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Panel: Contemporary Health and Social Policy Challenges

Paper Title: Managing Patient Demand in a Global Healthcare Market; Today's Challenges for Health Policy Leaders

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Abstract

The Canadian health policy landscape is complex and situated within an increasingly global context. The parameters surrounding access to health-related information, services and interventions are changing rapidly, and social media has become a formidable presence in the public engagement sphere, impacting social activism, knowledge-sharing and community formation. Along with these factors, the ease of international travel and the advent of the 'internet health care consumer' have contributed to the emergence of global, internet-based and often direct-to-consumer markets for health services. International private markets for both established treatments (e.g., organ transplants) and those that are emerging, experimental or unproven (e.g., many stem cell-based interventions), are growing. These phenomena are altering patterns of access to health services and in some ways shifting control from healthcare decision-makers and professionals in Canada to patients and providers in other jurisdictions. This paper will explore pressing issues currently facing Canadian health policy leaders in this context and reflect on future policy directions. Managing these developments in a way that respects individual rights and autonomy while minimizing risks and costs is especially critical given the largely public nature of healthcare in Canada.

I. INTRODUCTION

The health policy sphere has arguably always been complex, with decision makers called to grapple with a sometimes never-ending list of tensions surrounding funding, patient safety, quality of care and regulation of access, among other equally important and often divisive areas. In so doing, decision makers must balance priorities, make trade-offs and often operate with imperfect information. The increasingly global nature of health care adds another layer of complexity to these already challenging tasks. The ease of international travel sees people - patients and healthcare professionals alike - and health products routinely crossing borders, expanding access and care alternatives. Commonly cited rationales for why Canadians, for example, choose to participate in different forms of medical tourism include reducing wait times, accessing treatments not otherwise available at home, and seeking improved quality of care – although more research in this area is warranted (Snyder et al. 2011). Treatment options are further increased by virtue of the tremendous amount of information available on the internet. The transformative impact of the internet on consumer health information seeking has been the subject of attention (and concern) for some time now (Cline and Haynes 2001). More recently social media has been recognized as a formidable presence in the public engagement sphere given its role in the sharing of information, experiences and community formation – including for particular

patient groups (Petersen et al. 2015; Robillard et al. 2015), advocating for certain treatments – often through reliance on personal anecdotes (Mazanderani et al. 2013; Fox 2011), and its emerging influence in heath policy decisions, including regarding funding and access (Chafe 2011).

Priorities of public engagement and patient orientation are increasingly valued in health research, policy and practice (Woolf et al. 2016). When taken together with the above noted expansion of, and accompanying interest in, often relatively unfettered access to health information, products and services, the growth of - and sometimes vehement patient support for - global direct-to-consumer markets in the health sphere is perhaps unsurprising. These markets are numerous and diverse, and include both well established treatments as well as those that are emerging, unproven or experimental. In some instances, the products and services provided are fairly innocuous and uncontroversial; in other cases they carry significant risks of various forms for both individuals and health care systems.

In deciding how to respond to and manage these markets, policy leaders are called upon to consider a range of factors and sometimes competing priorities including, but not limited to, desires to harness the potential of emerging research and transformative technologies, respect individual autonomy, consider the interests and priorities of patients, manage potential risks (including to healthcare systems) and protect vulnerable individuals. The international, online nature of many of these markets and the involvement of a wide range of entities and individuals, including healthcare professionals, add further complexity to the decision-making matrix. Managing patient demands in the context of today's global health care market requires careful consideration of the diverse elements at play, a kind of evaluation that arguably demands a contextual approach. This paper will use three different lenses in an effort to capture the multi-faceted nature of the challenges facing decision makers in this context: the commercial market for organs; the direct-to-consumer market for genetic testing, and the market for unproven stem cell-based interventions. Despite their differences, these phenomena share some revealing commonalities that illustrate the complexities of the balancing act facing health policy leaders today and highlight key elements to be considered in future policy strategies.

II. THREE DIFFERENT LENSES

a. Organ Procurement Abroad ("Transplant Tourism")

Although initially cast as a revolutionary form of medical intervention, organ transplants are now widely accepted as a valuable treatment for individuals suffering from organ failure. Indeed, medical practice around organ donation has advanced to the point where the need for organs far outpaces the number available, a challenge faced worldwide (Shimazono n.d.). The imbalance between supply and demand means many individuals are dying on waitlists, while others live with significantly reduced quality of life. For example, in 2012, 230 Canadians died while on a waitlist for an organ transplant (CIHI 2014). Efforts to improve organ donation rates are wide ranging and include measures such as public information campaigns, paired donation schemes, presumed consent (or "opt-out") models, expanded criteria for the determination of death (i.e. from neurological death to also include cardiac death) and exploration of incentive structures, among others (Abouna 2008; Caulfield et al. 2014).

Notwithstanding these efforts – many of which may indeed have good long-term potential – unmet need for organs persists and some individuals elect not to wait and instead travel to obtain an organ transplant outside their country of residence. Research suggests that individuals who face long wait times, who have had a declined living donor, who do not make the wait lists and/or whose original country of origin presents an access option may be more likely to engage in travel for organ transplantation (Gill et al. 2011; Prasad et al. 2006). There are different forms of travel for organ transplantation (sometimes referred to as "transplant tourism"). The *Declaration of Istanbul on Organ Trafficking and Transplant Tourism*, which followed a World Health Assembly directive, provides the following instructive definitions:

> **Organ trafficking** is the recruitment, transport, transfer, harboring or receipt of living or deceased persons or their organs by means of the threat or use of force or other forms of coercion, of abduction, of fraud, of deception, of the abuse of power or of a position of vulnerability, or of the giving to, or the receiving by, a third party of payments or benefits to achieve the transfer of control over the potential donor, for the purpose of exploitation by the removal of organs for transplantation. **Transplant commercialism** is a policy or practice in which an organ is treated as a commodity, including by being bought or sold or used for material gain. **Travel for transplantation** is the movement of organs, donors, recipients or transplant professionals across jurisdictional borders for transplantation purposes. Travel for transplantation becomes transplant tourism if it involves organ trafficking and/or transplant commercialism or if the resources (organs, professionals and transplant centers) devoted to providing transplants to patients from outside a country undermine the country's ability to provide transplant services for its own population.
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> (Declaration of Istanbul 2008, 2, emphasis added).

For the purpose of this discussion, all three of these categories should be distinguished from unplanned organ transplants that follow an out-of-country medical emergency. Emergency transplants are unanticipated, generally unavoidable, and often funded by some form or combination of health insurance (e.g., public and private coverage). In contrast, the different forms of transplant tourism outlined in the *Declaration of Istanbul* involve a prospective organ recipient travelling outside their country of residency for the deliberate purpose of obtaining an organ transplant, often at direct personal expense. The size and scope of this practice are difficult to quantify with any degree of specificity. It has been estimated that between 5-10% of the kidney transplants (which are the most common form of living donation) taking place around the world annually use organs obtained through commercial transactions (Akoh 2012). Other estimates similarly suggest that transplant tourism accounts for up to 5-10% of transplants globally (Khamash and Gaston 2008).

In some cases, individuals travel to receive directed donation organs from genetically or emotionally connected donors (Delmonico 2009); in other instances, they may travel to jurisdictions with healthcare systems, such as the United States, that legally provide access to non-resident patients – albeit often at significant cost (Freeman 2007); in yet other instances individuals deliberately pursue the explicit (and generally illegal) purchase of an organ (Prasad et al. 2006). The latter activity can fall into the categories of organ trafficking and/or transplant commercialism, both of which are almost universally prohibited within the global health community, which strongly supports altruistic donation (WHO 2010, Declaration of Istanbul 2008).

Concerns about transplant tourism often largely focus on the potential harms suffered by the organ donors, including adverse physical, social and financial impacts (Cohen 2013). Indeed, Cohen (2013) suggests that even using the term "donor" may not be appropriate given it tends to imply a degree of altruism that may not be present in these individuals, particularly if they are forced or otherwise coerced or exploited in the process (Cohen 2013). As such, many countries explicitly prohibit transplant commercialism and organ trafficking. For example, in Canada transplant commercialism is outlawed in the provincial and territorial statues that govern organ donation across the country (e.g., Alberta's *Human Tissue and Organ Donation Act*, SA 2006, c H-14.5, s. 3(2); Ontario's *Trillium Gift of Life Network Act*, RSO 1990, c H.20, s. 10), and organ trafficking is a criminal code offence (s. 279.04(3)). Nonetheless, Canadians have been found to be among those participating in transplant tourism (Prasad et al. 2006; Gill et al. 2011). There admittedly are various legal ambiguities including what forms of incentives are and are not permitted under current legal frameworks, and regarding the reach of domestic criminal law over citizens' actions abroad – challenges that Canadian regulators are not alone in facing. Indeed, it has been suggested that "[t]he cross border and complex nature of this act possibly makes it one of the most difficult crimes to prove and prosecute" (Ambagtsheer et al. 2012, 5).

Equally complex from a health systems perspective are issues regarding how to manage the care of prospective and returning organ transplant tourists. Given the range of possibilities outlined above, it is important to note that not all cases of transplant tourism are illegal or unethical. It is also debatable whether the means through which an organ was obtained are or are not a relevant consideration for a domestic health care system in the context of care and resource allocation decisions. These issues can have significant impacts both in terms of health care practice and for resource consumption, the latter of which may be particularly pressing in health care systems that are largely publicly funded, as is the case in Canada.

Evidence indicates physicians and other health care professionals involved in organ transplant wait list processes are sometimes approached by patients interested in pursuing organ transplants outside their jurisdiction of residence (Ambagtsheer et al. 2012). These health care professionals may be asked for pre-transplant support such as information or advice about transplant destinations, access to medical records or supply of summarized documentation, pre-procedure testing and/or related prescriptions (e.g., immunosuppressive medication, preemptive antibiotics, immunization updates). Upon return from receiving an organ transplant in another jurisdiction, patients may seek follow-up care (emergent and non-emergent), ongoing medication support and/or assistance with reimbursement requests (e.g., from provincial health insurance programs), often with insufficient records about the care that was provided

(Prasad et al. 2006). Health care providers' obligations and duties to their patients as well as their professional ethics can be sorely tested in these situations, particularly if they suspect the patient intends to obtain (or has already obtained) an organ through either organ trafficking or transplant commercialism and have a resulting ethical conflict about providing care.

In Canada, eligibility for medical care is not reduced in any way by the precipitating actions of the patient, even where they may have been illegal (e.g., organ trafficking). Physicians are advised not to allow the quality of care they provide to organ recipients returning from a transplant obtained aboard, particularly when care is required on an emergent basis, to be negatively impacted by any personal opinions they may have about the nature or legality of the transplant (Ambagtsheer et al. 2012). Obtaining appropriate follow-up care upon is particularly important given evidence that patients who obtained kidneys abroad through transplant tourism, including via commercial translations, tended to have a high rate of adverse events, including serious and unusual infections and poorer outcomes (Prasad et al. 2006; Gill et al. 2008; Alghamdi et al. 2010). The Canadian Society of Transplantation and Canadian Society of Nephrology has issued a policy statement on organ trafficking and transplant tourism in which it provides advice to Canadian health care providers about their pre and post-transplant obligations (Gill et al. 2010). Clarity around physicians' legal and professional obligations to individual patients does not however answer the larger health system questions about how best to manage the associated resource and equity implications.

It is forecasted that transplant tourism in its various forms will continue to exist, at least until domestic supply of and demand for organs balances out (Wright et al. 2012; Gill et al. 2011). Achieving this goal will likely require a combination of concerted and coordinated efforts including legislative approaches, public education, improved practice standards, deterrence efforts by physicians (Gill et al. 2011), and investment in information technology and infrastructure, among others. Alongside these efforts however, it will also behoove health policy leaders to work to mitigate the risks – to both individuals and health care systems – of transplant tourism, in its various forms. Achieving this goal will admittedly not be a straightforward task, particularly given that this market operates (often illegally) outside the bounds of state-run medical systems.

b. Personalized Medicine and the Direct-to-Consumer Genetic Testing Market

History reflects a long – and sometimes problematic – interest in human genetics. The Human Genome Project was in many ways a key event in the modern history of genetics research. An ambitious, international initiative that started in 1990 and concluded in 2003, the Human Genome Project led to the mapping of the entire human genome and cost approximately $2.7 billion USD (1991 rates) (NHGRI et al. n.d). It was hailed as a remarkable scientific achievement that would change the face of medicine "through earlier diagnosis, more effective prevention and treatment of disease, and avoidance of drug side effects" (Collins 2005). Perhaps not surprisingly, many of these laudable goals remained largely aspirational at the project's ten year anniversary (Editorial 2010; Evans et al. 2011) and arguably still do today.

Emerging from the foundation laid by the completion of the Human Genome Project, personalized medicine has now risen to a prominent position in the genetics landscape. Broadly defined, personalized medicine is the tailoring of prevention, diagnosis and treatment to an individual's genetic make-up (NIH 2014). Personalized medicine has been made a research priority at national levels, including in Canada (CIHR 2012) and the United States, the latter most notably with President Obama's recent commitment to the Precision Medicine Initiative (see https://www.whitehouse.gov/precision-medicine). In 2015 it was identified as one of the five most promising areas for innovation in Canada by a federal government Advisory Panel on Healthcare Innovation (APHI 2015), and it continues to receive attention in popular press stories about individuals, including prominent public figures, seeking personalized medicine-based treatment approaches (e.g., CBC 2016).

The clinical promise of personalized medicine, while perhaps still speculative in many areas, is considerable. If actualized, personalized medicine may inform more targeted prevention strategies, support earlier diagnoses and lead to better patient outcomes through selection of more effective treatment approaches, with fewer adverse effects (Green 2011; Mirnezami 2012; Chan 2011). It also, by extension, may contribute to more efficient use of health care resources "by administering treatments only to those most likely to benefit" (McClellan et al. 2013 at 143). While it is beyond the scope of this paper to address this point in detail, it is important to note that efforts to stratify patients based on genetic information may raise practical and policy issues of their own (Caulfield and Zarzeczny 2014).

As outlined above, while much of the momentum surrounding the "genetic revolution" in general and personalized medicine in particular is situated largely in publicly funded biomedical research spheres, a private market for genetic testing services offered on a direct-to-consumer basis has also emerged (Caulfield and McGuire 2012). This market consists of private companies that offer a range of genetic testing services directly to the public, without requiring a referral from a healthcare provider. Specific claims about the nature of information provided range widely from identification of disease risk to physical characteristics (e.g., athletic abilities), from ancestry research to questions of lifestyle and health promotion (Caulfield et al. 2015; Caulfield and McGuire 2012). Similarly, there is considerable variation in the quality of the tests, the validity of the results and their potential clinical utility (McGuire et al. 2010).

For example, one leading company in this area offers ancestral information (e.g., DNA composition), personal traits (e.g., male pattern baldness), genetic risk (e.g., heart disease) and carrier status (e.g., cystic fibrosis) (see https://www.23andme.com/en-ca/, accessed April 5, 2016). Costs of these services differ but have decreased substantially over time; at the time of writing, the advertised cost for a 23andMe kit in Canada is $249.00, with 10% off of additional kits (see https://www.23andme.com/en-ca/, accessed April 5, 2016). The process involves ordering and paying for the kit, sending back a saliva swab taken from the inside of the cheek, and waiting for results to be returned.

There are a number of concerns raised in association with the direct-to-consumer market for genetic testing, including that people may act on inaccurate information, perhaps by engaging in fatalistic or deterministic behaviours. It is worth noting however that the evidence on this point is mixed, and equally that "there is little evidence to support the basic premise implied by empowerment rhetoric –

namely that individuals will use genomic risk information to adopt a healthier lifestyle (Caulfield et al. 2013, 3). Privacy is another area of concern, particularly where there is a lack of certainty regarding data release policies, restrictions around future potential uses, access controls for third parties (e.g., researchers, insurers, government, etc.) and protections in the event a company is sold or goes bankrupt, among others (Caulfield and McGuire 2012).

Ensuring appropriate consent is also challenge given that the physical sample is taken in a private space, without the involvement of a healthcare professional, and could conceivably be done without an individual's knowledge or consent. The question of testing of children raises related yet distinct issues, including the limits to parents' decision making power over the health-related interests of their children and what role a 'best interests' analysis should play (Caulfield et al. 2015). The recent introduction of supplemental newborn screening tests to the direct-consumer market is a useful illustration of some of the key concerns including testing of conditions known for "high false-positive rates, variability in onset, lack of treatment options, and counseling difficulties … [and] the return of variants of unknown significance" and has again triggered calls for stricter government controls (Borry et al. 2016).

Finally, enduring concerns about genetic discrimination led to the passing of the *Genetic Information Non-Discrimination Act* (GINA) in the United States and the tabling of Bill S-201, *An Act to Prohibit and Prevent Genetic Discrimination* (Short title: *Genetic Non-Discrimination Act*) in the Canadian Senate. In different ways, both pieces of legislation seek to protect against discrimination on the basis of genetics in particular contexts such as employment and insurance. The need for such legislation, particularly in Canada where other protections such as the *Charter of Rights and Freedoms* and provincial human rights legislation are already in place, remains an open question and matter of some debate (Pullman and Lemmens 2010).

From a health systems perspective, direct-to-consumer genetic testing also has the potential to be a considerable cost driver. For example, recent research by Van der Wouden et al. (2016) suggests that of over one thousand individuals who pursued direct-to-consumer genetic testing, sixty-three percent intended to discuss their results with their primary health care provider. McGuire and Burke (2009) adopt the phrase "raiding the medical commons" to describe the concern that individuals who obtain information on the direct-to-consumer market will then use publicly funded health care resources for questions, follow-up testing – a realistic concern given high false positive rates.

Given the various concerns often discussed in relation to the direct-to-consumer market for genetic testing, the question of regulation is an important one but also one that currently lacks international consistency. Indeed, the regulatory status of direct-to-consumer genetic testing services continues to evolve. In the United States, the FDA and the Federal Trade Commission (responsible for consumer protection) have provided warnings regarding particularly problematic claims (Annas and Elias 2014) and appear to be "deliberating about the best regulatory approach" (Caulfield and McGuire 2012, 30). Health Canada has yet to take to a strong stance with regard to tests sold directly to consumers (Webster 2010). In contrast, a number of European countries have taken a strong restrictive approach and have limited or prohibited the use of direct-to-consumer genetic testing by way of legislation (Borry et al. 2012; Caulfield et al. 2015). The lack of regulatory consensus may be explained partly by the

heterogeneity in the market which makes it difficult to apply any one standard, leading to suggestions that a risk stratified approach is required (McGuire et al. 2010), and by debates about whether the information provided is or is not appropriately characterized as medical advice (Magnus, Cho and Cook-Degan 2009).

In other ways, the regulatory questions here reflect tensions between proponents of individuals' interests in and perhaps rights to information about themselves, and desires to mitigate potential risks to both individuals and healthcare systems. The emergence of this private market may, at least in part, be explained by public demand for genetic services – a demand that is unsurprising given the tremendous amount of attention and enthusiasm genetics-based research, including personalized medicine, has received in very public forums. Nonetheless, autonomy-based access imperatives may need to be balanced against the stewardship obligations policy makers hold, particularly in publicly funded healthcare systems, as well as the *parens patriae* duties of the state to protect the interests of children and others unable to protect themselves.

c. Unproven Stem Cell-Based Interventions ("stem cell tourism")

Much like genetics, stem cell research is another area of biomedical research often credited with having considerable potential, both in terms of its clinical promise for producing better treatments and its prospective commercial strengths as an economic driver (Caulfield 2010). Much of the therapeutic potential of this field turns on the regenerative capacity of stem cells. Known as the "building blocks" of the body, stem cells have – to varying degrees, depending on the type of cell –the ability to replicate themselves and therefore replace dying or injured cells (Main et al. 2014). Hematopoietic stem cell transplants (often more commonly known as bone marrow transplants) as a treatment for cancers of the blood or bone (e.g., leukemia) are one of the few examples of well established stem cell-based interventions.

In addition to having considerable therapeutic potential, stem cell research is also a notoriously complex field of research, particularly when it comes to clinical translation (Main et al. 2014). Harnessing and controlling the regenerative capacities of stem cells is no small feat, nor is maintaining consistency in manufacturing or genetic stability in cell lines, or ensuring safe use in humans in the face of risks of tumour formation (Bubela et al. 2012), to name but a few factors. These challenges make it particularly difficult for researchers and clinicians alike to predict when stem cell treatments will actually be ready for routine clinical use. There are an increasing number of stem cell-related clinical trials registered worldwide, but at present the vast majority of these are in early phases (Main et al. 2014; Trounsen 2011).

Notwithstanding the relatively infancy of much of this investigational work, accounts in the popular press continue to emphasize optimistic timeframes for routine clinical use of stem cell therapies; research reflects consistent use of the 5-10 years timeframe in terms of when clinical applications can be expected, and further illustrates that this target does not appear to move even with the passage of time (Kamenova and Caulfield 2015). The tenor of the discourse surrounding the clinical potential of stem cell research has been referred to as "hype", and given these optimistic public portrayals of stem

cell research's state of readiness, it is perhaps not surprising that public (and especially patient) expectations and demand for stem cell treatments are high (Bubela et al. 2012).

Separate and apart from in vitro research into stem cell biology (i.e. research that takes place outside a living organism – e.g., in a culture dish) and the early clinical investigations described above, a private market has emerged where unproven stem cell-based interventions are marketed and sold directly to patients (Main et al. 2014; Connolly et al. 2014; Lau et al. 2008). Clinics offering a wide range of purportedly stem cell-based interventions for conditions ranging from aging to autism, spinal cord injury to ALS, can be found in countries around the world (Connolly et al. 2014). These interventions are referred to as unproven because they have not been established as being safe or effective by either the clinical trial process or other modes of responsible medical innovation (Lindvall and Hyun 2009), and the word 'intervention' is used in this context rather than treatment or therapy, because the clinical utility of what is provided remains to be established.

Obtaining robust data on this market is difficult, largely because it operates outside regulated medical systems. What is known has been gleaned from a variety of sources including reviews of clinic websites (Lau et al. 2008), interviews with patients (Levine and Wolf 2012), analysis of patient blogs (Ryan et al. 2010), analysis of media reports (Zarzeczny et al. 2010), including social media use (Kamenova et al. 2014), and published case reports (Amariglio et al. 2009). These services are often offered on a direct-to-consumer basis, meaning prospective patients contact the clinics directly – commonly after finding information about them on the internet – and make their own arrangements for care (Connolly et al. 2014). This process marks a significant departure from the specialist referral system used in Canada where primary care providers must provide referrals to specialists, thereby acting as a kind of 'gatekeeper'. Care is typically paid for out-of-pocket and not covered by state-run or private health insurance schemes, and the costs are often considerable. Reports from various sources including media stories, interviews, patient blogs and website reviews suggest ranges of $10,000 - $60,000 USD (Petersen et al. 2013; Zarzeczny 2010).

One of the potential problems with medical services provided on a direct-to-consumer basis outside regulated systems is the lack of oversight and quality control, which is particularly problematic when – as is the case with stem cell-based products - an intervention carries potential physical risk. There are a number of published case reports of harms following an unproven stem cell-based intervention such as lesions, tumours and meningitis (Thirabanjasak et al. 2010; Amariglio et al. 2009; Dobkin et al. 2006), among others, including accounts of deaths (Cyranoski 2010). The content of many of the clinic websites advertising these interventions has been found to be overly optimistic in that it portrays the treatments as safe, effective and even sometimes routine (Connolly et al. 2014; Lau et al. 2008). Little is known however about the nature of information provided to prospective patients, and specifically, whether sufficient information is provided for people to be able to give informed consent. In Canada, informed requires disclosure of the nature of the treatment and its seriousness, any material risks (i.e. including any that are particularly unusual or serious), treatment alternatives and answers to questions the patient may have (Peppin 2011). It seems likely that in at least some cases, individuals are exposing themselves (or loved ones who lack decision making capacity, such as minor children – Zarzeczny and

Caulfield 2010) to considerable physical and financial risk without necessarily fully appreciating the level of uncertainty and potential harms involved (Connolly et al. 2014).

Concerns about this market have triggered a range of responses. Some countries (e.g., Germany – Stafford 2009) have tightened their regulatory frameworks in an effort to restrict clinical use of stem cells falling into certain experimental or high risk categories, although robust enforcement in some cases (e.g., China – Cyranoski 2012) appears to be a challenge. Others are more actively enforcing existing regimes; for example in recent years the United States Food and Drug Administration has taken a fairly proactive approach through legal enforcement and public information campaigns (FDA 2011; FDA 2012). In some jurisdictions, professional regulatory bodies responsible for governing the practice of medicine have disciplined their physician members for different forms of involvement in this market (Zarzeczny et al. 2014). Leading international stem cell research organizations have issued guidance in the area (ISSCR 2008; ISSCR 2013), and a wide range of patient advocacy groups have engaged by providing informational supports and cautions to their members (e.g., ALS Canada n.d.).

Despite these various efforts to curtail this market, it continues to exist and perhaps even grow (Ogbogu et al. 2013). There are a multitude of reasons underlying its robustness. At the state level, market growth and commercialization agendas may conflict with regulatory imperatives to control for risk. Conflicting perspectives on the role of regulation in the context of emerging and experimental interventions are also a factor, reflected most recently in high profile debates in the United States and Australia about autologous stem cell interventions used primarily in an orthopedic context (DeFrancesco 2012). Different opinions regarding the scientific process and standards of proof are also in some ways feeding a perceived divide between 'Western' approaches to medicine and scientific research and those adopted in other parts of the world (Sleeboom-Faulkner et al. 2016).

This lack of global consensus is particularly problematic given the international and largely online nature of this market, for which coordinated efforts would be required for truly effective regulation. At the individual level, the power and importance of hope in this context cannot be underestimated, particularly given the tremendous challenges many patients and their loved ones who consider pursuing unproven stem cell-based interventions are facing (Petersen et al. 2015; Petersen et al. 2013). Arguments in favour of (relatively) unfettered access to interventions – proven or otherwise - often draw on autonomy-based principles, sometimes framed in the broader context of 'right to try' movements (Jacob 2015), while proponents of stricter controls focus on the value of minimizing risks to individuals, health care systems and the field of regenerative medicine research more broadly. Indeed, debates in this field are often heated and the potential for consensus may be remote at best.

III. EXPLORING THE POLICY BALANCING ACT

Despite their individual elements, these three cases highlight the often delicate and complex balancing act health policy leaders face when trying to develop sound policies for how patient demand for and access to global health market products and services will be managed. There are both practical issues to address, including matters of governance, as well as broader (some might say values-based) points of principle to consider when determining vital questions including whether and how access to private

markets for medical products and services should be restricted, what regulatory tools or policy levers are appropriate when it comes to controlling access, and how resource implications will be factored in. Notwithstanding the best of intentions, it must be acknowledged that in the end, as is true of many so-called "wicked" policy problems – a category which the three cases outlined above arguably fall into – consensus about both the precise problem definition and the measure of successful policy in these spheres may ultimately prove to be elusive (Weber and Khademian 2008).

Complex governance structures are evident in all three of these contexts, in that power and influence is held by a range of different players, both institutional and individual. State-level regulation is but one small element of these much larger frameworks, each of which crosses borders and operates largely outside of state-run systems. There are a range of stakeholders involved including both public and private actors. For example, as highlighted to varying degrees in the private markets for organs, direct-to-consumer genetic testing and unproven stem cell-based interventions, government regulators (e.g., FDA, Health Canada), international organizations (e.g., WHO, ISSCR), professional regulatory bodies (e.g., medical boards and colleges), advocacy groups, private market providers, domestic healthcare professionals (e.g., doctors) and patients and their supporters, as well as members of the public more broadly, all play important but highly varied roles.

This multiplicity of players on the field demands creative engagement strategies and, ideally, a collaborative approach to policy making. The persistence of transplant tourism in the face of clear legal prohibitions at national levels, the apparent nimbleness of the stem cell tourism market that has thus far largely eluded robust regulation at the state level, and the regulatory challenges arising in part from the considerable diversity in the direct-to-consumer market for genetic testing services all highlight limitations to traditional top-down legal regulatory approaches. As McGuire et al. (2010) have argued in the context of the direct-to-consumer genetic testing market, "[g]iven that this is largely an Internet-based industry, a comprehensive regulatory policy will need to consider international laws, local norms, and implications for stakeholders from diverse health systems. International cooperation will be required" (182).

Indeed, questions of when to use legal tools (e.g., regulation in the strictest sense) to control or restrict emerging technologies is a complex one, particularly when balancing is required between risks, uncertainties and social demand (Harmon et al. 2013). Challenges with extra-territorial regulation and law enforcement adds further complexity, given the cross-border nature of these markets and sometimes conflicting priorities (both within and between nation states) between economic imperatives (e.g., promotion of clinical translation, desire to promote trade and tourism, preference for allowing market-driven commerce, etc.) and more protectionist regulatory approaches .

Evidentiary limitations are another important factor. The value of evidence-based or evidence-informed policy is widely celebrated and yet in many areas of emerging biotechnology and medical developments, decisions must be made in the face of conflicting or imperfect evidence, or even disagreement regarding the hallmarks of valid evidence. For example, robust data on the size and scope of the three different markets discussed above is lacking, as is a clear and comprehensive understanding of the individual, social and economic impacts of the markets, or of individual outcomes. Stem cells and genetics are fast-

moving fields where the state of knowledge can change quickly. Concrete data about both harms and benefits of participation in the markets discussed above is sparse, and in its absence, some of the concerns raised could be viewed as largely speculative which raises debates about the value of precautionary versus permissive forms of regulatory approaches.

In all three of the areas discussed above, there has been much focus to-date on efforts to provide balanced, evidence-based information so that individuals (patients/consumers) can make informed decisions. However, given the vast amount of competing information available on the internet, it is highly questionable whether simply adding more will be effective. It is suggested that information must be paired with appropriate assistance, including perhaps interpretation by healthcare professionals, if we hope to support patients in exercising their autonomy in a legitimate way (Caplan 2012). However, it also cannot be ignored that doing so comes at a cost to publicly funded healthcare systems.

The suggestion that information is power has become a truism in many contexts, and the role of the internet in exponentially increasing access to information cannot be underemphasized here. Petersen et al. (2013) suggest that online direct-to-consumer advertising not only facilitates access to information and acts as a tool for generating demand, but also radically transforms relationships between the public and experts. Domestic healthcare professionals are now only one of various potential sources of information about medical conditions and treatment options, and patients are playing an ever larger role in decision-making about their care. Indeed, paternalistic approaches have fallen out of favour in Canadian health law jurisprudence, a trend paralleled in policy spheres with greater attention being paid to the value of public or citizen engagement (e.g., Health Canada 2000; Graham and Phillips 1997). It has been argued that in the context of new and emerging biotechnologies specifically, "governance frameworks, including the law, must include appropriate public engagement provisions", in order to promote both trust and legitimacy (Harmon et al. 2013, 2). Where personal beliefs and politics are engaged, as is often the case with transformative technologies including stem cell research, genetics and even the organ trade, public engagement and education have been identified as critical components of public trust, particularly if "calls for caution and restraint in the progress of medical therapies" are to be heard (Paylor et al. 2014, 410).

Even where these concepts may have appeal in principle their implementation will not be straightforward, and careful thought will need to be given to the role of (or place for) public engagement, citizen participation and demand-driven policy. Identifying the relevant public (or publics?) to consult, and how to do so effectively, will be important elements of this consideration. As Petersen et al. (2015) suggest:

> In understanding the role activists play within new treatment markets, and in particular how they use digital media to build communities of hope and create optimistic narratives that mitigate risk, regulators will be better placed to develop strategies that respond to the conditions of digitalized health, including the means for engaging with citizens that are more imaginative and personally meaningful. (11)

As is true in other policy spheres, larger questions about the role of the state will also need to be considered in the context of how far it is appropriate to go if seeking to achieve a balance between defense of individual autonomy and risk mitigation. It is suggested that, "[t]he modern biosciences require governance frameworks that are capable of simultaneously managing risk, coping with uncertainty, combating ambivalence, and building trust, all the while encouraging the delivery of those instrumental outputs that we value/demand (better health, new technologies, commercial reward)" (Harmon et al. 2013, 7). As the three cases outlined above illustrate, working to achieve this balance is perhaps an ambitious but also highly important objective for health policy leaders today – particularly given the high stakes involved for individuals and health systems alike.

IV. CONCLUSION

As illustrated above through the lenses of transplant tourism, direct-to-consumer genetic testing and unproven stem cell-based interventions, the emergence of private markets offering health products and services from jurisdictions around the world on a direct-to-consumer basis over the internet raises important challenges for policy makers. Indeed, these emerging sources of patient and public demand for access to health services and information create both opportunities and challenges for health system administrators, healthcare professionals, regulators, financing systems and policy makers. A balance must be struck between sometimes competing priorities, in a way that will promote public trust, respect individual rights and autonomy and reflect responsible stewardship of public resources, all while fulfilling the state's obligations to its most vulnerable members.

A central part of any policy strategy going forward must include a focus on research. Not only do we require a more fulsome understanding of individual market contexts, including but not limited to the three introduced here, but also of how to engage in meaningful patient and public engagement. In the context of managing access and demand in today's global healthcare market, effective engagement will require greater insight into stakeholders' (including patients and their supporters) values and priorities and decision-making processes, including how risk, benefit and uncertainty are understood and evaluated – a plea that echoes similar calls in relation to medical tourism more broadly (Johnston et al. 2012). It has been suggested that "[t]he growing use of digital media by patients to create communities of hope that campaign for access to unproven treatments should lead regulators to reflect on the implications and limitations of their own approaches to 'regulating risk'" (Petersen et al. 2015, 11). Indeed, the continued growth and diversification of private, direct-to-consumer markets for health services – including those not available through publicly funded domestic healthcare systems – is a complex issue facing policy leaders today, and one that will benefit from a collaborative response.

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