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The Oversight of Clinical Innovation in a Medical Marketplace

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29.1 INTRODUCTION

Clinical innovation is ubiquitous in medical practice and is generally viewed as both necessary and desirable. While innovation has been the source of considerable benefit, many clinical innovations have failed to demonstrate evidence of clinical benefit and/or caused harm. Given uncertainty regarding the consequences of innovation, it is broadly accepted that it needs some form of oversight. But there is also pushback against what is perceived to be obstruction of access to innovative interventions. In this chapter, we argue that this pushback is misguided and dangerous – particularly because of the myriad competing and conflicting interests that drive and shape clinical innovation.

29.2 CLINICAL INNOVATION AND ITS OVERSIGHT

While the therapeutics lifecycle is usually thought of as one in which research precedes clinical application, it is common for health professionals to offer interventions that differ from standard practice, and that have either not (yet) been shown to be safe or effective or have been shown to be safe but not yet subjected to large phase 3 trials. This practice is often referred to as 'clinical innovation'.[1] The scope of clinical innovation is broad, ranging from minor alterations to established practice – for example using a novel suturing technique – to more significant departures from standard practice – for example using an invasive device that has not been formally tested in *any* population.

For the most part, clinical innovation is viewed as necessary and desirable. Medicine has always involved the translation of ideas into treatment and it is recognised that ideas originate in the clinic as well as in the research setting, and that research and practice inform each other in an iterative manner.[2] It is also recognised that the standard trajectory of research followed by health technology assessment, registration and subsidisation may be too slow for patients with life-limiting or debilitating diseases and that clinical innovation can provide an important

[1] W. Lipworth et al., 'The Need for Beneficence and Prudence in Clinical Innovation with Autologous Stem Cells', (2018) *Perspectives in Biology and Medicine*, 61(1), 90–105.

[2] P. L. Taylor, 'Overseeing Innovative Therapy without Mistaking It for Research: A Function-Based Model Based on Old Truths, New Capacities, and Lessons from Stem Cells', (2010) *The Journal of Law, Medicine & Ethics*, 38(2), 286–302.

avenue for access to novel treatments.[3] There are also limitations to the systems that are used to determine what counts as 'standard' practice because it is up to – usually commercial – sponsors to seek formal registration for particular indications.[4]

While many clinical innovations have positively transformed medicine, others have failed to demonstrate evidence of clinical benefit,[5] or exposed patients to considerable harm – for example, the use of transvaginal mesh for the treatment of pelvic organ prolapse.[6] Many innovative interventions are also substantially more expensive than traditional treatments,[7] imposing costs on both patients and health systems. It is therefore broadly accepted that innovation requires some form of oversight. In most jurisdictions, oversight of innovation consists of a combination of legally based regulations and less formal governance mechanisms. These, in turn, can be focused on:

1. the oversight of clinical practice by professional organisations, medical boards, healthcare complaints bodies and legal regimes;
2. the registration of therapeutic products by agencies such as the US Food and Drug Administration, the European Medicines Agency and Australia's Therapeutic Goods Administration;
3. consumer protection, such as laws aimed at identifying and punishing misleading advertising; and
4. the oversight of research when innovation takes place in parallel with clinical trials or is accompanied by the generation of 'real world evidence' through, for example, clinical registries.

The need for some degree of oversight is relatively uncontroversial. But there is also pushback against what is perceived to be obstruction of access to innovative interventions.[8] There are two main arguments underpinning this position. First, it is argued that existing forms of oversight create barriers to clinical innovation. Salter and colleagues, for example, view efforts to assert external control over clinical innovation as manifestations of conservative biomedical hegemony that deliberately hinders clinical innovation in favour of more traditional translational

[3] B. Salter et al., 'Hegemony in the Marketplace of Biomedical Innovation: Consumer Demand and Stem Cell Science', (2015) *Social Science & Medicine*, 131, 156–163.

[4] N. Ghinea et al., 'Ethics & Evidence in Medical Debates: The Case of Recombinant Activated Factor VII', (2014) *Hastings Center Report*, 44(2), 38–45.

[5] C. Davis, 'Drugs, Cancer and End-of-Life Care: A Case Study of Pharmaceuticalization?', (2015) *Social Science & Medicine*, 131, 207–214; D. W. Light and J. Lexchin, 'Pharmaceutical Research and Development: What Do We Get for All That Money?', (2012) *BMJ*, 345, e4348; C. Y. Roh and S. H. Kim, 'Medical Innovation and Social Externality', (2017) *Journal of Open Innovation: Technology, Market, and Complexity*, 3(1), 3; S. Salas-Vega et al., 'Assessment of Overall Survival, Quality of Life, and Safety Benefits Associated with New Cancer Medicines', (2017) *JAMA Oncology*, 3(3), 382–390.

[6] K. Hutchinson and W. Rogers, 'Hips, Knees, and Hernia Mesh: When Does Gender Matter in Surgery?', (2017) *International Journal of Feminist Approaches to Bioethics*, 10(1), 26.

[7] Davis, 'Drugs, Cancer'; T. Fojo et al., 'Unintended Consequences of Expensive Cancer Therapeutics – The Pursuit of Marginal Indications and a Me-Too Mentality that Stifles Innovation and Creativity: The John Conley Lecture', (2014) *JAMA Otolaryngology – Head and Neck Surgery*, 140(12), 1225–1236; S. C. Overley et al., 'Navigation and Robotics in Spinal Surgery: Where Are We Now?', (2017) *Neurosurgery*, 80(3S), S86.

[8] D. Cohen, 'Devices and Desires: Industry Fights Toughening of Medical Device Regulation in Europe', (2013) *BMJ*, 347, f6204; C. Di Mario et al., 'Commentary: The Risk of Over-regulation', (2011) *BMJ*, 342, d3021; O. Dyer, 'Trump Signs Bill to Give Patients Right to Try Drugs', (2018) *BMJ*, 361, k2429; S. F. Halabi, 'Off-label Marketing's Audiences: The 21st Century Cures Act and the Relaxation of Standards for Evidence-based Therapeutic and Cost-comparative Claims', (2018) *American Journal of Law & Medicine*, 44(2–3), 181–196; M. D. Rawlins, 'The "Saatchi Bill" will Allow Responsible Innovation in Treatment', (2014) *BMJ*, 348, g2771; Salter et al., 'Hegemony in the Marketplace'.

pathways.[9] It has also been argued that medical negligence law deters clinical innovation[10] and that health technology regulation is excessively slow and conservative, denying patients the 'right to try' interventions that have not received formal regulatory approval.[11]

Second, it is argued that barriers are philosophically and politically inappropriate on the grounds that patients are not actually 'patients', but rather 'consumers'. According to these arguments, consumers should be free to decide for themselves what goods and services they wish to purchase without having their choices restricted by regulation and governance systems – including those typically referred to as 'consumer' (rather than 'patient') protections. Following this line of reasoning, Salter and colleagues[12] argue that decisions about access to innovative interventions should respect and support 'the informed health consumer' who:

> assumes she/he has the right to make their own choices to buy treatment in a health care market which is another form of mass consumption. . .[13]

and who is able to draw on:

> a wide range of [information] sources which include not only the formally approved outlets of science and state but also the burgeoning information banks of the internet.[14]

There are, however, several problems with these arguments. First, there is little evidence to support the claim that there is, in fact, an anti-innovative biomedical hegemony that is creating serious barriers to clinical innovation. While medical boards can censure doctors for misconduct, and the legal system can find them liable for trespass or negligence, these wrongs are no easier to prevent or prove in the context of innovation than in any other clinical context. Product regulation is similarly facilitative of innovation, with doctors being free to offer interventions 'off-label' and patients being allowed to apply for case-by-case access to experimental therapies. The notion that current oversight systems are anti-innovative is therefore not well founded.

Second, it is highly contestable that patients are 'simply' consumers – and doctors are 'simply' providers of goods and services – in a free market. For several reasons, healthcare functions as a very imperfect market: there is often little or no information available to guide purchases; there are major information asymmetries – exacerbated by misinformation on the internet; and patients may be pressured into accepting interventions when they have few, if any, other therapeutic options.[15] Furthermore, even if patients *were* consumers acting in a marketplace, it would not follow that the marketplace should be completely unregulated, for even the most libertarian societies have regulatory structures in place to prevent bad actors misleading people or exploiting them financially (e.g. through false advertising, price fixing or offering services that they are unqualified to provide).

This leaves one other possible objection to the oversight of clinical innovation – that patients are under the care of professionals who are able to collaborate with them in making decisions through shared decision-making. Here, the argument is that innovation (1) *should not* be overseen because it is an issue that arises between a doctor and a patient, and (2) *does not need* to be overseen

[9] Salter et al., 'Hegemony in the Marketplace'.
[10] Rawlins, 'The "Saatchi Bill"'.
[11] Dyer, 'Trump Signs Bill'.
[12] Salter et al., 'Hegemony in the Marketplace'.
[13] Ibid., 159.
[14] Ibid.
[15] T. Cockburn and M. Fay, 'Consent to Innovative Treatment', (2019) *Law, Innovation and Technology*, 11(1), 34–54; T. Hendl, 'Vulnerabilities and the Use of Autologous Stem Cells for Medical Conditions in Australia', (2018) *Perspectives in Biology and Medicine*, 61(1), 76–89.

because doctors are professionals who have their patients' interests at heart. These are compelling arguments because they are consistent with both the emphasis on autonomy in liberal democracies and with commonly accepted ideas about professionals and their obligations.

Two objections can, however, be raised. First, these arguments ignore the fact that professionalism is concerned not only with patient well-being but also with commitments to the just distribution of finite resources, furthering scientific knowledge and maintaining public trust.[16] The second problem with these arguments is that they are premised on the assumption that all innovating clinicians are consistently alert to their professional obligations and willing to fulfil them. Unfortunately, this assumption is open to doubt. To illustrate this point, we turn to the case of autologous mesenchymal stem cell-based interventions.

29.3 THE CASE OF AUTOLOGOUS MESENCHYMAL STEM CELL INTERVENTIONS

Stem cell-based interventions are procedures in which stem cells – cells that have the potential to self-replicate and to differentiate into a range of different cell types – or cells derived from stem cells are administered to patients for therapeutic purposes. Autologous stem cell-based interventions involve administering cells to the same person from whom they were obtained. The two most common sources of such stem cells are blood and bone marrow (haematopoietic) cells and connective tissue (mesenchymal) cells.

Autologous haematopoietic stem cells are extracted from blood or bone marrow and used to reconstitute the bone marrow and immune system following high dose chemotherapy. Autologous mesenchymal cells are extracted most commonly from fat and then injected – either directly from the tissue extracts or after expansion in the laboratory – into joints, skin, muscle, blood stream, spinal fluid, brain, eyes, heart and so on, in order to 'treat' degenerative or inflammatory conditions. The hope is that because mesenchymal stem cells may have immunomodulatory properties they may support tissue regeneration.

The use of autologous haematopoietic stem cells is an established standard of care therapy for treating certain blood and solid malignancies and there is emerging evidence that they may also be beneficial in the treatment of immunological disorders, such as multiple sclerosis and scleroderma. In contrast, evidence to support the use of autologous mesenchymal stem cell interventions is weak and limited to only a small number of conditions (e.g. knee osteoarthritis).[17] And even in these cases, it is unclear what the precise biological mechanism is and whether the cells involved should even be referred to as 'stem cells'[18] (we use this phrase in what follows for convenience).

Despite this, autologous mesenchymal stem cell interventions (henceforth AMSCIs) are offered for a wide range conditions for which there is *no* evidence of effectiveness, including spinal cord injury, motor neuron disease, dementia, cerebral palsy and autism.[19] Clinics offering these and other claimed 'stem cell therapies' have proliferated globally, primarily in the private

[16] Medical Professionalism Project, 'Medical Professionalism in the New Millennium: A Physicians' Charter', (2002) *Lancet*, 359(9305), 520–522.

[17] H. Iijima et al., 'Effectiveness of Mesenchymal Stem Cells for Treating Patients with Knee Osteoarthritis: A Meta-analysis Toward the Establishment of Effective Regenerative Rehabilitation', (2018) *NPJ Regenerative Medicine*, 3(1), 15.

[18] D. Sipp et al., 'Clear Up this Stem-cell Mess', (2018) *Nature*, 561, 455–457.

[19] M. Munsie et al., 'Open for Business: A Comparative Study of Websites Selling Autologous Stem Cells in Australia and Japan', (2017) *Regenerative Medicine*, 12(7); L. Turner and P. Knoepfler, 'Selling Stem Cells in the USA: Assessing the Direct-to-Consumer Industry', (2016) *Cell Stem Cell*, 19(2), 154–157.

healthcare sector – including in jurisdictions with well-developed regulatory systems – and there are now both domestic markets and international markets based on stem cell tourism.[20]

While AMSCIs are relatively safe, they are far from risk-free, with harm potentially arising from the surgical procedures used to extract cells (e.g. bleeding from liposuction), the manipulation of cells outside of the body (e.g. infection) and the injection of cells into the bloodstream (e.g. immunological reactions, fever, emboli) or other tissues (e.g. cyst formation, microcalcifications).[21] Despite these risks, many of the practitioners offering AMSCIs have exploited loopholes in product regulation to offer these interventions to large numbers of patients.[22] To make matters worse, these interventions are offered without obvious concern for professional obligations, as evident in aggressive and misleading marketing, financial exploitation and poor-quality evidence-generation practices.

First, despite limited efficacy and safety, AMSCIs are marketed aggressively through clinic websites, advertisements and appearances in popular media.[23] This is inappropriate both because the interventions being promoted are experimental and should therefore be offered to the minimum number of patients outside the context of clinical trials, and because marketing is often highly misleading. In some cases, this takes the form of blatant misinformation – for example, claims that AMSCIs are effective for autism, dementia and motor neuron disease. In other cases, consumers are misled by what have been referred to as 'tokens of legitimacy'. These include patient testimonials, references to incomplete or poor-quality research studies, links to scientifically dubious articles and conference presentations, displays of certification and accreditation from unrecognised organisations, use of meaningless titles such as 'stem cell physician' and questionable claims of ethical oversight. Advertising of AMSCIs is also rife with accounts of biological processes that give the impression that autologous stem cells are entirely safe – because they come from the patient's own body – and possess almost magical healing qualities.[24]

Second, AMSCIs are expensive, with patients paying thousands of dollars (not including follow-up care or the costs associated with travel).[25] In many cases, patients take drastic measures to finance access to stem cells, including mortgaging their houses and crowd-sourcing funding from their communities. Clinicians offering AMSCIs claim that such costs are justified given the complexities of the procedures and the lack of insurance subsidies to pay for them.[26] However, the costs of AMSCIs seem to be determined by the business model of the industry and by a determination of 'what the market will bear' – which in the circumstances of illness, is substantial. Furthermore, clinicians offering AMSCIs also conduct 'pay-to-participate' clinical trials and ask patients to pay for their information to be included in clinical registries. Such

[20] I. Berger et al., 'Global Distribution of Businesses Marketing Stem Cell-based Interventions',(2016) *Cell Stem Cell*, 19(2), 158–162; D. Sipp et al., 'Marketing of Unproven Stem Cell–Based Interventions: A Call to Action', (2017) *Science Translational Medicine*, 9(397); M. Sleeboom-Faulkner and P. K. Patra, 'Experimental Stem Cell Therapy: Biohierarchies and Bionetworking in Japan and India', (2011) *Social Studies of Science*, 41(5), 645–666.

[21] G. Bauer, et al., 'Concise Review: A Comprehensive Analysis of Reported Adverse Events in Patients Receiving Unproven Stem Cell-based Interventions', (2018) *Stem Cells Translational Medicine*, 7(9), 676–685; T. Lysaght et al., 'The Deadly Business of an Unregulated Global Stem Cell Industry', (2017) *Journal of Medical Ethics*, 43, 744–746.

[22] Sipp et al., 'Clear Up'.

[23] T. Caulfield et al., 'Confronting Stem Cell Hype', (2016) *Science*, 352(6287), 776–777; A. K. McLean et al., 'The Emergence and Popularisation of Autologous Somatic Cellular Therapies in Australia: Therapeutic Innovation or Regulatory Failure?', (2014) *Journal of Law and Medicine*, 22(1), 65–89; Sipp et al., 'Clear Up'.

[24] Munsie et al., 'Open for Business'; Sipp et al., 'Marketing'.

[25] A. Petersen et al., 'Therapeutic Journeys: The Hopeful Travails of Stem Cell Tourists', (2014) *Sociology of Health and Illness*, 36(5), 670–685.

[26] Worldhealth.net, 'Why Is Stem Cell Therapy So Expensive?', (WorldHealth.Net, 2018), www.worldhealth.net/news/why-stem-cell-therapy-so-expensive/.

practices are generally frowned upon as they exacerbate the therapeutic misconception and remove any incentive to complete and report results in a timely manner.[27]

Finally, contrary to the expectation that innovating clinicians should actively contribute to generating generalisable knowledge through research, clinics offering AMSCIs have proliferated in the absence of robust clinical trials.[28] Furthermore, providers of AMSCIs tend to overstate what is known about efficacy[29] and to misrepresent what trials are for, arguing that they simply 'measure and validate the effect of (a) new treatment'.[30] Registries that have been established to generate observational evidence about innovative AMSCIs are similarly problematic because participation is voluntary, outcome measures are subjective and results are not made public. There are also problems with the overall framing of the registries, which are presented as alternatives – rather than supplements – to robust clinical trials.[31] And because many AMSCIs are prepared and offered in private practice, there is lack of oversight and independent evaluation of what is actually administered to the patient, making it impossible to compare outcomes in a meaningful way.[32]

While it is possible that doctors offering autologous stem cell interventions simply lack awareness of the norms relating to clinical innovation, this seems highly unlikely, as many of these clinicians are active participants in policy debates about innovation and are routinely censured for behaviour that conflicts with accepted professional obligations. A more likely explanation, therefore, is that the clinicians offering autologous stem cell interventions are motivated not (only) by concern for their patients' well-being, but also by other interests such as the desire to make money, achieve fame and satisfy their intellectual curiosity. In other words, they have competing and conflicting interests that override their concerns for patient well-being and the generation of valid evidence.

29.4 IMPLICATIONS FOR OVERSIGHT OF CLINICAL INNOVATION

Unfortunately, the case of AMSCIs is far from unique. Other situations in which clinicians appear to be abusing the privilege of using their judgement to offer non-evidence-based therapies include orthopaedic surgeons over-using arthroscopies for degenerative joint disease,[33] assisted reproductive technology specialists who offer unproven 'add-ons' to traditional in-vitro fertilisation[34] and health professionals engaging in irresponsible off-label prescribing of psychotropic medicines.[35]

[27] D. Sipp, 'Pay-to-Participate Funding Schemes in Human Cell and Tissue Clinical Studies', (2012) *Regenerative Medicine*, 7(6s), 105–111.

[28] Sipp et al., 'Clear Up'.

[29] Sipp et al., 'Marketing'.

[30] R. T. Bright, 'Submission to the TGA Public Consultation: Regulation of Autologous Stem Cell Therapies: Discussion Paper for Consultation', (Macquarie Stem Cell Centres of Excellence, 2015), 4, www.tga.gov.au/sites/default/files/submissions-received-regulation-autologous-stem-cell-therapies-msc.pdf.

[31] Adult Stem Cell Foundation, 'Adult Stem Cell Foundation', www.adultstemcellfoundation.org; M. Berman and E. Lander, 'A Prospective Safety Study of Autologous Adipose-Derived Stromal Vascular Fraction Using a Specialized Surgical Processing System', (2017) *The American Journal of Cosmetic Surgery*, 34(3), 129–142; International Cellular Medicine Society, 'Open Treatment Registry', (ICMS, 2010), www.cellmedicinesociety.org/attachments/184_ICMS%20Open%20Treatment%20Registry%20-%20Overview.pdf.

[32] Sipp et al., 'Marketing'.

[33] P. F. Stahel, 'Why Do Surgeons Continue to Perform Unnecessary Surgery?', (2017) *Patient Safety in Surgery*, 11(1), 1.

[34] J. Wise, 'Show Patients Evidence for Treatment "Add-ons", Fertility Clinics are Told', (2019) *BMJ*, 364, l226.

[35] P. Sugarman et al., 'Off-Licence Prescribing and Regulation in Psychiatry: Current Challenges Require a New Model of Governance', (2013) *Therapeutic Advances in Psychopharmacology*, 3(4), 233–243.

Clinicians in all of these contexts are embedded in a complex web of financial and non-financial interests such as the desire to earn money, create product opportunities, pursue intellectual projects, achieve professional recognition and career advancement, and develop knowledge for the good of future patients[36] – all of which motivate their actions. Clinicians are also susceptible to biases such as the 'optimism bias', which might lead them to over-value innovative technologies and they are impacted upon by external pressures, such as industry marketing[37] and pressure from patients desperate for a 'miracle cure'.[38]

With these realities in mind, arguments against the oversight of innovation – or, more precisely, a reliance on consumer choice – become less compelling. Indeed, it could be argued that the oversight of innovation needs to be strengthened in order to protect patients from exploitation by those with competing and conflicting interests. That said, it is important that the oversight of clinical innovation does not assume that all innovating clinicians are motivated primarily by personal gain and, correspondingly, that it does not stifle responsible clinical innovation.

In order to strike the right balance, it is useful – following Lysaght and colleagues[39] – for oversight efforts to be framed in terms of, and account for, three separate functions: a *negative function* (focused on protecting consumers and sanctioning unacceptable practices, such as through tort and criminal law); a *permissive function* (concerned with frameworks that license health professionals and enable product development, such as through regulation of therapeutic products); and a *positive function* (dedicated to improving professional ethical behaviour, such as through professional registration and disciplinary systems). With that in mind, we now present some examples of oversight mechanisms that could be employed.

Those with responsibility for overseeing clinical practice need to enable clinicians to offer innovative treatments to selected patients outside the context of clinical trials, while at the same time preventing clinicians from exploiting patients for personal or socio-political reasons. Some steps that could be taken to both encourage responsible clinical innovation and discourage clinicians from acting on conflicts of interest might include:

- requiring that all clinicians have appropriate qualifications, specialisation, training and competency;
- mandating disclosure of competing and conflicting interests on clinic websites and as part of patient consent;
- requiring that consent be obtained by an independent health professional who is an expert in the patient's disease (if necessary at a distance for patients in rural and remote regions);
- ensuring that all innovating clinicians participate in clinical quality registries that are independently managed, scientifically rigorous and publicly accessible;

[36] T. E. Chan, 'Legal and Regulatory Responses to Innovative Treatment', (2012) *Medical Law Review*, 21(1), 92–130; T. Keren-Paz and A. J. El Haj, 'Liability versus Innovation: The Legal Case for Regenerative Medicine', (2014) *Tissue Engineering Part A*, 20(19–20), 2555–2560; J. Montgomery, 'The "Tragedy" of Charlie Gard: A Case Study for Regulation of Innovation?', (2019) *Law, Innovation and Technology*, 11(1), 155–174; K. Raus, 'An Analysis of Common Ethical Justifications for Compassionate Use Programs for Experimental Drugs', (2016) *BMC Medical Ethics*, 17(1), 60; P. L. Taylor, 'Innovation Incentives or Corrupt Conflicts of Interest? Moving Beyond Jekyll and Hyde in Regulating Biomedical Academic-Industry Relationships', (2013) *Yale Journal of Health Policy, Law, and Ethics*, 13(1), 135–197.

[37] Chan, 'Legal and Regulatory Responses'; Taylor, 'Innovation Incentives'.

[38] Chan, 'Legal and Regulatory Responses'.

[39] T. Lysaght et al., 'A Roundtable on Responsible Innovation with Autologous Stem Cells in Australia, Japan and Singapore', (2018) *Cytotherapy*, 20(9), 1103–1109.

- requiring independent oversight to ensure that appropriate product manufacturing standards are met;
- ensuring adequate pre-operative assessment, peri-operative care and post-operative monitoring and follow-up;
- ensuring that patients are not charged excessive amounts for experimental treatments, primarily by limiting expenses to cost-recovery; and
- determining that some innovative interventions should be offered only in a limited number of specialist facilities.

Professional bodies (such as specialist colleges), professional regulatory agencies, clinical ethics committees, drugs and therapeutics committees and other institutional clinical governance bodies would have an important role to play in ensuring that such processes are adhered to.

There may also be a need to extend current disciplinary and legal regimes regarding conflicts of interest (or at least ensure better enforcement of existing regimes). Many professional codes of practice already require physicians to be transparent about, and refrain from acting on, conflicts of interest. And laws in some jurisdictions already recognise that financial interests should be disclosed to patients, that patients should be referred for independent advice and that innovating clinicians need to demonstrate concern for patient well-being and professional consensus.[40]

With respect to advertising, there is a need to prevent aggressive and misleading direct-to-consumer advertising while still ensuring that all patients who might benefit from an innovative intervention are aware that such interventions are being offered. With this in mind, it would seem reasonable to strengthen existing advertising oversight (which, in many jurisdictions, is weak and *ad hoc*). It may also be reasonable to prohibit innovating clinicians from advertising interventions directly to patients – including indirectly through 'educational' campaigns and media appearances – and instead develop systems that alert referring doctors to the existence of doctors offering innovative interventions.

Those regulating access to therapeutic products need to strike a balance between facilitating timely access to the products that patients want, and ensuring that those with competing interests are not granted licence to market products that are unsafe or ineffective. In this regard, it is important to note that product regulation is generally lenient when it comes to clinical innovation and it is arguable that there is a need to push back against current efforts to accelerate access to health technologies – efforts that are rapidly eroding regulatory processes and creating a situation in which patients are being exposed to an increasing number of ineffective and unsafe interventions.[41] In addition, loopholes in therapeutic product regulation that can be exploited by clinicians with conflicts of interest should be predicted and closed wherever possible.

Although clinical innovation is not under the direct control of research ethics and governance committees, such committees have an important role to play in ensuring that those clinical trials and registries established to support innovation are not distorted by commercial and other imperatives. The task for such committees is to strike a balance between assuming that all researcher/innovators are committed to the generation of valid evidence and placing excessive burdens on responsible innovators who wish to conduct high-quality research. In this regard, research ethics committees could:

[40] Cockburn and Fay, 'Consent'; Keren-Paz and El Haj, 'Liability versus Innovation'.

[41] J. Pace et al., 'Demands for Access to New Therapies: Are There Alternatives to Accelerated Access?', (2017) *BMJ*, 359, j4494.

- ensure that participants in trials and registries are informed about conflicts of interest;
- ensure that independent consent processes are in place so that patients are not pressured into participating in research or registries; and
- consider whether it is ever acceptable to ask patients to 'pay to participate' in trials or in registries.

Research ethics committees also have an important role in minimising biases in the design, conduct and dissemination of innovation-supporting research. This can be achieved by ensuring that:

- trials and registries have undergone rigorous, independent scientific peer review;
- data are collected and analysed by independent third parties (e.g. Departments of Health);
- data are freely available to any researcher who wants to analyse it; and
- results – including negative results – are widely disseminated in peer-reviewed journals.

While this chapter has focused on traditional 'top-down' approaches to regulation and professional governance, it might also be possible to make use of what Devaney has referred to as 'reputation-affecting' regulatory approaches.[42] Such approaches would reward those who maintain their independence or manage their conflicts effectively with reputation-enhancing measures such as access to funding and publication in esteemed journals. In this regard, other parties not traditionally thought of as regulators – such as employing institutions, research funders, journal reviewers and editors and the media – might have an important role to play in the oversight of clinical innovation.

Importantly, none of the oversight mechanisms we have suggested here would discourage responsible clinical innovation. Indeed, an approach to the oversight of clinical innovation that explicitly accounts for the realities of competing and conflicting interests could make it easier for well-motivated clinicians to obtain the trust of both individual patients and broader social licence to innovate.

29.5 CONCLUSION

Clinical innovation has an important and established role in biomedicine and in the development and diffusion of new technologies. But it is also the case that claims about patients' – or consumers' – rights and about the sanctity of the doctor–patient relationship, can be used to obscure both the risks of innovation and the vested interests that drive some clinicians' decision to offer innovative interventions. In this context, adequate oversight of clinical innovation is crucial. After all, attempts to exploit the language and concept of innovation not only harms patients, but also threatens legitimate clinical innovation and undermines public trust. Efforts to push back against the robust oversight of clinical innovation need, therefore, to be viewed with caution.

[42] S. Devaney, 'Enhancing the International Regulation of Science Innovators: Reputation to the Rescue?', (2019) *Law, Innovation and Technology*, 11(1), 134–154.