

# International stem cell tourism: a critical literature review and evidence-based recommendations

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Stem cell tourism is an emerging area of medical tourism activity. Frustrated by the slow translation of stem cell research into clinical practice, patients with debilitating conditions often seek therapeutic options that are not appropriately regulated. This review summarises recent developments in the field of stem cell tourism and provides clinicians with the information necessary to provide basic pretravel health advice to stem cell tourists. PubMed and Scopus databases were consulted for relevant publications, using combinations of the terms 'stem cell', 'tourism', 'regenerative medicine', 'international', 'travel medicine' and 'environmental health'. The leading countries in the international stem cell tourism market are the USA, China, India, Thailand and Mexico. As the majority of clinics offering stem cell therapies are based in low- and-middle-income countries, stem cell tourists place themselves at risk of receiving an unproven treatment, coupled with the risk of travel-related illnesses. These clinics do not generally provide even basic travel health information on their websites. In addition to often being ineffective, stem cell therapies are associated with complications such as infection, rejection and tumorigenesis. Physicians, researchers, regulatory bodies, advocacy groups and medical educators are encouraged to work together to improve patient and physician education and address current legislative deficiencies.

Keywords: environmental health, ethics, medical tourism, regenerative medicine, stem cell, travel health.

## Introduction

Medical tourism is a global, multibillion dollar industry that facilitates travel to another country with the intent of accessing medical care.<sup>1</sup> This industry is driven by patients seeking available, affordable and timely healthcare that is not always accessible domestically. The expanding media culture, combined with advances in electronic communication and access to low-cost air travel, has fuelled the growth of this industry.<sup>1</sup> Stem cell therapies are emerging as a growing subset of medical tourism activity. The ability of stem cells to differentiate into numerous cell types<sup>2</sup> may play an important role in stimulating the body's innate repair mechanisms.<sup>3</sup> The promise of restoring function to previously damaged organs and tissues offers exciting therapeutic potential for many health concerns.<sup>2</sup>

The therapeutic potential of stem cell technologies has aroused significant interest in both the lay public and clinicians.<sup>4</sup> Research into using stem cells to treat debilitating conditions that are currently incurable with limited treatment options has focused on multiple sclerosis, anti-ageing, Parkinson's disease, stroke and spinal cord injury. As these technologies are largely in their infancy, there are significant barriers to the translation of stem cell technology from bench to bedside.<sup>5</sup> The extensive media coverage of this novel field generates false public expectations surrounding the clinical applications of stem cells.<sup>6</sup> These expectations are problematic because despite the optimism towards regenerative medicine, its progress has been sluggish to date.<sup>7</sup> Consequently, many patients who are desperate for a cure travel abroad to receive unproven and unregulated stem cell treatments, a phenomenon known as stem cell tourism.

Table 1 summarises the findings from previous review articles focused on stem cell therapy and stem cell tourism. Having a basic understanding of the current literature in this field will become an increasingly valuable asset for physicians who wish to effectively counsel patients about these treatments.<sup>8</sup> This review aims to summarise recent developments in the field of stem cell tourism and provide travel medicine practitioners with the key information necessary to provide pretravel health advice to stem cell tourists.

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Title	Author(s)	Journal	Year	Article focus
Regulation of Stem Cell Technology in Malaysia: Current Status and Recommendations	Nishakanthi et al.	Science and Engineering Ethics	2020	Examines the objectives and effectiveness of the current Guideline for Stem Cell Research and Therapy in Malaysia
Cell therapy for Lung Disease: Current Status and Future Prospects	Enes and Weiss	Current Stem Cell Reports	2020	Overview of the current status of the field of mesenchymal stromal cell therapies with an emphasis on patients with lung diseases
Current state of Health Canada regulation for cellular and gene therapy products: potential cures on the horizon	Chisholm et al.	Cytotherapy	2019	Overview of the regulatory framework of cell and gene therapies in Canada
The 'Growing' Reality of the Neurological complications of Global 'Stem Cell Tourism'	Julian et al.	Seminars in Neurology	2018	Examines the status of stem cell tourism in neurology
Concise Review: A Comprehensive Analysis of Reported Adverse Event in Patients Receiving Unproven Stem Cell- Based Interventions	Bauer et al.	Stem Cells Translational Medicine	2018	Comprehensive retrospective analysis of adverse events reported for patients receiving unproven SCIs
Regulation of stem cell therapy travel	Cohen and Simana	Current Stem Cell Reports	2018	Focuses on the regulatory challenges of stem cell tourism travel
Current and emerging global themes in the bioethics of regenerative medicine: The tangled web of stem cell translation	Chan	Regenerative Medicine	2017	Recent developments in stem cell therapy landscape
Concise Review: Stem cell Interventions for people with Cerebral Palsy: Systematic Review with Meta-Analysis	Novak et al.	Stem Cells Translational Medicine	2016	Assesses the efficacy and safety of stem cell interventions for people with cerebral palsy
Social Responsibility in Stem Cell Research - Is the News All Bad	Benjaminy et al.	Stem Cell Reviews and Reports	2016	Examined articles from leading news media about stem cell interventions for neurodegenerative diseases
Science, ethics and communication remain essential for the success of cell-based therapies	Dominici et al.	Brain Circulation	2016	Distinguishes 'proven cell-based therapies' from 'unproven' and unauthorised cell-based therapies
Clinically relevant aspects of stem cell technologies: current state of play	Stuart and Pattavilakom	ANZ Journal of Surgery	2015	Summarises current clinical trials, with an emphasis on therapeutic potential, mechanism of action and associated risks

Table 1. Summary of previous review articles relating to stem cell tourism and stem cell therapy

#### S. Lyons et al.

Table 1. Continue

Title	Author(s)	Journal	Year	Article focus
Cell therapy worldwide: an incipient revolution	Rao et al.	Regenerative Medicine	2015	Discusses regulation of regenerative medicine, cord blood banking, mesenchymal stem cell-based products and induced pluripotent stem cells
Ethical considerations when counselling patients about stem cell tourism	Tsou	Continuum	2015	Highlights ethical issues physicians should consider and provides practical resources to promote informed patient decision-making
Regulating the therapeutic translation of regenerative medicine	Cuchiara	Expert Opinion on Biological Therapy	2015	Article argues for policy changes at the FDA and other regulatory agencies to streamline the clinical trials process
Why regenerative medicine needs an extracellular matrix	Prestwich and Healy	Expert Opinion on Biological Therapy	2015	Argues that synthetic extracellular matrices is the most essential contributor for improving the outcomes of cell therapy
From bench to FDA to bedside: US regulatory trends for new stem cell therapies	Knoepfler	Advanced Drug Delivery Reviews	2015	Discusses the scientific, ethical and medical questions associated with the emerging trends in stem cell product development and their regulatory pathways in the USA
Human stem- cell research in gastroenterology: experimental treatment, tourism and biobanking	Hermerén	Best Practice and Research Clinical Gastroenterology	2014	Outlines the growing interest in the possibility of applying stem cell therapies to gastrointestinal diseases and discusses ethical issues raised by this kind of research
Representations of stem cell clinics on Twitter	Kamenova et al.	Stem Cell Reviews and Reports	2014	Review of Twitter posts discussing unproven stem cell therapies
Professional regulation: a potentially valuable tool in responding to 'stem cell tourism'	Zarzeczny et al.	Cell Press	2014	Considers the use of professional regulation to address physician involvement in stem cell tourism
Health consumers and stem cell therapy innovation: markets, models and regulation	Salter et al.	Regenerative Medicine	2014	Argues that the problem of stem cell tourism is embedded in the demand-supply relationship of the health consumer market and its engagement with different types of stem cell therapy innovation
The Ethics of Stem Cell-Based Aesthetic Surgery: Attitudes and Perceptions of the Plastic Surgery Community	Nayar et al.	Aesthetic Surgery Journal	2014	Characterises the attitudes of plastic surgeons regarding stem cell-based aesthetics

#### International Health

Table 1. Continue

Title	Author(s)	Journal	Year	Article focus
Curbing stem cell tourism in South Africa	Meissner- Roloff and Pepper	Applied and Translational Genomics	2013	Argues that a failure to understand the ethical, moral and cultural ramifications when new scientific concepts are introduced could hinder the efficacy and speed of bringing discoveries to the patient
Reassessing direct-to-consumer portrayals of unproven stem cell therapies: is it getting better?	Ogbogu et al.	Regenerative Medicine	2013	Assesses whether increased scrutiny of 'stem cell tourism' has resulted in changes to online claims by clinics that provide putative unproven stem cell treatments
Autologous cell therapies: Challenges in US FDA regulation	McAllister et al.	Regenerative Medicine	2012	Highlights the challenges the US FDA faces and present talking points for an improved regulatory framework for autologous CBTs
Stem cells in clinical practice: applications and warnings	Lodi et al.	Journal of Experimental and Clinical Cancer Research	2011	Discusses available stem cell subtypes and their rational use in the medical area, with a specific focus on their therapeutic benefits and side effects
The unregulated commercialization of stem cell treatments: A global perspective	Sipp	Frontiers of Medicine	2011	Provides an overview of pseudomedical stem cell treatments for amyotrophic lateral sclerosis and makes regulatory recommendations
Clinical translation of cell transplantation in the brain	Dunnett and Rosser	Current Opinion in Organ Transplantation	2011	Identifies the major recent advances in stem cell transplants into the brain of animal models and discusses preliminary results on feasibility, safety, efficacy in an a range of human neurodegenerative diseases
Stem cell stratagems in alternative medicine	Sipp	Regenerative Medicine	2011	Discusses the stem cell industry as practised by alternative medicine providers and highlights points of commonality in their strategies for marketing
Abbreviations: CBTs, cell-based there	pies: SCIs, stem cell inter	ventions.		

## Search strategy and selection criteria

This narrative literature review was conducted in January 2021. PubMed and Scopus databases were consulted for relevant publications, with a preference for more recent literature (from 2010 through 2020), using combinations of the terms 'stem cell', 'tourism', 'regenerative medicine', 'international' and 'travel medicine'. All articles retrieved were screened from their title and abstract. Articles with a focus on stem cell tourism were in-

Descending rank	Clinical indication
1	Multiple sclerosis
2	Anti-ageing
3	Parkinson's disease
4	Stroke
5	Spinal cord injury
6	Cerebral palsy
7	Autism
8	Amyotrophic lateral sclerosis
9	Alzheimer's disease
10	Arthritis

**Table 2.** Leading clinical indications for stem cell therapy (afterConnolly et al.<sup>15</sup>)

cluded, and relevant references cited in retrieved articles were also consulted. Only articles published in the English language were included. The final reference list was agreed upon by all authors.

## Motivations for stem cell tourism

Many factors influence patients in their decision to pursue medical services abroad.<sup>9</sup> These include cost, perceived quality of care, long waiting times, domestic restrictions, inability to participate in clinical trials and lack of access to unapproved treatments.<sup>9</sup> Primarily advertised online, stem cell therapies target a broad spectrum of diseases and disabilities,<sup>10</sup> cosmetic procedures, sports performance enhancement and injury recovery.<sup>5</sup> Recently, in the face of the COVID-19 pandemic, stem cell clinics have begun marketing putative therapies that counter the effects of the virus.<sup>11</sup>

While individual motivations to seek unproven and unregulated therapies may vary, they are underpinned by hope and the desire to exhaust all available options.<sup>9</sup> Many patients pursue these treatments in desperation<sup>12</sup> and when conventional medicine fails to adequately alleviate their symptoms.<sup>13</sup> Although disease-modifying treatments exist for some conditions, patients living with progressive diseases are largely limited to symptomatic therapies.<sup>14</sup> It is not surprising then that patients suffering from serious long-term medical conditions are willing to explore experimental options including stem cell therapies.<sup>14</sup>

# Medical and financial risks

Patients seeking stem cell interventions overseas are often afflicted with underlying debilitating conditions that frequently exist as comorbidities (Table 2).<sup>15</sup> As the majority of clinics offering these unproven treatments are based in low- and middle-income countries (LMICs) with endemic risks of infectious disease transmission, these stem cell tourists place themselves at risk of receiving an unproven treatment,<sup>15</sup> coupled with the risk of travel-related illnesses from both communicable and

non-communicable diseases.<sup>16</sup> Notwithstanding this, the clinics offering these treatments do not generally provide even basic travel health information on their websites.<sup>15</sup>

In addition to often being ineffective, stem cell therapies have been associated with complications such as infection, rejection, tumorigenesis and death.<sup>5</sup> A recent case study by Madhavan et al. described a 74-y-old man from the USA who received intravenous and intrathecal stem cell injections in Russia, to treat chronic fatigue and decreased exercise tolerance. His treatment resulted in the formation of an intrathecal mass and cauda equina nerve root thickening, resulting in a substantial neurological deficit. He experienced progressive bilateral lower extremity weakness and developed urinary incontinence, both of which were refractory to medical and surgical therapy. This case study forms part of a growing body of evidence that highlights the dangers of unregulated stem cell therapies.<sup>17</sup>

Stem cell tourism may also give rise to severe financial and socioeconomic consequences that leave patients in poverty.<sup>13</sup> It is estimated that the cost per stem cell treatment is between US\$10000 and US\$60000, excluding travel expenses.<sup>18</sup> While the entire financial burden of the treatment lies in the hands of patients, there is rarely any form of follow-up with patients once they have been discharged from the treatment facilities.<sup>5</sup> This has wide-reaching economic implications for patients' native healthcare systems,<sup>19</sup> especially if patients require follow-up care to treat complications and infections incurred from the procedure they received abroad.<sup>20</sup> The cost burden is significant, not only for patients, but also for public health programmes, insurance companies and hospitals.<sup>21</sup> This presents challenges for countries like Canada that are publicly funded, as the follow-up care tends to be complex and expensive.<sup>22</sup> Medical tourism also has global public health security implications through the heightened risk of importation of multidrug-resistant bacterial strains from countries with lower levels of antimicrobial stewardship.

## Influence of social media on stem cell tourism

Stem cell therapies that have not been approved for clinical use are not routinely discussed, recommended or advertised by physicians.<sup>23</sup> This has created an opportunity for social media platforms to propagate information regarding stem cell interventions directly to patients from across the world.<sup>23</sup> This direct-toconsumer advertising employs various techniques to legitimise providers and their products.<sup>24</sup> They use strong emotional appeals such as patient-based testimonials, blogs and third-party endorsements to connect and engage directly with their audiences.<sup>24</sup> They also use terms such as 'clinical data', 'scientific publications' and 'conference proceedings' on their websites in an attempt to lend credibility to their interventions.<sup>5</sup> In a study of the geographical representation of stem cell therapies marketed online, 21 countries spanning 5 continents were found to be offering and marketing their therapies virtually.<sup>15</sup> Another study reported that >400 websites currently advertise stem cell-based interventions online for a wide range of conditions.<sup>25</sup> The leading countries in the international stem cell tourism market are the USA, China, India, Thailand and Mexico (Table 3).<sup>15</sup>

Most media coverage is highly optimistic about the therapeutic potential of stem cell therapies while simultaneously

Stem cell tourism destination	Proportion of clinics (%)			
USA	27			
China	12			
India	12			
Thailand	11			
Mexico	9			
Argentina	3			
Australia	3			
Austria	3			
Germany	3			
Ukraine	3			
Malaysia	3			
Colombia	1			
Dominican Republic	1			
Israel	1			
South Korea	1			
Lebanon	1			
New Zealand	1			
Panama	1			
Philippines	1			
Russia	1			
Spain	1			

**Table 3.** Global distribution of stem cell clinics marketed to medical tourists (after Connolly et al.<sup>15</sup>)

forecasting unrealistic timelines for clinical use.<sup>26</sup> Studies have examined the Twitter profiles of stem cell clinics and the content of messages they have posted online and found that the tone of most tweets was unduly positive and that critical discussions of the social and ethical implications of unproven stem cell therapies or their health risks were rarely entertained.<sup>27</sup> While portraying the results of these unproven treatments positively,<sup>28</sup> these media reports often underestimate their risks and sensationalise the preliminary scientific findings.<sup>29</sup> A study of Australian stroke survivors found that most respondents knew very little about the risks and benefits associated with stem cell treatments, with most relying on the media and online advertisements as their primary sources of information.<sup>30</sup> This is problematic because a growing number of interventions are being offered outside of clinical trials and marketed online, where there is little scientific justification for their use.<sup>24</sup>

The reach of social media influencers, athletes and other high profile individuals<sup>31</sup> has generated much attention in the news and on social networks.<sup>32</sup> A recent example is that of the Canadian ice-hockey player, Gordie Howe, who travelled to Mexico following a stroke to receive stem cell treatments.<sup>32</sup> When Howe's stem cell travel was reported in the news, the public assumed the efficacy of his treatment without acknowledging or considering the lack of scientific evidence and potential risks associated with the procedure.<sup>33</sup> Reports of athletes seeking sports performance enhancement and injury recovery have contributed to the hype surrounding stem cell tourism. This is challenging for patients with debilitating medical conditions because they are especially vulnerable to the influence of success stories<sup>34</sup> and tend to view these apparent favourable outcomes as an indicator that treatments are both safe and effective.  $^{\rm 35}$ 

## **Regulation of stem cell therapies**

Stem cell clinics that lack accreditation have proliferated worldwide due to weak regulations,<sup>36</sup> bridging the gap between the growing patient demand for unmet medical needs and the potential of medical innovation.<sup>37</sup> While neither scientifically established nor approved clinically, direct-to-consumer offerings of these treatments present scientific, patient and public welfare issues.<sup>38</sup> Protecting patients from expensive, unproven, ineffective and potentially harmful therapies requires legal, ethical and public health oversight.<sup>39</sup>

Stem cell clinics that offer unproven therapies often operate in a regulation vacuum, via regulatory loopholes, or in violation of existing regulatory standards.<sup>5</sup> While the administration of these unproven therapies occurs globally, most involve LMICs<sup>40</sup> such as India, Thailand, Mexico and the Dominican Republic.<sup>15</sup> This is attributable primarily to the ease of travel and globalisation, which enables patients to circumvent local restrictions.<sup>40</sup> The increasing use of unproven stem cell therapies has created an urgent need for universal agreement between national and international bodies over the commercialisation of medical practices and products.<sup>41</sup>

While some countries have implemented regulations to curb stem cell tourism, many have inadvertently created loopholes whereby the regulations leave room for varied interpretation.<sup>42</sup> These clinics may then exploit these loopholes and offer unproven and risky treatments directly to patients.<sup>42</sup> In the USA, stem cell products are regulated by the Food and Drug Administration (FDA). In order to circumvent the rigorous regulatory approval process mandated by the FDA, many clinics have classified their stem cell therapies as human cellular and tissue-based products (HCT/P) rather than as biological drugs,<sup>42</sup> because HCT/Ps that are minimally manipulated and intended for homologous use are not subject to FDA regulations.<sup>2</sup> This vague language created a loophole for US clinics to exploit in the early 2000s. In 2014, the FDA updated their regulations by clarifying the meaning of the terms 'minimal manipulation' and 'homologous use' to reduce the areas of uncertainty that arose within the regulations.<sup>2</sup>

Another legislative challenge is the lack of harmonised regulatory schemes across the world.<sup>42</sup> The legal divergences between countries in relation to codes of conduct, practice or ethics, as well as the enforcement patterns and bounds of a disciplinary authority, enable clinics to evade regulatory oversight.<sup>10</sup> The concern is that these jurisdictional variations create a platform by which clinics can seek out the most lenient regulatory environment.<sup>10</sup> In Japan, if early phase trials show promise of safety and efficacy, clinics can advertise regenerative medicine therapies for up to 7 y without demonstrating ongoing treatment effectiveness.<sup>43</sup> The goal of this strategy appears to be the expedited commercialisation of stem cell products that will help to encourage future investment in the field of regenerative medicine.44 This has created a multinational research market whereby clinics can relocate their operations or clinical trials to less-regulated jurisdictions.44

In an attempt to distance the scientific community and stem cell research from clinics offering unproven and unregulated stem cell-based interventions,45 the International Society for Stem Cell Research (ISSCR) has developed guidelines that seek to promote rigour, oversight and transparency in all areas of practice.<sup>46</sup> They caution patients against use of fraudulent stem cell therapies and recommend patients only to undergo procedures that have been registered with the FDA or European Medicines Agency.<sup>47</sup> Unregulated and unproven practices undermine the credibility and validity of leaitimate stem cell research and threaten to compromise the future development of the field.<sup>15</sup> Furthermore, participation in unregulated stem cell treatments may deem patients ineligible for future enrolment in approved stem cell clinical trials, should these become available.<sup>48</sup> Fundamentally, stem cell tourism may indirectly hinder the progression and advancement of stem cell science.<sup>7</sup>

#### **Bioethical considerations**

Providing patients with trustworthy, accurate and scientific information can have a dissuasive effect against the pursuit of unproven therapies. Educating patients and caregivers can help them make better informed healthcare decisions.<sup>49</sup> Informed healthcare consent is important because it helps to safeguard patient autonomy, empower patients during the course of their care and cultivate trust between physicians and their patients.<sup>28</sup> Many believe that patients have the right to autonomy in pursuing any available treatment option in the face of terminal or disabling illnesses.<sup>50</sup> This has led to the introduction of the Right to Try Act (RIT) in the USA, which gives terminally ill patients access to experimental drugs that have passed phase I testing.<sup>51</sup> Supporters of the RIT argue that if there is hope that a treatment might be effective, patients should have the right to fight for their own lives.<sup>39</sup> Petersen et al. has suggested that for many patients and carers who have exhausted conventional treatment options, the hope offered by stem cell therapy providers may be preferable to the option of taking no action.<sup>52</sup> Opponents of this movement argue that liberal access to experimental therapies could negatively impact patients by offering false hope when they are in a highly vulnerable state, ultimately leading to an increased burden of suffering.<sup>39</sup> This phenomenon is known as therapeutic misestimation.<sup>53</sup> It describes the tendency of patients and their loved ones to misinterpret the therapeutic potential of a treatment as well as the risks involved.<sup>53</sup> This is ethically problematic as patient expectations and estimation of medical benefits and risks are largely inaccurate, undermining the autonomy of a patient's choice to consent to experimental stem cell research participation.54

While patient autonomy must be respected, clinicians have a responsibility to provide patients with all relevant information to enable them to make a genuinely informed decision regarding their own care.<sup>55</sup> Patients should be informed of all risks related to both the procedure and travel<sup>56</sup> before engaging in stem cell tourism.<sup>22</sup> If the physician can demonstrate an evidence-based understanding of the advantages and disadvantages that these therapies entail,<sup>28</sup> it will help to foster transparency and enhance the physician-patient relationship.<sup>45</sup> This will help to ensure that patients feel comfortable approaching their physicians before enlisting in unproven and unregulated therapies. Properly educating

patients about the fraudulent claims made by stem cell clinics will ultimately protect against their exploitation.<sup>47</sup>

# Future directions and research priorities

Faced with life-threatening conditions, many patients are willing to pursue unregulated and unproven stem cell treatments in anticipation of a cure or disease amelioration. These circumstances allow stem cell clinics the opportunity to exploit the therapeutic hope of patients and their families. Improvement in educational and regulatory efforts at both a national and international level is essential. While acknowledging the differences in legal frameworks across nations, professional guidelines, such as those published by the ISSCR, should be formalised into international governmental regulations.<sup>42</sup> A global accreditation system operated by the WHO or Joint Commission International should be established,<sup>57</sup> whereby review boards can examine the quality of the information provided by clinics.<sup>42</sup> National authorities should enforce penalties against clinics making false claims.<sup>58</sup> From common law fraud to consumer fraud, action should be taken against clinics that violate truthful advertising regulations.<sup>59</sup> Finally, these clinics should be required to demonstrate evidence of review and approval for human subject protection and requlatory oversight.<sup>42</sup> This is especially important as serious complications following the administration of unproven stem cell interventions have been documented, and research suggests that they may be significantly under-reported.<sup>60</sup> This calls for the creation of a national registry of well-documented cases of stem cell tourism clinical outcomes. Universal approaches to the provision of standardised, accessible stem cell therapy-based care should be pursued.

Providing evidence-based education to both clinicians and their patients may help combat unethical and dangerous practices surrounding stem cell tourism.<sup>60</sup> There is an urgent need to assess physician competence in counselling patients regarding the safety and efficacy of these treatments.<sup>60</sup> Currently, the number of patients who approach their physicians to inquire about such therapies is unknown. Thus, a research opportunity exists to assess whether physicians feel adequately prepared to educate their patients when asked about these therapies and how often this occurs.<sup>47</sup> Furthermore, there is a need to create unified, evidence-based guidelines to help standardise provider education.<sup>61</sup> Instruction in regenerative medicine should be included in undergraduate and postgraduate medical curricula to provide future practitioners with the skills to address patient queries regarding stem cell tourism.

Patient advocacy groups in conjunction with regulatory agencies have been encouraged to work together to promote patient and physician education to help limit and eliminate these practices.<sup>37</sup> Patients view these advocacy groups as a trusted source of information, and so greater efforts should be made to create up-to-date educational resources for patients who are considering stem cell treatments.<sup>62</sup> These resources should include information regarding medical and financial risks, credible and objective patient testimonials, and the potential of being excluded from future clinical trials, should they become available.<sup>48</sup> Providing patients with reliable information can help empower them to be effective advocates for their own health<sup>63</sup> and ensure they have the requisite knowledge to make an informed decision.  $^{\rm 15}$ 

Given that the current educational resources available cover a broad range of medical conditions, it is possible that the desian and content of the current materials are not optimised for all patients.<sup>64</sup> Stroke survivors, for example, often experience cognitive, language, communication or visual problems.<sup>48</sup> It has been suggested that using more interactive and appealing methods of communicating health information may be more effective for these patients.<sup>30</sup> Research has also shown that, in order to deliver health information effectively, it must be perceived as both meaningful and comprehensive to the consumer.<sup>64</sup> Resources should be created in both audio-visual and written formats to accommodate different patient needs.<sup>64</sup> Summaries of current research findings and new and emerging treatment options should be actively promoted to patients via the media and online platforms in easily understandable language.<sup>48</sup> Keeping patients up to date with the current literature will help challenge the unsubstantiated claims being made by unscrupulous stem cell clinics worldwide.27

A recent review article by Master et al. reflects on the flourishing 'unproven stem cell intervention industry' as a health problem of global significance. The authors propose the adoption of a global approach with the creation of a WHO Expert Advisory Committee on Regenerative Medicine to promote international cooperation on the subject, harmonise with national scientific societies, issue universal recommendations, promote regulatory frameworks that address unmet clinical needs and counter misinformation through an educational campaign.<sup>65</sup>

## Limitations of literature review

Although we used broad search terms to identify sources pertinent to stem cell tourism, some may have been overlooked. Our search strategy was restricted to two databases: Scopus and PubMed. While these represent two major databases, only articles published during 2010–2020, with a preference for newer evidence, were reviewed. This review was primarily restricted to articles published in the English language, and potentially relevant studies published in Spanish and other languages may have been omitted for consideration. As a narrative literature review, there was no formal assessment of the quality of the evidence included or any potential for bias on behalf of the authors in their selection methods. However, we have attempted to view the literature through as critical a lens as possible.

#### Conclusions

Stem cell technologies are often associated with inflated expectations of their therapeutic potential. While this has fostered substantial financial support for legitimate stem cell research, significant challenges remain in their translation from bench to bedside. Frustrated by apparently slow progress in the field, patients with debilitating and terminal conditions have begun pursuing alternative options that are neither approved clinically nor appropriately regulated. While regenerative medicine offers significant therapeutic potential, measures need to be put in place to ensure patient safety. Physicians, researchers, scientists, regulatory bodies and advocacy groups are encouraged to work together to improve patient and physician education and address current legislative deficiencies. As stem cell research is still largely in its infancy, it will be interesting to observe if COVID-19 will have an impact on stem cell tourism as it continues to restrict travel across international borders.

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