Health Technology Management and Canada's Medical Devices Special Access Program

by

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ABSTRACT

Health Technology Management (HTM) encompasses a broad array of processes spanning technical, clinical, and administrative disciplines in order to optimize the efficient use of healthcare resources. It employs a 'lifecycle' approach, evaluating technologies at each stage of maturity from concept through use and finally discontinuance.

Health technologies exist in various forms; one of them being medical devices. In Canada, medical devices are controlled through the federal Food and Drugs Act and Regulations. While most medical devices require licensing to be sold in the market, provisions exist in the regulations for healthcare professionals to access unlicensed devices. One mechanism is through application to Health Canada's Medical Devices Special Access Program (MDSAP).

This thesis examined the MDSAP in order to understand its role in HTM. Three separate, yet related studies, were conducted. The first study employed a scoping literature review to determine the landscape of available information and to identify more focused areas of required research. The second study reviewed two cases to determine why and how the MDSAP was used to obtain devices in a hospital setting. The third study conducted key informant interviews to compare and contrast key stakeholder perspectives on roles and responsibilities, knowledge and information needs, and program utilization.

Each study employed qualitative content analysis to generate findings. The scoping study determined that the literature was generally limited, yet suggested the MDSAP roles in HTM are: as an arbiter in technology selection, as a route to technology procurement, and as a facilitator of health technology innovation.

The two-case study determined the MDSAP was used for the introduction of new health technology, which comprised 5 general processes: Technology Development, Knowledge Transfer, Evaluation, Acquisition, and Patient Management, and the program played an essential role in the Acquisition stage for the two novel technologies under consideration. Four drivers of program use were identified. These were: change agents, clinical need, innovation, and new evidence. The combination of driving forces triggered the sequence of processes. The MDSAP is a regulatory policy that impacts the management of

health technology. It can result in the accelerated replacement of existing technology, organizational change, and innovation in the development of best clinical practice.

The study on stakeholder perspectives produced four themes: the MDSAP authorizes access to needed medical devices, physicians drive MDSAP demand in the interest of patient care, global forces impact the MDSAP, and the improved management of health technology is a priority need. This study suggests HTM's next steps should include initiatives that enhance the collection and dissemination of unlicensed medical device data.

The three studies' findings were aligned. They inform components of the four major stages of the technology lifecycle – premarket, adoption, real-world use, and decommissioning – and demonstrate the role and impact of the MDSAP in HTM.

PREFACE

This thesis is an original work by Roland Maier. The research project, of which this thesis is a part, received research ethics approval from the University of Alberta Research Ethics Board 2, Project Name "Decision-making on new non-drug health technologies (NDHTs) by hospitals and health authorities in Canada", no. Pro00041926, September 3, 2013.

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And to Kathryn, who has been on this long journey with me, for being my friend.

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INTRODUCTION

Health technology, as defined by the World Health Organization (WHO), is a broad term that denotes the application of products, processes and systems to the provision of healthcare. This includes the use of inventions, such as drugs, devices, and software, as well as techniques such as medical procedures (WHO 2017). Optimizing the efficient use of this array of healthcare 'tools' is the discipline of health technology management (HTM), and is the focus of this present work.

Current interest in HTM has arisen from the need to ensure sustainability of healthcare systems. HTM is inherently broad, inclusive, and dynamic. It adopts a 'lifecycle' approach to the management of technologies, extending both before and beyond the identification and selection of novel technologies. HTM continuously evaluates the effectiveness of technologies in their contextual settings in order to maximize the use of scarce healthcare resources (CADTH 2017).

Where HTM differs from other areas of management, for example, human resources, risk, or facilities, is in its 'techno-centricity' – the management metrics are designed and defined on technological grounds (Lenel et al. 2005; Hegarty et al. 2016). This technological 'lens' has a long history in Canada, and is embodied in federal law in the *Foods and Drugs Act* and *Medical Devices Regulations* (MDR). The Act and Regulations provide legal definitions for the different types of health technologies (among them, medical devices) and establish the safety and effectiveness framework that governs their licensing and sale in Canada.

Built into this governing framework, also, are provisions for exceptions. While most medical devices require product or manufacturer licensing to be sold, Part II of the MDR permits unlicensed devices to be sold in prescribed circumstances. The mechanism for this is through application to Health Canada's Medical Devices Special Access Program (MDSAP). Although the MDR have been in effect since 1998, little is currently known concerning the MDSAP. The Canadian Agency for Drugs and Technologies in Health (CADTH) (2017) recently stated that, "limited work is being done on evaluating technology use in the pre-market space, and in the real world." This makes improvements in the management of health technologies obtained through the MDSAP particularly challenging.

The chapters in this thesis begin to add to our current knowledge through the presentation of three studies. The first chapter, a scoping study, surveys the depth and breadth of information available in academic and non-academic sources and clarifies current knowledge gaps. It provides the first publicly available list of known devices, which suggest clinical program usage patterns. It also describes the literature themes, which suggest what the roles of the MDSAP are in HTM. The findings from this introductory study form the basis for the two subsequent studies.

The second chapter reviews two cases of real-world use of the MDSAP. The actors, information sources, and processes in each case are described, and the nature of the driving forces are explained. These cases advance our understanding of how and why the MDSAP is used to obtain unlicensed technologies in Canada, and demonstrate the clinical and operational impacts of the MDSAP.

The third chapter examines the perspectives of key stakeholders. Through key informant interviews, viewpoints regarding roles, responsibilities, challenges and opportunities pertaining to the MDSAP are presented. Recommendations from these subject experts can be used by Canadian decision makers to guide the design or improvement of leading health policies and practices.

Collectively, these three studies provide new knowledge that spans the four major stages of the technology life cycle: premarket, adoption, real-world use, and decommissioning. This is a step forward in the journey of optimally managing health technology in Canada.

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CHAPTER 1 The Medical Devices Special Access Program in Canada: A Scoping Study

INTRODUCTION

Although healthcare organizations across Canada have made significant progress in developing health technology assessment (HTA) systems, there has been growing concern that their capacity to better manage health technology, more broadly, is lacking. In December 2016, the Federal/Provincial/Territorial Conference of Deputy Ministers of Health tasked the Canadian Agency for Drugs and Technologies in Health (CADTH) to propose a pan-Canadian health technology management (HTM) strategy.

HTM requires knowledge of how new health technologies enter organizations. A recent survey of 47 healthcare organizations across Canada revealed a variety of mechanisms, one of which was the MDSAP (Stafinski et al. 2017).

The MDSAP is laid out in Part 2 of the Canadian *Medical Devices Regulations* under the *Food and Drugs Act* – Custom-Made Devices and Medical Devices Imported or Sold for Special Access (defined as "access to a medical device for emergency use or if conventional therapies have failed are unavailable or are unsuitable") (Government of Canada 1985, 1998a, McAllister and Jeswiet 2003, Gibson and Lemmons 2015). While the program has existed for almost 20 years, how it has been perceived and used remain unclear.

The objective of this study was to determine the landscape of information related to the MDSAP in Canada using scoping review methodology, and gain insights into its role in HTM.

METHODS

The scoping study approach (initially developed by Arksey and O'Malley) was selected because it is ideally suited to situations where the field of evidence is anticipated to be small and when a wide range of research and non-research material needs to be consulted (Anderson et al. 2008, Davis et al. 2009, Levac et al. 2010). It consists of an iterative design with up to 6 stages.

Stage 1 - Identify the research question

The study question was developed iteratively while simultaneously keeping in constant focus the underlying aims of the review (Mays et al. 2005). As the overall aim was to understand broadly what scholarly work had been done to date, and what the sources, volume, and types of information were, the research question was defined as, "what is known from the existing literature about Health Canada's Medical Devices Special Access Program (MDSAP)?"

Stage 2 – Identify relevant studies

The search for relevant material was not limited to peer-reviewed sources as the research purpose was to capture the breadth and range of information available. A list of keywords was developed iteratively, and a search strategy developed with the assistance of an information specialist. For peer-reviewed references, 13 electronic bibliographic databases were searched. A number of approaches to searching the grey literature were attempted with Google Scholar providing the most fruitful results. Links within web pages were also explored.

Searches were conducted between April 2015 and January 2017 (see Appendix 1-1).

Stage 3 – Select studies

As recommended by Levac et al. (2010), the broad research question was then "[combined] with a clearly articulated scope of inquiry in order to guide the search strategy and establish parameters around study selection and data extraction." Inclusion and exclusion criteria were developed *post hoc* and were applied to all material by two reviewers. Material was considered in-scope if it related directly to Health Canada's MDSAP, including custom-made devices accessed through the program. Conversely, material was considered out-of-scope if it did not meet the inclusion criteria. Topics that were explicitly identified as being out of scope included:

- programs from other countries,
- special access programs for drugs or biologics (e.g., blood products),
- investigational trials access,
- health care delivery programs,
- off-label use, or
- reimbursement mechanisms.

Press releases, patents, book chapters and non-English material were also excluded.

Importantly, the quality of the material was not formally assessed and did not form a basis for exclusion.

Stage 4 – Chart the data

A standardized form was developed to record extracted information (see Appendix 1-2). Two reviewers independently pilot-tested the form prior to full use. It contained two sections: one for general data (type and purpose of document, location, date of publication, authorship, and sponsorship or affiliation disclosure) and one for specific data about medical devices (device name, type, and manufacturer; dates and quantities used) where these were provided.

Stage 5 – Collate, summarize and report the results

Two separate "maps" were produced (Davis et al. 2009). The first, a literature map, characterized the range and depth of literature. The second, a device map, compiled the MDSAP-authorized medical

devices found in the literature and categorized them by medical specialty using the Preferred Name Code classification system employed by Health Canada (Health Canada 2006)

In addition to these two mapping constructs, a thematic analysis and synthesis was conducted which yielded a concept map (Attride-Stirling 2001; Thomas and Harden 2008; Gale et al. 2013).

Stage 6 – Consult expert opinion

A subject matter expert consultation exercise was conducted. In stable contexts such as the health management field, relevant stakeholders are often 'visible' (Varvasovsky and Brugha 2000), and the aim in selecting stakeholders is to secure competencies rather than to assure representativeness of all possible interest groups (Welp et al. 2006). Accordingly, individuals with extensive background in regulatory affairs and Health Canada's MDSAP were required. Stakeholder groups were identified from the literature review, and individuals in industry and from the regulator were approached.

The subject matter experts were presented with background information on study rationale, methods, and preliminary findings, and were asked to consider the completeness of the literature search and to identify additional references (Levac et al. 2010). These suggestions were incorporated back into Stage 2, and a second round of stages 3 through 5 was performed.

RESULTS/FINDINGS

Literature Map

A total of 161 documents were retrieved (see Appendix 1-3).

Medical Device Map

No single source of information comprehensively listed the names of all medical devices obtained through the MDSAP. Information published by Health Canada was limited to national aggregate numbers of device applications processed annually (Health Canada 2013, 2014).

Fifty-three devices were identified, although some devices had more than one associated manufacturer or vendor due to corporate mergers and acquisitions. Forty-one of these devices were in the cardiovascular category (see Appendix 1-4).

Literature Themes

Most of the peer-viewed papers that were found focused on individual technologies, and not on the MDSAP, which was frequently referenced only as the means to obtain access to the unlicensed technology. However, basic themes still emerged, and were categorized into organizing themes and then into "global" themes. The resulting concept map contained the following 3 global themes described below (Figure 1).

Theme #1: *The MDSAP as an arbiter in health technology selection, playing an "approval" role*

1.1 APPROVAL IS FOR PATIENTS AND CLINICAL INDICATIONS

The MDSAP provides approval for the patient as an individual, not patients in aggregate or at the population level, and is described as having "a single patient focus" (Health Canada 2007). "… all patients received approval to have surgery from Health Canada on the Special Access Program ..." (Pop 2002). Additionally, small batches of devices for multiple individuals may be approved on a case-by-case basis (Health Canada 2014).

Many authors indicated that patient eligibility was dependent upon the clinical indication. Peters (2002) explained that MDSAP "provides approval for the use of silicone gel implants for the following patients: mastectomy, augmentation after failed saline implants (usually with ripples and folds) and primary augmentation if a saline failure is strongly predicted. Health Canada has not approved the use of gel implants for general use." More recently, de Varennes (2016) reported that "These cases were not "run-of-the-mill" AVRs [aortic valve replacements]. Health Canada would not have authorized us to use a valve in that setting."

1.2 APPROVAL IS FOR TECHNIQUES AND PROCEDURES

Regarding percutaneous aortic valve implantation, Webb et al. (2006) wrote, "The procedure was approved by the Therapeutic Products Directorate, Department of Health and Welfare, Ottawa, Canada, for compassionate clinical use …".

Further examples include needle ablation (Sapp et al. 2013), left atrial appendage closure (Saw et al. 2015), and left atrial decompression (Amat-Santos et al. 2015). Some authors attributed approval of not only a procedure but also an entire program to the MDSAP. "In 2005, the Canadian TAVI [transcatheter aortic valve implantation] program was approved by the Department of Health and Welfare (Ottawa, Ontario, Canada) for compassionate clinical use…" (Rodés-Cabau et al. 2010a).

1.3 APPROVAL IS FOR DEVICES

The MDSAP approves the use of unlicensed alternatives to licensed medical devices when they are perceived to be clinically superior. (Raymond et al. 2001; Almasham et al. 2008; Humpl et al. 2010; Abraham et al. 2012; Nietlispach et al. 2010). Peters' (2002) review of breast implants noted the availability of two types of implants, saline filled (comprising 95% of implants) which were licensed and gel filled (5%) which, at the time, were unlicensed. Gel filled implants were being used for "patients with exceptional circumstances, who received approval on compassionate grounds, because the quality of their final results would be more compromised with saline implants … than with gel implants."

The uniqueness of the device (is it sufficiently different from a licensed alternative?) was a consideration in approval. Minor variations in design and incremental improvements were considered insufficient for granting approval (Health Canada 2016).

The MDSAP also approves custom-made devices (Government of Canada 1998a, Health Canada 2016). One example is custom-made endovascular stents (Nietlispach et al. 2010; Mewhort et al. 2011; Lioupis et al. 2012).

1.4 APPROVAL DEPENDS UPON MORAL JUDGMENTS

"Compassionate use" was noticeably absent in government documents, but in primary studies, justification for MDSAP approval often related to compassion (Cheung et al. 2010; Cheung et al. 2014).

The requirement for patient consent is found in the "Undertaking" section of the application form. However, Health Canada has recognized that it has no jurisdictional authority in this area, since patient consent is established in the physician-patient relationship, and regulated at the provincial/territorial level through colleges of medicine (Government of Canada 2007). Soon et al. (2011) wrote, "The prosthesis was approved for compassionate use by the department of Health and Welfare, Ottawa, Canada, in consenting patients declined for conventional reoperative surgery." Similarly, Gurvitch et al. (2010) wrote, "All patients were approved on a compassionate-use basis and gave written informed consent."

Institutional review was not a requirement for approval, but was mentioned as being sought in select cases. Asch (2002) noted, "In cases in which it was deemed that filter removal had to be postponed beyond 12 weeks for a medical indication, specific approval from both the ethics department and the Health Protection Branch was sought and granted." The requirement for approval from all three parties was noted by Dahdah et al. (2007). "Given the investigational status of the device used in this case report, approval was obtained from an institutional government-designated pediatric ethics committee and from the Canadian Special Access Programme of the Therapeutic Products Directorate, Health Canada. Parental written informed consent was obtained prior to the intervention."

1.5 APPROVAL DEPENDS UPON EVIDENCE ADEQUACY

Approval depends upon satisfying minimum evidence requirements as defined by Health Canada. Its Special Access Unit, with scientific reviewers and medical experts in the Bureau, decides on authorization based on the medical rationale provided and other information available (Health Canada 2016). These evidence requirements are unique to the MDSAP due to their separate position (in Part 2) within the Medical Devices Regulations. A number of documents described this evidentiary uniqueness through comparisons with other programs.

Health Canada (2007) noted: "Separate regulatory provisions for drugs and devices have created inconsistencies between two programmes even though they have the same overarching intention, namely to provide emergency use access to products unavailable on the Canadian market." Walker et al. (2014) concluded that many jurisdictions have "a lower evidentiary standard for devices compared to drugs."

Two articles compared the denial of a request for AIDS drugs with the approval of requests for breast implants and argued that there was less evidence of benefit to breast implant recipients (cosmetic) than

there was to AIDS drug recipients (life-saving) (Christie and Montaner 2006; Government of Canada 2006b).

Differences in evidence requirements for investigational testing, licensing, and obtaining devices via special access were also raised. As indicated by Health Canada, “Medical devices authorized under Special Access do not undergo the same level of scrutiny required to obtain a medical device license or an authorization for investigational testing” (Health Canada 2016).

Evidence thresholds were seen as being open to interpretation. A report of the Standing Committee on Health captured this sentiment with a committee member’s question, “So I am wondering how you can determine that the risk is acceptable and therefore offer breast implants to all these women without having any long-term studies?” (Government of Canada 2005b).

Theme #2*: The MDSAP as a route of health technology procurement*

2.1 PRE-MARKET ACCESS

The MDSAP provided an early route for professionals to access unlicensed products which subsequently were licensed, e.g., the Thermablate™ endometrial ablation technology (Vilos and Edris 2007) and the product Bio-Alcamid™ (Ellis and Sardesai 2008). Both were first used through MDSAP before receiving regulatory approval. More recently, Health Canada has stated that although the SAP plays a role by providing access to products that have not yet obtained market authorization (Health Canada 2007), it is not intended as an “early market access” route for devices that are still in trials, still in development, or awaiting licensure (Health Canada 2016).

However, the MDSAP does appear to play a role in commercialization based on the sequential licensing of a device at an international level. The product may have been licensed in one jurisdiction and obtained via special access before receiving market approval in Canada or an additional jurisdiction. The Amplatzer Plug III (a CE marked device) was accessed via MDSAP in Canada while under evaluation by the Food and Drug administration in the US (Jilaihawi and Ibrahim 2010). A second example was the international roll-out of Thermablate, initially approved for sale by the State Drug Administration in China and also used to treat 54 women in Canada via the MDSAP before it received licensing. Approval for sale in Europe with CE marking followed (Yackel and Vilos 2004).

A variation of the pre-market access concept was the case of silicone gel implants, whereby the products were initially licensed, then withdrawn from the market and obtained only by SAP, and later marketed again after additional studies had demonstrated the products were safe (Brown et al. 2005; Spear and Hedén 2007; Hall-Findlay 2011).

2.2 NON-MARKET ACCESS

Certain devices obtained through the MDSAP have never been licensed in Canada. Accumulating the clinical evidence needed for market approval is sometimes seen as an insurmountable barrier. For heart

valves, Webb et al. (2010) explained, “It is unlikely that we will see rigorous testing of all potential combinations of available surgical and transcatheter valve types, frames configurations, and sizes.” Interventions to treat rare diseases are also difficult to evaluate through clinical trials, because of the small number of patients (Walker et al. 2014). Custom-made devices are also challenging to evaluate for efficacy because each device is designed specifically for one individual (Klepinski 2006; Lioupis et al. 2012).

Also, Canada represents a small potential market; e.g., the CE-labeled Innogenetics Inno-LIA HIV I/II Score, an unlicensed assay, can only be obtained through the SAP (Kadivar et al. 2013).

2.3 LOGISTICS

The logistics of procurement were described in several papers, including Health Canada’s recently-issued Guidance document (Health Canada 2016). Collectively, they provide information relevant to manufacturers, importers and healthcare professionals on topics such as: applicant qualifications, individual and batch requests, advertising, labeling, purchasing and sale, return of unused products, etc. within the context of the MDSAP

The volume of SAP requests is also a logistics issue. In 2004, the Auditor General’s report stated: “In 2002, Health Canada received 5,000 requests through the Special Access Program, a 683 percent increase in the last four years. Since the staff who process requests through the Special Access Program are the same as those who conduct pre-market evaluations, time spent dealing with these requests is time taken away from working on pre-market evaluations” (Government of Canada 2004). Health Canada (2016) similarly advised, “the Special Access Unit experiences a high volume of requests and follow-up communications”, and the Therapeutic Products Directorate’s annual performance reports drew attention to the application processing metrics of the MDSAP (Health Canada 2013; Health Canada 2014).

2.4 COSTS

The 2 relevant types of costs associated with the MDSAP are program costs, and device costs. Devices being requested through MDSAP are exempt from application fees on the basis of the determination that “these devices have been exempted … for public good reasons” (Government of Canada 1998b). It is not clear how institutions pay for them, but Health Canada has offered guidance on two matters: (1) devices do not have to be provided free of charge by the manufacturer, and (2) cost savings of the device are not an adequate justification for granting access (Health Canada 2016). Only one study of cost-effectiveness of a device being acquired by SAP was found in the literature (Hancock-Howard et al. 2013).

Walker et al. (2014) discussed the cost of these devices to society from an ethical standpoint. “Potential cost burdens to society are difficult to predict as the funding implications of SAPs vary by location and program. Where health care payment systems are structured around evidence of safety, efficacy, and cost-effectiveness, SAPs have the potential to open the door to costly and unproven interventions, thereby subverting attempts to contain costs based on sound reasoning and evidence. Supplying

unproven interventions entails opportunity costs; manufacturers may not develop alternative options and governments have less to spend on more effective interventions."

Theme #3. *The MDSAP as a facilitator of health technology innovation*

3.1 TECHNOLOGY INTRODUCTION

The MDSAP enables access to emerging technologies (Webb et al. 2006; Osten et al. 2010; Sinclair and McGregor 2013; Government of Canada 2004, Health Canada and the Public Health Agency of Canada 2014; Health Canada 2016).

Several papers discussed technical feasibility, safety, procedural success rate, efficacy, or short-term patient outcomes, all key information elements for technology uptake and diffusion (e.g., Helton et al. (2011) and Purdham et al. (2012) on cardiac valves). Health Canada has acknowledged the importance of publishing studies that report on such elements in order to communicate findings to the relevant clinical community (Health Canada 2016).

The MDSAP has also been used to facilitate first-in-man-use applications of devices, for patients, "who would otherwise have no clinical options" and were given "careful scrutiny" (Health Canada 2016). In 2005 during meetings of the Standing Committee on Health, the program was portrayed as providing access, with the healthcare professional described as the initiating force or the technology pioneer (Government of Canada 2005a, 2005b)

3.2 TECHNOLOGY EVOLUTION

The MDSAP provides access to evolving technologies (evolution of the device or of its use). In several papers, device evolution was phrased in the language of 'generations,' such as the third generation HeartWare HVAD (Rao et al. 2013), or second-generation endometrial ablation technologies (Vilos and Edris 2007), or in terms of improvement or evolution in time (Velasco-Sanchez et al. 2013; Purdham et al. 2012; Stein and Stein 2014). Device evolution was expressed in terms of novel techniques, or additional clinical indications. For example, Osten et al. (2011) described how TAVI evolved from an antegrade transvenous transseptal approach to percutaneous retrograde transfemoral and anterograde transapical approaches. Occasionally, off-label use was reported as being intertwined with special access use; "The use of CSs [covered stents] in this study were obtained as an off-label application through a special-access government medical programmer [sic] (Kundu et al. 2011)." However, Health Canada distinguishes between the two and provides oversight of off-label use through the Investigational Testing provisions of Part 3 of the regulations (Health Canada 2016).

3.3 TECHNOLOGY ROUTINELY USED

The MDSAP can influence the path of a technology to routine use. In some cases, after the first MDSAP approval, requests for the device have accelerated as its adoption became more widespread. TAVI was one of the most documented technologies accessed through the MDSAP in Canada, its use rising

exponentially as it became well-established for treating select patients (Jilaihawi et al. 2012; Del Trigo et al. 2015). Silicone breast implants experienced a large increase in use in Ontario between 2000 and 2005 as plastic surgeons gained confidence in its safety (Snell et al. 2008).

Health Canada's position on the general use of devices obtained via SAP is that health care facilities should not expect to obtain individual devices on an ongoing basis, and that SAP approval does not suggest that the device is appropriate or suitable for general use (Health Canada 2016). However, batch requests for devices routinely required in urgent, life-threatening circumstances are available on a case-by-case basis (Health Canada 2014).

3.4 TECHNOLOGY LEARNING CURVE

Many non-drug health technologies are associated with learning curves, of which an important component is appropriate patient selection (Zamorano et al. 2011). This is reported as being particularly true with MDSAP devices (Wong et al. 2010; Soon et al. 2011). The MDSAP has advised that, where device training is required prior to use, the timing of training prior to submitting the SAP application should be considered (Health Canada 2016).

Once devices are accessed, there is limited monitoring (Government of Canada 2006a). To assist with the collection of outcomes data about specific new technologies, a number of registries have been created (Cribier and Zajarias 2008; Purdham et al. 2012; Guerrero et al. 2015).

Some papers referred to the MDSAP in terminology associated with research, such as the "Canadian special access trial" and "Canadian special access study" (Del Valle-Fernandez et al. 2010; Hancock-Howard et al. 2013). Other research-oriented articles noted that the device was initially obtained via special access, and then became licensed. "During the initial portion of this study, the PED was only available through a Health Canada compassionate-use program (O'Kelly et al. 2013)."

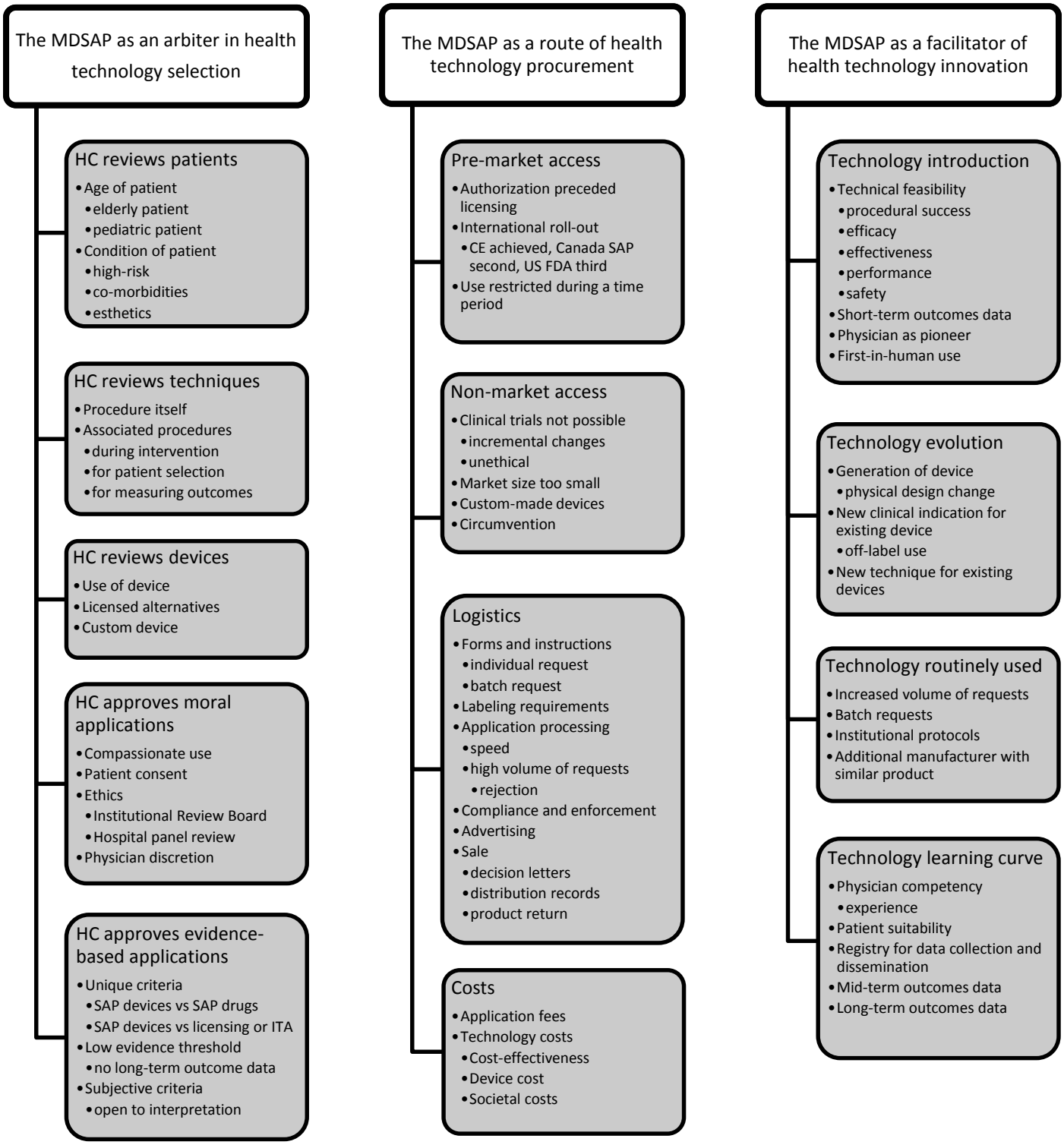

Figure 1-1. Concept map derived through thematic synthesis of the literature. MDSAP = Medical Devices Special Access Program. HC = Health Canada.

DISCUSSION

The three global themes of technology selection, procurement, and innovation determined through the scoping review suggest that the MDSAP is one mechanism of health technology management in Canada. By providing access to emerging new devices, the program facilitates the adoption and diffusion of innovations in healthcare, as well as the start of the technology life cycle (Figure 2).

Diffusion of innovations starts from individual use cases, where authorizations are granted on ethical grounds after assessment of safety, effectiveness, and risk/benefit for *individuals*. While the MDSAP is not intended to be an early market access route for medical devices, it involuntarily plays that role. As additional authorized requests for the emerging technology continue to build the evidence base, a critical mass is reached that permits (or disqualifies) device licensing and marketing. This decision is now no longer made on the basis of optimal care for an *individual*, but on the ethical grounds of safety and effectiveness at the *population* level.

Thus, the special access program does not appear to be used to circumvent licensing. The MDSAP allows an emerging or evolving technology to demonstrate that it has promise and gather support and momentum. Where evidence is limited, the healthcare professional bridges the evidence gap by providing the medical rationale to Health Canada on the application form. This enables ethically desired patient outcomes as well as product commercialization.

The findings from this scoping review suggest that the MDSAP may be an effective commercialization strategy for industry. By providing education and training in the use of new technologies to physician pioneers, industry has a commercialization mechanism available for cases in which clinical trial data is difficult to obtain. Bates (2008) investigated similar programs in the pharmaceutical context, known in Europe as named patient programmes, and provided evidence that these programs were effective in increasing market share.

The limitations of this study include its reliance upon publicly available sources. There are two potential implications of this: 1) incompleteness of the medical devices identified and 2) over-representation of emerging technology and technology adoption themes, due to the nature of the research articles reviewed.

The review identified a number of evidence gaps and, in turn, areas for future research. They include investigating the magnitude and level of significance of the MDSAP in Canada. To what extent does it shape the healthcare landscape – in which medical specialties, or for which diseases? What is the health economic impact? Of note, in the area of custom-made devices, very little information is currently publicly available. Concept maps stratified by stakeholder group should also be developed. The special access program is a unique federal route with a different mandate than the standard licensing route. Are the unique circumstances, opportunities, and risks surrounding special access devices sufficiently understood

at the provincial and territorial level? At the institutional level? And, as Bryan et al. (2014) implore, are they optimally managed?

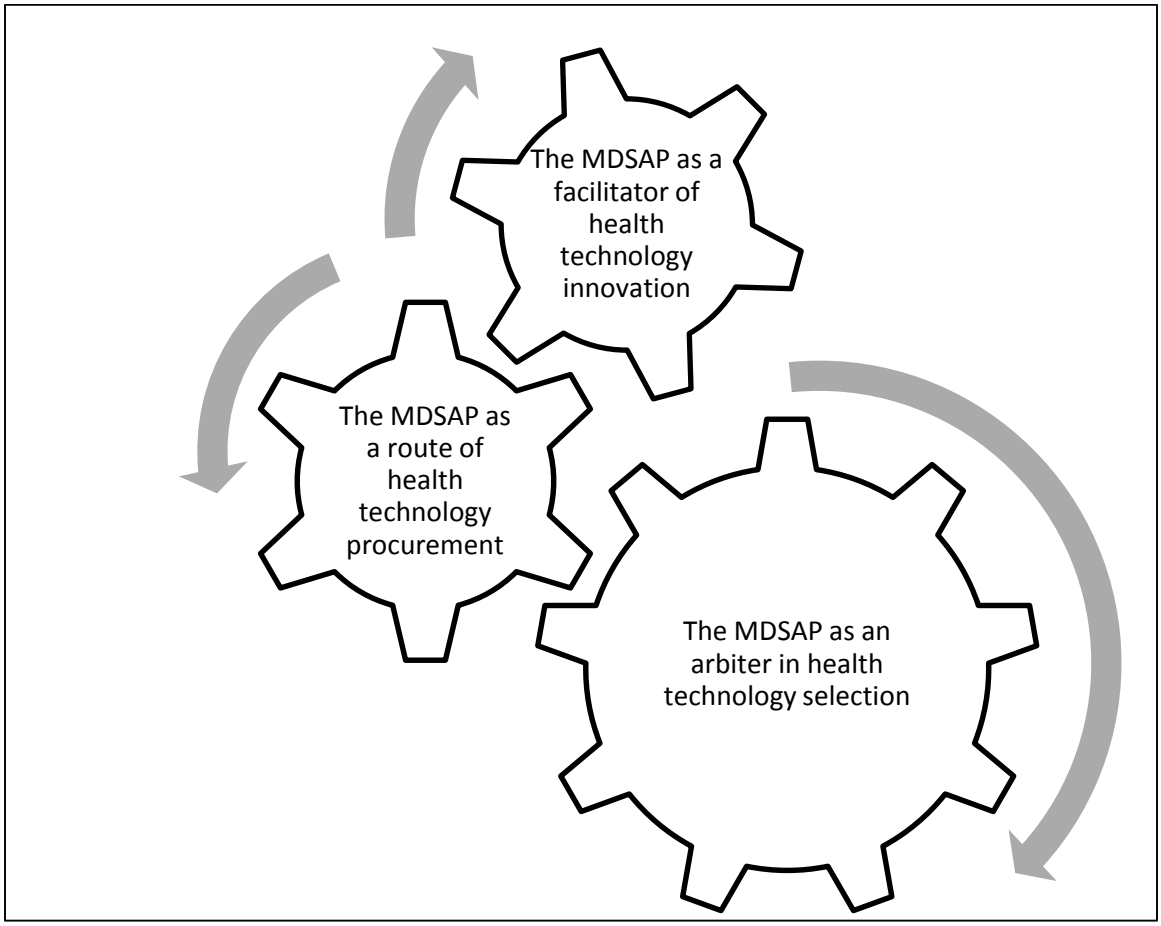

Figure 1-2. Graphical depiction of the mechanism of action and the interrelated functions of the MDSAP in health technology management.

CONCLUSION

This paper provides the first scoping review and analysis of publicly available information pertaining to the Canadian Medical Devices Special Access Programme. This is an important step for managing health technology, building evidence into decision-making, and refining policy.

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APPENDIX 1-1. Literature search strategy

Electronic Database Searches

Date: February 2, 2016

Limits: No limits were used

Databases:	Hits
1. Medline	10
2. EMBASE	19
3. CINAHL	2
4. PsycInfo	2
5. Web of Science	14
6. HealthSTAR	9
7. Scopus	3
8. Canadian Research Index	2
9. Index to Canadian Legal Literature	0
10. Canadian Legal Information Institute	0
11. Canadian Health Facilities Law Guide	0
12. Law Source	0
13. Health Policy Reference Center	22

Concept 1	**Concept 2**	**Concept 3**
Non-MeSH	**Non-MeSH**	
Special access program	Prosthesis	Canada
SAP	Implant*	
	Custom	

Total number of records found before duplicate removal = 83

Total after duplicates removed = 44

Date: February 5, 2016

PubMed search

Query	**Items found**
Search ((((“compassionate grounds”) OR (“compassionate access”) OR (“compassionate release”) OR (“special access”) OR (“special access program”) OR (“special access programme”) OR (Health Services accessibility/legislation and jurisprudence [MESH]))))) AND (((implant) OR (non-drug0 OR 9device*) OR (“medical device”) OR (prosthesis) OR (prosthetic) OR (custom))) Filters: English	185

Grey Literature Searches

Google Scholar

Terms	Date	Number of references
“special access program” Canada	September 19, 2015	588
“special access programme” Canada	September 19, 2015	174
custom “special access” Canada	October 2, 2015	First 100
“special access” Canada prosthesis	October 26, 2015	138
Canada implant “special access”	November 22, 2015	First 100
“special access” prosthesis Canada	November 22, 2015	First 100

Government Websites

Website	Search Terms	Number of references	Date
Parliament of Canada www.parl.gc.ca	“medical device” “special access”	First 100	July 24, 2016
Canada Gazette gazette.gc.ca	With the exact phrase: special access programme	17	January 26, 2017

APPENDIX 1-2. Data extraction form

Section 1. Document information
Title:
Year of publication:
Publication location: e.g. journal name e.g. website
Primary author name:
Type of document: e.g. peer-reviewed journal article e.g. form
Purpose of document: e.g. demonstration of technology feasibility e.g. guidance on process

Section 2. Contributing author information
Name(s) of author(s) organization(s):
Type of organization: e.g. university, hospital, regulator, industry, academic journal
Financial interest or affiliation by authors: e.g. funding source stated? e.g. materials from vendor gratis? e.g. not applicable? e.g. other?

Section 3. Special Access Program information
Document statements about SAP: e.g. role of SAP

Section 4. Technology-specific information (if available)
Date technology was used From: To:
Number of patients:
Device vendor:
Device name:
Device type:
Device classification by practice: e.g. cardiology, surgery, ophthalmology, …
Device classification by generation: e.g. first generation e.g. device succeeds which predecessor

APPENDIX 1-3. Literature characteristics

Venue of publication	Types of publication	Author affiliation
Academic journals, including publications of professional societies	• Primary studies • Reviews • Editorials • Conference abstracts • Letters to the editor • Consensus statements	• Hospital • Academic medical center • University • Manufacturer • Clinic or private practice • Public health agency • Private consultant practice • Law firm
Health Technology Assessment (HTA) producer	• HTA reports	• Self-published
Universities	• Theses and dissertations	• Self-published
Federal government websites and webpages	• Forms • Laws, regulations • Guidelines, instructions • White papers • Meeting agendas and minutes • Performance reports • Committee reports	• Parliament • House of commons committee • Health ministry • Auditor General
Law firm websites	• Bulletins • Presentation materials	• Self-published • Health ministry
Manufacturer association website	• Presentation materials • Code of conduct	• Self-published • Health ministry

APPENDIX 1-4. Medical devices obtained via Special Access Program authorization

Device manufacturer/vendor	Device name	Medical Specialty
Abbott Laboratories	MitraClip	Cardiovascular
Abbott Medical Optics (acquired Visiogen)	Synchrony	Ophthalmology
Abiomed	Impella Right Direct	Cardiovascular
Abiomed	Impella Right Peripheral	Cardiovascular
AGA Medical Corporation	Amplatzer Cardiac Plug	Cardiovascular
AGA Medical Corporation	Amplatzer Membranous VSD Occluder 2	Cardiovascular
Allergan (see also Inamed)	Style 410	General & plastic surgery
Bard	Recovery	Cardiovascular
Bard Peripheral Vascular	Fluency Plus	Cardiovascular
Berlin Heart	Berlin Heart Excor Pediatric	Cardiovascular
Biosense Webster	(not stated)	Cardiovascular
Boston Scientific	Watchman	Cardiovascular
Cook Medical	Custom-made stent graft	Cardiovascular
CoreValve	CoreValve revalving system	Cardiovascular
Correx	Not indicated	Cardiovascular
Edwards Lifesciences	Ascendra transapical catheter	Cardiovascular
Edwards Lifesciences	Cribier Edwards	Cardiovascular
Edwards Lifesciences	Forma Repair System	Cardiovascular
Edwards Lifesciences	Fortis	Cardiovascular
Edwards Lifesciences	RetroFlex delivery catheter	Cardiovascular
Edwards Lifesciences	RetroFlex II delivery system	Cardiovascular
Edwards Lifesciences	Sapien	Cardiovascular
Edwards Lifesciences	Sapien XT	Cardiovascular
Edwards Lifesciences	Sapien 3	Cardiovascular
Ev3 Endovascular Inc	Pipeline Embolization Device	Neurology
Flowcardia	CROSSER system	Cardiovascular

Fresenius Kabi	Freka Pexact	Gastroenterology & Urology
HeartWare	HVAD	Cardiovascular
Inamed Aesthetics (see also Allergan)	Style 410	General & plastic surgery
Innogenetics	Inno-LIA HIV I/II	Microbiology
MDMI Technologies	Thermablate	Obstetrics & gynaecology
Medtronic (see CoreValve)	CoreValve	Cardiovascular
Medtronic	ATS 3f	Cardiovascular
Medtronic	ATS Enable Model 6000	Cardiovascular
Medtronic	Talent	Cardiovascular
Mentor	(not stated)	General & plastic surgery
Neovasc Inc	Tiara system	Cardiovascular
NMT Medical	Recovery	Cardiovascular
NuMed Inc	Cheatham-Platinum stent	Cardiovascular
Ophtec	Artisan iris-claw	Ophthalmology
PhysIOL	FineVision	Ophthalmology
Polymekon	Bio-Alcamid	General & plastic surgery
St Jude Medical	Amplatzer Vascular Plug III	Cardiovascular
St Jude Medical	Amulet	Cardiovascular
St Jude Medical	Portico valve system	Cardiovascular
Standard Diagnostics	SD Bioline Syphilis 3.0 Test	Microbiology
Target Therapeutics	TriSpan	Neurology
Teleflex Medical	Rusch Trachflex Plus	Anaesthesiology
Thoratec	Aria	Cardiovascular
V-Wave Ltd	V-Wave	Cardiovascular
Visiogen (see Abbott Medical Optics)	Synchrony	Ophthalmology
William Cook Europe	Cook Zenith TX2	Cardiovascular
Zeiss	AT LISA 809	Ophthalmology

CHAPTER 2 Use of the Medical Devices Special Access Program for the Introduction of Innovative Medical Devices in a Canadian Hospital: A Two-case Study

INTRODUCTION

Health technology management (HTM) involves the organization and coordination of a variety of activities, including technology assessment, appropriate procurement, and maintenance programs, which collectively require skills in the management of areas as diverse as clinical judgement and use, financing, and training and development (Lenel et al. 2005). In Canada and abroad interest in HTM has heightened as healthcare systems strive to provide appropriate *and* sustainable services (Bryan et al. 2014; Sampietro-Colom and Martin 2016; Pan American Health Organization 2017). For example, the Organization for Economic Cooperation and Development has stated that "Good management is key, both for anticipating budgets needed for new treatments, and for assessing any new technological innovations coming on the market" (Skinner and Chandra 2017).

In Canada, medical devices may be procured by healthcare organizations in a variety of ways. With the exception of the lowest-risk 'Class I' devices, most require licensing before they can be marketed or sold. Authority over the licensing of medical devices rests within the federal government (Health Canada), through its Medical Devices Regulations (Government of Canada 1998). Unlicensed devices may be accessed by a healthcare professional upon application to Health Canada through its Medical Devices Special Access Program (MDSAP) (Health Canada 2007).

A recent Canadian survey identified the MDSAP as one mechanism by which new non-drug technologies become introduced into health institutions (Stafinski et al. 2017). It has been suggested that this program plays important roles in health technology selection, procurement, and innovation; however, the extent of the program's use, and the implications, are not well understood (Maier et al. 2017). Due to patient privacy and business confidentiality constraints, detailed public reporting is not available. This knowledge gap makes efforts at optimizing local policy and processes more challenging (Walker et al. 2014).

The need remains to provide a more detailed account of the MDSAP's use within a contextual setting, and its impact on HTM. This study was conducted to investigate how and why the program was used in Alberta, Canada. Our objectives were to determine the drivers of use, the stakeholders involved, and the information sources and processes used in decision making.

METHODS

A two-case study approach was selected (Yin 2014). Case studies are well-suited to the investigation of processes in which multiple variables interact simultaneously. They can examine non-linear

interdependencies and interrelationships and can explain *how* a series of events are related and *why* they produce an ultimate outcome (Ibid., pp. 154, 156, 167). Among case study designs, the 'two-case' study approach can produce more robust conclusions than the 'single case', due to its ability to identify replicated elements across cases (Ibid. pp. 57,164).

A review of program usage data (Health Canada, personal communication) and findings from a scoping study (Maier et al. 2017) suggested that healthcare professionals in cardiovascular medicine were key users of the program. Consultations with local cardiologists in Edmonton confirmed the study's importance and identified 2 specific medical devices for which sufficient data were available: 1) the Absorb Bioresorbable Vascular Scaffold System (BVS), and 2) the Melody™ Transcatheter Pulmonary Valve (Melody).

Approval for the study was obtained from the University of Alberta Research Ethics Board 2, and data collection proceeded as follows. The key information items that needed to be obtained through the planned interviews were identified in 4 categories: actors involved, processes followed, technology details and knowledge/evidence considered (see Appendix 2-1 for the list of items). These formed the basis for the interview questions. Healthcare professionals who had direct knowledge of each case were contacted and provided with a briefing note, after which semi-structured interviews were conducted. Supplementary documentation, such as written departmental procedures, completed applications, and records, were requested where available to further support and 'triangulate' the interview responses. Data that could be used to identify specific patients were not collected.

Data analysis followed a descriptive framework strategy (Yin 2014, p.139). Initially, narrative descriptions were developed from the key informants' responses. Flexibility in the structure of the descriptions was permitted in order to incorporate the unique characteristics of each case. For the first case (BVS), a task flow diagram was constructed to visually support the complexity of the case. Task flow diagrams are administrative tools designed to depict, evaluate, and improve operational processes and are commonly used in healthcare settings (Public Health Informatics Institute 2006). They are constructed using process analysis techniques, and they identify, and show the relationships between, actors, tasks, and decisions (American Society for Quality 2017). For the second case (Melody), which had less complexity, the interview responses were tabulated.

Following the case descriptions, cross-case comparisons were performed to identify patterns. A thematic analytic approach was used to identify both important topics and common and contrasting elements. Generalizations were derived by using literal replication logic (Yin 2014, p.57). Plausible explanations for each pattern were developed based upon an examination of the relationships among each pattern's variables.

The first cross-case comparison examined process elements to answer the key research question of *how* the MDSAP was used. Events were examined to see if they were sequential, overlapping, or completely

concurrent. Overlapping or concurrent events were interpreted as evidence of non-causal interactions, while sequential events were further examined for dependency. The second cross-case comparison examined factors of use to answer the key research question of *why* the MDSAP was used. Factors were examined for their mechanisms of action and whether they acted independently.

The two cross-case comparisons were then combined to form a general explanation of how the driving forces triggered the process elements (Yin 2014, p.170). This explanation can be used as a conceptual model to predict the circumstances under which use of the MDSAP may plausibly re-occur.

RESULTS

Case 1. The Absorb BVS System

The Absorb Bioresorbable Vascular Scaffold System (Abbott Vascular, Santa Clara, CA), or 'BVS', is a combination device/drug product used for the treatment of coronary artery disease. It is comprised of four main components: a bioresorbable scaffold, a bioresorbable coating, the antiproliferative drug Everolimus, and a delivery system. The scaffolds are manufactured in several different lengths and diameters which must be matched to the size of the artery in which they are to be implanted. The original delivery component used in the clinical trials was later replaced with a 'rapid exchange' version, and the complete system then became the Absorb GT1™ Bioresorbable Vascular Scaffold System (Abbott 2016). It was licensed as a Class 4 device in Canada in June, 2016.

BVS was reviewed by the University of Alberta Hospital Division of Cardiology prior to its becoming licensed. Performance of the system had been established in international clinical trials and information pertaining to its safety and effectiveness had been published. BVS was considered an important improvement over the best licensed technology in use at the time. Compared to drug eluting stents it provided numerous clinical advantages to patients and no known additional risks.

The decision to adopt BVS was made by the senior medical and administrative leadership team of the cardiology division. As it was perceived as an incremental or evolutionary step in technology, it was not considered a candidate for a health technology assessment (HTA) or a business case; formal HTAs and business cases are normally required for larger 'disruptive' or costly technologies. In addition to safety, clinical effectiveness and outcomes, the adoption decision considered the following factors:

- Volumes (frequencies and quantities)
- Alternative options
- Affordability, and health of the department budget
- Department priorities, and tradeoffs

These were standard decision-making criteria used by the division (i.e.,not unique to the BVS case).

Being unlicensed at the time, BVS was not available through a negotiated procurement contract and pricing was full list price. The then-current licensed alternative (drug eluting stents) had been on the market for a number of years and prices had gradually decreased. Compared to drug eluting stents, the new BVS was more expensive. The incremental cost of BVS was absorbed by the department budget.

Until it was licensed, BVS could only be obtained through the MDSAP, which involved completion and submission of the standard Application form to Health Canada. The cardiology division cardiac catheterization and interventional cardiology director submitted a batch request of two units of each available size (seven sizes in total) to be kept on hand. A batch request was required in this setting as patients presented in emergency settings and the appropriate size of the device could not be determined in advance.

Because the number of devices authorized by Health Canada through the MDSAP was limited to a one-month supply, the on-hand inventory had to be carefully managed. An additional complicating factor was the short expiry date of the product due to the drug component (since improved), and, as required by the MDSAP, unused product needed to be returned to the manufacturer or importer. Used or returned product then needed to be replenished through re-applications to Health Canada for new product. This process was in effect until BVS was licensed, after which authorizations from Health Canada were no longer required (see Appendix 2-2).

Case 2. The Melody Transcatheter Pulmonary Valve

Dr. Philip Bonhoeffer, a European based professor and cardiologist, pioneered the development of a prosthetic heart valve that could be implanted via transcatheterization, thus sparing the patient from an open surgical approach with its attendant harms. Known as the Melody™ Transcatheter Pulmonary Valve (Medtronic, Minneapolis, MN), this novel device was first implanted in a human by Dr. Bonhoeffer in the year 2000. Deployment of the valve required development of a separate delivery system, known as the Ensemble™ Delivery System. Over the next five years an additional 88 patients underwent the procedure, which led to a design modification to the valve (McElhinney and Hennesen 2013). The Melody system received CE marking in 2006, Health Canada licensing in 2006, US Humanitarian Device Exemption in 2010, and FDA pre-market approval in 2013.

Prior to receiving Canadian licensing, practicing cardiologists in Edmonton, Alberta at the University Hospital became aware of the innovation as reports of the device and technique began to emerge. Relying primarily on the published literature on structural heart disease, clinicians reviewed evidence on procedures, outcomes (only short-term data were available at the time), and complications. Peer-to-peer learning was an important factor, as physicians discovered, shared and discussed new articles among themselves (see Appendix 2-3). The Melody valve was perceived as a first-in-class innovation as there was no other device that offered a non-surgical approach.

At the time, the primary uncertainty over the new technology was whether it was sufficiently durable. The standard surgical valve prostheses then in use had known function and durability and could, at least theoretically, last the patient's lifetime. Patients requiring the valves were in typically their mid-teenage years, had already had previous operations, and were now experiencing sequelae that required a new valve. The Melody valve was perceived as a temporary measure and not a replacement for open heart surgery, the premise being that patients would still eventually require surgery but the new valve could delay that for a number of years. This would potentially provide significant clinical benefit. However, as the evidence on longevity was not yet available, there was a risk that the Melody would not last long enough and that surgery would be required too soon. Ultimately, the devices lasted longer than expected.

The decision to proceed with the new technology was made within the catheterization lab environment, and in 2006, two physicians from Edmonton proctored with Dr. Bonhoeffer at the Great Ormond Street Hospital for Children in London. The two days of proctoring covered a diversity of topics, including case selection. Half of each day was spent in seminars and the other half was spent observing demonstrations and performing procedures.

Upon return to Canada, an application to import the unlicensed device was made to Health Canada through the MDSAP. A key consideration for the first cases was to select 'straight forward' patients with high likelihoods of success. Completion and submission of the form was supported by the department manager. Sufficient devices were requested in a single batch application to support three cases, including a small quantity of extra supplies. During the time the application was being processed by Health Canada, physician schedules were arranged and patients were prepared. After authorization had been received from Health Canada, the product was procured from the vendor.

Dr. Bonhoeffer travelled to Edmonton in July 2006 and performed the first three procedures with the two physicians. His on-site presence was considered important for the first cases. Patient follow-up was performed at the clinic as per standard procedures, as implantation of the Melody valve was considered a minimally invasive procedure. Additional cases followed (Coe and Taylor 2011). The Melody was licensed by Health Canada in December of that year.

Cross-case comparison of process elements

The sequence of events of each case followed a similar pattern, comprised of a succession of five general processes (Table 1). The first general process of *Technology Development* entailed three similar stages for both BVS and Melody, as each technology was designed and iteratively modified, tested in formal clinical trials, and licensed for sale in Europe.

The second general process of *Knowledge Transfer* was similar in some respects but differed in others as a result of the difference in magnitude of innovation of the respective medical devices. While physician education through presentation attendance and literature review was important in both cases, peer-to-

Table 2-1. Cross-case comparison of process elements

Process	Case 1. BVS	Case 2. Melody
1. Technology Development		
a. Design and manufacture	• Device/technique invention • Product modifications	• Device/technique invention • Product modifications
b. Evidence development	• Clinical trials	• Clinical trials
c. Conformity assessment	• CE marking	• CE marking
2. Knowledge Transfer		
a. Education	• Conference/presentation attendance • Published article review	• Conference/presentation attendance • Published article review • Peer-to-peer learning
b. Training		• Proctoring
3. Evaluation		
a. Clinical effectiveness assessment	• Technology approval	• Technology approval
b. Cost effectiveness assessment	• Budget approval	• Budget approval
4. Acquisition		
a. MDSAP application	• Health Canada authorization	• First case selections • Health Canada authorization
b. Procurement	• Device purchasing • Device use • Inventory management • Product expiry/return	• Device purchasing • Device use
c. Re-application	• Device re-order	• Device re-order
5. Patient Management		
a. Case readiness	• Case preparations	• Patient scheduling • Case review • Additional case selections
b. Patient care	• Emergency Intervention	• Scheduled intervention • Patient follow-up

peer learning was identified as an important element for the introduction of the highly innovative first-in-class Melody. Further, for the Melody, physician education was supplemented with personal training through proctoring.

The third general process of *Evaluation* had similar elements in the review of evidence of clinical and cost effectiveness and in budget approval by decision-makers within the hospital division. Costs for both were managed 'in-house' and there were no additional funds requested or received.

The role of the MDSAP first became evident during the fourth general process, *Acquisition,* as neither device was licensed by Health Canada. Minor differences in the application stage reflected the use case of the device. The BVS was requested in small batches to be kept on hand in case of emergency while the Melody was requested for known individuals. This resulted in more actively managed inventory at the procurement stage for the BVS. Both devices required re-application to Health Canada for use in additional patients until ultimately, in both cases, the devices were licensed.

The fifth general process of *Patient Management* had similar as well as different elements. For BVS, patients were managed in emergency settings as per established protocols, while for the Melody, new protocols were established and first case selection was an additional important consideration.

***How* was the MDSAP used?**

The sequence of events proceeded in linear fashion with occasional overlapping and iterative activities. One iterative relationship was between technology design and evidence development. While the device was designed and manufactured before it could be tested, subsequent modifications to the design were based upon the initial learnings from product use. An example of an overlap in processes occurred during Acquisition and Patient Management, where in the case of the Melody, detailed knowledge of the patients' clinical conditions formed part of the application to the MDSAP.

Each of the five general processes needed to occur for the medical device to be used in patient care. The first process (Technology Development) was *independent* of any other process, whereas the second and subsequent processes were all *dependent* upon completion of the prior process. The nature of the relationship among processes was one of contingency. They were non-causal.

The MDSAP was used to complete the process of Acquisition. Authorization from Health Canada was a required constituent element without which the device could not have been obtained. Functionally, the MDSAP was used in the introduction of innovative medical devices and in their repeated use until they were established.

Cross-case comparison of factors driving MDSAP use

Four factors can be identified from these case studies as driving use of the MDSAP (Table 2):

1. Change agents
2. Clinical need
3. Innovation
4. New evidence.

Table 2-2. Cross-case comparison of factors of MDSAP use.

Driving Force	Case 1. BVS	Case 2. Melody
1. Change Agents		
a. External	• Manufacturer/importer	• Developer
b. Internal	• Physician champions • Department/division	• Physician champions • Department/division
2. Clinical Need		
a. Indication	• Well-known, predictable, routine • Emergency setting	• Well-known, predictable, routine • Scheduled appointment
b. Patient outcomes (short-term)	• Improved over current	• Improved over current
c. Patient outcomes (long-term)	• Not known	• Not known
3. Innovation		
a. Device design	• Incremental change • Improved effectiveness	• First-in-class • Inferior effectiveness
b. Technique	• Similar to current	• Superior safety
c. Device costs	• Affordable (higher)	• Affordable (unknown change)
d. Maturity	• CE marked	• CE marked
4. New Evidence		
a. Sources and channels	• Clinical trials • Conferences/presentations • Peer-reviewed articles	• Clinical trials • Conferences/presentations • Peer-reviewed articles • Peer-to-peer learning • Proctoring
b. Strength	• Low uncertainty	• Low uncertainty

In both cases, persons external and internal to the hospital promoted adoption of the new technology. The main difference between the two cases was the pivotal role of the device developer in the Melody case. As the Melody was a first-in-class product and technique, the expertise and guidance provided by the developer was an important factor in its adoption. There was no equivalent external product champion for the BVS case. Internally, within the hospital setting, the change impetus came from two levels: the individual physician champions, and the divisional pro-innovation culture.

Ongoing clinical need was a second driving force of MDSAP use. In both cases, clinical indications for use were well-understood and medical interventions for the respective patient groups had already been established. Compared to current practice, use of the new devices was expected to be beneficial to patients over the near-term. Long-term outcomes were unknown but were not anticipated to be worse than current practice.

A third driving force was the innovation, itself. The technology behind each innovation was emerging. Each had obtained European CE-marking but neither was licensed in Canada. For the BVS, the innovation was an incremental design improvement to the device only, while for the Melody, the device *and* the technique were both new. In both cases, the devices were seen as innovations that would become the next standard of care. Neither of these devices were seen as 'one-off' uses; rare exceptions based on the unique clinical circumstances of a single patient. For the Melody, even though the device, itself, was less durable than the currently available option, the large reduction in harm to the patient afforded by the new technique was the driving force for adoption. Importantly, neither device was selected based on cost and budget impact was manageable.

A final driving force was the availability, communication, and level of quality of new evidence. In both cases, the conduct of formal clinical trials yielded evidence of sufficient strength for informed decision-making. While direct advertisement for sale of the unlicensed medical devices did not occur in Canada, the scientific evidence for each device was widely disseminated through medical education channels.

***Why* was the MDSAP used?**

The four forces collectively drove use of the MDSAP. Each single force was a necessary but insufficient factor on its own. Change agents, faced with ongoing clinical need, triggered the process of Technology Development. Once the innovation and the evidence were available, the change agents triggered the processes of Knowledge Transfer, Evaluation, and Acquisition, which enabled the provision of improved patient care. Without the innovation or evidence of its benefit, or knowledge of the ongoing clinical need, the change agents would not have triggered the processes in these cases. Therefore, it was the combination of all four factors that drove use of the MDSAP.

DISCUSSION

The MDSAP is used during the introduction of new health technologies in Canada. Its function is to enable procurement of non-accessible medical devices. In this setting, the distinguishing characteristic of MDSAP cases is the combined presence of expert practitioners, well-characterized clinical need, an emerging technology, and strong evidence of short-term incremental effectiveness. The goal of institutional cost reduction is not a driver of MDSAP use.

The two cases examined in this study pertained to the introduction of new technologies from within the cardiovascular discipline. In each case, long-term patient outcomes were considered, although data at the time of technology introduction were limited. Boudard (2013) investigated cardiovascular device innovations in France and argued that, as long-term data were not required for CE-marking, the safety and efficacy of these innovations were not known. Boudard recommended that, since it was not feasible to collect long-term data via randomized controlled trials, post-implementation observational studies be conducted instead for follow-up. Our recommendation for further study includes investigating cases from other disciplines known to regularly use the MDSAP, such as orthopedics or ophthalmology, as results from studies of cardiovascular devices may be different from results of devices in other fields.

Dutot (2017) examined the adoption of innovative medical devices in France and affirmed the primary role of hospitals in introducing new health technologies. While our 2-case study was situated in the Canadian hospital setting, we suggest that additional studies of MDSAP in non-hospital contexts are warranted as 'special access' programs differ from conventional licensing in their purpose and operational mechanism, and this has not yet been fully explored.

'Early access' or 'compassionate access' programs exist in many developed countries. In the United States and the European Union, there are mechanisms to allow this, as an important pathway for patients who have life-threatening conditions to have access to unlicensed devices (Tsuyuki et al. 2016). However, there is little in the literature that describes how such mechanisms actually function within the overall context of health technology adoption and rational technology management, especially within institutions. More has been elucidated with respect to special access to drugs, compared to medical devices (Balasubramaniam et al. 2016). The authors conclude that 'further research and periodic reviews are warranted to understand the contemporary and future regulatory trends in early access programs'.

As a regulatory policy instrument, Health Canada's MDSAP affects HTM in several ways. The program enables the replacement of existing technologies with emerging technologies. It impacts organizational processes in procurement. It allows the provision of best clinical practice. And it accelerates the introduction of change. Further studies that can quantify these impacts are needed.

STRENGTHS AND LIMITATIONS

This 2-case study had both strengths and limitations. Among the strengths was the first-hand knowledge of the internal processes that was had by the contributors and the level of detail available. The study limitations included its dependency upon re-call and memory and that the supporting documentation was limited. The conclusions reached from this study were derived from two cases, and may have been more robust with the investigation of additional cases.

CONCLUSION

The optimal management of health technologies requires an understanding of the impact of regulatory policies. In Canada, the MDSAP plays a procurement role in the introduction of new health technologies in hospital settings. Program use is driven by a combination of necessary factors. This results in an accelerated replacement of existing technology, organizational changes, and best clinical practice.

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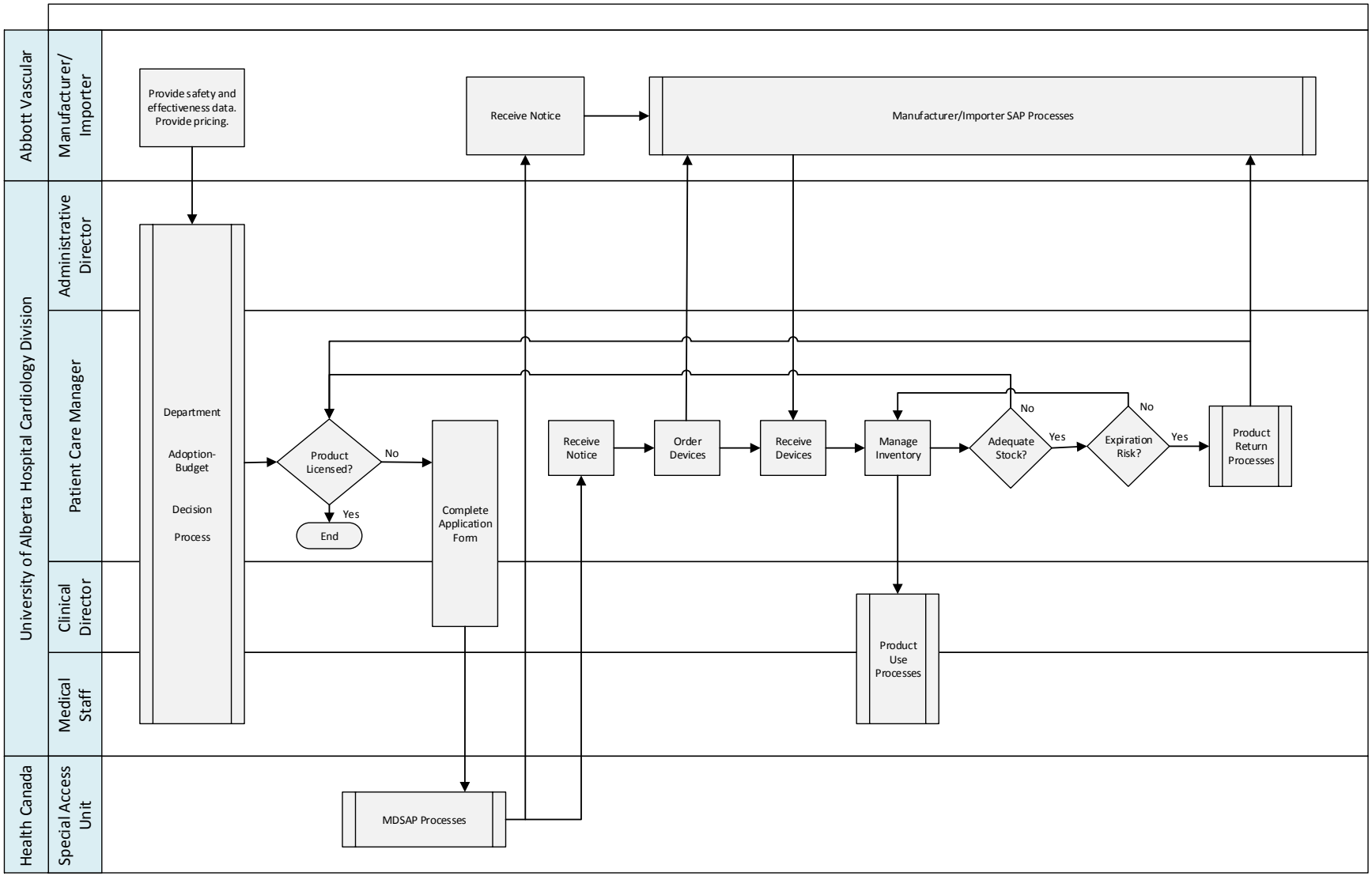
APPENDIX 2-1. Information collected for each case study

1. Actors
    a. Who made the request
    b. Who made decisions
    c. Who all was involved in executing the request (which departments, which staff)
    d. Who managed the process
    e. Other important information pertaining to Actors

2. Processes
    a. What the sequence of events was from point of request to initial use in a patient
    b. What the decision points were in the process
    c. What the time frame was
    d. What the sequence of events was in following up on the performance of the device
    e. Other important information pertaining to Processes

3. Technology
    a. Whether the request was routine or uncommon for the healthcare provider
    b. What device was requested
    c. Whether the device was an emerging technology, or well established
    d. What the unique feature of the device was that precluded use of a licensed alternative
    e. Whether individual or multiple requests were needed for individual or multiple components
    f. What the technique or procedure was for which the device was used
    g. Whether requests were made for on-hand stock (and therefore not a 'named patient' request)
    h. Other important information pertaining to Technology

4. Knowledge
    a. What the patient condition or clinical indication was that required/justified use of the technology
    b. What evidence sources about the technology were used (e.g. published literature, conference attendance, personal experience, vendor materials) by the decision-makers
    c. Whether there were factors, other than device-related features, that determined use of the unlicensed technology
    d. What type(s) of evidence was (were) provided on the application form
    e. How gaps in knowledge and uncertainty (risk) were managed
    f. Other important information pertaining to Knowledge



APPENDIX 2-2. Task flow diagram for BVS case

APPENDIX 2-3. Characteristics of Melody case

Activity	Actors	Information Needs	Decisions
1. Discovery	Physicians and their Peers	Technology; procedures; outcomes; complications	
2. Evaluation	Catheterization lab administrative leadership team	Clinical effectiveness; Cost effectiveness	Technology adoption
3. Proctoring	Developer Physicians	Specialized training and experience	
4. Patient selection	Physicians	Patient clinical information	First case identification
5. MDSAP application	Physicians Clinical managers	MDSAP criteria Form categories	
6. Application processing	Federal regulator	MDSAP criteria Form categories	Device importation/sale authorization
7. Procurement	Catheterization lab manager Procurement department	Product-related purchasing information	Device procurement
8. Patient scheduling	Clinical departments Developer	Schedule availability	Date of procedure
9. Case review	Physicians Developer	Patient clinical information	
10. Procedure performance	Physicians Developer	Direct personal guidance and feedback	
11. Patient care	Clinic	Patient health better/worse/same than before intervention	Patient follow-up

CHAPTER 3 Balancing Regulation, Innovation, and Care: Stakeholder Perspectives of Health Canada's Medical Devices Special Access Program

INTRODUCTION

The Special Access Program administered by Health Canada's Medical Devices Bureau (MDSAP) is a mechanism whereby healthcare professionals may apply for access to unlicensed technologies "for emergency use or if conventional therapies have failed, are unavailable, or are unsuitable" (Health Canada 2007). Several thousand applications are processed on an annual basis by Health Canada (Health Canada 2013, 2014). While the federal regulations are relatively clear, the contexts surrounding stakeholder use of the program are less understood.

The three key stakeholder groups of the MDSAP are the regulator (Health Canada), the medical device industry (manufacturers, importers), and the healthcare professionals requesting access to the devices (Government of Canada 1998). It is known from the arena of health technology assessment that perspectives among stakeholders can vary widely and that addressing these gaps is a key requirement for resolving important issues in decision making (Henshall and Schuller 2013).

The objective of this present study was to gain a deeper understanding of stakeholder perspectives of the MDSAP, with the underlying aim to advance policy and practice in health technology management in Canada. More specifically, it explored key stakeholder attitudes and opinions about MDSAP intent, scope, process, challenges and opportunities, and each other's roles and responsibilities,

METHODS

Approval for the study was obtained from the University of Alberta Research Ethics Board 2, and data were collected through key informant interviews. Interviewees were identified using a 'snowball' approach. Using existing relationships, each stakeholder group was contacted and solicited for interview candidates. Potential candidates were then contacted, provided with an overview of the study's purpose, and asked to participate in qualitative semi-structured interviews. During the interview, suggestions for additional contacts were requested; this continued until content saturation had been reached (i.e., no new ideas emerged). Interviews were conducted by email, telephone, and in-person, between December 2014 and November 2016.

Information was gathered under three broad headings: stakeholder roles and responsibilities, knowledge and information needs, and program utilization (see Appendix 3-1 for the detailed list). Open-ended questions were designed in advance (Dillman et al. 2014, p.128). Flexibility during the interview was allowed in order to capture concepts that may not have been anticipated and permit omission of

questions for which interviewees had no expert knowledge. Analogous to the 'pearl growing' technique used in literature searches (Ramer 2005), the interview questions evolved over the course of the study as learnings from the earliest interviews led to the design of expanded questions for later interviews. Telephone and in-person interviews were not recorded electronically, but notes were made and transcribed. Documents cited by the interviewees were retrieved and formed part of the interview responses.

Data were analyzed and synthesized using a thematic approach (Attride-Stirling 2001). Source information, categorized by stakeholder group, was entered into a common electronic table to facilitate identifying common themes and contrasting elements. Special emphasis was given to the more salient concepts as indicated by stakeholders.

RESULTS

Responses from eleven subject experts (three from the regulator, two from industry, and six healthcare professionals) were included in the analysis. Four common themes were expressed, for which there was broad agreement among stakeholders. Within each theme, however, unique elements that emerged reflected contextual roles and responsibilities. Additionally, there was some individual variation among group members.

Theme #1. *The MDSAP authorizes access to needed medical devices*
Stakeholders agreed that the MDSAP provides access to needed medical devices for emergency use, or when conventional therapies have failed or are unsuitable or unavailable. This includes access to custom-made products. A single device may be requested for a known patient, or a small batch may be requested to be kept on hand for emergency use. The decision whether to grant access depends in part upon the risk-benefit profile of the device.

Additional viewpoints from clinicians:

1. The processing time for applications varies; it may be quick or slow.
2. While batch requests are useful, the need for repeated applications for small quantities creates inefficient workflows.
3. The strength of the evidence for the device is situational: it may be limited, adequate, or strong.
4. The decision for authorization or refusal can appear arbitrary.
5. Unlicensed devices are more expensive as they must be purchased at list price; vendors are not permitted to negotiate lower prices. The healthcare system pays for the 'increased' costs.

Additional viewpoints from industry:

1. Industry is not a co-applicant so may not be aware that an application is being processed. A 'heads up' would allow industry to respond earlier and provide the device more quickly.
2. Industry has dual roles – gatekeeper and facilitator – and considers requests based upon appropriateness and readiness of device.
3. Stakeholder trust is built upon reputation of integrity.
4. Maintaining compliance in providing unlicensed products entails considerable 'behind-the-scenes' complexity.
5. Licensing is beneficial to industry as it allows advertising and sale.
6. One reason the MDSAP is needed is to provide access to niche items for which the economics cannot support licensing.

Additional viewpoints from the regulator:

1. Two processing streams exist: initial requests, and subsequent.
2. Processing speed is important and is publicly reported.
3. 24-hour urgent processing is available.
4. Information (in)completeness is a factor in turnaround.
5. Industry is not required to provide the device, or to provide it at no cost.
6. Health Canada may consider information from a variety of sources in making its authorization decision.
7. The MDSAP is not to be used to circumvent licensing.
8. Licensing fees help recover government costs. Manufacturers may be eligible for fee remission for 'small market' items.

Theme #2. *Physicians drive MDSAP demand in the interest of patient care*

All stakeholders agreed that physicians, in the interest of providing the best possible patient care, drive use of the MDSAP. Although industry provides technical information the first time a product is requested, industry's role is restricted in that it may not promote product access through the MDSAP or initiate the application process.

Additional viewpoints from clinicians:

1. Physicians learn of technological innovations through conference attendance, from peers, and from medical journals. Industry may be one additional source of information.
2. Patient care contexts vary tremendously and physicians use the single MDSAP for a variety of patient needs.
3. Physicians, as a group, have varied risk tolerances.

4. A physician may request a device from Health Canada, but the hospital may not have financial room to pay for it.

Additional viewpoints from industry:

1. Physicians that use the MDSAP are typically early adopters.
2. Not all physicians are aware of the MDSAP. Opportunities for optimal patient care may be lost when physicians are not aware.
3. Physicians protect patient information. Confidentiality enhances patient security (e.g. cybersecurity against 'hacked' devices).
4. Devices are personally owned by the physician, not the hospital.

Additional viewpoints from the regulator:

1. Any healthcare professional (HCP), not only a physician, licensed by their provincial body can apply.
2. The HCP should be highly knowledgeable about the device and not be reliant on industry.
3. HCP knowledge of specific cases is essential as medical devices obtained under MDSAP are not given the same level of scrutiny as devices obtained under licensing.
4. The importance of physicians obtaining informed consent in the MDSAP setting is reflected in the existence of a separate attestation section on the Application Form.
5. Hospitals should not include unlicensed devices in their published standards of care with the assumption that they will be available through the MDSAP.

Theme #3. *Global forces impact the Canadian MDSAP*
Stakeholders expressed the view that activities and events beyond Canada's borders directly and indirectly impact the design or use of the MDSAP.

Additional viewpoints from clinicians:

1. Clinical trials are conducted internationally, communicated globally, and provide evidence well before the novel device becomes licensed in Canada. This time lag is one driver of use of the MDSAP.
2. Patients may have no ability to participate in on-going international clinical trials.
3. The MDSAP is used for European (CE-marked) products until they are licensed in Canada.
4. Devices can update frequently and not all devices can be tested ethically.
5. While some devices are only minor updates, others are truly new and life-saving.

Additional viewpoints from industry:

1. Industry is aware when the critical mass of data needed to support product launch has been developed.
2. Global product cycles can be very short. Canada is not the only jurisdiction in which to launch innovations, and is not always the first.
3. Changing international regulations, e.g. in product labeling, may impact products destined for Canada.

Additional viewpoints from the regulator:

1. The MDSAP is not intended to be an early market access route. Investigational Trial Access (ITA) should be used for emerging technologies in Canada. ITA can be used for new 'off-label' indications for use.
2. Some medical devices requested through the MDSAP appear very similar to licensed alternatives. Incremental changes are not sufficient grounds for using MDSAP.
3. Periodic reviews are conducted for devices that have been made available under MDSAP for an extended period of time, e.g. over one year.
4. International regulations are carefully considered, e.g. Canada is a participant in the International Medical Device Regulators Forum, and there is considerable alignment.

Theme #4. *Improved health technology management is a priority need*
Currently, mandatory incident reporting, based upon awareness, applies to the HCP who received device authorization. Stakeholders agreed that an opportunity exists for the improved management of medical devices throughout the technology life cycle.

Additional viewpoints from clinicians:

1. Physicians are responsible for patient management – both before *and after* the device is licensed. Patient care extends beyond the 'sale' event. Post-use reporting of device effectiveness is important for ongoing patient care.
2. The physician that originally accessed the device may not be the physician responding to the subsequent adverse event. The patient may have relocated or otherwise changed physicians.
3. Considerable time may have elapsed since the device was authorized. In this situation, determining whether the incident is due to device failure or normal wear is subjective.
4. Discerning incident causality as device failure, or user error, can also be subjective.
5. Health Canada could and should provide ethics oversight for emerging technologies.
6. Health Canada could and should provide leadership in real-world data collection and dissemination after licensing.

Additional viewpoints from industry:

1. How a device is used is the practice of medicine, which is regulated by provincial colleges.
2. Vanessa's Law has been recently enacted and the regulations, now in development, may create changes to device reporting. (Note: Vanessa's Law amended the *Food and Drugs Act* and "improves Health Canada's ability to collect post-market safety information and take appropriate action when a serious health risk is identified" (Government of Canada 2014)).
3. Physicians have visibility on real-world data that no one else has and therefore have an opportunity to shape conversations.
4. The generation of long-term data prior to licensing is not feasible due to high costs, and may not be desirable as potentially beneficial products would be delayed from introduction.

Additional viewpoints from the regulator:

1. The MDSAP authorizes the importation and sale of devices; the *use of* devices after the sale is not regulated by the MDSAP.
2. If a medical device becomes licensed, the MDSAP no longer applies.
3. Voluntary feedback of device performance is encouraged.
4. Health Canada monitors international product recalls and other post-market information sources.
5. Health Canada cannot disclose confidential business information. However, Vanessa's Law and the upcoming regulations are modernizing the definition of disclosure.

DISCUSSION

Clinicians, industry, and the regulator hold common perspectives on the fundamentals of MDSAP design and function. Perspectives on the finer details of the program vary. These may represent opportunities for enhancing current practices or in shaping future policy discussions.

The MDSAP permits access to needed medical devices, and physician demand in the interest of patient care drives program use. Considering the rationale for the program's existence is to be an option for emergency access to healthcare technology, its promotion appears relatively muted. The recently released Guidance from Health Canada could be used to increase awareness among clinicians, health system administrators, and professional colleges on the appropriate use of the program (Health Canada 2016). The Guidance could also be used to enhance awareness regarding the ethics and unique risks associated with devices made available through the MDSAP. In hospitals, procurement and biomedical equipment departments may wish to explore the implications of personal ownership of medical devices by healthcare professionals (for example, in terms of asset management: inventory control, maintenance of personal property, recall notification) and whether their institutional policies and practices are optimally designed and managed.

Canada's MDSAP is impacted by the regulatory frameworks of other jurisdictions. Medical device licensing regulations in Europe have lower evidentiary requirements than their North American counterparts, although these are currently evolving (Tarricone et al. 2014). In the US, high premarket standards are viewed as a barrier to investment in new technology, and enhanced post-market surveillance has been proposed as an alternative for device evaluation (Califf et al. 2012). The effect on the Canadian landscape is increased MDSAP utilization, and this is unlikely to change in the near future. Alternative approaches to the current Canadian regulatory framework have been considered. In 2005, Health Canada proposed Progressive Licensing (known also as adaptive licensing), which advocated the use of a contextual risk-benefit assessment for product licensing during each stage of a technology's 'lifecycle' (clinical trials through post-market). Progressive Licensing failed to pass through parliament in 2008 and has not been revisited by government (Gibson and Lemmens 2015). However, researchers continue to deliberate this option. For example, Husereau et al. (2014) identified several key issues that must be addressed for adaptive licensing to be successful, including: stakeholder role clarity, legal implications, and costs.

The improved management of health technology remains a Canadian challenge. Medical devices, obtained through the MDSAP or otherwise, have characteristics that make their evaluation and use different from other health technologies such as drugs (Drummond et al. 2009). They have a user learning curve, are situated in dynamic organization-specific contexts, and evolve incrementally over time. This necessitates ongoing evaluations of clinical and cost-effectiveness. Recently, the Canadian Agency for Drugs and Technologies in Health (CADTH) proposed a new framework for the improved management of health technology, which if implemented, may be a means for the improved management of devices obtained through MDSAP (CADTH 2017). However, the effectiveness of this approach would still be dependent upon the timeliness and completeness of data collection and dissemination.

Currently, the management of medical device data is fragmented and improvements are desired. This is broadly acknowledged, but the way forward has yet to be determined. In 2013, a senate committee recommended against the establishment of a national medical device registry. Among the reasons cited were: Canada has rigorous pre-market evaluation requirements, medical device safety is a shared responsibility, patient privacy, and poor use of taxpayer dollars. It recommended a "comprehensive national integrated electronic health records system" as an alternative (Senate of Canada 2013). However, this decision did not consider that devices obtained through the MDSAP fall *outside of pre-market evaluations*, and that MDSAP device data is *restricted information, not shared*. An alternative, a more limited application of a registry, was not considered.

Greater transparency on devices accessed through the MDSAP could enhance health technology management in Canada. Disclosing device information would allow all health leaders to more fully and meaningfully participate in the responsible selection and management of these technologies. This can

only happen if industry and Health Canada design or enable a comprehensive communication channel. Oortwijn and der Wilt (2016), revisited the four-fold criteria for 'accountability for reasonableness,' (publicity, relevance, revisability, enforcement), and argued that these elements should all be present when evaluating health technologies. The enactment of Vanessa's Law fulfills each of these criteria to some degree, and Health Canada has recently (June 2017) initiated stakeholder consultations into medical device incident reporting, with the aim of increasing the quantity and quality of reporting and thereby enhancing the ability to detect safety problems. This is an important, although incremental, step forward. Additional deliberations among all stakeholders on the use of administrative databases, registries, and electronic records outside the 'incident' context are still needed.

STRENGTHS AND LIMITATIONS

This study is not an exhaustive presentation of all Canadian stakeholder views. Rather, its chief objective was to capture and communicate current themes and thereby stimulate further discussion.

CONCLUSION

The MDSAP balances regulation, innovation, and the delivery of care. Global forces and Canadian stakeholders shape the program's use. Health technology management's next steps should include initiatives that enhance the collection and dissemination of unlicensed medical device data.

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APPENDIX 3-1. Key Informant Interview Guide

Date	
Participants	

INTRODUCTION

(Present the points below in conversational style, do not read verbatim)

- Personal introduction of the interviewer
- Introduction of the present study as one of a number being conducted to build understanding of decision-making in the area of non-drug health technologies.
- The present study is focused on medical devices, in particular, the Medical Devices Special Access Program.
- A review of the literature is nearly complete, and suggests that the regulations surrounding the program are relatively well documented and understood. What is less well understood, however, are the perspectives that key stakeholders of the program hold.
- The key stakeholder groups of the MDSAP are principally the regulator (Health Canada), the medical device manufacturers, and the healthcare professionals requesting access to the devices.
- Owing to the different context in which each group is situated, each group is likely to perceive the program from a different perspective, and may therefore have unique insights into different aspects or areas of the program.
- The objective of the interview is to capture the perspectives of each stakeholder group
- Key stakeholders' willingness to share perspectives and possible experiences of the MDSAP are appreciated.
- Request permission to ask questions.
- Advise that the interview is not being recorded, and request permission to write notes

(Optional at end of the interview: advise that the notes will be typed and request permission to send back to interviewee for review)

QUESTIONS

1. STAKEHOLDER ROLES and RESPONSIBILITIES

The first set of questions is designed to explore perceptions around what the roles and responsibilities are for each stakeholder group – regulator, healthcare professional, and manufacturer – in the context of the MDSAP.

1.1 What do you see are the roles and responsibilities of Health Canada? What should the role be?

1.2 What do you see are the roles and responsibilities of the device manufacturer? What should the role be?

1.3 What do you see are the roles and responsibilities of the Healthcare professional? What should the role be?

1.4 'Transparency' is a term currently in vogue in healthcare, in industry as well as in government. Each stakeholder group holds information that the other group does not. What is your perspective on each stakeholder's responsibilities for protecting and disclosing information about medical devices obtained through Special Access? What should be protected? What should be publicly available? When?

1.5 The application form has a section called "undertaking", whereby the health care professional attests to inform the patient of the risks and benefits associated with the use of the unlicensed medical device. In your opinion, do healthcare professionals provide informed consent to their patients differently for licensed products than they do for SAP-obtained products? Is this a responsibility of the healthcare institution? How is this monitored, if at all? How is this enforced?

1.6 When it comes to device incident reporting, what is your perspective on each stakeholder's roles and responsibilities? What should the healthcare professional be expected or required to do? The healthcare institution? The manufacturer? The federal government?

1.7 I would like to get your perspective on the area of jurisdictional constraints. For example, the HC and PHAC 2014 Evaluation Report describes a review undertaken by Health Canada of its regulatory authorities whereby HC concluded that, "it does not have the authority to regulate the use of a device after its sale …". Can you think of any other examples of limitations of regulatory authority? (compelling manufacturers to proceed with licensing) (oversight of physician licensing/competency) (patient privacy legislation)

1.8 Do you feel the SAP (authorized use of an unlicensed technology) and off-label use (unauthorized use of a licensed technology) are distinctly different categories? What should each stakeholder's role and responsibility be in regards to off-label use of medical devices? Healthcare professional? Manufacturer? Health Canada? How does, or doesn't, Health Canada manage off-label use of medical devices when it does not have regulatory authority to do so?

1.9 Some emerging devices have a learning curve associated with their use. Whose responsibility is it to ensure this has been taken into consideration?

1.10 The HC and PHAC 2014 Evaluation Report notes that “HC does not derive its authority solely from legislation; indeed much of its role is through the exercise of the federal spending power.” Does this ‘role’ apply to SAP?

1.11 Is there anything else pertaining to Stakeholder Roles that you feel is important?

2. INFORMATION REQUIREMENTS

The next set of questions is designed to explore perceptions around information requirements.

2.1 To start off with, what kinds of information, and to what depth, does Health Canada require?

2.2 In relation to what you had just described as being Health Canada’s role, does that seem reasonable to you? Do you feel any of that information isn’t necessary? If yes, which? Do you feel some important information is being missed? If yes, like what?

2.3 I’d like to talk about the Medical Rationale section. Of the four or five questions that need to be answered, in your experience, how much or how long of an answer is given? Some of these could have entire books written on the subject; some of these might be given a simple “not applicable” answer. How comprehensive of an answer is usually provided, or does this vary from case to case, or by applicant? Can you explain?

2.4 Have the information requirements changed over time? If so, how?

2.5 What about information generated outside of Canada. How well accepted is it?

2.6 The HC and PHAC 2014 Evaluation Report identified an increased number of requests for additional information from Health Canada for the routine licensing submission review process. The reasons behind this were stated to be the “implementation of Good Review Practices (GRP) and increased scientific scrutiny of applications.” Has there been an increase in the amount of requests for additional information for SAP applications between 2003-2012? If yes, what kind of information is being requested?

2.7 Not everything can be known about how effective a medical device is. Some uncertainty will remain and this will create risk to the patient. By increasing evidence level requirements, products that would be of benefit could be denied. Conversely, with low evidence level requirements, products that could be more harmful than anticipated would be authorized. Is the balance currently ‘right’ in your opinion? Why or why not?

2.8 The HC and PHAC 2014 Evaluation Report identified combination products as an area of urgent concern. “Reported difficulties include inconsistent application of the criterion for classifying products; inappropriate classifications of some products as medical devices, which some internal key informants suggested may result in under-estimating their risks; and difficulties in completing reviews of combination products in a timely fashion.” There is also a difference in fee structure;

fees for drug submissions are “substantially higher.” The report recommended the development and implementation of policy and guidance relating to the review and licensing of combination products. In your opinion, do combination products pose unique challenges in gathering, providing or evaluating evidence?

2.9 What are the current challenges with device incident reporting?

2.10 The Medical Devices Regulations require the healthcare professional to report an incident with the device to Health Canada as well as the manufacturer. Some devices obtained via SAP can be in use for many years before any problems develop. In that time, patients may move and physicians may change. How is the healthcare professional supposed to keep track of this? What are the consequence for not reporting a device incident? How is this monitored? How is this enforced? What is your perspective on ‘failure of the device’ or ‘deterioration of its effectiveness’ in the context of the SAP? When these devices are placed in high-risk settings on ‘compassionate’ grounds, where patient outcomes are frequently poor, and the evidence on the device, the method of deployment, and the cohort of patients for which the device is suitable is all emerging – how does one attribute ‘failure’ or ‘deterioration’ to the device itself?

2.11 What are the opportunities with device incident reporting?

2.12 The HC and PHAC 2014 Evaluation Report suggested “enhancing collaboration with international regulators to collect and monitor safety information.” In the context of the SAP, do you feel this is advisable or feasible?

2.13 What are the challenges with long-term data collection, e.g. via device registry or patient registry?

2.14 What are the opportunities with long-term data collection?

2.15 Registration cards are required for implanted devices obtained via SAP. What are the challenges or opportunities with this system?

2.16 The Standing Senate Committee on Social Affairs, Science and Technology recommended that Bill S-202, An Act to establish and maintain a national registry of medical devices, not proceed. Reasons for this were:

1) Health Canada has the necessary authorities in place to adequately regulate medical devices,
2) Canada’s pre-market evaluation requirements are rigorous in comparison to other jurisdictions,
3) The safety of medical devices in Canada is a shared responsibility. Any requirements to provide patient information to a national registry goes beyond the federal role,
4) A registry containing names and addresses of patients would pose privacy concerns,
5) the cost to the taxpayer would outweigh the benefits

The committee recommended as an alternative the establishment of a comprehensive national integrated electronic health records system. What are your perspectives on Bill S-202 or the topic in general?

2.17 The HC and PHAC 2014 Evaluation Report suggested “implementing a public database of medical device problem reports”. In the context of the SAP, do you feel this is advisable or feasible?

2.18 Is there anything else pertaining to information requirements that you feel is important to mention?

3. UTILIZATION FACTOR

The next set of questions is designed to capture your perspective on what drives MDSAP use.

3.1 What do you feel drives use of the MDSAP?

3.2 John Webb (2010) wrote in his article on TAVI, “It is unlikely that we will see rigorous testing of all potential combinations of available surgical and transcatheter valve types, frames configurations, and sizes.” He seems to imply that the nature of some technologies is such that it is infeasible to meet licensing requirements. Do you feel that all technologies could realistically become licensed? Why or why not? If no, does this drive MDSAP use?

3.3 Thinking again about combination technologies, does the integration of different types of underlying technologies into the final product become a barrier to licensing?

3.4 Do highly complex products require different licensing strategies than very simple ones?

3.5 When thinking about industry, do you feel industry considers MDSAP as a market entry strategy?

3.6 Do you feel industry uses the MDSAP to circumvent licensing? Do you feel industry is perceived that way?

3.7 Do you feel any macro-environmental business drivers impact MDSAP use, such as:

- Changing Markets?
  - Emerging markets (such as China or India)
- Globalization?
  - Resources allocated to R & D; comparisons between countries
  - Location of manufacturing facilities; comparative advantage of nations
- Time compression?
  - Shortened product life cycles
  - Shortened development times
  - Decreased payback periods

3.8 Health Canada monitors and publicly reports ‘performance’ metrics. Do you feel application turnaround time impacts program use, either for or against? Do you have an example?

3.9 As discussed earlier, Health Canada has evidence requirements that inform the application decision. Do you feel the *amount* or *type* of evidence needed encourages or dissuades program use?

3.10 Do you feel the admissibility of foreign information is a factor?

3.11 Standard forms have been created and modified over the years, and more recently, Health Canada has piloted electronic submissions. Do you feel the application mechanism impacts program use? Does it impact program use for *batch requests*?

3.12 Health Canada has implemented a new cost recovery framework with the intention of increasing the efficiency of the submission review process for licensing. Do you feel the licensing fees impact SAP use?

3.13 Do you feel the way the regular *licensing route* operates has a bearing on SAP use? In what way?

3.14 Do you feel the way the *investigational trial access* route operates has a bearing on SAP use? Do you have an example?

3.15 What do you perceive to be the reasons that healthcare professionals have for using MDSAP? For example, is it for situations "where conventional therapies have failed, are not suitable, or are unavailable?"

3.16 Are there other contributing personal or institutional factors? Are there other pragmatic or contextual factors?

3.17 Is there anything else pertaining to Utilization Factors that you feel is important? (Probing questions, optional):

- For example, in the past *the media* has covered SAP use at various time and for various devices. This in turn appears to have created an increased level of discussion activity by the federal government. Have you had any experience with this?
- For example, the *Auditor General* has released reports that reviewed various programs within Health Canada, such as the SAP. Have these had indirect or direct influence on program utilization?
- What about the policies of other governments, most notably the US, or in the European Union. Do international policies indirectly or directly influence Canada's SAP program? (i.e. have a hegemonic effect)?
- What about the other SAP programs in Canada, e.g. the one for pharmaceuticals? Do discussions arising from the drug SAP program impact the medical device SAP program?

CONCLUSION

This thesis examined the relationship between HTM and Canada's MDSAP. The three studies investigated: the landscape of available information, two cases of use, and key stakeholder perspectives. Through qualitative content analysis, each study provided knowledge that informs components of the four major stages of the technology life cycle – *premarket, adoption, real-world use, and decommissioning* – thus supporting the optimal management of health technology.

The three themes from the first study were: the MDSAP as an arbiter in health technology selection, as a route of health technology procurement, and as a facilitator of health technology innovation. These themes suggested the MDSAP has roles in all four stages of the technology life cycle. By regulatory design, the MDSAP is frequently used in a premarket setting for technology adoption. Through the authorization of unlicensed innovations, the MDSAP impacts the premarket and adoption stages of health technologies. Data on the real-world use of the MDSAP was provided in the form of the medical device map, which suggested significant program utilization by the cardiovascular community. The MDSAP impact in decommissioning, while not extensively investigated, could be seen, as one example, in the case of breast implants. Although silicone breast implants had been removed from the market for a period of time, they were still regularly accessed due to MDSAP authorization.

Building on the first study, the second study examined two cases of MDSAP use. This study determined that the MDSAP had significant roles in the premarket adoption of important new technologies, and that after introduction, these technologies became 'routinized.' The second study also mapped contextual processes, determined the MDSAP had a direct impact in procurement, and identified real-world drivers of program use. Finally, in one of the cases examined, the MDSAP was shown to enable the decommissioning of legacy technology by providing access to a newer alternative.

Also building on the first study, the third study examined the unique perspectives of each key stakeholder group. The four themes expressed by stakeholders were: the MDSAP authorizes access to needed medical devices, physicians drive MDSAP demand in the interest of patient care, global forces impact the MDSAP, and the improved management of health technology is a priority need. Stakeholders described the role the MDSAP has in the premarket adoption of novel technologies, as well as its real-world use in accessing 'niche' items. The contrasting elements in stakeholder perspectives spoke to the real-world contexts and challenges in which each group must find their balance.

Further, the themes from the first and third study consistently align with each other and with the findings from the second study. Six examples follow. The themes of 'approval' and 'procurement' from the first study were echoed by the theme of 'authorized access' in the third study. The theme of 'procurement' from the first study was observed in the 'Acquisition' process in the two-case study. The theme of 'innovation' from the first study was supported in the finding that the MDSAP was used for the introduction

of new technologies in the second study. The concept of ‘learning curve’ noted in the first study, was observed in the role of the mentor/developer in the second case study. Physicians as a driving force was observed in the two case studies, and articulated by the stakeholders. Finally, the development/licensing maturity of the technology (the accessed device being CE-marked) was noted across all three studies.

However, not everything is yet understood about the MDSAP. These three studies were qualitative in nature, and as noted, additional value to HTM is likely to be gained from further quantitative assessments of the MDSAP’s impact. And, in the spirit of the lifecycle ethos of HTM, a future re-evaluation of the MDSAP will be warranted as the landscape of healthcare in Canada continues to evolve.

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