

The Globalization of Healthcare: Implications of Medical Tourism for the Infectious Disease Clinician

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Travel abroad for healthcare has increased rapidly; interventions include organ transplant; cardiac surgery; reproductive care; and joint, cosmetic, and dental procedures. Individuals who receive medical care abroad are a vulnerable, sentinel population, who sample the local environment and can carry home unusual and resistant infections, documented in many reports. Medical tourists are at risk for hospital-associated and procedure-related infections as well as for locally endemic infections. Patients may not volunteer details about care abroad, so clinicians must inquire about medical procedures abroad as well as recent travel. Special infection control measures may be warranted. Healthcare abroad is associated with diverse financial, legal, ethical, and health-related issues. We focus on problems the infectious disease clinician may encounter and provide a framework for evaluating returned medical tourists with suspected infections. A better system is needed to ensure broad access to high-quality health services, continuity of care, and surveillance for complications.

Keywords. medical tourism; cross-border healthcare; multidrug-resistant organisms; transplant tourism; healthcare globalization.

Healthcare is undergoing dramatic globalization. Throughout history, the sick and lame have embarked on pilgrimages to find cures. In the past, this was primarily to access facilities or technologies unavailable at home. Now travel for medical treatment has expanded enormously and many travel from developed countries to low- or middle-income countries, often to avoid high costs or long delays. Travel to another country for medical treatment has been called “medical tourism” and “cross-border healthcare” [1, 2]. Globalization of medical care is a multi-billion-dollar phenomenon, associated with economic, cultural, ethical, legal, and

health consequences. A growing literature describes its dimensions and complexities [3–6]. This paper will focus on infectious disease implications.

MAGNITUDE/OVERALL VOLUME

Common destinations for medical tourists include India, Thailand, China, Mexico, Latin America, the Caribbean, Europe, Singapore, the Middle East, and Pakistan [7]. Notably, destinations include many low- and middle-income plus a few high-income countries. Patients often seek treatment in their World Health Organization (WHO) region of residence, but the diaspora population may combine medical treatment with family visits [8]. Seventy percent of patients going to Singapore and Malaysia are from countries in the Association of Southeast Asian Nations; those going to Cuba are mainly from the Caribbean and Central America, and those going to Jordan are mostly from Middle Eastern countries [8]. The main constraint on medical tourism is the challenge of insurance

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portability. High-quality medical professionals, often trained in the United States or United Kingdom, are found in many institutions treating medical tourists; US medical schools are increasingly cooperating with foreign institutions in educational efforts. Meanwhile, lower costs of services, including labor, provide developing countries a substantial cost advantage [8].

Complete and accurate data on medical tourism volume, destinations, services, and procedures are unavailable. One source estimated 4 million international patients annually [8]. Thailand attracted 1.28 million international patients in 2005, [9] with India, Singapore, and Malaysia each approaching this number by 2012 [8]. The Asian market had been forecast to generate \$4.4 billion in 2012 [8]. Singapore has launched an initiative to develop new areas, such as stem cell treatment and transplant. Widely variable estimates of global medical tourism value (US\$20–\$60 billion) are unreliable [10]. Guidelines for consistent definitions and reporting methodologies for medical tourism have been recently published (2011) [11] and may permit more accurate reporting.

One debatable source estimated that 750 000 Americans traveled abroad in 2007 for medical procedures (45% to Asia in 2005) [12]. In 2005, an estimated 55 000 Americans received care at Bumrungrad Hospital (Bangkok), a hospital that currently estimates treating 420 000 international patients annually [13].

REASONS FOR SEEKING CARE ABROAD AND PROBLEMS ASSOCIATED WITH MEDICAL TOURISM

Among the motivations for medical tourism (Table 1) are lower cost, avoidance of long waits, legal or cultural restrictions at home, privacy and opportunity to recover away from home, incentives offered by employers or insurers, and interest in combining an exotic vacation with a medical procedure [1, 2, 7, 14]. Common procedures include dental work; arthroplasty; cataract, bariatric, cosmetic, and cardiac surgery; reproductive care; and tissue and organ transplant. More than 40% of unrelated stem cell transplants worldwide involve donors from a different country [15]. Vast cost differences exist: a hip replacement may cost \$7000–\$12 000 (India) or \$6500–\$14 000 (Thailand) versus \$43 000–100 000 (United States) [12]. Medical tourism is sufficiently common that the Centers for Disease Control and Prevention and professional societies have developed patient guidelines (Table 2).

Problems associated with medical tourism have become evident: lack of regulation, complications and poor outcomes, exploitation of donors and surrogates, diversion of skilled specialists to hospitals serving foreigners, and fragmented follow-up care (Table 1). Some professional associations and international organizations have developed quality-of-care standards and have

established accreditation procedures [1, 3] (Table 2). The International Organization for Standardization (ISO) and Joint Commission International (JCI) perform procedural assessments on quality and safety associated with medical tourism, although they do not assess outcomes. JCI had accredited 368 international hospitals as of March 2012 [16]. Globally, 55 countries have JCI-certified hospitals; Singapore alone had 22 (2013).

INFECTIOUS DISEASES ASSOCIATED WITH MEDICAL TOURISM

Medical tourists are at risk for procedure-related infections—eg, wound and blood-borne infections—and those related to regional travel. Broader population consequences can follow if pathogens or resistance determinants spread during care or after return home. Consequences following healthcare abroad can appear early or late. Although this paper focuses on individuals who travel to obtain healthcare, similar risks exist for travelers who require care during travel (inadvertent medical tourists) and persons visiting friends and relatives who undergo procedures while abroad (incidental medical tourist). A Boston-area survey found that about half of international travelers experienced health problems, 7% sought medical care, and 1% required hospitalization [17].

Healthcare-associated infections overlap with those elsewhere, though the prevalence in developing countries is substantially higher than in Europe and the United States [18]. A meta-analysis found that developing-country adult intensive care units had infection rates at least 3-fold higher than those reported from the United States, and surgical site infection rates were also higher (5.6 vs 1.6–2.9 per 100 surgical procedures) [18]. Higher rates of infections [19] complicate procedures done abroad, but no system-wide database currently tracks procedures and outcomes. Because quality of care varies greatly by institution, it is difficult to make meaningful generalizations about risks outside the United States.

Many countries with robust medical tourism programs lie in tropical and subtropical regions where malaria, dengue fever, enteric fever, and other endemic infections exist. Many have high background rates of tuberculosis, antibiotic resistance, and hepatitis B, hepatitis C, and human immunodeficiency virus (HIV). Blood and blood products used in hospitals certified by JCI are expected to be screened for common blood-borne pathogens, but not necessarily for all region-specific agents. Dengue and West Nile viruses, for example, cause rare infections after transfusion, and screening for these is not done in most regions [20].

Kidney Transplantation

As of 2010, 98 countries reported having organ transplant services and together performed about 100 000 transplants annually [21, 22]. An estimated 10% of organ transplants worldwide

Table 1. Summary of Reasons for Seeking Overseas Medical Treatment, Potential Benefits to Receiving Countries, and Current Challenges and Concerns Associated With Medical Tourism

Reasons and Motivations for Seeking Medical Treatment Abroad	Potential Benefits to Receiving Countries of Medical Tourism	Current Challenges and Concerns Regarding Medical Tourism
<p>Attributed to country of residence:</p> <ul style="list-style-type: none"> • Treatments not covered by health insurance in home country • Lack of health insurance making some care unaffordable in home country • Lack of technology or medical expertise in own country; procedure or treatment unavailable • Legal or cultural constraints in home country (eg, termination of pregnancy; in vitro fertilization; sexual reassignment surgery; surrogates for pregnancy; stem cell treatments) • Medical insurance plans include coverage and may even offer incentives for out-of-country procedures 	<ul style="list-style-type: none"> • Improve overall quality of care due to standards for treating foreign patients • Revenue from medical tourism may provide opportunities to improve access and quality for local residents • Physicians and other healthcare workers trained elsewhere may repatriate to countries of origin to work and improve local access and quality of care • Patients and their families may stay in country or region for sightseeing during recovery and bring money to local economy 	<p>Associated with direct impact on medical tourist:</p> <ul style="list-style-type: none"> • Lack of regulation of medical tourism companies • Accreditation of care providers may be lax and highly variable • Ethical concerns about doing procedures that are not supported by scientific evidence • Fragmented or poor follow-up care; lack of communication between institutions abroad and at home; poor medical records • Late complications following surgery • High nosocomial infection rates; early and late infections • Lack of oversight to identify reasons for adverse events and effect change • Major surgery may be associated with increased risk for perioperative deep vein thrombosis from long-haul flights • Lack of liability for poor results or malpractice • Lack of standards regarding patient privacy and confidentiality
<p>Attributed to country providing care:</p> <ul style="list-style-type: none"> • Low cost; more affordable medical care • Treatment available without long waiting periods • Modern facilities, including accreditation by Joint Commission International, giving patients confidence in the quality of care • Expanding capacity to care for patients from developed countries and concierge services to assist with planning; personalized assistance • Option to receive care and remain anonymous • Well-organized promoters of medical tourism, including professional organization, regular international meetings, websites, journal, and written materials • Sightseeing and touring in an exotic location in addition to obtaining medical care 		<p>Associated with impact on country providing care:</p> <ul style="list-style-type: none"> • Rise in cost of medical care for local residents • Focus on wealthier foreign patients may undermine resources for impoverished local residents who may have less access to care • Exploitation of local donors or surrogates for certain procedures • Imbalance of specialties; financial incentives for care of foreign patients affects specialty choices

Source: Heible [1], Milstein and Smith [2], Horowitz et al [7], Turner [14].

in 2007 resulted from transplant tourism [23]. The US national waitlist removal data from 1987–2006 indicated 373 likely cases of transplant tourism; male sex, Asian ethnicity, resident alien status, and college education were independently associated with overseas transplant, most often in China, the Philippines, and India [24]. It seems that Chinese transplant programs routinely sold organs to nationals and foreigners until 2007 when the practice was banned [25]. India outlawed buying and selling kidneys in 1994 [26]. Organ vending is illegal in all countries except Iran, yet the practice persists [27]. Formalized at the

63rd World Health Assembly, the WHO Guiding Principles on Human Cell, Tissue and Organ Transplantation stated that “organs should be donated freely without any monetary payment or reward of monetary value” [28]. Despite their promulgation, the guiding principles are not necessarily followed; a thriving black market persists in some countries.

Although kidney transplants have raised many concerns about human rights [27]—including transplanting organs from executed prisoners—they are similar to other solid organ transplants where the organ can be a source of infection and complications arise

Table 2. Internet Resources From Professional Societies and International Organizations Focusing on Quality and Safety and Accreditation of Healthcare Abroad

Organization	Resource	Website
Organizations that provide guidance and information about quality and safety		
Centers for Disease Control and Prevention (CDC)	A chapter in <i>Health Information for International Travel 2014</i> is devoted to medical tourism with advice and guidance for medical tourists	wwwnc.cdc.gov/travel/yellowbook/2014/chapter-2-the-pre-travel-consultation/medical-tourism.htm
American Medical Association	Guidelines for employers, insurance companies, and entities that "facilitate/offer incentives" for care abroad	http://www.ama-assn.org/ama1/pub/upload/mm/31/medicaltourism.pdf
American College of Surgeons	Summary of information and internet resources on Nora Institute for Surgical Patient Safety website, including websites and companies that specialize in medical tourism	www.surgicalpatientsafety.facs.org
American Society for Plastic Surgery	Information on medical tourism with emphasis on issues at home and abroad	www.plasticsurgery.org/articles-and-galleries/patient-and-consumer-information/patient-safety/medical-tourism.html
International Society of Aesthetic Plastic Surgery	Certifies 1500 surgeons in 73 countries who meet US standards	www.isaps.org
American Dental Association	Information regarding travel, dental care, dental tourism, via Global Dental Safety Organization for Safety and Asepsis Procedures	www.osap.org
Global Observatory on Donation and Transplantation	World Health Organization-Organization National de Transplantes (WHO-ONT), a collaboration that provides worldwide transplant data, and information on organizational and legal aspects	www.transplant-observatory.org/pages/home.aspx
World Health Organization (WHO)	Guiding principles on human cell, tissue, and organ transplant	www.who.int/transplantation/Guiding_PrinciplesTransplantation_WHA63.22en.pdf
World Health Organization	World Alliance for Patient Safety	www.who.int/patientsafety/en
Organizations that provide healthcare standards and accreditation internationally		
International Organization for Standardization (ISO)	A nonprofit organization that has developed standards that certify hospital quality-management programs internationally	www.iso.org
Joint Commission International (JCI) (affiliate of the Joint Commission on Accreditation of Healthcare Organizations [JCAHO])	Provides accreditation of healthcare facilities internationally	www.jointcommissioninternational.org
International Society for Quality in Health Care (ISQua)	Umbrella organization that accredits JCI and other accrediting agencies	www.isqua.org
QHA Trent (Quality Healthcare Advice)	A private British company that provides accreditation to hospitals, clinics, primary care providers, residential care homes, and home care	www.qha-international.co.uk
Australian Council for Healthcare Standards International (ACHS)	An independent not-for-profit organization that is the leading healthcare assessment and accreditation provider	www.achs.org.au
Canadian Council on Health Services Accreditation	Accreditation Canada International promotes health accreditation and quality improvement worldwide	www.accreditation.ca/accreditation-programs

from immunosuppression. Some transplant-associated infections are geographically restricted, including human T-lymphotropic virus types 1 and 2, West Nile virus, rabies, malaria, *Leishmania*,

Trypanosoma cruzi, and several fungi, among others [29]. The source of infection may be the transplanted organ or transfused blood [29]. At least 45 cases of malaria have occurred in organ

transplant patients (36 renal); at least 14 (3 heart, 5 liver, 6 renal transplants) had evidence supporting donor-to-host transmission via the graft [29]. *Strongyloides stercoralis*, endemic in tropical and subtropical regions, has been transmitted from a donor with unrecognized infection to kidney and liver transplant recipients [30].

A systematic review of outcomes found inferior patient and graft survival after commercial transplants (performed in South Asia, East Asia, and the Middle East) compared to results described in the United Network for Organ Sharing [26]. Commercial transplants had a higher incidence of infections including hepatitis B, hepatitis C, malaria, HIV, and tuberculosis, and markedly increased incidence of postoperative surgical interventions [26]. Likewise, patients who had renal transplants overseas (n = 87, mostly in China) followed at Seoul National University Hospital, Korea (2000–2009), had higher risk of infections, acute rejection, and hospitalization than did patients with local donors (n = 577) [31]. A meta-analysis (39 centers globally) concluded that transplant tourists had lower 1-year graft and patient survival than domestic kidney transplant recipients and were more likely than domestic kidney transplant recipients to develop cytomegalovirus, hepatitis B virus, HIV, and wound infections [32].

Cosmetic Surgery

A cluster of wound infections caused by *Mycobacterium abscessus* following cosmetic surgery (including abdominoplasty, breast surgery, liposuction) in Santo Domingo, Dominican Republic, was reported in the United States in 2003–2004 [33]. A 2005 survey of North American infectious disease specialists found that 6% of 425 respondents had encountered infectious complications from cosmetic surgery performed abroad in the previous year [34]. No comparator or denominator data were available.

Resistant Organisms

Prominent bacterial species causing nosocomial infections and resistance patterns vary geographically. In many countries, antibiotics are available without prescription; overuse is common and resistance widespread, so nosocomial infections may be caused by unusually resistant bacteria that reflect problem pathogens in that hospital or region. For example, extended-spectrum β -lactamase (ESBL) rates exceed 80% in India, and vancomycin-intermediate-resistant *Staphylococcus aureus* is prevalent in parts of Asia [35, 36].

Travelers sample the microbial milieu of another region and can acquire resistant bacteria in the absence of illness or medical treatment [37]. Travelers cultured before, during, and after travel to Mexico showed increase in resistance in their fecal *Escherichia coli*, even if they took no antibiotics [38]. In a Canadian study, patients with diarrhea who had recently traveled had a 5.2-fold increase in colonization with ESBL-

producing *E. coli* [39]. Twenty-four of 100 Swedish travelers acquired new ESBL-producing *E. coli* during travel (median duration, 2 weeks), with highest rates from India (7 of 8 travelers) [40]. The ESBL colonization rate in Australians increased from 7.8% pretravel to 49% posttravel, with resistant *E. coli* isolated from 50% to 79% of travelers to Asia (excluding Japan), South America, and/or Middle East/Africa [41]. At 6 months posttravel, 18%–24% remained colonized [40, 41]. Resistance enzymes varied by region: CTX-M-15 from India, Europe, and Africa, and CTX-M-14 from elsewhere in Asia [42]. CTX-M β -lactamases carried in feces also spread within households [43]. A UK study found that recent international travel or antibiotic use were independent risk factors for septicemia following transrectal prostate biopsy. All blood and urine *E. coli* isolates from septic patients were resistant to ciprofloxacin, the agent used for prophylaxis [44]. Many studies document the role of travelers, including medical tourists, in moving bacteria and resistance genes globally [45–48].

Current Gram-Negative Concerns

Resistance genes may be found in commensals as well as in pathogenic organisms; international travel played a key role in the global dissemination of CTX-M-, KPC (*Klebsiella pneumoniae* carbapenemase)-, VIM (Verona integron-encoded metallo- β -lactamase)-, OXA-48 (oxacillinase group of β -lactamases)-, and NDM (New Delhi-metallo- β -lactamase)-producing Enterobacteriaceae [45–49]. Although some infections resulted from treatment for injuries or acute during-travel problems, many were acquired via medical tourism [45, 49]. In one case, carbapenem-resistant *K. pneumoniae* in Colombia in 2008 was traced to a medical tourist from Israel who traveled for liver transplant, exemplifying the ability of the medical tourist to introduce resistant organisms to the country providing medical care [50].

Travelers have provided specimens that have helped to map the global distribution of NDM enzymes [48, 51]. This metallo- β -lactamase was first characterized from an isolate in a Swedish patient (Indian origin) who had been hospitalized in India in late 2007 and early 2008 [52]. In Sweden, a multidrug-resistant *K. pneumoniae* from his urine and an *E. coli* cultured from a fecal sample were both positive for what was subsequently designated NDM. These carbapenemases have been identified primarily in Enterobacteriaceae but can spread to multiple gram-negative bacterial species, including other pathogens (eg, *Vibrio cholerae*, *Pseudomonas aeruginosa*, *Salmonella*), and to commensals. Bacteria may carry NDM-1 along with other resistance determinants; they are typically pan-resistant. The genetic element encoding NDM-1 is carried on plasmids and occasionally on chromosomes [53]. A 2010 paper identified 37 NDM-1-producing isolates in the United Kingdom, a high proportion in travelers to India or Pakistan within the previous year (n = 17/37); 14 had antecedent hospital treatment abroad,

including renal or bone marrow transplant and cosmetic surgery [46]. The earliest documented NDM-1-producing isolates were in India in 2006 [54]. NDM-1-producing isolates are widespread in clinical isolates in India and Pakistan (Varanasi 6.9%, Mumbai 8%, and Rawalpindi, 18.5%), [54–56] and were also found in environmental samples (eg, water samples, Delhi) [57]. Nosocomial spread has been documented in multiple regions (Europe, Africa, Middle East, North America) [48].

Since first detected in the United States in 2010, 14 of 16 NDM-producing isolates were linked to medical care in South Asia [58]. In 2012, a hospital outbreak in Denver, Colorado, involved 8 patients [58]. Although the source of introduction was unclear, 5 isolates were from asymptotically colonized patients, a reminder of potential spread by unrecognized carriers [58].

Current Gram-Positive Concerns

Transfer of resistant gram-positive organisms, including methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* (VRE), and hypervirulent *Clostridium difficile*, also occurs [35, 36, 45, 59]. Reportedly, a quarter of MRSA cases from 2000 to 2003 in Sweden were attributed to exposure abroad, and the majority were healthcare-associated [45]. Ireland, France, and Australia have described the transfer of hypervirulent *Clostridium difficile* (ribotype 027) from the United Kingdom, Belgium, and North America, respectively [45].

Mycobacterium Tuberculosis

Resistance to antituberculous medication is a global problem; high levels of resistance are found in parts of Asia and exposures can occur in hospitals [36]. In Singapore, extensively resistant tuberculosis was diagnosed in 2010 in a patient from Indonesia who required several months of multidrug treatment and surgery before being able to return home [60].

Other Concerns

Other concerns related to medical procedures abroad include reuse of syringes or equipment without adequate sterilization, exposure to falsified or substandard medications [61], and inadequately screened blood donations. Travelers to tropical and developing countries risk acquiring locally endemic infections; recent studies provide destination-specific risks [62]. Medical tourists, sometimes with family, may travel regionally, thus facing risk for vector-borne and other locally endemic infections. They may encounter new and emerging threats such as influenza A(H7N9) or novel coronavirus, which may spread nosocomially. The SARS (severe acute respiratory distress syndrome) outbreak led to nosocomial transmission in countries with substantial medical tourism, although medical tourists were not specifically identified then. Finally, major surgery

away from home environment carries the risk of perioperative deep vein thrombosis from long-haul flights.

MEASURES TO ASSURE QUALITY AND SAFETY FROM MEDICAL TOURISM AND CONTROL OF INFECTIONS

Patients contemplating medical tourism should be advised of procedure-related as well as typical travel-associated risks. The public should be informed of potential infectious disease risks associated with overseas hospital care. Efforts such as the Chennai Declaration—a consensus report resulting from a 2012 meeting in Chennai, India, of healthcare representatives, experts, and policy makers from India and WHO, which aimed to formulate a plan to address the global challenge of antimicrobial resistance from the Indian perspective—attempt to tackle the resistance problem [63]. For medical tourists, a tracking system is needed as patients from one institution may return to many different countries and institutions, making it difficult to identify problems at a particular institution. Improved communication is essential to optimize continuity of care of medical tourists who may have follow-up on a different continent by a clinical team unaware of site(s) of medical and surgical care. Medical tourists may carry home unusually resistant microbial flora; patients hospitalized after return from medical care in high-risk destinations such as South Asia should be placed on contact isolation and cultured for resistant organisms. Decisions about empiric therapy and surgical prophylaxis should consider recent travel history and procedures abroad. Surveillance networks such as GeoSentinel (55 travel-tropical medicine clinics on 6 continents) can be refined to capture data on antimicrobial resistance. The International Health Regulations 2005 contain criteria to determine whether an event may “constitute a public health emergency of international concern” [64]; thus, WHO can potentially champion coordinated global surveillance of antimicrobial resistance as well as international response [65].

SUMMARY

Travel abroad for healthcare will likely continue to increase, given the market forces. Knowledge of this trend is critical in incorporating a global perspective into clinical care. Patients may not freely volunteer information about medical care, so today’s medical history must include explicit queries about travel and details of medical care or procedures carried out abroad. The differential diagnosis of illness after a procedure in another country is often broader than that in the United States. Infection control issues must be considered, as patients may be colonized or infected with multidrug-resistant bacteria. Complicating infections may appear early or late, with the latter

more common in those who have received blood or blood products, tissue or organ transplants, and immunosuppressed hosts. Healthcare abroad is an integral part of the knowledge base required of infectious disease clinicians. More generally, a better system is needed to gather information on these global patients and the outcomes of their treatment. Infectious diseases associated with medical tourism have been recognized primarily through case reports or case series. Collection of data including demographics, procedures sought, and outcomes in a systematic and standardized fashion is needed to inform physicians caring for patients seeking medical care abroad or returning from their overseas medical treatments. Policy makers must consider economic, ethical, and legal aspects of medical tourism in trying to balance healthcare access and affordability.

Notes

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References

- Heible M. The movement of patients across borders: challenges and opportunities for public health. *Bull World Health Organ* **2011**; 89:68–72.
- Milstein A, Smith M. America's new refugees—seeking affordable surgery offshore. *N Engl J Med* **2006**; 355:1637–40.
- Reed CM. Medical tourism. *Med Clin North Am* **2008**; 92:1433–46, xi.
- Hodges JR, Turner L, Kimball AM, eds. Risk and challenges in medical tourism. Understanding the global market for health services. Santa Barbara, CA: Praeger, **2012**.
- Lee CV, Balaban V. Medical tourism. In: CDC health information for international travel 2014. New York: Oxford University Press, **2014**:127–31.
- Cohen IG. Introduction. In: Cohen IG, ed. The globalization of health care: legal and ethical issues. New York: Oxford University Press, **2013**: xiii–xxiv.
- Horowitz MD, Rosensweig JA, Jones CA. Medical tourism: globalization of the healthcare marketplace. *Med Gen Med* **2007**; 9:33.
- Smith RD, Chanda R, Tangcharoensathien V. Trade in health-related services. *Lancet* **2009**; 373:593–601.
- Deloitte Center for Health Solutions. Medical tourism: the Asian chapter. Available at: http://www.deloitte.com/view/en_GX/global/industries/life-sciences-health-care/health-care/5fa663ec49101210VgnVCM100000ba42f00aRCRD.htm#.UUZaGxn6GPc. Accessed 13 December 2012.
- Deloitte Center for Health Solutions. Medical tourism: consumers in search of value. Available at: [http://www.deloitte.com/assets/Dcom-UnitedStates/Local%20Assets/Documents/us_chs_MedicalTourismStudy\(3\).pdf](http://www.deloitte.com/assets/Dcom-UnitedStates/Local%20Assets/Documents/us_chs_MedicalTourismStudy(3).pdf). Accessed 13 December 2012.
- Organisation for Economic Co-operative and Development. Improving estimates of exports and imports of health services and goods under the SHA framework. OECD, **2011**. Available at: www.oecd.org/dataoecd/4/18/49011758.pdf. Accessed 24 February 2013.
- Kumar S, Breuing R, Chahal R. Globalization of health care delivery in the United States through medical tourism. *J Health Commun* **2012**; 17:177–98.
- Bumrungrad International Hospital. Fact sheet. Available at: <http://www.bumrungrad.com/en/about-us/bumrungrad-factsheet>. Accessed 13 December 2012.
- Turner LG. Quality in health care and globalization of health services: accreditation and regulatory oversight of medical tourism companies. *Int J Qual Health Care* **2011**; 23:1–7.
- World Health Organization. Transplantation: stem cells are daily circulating around the world. Available at: http://www.who.int/transplantation/stem_cells/en/index.html. Accessed 5 February 2013.
- Joint Commission International. Available at: www.jointcommissioninternational.org/JCIAccredited-Organizations. Accessed 1 March 2013.
- Chen LH, Han P, Jentes E, et al., for the Boston Area Travel Medicine Network (BATMN). Health problems during and after travel among Boston-area international travelers. In: Abstracts of the 13th Conference of the International Society of Travel Medicine (ISTM), Maastricht, the Netherlands, 19–23 May 2013. FC3.1.
- Allegranzi B, Bagheri Nejad S, Combesure C, et al. Burden of endemic health-care-associated infection in developing countries: systematic review and meta-analysis. *Lancet* **2011**; 377:228–41.
- Rosenthal VD, Richtmann R, Singh S, et al.; International Nosocomial Infection Control Consortium. Surgical site infections, International Nosocomial Infection Control Consortium (INICC) report, data summary of 30 countries, 2005–2010. *Infect Control Hosp Epidemiol* **2013**; 34:597–604.
- Stramer SL, Linnen JM, Carrick JM, et al. Dengue viremia in blood donors identified by RNA and detection of dengue transfusion transmission during the 2007 dengue outbreak in Puerto Rico. *Transfusion* **2012**; 52:1657–66.
- Global Observatory on Donation and Transplantation. Organ donation and transplantation: activities, laws and organization, **2010**. Available at: <http://www.transplant-observatory.org/Data%20Reports/2010%20Report20final.pdf>. Accessed 5 February 2013.
- Delmonico FL, Monintuez-Gil B, Matesanz R, Noel L. A call for government accountability to achieve national self-sufficiency in organ donation and transplantation. *Lancet* **2011**; 378:1414–8.
- World Health Organization. WHO proposes global agenda on transplantation, **2007**. Available at: <http://www.who.int/mediacentre/news/releases/2007/pr12/en/index.html>. Accessed 5 February 2013.
- Merion RM, Barnes AD, Lin M, et al. Transplants in foreign countries among patients removed from the US transplant waiting list. *Am J Transplant* **2008**; 8(4 Pt 2):988–96.
- Alcorn T. China's organ transplant system in transition. *Lancet* **2011**; 377:1905–6.
- Sajjad I, Baines LS, Patel P, Salifu UO, Jindal RM. Commercialization of kidney transplants: a systematic review of outcomes in recipients and donors. *Am J Nephrol* **2008**; 28:744–54.
- Cohen IG. Transplant tourism: the ethics and regulation of international markets for organs. *J Law Med Ethics* **2013**; 41:269–85.
- World Health Organization. WHO guiding principles on human cell, tissue and organ transplantation. Available at: http://www.who.int/transplantation/Guiding_PrinciplesTransplantation_WHA63.22en.pdf. Accessed 28 February 2013.
- Martin-Davila P, Fortun J, Lopez-Velez R, et al. Transmission of tropical and geographically restricted infections during solid-organ transplantation. *Clin Microbiol Rev* **2008**; 21:60–96.
- Centers for Disease Control and Prevention. Transmission of *Strongyloides stercoralis* through transplantation of solid organs—Pennsylvania, 2012. *MMWR Morb Mortal Wkly Rep* **2013**; 62:262–66.
- Cha RH, Kim YC, Oh YJ, et al. Long-term outcomes of kidney allografts obtained by transplant tourism: observations from a single center in Korea. *Nephrology (Carlton)* **2011**; 16:672–9.

32. Anker AE, Feeley TH. Estimating the risks of acquiring a kidney abroad: a meta-analysis of complications following participation in transplant tourism. *Clin Transplant* **2012**; 26:E232–41.
33. Centers for Disease Control and Prevention (CDC). Nontuberculous mycobacterial infections after cosmetic surgery—Santo Domingo, Dominican Republic, 2003–2004. *MMWR Morb Mortal Wkly Rep* **2004**; 53:509.
34. Furuya EY, Paez A, Srinivasan A, et al. Outbreak of *Mycobacterium abscessus* wound infections among “lipotourists” from the United States who underwent abdominoplasty in the Dominican Republic. *Clin Infect Dis* **2008**; 46:1181–8.
35. Molton JS, Tambyah PA, Ang BS, Ling ML, Fisher DA. The global spread of healthcare associated multidrug-resistant bacteria: a perspective from Asia. *Clin Infect Dis* **2013**; 56:1310–8.
36. Jean SS, Hsueh PR. High burden of antimicrobial resistance in Asia. *Int J Antimicrob Agents* **2011**; 37:291–5.
37. Leverstein-Van Hall MA, Stuart JC, Voets GM, et al. Global spread of New Delhi metallo- β -lactamase-1. *Lancet Infect Dis* **2010**; 10:830–1.
38. Murray BE, Mathewson JJ, DuPont HL, Ericsson CD, Reves RR. Emergence of resistant fecal *Escherichia coli* in travelers not taking prophylactic antimicrobial agents. *Antimicrob Agents Chemother* **1990**; 34:515–8.
39. Peirano G, Laupland KB, Gregson DB, Pitout JD. Colonization of returning travelers with CTX-M-producing *Escherichia coli*. *J Travel Med* **2011**; 18:299–303.
40. Tängdén T, Cars O, Melhus A, Löwdin E. Foreign travel is a major risk factor for colonization with *Escherichia coli* producing CTX-M-type extended-spectrum β -lactamases: a prospective study with Swedish volunteers. *Antimicrob Agents Chemother* **2010**; 54:3564–8.
41. Kennedy K, Collignon P. Colonisation with *Escherichia coli* resistant to “critically important” antibiotics: a high risk for international travellers. *Eur J Clin Microbiol Infect Dis* **2010**; 29:1501–6.
42. Laupland KB, Church DL, Vidakovich J, Mucenski M, Pitout JD. Community-onset extended-spectrum beta-lactamase (ESBL) producing *Escherichia coli*: importance of international travel. *J Infect* **2008**; 57:441–8.
43. Lo W-U, Ho P-L, Chow K-H, Lai EL, Yeung F, Chiu SS. Fecal carriage of CTXM type extended-spectrum beta-lactamase-producing organisms by children and their household contacts. *J Infect* **2010**; 60:286–92.
44. Patel U, Dasgupta P, Amoroso P, Challacombe B, Pilcher J, Kirby R. Infection after transrectal ultrasonography-guided prostate biopsy: increased relative risks after recent international travel or antibiotic use. *BJU Int* **2012**; 109:1781–5.
45. Rogers BA, Aminzadeh Z, Hayashi Y, Paterson DL. Country-to-country transfer of patients and the risk of multi-resistant bacterial infection. *Clin Infect Dis* **2011**; 53:49–56.
46. Kumarasamy KK, Toleman MA, Walsh TR, et al. Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study. *Lancet Infect Dis* **2010**; 10:597–602.
47. Struelens MJ, Monnet DL, Magiorakos AP, Santos O'Connor F, Giesecke J; European NDM-1 Survey Participants. New Delhi metallo-beta-lactamase 1-producing Enterobacteriaceae: emergence and response in Europe. *Euro Surveill* **2010**; 15.
48. Wilson ME, Chen LH. NDM-1 and the role of travel in its dissemination. *Curr Infect Dis Rep* **2012**; 14:213–26.
49. van der Bij AK, Pitout JD. The role of international travel in the worldwide spread of multiresistant Enterobacteriaceae. *J Antimicrob Chemother* **2012**; 67:2090–100.
50. Lopez JA, Correa A, Navon-Venezia S, et al. Intercontinental spread from Israel to Colombia of a KPC-3-producing *Klebsiella pneumoniae* strain. *Clin Microbiol Infect* **2011**; 17:52–6.
51. Nordmann P, Naas T, Poirel L. Global spread of carbapenemase-producing Enterobacteriaceae. *Emerg Infect Dis* **2011**; 17:1791–8.
52. Yong D, Toleman MA, Giske CG, et al. Characterization of a new metallo-beta-lactamase gene, bla(NDM-1), and a novel erythromycin esterase gene carried on a unique genetic structure in *Klebsiella pneumoniae* sequence type 14 from India. *Antimicrob Agents Chemother* **2009**; 53:5046–54.
53. Nordmann P, Poirel L, Walsh TR, Livermore DM. The emerging NDM carbapenemases. *Trends Microbiol* **2011**; 19:588–95.
54. Castanheira M, Deshpande LM, Mathai D, Bell JM, Jones RN, Mendes RE. Early dissemination of NDM-1- and OXA-181-producing Enterobacteriaceae in Indian hospitals: report from the SENTRY Antimicrobial Surveillance Program, 2006–2007. *Antimicrob Agents Chemother* **2011**; 55:1274–8.
55. Seema K, Ranjan Sen M, Upadhyay S, Bhattacharjee A. Dissemination of the New Delhi metallo- β lactamase-1 (NDM-1) among Enterobacteriaceae in a tertiary referral hospital in north India. *J Antimicrob Chemother* **2011**; 66:1646–7.
56. Perry JD, Naqvi SH, Mirza IA, et al. Prevalence of faecal carriage of Enterobacteriaceae with NDM-1 carbapenemase at military hospitals in Pakistan, and evaluation of two chromogenic media. *J Antimicrob Chemother* **2011**; 66:2288–94.
57. Walsh TR, Weeks J, Livermore DM, Toleman MA. Dissemination of NDM-1 positive bacteria in the New Delhi environment and its implications for human health: an environmental point prevalence study. *Lancet Infect Dis* **2011**; 11:355–62.
58. Centers for Disease Control and Prevention. Hospital outbreak of carbapenem-resistant *Klebsiella pneumoniae* producing New Delhi metallo-beta-lactamase—Denver, Colorado, 2012. *MMWR Morb Mortal Wkly Rep* **2013**; 62:108.
59. He M, Miyajima F, Roberts P, et al. Emergence and global spread of epidemic healthcare-associated *Clostridium difficile*. *Nat Genet* **2013**; 45:109–13.
60. Phua CK, Chee CB, Chua AP, et al. Managing a case of extensively drug-resistant (XDR) pulmonary tuberculosis in Singapore. *Ann Acad Med Singap* **2011**; 40:132–5.
61. Institute of Medicine. Countering the problem of falsified and substandard drugs. Washington, DC: The National Academies Press, **2013**.
62. Leder K, Torresi J, Libman MD, et al.; for the GeoSentinel Surveillance Network. GeoSentinel surveillance of illness in returned travelers, 2007–2011. *Ann Intern Med* **2013**; 158:456–68.
63. Ghafur A. The Chennai Declaration: a solution to the antimicrobial resistance problem in the Indian subcontinent. *Clin Infect Dis* **2013**; 56:1190.
64. World Health Organization. International health regulations (2005). Geneva, Switzerland: WHO, **2008**.
65. Wernli D, Hausteil T, Conly J, Carmeli Y, Kickbusch I, Harbarth S. A call for action: the application of the International Health Regulations to the global threat of antimicrobial resistance. *PLoS Med* **2011**; 8: e1001022.