

Medical societies, patient education initiatives, public debate and marketing of unproven stem cell interventions

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Abstract

Businesses marketing unproven stem cell interventions proliferate within the U.S. and in the larger global marketplace. There have been global efforts by scientists, patient advocacy groups, bioethicists, and public policy experts to counteract the uncontrolled and premature commercialization of stem cell interventions. In this commentary, we posit that medical societies and associations of health care professionals have a particular responsibility to be an active partner in such efforts. We review the role medical societies can and should play in this area through patient advocacy and awareness initiatives

Key Words: *medical societies, health care professionals, unproven stem cell interventions, “stem cell” clinics, patients*

Introduction

As businesses marketing unproven stem cell interventions proliferate within the USA and in the larger global marketplace, researchers from a variety of academic disciplines and clinical specialties are calling for more robust regulatory oversight, patient education initiatives and public policy debate concerning ethically and scientifically justifiable governance standards for cell-based therapeutics. A recent publication by Sipp *et al.* [1] is an important and timely contribution to global efforts to counteract the rapid increase in businesses selling unproven and unlicensed “stem cell” interventions. The authors rightly emphasize the need for mobilization of various stakeholders and coordinated actions at multiple levels of governance. Building upon their critical analysis and “call to action,” along with recent Food and Drug Administration (FDA) actions sanctioning specific outfits offering unproven cell-based therapies [2,3], we propose that medical societies have a particular responsibility to the patient communities they serve to participate in the struggle to counter the widespread promotion of unproven stem cell interventions. In this perspective, we review the role medical societies can and should play in pursuing

this objective through patient advocacy, education, awareness and engagement initiatives.

As the authors note, medical specialties ranging from respiratory medicine to sports medicine and ophthalmology have issued cautionary statements alerting patients to risks associated with undergoing unproven stem cell interventions [4–6]. These important documents articulate the considered positions of societies representing thousands of medical professionals and provide insight into how such organizations are trying to protect patients from risk of avoidable injuries and even possibility of fatal outcomes, significant financial harm and psychological harms associated with dashed hopes. Such statements also help to clarify what distinguishes carefully designed and properly conducted clinical research involving administration of stem cells or their derivatives as investigational agents from predatory marketing schemes based on little or no credible scientific evidence. However, both the strategies used by businesses marketing unproven stem cell interventions and the global regulatory landscape are in constant flux. Medical societies and associations of health care professionals need to respond to these challenges in a dynamic and sustained manner.

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First, education efforts organized by medical societies should be multifaceted and directed at both patients and their loved ones and practicing physicians and other related caregivers. Physicians, nurses and other health care professionals are in the unique position of actively participating in the care and decision-making processes of patients. They play a crucial role in providing information to patients and their family members and helping them make informed decisions about medical interventions. Given their role in helping patients weigh options, gather information and make difficult health-related decisions, it is essential that physicians and other caregivers play an active and engaged role in educating and counseling patients who are considering unproven stem cell interventions [7,8]. For a number of medical conditions, there are promising regenerative medicine-based approaches at various stages of development, extending from basic research to pre-clinical studies and clinical trials [9]. Unfortunately, due to time constraints and challenges associated with tracking the often substantial number of clinical studies associated with particular diseases and other medical conditions, many medical professionals are ill-equipped to discuss the current status of stem cell-based interventions in their clinical specialty. Medical societies have a vital role to play in keeping clinicians informed of such developments and helping patients better understand the current state of clinical research, whether related to stem cells or other possible therapies [10].

Medical societies are well-positioned to distribute to their members and to patients specialty-specific information about developments in stem cell research. Dedicated stem cell-related sessions at medical conferences, literature reviews in specialty and society journals, webinars, patient education guides, succinct summaries of the current state of stem cell research related to particular diseases and other medical problems and regular updates concerning relevant regulatory developments can all be used to keep physicians informed, current and able to respond to their patients' questions and concerns. Similarly, medical societies need to develop, regularly update and widely distribute patient information sheets on the current status of stem cell treatments and clinical research, written using accessible language [11,12]. Patients and their advocates should be encouraged to participate in the development of such guides.

There are currently volunteer physician/scientist organizations, such as ALSUntangled, that publish scientific reports critically evaluating the therapeutic claims of particular "stem cell" clinics [13–15]. These reports appear to have an impact within patient communities and help promote informed, evidence-based decision-making. The ALSUntangled model of paying

attention to businesses marketing unproven stem cell interventions and critically assessing their marketing claims and clinical activities provides insight into how medical societies might better educate and inform physicians and patients. Caution would need to be exercised when producing such reports because some businesses selling unproven stem cell interventions have displayed a willingness to threaten and attempt to intimidate critics. Medical societies, therefore, need to decide whether to address the problem of widespread marketing of unproven stem cell interventions in general terms or grapple with the promotional claims of specific businesses. Acknowledging the importance of engaging in such work in a careful manner that minimizes the threat of litigation, we suggest that the ALSUntangled approach to examining the claims of businesses selling unproven stem cell interventions has lessons that extend beyond the amyotrophic lateral sclerosis community to other groups of patients and clinicians. For example, medical societies can help patients identify marketing claims that are unsupported by scientific evidence. Medical societies can also play a role in bringing particular businesses and clinicians to the attention of regulatory authorities. In some instances, it will be prudent for medical societies to seek the advice of legal counsel before deciding how best to report to authorities clinical and commercial practices that do not appear to comply with applicable regulatory standards.

Next, medical associations should take steps to ensure that they are not endorsing or otherwise enabling clinicians and businesses advertising unproven stem cell-based interventions. Sipp *et al.* summarize the many tokens of scientific legitimacy that have been co-opted by clinics selling unproven "stem cell" interventions [1]. Medical specialties have an important role to play in exposing such tokens. For instance, presentation of data originating from pay-to-participate stem-cell "studies," when such studies have not been properly subject to review by institutional review boards and national regulatory authorities such as the FDA or Health Canada, should not be permitted at medical conferences [16]. The pledges required for members of the International Society for Cellular Therapy (ISCT) [17] and the International Society for Stem Cell Research (ISSCR) may serve as models for medical associations that wish to deter their members from engaging in unethical and unprofessional cell-based interventions. Such pledges can be tied to expectations regarding professional conduct associated with membership in particular medical societies. For example, individuals interested in becoming members of medical societies could first be required to read key resources on ethical, legal and scientific issues related to unproven stem cell interventions and to pledge that they will not be involved in stem

cell-based clinical activities that fall outside the scope of evidence-based medical practice or properly reviewed, conducted and regulated clinical trials or medical innovation [18]. At the same time, it should be recognized that such an honor system will not necessarily dissuade unscrupulous individuals or groups. As a result, medical societies may need to implement more stringent self-regulation approaches. One such approach can involve close collaboration and information exchange with professional bodies that have wide disciplinary authority in issues of professional misconduct, such as state medical boards (USA), provincial medical colleges (Canada) and national medical councils or health ministries (UK, India, China and Mexico) [19].

The regulation of regenerative medicine and stem cell products is another area that calls for greater engagement by medical societies. In many countries at present there is increased pressure to proceed with regulatory models, such as conditional approval, which favor patient access to experimental interventions at early stages of clinical testing [20]. However, there are valid concerns that implementation of such regulatory frameworks will lead to lower safety and efficacy standards and increased risks to patients and research subjects. National, regional and international medical societies should monitor regulatory developments, provide regulatory updates for their members and make informed contributions to regulatory debates by submitting comments to regulatory agencies, issuing statements alone or in common with other societies and supporting responsible news media coverage of possible changes to regulatory standards. Many countries provide opportunities for public responses before new laws and regulations are passed. For example, in the USA, the FDA recently sought public comments on four draft guidance documents related to stem cells and other human cells and tissues as part of its process of developing a new regulatory framework for stem cells and regenerative medicine. Medical associations should take advantage of such mechanisms for democratic engagement and make informed, timely contributions to the development of public policies.

To maximize the impact of their education and advocacy efforts, medical communities should cultivate relationships and build alliances with other important stakeholders such as scientific societies and patient advocacy groups. For instance, development of clinical guidelines related to cell-based interventions would greatly benefit from the inclusion of stem cell scientists, bioethicists and experts in public policy and regulatory science. The ISCT Presidential Task Force on the Use of Unproven Cellular Therapies provides a good example of a working group with involvement of experts from various fields related to cell and gene therapy. This approach has been proven partic-

ularly productive as shown by the recent publication of a reference guide covering a variety of challenges posed by the proliferation of unproven stem cell interventions [21–23]. In a similar vein, the ISSCR has been actively engaged in educational activities on the marketing of unproven stem cell interventions for the past 10 years, including deployment of patient-centered online resources [24]. These efforts culminated in the publication in 2016 of the revised and expanded guidelines for Stem Cell Research and Clinical Translation that call, among others, for sensible science communication that avoids hype regarding stem cell research [25,26]. Similarly, patient advocacy groups and foundations are vital partners when promoting public awareness initiatives concerning the state of the art of cell-based treatments for their diseases of interest.

We acknowledge that the task of countering the misleading promotional claims of “stem cell” outfits and the powerful narratives of on-line patient “communities of hope” [27] will be difficult. Responding in a sensitive manner to the powerful role of hope in shaping attitudes toward stem cell interventions is a particularly challenging issue. Furthermore, we recognize that some patients face life-threatening illnesses or injuries, are desperate and are particularly vulnerable to dramatic but unsubstantiated marketing claims about treatments and cures. For these reasons, the communication and education efforts we outline must move beyond the largely discredited “knowledge deficit” model and draw instead on evidence-based scientific communication practices [28–30]. Grappling with these difficult issues is far from straightforward, but medical societies have too often been absent from this arena. It is time they adopted a more active and engaged role in patient education initiatives and public awareness efforts intended to draw attention to the many risks associated with businesses selling unproven and unlicensed stem cell interventions. Organizations such as the ISSCR and the ISCT provide insight into the contributions medical societies need to make to public debate.

References

- [1] Sipp D, Caulfield T, Kaye J, Barfoot J, Blackburn C, Chan S, et al. Marketing of unproven stem cell-based interventions: a call to action. *Sci Transl Med* 2017;9:5.
- [2] Food & Drug Administration. FDA acts to remove unproven, potentially harmful treatment used in ‘stem cell’ centers targeting vulnerable patients; 2017. Available from: <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm573427.htm>. [Accessed 27 September 2017].
- [3] Food & Drug Administration. FDA warns US Stem Cell Clinic of significant deviations; 2017. Available from: <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm573431.htm>. [Accessed 27 September 2017].

- [4] Ikonomou L, Freishtat RJ, Wagner DE, Panoskaltis-Mortari A, Weiss DJ. The global emergence of unregulated stem cell treatments for respiratory diseases professional societies need to act. *Ann Am Thorac Soc* 2016;13:1205–7.
- [5] Osborne H, Anderson L, Burt P, Young M, Gerrard D. Australasian college of sports physicians-position statement: the place of mesenchymal stem/stromal cell therapies in sport and exercise medicine. *Clin J Sport Med* 2016;26:87–95.
- [6] Parke DW, Lum F, McLeod SD. Stem cell treatment: think twice if they ask for payment. *Ophthalmology* 2016;123:S62–3.
- [7] Levine AD, Wolf LE. The roles and responsibilities of physicians in patients' decisions about unproven stem cell therapies. *J Law Med Ethics* 2012;40:122–34.
- [8] Zarzeczny A, Clark M. Unproven stem cell-based interventions & physicians' professional obligations; a qualitative study with medical regulatory authorities in Canada. *BMC Med Ethics* 2014;15:75.
- [9] Rao M, Mason C, Solomon S. Cell therapy worldwide: an incipient revolution. *Regen Med* 2015;10:181–91.
- [10] Bowman M, Racke M, Kissel J, Imitola J. Responsibilities of health care professionals in counseling and educating patients with incurable neurological diseases regarding "stem cell tourism" caveat emptor. *JAMA Neurol* 2015;72:1342–5.
- [11] Ikonomou L, Panoskaltis-Mortari A, Wagner DE, Freishtat R, Weiss DJ. Unproven stem cell treatments for lung disease-an emerging public health problem. *Am J Respir Crit Care Med* 2017;195:P13–14.
- [12] Jin J. Stem cell treatments. *JAMA* 2017;317:330.
- [13] The ALSUntangled Group. ALSUntangled update 4: investigating the XCell-center. *Amyotroph Lateral Scler* 2010;11:337–8.
- [14] The ALSUntangled Group. ALSUntangled update 3: investigating stem cell transplants at the hospital san jose tecnologico de monterrey. *Amyotroph Lateral Scler* 2010;11:248–9.
- [15] The ALSUntangled Group. ALSUntangled No. 27: precision stem cell. *Amyotroph Lateral Scler Frontotemporal Degener* 2015;16:282–5.
- [16] Turner L. ClinicalTrials.gov, stem cells and 'pay-to-participate' clinical studies. *Regen Med* 2017;12(6):705–19.
- [17] International Society for Cellular Therapy. ISCT Membership; 2017. Available from: <http://www.celltherapysociety.org/?page=MemberType>. [Accessed 27 September 2017].
- [18] Lindvall O, Hyun I. Medical innovation versus stem cell tourism. *Science* 2009;324:1664–5.
- [19] Zarzeczny A, Caulfield T, Ogbogu U, Bell P, Crooks VA, Kamenova K, et al. Professional regulation: a potentially valuable tool in responding to "stem cell tourism". *Stem Cell Reports* 2014;3:379–84.
- [20] von Tigerstrom B. Revising the regulation of stem cell-based therapies: critical assessment of potential models. *Food Drug Law J* 2015;70:315–37.
- [21] Dominici M, Nichols K, Srivastava A, Weiss DJ, Eldridge P, Cuende N, et al. Positioning a scientific community on unproven cellular therapies: the 2015 international society for cellular therapy perspective. *Cytotherapy* 2015;17:1663–6.
- [22] Nichols K, Janssen W, Wall D, Cuende N, Griffin D. Part 4: interaction between unproven cellular therapies and global medicinal product approval regulatory frameworks. *Cytotherapy* 2016;18:127–37.
- [23] Srivastava A, Mason C, Wagena E, Cuende N, Weiss DJ, Horwitz EM, et al. Part 1: defining unproven cellular therapies. *Cytotherapy* 2016;18:117–19.
- [24] International Society for Stem Cell Research. A Closer Look at Stem Cell Treatments; 2017. Available from: <http://www.closerlookatstemcells.org/>. [Accessed 27 September 2017].
- [25] Caulfield T, Sipp D, Murry CE, Daley GQ, Kimmelman J. Confronting stem cell hype. *Science* 2016;352:776–7.
- [26] Daley GQ, Hyun I, Apperley JF, Barker RA, Benvenisty N, Bredenoord AL, et al. Setting global standards for stem cell research and clinical translation: the 2016 ISSCR guidelines. *Stem Cell Reports* 2016;6:787–97.
- [27] Petersen A, MacGregor C, Munsie M. Stem cell miracles or Russian roulette?: patients' use of digital media to campaign for access to clinically unproven treatments. *Health Risk Soc* 2016;17:592–604.
- [28] Simis MJ, Madden H, Cacciatore MA, Yeo SK. The lure of rationality: why does the deficit model persist in science communication? *Public Underst Sci* 2016;25:400–14.
- [29] Scheufele DA. Communicating science in social settings. *Proc Natl Acad Sci USA* 2013;110:14040–7.
- [30] Nisbet MC, Mooney C. Framing science. *Science* 2007;316:56.