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COMMENTARY

Making Choices: Health Consumers, Regulation and the Global Stem Cell Therapy Market

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Existing modes of regulation in stem cell therapy innovation offer little recognition of the role of health consumer choice in the governance of this emerging global market. Instead, there is a strong and familiar emphasis on the roles of scientists, clinicians and bioethicists in determining what regulation should be provided, when and by whom. For the most part, it is assumed that health consumers (patients) should be protected from themselves through regulation that renders consumer choice redundant because the apparatus of the state or professions has ensured on their behalf that available treatments are safe and efficacious. Their best interests are served, it is maintained, by their continuing faith in their regulatory guardians. This article argues that such an approach to regulation is outmoded and inefficient because it fails to address the governance needs of motivated, mobile consumers in the global stem cell therapy market. Such consumers require a balance between information that facilitates their ability to make rational choices and the confidence that provider regulation is fit for their purpose.

The orthodox approach to governance works so long as the authority of science, medicine and, to a lesser extent, bioethics is able to control the operation of the health care market by convincing consumers that their choices of treatments should be what science, medicine and bioethics say they should be. The logic of this interpretation of the market is that consumer demand for stem cell therapies should adjust to the available supply generated by the orthodox scientific model of stem cell innovation characterised by the sequence of basic research, clinical experimentation, product development, clinical trials, product approval and clinical application, regardless of the timescale involved. In the case of stem cell therapies, this approach to market governance has clearly failed. The rapid and continuing expansion of a global market of innovative treatments measured in terms of hundreds of clinics treating thousands of patients has occurred independently of the very small stem cell therapy market supplied by the outputs of the orthodox model [1]. Alternative, practice-based models of stem cell innovation have emerged that respond to consumer demand much more readily than the orthodox model. This poses demand-side governance challenges which need to be recognised and addressed.

To an extent, recognition of the governance challenge is hampered by the analysis of the latter market offered by proponents of the orthodox model. Essentially a normative approach, this analysis suggests that innovative activities that deviate from the tenets of the orthodox model are, ipso facto, illicit, immoral and indicative of a failure of national and transnational regulation to insist that the orthodox model is preserved unchallenged [2, 3]. Health consumers are dismissed as 'stem cell tourists' whose market choices are invalid, insincere, potentially self-damaging or misinformed and providers are categorised as crooks, charlatans or worse. This is an unhelpful analysis because its categorical value assumptions prevent a discussion of the governance implications of models of innovation that deliberately position themselves between health consumer demand and stem cell therapy supply with the intention of bringing the two closer together.

Nor is health consumer demand for stem cell therapies something that is easily diverted by the advice of leading authorities. It is not, as is frequently implied, merely a matter of toning down the hype and consumer demand

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'pull' generated by the competing optimistic visions of the factions of stem cell science and stem cell clinics; there is also the very considerable demand 'push' created by the engagement between a consumer's health status and the domestically available health care supply. The constraints imposed by a particular disease condition, the proximity of pain and/or death, and the limits of local treatment serve to structure a calculation of risks and benefits with its own internalist rationality [4]. Such a subjective rationality may be at odds with the rationality of the external observer, be they scientist, bioethicist or state regulator, and generates a consumer demand with both a limited sensitivity to negative information about stem cell therapies and a greater preparedness to take risks [5]. Where patient organisations are well organised, this economic demand for treatment may translate into political demand for changes in the orthodox model and its governance, for example, in the cases of AIDS and neuromuscular disorders [6, 7]. Most recently, in Italy, protests from patient groups led the Italian Parliament to introduce legislation in May 2013 to allow experimental stem cell therapies on 32 terminally ill patients to proceed [8].

Whilst the orthodox scientific model of stem cell innovation is relatively impervious to health consumer demand, practice-based models of innovation have proved more responsive. Their common characteristic is that they are examples of *medical innovation*, where the goal is the benefit of the individual patient, as distinct from the *scientific innovation* of the orthodox model, where the goal is scientifically generalizable results [9]. Thus defined, 'Medical innovation in cellular therapy may be viewed as the ethical and legitimate use of non-approved cell therapy by qualified healthcare professionals in their practice of medicine' [10]. Underpinned by quite different legitimising values embodying different priorities, scientific and medical innovation frequently find themselves in tension with one another. Proponents of the orthodox model of stem cell innovation, guided as they are by the research ethic which 'aims to produce generalizable knowledge about new cellular or drug treatments, or new approaches to surgery', often take the view that medical innovation should be used 'only in exceptional circumstances' with seriously ill patients because such innovation is not driven by the principles of the scientific method [11].

In the West, the view that medical innovation is to be regarded as exceptional rather than customary has dominated the governance debate in this field. However, against this, the emerging recognition that, as the International Society for Cell Therapy (ISCT) puts it, patients, families and partners 'should have the right to seek treatment for their diseases. No entity should withhold this fundamental right unless there is a high probability of harm to the patient' [10]; this has begun to raise the profile of consumer choice. Once established as a legitimate component of the debate, this in turn leads to an assessment of the appropriateness of models of scientific and medical innovation in terms not only of their scientific integrity but also their ability to respond to health consumer demand. The more that consumer choice is accorded an explicit role in discussions about innovation governance, the more medical innovation is likely to become respectable.

In Europe, the Hospital Exemption within the EU's Advanced Medicinal Therapy Product (ATMP) Regulation 1394/2007 and national provisions, such as the UK's 'Specials' scheme operating under an exemption within Article 5 [1] of Directive 2001/83/EC, have provided one route for medical innovation by clinicians to meet consumer demand earlier rather than later. More generally, because by definition medical innovation is not research, its governance falls within the normal regulation of the professional standards of medical practice by licensing bodies and medical malpractice laws. Hence, for example, the UK General Medical Council's Fitness to Practice panel struck off Dr Robert Trossel for exploiting vulnerable patients and unjustifiably administering inappropriate stem cell treatments.

However, much of the expansion in the supply of stem cell therapies has taken place in non-Western countries such as China and India, where the assumptions of the orthodox model of stem cell innovation are less comprehensively embodied in regulatory arrangements and there is a greater tolerance of clinician-led medical innovation. Whereas, in Europe, medical innovation supplies therapies for single or small groups of patients in what is presented, in the case of the Hospital Exemption at least, as a non-routine exercise, in non-Western countries, this model routinely provides therapies for large populations of patients (e.g. NutechMediworld, Zhongyuan Union Stem Cell, Celltex and Unique Cell Treatment Clinic). In other words, medical innovation and consumer demand responsiveness are regarded as normal rather than exceptional. In an interesting variant, some companies have combined elements of medical innovation and scientific innovation into a single business model. Here, profits from the stem cell medical innovation treatments for one set of diseases are re-invested in the funding of registered clinical trials for stem cell scientific innovation (orthodox model) with regard to a different set of diseases (e.g. Beike Biotechnology, Chaitanya Stem Cell Therapy Centre).

The governance challenge resides in the fact that this market has emerged largely outside the jurisdictions of the dominant Western powers in biomedical innovation, falls within the governance of practice not research, is propelled by a consumer demand ('stem cell tourists') often labelled as illicit by these jurisdictions, and is agile enough to move across jurisdictions where necessary. In this situation, demand-side governance, the enabling of consumer choice

through the provision of accurate and impartial information, is a flexible option to pursue. As the ISCT puts it:

> 'Patients therefore need to be equipped to understand the difference between (a) formal clinical trials and the innovative practice of medicine (where their rights are protected and risks are communicated) and (b) fraudulent cell therapy practice (where there are no protections, no demonstration of competency and misinformation is the rule). In practice, a continuum exists between these two extremes, with varying levels of scientific diligence.' [10]

However, at present, much consumer information is still asymmetric, reinforcing the promises of stem cell science through positive information on the websites of private companies, patient blogs and internet articles, with the majority of stem cell suppliers claiming that their therapies offer a safe and efficient treatment for diseases that orthodox Western medicine regards as incurable or difficult to treat [3, 12]. Consumers lack the evidence to make fully informed choices. Websites such as the International Society for Stem Cell Research (ISSCR) 'A Closer Look at Stem Cell Treatments' offer alternative information, but it is, firstly, general rather than disease specific in scope and, secondly, predicated on the assumptions of the orthodox scientific model of stem cell innovation.

It is likely that both public and private governance have a contribution to make, not least because there is an available global market of standards measurement relevant to the stem cell therapy field, one keen to sell its products to stem cell clinics which need to bolster their clinical respectability in the eyes of potential clients. In terms of quality of process and safety, there is an existing market of standardised measures [e.g. Good Laboratory Practice (GLP), Good Manufacturing Practice (GMP), Good Clinical Practice (GCP)] provided by national, international and private organisations [e.g. Food and Drugs Administration (FDA), Medicines and Healthcare products Regulatory Agency (MHRA), International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), World Health Organisation (WHO)] which some clinics already claim to access. More specifically, the International Cellular Medicine Society (ICMS) has produced guidelines for best practice in cell-based medicines and has recently formed an alliance with the American Association of Blood Banks (AABB) for the production of a global accreditation programme for stem cell clinics [13]. If health consumers are to make an informed choice about the safety of the stem cell therapy product they are considering purchasing, then clearly they should be aware of the importance of these standards indicators. Patient and scientific organisations could act as educative vehicles for the dissemination of such information. Equally, in terms of efficacy, although stem cell clinics do not publish systematic data on the results of their interventions, there is no reason why consumers should not provide evidence of their experiences through a patient-centred website.

The general reticence to engage with the reality of the global market of stem cell therapies serves to perpetuate the present neglect of consumer demand-led medical innovation and the forms of governance it requires. It is a reticence that has both supporters and opponents and is unlikely to remain politically unchallenged for long, and bioethicists are beginning to acknowledge the issues posed by medical innovation in the stem cell field [14]. It is important, also, that the present governance vacuum surrounding practice-based medical innovation is addressed by the medical profession itself through changes in its normal systems of self-regulation and professional guidance. Commenting on the 'sclerotic' qualities of the established drug innovation model traditionally sponsored by the USA and EU, Joyce Tait observes of China and India that 'these increasingly powerful components of the bioeconomy may see a competitive advantage in leading regulatory reform so as to encourage more innovative health care sectors to develop, initially for their large and increasingly wealthy home markets, and perhaps also to encourage change in the United States and European regulatory systems' [15]. Given the market benefits that may accrue from the association of these emerging economies with stem cell medical innovation as documented in this paper, it would be irrational of them to do otherwise.

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