus influenzae B	+ (≤5 yrs)	ø	ø	ø
Human Papilloma Virus	ø	+ (F, ±M)	c/u	ø
Influenza, seasonal	(§ , risk)	(§ , risk)	Risk, (§)	++
MMR	+++	c/u (2 doses)	c/u	ø
Pneumococcal disease	§	Risk	Risk	§
Rotavirus	§	ø	ø	ø
Tuberculosis	§	ø		
Varicella	§	c/u — §		ø

To check at every travel health consultation → catch-up dose

+ to +++ = routine, ø = not indicated, c/u = catch-up if previously missed,
§ = see national recommendations — Expanded Programme on Immunizations (EPI)

Vaccinations performed for travellers

Zurich University Travel Clinic 2022

• Rabies	7,544
• Yellow fever	4,446
• **Tick-borne encephalitis**	**3,074**
• Hepatitis A	2,491
• Typhoid (Ty21a)	2,322
• Polio (IPV only)	2,254
• **HPV (Gardasil 9)**	**1,513**
• Hepatitis A + B (Twinrix)	1,387
• **MMR (Priorix)**	**1,224**
• Influenza	615
• H. zoster (Shingrix)	436

Unpublished data

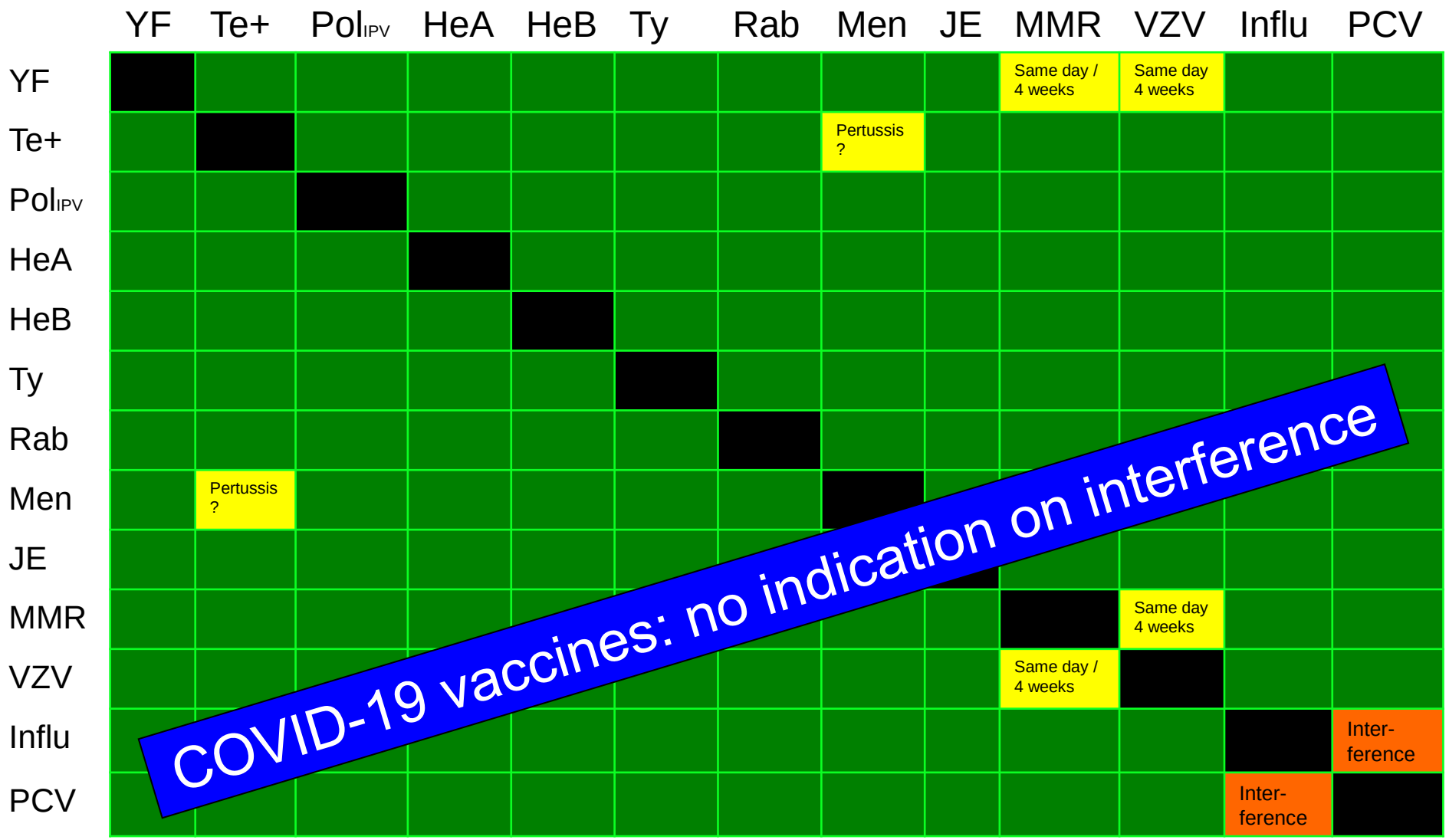
6 US Health Care Systems 2009-18

N = 1,026,822 travelers

• Typhoid (IM + oral)	81 %
• Yellow fever	12 %
• Rabies	5 %
• Japanese encephalitis	2 %
• Other	No data
• Routine, just in text	No data
• Cholera (lowest)	N = 29

Lewis B et al. Vaccine. 2022; 40:5904-11.

Co-administration of travel vaccines



Jelinek T et al. Travel Med Infect Dis. 2015; 13:241-50.
Barnett ED et al. in Plotkin et al. Vaccines, 8th ed., 2022.
Bonanni P et al. Hum Vaccin Immunother. 2023; Apr 11;2195786.

Conclusions

- Substantial health burden of VPIs (but low mortality)
- No satisfactory GRADE criteria for travel vaccination recommendations by WHO
- Illusionary to conduct costly cohort studies (funding!)
- The gaps will remain

Nevertheless — relying on limited evidence:

- Create awareness in the public, particularly in VFR
- Follow national guidelines — frequent updates!
- Many health professionals use pre-travel consultation to give catch-up (routine) vaccine doses

VFR = Visiting Friends and Relatives

Questions — comments?

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istm.org/cistm18