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## Review

# Human Mobility and the Global Spread of Infectious Diseases: A Focus on Air Travel

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Greater human mobility, largely driven by air travel, is leading to an increase in the frequency and reach of infectious disease epidemics. Air travel can rapidly connect any two points on the planet, and this has the potential to cause swift and broad dissemination of emerging and re-emerging infectious diseases that may pose a threat to global health security. Investments to strengthen surveillance, build robust early-warning systems, improve predictive models, and coordinate public health responses may help to prevent, detect, and respond to new infectious disease epidemics.

#### Human Mobility and the Spread of Infectious Diseases

Increases in the global mobility of humans, nonhuman animals, plants, and products are driving the introduction of infectious diseases to new locations. In recent years we have witnessed several infectious diseases spread well beyond their previously understood geographic boundaries, as was demonstrated by the introduction of Zika virus to the Americas. We have also witnessed the emergence and spread of novel pathogens, such as the discovery of a previously unknown Middle Eastern respiratory syndrome coronavirus (MERS-CoV) in Saudi Arabia spreading to distant countries such as South Korea [1].

Many factors contribute to the global spread of infectious diseases, including the increasing speed and reach of human mobility, increasing volumes of trade and tourism, and changing geographic distributions of disease vectors. In particular, human travel and migration (especially via air travel) is now a major driving force pushing infections into previously nonendemic settings. Year by year, there are increasing numbers of international tourists [2], more international refugees and migrants [3], greater capacity for shipping by sea [4], and greater international air travel passenger volumes [5]. Air travel poses a growing threat to global health security, as it is now possible for a traveler harboring an infection in one location on earth to travel to virtually any other point on the planet in only 1–2 days. Infections introduced via travel may be sporadic and have little potential for further transmission, such as Lassa fever introduced into European settings [6]. In other situations, infections introduced by air travel may cause self-limited local epidemics such as Chikungunya virus in Italy [7]. More recently, there are a growing number of examples of infections introduced to a new region that ultimately become endemic, such as Chikungunya virus in Latin America and the Caribbean [8].

Vector-borne infections, including arthropod-borne viruses (arboviruses) present unique challenges as disease vectors such as mosquitoes can be carried overland, in boats, or on planes, and may travel between any two points on the globe within their lifespan. Such vectors have the potential to infect nontravelers in their new destination, as is seen in airport malaria [6]. Even if a vector is not infected, that vector may become endemic to a new region if there are suitable environmental conditions, and then potentially enable future epidemics. The most well-known example of this is the now-global distribution of *Aedes aegypti* and *Ae. albopictus* mosquitoes,

#### Highlights

The volume of global air travel continues to increase annually, and passengers have the capacity to introduce infections to new regions in short time frames.

Infections transported through air travel may initiate or facilitate epidemics.

Front-line healthcare providers and public health teams require training and tools to properly identify and respond to infectious diseases transported through air travel, some of which may have epidemic potential.

Developing more effective global surveillance tools and mechanisms to better communicate and coordinate between countries can facilitate more rapid and effective responses to epidemics.

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the vectors responsible for a number of arbovirus infections including dengue, Chikungunya, and Zika viruses [9]. Vector introduction is further facilitated by ecological factors, such as climate change and urbanization, that may enable vectors to flourish in new regions.

Clinical and public health care providers must be aware of the fluid boundaries of infectious diseases and be cognizant of the potential for imported infections. Front-line healthcare providers must now have knowledge of an increasingly broad spectrum of emerging illnesses from around the world, and public health teams must be prepared to respond to individual cases that have epidemic potential (e.g., Ebola virus), and coordinate responses at local, national, and international levels. Preparation for planning mass gatherings, such as large sporting events or an annual religious pilgrimage, require special consideration for the potential of these events to contribute to global outbreaks. Here, we outline emerging and re-emerging infectious diseases that are spread via human mobility, with a focus on air travel. We discuss sporadic cases and localized epidemics, international epidemics, and then focus on clinical and public health implications.

## Air Travel Contributing to Sporadic Travel-Related Infections of Epidemic Potential, and to Localized Epidemics

Travel-related illnesses are common and mostly mild and self-limited, such as traveler's diarrhea. However, the list of infections imported by returned travelers is growing [10], and many are capable of causing local epidemics (Table 1).

#### Malaria

Despite a global push for eradication, malaria continues to cause significant global morbidity and mortality. This protozoal vector-borne infection is transmitted to humans by the bite of infected *Anopheles* mosquitoes that are found in many tropical and temperate countries [11]. Malaria is a common cause of febrile illness in returned travelers [12], and delays in diagnosis may lead to poor patient outcomes, including death [13]. The incubation period varies from weeks to more than a month depending on the species, which frequently contributes to the delayed diagnosis of imported cases.

Airport malaria, where non-travelers near airports are infected by mosquitoes that have been imported by air travel [14], is a challenging diagnosis as local clinicians may not suspect this infection. Although the spraying of arriving planes has reduced the incidence of cases, it continues to be a concern as volumes of travel continue to increase [15] and case reports of malaria in non-travelers continue to grow [16]. Regions that have eradicated malaria but still have *Anopheles* vectors present are at risk of malaria reintroduction, for example in Sri Lanka [17].

The global distribution of drug-resistant malaria is also changing, and strains of multidrugresistant *Plasmodium falciparum* appear to be spreading [18]. Although multidrug-resistant strains are still generally rare, there is growing concern that such strains may expand beyond their current boundaries through boat and air travel, heightening the need for better surveillance.

#### Schistosomiasis

Chronic infection with schistosomiasis is associated with gastrointestinal or urogenital pathology [19]. Schistosomiasis is acquired via contact with contaminated fresh water and requires specific snail intermediate hosts for disease transmission [19]. Locally acquired cases of schistosomiasis were discovered recently in France, and these were most certainly introduced



## Table 1. Recent Emerging and Re-emerging Infectious Diseases of Global Health Significance, Whose Spread Was Facilitated by Air Travel

Origin (Year)	Destination
Mexico (2009) [48]	Pandemic [50]
South Asia (2002, 2008)	Haiti epidemic (2010) [117]
India (2009) [84]	Australia, Austria, Belgium, Canada, China, Croatia, Czech Republic, Denmark, France, Germany, Ireland, Italy, Japan, Kuwait, Lebanon, The Netherlands, New Zealand, Norway Oman, Singapore, South Africa, Spain, Sweden, Switzerland, Taiwan, Turkey, United Kingdom, USA [85]
China (2014) [118]	Algeria, Argentina, Belgium, Brazil, Cambodia, Canada, China, Denmark, Egypt, France, Germany, Great Britain, Italy, Japan, Laos, Lithunia, Malaysia, The Netherlands, Nigeria, Poland, Portugal, South Africa, Spain, Switzerland, Taiwan, Thailand, Tunisia, USA, Vietnam [87]
Primarily Southeast Asia (1950s) [55]	Global emergence over the past five decades [55]
Saudi Arabia (2012) [25]	Epidemics in South Korea and Saudi Arabia, with cases detected in Algeria, Austria, China, Egypt, France, Germany, Greece, Iran, Italy, Jordan, Kuwait, Lebanon, The Netherlands, Oman, Philippines, Qatar, Thailand, Tunisia, Turkey, Turkey, United Arab Emirates, United Kingdom, USA, Yemen [119]
Africa and Asia [69]	First detected in Latin America and the Caribbean in 2015 with ongoing transmission in the South Pacific, Latin America and the Caribbean [71]
Asia and Africa [8,121]	Latin America and the Caribbean in December 2013 with ongoing transmission in this region [120], and autochthonous cases in Europe [60]
Southern China (2002) [22]	Epidemics in Hong Kong, Canada, USA, Vietnam, Singapore,
	Philippines, and Mongolia [22]
	Origin (Year)Mexico (2009) [48]South Asia (2002, 2008)India (2009) [84]China (2014) [118]China (2014) [118]Primarily Southeast Asia (1950s) [55]Saudi Arabia (2012) [25]Africa and Asia [69]Asia and Africa [8,121]

by travelers from endemic settings in Africa [20]. Snails local to Corsica were found to be competent hosts of *Schistosoma haematobium*, *Schistosoma bovis*, and hybrids of the two infections. There is the potential for further disease expansion given ongoing human travel and migration from schistosomiasis-endemic regions to nonendemic areas with the requisite intermediate snail hosts.



#### Air Travel Contributing to International Epidemics and Pandemics

Air travel has contributed to several epidemics of global health significance in recent years. Typically, an infected individual, either symptomatic or within an incubation period, flies to a distant location and introduces this infection to the local population. Below, we discuss major international epidemics relevant to air travel after 2000.

#### Severe Acute Respiratory Syndrome (SARS)

The severe acute respiratory syndrome (SARS) outbreak of 2002–2003 is an example of an emerging infection causing several simultaneous epidemics in noncontiguous geographic regions. SARS is a respiratory tract infection caused by a zoonotic coronavirus (SARS-CoV), and is thought to have arisen in horseshoe bats and subsequently transmitted to humans through civets as intermediate hosts [21].

The 2002 SARS epidemic originated in southern China and spread via air travel to 29 countries, causing local epidemics in Hong Kong, Taiwan, Canada, Singapore, Vietnam, and the Philippines [22]. The global epidemic lasted about 8 months, with 8096 probable cases and 774 deaths for a case-fatality rate of 10% [22]. SARS caused widespread panic and cost an estimated US\$11 billion worldwide [23]. Although the public health response was swift and ultimately effective, this epidemic highlighted the need for increased international cooperation in the era of rapid global transit. This epidemic spurred revisions to the International Health Regulations (IHR) and introduced the most significant changes since their adoption [24].

#### Middle East Respiratory Syndrome (MERS)

Another novel zoonotic respiratory coronavirus, MERS-CoV, originated in Saudi Arabia in 2012 [25]. Its reservoir is thought to be the dromedary camel. Similar to SARS-CoV, MERS-CoV causes a respiratory infection, though with a higher case-fatality rate of about 35% [26].

Since 2012, over 2000 cases have been detected in 27 countries. South Korea experienced the largest epidemic outside of Saudi Arabia, which was initiated by a single infected business traveler returning from that country. This one index case at a single hospital resulted in an additional 184 confirmed cases at 17 hospitals, and caused 33 deaths before the epidemic ended 2 months later [27]. Infection risk appeared to be primarily through hospital-based contact and fomites rather than through household contacts [28].

Although the virus is thought to have low epidemic potential, epidemics such as the one in South Korea are not unexpected [29]. There are a number of countries at risk of importing cases via air travel due to close trade and tourism ties to Saudi Arabia [30]. Additionally, the annual Hajj pilgrimage brings millions of pilgrims from around the world to Saudi Arabia, raising the potential for future epidemics [31].

#### Ebola Virus

The 2014 Ebola virus disease (EVD) epidemic in West Africa also highlighted the risks of global infectious disease transmission in an increasingly connected world. This zoonotic virus has a probable bat reservoir [32] and is spread between humans through contact with infected body fluids. EVD can incubate for up to 3 weeks before presenting as a severe febrile illness with multisystem organ failure and hemorrhagic tendencies. Epidemics have largely been confined to Africa, with case fatality rates between 30% to upwards of 80% [33].

The largest EVD epidemic began in Sierra Leone in 2014. Starting in a rural town, the epidemic spread via land travel to bordering Guinea and Liberia. From there, cases began appearing on

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several continents via international air travel. In the USA, for instance, one returned traveler infected two healthcare workers before local transmission stopped [34]. Similar imported cases were seen in Italy and the United Kingdom, and a short chain of healthcare-related transmission was documented following the return of an infected Spanish citizen back to Spain [35,36]. An infected individual flew to Nigeria and initiated a larger epidemic, with 19 confirmed cases in two cities resulting in seven deaths [37]. Ultimately, the Nigerian epidemic was halted by the heroic efforts of local public health teams [38]. By the time the West African EVD outbreak ended in 2016, there were 21 868 reported cases and 11 310 deaths, with imported cases in seven countries.

During the 2014 EVD epidemic, many countries hastily instituted policies that limited travel to and from EVD-affected countries. Some countries closed land and air borders with Guinea, Liberia, and Sierra Leone [39,40], and others, including Australia and Canada, temporarily refused to issue visas to travelers from affected countries [41], a policy not aligned with the World Health Organization (WHO)'s IHR. The USA imposed enhanced screening procedures that measured the temperature of returned travelers from affected countries for up to 3 weeks. The 2014 EVD epidemic highlighted how governments may rapidly impose policy related to an emerging infection of epidemic potential, although the effectiveness of many of these policies is still debated.

#### Influenza

Influenza A virus causes predictable seasonal epidemics in both northern and southern hemispheres. Influenza A virus also circulates in birds and pigs and has the potential to mutate more rapidly compared to influenza B virus, allowing the virus to recombine with different strains and cause epidemics. Many individuals infected with influenza A virus will experience a self-limited febrile illness punctuated with myalgia and malaise, and this infection is also associated with severe illness and is responsible for roughly 300 000–600 000 deaths per year, globally [42].

The 1918 influenza pandemic demonstrated the ability of influenza A virus to cause a global catastrophe in the era of increasing global mobility, as it resulted in an estimated 50 million deaths worldwide [43]. Seasonal influenza strains are now more mobile than ever, and the effect of air travel is a well-established mechanism for facilitating global influenza transmission [44–47]. The 2009 H1N1 influenza pandemic demonstrated the potential for global air travel networks to rapidly disseminate a novel influenza virus that emerged on a pig farm in Mexico and spread to the rest of the world [48,49], resulting in approximately 123 000–203 000 deaths, globally [50].

#### Air Travel Contributing to Infections with New Areas of Endemicity

Human mobility continues to introduce infections to new geographic locations, and air travel contributes to this process. Occasionally, infections introduced to new regions may become endemic.

#### Aedes spp. Mosquitoes

The global emergence of arboviruses, such as dengue, Zika, and Chikungunya viruses, demonstrates how certain infections may become endemic in new regions if they are imported to areas with suitable ecological conditions. These arboviruses require *Ae. aegypti* or *Ae. albopictus* mosquito vectors for transmission, and at least one of these species of mosquito is now present on every continent except Antarctica [9]. *Ae. albopictus*, the Asian tiger mosquito, is well adapted to urban environments [51] and has contributed to recent arboviral epidemics.



These mosquito vectors have spread along human trade and travel routes [51,52], and diseases carried by such vectors are quickly following the same path.

#### Dengue Virus

Dengue virus, transmitted primarily by *Ae. aegypti*, is one of the most important re-emerging infectious diseases, with an estimated 2.5 billion people living in regions suitable for infection [53]. Dengue virus has four serotypes, each of which circulates independently, causing outbreaks in populations that are naïve to that serotype [54]. Though once well controlled, dengue virus re-emerged in Asia in the 1950s, and is now endemic or epidemic in many tropical and subtropical regions around the world. Its re-emergence over the past half-century has been driven by urbanization, globalization, inadequate vector control [55], and, notably, increasing human travel [56,57]. Autochthonous transmission has now been described in the USA, France, Croatia, and Madeira [58–60], all imported by infected travelers. Air travel is contributing to the increasing frequency of epidemics as new serotypes are introduced into susceptible populations by travelers [61,62]. Interestingly, there is emerging evidence that individuals infected with dengue virus who are asymptomatic or presymptomatic (and presumably have lower levels of viremia) are still able to infect competent mosquito vectors. Such individuals may be more prone to traveling given their lack of symptoms, and are likely contributing to global dengue virus transmission [63,64].

#### Chikungunya Virus

Chikungunya virus is another arbovirus that is transmitted by *Ae. aegypti* and *Ae. albopictus* mosquito vectors. It causes a self-limited febrile illness with a syndrome of arthralgia or arthritis that may last for weeks to months after infection. Chikungunya virus was originally endemic in African and Asian settings, but has caused localized epidemics in Italy in 2007, and in Italy and France in 2017 [7,60,65,66]. The 2007 epidemic in Italy was initiated by a single viremic traveler returning from India [7], highlighting the role of air travel in its spread. In December of 2013, autochthonous cases of Chikungunya infection appeared in Saint Martin, also likely introduced by a viremic traveler. Given the appropriate ecological suitability and competent vectors for transmission, Chikungunya virus rapidly spread throughout Latin America and the Caribbean, affecting 46 countries and over 3 million people, and is now endemic in the Americas [67]. An evaluation of global travel patterns from endemic locations predicted that imported cases of Chikungunya would be common in New York, Miami, and Puerto Rico, with autochthonous transmission in the latter two regions [8], which was ultimately realized 1 year later [68].

#### Zika Virus

Zika virus is also transmitted by *Ae. aegypti* and *Ae. albopictus* vectors and typically causes a self-limited febrile illness in approximately 20% of those affected [69]. The virus has a predilection for developing nervous systems, and microcephaly is well documented in children born to infected pregnant mothers [70]. Zika virus originated in Africa and spread slowly eastward to Asia during the second half of the 20th century, culminating in a large outbreak on the Yap island in 2007 [69]. This was followed by a number of smaller outbreaks in Pacific islands, eventually resulting in an unprecedented epidemic in Brazil in 2015 that spread through much of Latin America and the Caribbean [71]. Although the index case was not identified, molecular clock analyses suggest that the virus was introduced multiple times in 2013 or 2014 from viremic travelers [71]. The virus was accurately predicted to spread throughout Latin America and the Caribbean based on human air travel patterns from Brazil, to regions with suitable ecological conditions and competent mosquito vectors for disease transmission [72]. Similarly, Zika virus is predicted to be reintroduced to African and Asia-Pacific nations based on current air travel patterns [73,74]. It is currently unclear if Zika virus will be established as an endemic



infection in Latin American and Caribbean nations, though there are several parallels with Chikungunya virus in this region, suggesting that this is a likely scenario [75].

#### Antimicrobial Resistance

The discovery of antibiotics heralded a new era in medicine, but was almost immediately followed by the emergence of drug resistance, such as the early descriptions of penicillin resistance in *Staphylococcus aureus* species [76]. Treatment of organisms harboring antimicrobial resistance (AMR) genes is associated with treatment failures, worse clinical outcomes, and greater expense [77]. The devastating economic and health impacts of AMR are expected to be amplified in low-income countries [78]. The rapid rise of broad-spectrum AMR among Gram-negative bacteria, especially the Enterobacteraciae, is a growing public health threat. Soon after the development of extended-spectrum cephalosporins in the 1980s there emerged Enterobacteraciae with extended-spectrum beta-lactamases (ESBLs) and AmpC cephalosporinases [79]. These resistance genes were soon found worldwide in a variety of Gram-negative organisms, including *Klebsiella, Escherichia coli, Salmonella*, and others [80]. Carbapenemases are now increasingly commonplace, conferring resistance to some of the broad-est-spectrum antibiotics [81].

International air travel is contributing to this global spread of resistant organisms. Travelers returning from areas with a high prevalence of AMR often return colonized with resistant organisms, and these individuals can transmit AMR organisms to others [82]. The New Delhi metallo-beta-lactamase-1 (NDM-1) gene is a recent example of the potential for AMR to spread rapidly. Organisms with NDM-1 are resistant to essentially all cephalosporins and carbapenem antibiotic classes [83]. The first case report of NDM-1 was in a traveler who acquired a urinary infection while in India in 2008 [84]. By 2010, NDM-1 was detected in the USA, Canada, Japan, Kenya, Oman, Australia, the United Kingdom, and multiple other European countries [85]. Similarly, colistin resistance with the mobilized colistin resistance-1 (mcr-1) gene is a very concerning development. From its likely origin in China, mcr-1 has been detected in returned travelers around the world [86,87]. Like NDM-1, it can colonize travelers returning from endemic areas [88], and local transmission is now being seen outside of China [89]. These bacteria are emerging far from their site of origin largely due to human travel and agricultural trade. The WHO has recognized AMR as a major global health threat and has enacted a Global Action Plan to help combat its spread [90]. However, large-scale antimicrobial stewardship programs are currently not realized in much of the world.

#### Clinical Implications of Infections Transmitted via Air Travel

Given the increases in global tourism and human migration, physicians and other healthcare workers are seeing more travel-related infections. Since infections from distant locales can present to virtually any clinic or hospital in the world in a matter of days, healthcare workers must be aware of both local and international epidemics. For example, the index case of MERS in Korea had visited four healthcare facilities over 8 days before a diagnosis was established [91], and this delayed diagnosis contributed to the epidemic. The ability of a clinician to obtain a quality travel history is increasingly important, even for routine infectious syndromes like an upper respiratory tract infection. Several tools now exist for clinicians to help keep abreast of distant epidemics that may be relevant to their clinical practice, such as ProMED-Mail [92] and HealthMap [93]. However, questions still remain about the best way to consume and process a large volume of data for which there may only be limited pertinent information.

It is also important for clinicians to ask about a more remote travel history. For example, tuberculosis testing is usually considered before starting immunosuppressive medications.



However, asking about potential exposures to parasitic infections, such as *Strongyloides stercoralis*, is frequently forgotten. *Strongyloides* infections can disseminate following immunosuppression and cause a severe and frequently fatal disease [94]. Screening for *Strongyloides* is now recommended prior to initiating immunosuppressive medications in patients who have spent significant time in endemic countries [95]. Similarly, neurocysticercosis should be considered in those with seizure disorders from endemic countries, even if they have not visited an endemic region in many years. The differential diagnosis for common syndromes often expands when a lifetime travel history is considered, and this information has potential to significantly impact clinical decision-making.

#### Public Health Implications of Infections Transmitted via Air Travel

Epidemics such as those caused by SARS, MERS, and Ebola viruses highlight the importance of rapid public health responses to emerging epidemics in the era of expanding global air travel. Public health agencies at local and international levels must be aware of global outbreaks and emerging threats, and have the tools to initiate a rapid and coordinated response. Several systems need to be in place to facilitate such coordinated responses, including surveillance tools and methods of communication and management in various jurisdictions.

The revised IHR adopted after the 2002 SARS outbreak was designed to improve global reporting of outbreaks [24] and this document continues to function as an effective datasharing agreement. While SARS and the revised IHR have resulted in an increased investment in surveillance among higher-income countries, countries with fewer resources but a higher burden of infectious disease epidemics have ongoing challenges operating surveillance programs. Improving global surveillance capacity is a priority, and countries with limited public health capacity may require logistic and infrastructure support for these global systems to function effectively [96,97]. In addition to disease surveillance networks, early-warning systems are increasingly helpful for monitoring the global spread of infectious diseases. Such systems utilize multiple data sources, including voluntary reports, international news, and social media [92,93,98,99]. Other systems, such as GeoSentinel and TropNet, coordinate tropical and travel medicine clinics that collect data on illnesses in returned travelers. These travelers essentially act as sentinels of emerging epidemics when a source country does not have the capacity to detect these infections in a timely manner. Such networks have detected a sarcocystis outbreak in Malaysia [100], dengue virus outbreaks in Angola [101], and tracked the spread of Zika virus globally [102]. With improved surveillance and early warning systems, and by harnessing travelers as sentinels, it is possible to piece together a global picture of emerging and re-emerging infectious diseases. Responding to these epidemics, though, still poses several challenges.

Travel-related policy and public health responses to epidemics take several approaches, and include travel restrictions to and from affected areas, and passenger screening. Travel bans and restrictions are generally not helpful in halting the spread of infectious diseases [45,103–106]. Such policies also may hinder affected countries coping with the epidemic and can impose significant economic burden above the direct costs of the infectious outbreak [107]. Travel restrictions also violate the revised IHR, effectively punishing countries for participating in global disease surveillance and discouraging open communication [108]. Screening of travelers from affected counties also poses logistical problems. Screening commonly relies on either self-reported symptoms (such as an influenza-like illness), which may be inaccurate, or on periodic body temperature screening such as using thermometers or thermal imaging technology. Travelers may be completely asymptomatic if they are in an incubation period during the time of travel, and this may be especially pertinent for infections with longer incubation periods



such as Ebola virus [109]. Ultimately, resources may be better channeled to controlling the epidemic at the source.

#### Travel-Related Infectious Diseases in Low-Income and Lower-Middle-**Income Countries**

The burden of infectious diseases is disproportionately high in low-income and lower-middleincome countries (LICs and LMICs, respectively) [110]. Improving disease surveillance capabilities, vector control initiatives, developing laboratory capacity [111-113], and supporting public health interventions such as vaccination, is essential to mitigate local impact and future dissemination of epidemics [114]. If an epidemic of global health significance is detected in an LIC or LMIC, communication and coordination with local public health teams is essential, as is supporting the capacity of local laboratories and personnel. This was recently helpful in halting the 2018 Madagascar plague epidemic [115,116].

#### **Concluding Remarks**

The capacity for an infected human to rapidly travel between any two points on earth has heralded a new era in global health security as infectious diseases are able to spread more effectively than at any other time in history. The global public health response must be proportional.

Quality surveillance, open communication, and global coordination are key elements to prevent, detect, and extinguish epidemics early. Similarly, vaccine development and vector-control efforts may proactively prevent the emergence of epidemics. New tools are needed to enable front-line healthcare workers to diagnose non-local infections, as well as to facilitate rapid data sharing during outbreaks (see Outstanding Questions). Investing in capacity building targeted at detecting and responding to epidemics in LICs and LMICs is likely to be a very effective and cost-effective mode of preventing disease transmission worldwide.

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#### **Outstanding Questions**

How do we most effectively harness the current global infectious disease surveillance capacity given the existing gaps?

Can stronger modeling more accurately predict where infections will spread through air travel, and can this determine what the next epidemic of global health significance will be?

How can we enable local healthcare workers to more effectively utilize global infectious diseases surveillance data?

How do we develop better methods to screen for passengers harboring infectious diseases prior to traveling, or after arrival?

How can international and local travelrelated policies be strengthened to more effectively respond to infectious diseases of epidemic potential?

What is the best way to support lowincome and lower-middle-income countries responding to infections with epidemic potential?

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