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.
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

<table>
<thead>
<tr>
<th>Reasons and Motivations for Seeking Medical Treatment Abroad</th>
<th>Potential Benefits to Receiving Countries of Medical Tourism</th>
<th>Current Challenges and Concerns Regarding Medical Tourism</th>
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<tbody>
<tr>
<td>Attributed to country of residence:</td>
<td></td>
<td>Associated with direct impact on medical tourist:</td>
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<tr>
<td>• Treatments not covered by health insurance in home country</td>
<td>• Improve overall quality of care due to standards for</td>
<td>• Lack of regulation of medical tourism companies</td>
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<tr>
<td>• Lack of health insurance making some care unaffordable in</td>
<td>treating foreign patients</td>
<td>• Accreditation of care providers may be lax</td>
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<td>home country</td>
<td>• Revenue from medical tourism may provide opportunities</td>
<td>and highly variable</td>
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<td>• Lack of technology or medical expertise in own country;</td>
<td>to improve access and quality for local residents</td>
<td>• Ethical concerns about doing procedures that are not</td>
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<tr>
<td>procedure or treatment unavailable</td>
<td>• Physicians and other healthcare workers trained elsewhere</td>
<td>supported by scientific evidence</td>
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<tr>
<td>• Legal or cultural constraints in home country (eg,</td>
<td>may repatriate to countries of origin to work and</td>
<td>• Fragmented or poor follow-up care; lack of</td>
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<td>termination of pregnancy; in-vitro fertilization;</td>
<td>improve local access and quality of care</td>
<td>communication between institutions abroad and at</td>
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<td>sexual reassignment surgery; surrogates for pregnancy;</td>
<td>• Patients and their families may stay in country or</td>
<td>home; poor medical records</td>
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<td>stem cell treatments)</td>
<td>region for sightseeing during recovery and bring</td>
<td>• Late complications following surgery</td>
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<td>• Medical insurance plans include coverage and may even</td>
<td>money to local economy</td>
<td>• High nosocomial infection rates; early and late</td>
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<td>offer incentives for out-of-country procedures</td>
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<td>infections</td>
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<td>Attributed to country providing care:</td>
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<td>• Lack of oversight to identify reasons for adverse</td>
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<td>• Low cost; more affordable medical care</td>
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<td>events and effect change</td>
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<td>• Treatment available without long waiting periods</td>
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<td>• Major surgery may be associated with increased risk</td>
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<td>• Modern facilities, including accreditation by Joint</td>
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<td>for perioperative deep vein thrombosis from long-haul</td>
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<td>Commission International, giving patients confidence in</td>
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<td>flights</td>
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<td>the quality of care</td>
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<td>• Lack of liability for poor results or malpractice</td>
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<td>• Expanding capacity to care for patients from developed</td>
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<td>• Lack of standards regarding patient privacy and</td>
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<td>countries and concierge services to assist with planning,</td>
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<td>confidentiality</td>
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<td>personalized assistance</td>
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<td>• Option to receive care and remain anonymous</td>
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<td>• Well-organized promoters of medical tourism, including</td>
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<td>professional organization, regular international</td>
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<td>meetings, websites, journal, and written materials</td>
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<td>• Sightseeing and touring in an exotic location in addition</td>
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<td>to obtaining medical care</td>
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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
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 asymptptomatically 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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