Title: Real-time incidence of travel-related symptoms through a smartphone-based app remote monitoring system: a pilot study

Running title: Smartphone surveillance system for travel-related infections

Keywords: travel medicine, smartphone, medical apps, real-time health recordings, digital participatory surveillance system

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Abstract

Trip Doctor®, a Smartphone-based app monitoring system, was developed to detect infections among travelers in real-time. For testing, 106 participants were recruited (62.2% male, mean age 36 years (SD=11)). Majority of trips were for tourism and main destinations were in South East Asia. Mean travel duration was 14 days (SD=10). Diarrhea was the most frequently reported symptom (15.5%). The system demonstrated adequate usability and is ready to be used on a larger scale.

Introduction

International travel have been steadily growing for six consecutive decades, with an estimated increase of 3.3% per year in tourism and, only in 2015, 14% of travels were related to business. [1] A greater increase is observed and forecasted in travel to tropical and subtropical destinations in Asia, America and Africa. A median of 51% (Interquartile range: 6-87%)[2] travellers are estimated to present travel-related symptoms during or after the travel, of them up to 55% seek medical care during the trip[2] , additionally in some reports, at least 21% of the travelers stopped their planned activities due to illness.[3] Most studies evaluating travel-related infections[2] are based on questionnaires conducted in post-travel clinics in symptomatic travelers once returned, conferring strong recall bias, providing inaccurate temporal symptom sequence and not taking into account the number of asymptomatic travelers to calculate incidence rates. The most common symptoms of travel-related infections shown in previously published studies are: fever (8-17%), travelers' diarrhea (33-69%) and cutaneous lesions (7-17%).[3,4,5]

A way to overcome the limitations cited above is the use of telemedicine. There are many mobile applications for travel medicine[6,7] but few of them evaluating health travel risks real-time.[8]

Our aim was to develop and test a new telemedicine and digital participatory system in order to detect travel related-symptoms and provide with remote care to the travelers attending our travel clinic; alongside testing the surveillance capacity of the system.

Methods

Our group developed and tested a Smartphone-based app remote digital participatory and monitoring system[9] to detect symptoms of the main infectious diseases among

international travelers in real-time, called Trip Doctor®. The app was uploaded in PlayStore® and Apple Store® to be used with a code that we provided to the travelers after agreed to participate into the study. Trip Doctor® app monitored the status of the travelers on a daily basis at a predetermined time, providing specific medical advice and offering remote contact with the study physicians to those reporting symptoms. All travel and clinical data, including malaria prophylaxis indication and intake, travel dates, and purpose of travel, health status and symptoms, and approximate daily geolocation, for each health check during travel, were recorded automatically in a specific web back-end remote monitoring system. Real-time data of participants could be visualized by medical specialists through the web monitoring system and could be transformed into a dataset automatically for the purpose of analyzing the data (Figure 1). Trip Doctor® app was developed following privacy by design strategies so only medical specialists monitoring the backend can access to patient information. Additionally the app acted as a reminder for malaria prophylaxis in case it was indicated by the attending physician. Daily predetermined symptoms captured were "diarrhea", "abdominal pain", "fever", "joint pain", "headache", "cutaneous lesions" and "other". Symptoms were chosen by the medical team of the study in order to detect the most frequent symptoms associated to the main tropical infections including those posing a risk of the traveler abroad. Moreover, possible associated symptoms of malaria chemoprophylaxis were also recorded in the database: oral ulcers, insomnia. A real-time alarm system was implemented in the database to automatically identify travelers with symptoms compatible with arboviral disease (defined as fever + joint pain + travelling to an area endemic for arbovirus) to test the system's potential to contribute to the identifications of suspects to control the introduction of arboviral diseases in Spain. All travelers were followed-up during 21 days after the travel.

This study was approved by the Ethics Committee of Hospital Clinic Barcelona (reference HCB/2015/0995) and the clinical investigation has been conducted according to the principles expressed in the Declaration of Helsinki. A written informed consent was signed by the participants before using the Trip Doctor®.

We invited to participate in this pilot study those travelers attending our pre-travel clinic older than 18 years and travelling for one month or less. Travelers taking malaria chemoprophylaxis with other drugs than atovaquone-proguanil were excluded due to safety because the App was not configured to remind other prophylaxis schemes than atovaquone-proguanil.

Results

During the study period 106 travelers agreed to participate in the study. Mean age was 36 years (SD=11) and 62.2% were male. The most visited regions were Sub-Saharan Africa 34.6%, followed by South East Asia 32%, Americas 16.4%, Western Pacific 16% and Eastern Mediterranean 1.9%.The top 5 destination countries were: Thailand (12%), followed by India (8%) and Indonesia (8%), Mozambique (6%) and China (5%). Mean duration of travel was 14 days (SD=10). The main purpose of travel was tourism in 58%, followed by work 30%, volunteering or humanitarian work 9% and Visiting Friends and Relatives (VFR) 3%. Thirty three percent of participants were prescribed with malaria chemoprophylaxis for a mean duration of 15 days (SD=6).

Incidence rates of recorded symptoms are shown in Table 1. No associations between symptoms were observed with sex, purpose of travel, age, duration of the trip or prophylaxis status. Moreover, no cases fulfilling the definition of arbovirus suspicion were found during the period of the study.

During the period of the study 2 telemedicine calls were received, both for mild

abdominal pain associated with constipation and they could be resolved by telemedicine itself. No further medical visits were needed. During the follow-up period, a phone interview was made to all participants, at least 3 patients sought medical care abroad, two of them because of diarrhea and fever, but no more information could be collected.

In terms of usability, number mean of days with a complete daily health check for all users was 9.9 (SD=6.9) and number mean of days not using the App, meaning not completing the health daily check, was 5.7 (SD=8.8). The participants used the app, completing the health daily check, more than 50% of the days of the travel.

Discussion

We evaluated the new Smartphone app Trip Doctor® in a pilot study to show that our remote monitoring system is able to capture real-time incidence of travel-related infections, together with a number of epidemiological and geographical data that can be evaluated as risk factors for disease in further studies. The platform allows overcoming common limitations of conventional studies: providing a reliable time sequence of medical events, avoiding recall bias, and providing a denominator of healthy travelers to calculate incidence rates, as well as offering care to travelers if necessary.

The main limitation of this pilot study is the small number of participants and the short duration of travel, this is reflected in the absence of association between symptoms and duration of travel, a main factor for illness in other studies.[4,5] Other limitations are those related to generalizability, our cohort is a selected population who attend to a travel clinic and that fact could influence their behavioral risk. Also, VFR and vulnerable population (pregnant women, children and people aged more than 65 years) are not well represented.

In spite of these limitations, it was shown that 13% of them presented at least one symptom of travel-related infection, with diarrhea and abdominal pain the most common in 15% of the cases, less than in other studies.[10,5].

Conclusion

This is a pilot test of a broader initiative to implement remote monitoring of health in travelers to high risk areas. If scaled-up, the outputs of this initiative will facilitate big data analysis, providing a better understanding of health-related risks for travelers and having a positive impact in pre-travel advice and disease prevention. This traveler's platform could be then used as a surveillance mechanism for the epidemiology of infectious imported diseases, enhancing mechanisms to control the introduction of infectious diseases (in particular arboviral diseases) in countries at-risk harboring *Aedes* mosquitoes. Moreover, tracing traveler's symptoms could be an excellent data source to detect outbreaks of infectious diseases in remote destinations in a real time basis.

Declarations

We do not have conflicts of interest to disclose and this work was supported by ISDIN,Fundació La Caixa and grants COOP-XVII-02 and COOP-XVI-14 from Universidad Politécnica de Madrid.

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188 Table1. Incidence of travel-associated symptoms during travel in the cohort (N=106)

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Symptom (for a 12 day mean travel)	Accumulated incidence or incidence proportion	Incidence Rate*
Diarrhea	15.5%	1.4%
Abdominal pain	13.1%	1.2%
Articular pain	8.3%	0.8%
Headache	9.5%	0.9%
Cutaneous lesions	9.5%	0.9%
Other symptoms	10.7%	1%
Fever	3.6%	0.3%
Oral ulcers	3.6%	0.3%
Insomnia	3.6%	0
***cases person-day**		

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