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Original Article

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The antimicrobial resistance travel tool, an interactive evidence-based educational tool to limit antimicrobial resistance spread

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Abstract

Background: International travel has been recognized as a risk factor contributing to the spread of antimicrobial resistance (AMR). However, tools focused on AMR in the context of international travel and designed to guide decision-making are limited. We aimed at developing an evidence-based educational tool targeting both healthcare professionals (HCPs) and international travellers to help prevent the spread of AMR.

Methods: A literature review on 12 antimicrobial-resistant bacteria (ARB) listed as critical and high tiers in the WHO Pathogen Priority List covering four key areas was carried out: AMR surveillance data; epidemiological studies reporting ARB prevalence data on carriage in returning travellers; guidance documents reporting indications on screening for ARB in returning travellers and recommendations for ARB prevention for the public. The evidence, catalogued at country-level, provided the content for a series of visualizations that allow assessment of the risk of AMR acquisition through travel.

Results: Up to January 2021, the database includes data on: (i) AMR surveillance for 2.018.241 isolates from 86 countries; (ii) ARB prevalence of carriage from 11.679 international travellers and (iii) 15 guidance documents published by major public health agencies. The evidence allowed the development of a consultation scheme for the evaluation of risk factors, prevalence of carriage, proportion and recommendations for screening of AMR. For the public, pre-travel practical measures to minimize the risk of transmission were framed.

Conclusions: This easy-to-use, annually updated, freely accessible AMR travel tool (https://epi-net.eu/travel-tool/overview/), is the first of its kind to be developed. For HCPs, it can provide a valuable resource for teaching and a repository that facilitates a stepwise assessment of the risk of AMR spread and strengthen implementation of optimized infection control measures. Similarly, for travellers, the tool has the potential to raise awareness of AMR and outlines preventive measures that reduce the risk of AMR acquisition and spread.

Key words: Surveillance, International travelling, AMR

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Background

Antimicrobial resistance (AMR) is a global public health issue that is limiting the ability to successfully treat infections. International travel has been recognized as one of the risk factors for the acquisition and spread of antibiotic-resistant bacteria (ARB),[1] together with human and animal antibiotic misuse, healthcare transmission, suboptimal antibiotic dosing and environmental contamination.[2]

At international, national and local levels, surveillance programs, implementation of infection prevention and control (IPC) measures and antimicrobial stewardship (AMS) interventions are recognized as key components of the AMR control strategies. Surveillance systems and repositories, such as the European Antimicrobial Resistance Surveillance Network (EARS-Net), the Global Antimicrobial Resistance Surveillance System (GLASS), the Centre for Disease Dynamics, Economics & Policy's (CDDEP) and the COMBACTE-MAGNET Epidemiology Network (EPI-Net), allow the monitoring of AMR through the timely sharing of data and provide a valuable source of information, particularly with regard to documenting trends in AMR at global level. So far, surveillance reports focusing on imported cases due to travelling are limited and recommendations on the ideal population among travellers to be targeted by screening activities are still to be defined.[3]

Constant monitoring and extraction of AMR data from surveillance systems is one of the mainstay of the COMBACTE-MAGNET EPI-Net project in the fight against the spread of AMR. AMR epidemiological data from surveillance systems across Europe are collected, regularly updated and made freely available through a web-based platform (www.epi-net.eu). Since its launch in September 2018, the EPI-Net platform is continuously developing new visualization tools to facilitate consultation of AMR data from different sources.

Although international travel has been recognized as a relevant contributing factor to AMR, no traveller-based clinical algorithms exist to support healthcare professionals (HCPs) decision-making in terms of IPC and AMS strategies to be adopted in the daily practice when dealing with individuals returning from travel.

With the purpose of retrieving and displaying data specifically focusing on AMR and international travel, a multi-pronged review of the literature was conducted, covering four key areas including AMR surveillance, ARB carriage and IPC guidance.

The collected evidence set the groundwork to build the framework of the 'AMR travel tool', an *ad hoc*, evidence-based, dynamic tool designed for both HCPs and international travellers. The AMR travel tool has been successfully integrated in the existing EPI-Net online platform.

Methodology

Data collection

Data were obtained through a comprehensive multi-step literature review covering the following four key areas:

i) Public access to national/international AMR surveillance databases and repositories reporting the most recent AMR data for invasive and non-invasive clinically relevant resistant isolates.
ii) epidemiological studies reporting prevalence data on ARB carriage in returning international travellers,
iii) guidance documents from main public health agencies published between January 2010–December 2020 reporting indications on screening for ARB in individuals returning from international travel,
iv) guidance documents and official websites reporting practical recommendations to prevent AMR targeting the public.

The target ARB were those listed at critical and high tiers in the World Health Organization (WHO)'s global Pathogen Priority List (PPL)[4]: carbapenem-resistant *Acinetobacter baumannii* (CRAB), carbapenem-resistant *Escherichia coli*, carbapenem-resistant *Klebsiella pneumoniae*, carbapenem-resistant *Pseudomonas aeruginosa* (CRPA), third-generation cephalosporins-resistant *E. coli*, third-generation cephalosporins-resistant *K. pneumoniae*, vancomycin-resistant *Enterococcus faecium* (VRE), methicillin-resistant *Staphylococcus aureus* (MRSA), fluoroquinolone-resistant (FQR) *Neisseria gonorrhoea*, FQR-*Salmonella spp*, FQR- *Campylobacter spp*, third-generation cephalosporins-resistant *Neisseria gonorrhoea*. The modified PICO inclusion/exclusion criteria and a comprehensive list of the variables collected for each key area is displayed in Supplementary Tables 1 and 2.

Search strategy

Mapping of surveillance systems and proportion of AMR. An existing list of national surveillance sources and international repositories (EPI-Net,[5]) including data on at least one of the target ARB (Supplementary Table 3) was updated and used to retrieve country-level data. The mapping update of the existing inventories was performed from January 2017 to December 2020 in English language. The list and the main characteristics of surveillance systems and networks identified for ARB data collection are summarized in Supplementary Table 3. Information on proportion of resistance for the target pathogens isolated from invasive or clinically relevant samples were extracted. When data on ARB targets could not be retrieved from surveillance reports, an additional pathogen-based search targeting the missing data for specific pathogens or countries was performed. Multicentre studies published between January 2017 and December 2020 reporting surveillance data for at least two hospital centres and for at least one continuous year were included. Reviews were excluded and used only to identify original research articles reporting proportion of resistance. When resistance data for less than 30 isolates were reported by a surveillance system or study, data were not extracted. The search terms used are listed in Supplementary Table 4, and the studies for which data were extracted are listed in Supplementary Table 5.

Prevalence of ARB carriage in returning travellers. A search for studies reporting data on carriage of ARB targets in individuals returning from international travel was conducted using PubMed database. Studies published between January 2015 and December 2020 in English language were searched using the following terms: ((('travel' OR 'migration' OR 'migrant' OR 'spread') AND ('antibiotic' OR 'drug' OR 'antimicrobial' AND resistant*) AND ('colonization' OR 'carriage')). No restriction by study type was

applied. Reviews were excluded and used only to identify original research articles reporting proportion of resistance in returned individuals.

Guidance documents on AMR screening in individuals with a history of travel. A literature search on the most relevant guidance documents reporting recommendations on screening activities among individuals with a history of travel was conducted using PubMed and Google search engine from January 2010 and December 2020 and was restricted to English language. The following search strategy was applied: ('antimicrobial resistance' OR 'antibiotic resistance' OR 'AMR' OR 'multidrug resistant-bacteria') AND 'screening' AND ('travel' OR 'international travel' OR 'travellers' OR 'transfer abroad') AND 'pathogen name' AND 'country name'. Clinical guidelines for ARB prevention and control that did not provide recommendations specifically targeting international travellers were excluded.

Practical recommendations for international travellers. Published literature from international public health societies and agencies, such as the WHO, ECDC and CDC providing practical recommendations dedicated to preventing the risk of acquiring ARB, were comprehensively reviewed. General information on AMR and practical recommendations were additionally searched through Google search engine using the following combination of terms: 'antimicrobial resistance' AND ('international travel' OR 'travel health') AND ('education*' OR 'advice').

Data synthesis, tool design and validation process

The data collected were grouped at country-level and used to develop a graphical consultation tool to be integrated in the already established COMBACTE-MAGNET EPI-Net website.

In order to optimize the communication of the web tool content to the target audience, a beta version was sent for revision and approval to a panel of 12 experts in AMR surveillance from all over the world and to the Patient and Public Involvement (PPI) panel of COMBACTE-MAGNET.[6]

The primary structure of the tool is centred on a straightforward query of 'base country' and 'country of travel' to output in two separate user-specific sections: (a) decision support for HCPs and (b) pre-travel educational indications for travellers. Raw data from target knowledge sources were collected and transformed into a stepwise decision aid to guide HCPs in considering the overall risk factors associated with travel, proportion of resistance and colonization rates related to travel destinations, and indications to screen patients. Qualitative data were tabulated while quantitative data were charted on bar graphs, sunburst plots or interactive matrices, and the main information displayed by ARB type. The studies on AMR carriage are graphically displayed using bar charts that underline the number of travellers identified as carriers upon return from travel in a specific country of destination. Surveillance data are shown in two different visualizations: (a) sunburst plots displaying the country-to-country differences in the proportion of AMR and (b) interactive infographics that show matched country-to-country AMR proportions using colour to represent the scale of the difference. All the displayed graphics are freely downloadable through the website.

Likewise for travellers, a series of practical recommendations on how to minimize AMR acquisition during travel and ARB-specific infographics were developed as freely downloadable, printable and user-friendly flyers summarizing: pathogens, at-risk populations, the level of risk, route of transmission and key tips on how best to prevent infections during planned travel.

Results

AMR surveillance data availability worldwide

The mapping and review retrieved a total of 12 surveillance systems and two international repositories reporting data on the 12 ABR targets. Data were extracted from: the COMBACTE-MAGNET EPI-Net and CDDEP repositories, which include several surveillance systems and sources; four international surveillance systems, namely GLASS, EARS-Net, FWD-Net and Euro-GASP; seven national surveillance systems, namely AGAR-AURA (Australia), ANRESIS (Switzerland), CARA (Canada), CARSS (Canada), ICMR (India), Ministry of Health New Zealand (New Zealand) and SWEDRES (Sweden); and eight surveillance studies.[7–14] Out of 436 papers screened, eight studies met inclusion criteria. Overall, data for a total of 2.018.241 isolates from 86 countries were extracted. Publicly accessible surveillance data on the ARB target are lacking in 111 countries.

Eleven surveillance systems/repositories (1.707.410 isolates, 84,6% of the data retrieved) reported data for high-income countries (HIC), three (238.514 isolates, 11,8%) for upper middle-income countries (UMIC), three (65.181 isolates, 3,2%) for lower middle-income countries (LMIC) and two (7.136 isolates 0,4%) for low-income countries (LIC). The most comprehensive surveillance systems in terms of ARB and countries monitored were the ones from WHO (GLASS) and ECDC (EARS-Net). The list of countries, surveyed bacteria and sources are detailed in Supplementary Tables 3 and 5.

The most commonly surveyed bacterial phenotypes were third-generation cephalosporin-resistant (3GCR) enterobacterales (3GCRE) and carbapenem-resistant enterobacterales (CRE) (35,5 and 36,5% of the entire data collection of tested isolates, respectively) followed by MRSA (12,9%) and CRAB (1,9%). CRPA and VRE were monitored by four surveillance systems/repositories with 2,5 and 2,0% of tested isolates, respectively. FQR- and/or 3GCR *N. gonorrhoea* and FQR *Salmonella* spp and *Campylobacter* spp were included in a limited number of surveillance systems (five systems, 1,5% of tested isolates; four systems, 1,6% of tested isolates; eight systems, 2,7% of tested isolates and four systems, 2,8% of tested isolates, respectively). The overall proportions of resistance, current gaps in data reporting and availability, are shown in Figure 1.

Prevalence of carriage of antibiotic-resistant bacteria in individuals returning from international travel

The literature search retrieved 368 articles, which were assessed for eligibility. Thirty-four studies were included and resistance data extracted, accounting for data from overall 11.679 international travellers tested.[15–48] All the included studies were conducted in HIC, mostly in Europe (29/34, 85%). Twenty-four (71%) prospectively enrolled individuals before their departure.

Figure 1. Proportion of antimicrobial resistance (AMR) worldwide, stratified by country and displayed by ARB type and specimen. In bold the percentage of resistance is reported, in parenthesis is reported the year to which data refer. The number of tested isolates for each ARB target is shown in Supplementary Table 3. On the right side (grey) the income-status of each country is displayed (HIC: high-income country, UMIC: upper medium-income country, LMIC: lower medium-income country, LIC: low-income country). Warm-to-cool colour scheme corresponds to numerical data of resistance rates for each ARB target, with warm colours representing high-value resistance data points and cool colours representing low-value data points.

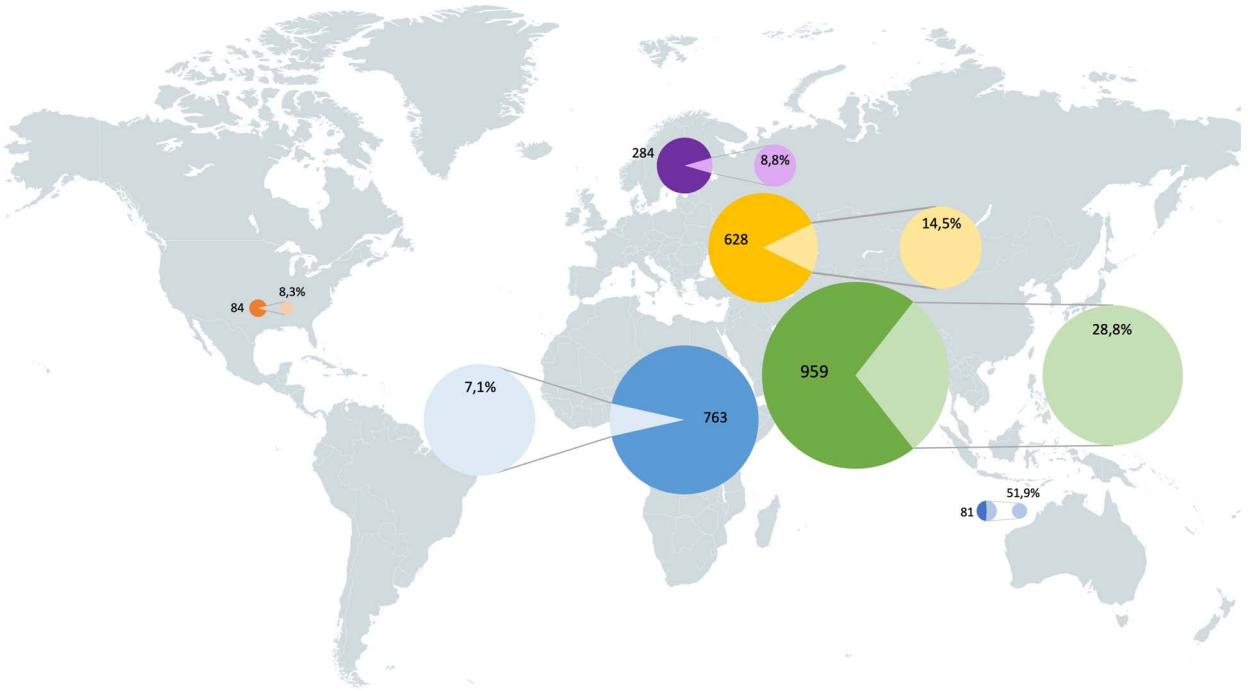

Figure 2. Data on carriage of third generation cephalosporin-resistant Enterobacterales in international travellers returning from six world regions: African Region (light blue), Eastern Mediterranean Region (yellow), European Region (purple), Region of the Americas (orange), South-East Asian Region (green) and Western Pacific Region (blue). Total number of travellers reported visiting the world regions and the corresponding percentage of antimicrobial-resistant bacteria upon return are displayed. The dimension of the pie charts corresponds to the sample site (number of travellers tested).

The length of stay abroad was specified in 19 (56%) studies and reported as mean value of the study population.

Overall, 30 studies (88%) assessed colonization risk for 3GCRE, eight (24%) for CRE, three for MRSA, two for VRE and one for CRAB. The pre-travel colonization status was reported in 17/24 (71%) of the prospective studies. Among them, 3GCRE acquisition rate was 31,6% and CRE acquisition rate was 0,7%. Figure 2 shows the overall colonization rate of returning travellers with 3GCRE carriage for six different world regions: African Region, Eastern Mediterranean Region, European Region, Region of the Americas, South-East Asian Region and Western Pacific Region.

Guidance documents on AMR screening in returning travellers

The search retrieved 15 documents meeting the inclusion criteria.[49–63] Among them, four (27%) were published by three main international agencies: WHO, ECDC and CDC, while eleven documents (73%) were national or regional guidance documents, all of which (with the exception of South Africa) were from HIC. The indications were grouped by drug-resistant bacteria species and presented as follows: (i) 'who to consider for screening': recommendations provided for individuals with/without hospitalization abroad (ii) 'when to screen': recommendations specifying the screening timeframe and (iii) 'what screening': recommendations detailing screening sites (Table 1).

Thirteen out of 15 documents provide indications on screening activities in returning travellers for Gram-negative resistant bacteria (Table 1). Specifically, indications for CRE were described in 12 documents (80%), for CRAB and CRPA in two documents (13%) and for 3GCE in three documents (20%). Indications for screening for Gram-positive-resistant bacteria were reported in five documents: three (27%) and two (13%) documents on MRSA and VRE, respectively. No specific screening recommendations related to returned travellers were found for the remaining ARB target.

Seven documents suggested screening all returning travellers from 'high-risk' countries: three documents further detailed which countries, while four documents referred to 'high endemic' settings. None of these documents clearly explain resistance rates, thresholds for empiric therapy, or definitions of 'high-risk' populations or 'high endemic' countries.

The most common criteria considered in the guidance documents were hospitalization abroad, country of travel, and time since hospitalization abroad. Eleven out of 15 (73%) documents specify the ideal timeframes to screen travellers that had been previously hospitalized abroad (Table 1). For CRE, seven guidance documents recommend to screen patients that were hospitalized abroad within the preceding 12 months. Regarding MRSA, one document recommends to screen patients within 6 months, and two documents recommend a timeframe of 12 months from hospitalization abroad. For VRE, one document indicates to screen individuals within 12 months from hospitalization.

The majority of the documents (10/15, 67%), do not specify whether and how often screening should be performed among individuals with a history of international travel that were not hospitalized during the trip.

Table 1. List of the 15 guidance documents included in the review and summary of the main information collected

	Guidance document title	Agency	Country/Year region	Pathogen	Who? Screening recommendations for individuals non-hospitalized abroad	Who? Screening recommendations for patients hospitalized abroad	When? Screening timeframe	What? Screening procedure (site)
1	Risk assessment on the spread of carbapenemase-producing Enterobacteriaceae (CPE) through patient transfer between healthcare facilities, with special emphasis on cross-border transfer	ECDC	Europe 2011	CRE	Not detailed	Screening for CPE strongly recommended for any patient transferred across borders into a healthcare facility.	Not detailed	Rectal
2	Risk assessment on ESBL-E in transfer between facilities with emphasis on cross-border transfer based on systematic review	ECDC	Europe 2014	3GRE	Not detailed	Screening to be considered for individuals that have been admitted in hospitals/wards abroad.	Not detailed	Rectal
3	Infection prevention and control measures and tools for the prevention of entry of carbapenem-resistant Enterobacteriaceae into healthcare settings: guidance from the European Centre for Disease Prevention and Control	ECDC	Europe 2017	CRE	Not detailed	Screening recommended for any patient with a history of overnight stay in a healthcare setting, regardless of country visited	Within 12 months	Rectal or perirectal, any other site, which is either actively infected, e.g. draining wounds or considered to be colonized
4	Guidelines for the prevention and control of carbapenem-resistant Enterobacteriaceae, *Acinetobacterbaumannii* and *Pseudomonas aeruginosa* in health care facilities	WHO	Global 2017	CRE	Not detailed	Screening recommended for patients that have been hospitalized in 'endemic areas'	Not detailed	Faeces, rectal swabs, perianal
				CRAB, CRPA	Not detailed	Not reported, further research is needed	Not detailed	Not detailed
5	Carbapenemase-producing Enterobacteriaceae (CPE). New Regulations for Reporting CPE	Public Health Ontario	Canada 2019	CRE	Consider screening individuals who travelled to India, Pakistan, Bangladesh, USA	Screening to be considered for patients that have been hospitalized abroad (particularly in India, Pakistan, Bangladesh, USA)	Not detailed	Stool or rectal
6	Screening, testing and surveillance for antibiotic-resistant organisms (AROs)	Public Health Ontario	Canada 2013	CRE	Consider screening individuals who travelled to Bangladesh, Bhutan, India, Maldives, Nepal, Pakistan, Sri Lanka	Screening recommended for individuals who received care in hospitals in USA-especially eastern seaboard region (e.g. New York City), Greece, Israel, Indian subcontinent (e.g. India, Sri Lanka, Bangladesh, Pakistan) and in any hospital that has reported transmission of CPE	Within 12 months	Stool, rectal or urine, wound, endotracheal suction (critical care), exit sites (critical care)
				3GRE	Not detailed	Screening recommended for individuals hospitalized abroad, regardless of country visited	Not detailed	Rectal, stool or urine
				MRSA	Not detailed	Screening recommended for individuals hospitalized abroad, regardless of country visited	Within 12 months	Anterior nares (both nares with one swab), perianal/ perineal skin or groin, open wounds/lesions/incisions, exit sites of indwelling devices
				VRE	Not detailed	Screening recommended for individuals hospitalized abroad, regardless of country visited	Within 12 months	Stool or rectal

(Continued)

Table 1. (Continoued)

	Guidance document title	Agency	Country/ region	Year	Pathogen	Who? Screening recommendations for individuals non-hospitalized abroad	Who? Screening recommendations for patients hospitalized abroad	When? Screening timeframe	What? Screening procedure (site)
7	Guidance on preventing the spread of MRSA, 3rd Edition	Danish Health Authority	Denmark	2016	MRSA	Not detailed	Screening recommended for individuals hospitalized abroad, regardless of country visited	Within 6 months	Nasal, throat (tonsils), perineum (for hospitalized patients and citizens in 24-hour care)
8	Recommendations for the control of carbapenemase-producing Enterobacteriaceae (CPE). A guide for acute care health facilities	The Australian Commission on Safety and Quality in Health Care	Australia	2017	CRE	Screening is not recommended	Screening is recommended for individuals who have been directly transferred from an overseas hospital, or who have been recently in an overseas hospital; screening to be considered for staff who have worked in overseas hospitals	Within 12 months	Rectal swabs, faeces
9	Australian guidelines for the prevention and control of infection in healthcare	NHMRC		2019	CRE	Consider screening individuals who travelled to areas of high endemicity	Screening recommended for individuals hospitalized abroad, regardless of country visited	Within 12 months	Rectal, faeces or urine from catheterised patients, wounds, aspirates from any tubes or drains
					3GRE	Consider screening individuals who travelled to areas of high endemicity	Screening recommended for individuals hospitalized in 'endemic areas'. Screening on admission to be considered regardless of country visited	Not detailed	Rectal or perianal, nasal, groin, wounds, ostomy sites and respiratory secretions or tracheal aspirates depending on the infectious agent
					CRAB, CRPA	Consider screening individuals who travelled to areas of high endemicity		Not detailed	Rectal or perianal, nasal, groin, wounds, ostomy sites and respiratory secretions or tracheal aspirates depending on the infectious agent
					MRSA	Not detailed	Screening recommended for individuals, regardless of healthcare facilities and country visited	Not detailed	Nasal and other mucosal surface; wounds, sites of catheters, urine, ostomy sites, groin/perineum, tracheostomy and other skin break; umbilicus in all neonates
					VRE	Not detailed	Screening recommended for individuals hospitalized abroad, regardless of country visited	Not detailed	Rectal or perianal, groin, wounds, ostomy sites and respiratory secretions or tracheal aspirates
10	Facility Guidance for Control of carbapenem-resistant Enterobacteriaceae (CRE)	CDC	USA	2015	CRE	Not detailed	Screening recommended for individuals hospitalized in 'endemic areas'	Not detailed	Stool, rectal or peri-rectal
11	Acute trust toolkit for the early detection management and control of CPE	PHE	UK (England)	2013	CRE	Not detailed	Screening is recommended for individuals hospitalized in Bangladesh, the Balkans, China, Cyprus, Greece, India, Ireland, Israel, Italy, Japan, North Africa, Malta, Middle East, Pakistan, South East Asia, South/Central America, Turkey, Taiwan, USA, and UK regions/areas where problems have been noted (North west especially Manchester, London). Screening to be considered also for patients on admission regardless of country visited.	Within 12 months	Rectal or stool
12	Framework of actions to contain carbapenemase-producing Enterobacterales			2020	CRE	Not detailed	Screening for CPE is recommended in case of hospital admission overseas or in case of direct transfer from hospital abroad	Within 12 months	Rectal
13	Toolkit for the early detection, management and control of carbapenemase-producing Enterobacteriaceae in Scottish acute settings	HPS	UK (Scotland)	2016	CRE	Not detailed	Screening is recommended for patients hospitalized outside Scotland	Within 12 months	Rectal or stool
14	Prevention and control methicillin-resistant *Staphylococcus aureus* (MRSA)	HPSC	Ireland	2014	MRSA	Pre-employment screening is recommended when prior workplace was in a country recognized to have specific problems with high rates of MRSA	Screening is recommended for patients transferred from a hospital abroad or patients who have been an in-patient in a hospital abroad	Within 12 months	Swabs from nose, perineum/groin, throat, areas of broken skin and urine if a urinary catheter is present
15	The SASCM CRE-WG: consensus statement and working guidelines for the screening and laboratory detection of carbapenemase-producing Enterobacteriaceae	DHET	South Africa	2014	CRE	not detailed	Screening is recommended to any patient hospitalized abroad, particularly on the African continent, but also in non-African countries	Within 3–6-12 months	Stool

All guidance documents mention the recommended sampling procedure and underline the fact that, in parallel to the targeted screening activities, adherence to universal IPC measures reduces the potential for horizontal transmission. Table 1 summarizes the information collected from the included guidance documents.

Tool design

After approval from both the panels involved, the tool was made available for free consultation in January 2021 (https://epi-net.eu/travel-tool/overview/). Its structure is characterized by two main parts, one dedicated to the HCPs and the other to international travellers. A flow chart on how the consultation tool can be assessed by HCPs in daily practice is shown in Figure 3, and two hypothetical scenarios for application are presented in Figure 4a and b. In detail, the HCPs-dedicated part is structured in five different sections:

i) general factors, tabulated as list of factors to be assessed in order to rapidly drive users through the main AMR-related risk factors when dealing with a patient recently returned from international travel (Supplementary Figure 1);
ii) proportion of ARB in clinical isolates, shown in two different visualizations: a) sunbursts displaying the country-to-country differences in AMR rate by ARB type, and a series of interactive matrices (one for each ARB) showing the 'match' between home countries and countries of destination in terms of AMR rate difference, with the colour in each cell displaying the scale of this difference. The two types of visualizations can support clinical decisions on starting the appropriate empiric therapy or implementing screening strategies and/or infection control measures (Supplementary Figures 2 and 3);
iii) prevalence of carriage in returning travellers, charted on bar graphs and displayed by ARB type that can further support healthcare providers' decisions (Supplementary Figures 4 and 5);
iv) guidance documents on screening, including international, national and regional, for which the availability and main information are displayed by ARB type (Supplementary Figures 6 and 7).

The travellers section is organized to provide information on AMR and tips that can help to avoid potential ARB colonization/infection during travel.

Discussion

The risk for AMR acquisition in travellers is multi-faceted and should take into account a range of factors including epidemiological data (e.g. resistance rates of destination country) as well as individual-level features, such as the type of travel and the planned length of stay. From a clinical perspective, an assessment of the AMR risk by HCPs represents an important part of the diagnostic evaluation of a patient with history of travel who requires hospital admission. However, specific risk-based guidelines are not available, and a thorough assessment of available sources, to estimate the risk is time-consuming and not feasible in current daily practice for each patient. Through a multi-step literature review and surveillance data on 12 ARB listed as critical and high tiers in the WHO PPL, we have developed an evidence-based consultation tool targeting both HCPs and the general public. The primary objective of this tool is to prevent ARB acquisition and spread and to support HCPs when clinically assessing international travellers. To our knowledge, this is the first educational and consultation tool dedicated to the risk assessment for ARB acquisition among international travellers that can facilitate HCPs' sequential evaluation of AMR risk factors, prevalence of ARB carriage, proportion of AMR and recommendations for appropriate screening. In the clinical context, the AMR travel tool represents a valid support for HCPs in driving proper IPC strategies (e.g. should I screen the patient for ARB colonization? Should I isolate the patient?) and appropriate empiric antibiotic treatment (e.g. should the initial antibiotic therapy cover ARB?).

From the traveller perspective, preventing colonization through active advice from HCPs has been suggested as a possible approach to limit travel-related spread.[64] The AMR travel tool is also designed, to provide information and advice directly to the traveller on prevention measures that can be adopted to limit travel-related AMR acquisition.

The tool delivers an easy-to-access and comprehensive overview of: (i) AMR surveillance data from 86 countries (44% of the 197 countries worldwide); (ii) recommendations on screening for ARB compiled from major public health agencies ($n = 15$ documents); (iii) ARB carriage data from returning international travellers across all continents ($n = 34$ studies) and (iv) information on AMR for the public.

The included studies on ARB carriage are a valuable source of information that can complement data from surveillance systems, further define AMR prevalence in both healthcare and community settings and support strategies to reduce AMR acquisition risks during travel. Consistently with previously reported data for antibiotic-resistant Enterobacteriaceae[65] and considering only the studies in which individuals were confirmed to not be colonized before travelling, the acquisition rate associated with travel reported for 3GCE was 31,6 and 0,6% for CRE. There are a number of limitations that were identified during our literature revision. Most of the published data on ARB carriage were aggregated by world regions or continents, and were not available for country-level stratification. Therefore, we could only group AMR data at country level for 17 studies (50% of the included publications), and provide by-country visualization on the tool. Additionally, the majority of the included studies did not report length of travel (16/34, 47%) or hospitalization abroad (27/34, 79%). Determining whether a returned traveller had been hospitalized abroad is an important factor to be evaluated in returning travellers and this information should be included in the epidemiological studies focused on ARB acquisition.

Although it is clear that international travel contributes to the spread of AMR across countries,[1,65] current evidence does not provide detailed recommendations for individuals returning to their home country. The majority of the included guidance documents recommend to screen all returned travellers who had a hospital admission whilst abroad, irrespective of the country visited or the length of time spent abroad. Evidence suggests that universal screening of returned travellers with a prior hospitalization may not be the most cost-effective[66] and feasible approach.

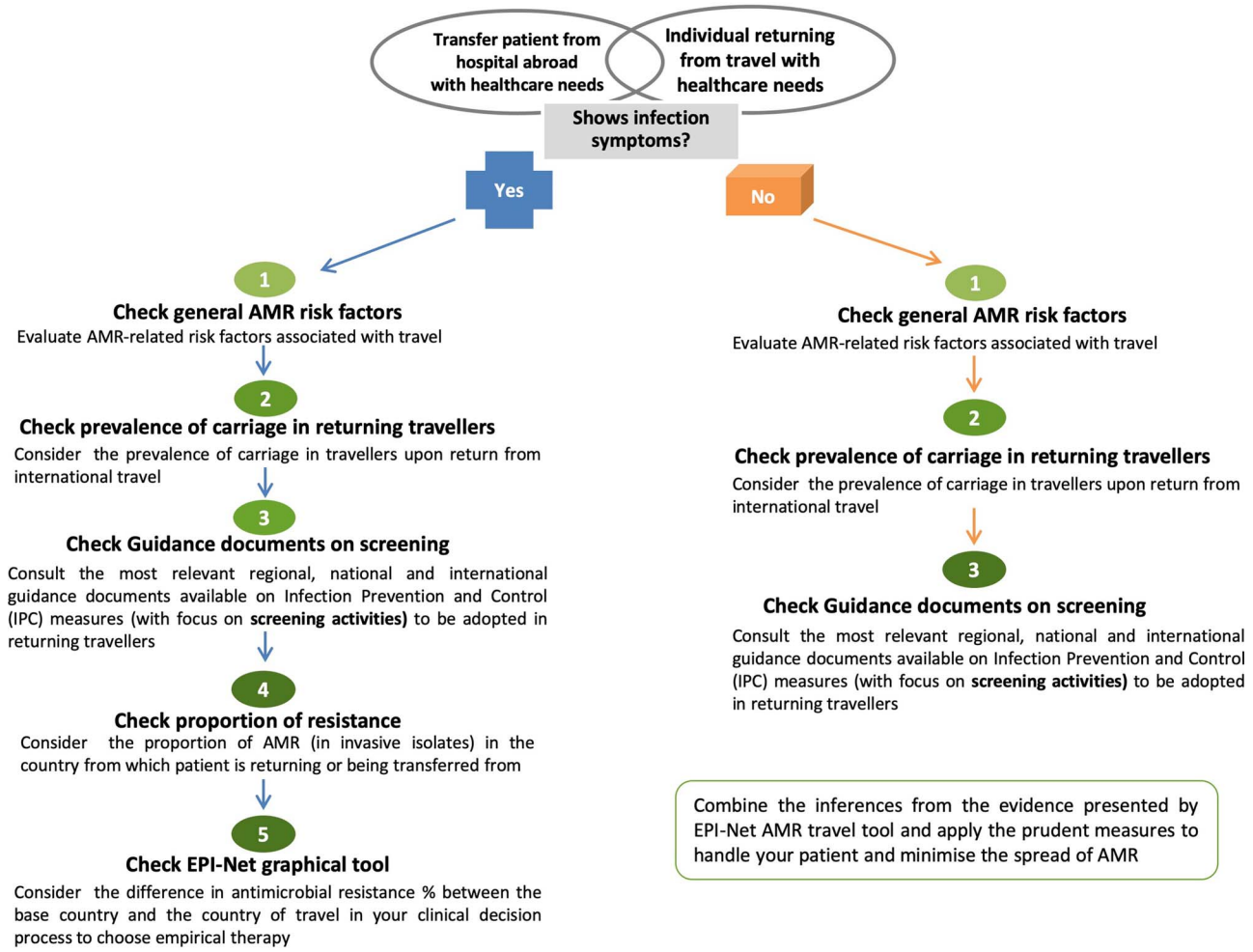

Figure 3. The flow chart presents how the different sections of the online tool can be used by health care professionals.

Despite the limited number of available guidance documents and studies focused on carriage in returning travellers (particularly for LMIC/LIC), collected evidence was used to develop a consultation webtool characterized by a series of interactive visualizations.

The interactive visualizations targeting the HCPs originate from surveillance data on AMR that are still fragmentary. In fact, a major limitation of the tool is the absence of AMR data from many countries. Only for 44% of the world countries, we were able to find surveillance data and for some of them, the number of tested isolates was less than one hundred (Supplementary Table 3). Therefore, the data provided should be interpreted with caution and as a means to accessing additional information or as educational material for teaching and in the process of clinical decision. However, current and future efforts in AMR surveillance at global level will allow to evaluate outcomes of the tool and confirm its intended benefit. The data collected were also used to frame recommendations on AMR for the general public, displayed in the international travellers-dedicated section of the tool. The information provided includes pre-travel recommendations as follows: (i) general advice (e.g. 'only use antibiotics when prescribed by a certified healthcare professional' and 'never share or use leftover antibiotics, complete the full treatment course') and (ii) ARB-specific information such as pathogen description, acquisition risks, route of transmission and tips to prevent infections that are presented in downloadable sections and infographics. A practical example is shown in Supplementary Figure 8.

All the different sections of the tool have been submitted to, revised and approved by a panel of experts on AMR surveillance and by members of the PPI panel of COMBACTE-MAGNET, and made available online. The information provided by the tool will be updated annually to continuously improve their performance and reliability. Ecraid (www.ecraid.eu), as the successor of the COMBACTE project, offers an avenue to the future sustainability of the AMR travel tool.

Conclusions

Our work highlights the value of consolidated AMR surveillance data and of infection prevention and control guidelines to contain the spread of ARB through international travel. Additionally, it shows how such data, combined with indications on screening and reinforced by epidemiological information on carriage of

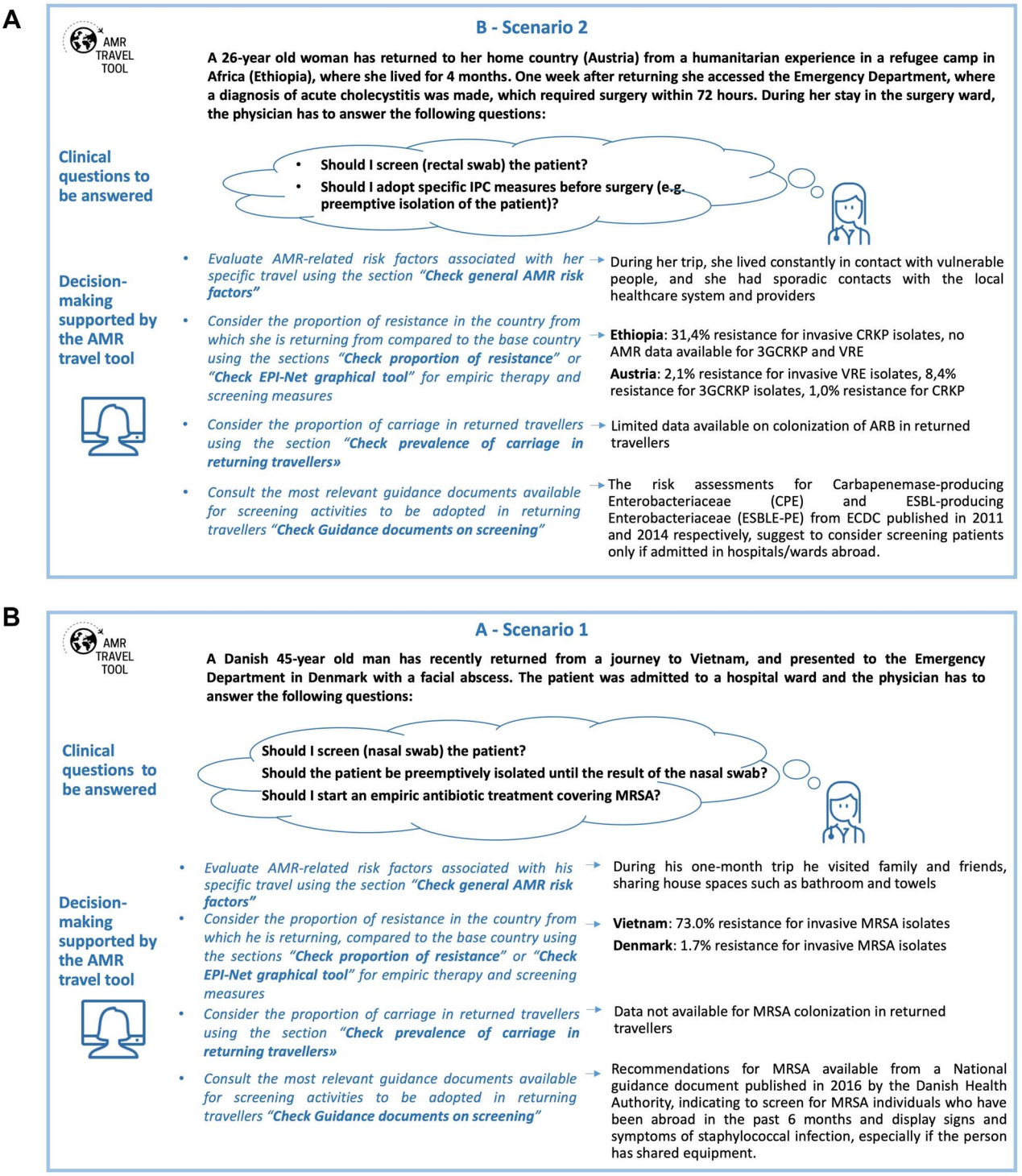

Figure 4. Hypothetical scenario 1 (4a) and hypothetical scenario 2 (4b) on how the tool can practically be used by healthcare professionals.

ARB in returning travellers, can be used to create a framework that supports clinical practice and the delivery of preventive messages to the public at large. All these aspects are crucial to fight the silent pandemic of AMR and its spread across countries. The AMR travel tool represents the first evidence-based tool driven by publicly available surveillance data and individual-level data that supports decision-making processes of HCPs treating returned travellers. The AMR travel tool is easy-to-use, periodically updated and freely accessible on https://epi-net.eu/travel-tool/overview/. The tool can prospectively have an impact at three different levels: (i) strengthening the implementation of optimized IPC measures in hospital and community

settings when an international traveller is admitted to hospital or examined by a general practitioner; (ii) increasing knowledge of global AMR epidemiological data and making knowledge available for decision-making on personalized antibiotic therapies, screening activities and guidelines development; (iii) raising awareness on the travel-related risks associated with AMR, and the importance of limiting the spread of AMR whilst preserving antibiotics for future generations. These considerations may prove even more pressing in light of a future scenario of the upcoming 'post-COVID era', when international travel will be restored.

Meeting at which the paper has been presented

European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) 2021, ePoster.

Author contributions

ET, FA conceived the idea for this project. FA, MS, AS and MDP designed the study. FA, AS, MT and TW contributed to literature research, data collection and analysis. FA and NBR developed the tool structure and visualizations. AG contributed to the visualizations and data analysis. FA wrote the first draft of the paper. All authors contributed to the manuscript revision and finalization. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Supplementary data

Supplementary data are available at *JTM* online.

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Conflict of Interest

The authors have declared no conflict of interest.

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