

REPORT OF AN INTERNATIONAL CONSULTATION

International Travel and Health

PRE-MEETING TO THE 12TH ASIAN PACIFIC TRAVEL HEALTH CONFERENCE
21 MARCH 2018, BANGKOK, THAILAND



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This publication contains the report of an international consultation Methodology for risk mapping of the international spread of vector-borne diseases via air travel, including views and data supplied by participants, and does not necessarily represent the decisions or policies of WHO.

Executive summary

WHO convened a one-day meeting in March 2018 prior to the Asia Pacific Travel Health Conference (APTHC), with the aim to understand key needs and challenges of the travel health community with regards to health advice for travellers. The meeting was logistically supported by APTHC organizers and Shoreland ¹, a long-standing partner of WHO in travel health.

In a globalised world with ever increasing travel and population movements, the risk of importing or exporting diseases is constantly growing. Under the International Health Regulations (IHR 2005)², WHO works with Member States and partners to establish and implement the required policies and procedures for managing the potential public health risks associated with the international movement of people and goods. Because infected travellers may spread disease internationally travel medicine is of strategic importance for public health worldwide to prevent the introduction and further spread of infection at destinations, particularly in vulnerable environments. The WHO travel health activities have been reduced in the past few years, and WHO is now reaching out to partners, donors, academic institutions and private sectors³ to strengthen its work in this field.

WHO provides the latest, evidence-based, travel health guidance for medical professionals, travellers and Member States. Its flagship publication, “International travel and health” (ITH), the “green book”, requires regular, evidence-based updates. The revision process of this and other key travel health publications (CDC yellow book and the UK NaTHNaC eBook) were discussed. It was noted that the WHO green book revision process is the most stringent one but has fewest available resources. Since 2012, the revision process follows the procedures of the WHO Guidelines Review Committee (GRC) and includes, as far as possible, a systematic and rigorous evaluation of available evidence and a transparent decision making process for issuance of recommendations. In general, experts expressed their strong interest in having the ITH book revised as it is the only guide with a worldwide scope. In addition participants recommended that WHO, US CDC⁴, and NaTHNaC⁵, establish a common core of evidence and identify gaps as a starting point for collaborative studies. A platform to share this scientific review and documenting the rationale for national differences depending on cultural aspects would be of great interest for the travel health community.

Given the resource constraints, the group identified 9 top priorities for immediate update of the ITH book: deep vein thrombosis, malaria prophylaxis and stand-by treatment, Japanese encephalitis, altitude sickness prevention and treatment; jet lag; rabies prevention; insect repellents; hepatitis A prevention; and dengue vaccines. The meeting ended with proposals to engage with partners in academic institutions for systematic reviews of the literature for the nine priority areas, to support WHO in regularly updating the “green book”. Participants also discussed more effective ways of presenting and sharing the travel advice, including, for example, online travel booking platforms,

¹ <https://www.shoreland.com/>

² IHR (2005), third edition, <http://www.who.int/ihr/publications/9789241580496/en/>

³ Under the Framework of engagement with non-State actors agreements (FENSA), see WHO’s engagement with non-State actors web site, <http://origin.who.int/about/collaborations/non-state-actors/en/>

⁴ Centers for Disease Control and Prevention, Travelers’ Health web page, yellow book, <https://wwwnc.cdc.gov/travel/page/yellowbook-home>

⁵ UK Travel Health web site, <https://travelhealthpro.org.uk/>

social media or mobile applications for both provision of travel medicine recommendations and also for the surveillance of travellers' illness.

Contents

Executive summary	3
Scope of the meeting.....	5
Revision process for key publication on travel and health	6
WHO International Travel and Health “green book”	6
Yellow book, CDC	6
The National Travel Health Network and Centre eBook	8
Needs and gaps in evidence & format for travel advice.....	9
Empirical treatment against traveller’s diarrhoea - How was the evidence generated?.....	11
Pre-hospital hypothermia	12
Digital formats for publishing travel advice.....	12
Infection tracking and surveillance in travellers.....	14
Closing.....	15
Appendix 1. Agenda	16
Appendix 2. List of Participants	17

Scope of the meeting

Carmen Dolea introduced the aim of the meeting, which was to discuss ways and methods for the revision of the WHO International Travel and Health book (ITH)⁶. The meeting focused on various aspects of the revision process: the evidence based approach to issue recommendations, capacity and resources needed to develop such a guideline as well as a review of existing and new means for dissemination of travel health advice worldwide.

The ITH, commonly named the “green book”, is addressed primarily to medical and public health professionals who provide health advice to travellers. It is, however, also intended to provide guidance to travel agents, and organisers, airlines and shipping companies. As far as possible the information is presented in a form readily accessible to interested travellers and non-medical readers. For medical professionals other sources of additional material are available and essential information is given as concisely as possible.

Since 2012, the development of WHO guideline follows a strict process to ensure a high quality, transparent and clear process. This process follows the procedures of the WHO Guidelines Review Committee (GRC)⁷ and includes, to the extent possible, a systematic and rigorous evaluation of evidence available and a transparent decision making process for issuance of recommendations.

The ITH is considered by the GRC as a compilation of WHO guidelines, providing compiled guidance on a full range of significant health issues associated with travel. An overview of the step-by-step process on how to plan, develop and publish a WHO guideline⁸ was presented. The first phase is seeking the GRC approval of the project and includes 1) definition of the scope of the guidelines and targeted audience; 2) management of conflict and declaration of interests; 3) setting up of a Guideline Development Group and an external review group; 4) formulation of Population, Intervention, Comparison and Outcome (PICO) questions and selected outcomes.

Upon approval by the GRC, the implementation stage is initiated and includes: 1) evidence retrieval, assessment and synthesis; 2) a Grading of Recommendations Assessment, Development and Evaluation (GRADE) process where the quality of evidence is assessed; 3) the formulation of recommendations with explicit consideration for benefit and harms, resource use, feasibility, equity and acceptability. Upon GRC approval, the guideline can be disseminated and its impact evaluated.

Participants welcomed and strongly supported the revision of the ITH as this document is valuable for the travel health community. This document is considered to be a key resource thanks to its worldwide scope and the fact that it is not constrained by national ideologies. The ITH is perceived to complement other important national guidelines such as the US yellow book or the UK travel health advice eBook developed by NaTHNaC.

⁶ WHO web site, International Travel and Health web site, <http://www.who.int/ith/en/>

⁷ WHO web site, Guidelines Review Committee (GRC), http://www.who.int/publications/guidelines/guidelines_review_committee/en/

⁸ WHO handbook for guideline development, 2nd edition http://www.who.int/publications/guidelines/handbook_2nd_ed.pdf?ua=1

Revision process for key publication on travel and health

WHO International Travel and Health “green book”

Gilles Pomerol provided a historical overview of WHO’s work on travel health. Some 60 years ago, the WHO published the “vaccination certificate requirements for international travel”, as part of the obligations under the International Health Regulations; the publication later integrated health advice to travellers. In 2002, WHO published the first complete version of the “International travel and Health” green book (ITH). Subsequent revisions were made regularly until the 2012 version. The publication covers a large range of topics and is the international reference for Yellow fever vaccination requirements, recommendations and risks (annex 1 and country list). This joint effort between WHO staff, other external experts and multiple organizations became one of WHO bestselling publication and was translated in to seven languages. The publication was made available as an e-Book on line. The webpage which also includes updates for travellers was visited on average 2000 times a day and downloaded a million times in 2011.

As of 2013-14, a methodologist reviewed the ITH content as per the WHO Guideline Review Committee (GRC) requirements.. Ten recommendations were identified as necessitating a systematic review of evidence: antibiotics for traveller diarrhoea, anti-diarrhoeal agents, HIV PrEP, aspirin for Deep Vein Thrombosis, use of sleep inducing medication for long flights, melatonin for jet lag, hypothermia, Hepatitis B post-exposure prophylaxis and phobia of flying. Since 2014, evidence has been documented for the first three items listed above. A five years plan of work was prepared for the GRC and 3 GRC support groups were formed. However, due to a reduction in resources and competing priorities such as the outbreaks of Ebola, Zika and Yellow Fever it was not possible for the secretariat to implement the plan, although yearly online updates of maps, yellow fever information, vaccine preventable diseases and malaria were maintained.

Yellow book, CDC

Gary Brunette introduced the CDC Health Information Travel (commonly known as the “yellow book”), which is a reference for health professionals providing pre-travel health advice to international travellers and is a useful resource for staying healthy abroad. Back in 1950 this document was only focusing on yellow fever requirements and recommendations and the scope expanded with further recommendations for travellers. Now the “yellow book” codifies the US government’s most current travel health guidelines, including pre-travel vaccine recommendations, destination specific advice, and easy-to-reference maps, tables and charts.

The revision process for the “yellow book” is a continuous process over a 2-year period with its final launch at the International Society for Travel Medicine meeting. The process is scheduled as follows: planning (Months 1st -3rd); preparation (Months 4th -5th); writing (Months 6th -8th); editing (Months 9th -14th); clearance & approvals; copy editing and page proofing (Months 16th -18th); printing and distribution (Months 19th -21st); promotion (Months 22nd -24th month). The production team involves an Editor in Chief (10% time); Chief medical editor (40% time); Technical editor (40% time); Board of medical editors (5 internal and 5 external); Managing editor (project manager) (70% time); Design editor (10% time); Editorial assistant (30% time); Cartographers (2) (50% time). The current publisher of the yellow book is the Oxford University Press. The printing agreement is that CDC provides all informational content which remains in the public domain and

Oxford provides design, format and printing expertise. This book is available in full online (cdc.gov/travel) with 6.5 million total page views in 2016. The most viewed chapters are the pre-travel consultation on infectious diseases. Discussions are on-going to develop also a mobile application.

The content of this book is developed after consultation with travel medicine experts and disease-specific subject matter experts (SMEs), with the aim to assess evidence and find a consensus on an accepted evidence base. SMEs are working in disease area such as malaria, rabies, food-borne and vector-borne diseases and are kept up to date on the literature. The Advisory Committee on Immunization Practices (ACIP) issue vaccine recommendations for U.S. civilian population. They are developed and voted on by medical and public health experts, using GRADE to assess the strength of the evidence. Reviews of the literature are published in the Morbidity and Mortality Weekly Reports (MMWR).

About 230 authors were involved in the 2018 edition of the “yellow book”, including internal CDC authors (SMEs for each topic, multiple SMEs for consensus panel) and external authors. Very detailed instructions are provided to authors as well as a template to ensure consistency of drafting method throughout the book. The final version goes through an internal CDC clearance process for final acceptance. The “yellow book” does not use in-text citations but rather references a few key and recent references for bibliography focusing on travellers. Recommendations issued by CDC are evidence based to the extent possible knowing that most study results often cannot be generalizable. Other challenges in the decision making process are differences in interpretation, distinct target populations and the difference of risk tolerance specific to the audience as well as the cultural acceptability of the recommendations. It is of importance to note that travel recommendations are often different from local recommendations for endemic population.

Several proposals were presented to participants to improve collaboration and synergy for travel health advice. A global scientific consensus on the disease-specific epidemiology should be developed to agree on accepted evidence base recommendation and a common interpretation of evidence by establishing common core of evidence and identify gaps in evidence (as a starting point for collaborative studies). On this scientific basis it is acceptable that recommendations diverge due to risk tolerance, medication availability and cultural differences. Recommendations by countries may differ. European, US and WHO guidelines disagree in many aspects, participants requested that explanation be given on the decision making process. Documenting the rationale for such differences would be of great interest for the travel health community.

In general, participants expressed their gratitude to the US CDC as an important resource for travel health, acknowledging the fact that it remains a national guideline and is US oriented. This document should be complemented by strong WHO recommendations. Participants also acknowledge the fact that recommendations issued for travellers may not always be in accordance with guidelines developed for endemic population. In general it was concluded that resources to develop the “yellow book” were greater than the resources available for WHO, and the process for the development of the “yellow book” was less stringent compare to the one required by the WHO GRC. A process to avoid duplication of effort and synergy between these institutions should be established.

The National Travel Health Network and Centre eBook

Dipti Patel presented the work of the National Travel Health Network and Centre (NaTHNaC) for protecting the health of UK travellers. NaTHNaC was set up in 2002 with the aim to improve the quality of travel health advice given by General Practitioners, travel clinics, pharmacies and other health care providers, and to provide up to date and reliable information for the travellers, travel industry and national government. It is commissioned by Public Health England and hosted by the University College London hospitals NHS foundation trust. Main partners are LSTM, LSHTM and HTD.

There are around 70 million UK travellers going abroad every year with about 3400 yellow fever centres across England, Wales and Northern Ireland. The production of guidance involves about 15 staff who follow standards and principles such as a clear process for production and based on best evidence available. Its content is user friendly with constant adjustment of the content thanks to multiple feedback mechanisms.

A new web site Travel Health Pro⁹ was developed almost 3 years ago involving travellers, government, health professionals, and travel health experts. Originally 2 audiences were determined, travel health professionals and travellers. The 2 sites were finally merged so as to facilitate coherence and maintenance and at the request of users. This web site was developed being attentive to both content and design of the information delivered. Recommendations are based on the best credible, evidence-based information and delivered in a very personalised manner. The web site is divided in 4 main areas: country, news item, outbreaks and fact sheets. On the country page the user can find information on general risk, resources, certificate requirements, vaccination recommendations for most travellers as well as for some travellers, malaria recommendations where appropriate and other travel risks. In general, recommendations for polio, yellow fever and meningitis are based on WHO recommendations. For other country specific diseases, recommendations are issued after a review by an expert panel. For vaccine issues: the joint expert committee for vaccines and immunization produce guidelines, see guidelines reference. Recommendations for malaria are based on the guidelines for malaria prevention in travellers from the UK published in 2017. The outbreak and news item page is focused on UK travellers and may be based on ECDC information.

NaTHNaC decided to avoid publishing travel advice in book-format as it was considered that a book becomes out of date soon from the moment of its publication. Instead, it went for an electronic publication, which is constantly updated. It is also complemented by a telephone advice line to focus on priorities. To improve its utility, the website is also complemented with input from multiple stakeholders such as social media, focus groups, surveys and advice line analysis. These electronic tools allow an analysis of users' needs which for example change with the season. In addition, educational webinars are produced on YouTube to increase health professional and traveller's awareness with risks when travelling. The content development of the eBook is conducted by NaTHNaC staff with subject experts at Public Health England and network partner subject matter experts where relevant.

Participants underlined the need for the 3 resources to talk to each other on a regular basis. It was noted that WHO resources were very low compare to US CDC and NaTHNaC. These institutions

⁹ TravelHealthPro, <https://www.travelhealthpro.org.uk/>

should synergise their effort to collect and assess the evidences for key recommendations accepting the fact that all recommendations cannot be grade and that they may differ due to different risk benefit analysis and cultural approaches.

Needs and gaps in evidence & format for travel advice

Karin Leder and Robert Steffen chaired a plenary discussion on the needs and gaps in evidence and on the need for various formats for travel advice. Grading is applicable when there is data. It is difficult to work on grading recommendations in travel medicine because often there are insufficient data on incidence of infection (numerator) and size of population at risk (denominator). In addition, baseline risk estimates vary in different geographic regions and by season. Also data generated in endemic population are not always applicable to travellers (i.e. malaria treatment). There are data gaps in disease risk and vaccine efficacy for some vaccine preventable diseases in travellers - such as flu, Japanese encephalitis (JE) or meningococcus - as well as travel related issues such as diarrhoea or malaria. There is a variability in each disease risk gradient according to specific individual travel scenarios.

Many segments within the current WHO ITH book would not be amenable to GRADE, but the areas that would be most likely to be addressed would be:

- Vaccine-preventable diseases (VPDs): variable degree of available data to underpin GRADE recommendations, some vaccines already have systematic reviews on efficacy albeit not always specifically addressing the travelling population
- Non VPDs: Systematic reviews on melatonin, DVT prophylaxis and altitude illness already exist, but the current WHO ITH includes only limited information on these factors so would need a significant, major overhaul

Data on traveller values and preferences is often lacking (especially for low-incidence/high-impact infections), so an arbitrary risk cut-off is likely to be required. A review of methods by which data on vaccine preventable diseases in travellers residents in industrialized countries concluded that the confidence as per GRADE was mostly moderate to very low. Data on risks among “non-Western travellers” are almost entirely lacking – this is an important area for WHO.

The Canadian Committee to Advise on Tropical Medicine and Travel (CATMAT) has been developing travel and tropical medicine guidelines and recommendations for the Public Health Agency of Canada, using an "evidence based" approach since 1994. CATMAT has updated its guideline development process¹⁰ and since 2013 uses the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) method for certain recommendations. . On the topic of prevention and treatment of travellers’ diarrhoea both CATMAT and the Journal of Travel Medicine published recommendations based on GRADE, the latter with 20 graded and three ungraded statements, based on an expert meeting sponsored by the ISTM Foundation. WHO is releasing in April a SAGE-graded revision of the policy on rabies vaccine and rabies immunoglobulins¹¹. More

¹⁰ <https://www.canada.ca/en/public-health/services/publications/diseases-conditions/evidence-based-process-developing-travel-tropical-medicine-guidelines-recommendations.html#a4>

¹¹ http://www.who.int/rabies/resources/who_wer9316/en/

graded recommendations have been generated by the U.S. ACIP on vaccines (partly included in the Yellow Book), on non-drug interventions against malaria (ISTM), on altitude illness (Wilderness Medical Society). Grading would rather easily be possible for other domains, such as hepatitis A prevention, as there is ample incidence data in unprotected travellers in lower income countries. Also with respect to travel associated influenza there is plenty of epidemiological evidence. However, there are data gaps in disease risk, even more so in risk profiles for other vaccine preventable diseases in travellers such as Japanese encephalitis (JE) — but nevertheless that is currently being graded by CATMAT. There is limited data on the WHO priorities formulated five years ago which were aspirin for DVT, sleeping pills, and/or melatonin against jet lag, phobia of flying, hypothermia, and HBV PEP.

In conclusion GRADE recommendations exist in various domains of travel health (many by CATMAT) and additional GRADE guidelines would be feasible. If WHO decides that we must grade the advice given in ITH we need to be aware of challenges: epidemiological conditions are moving targets, as there may be hygienic improvement or deterioration at the destination, antimicrobial resistance may develop, climatic changes may play a role. Consequently, recommendations would need to be regularly reconsidered or even revised, which usually is a resource-intensive process. There is also the issue of the threshold for recommendations based on risk perception and acceptance by the public ('belief'). That varies in different cultures, e.g. Western vs. non-Western travellers, there are even transatlantic differences. A fundamental question in travel health strategy needs to be 'is the health risk greater as compared to home?' Many would agree that efforts need to be made to harmonize recommendations across countries and to improve compliance by experts by counteracting tradition, industry and for-profit interests in commercially oriented institutions. Otherwise travellers at their destination comparing differing advice would not only conclude that their advisors were incompetent, but also question any preventive measures in the future.

Comments from the plenary pointed out that WHO guidelines are usually written for endemic populations and also that some WHO ITH chapters (such as malaria) have to take global opinion and cannot provide a detailed direction. Severe mortality in travellers is related to accidents and vehicle trauma. This is factual and does not need grading. When there are no or few data, it just should be made transparent, so that taking into account the limitations, the risk and benefits become very clear. A lot of information is available for jetlag and DVT systematic reviews, and grading could be easily done. Instead of using GRADE we should consider using the PRISMA¹² approach.

Looking at the evidence is the role of WHO. The WHO list of recommendations for evidence/systematic reviews came from a methodologist 5 years ago. ITH now needs to be reviewed to identify gaps and where there is a need to get evidence. The focus should be on science, and adaptation made on national guidelines, although for countries where there are no guidelines, general recommendations might be useful. There is a group in Europe discussing about evidence for travellers with the goal to standardize the recommendations at the national level. In Israel recommendations are based on evidence which go beyond the GRADE, looking at benefit and harm, also including economic aspects. Some now stress personalised medicine and travellers to decide on their own risk level.

¹² <http://www.prisma-statement.org/>

Empirical treatment against traveller's diarrhoea - How was the evidence generated?

Michael Libman introduced the experience with the CATMAT's¹³ systematic review and grading of recommendations for prevention and treatment of traveller's diarrhoea (TD). The working group was formed of volunteer members from the University of Montreal, with strict review of potential conflict of interest. One epidemiologist was recruited full time for 18 months. It was a heavy process which took two years. It was also a learning experience mostly because of the large amount of data. Some recommendations were not graded because of lack of credible alternatives (e.g. handwashing) or sounded logic but with insufficient evidence (e.g. food and beverage choice) and the lack of credible alternatives. Only studies with a classical definition of diarrhoea and with recent data on use of antibiotics were retained. The evidence based conclusions were committee driven (at difference of CDC where it is editor driven and cleared by hierarchy). Due to insufficient data, risk factors (such as destination, type of travel) and type of food were not evaluated. At the end, the recommendations may be subjective but transparent. Grade results are available in Annex of the publication¹⁴.

Options for prevention:

- Dukoral not recommended (after exclusion of a study performed in the endemic population of Bangladesh and not travellers);
- Bismuth subsalicylate (BSS) recommended four times a day if significant risk (strong recommendation, high confidence) with a 50% efficacy
- Rifaximine: prevention 58%.

Options for treatment:

- BSS: no GRADE assessment, no recommendation and only narrative review; Quinolone, conditional recommendation due to more harms, old data (all > 20 years) overall RR = 12%, but absolute reduction 300 cases per 1000 travellers (similar to BSS)
- Loperamide: conditional, low to moderate confidence in estimate of benefit, possible superiority to BSS, no evidence of adverse events, similar to antibiotics in efficacy. Combo superior to antibiotics alone;
- Azithromycin no data available
- Rifaximine : RR for cure 1.29, 177 more cures per 1000 treated; randomized controlled trials (RCT) comparisons to Ciprofloxacin = no difference. Also resistance issues unknown.
- Probiotics were excluded because too broad, lot of potential bias and lack of regulatory activity

At the end the efficacy was rather good, moderate quality, see appendix 2: GRADE tables for each TD intervention. Comments from the participants emphasized that TD is very well documented. In many other areas, there are fewer data and the review / grading should be easier and faster. It was pointed that every single vaccine went through this heavy process with WHO SAGE group, however, data are for endemic population and travellers are not included. In absence of data, expert advice

¹³ <https://www.canada.ca/en/public-health/services/travel-health/about-catmat.html>

¹⁴ <https://www.canada.ca/en/public-health/services/travel-health/about-catmat/statement-travellers-diarrhea.html>

needs to be considered. Note was made that there is a software available for GRADE analysis and that a training workshop could be organized

Pre-hospital hypothermia

Prativa Pandey presented on current research and gaps in the evidence in pre-hospital hypothermia. Body heat loss occurs through convection, respiration, evaporation, radiation and conduction. When body temperature drops below normal, the nervous system signals skin blood vessels to constrict, sweat glands to remain inactive and muscles to contract involuntarily causing shivering to generate heat and raise the body temperature. Heat loss increases 5 times by wet clothing and 25 five times by immersion in cold water.

Accidental hypothermia is an unintentional drop in core temperature below 35°C (Core temperature: 37° C +/- 0.5° C) and occurs in persons doing outdoor work or recreation, adventure travellers (climbing, trekking), after cold water immersion. It is also observed in homeless (sleeping outdoors) people, after trauma or with sepsis. While the brain can tolerate the cold, respiratory and cardiovascular effects can be very serious (hypoventilation with respiratory acidosis, bradycardia, hypotension, atrial and ventricular arrhythmias and below 28°C, risk of Ventricular Fibrillation (VF)).

Mild hypothermia treatment consists in removing the patient from cold environment, removing/cutting wet clothes (only with shelter), allowing patient to shiver, insulating the patient with a vapor barrier: in plastic sheet or wrap and then in a sleeping bag or blanket, insulating from the ground, covering head and neck and administering sugar containing fluids. Moderate and severe hypothermia treatment consists in insulation and vapor barrier as in mild hypothermia, active external rewarming and internal rewarming (warm IV fluids to 38-40C) while keeping patient horizontal with no sitting or standing. If no carotid pulse for 1', CPR and defibrillation for VF. Severely hypothermic patients have been resuscitated with Cardio Pulmonary Resuscitation (CPR) lasting 6 hours. Full neurological recovery seems possible.

Cardiovascular instability can occur in persons during afterdrop (further drop in core temperature that can initially occur during rewarming) who are near the threshold of moderate to severe hypothermia. There is some evidence that afterdrop along with drop in blood pressure occurs more often after rapid warm water rewarming and not during inhalation or spontaneous rewarming. Spontaneous rewarming by shivering or active external rewarming by various means like insulation with vapor barrier, body to body rewarming, use of chemical packs, electric pads or hot water bags in axillae, chest and back or forced air warming have been shown in small randomized cross-over trials to be effective in raising core temperature and are methods currently recommended. Active internal rewarming by warmed IV fluids help prevent heat loss as compared to room temperature fluids and seems beneficial while the benefit of inhalation of warm air/oxygen has been equivocal

Although large controlled studies in the field for pre-hospital hypothermia are lacking rapid rewarming in warm water as recommended by WHO ITH 2012 version is now not considered an option for hypothermia management

Digital formats for publishing travel advice

Sarah L. McGuinness introduced this topic. Travel has embraced the digital age with online airline booking set in a few minutes and digital information at our fingertips. We can travel anywhere by plane in less than 20 hours. However, we in the medical profession, seem to be lagging behind.

Because mobile devices are cheaper, more accessible and require less infrastructure than computers, smartphones and other hand-held devices are overtaking computers as the primary gateway to the Internet. This is not just a trend in the Western world, it is global.

While many travellers don't seek pre-travel health advice or don't do research when it comes to travel health, they do plenty of travel research online. Digital information sources consulted by travellers include travel advice forums, booking sites, and social media. Each of these digital contacts is a potential opportunity to provide travellers with links to travel health advice. The potential reach of digital travel health messaging is enormous. Social media is another digital resource with huge potential for the promotion and delivery of travel health advice. There is enormous potential to integrate travel health advice into other digital traveller tools and some travel insurance companies have already made a start by integrating travel health advice and health tips (such as global hospital finder) into mobile apps for travellers.

There are a number of digital formats that are available for delivering travel health advice: (i) **eBooks** are an electronic version of a printed book which can be read on a computer or specifically designed handheld device - their advantages include that they can be available offline and they are cheap to develop, but disadvantages include their lack of customisability and interactivity and that they become outdated quickly; (ii) **mobile apps** are software applications developed specifically for use on handheld devices - their advantages are that they are customisable, they can utilise existing smartphone functions, such as the in-built GPS or camera, and can be used online and offline- their major disadvantages are that they are costly to develop, require complex maintenance, and plagued with high user expectations; (iii) **clinical decision support tools** are essentially tools designed to enhance decision-making within the workflow of clinical practice (such as Shoreland Travax and Tropimed) - these are arguably the most powerful digital resources out there as they are highly customisable and able to aggregate data from multiple sources in real time, however their disadvantages are that they are resource-intensive (as they require constant updates) and subscription-based with a cost to the user.

When developing and evaluating digital health resources, we need to: (i) consider our target audience – provider or traveller; (ii) ensure the content is appropriate – it should be good quality, comprehensive but concise, and up-to-date; (iii) consider the usability, customisability and interface design.

Comments from the participants emphasized that working with private travel companies can be problematic since their goal is to sell holidays and not travel health (which in fact can be detrimental). Tripadvisor, may be the most appropriate since it has a good platform as well as social media, but there would be a cost. Insurance industry are now including travel advice to reduce their expenses, but their source of information is not known. Be aware of risk/ prevention work well. Mobile phones can be very useful (e.g. SMS for malaria messages in south Africa). CDC has been approached by google and asked to prepare health messages and it is currently piloted. Travellers could receive health message depending on their research or their itinerary.

Infection tracking and surveillance in travellers

Patricia Schlagenhauf introduced the ITIT project. ITIT is short for “Infection Tracking in Travellers”. The aim of this project is **to develop, pilot and make commercially available an application (ITIT App) and platform that will enable travellers to contribute data themselves on health and infection, both actively and passively**. The project will enable the creation of large, complex and versatile sets of data that are constantly evolving and include data from pop-up questionnaires, geolocation data and social media data. Analyses of these data will have societal impact and will constitute a tool for global infectious disease surveillance and an evidence base to inform public health policy and action. For tourists and business travellers, the data from the ITIT APP will be the basis for personalised travel medicine and will identify risk groups, risk destinations and behaviours, will provide advice and, in certain circumstances, health messages and alerts. The World Tourism Organization (WTO) predicts 1.8 billion travellers in 2030. Travellers play an important role in the spread of infection. Travellers are also good sentinels for infectious diseases when visiting countries and the data collected can contribute to monitor travel related infections. Current surveillance national and supranational surveillance (i.e. ECDC, WHO); surveillance networks (i.e. GeoSentinel, EuroTravNet); insurance data; proMED and epicore, are “Top Down”, ie professionals and institutions report on illness in travellers. ITIT will allow for a “Bottom Up” approach and self-reporting by travellers which will provide a major resource for infection surveillance. The ITIT app will also provide health advice and pop up alerts for travellers.

A recent example of the sentinel role of travellers for infection surveillance is the cluster of 5 recently imported cases of yellow fever among travellers coming back from previously unaffected areas of Brazil (2 deaths between January and March 2018) and a cluster of epidemiologically unexpected cases of schistosomiasis in travellers returning from Corsica, France.

Considering that smart phone coverage is 96% of the world’s population, that 82% online use social media and networks, that 46% use their phone to look up health advice, better use should be made of this for bottom up surveillance. Nowadays a large proportion of online users publicly share information on social media. Digital epidemiology, leveraging widespread use of the internet, mobile phones and social media, can supplement lab reports and traditional surveillance and can be used for early detection of outbreaks.

An example is the study performed in Thailand with 100 travellers geo-localized who reported accidents, mental health problems, wounds, bites, licks, diarrhoea and sunburn. It could be possible to pop up simple, standard messages when the traveller posts such information and symptoms. The digital technology could also be used to support IHR requirements for surveillance and notification. The Big Data generated could support global surveillance of infection. Issues of concern with digital data are fake news and privacy.

The ITIT project aims at creating a big data platform and mobile application framework to acquire, fuse, warehouse, analyse and exploit real time big data on travel-related infection. Data would be generated by the travellers themselves using an app with a graphical way to enter symptoms - touch interface of mobile devices. This would contribute to signal detection, outbreak recognition, spatio-temporal analyses and machine learning. Big Data would then inform public health policy on infection with travellers as sentinels. Incentives for the traveller to contribute would be in the form of health messaging and alerts and a “GAME” feature. Additional funds need to be raised for this

project that aims at recruiting 100,000 travellers. Many apps are available for travellers. They cover pretravel and/or during travel and/or post travel. There is a need for a gold standard (WHO, CDC). Smart phones apps can also support migrants for in-travel health advice and record keeper for those without documentation.

Comments from the participants emphasized the workload generated by such system and the need for an automated process. Concerns were expressed on big data and ethical problems and the need to establish guidelines.

Closing

Dr Carmen Dolea expressed her gratitude to all participants for the fruitful discussion. This meeting was extremely useful to build a common understanding and vision on how go ahead with the ITH revision process and possibility to use new technologies to strengthen travel health. During the meeting experts were asked to propose three recommendations that would need to be updated and may go through a GRADE review process. Only those receiving more than 2 votes are listed below:

1. Deep Vein Thrombosis
2. Malaria prophylaxis and stand-by treatment
3. Japanese encephalitis
4. Altitude sickness prevention and treatment
5. Jet lag
6. Rabies prevention
7. Insect repellents
8. Hepatitis A prevention
9. Dengue vaccines

The GRADE process is a methodology to analyse currently available scientific evidence and document decision making process for issuance of recommendations. This is a very time and resources consuming process. For that reason Dr Carmen Dolea reiterated the need for support to the Travel and Health activities at WHO in terms of collaboration, seconded staff, support for meetings and financing the next revision of the ITH, including conducting systematic reviews and organizing guidelines development expert meetings. The need to further explore options to use digital format for publishing travel advice and the ITH document was also emphasized and the use of apps for surveillance. The next steps included also follow up discussions with various partners to agree on specific deliverables and review process.

Appendix 1. Agenda

WHO consultation with experts in travel medicine to review gaps in evidence for International Travel and Health Asia Pacific Travel Health Conference – Bangkok, 21.03.2018, 11AM – 5PM		
Time	Item and Speakers	Chair
11:00– 11:15 am	Welcome and opening remarks <i>Leo Visser</i> <i>Pornthep</i> <i>Chanthavanich</i>	<i>Patricia Schlagenhauf</i>
11:15 – 11:40 am	Introduction <ul style="list-style-type: none"> • The ITH Green Book • Scope of the meeting <i>Gilles Pomerol</i> <i>Carmen Dolea</i>	
11:40– 12:00 am	Other travel and health guides <ul style="list-style-type: none"> • CDC • NaTHNaC <i>Gary Brunette</i> <i>Dipti Patel</i>	
12:00 – 12:30 pm	Views from travel health practitioners. Needs and gaps in evidence and format for travel advice. <i>Karin Leder</i> <i>Robert Steffen</i>	
Lunch break		
1:30– 2:00 pm	Priorities for review of evidence on travel health <i>Carmen Dolea</i>	<i>Robert Steffen</i>
2:00 – 3:45 pm	Evidence base for travel health recommendation <i>Michael Libman</i> <ul style="list-style-type: none"> • Empirical treatment against traveller’s diarrhea - How was the evidence generated • Treatment of Hypothermia - Current research and gaps in the evidence <i>Prativa Pandey</i> Round table: Gaps in evidence and current research	
3:45 – 4:45pm	IT tools for travel medicine advice and surveillance <i>Sarah L McGuinness</i> <ul style="list-style-type: none"> • Digital formats for travel advice • Infection Tracking and Surveillance in Travellers <i>Patricia Schlagenhauf</i>	
4:45 – 5:00pm	Closing and way forward <i>Carmen Dolea</i>	

Appendix 2. List of Participants

International / Regional Organizations and Societies

Asia Pacific Travel Health Conference

Pornthep Chanthavanich

President
Associate Professor Tropical Pediatrics, Mahidol
University
Bangkok, Thailand

International Society of Travel Medicine

Leo Visser

President
Professor, Leiden University, Netherlands

Lin Chen

President-Elect
Associate Professor, Harvard Medical School
Boston, USA

David Hamer

Director GeoSentinel
Professor Boston University
Boston, USA

WHO Collaborating Centres

Chinese Academy of Inspection and Quarantine (CAIQ),
China

Jing Wang

Professor, Chinese Academy of Inspection and
Quarantine,
WHO CC for ITH - Beijing

Gang Li

Director of the Division of Disease surveillance,
AQSIQ,
WHO CC for ITH – Beijing

University of Zurich,
Switzerland

Patricia Schlagenhauf

Professor, EBPI, University of Zurich.
WHO CC for ITH. – Zurich

Centres for Disease Control and Prevention (CDC),
USA

Gary Brunette

Chief Travellers Health, Centers for Disease Control
and Prevention,
WHO CC for ITH – Atlanta

National Centers

South Africa
National Institute for Communicable Disease (NICD)

Lucille Blumberg

Consultant, National Institute for Communicable
Disease (NICD) - Johannesburg

United Kingdom
National Travel Health Network and Centre

Dipti Patel
Director,
National Travel Health Network and Centre and
Occupational Medicine consultant for the UK
Foreign & Commonwealth Office - London

Canada
CATMAT

Michael Libman
Professor and Director McGill Centre for Tropical
Medicine,
Committee to Advise on Tropical Medicine and
Travel (CATMAT) - Montreal

Germany
Deutsche Gesellschaft für Tropenmedizin
und Internationale Gesundheit (DTG)

Hans Nothdurft
Tropical Disease Clinic Ludwig Maximilian Univ. –
Munich

Japan
Japanese Society of Travel Medicine

Tadashi Shinozuka
Executive Director - Tokyo

Private Sector

Shoreland Travax

David Freedman
Professor Emeritus of Infectious Diseases, UAB
Medical Director Shoreland Travax - Birmingham

Experts

Annelies Wilder Smith
Professor for Infectious Diseases Research LSHTM,
London,
Lee Kong Chian School of Medicine - Singapore

Karin Leder (tbc)
Professor and Head of the Infectious Disease Unit
in Epidemiology Department, Monash University –
Melbourne

Prativa Pandey
Director CIWEC Clinic Travel Medicine Center –
Kathmandu

Robert Steffen
Emeritus Professor Univ of Zurich - Zurich

Sarah McGuinness
Infectious disease physician, Monash University –
Melbourne

World Health Organization

Secretariat of the International Health Regulations

Carmen Dolea
Team Leader
IHR Committees, Travel & Trade
WHO Health Emergencies Programme
Geneva

Corinne Poncé
Technical Officer
IHR Committees, Travel&Trade
WHO Health Emergencies Programme
Geneva

Gilles Pומרول
Public Health Consultant to WHO
Geneva

Observers

Alain Bouckenhooghe
Assoc. VP, Head Clinical Sciences Hub Asia
Pac Sanofi Pasteur
Singapore

Chhor Nareth
Physician, Calmette Hospital
Phnom Penh

Christian Popescu
Intern World Health Organization
Geneva

Christoph Klose
German Federal Foreign Office,
Regional Medical Director for Southeast Asia
Jakarta

David Warrell
Emeritus Professor of Tropical Medicine
University of Oxford
Oxford

Eli Schwartz
Professor and Director Tropical Medicine,
Chaim Sheba Medical Center
Tel Aviv

Eyal Leshem
Infectious Disease Physician,
Chaim Sheba Medical Center
Tel Aviv

Joan Ingram
Infectious and Travel Medicine Physician

Auckland

Jonathan Cohen

Medical Director, Travel Clinics Australia
Melbourne

Joon Sup Yeom

Division of Infectious Diseases, Yonsei
University
Seoul

Kate Gaynor

Physician, United Family Hospitals
Guangzhou

Liu Zhiyong

China International Travel Healthcare
Association
Beijing

Mary Warrell

Oxford Vaccine Group, University of Oxford,
Centre for Clinical Vaccinology & Tropical
Medicine
Oxford

Masatoki Adachi

Travel Medicine Physician
Osaka/Kobe

Min Zhang

Guangdong International Travel Healthcare
Centre,
WHO CC for ITH
Guangdong

Priscilla Rupali

Professor and Head, Department of
Infectious Diseases, Christian Medical College
Vellore

Santanu Chatterjee

Consultant Physician Travel and Tropical
Medicine
Kolkata

Scott Tidwell

Director, International Partners Program,
Shoreland Travax
Birmingham

Tamar Lachish

Infectious Diseases Physician, Shaare-Zedek
Medical Center
Jerusalem

Theodore Tsai

VP Immunizations Science and Policy, Takeda
Vaccines
Boston

Tony Gherardin

Senior Medical Advisor
Department of Foreign Affairs and Trade
Australia
Canberra

Watcharapong Piyaphanee

Travel Medicine Physician
Faculty of Tropical Medicine, Mahidol
University
Bangkok

Woo-Yun Sohn

Area Medical Lead, Medical Affairs, Asia
Pacific, GSK
Singapore



