

**SUFFERING INDIVIDUALS AND THE SUSTAINABLE COLLECTIVE:
RARE DISEASE DRUG ACCESS AND CARE IN CANADA'S PUBLICLY FUNDED
HEALTH CARE SYSTEM**

by

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Abstract

This dissertation is about how public drug payers, pharmaceutical company representatives, policymakers/researchers, patients and families, and patient advocates make and manage meaning around controversial costly ‘orphan’ drugs for rare genetic disease in Canada.

Based on 18 months of multi-sited ethnographic fieldwork across Canada, I argue that practices around rare disease drug development and access have created two competing moral/ontological frames. When a drug costs hundreds of thousands to millions of dollars a year, some focus on relieving the ‘suffering individual’ no matter what the costs. Others focus on the importance of the ‘sustainable collective’ to protect the health care system. These individual/collective politics work to control the circulation and use of extremely expensive rare disease drugs within a publicly funded but fragmented health care system. These are framed by social actors as different versions of ‘Canadian values,’ which throws rare disease patients into the epicenter of a difficult politics of deservingness for social investments.

My analysis centers around the questions: 1) what do high drug prices *do*? 2) what are the different politics of care performed in rare disease drug access disputes? 3) how do practices around costly drugs affect and inflect the experience of being ‘rare’ for patients and families? Working at the intersections of medical anthropology and science and technology studies, I show how this individual/collective binary tension is situated in economic conditions of financialized pharmaceutical development and discourses of Canadian nation-making around the public/private tensions of the health care system.

The chapters in this dissertation juxtapose ethnography of ‘macro’ level negotiations and practices of rare disease drug resource allocation with the ‘micro’ level experiences of families

learning to live with and care for disease among emerging options for treatment. In doing so, I show that this suffering individual/sustainable collective binary works to separate patients from wider questions of collective concern vis-à-vis the health care system and the welfare state.

However, paying attention to the ways that the care needs of patients and families get simplified within these politics points to other possibilities for care in drug development and health system relationalities.

Lay Summary

This dissertation is about costly drugs for rare disease in Canada's publicly funded health care system. When drugs cost hundreds of thousands to millions of dollars a year, some focus on relieving the 'suffering individual' no matter what the costs. Others focus on the importance of the 'sustainable collective' to protect the health care system. I show how drug development and access practices create this individual/collective binary, forcing families to 'become' worthy sufferers deserving of resources. I juxtapose macro negotiations around rare disease policies by drug payers, policymakers/researchers, pharmaceutical companies, patient advocates and others, with the micro world of care practices enacted within families of children with rare disease to show how health resource allocation, care, and illness are always situated within political and economic contexts. This work urges a new politics of care for universal health care systems in an economy structured around inequality, trade-offs, and profit.

Preface

This dissertation is the original work Marlee McGuire, who identified and designed the research program independently, and conducted all of the research and data analysis and writing. This research was approved by the Research Ethics Board at the University of British Columbia, certificate number H14-03255. This research also draws upon data gathered as part of an earlier study, also approved by the Research Ethics Board at the University of British Columbia, certificate number H10-01512.

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List of Abbreviations

A4R	Accountability for Reasonableness
CADTH	Canadian Agency for Drugs and Technology in Health
CDEC	Canadian Drug Expert Committee
CDR	Common Drug Review
CEDAC	Canadian Expert Drug Advisory Committee
CEO	Chief Executive Officer
CIHR	Canadian Institutes of Health Research
CIHI	Canadian Institute of Health Information
CEO	Chief Executive Officer
CF	Cystic Fibrosis
CFHI	Canadian Foundation for Healthcare Improvement
CORD	Canadian Organization for Rare Disorders
CSF	Cerebrospinal fluid
DCE	Discrete Choice Experiment
DIN	Drug Identification Number
EBM	Evidence-Based Medicine
EMA	European Medicines Agency
EU	European Union
FDA	Food and Drug Administration (United States)
GAO	Government Accountability Office
GDP	Gross Domestic Product

HTA	Health Technology Assessment
IQ	Intelligence Quotient
MPS	Mucopolysaccharidosis
NDP	New Democratic Party
NOC	Notice of Compliance
ODA	Orphan Drug Act
PMPRB	Patented Medicines Pricing Review Board
R&D	Research and Development
RCT	Randomized controlled trial
SAP	Special Access Program
STS	Science & Technology Studies
QALY	Quality Adjusted Life Year
US	United States

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This dissertation is for my grandmothers, Huguette Lemay and Pauline Mongeau.

Chapter 1: Introduction

On a crisp spring morning in the prairie city of Saskatoon, delegates at the annual symposium held by the Canadian Agency for Drugs and Technology in Health (CADTH), Canada's main centralized health technology assessment (HTA) agency, piled into the convention center ballroom to watch the 2015 symposium's plenary panel. The Canadian flag and the flag of each province and territory were set up along the back edge of the stage. The display of nationalism looked regal—official and strong.

The plenary panel was titled 'Evidence of Value or Value of Evidence?' and panelists from Canada, Germany, Scotland, and the United States each reflected on the evolving world of evidence in their particular jurisdiction. While the issue of rare disease drugs was not *explicitly* in the panel title, everyone knew in advance that the panel was really *about* 'orphan' drugs for rare genetic diseases, which are extremely high cost with often very little solid evidence to support their reimbursement by the public health care system—at least using traditional decision-making standards. But the conditions these drugs treat are often severe, progressive, and life-limiting pediatric diseases, raising questions about Canada's somewhat fragmented commitment to universal health care for all and throwing the gaps in the health care system into relief.

Each panelist reflected on how both HTA drug review and health resource allocation are not hyper-rational processes at all, but instead are connected with the culture and structure of a particular country and their health care system. They all agreed that for rare disease drugs, if drug payers or decision-makers insisted on absolute certainty then no one would ever get treatment. But allocating resources responsibly is not simple, they all agreed. While sometimes patient input can help change the course of a funding decision, it remains hard to balance individual patient reports which can be "quite glowing about the medicines" to use the Scottish

delegate's words with clinical trial datasets that can indicate the exact opposite—uncertain outcomes, 'heroic' economic modeling assumptions, poor quality data, and with price tags of \$150,000 to \$950,000 per year and rising.

When asked to give closing statements, the Canadian delegate, Dr. Tony Fields, who at the time was chair of the agency's pan-Canadian Oncology Drug Review process, reflected:

I'd like to say something, it's a little interpretive or philosophical I don't know, but as we've discussed this evidence of value or value of evidence here, it reminds us how we in health technology assessment are working in that turbulent tension between the needs, wants, and aspirations of the individual and the needs, wants, and aspirations of the collective. This is one of the defining characteristics of human society in so many ways, and it behooves us to pause from time to time, as we struggle between the individual and the collective: are we managing to serve them both?

I looked around the packed convention center ballroom at this point, the lone anthropologist interloper (or so I assumed) surrounded by health technology assessment specialists but also public and private drug payers, pharmaceutical industry representatives, patients and patient advocacy group representatives, health economists, and clinicians, all listening carefully, some nodding their heads at this 'defining characteristic' of human society. As my fieldwork continued, I increasingly noticed how social actors made use of this individual/collective binary opposition to both make sense of rare disease and stake their claims about the future of rare disease drug access in Canada. The binary seemed to fit in to multiple goals across different groups of social actors. It emerged in my data as a concept that traveled across discourses of evidence, deservingness, advocacy, care, morality, and policymaking.

This dissertation is about how practices and disputes around rare disease and rare disease drug access in Canada draw upon the binary that Dr. Fields above references in his statement above: "*that turbulent tension between the needs, wants, and aspirations of the individual and the needs, wants, and aspirations of the collective.*" I examine the ways that this binary

opposition figures into Canadian nation-making practices across groups of ‘stakeholders’ who hold different visions of the Canadian health care system with respect to the relationships between the public health care system, new drugs and technologies, and the power of the private pharmaceutical industry to call the shots around resource allocation standards and principles. In the pages that follow, I will show how social actors articulate different versions of this individual/collective binary tension to build moral, scientific, and political cases to shape the world they want to see around them in a highly charged and high stakes politics of care. In doing so, they work to create two different ontological and moral realities through practices: one around a capital-driven discourse of the ‘suffering individual’ and one around a strategy of bureaucratic impartiality based around ‘the sustainable collective.’ I anchor analysis of these negotiations with the stories and lives of patients and families living with rare disease as new treatment options come into their lives, and the ways these individual/collective politics inflect the illness experience.

My aim in investigating this ethnographically in this dissertation is not to reify it, but rather to examine its production and use within porous social orders and practices. I will show how the way social actors work with this binary frequently refracts the issue of rare disease drug access into one of ‘suffering individuals’ and ‘the sustainable collective’ as a matter of different versions of Canadian ‘social values’ to try and channel and control social investments toward controversial drugs for ‘rare disease.’ These different moral absolutes figure into nation-making practices that inform health policy in a publicly funded but fragmented health care system. I juxtapose ethnographic material that analyzes what is at stake for social actors in these articulations with phenomenological material on the illness experience to show how these

pragmatic enactments to shape the health care system affect the illness experience, at the same time as the stories of patients and their families crack this conceptual binary apart.

Building from feminist traditions of ontological politics and multiplicity and the anthropology of care, at the heart of this dissertation are the questions: what do practices around high drug prices *do* to the relations they draw from and the relations they create? What are the different kinds of politics of care performed in rare disease drug access disputes? How do pragmatic enactments and practices at policy, government, industry, and advocacy levels affect and inflect the experience of being ‘rare’ for patients and their families?

Following the implementation of the 1983 Orphan Drug Act in the United States and similar rare disease drug incentivizing legislations worldwide (with Canada being an important exception as a high-income country that has not developed one), drugs for low prevalence conditions such as the rare genetic metabolic disorders that I will discuss in this dissertation started coming to market. They are called ‘orphan drugs’ because the diseases are considered orphans of the medical market, and companies need to be incentivized (with tax breaks and research grants and extended market protections) to ‘adopt’ them. However, orphan drugs are priced very high: between \$100,000 to \$950,000 per patient per year. Gene therapies for rare conditions are now entering the market, priced at over \$2 million. These drugs are indicated for a very small amount of patients, necessitating to a certain degree higher price points to recuperate a company’s investments in the development, listing, and marketing of a drug. However, there is a general concern among health systems experts that the prices have gone ‘too far’ and that lower thresholds for safety measures and a quicker bureaucratic process for ‘rare disease drugs’ are being taken advantage of by the pharmaceutical industry (Wellman-Labadie and Zhou 2010; Herder 2013; Hollis 2019). These prices force explicit conversations about the boundaries

between public health care systems and the pharmaceutical market as multiple versions of ‘solidarity’ and ‘care’ circulate across groups of social actors, and the tension between the individual good and the collective good deepens.

In 2005, ten years before the plenary panel referenced above, a rally was organized outside of a meeting of federal, provincial and territorial health ministers that in many ways kicked off what would become a major rare disease advocacy movement centering primarily on drug access. At the time, Durhane Wong-Rieger, President and CEO of the Canadian Organization for Rare Disorders (CORD) expressed to the media how shameful it is that Canada wouldn’t cover the costs when other countries, including the United States, England, Australia, and Argentina would. “Canadians with rare disorders are among the most neglected in terms of access to health care and treatment,” she proclaimed (The Guardian Charlottetown 2005). The issue is still not settled today, with frequently public and protracted access struggles when public drug plan managers hesitate to reimburse these controversial treatments.

In 2017, 45 percent of the new pharmaceutical treatments listed in Canada were drugs with an ‘orphan’ designation for rare diseases (PMPRB 2019), most of them for low prevalence genetic subdivisions of cancer. By 2022, worldwide orphan drug sales are forecast to total US \$209 billion and account for 21.4 percent of worldwide prescription sales (Hadjivasiliou 2017: 6). While there remain many genetic conditions considered rare in current prevalence measures for which there is no treatment, the orphan drug market is characterized by “steady and inexorable growth” (Hadjivasiliou 2017: 4). This growth is heralded by some as a success that indexes that the Orphan Drug Act should not be tampered with (US Institute of Medicine 2009; Celgene 2019; Cohen 2018; Yates 2019), but critiqued by others as a signal of the failure of incentivizing legislations to prevent exploitation and monopoly, indicating a need for the reform

of the Orphan Drug Act (Bagley et al 2018; Daniel et al 2016; Thomas and Caplan 2019; Simoens et al 2012). Patient and industry led movements to institute a similar set of incentivizing legislations and regulatory pathways in Canada have been met with a similar heterogeneity of response (see Clarke 2006; Herder 2013; Wellman-Labadie and Zhou 2010; McMillan and Campbell 2017; Rawson and Adams 2018).

What is and is not a rare disease depends on who you ask, and what definitions are in place in a jurisdiction as part of a formal rare disease and/or orphan drug policy. The United States operates on a definition of any condition that affects 1 in 200,000, whereas the European Union operates on a definition of 5 in 10,000. Canada has yet to adopt a firm definition of rare disease, or set a clearly delineated policy. This dissertation focuses on a very narrow ‘slice’ of conditions that get labelled within these politics as rare—those that have a biopharmaceutical therapy to treat them. However, there are an estimated 6000-8000 ‘rare’ diseases, only 6% of identified rare diseases have a pharmaceutical therapy to treat them (Boycott and Ardigó 2018). It is important to note that this estimated ‘6000-8000 rare diseases’ figure does political and economic work which tends to obscure the political-economic motivations behind such a figure. There is a distinction between the many genetic conditions that happen to be rare in prevalence and the highly debilitating rare genetic diseases of the metabolism that ‘orphan drugs’ target. Lumping all possible rare genetic conditions (many of which may be quite mild) in with these ‘orphan diseases’ has more to do with opening a market for treatments that must meet lower regulatory and reimbursement thresholds than it does with relieving suffering from devastating diseases, as I will return to in Chapter 5. However the ‘6000-8000 rare diseases’ figure is often utilized to urge more investment in and incentivization of rare disease drug development. This begs the question of whether systems should be formatted around finding therapies for all

identified rare genetic disorders, or, if in a profoundly unequal world with many unaddressed disparities in health status and access to basic health care, there are ‘bigger fish to fry’ so to speak (Bartfai and Lees 2013).

When rare disease drug development was considered inherently unprofitable, the rationale for providing special regulatory provisions and incentives was that companies needed to be encouraged to ‘adopt’ these orphans and participate in working toward the social good for all. Over the last two decades, however, rare disease ‘orphan drugs’ have become highly profitable. While pharmaceutical companies argue that high drug development costs make high prices necessary to ensure a return on investment, estimating actual drug development costs relative to revenues is challenging and augments the controversy around these drugs. Accurate information is not readily provided by drug manufacturers—as Morgan et al (2011: 11) note, any knowledge that the public has on drug development costs is based on the company’s word rather than auditable financial records, which makes it “impossible to assess validity and reliability.” Actual prices paid for drugs is considered ‘confidential business information’ and health care systems are not permitted by companies to make that information public.

One drug where enough information is publicly available to make a reliable estimate of profits is Vertex Pharmaceutical’s genetic mutation specific drugs for Cystic Fibrosis, ivacaftor (Kalydeco, which is priced at about \$350,000 per year) and a combination of ivacaftor and lumacaftor (Orkambi, priced at about \$300,000 per year). These drugs have posed a major challenge to health care systems as the high costs and low levels of evidence provided by the trial far exceed the general standard set by the health care system. Early development costs for these treatments were de-risked by a patient advocacy group, the Cystic Fibrosis Foundation, in exchange for royalty rights which they sold in 2013 for \$3.3 billion. Hollis (2019) analyzed

financial statements and expectations of profit based on the royalty right purchase and found that a conservative estimate of Vertex's combined profits on these two small market products, adjusted for research and development costs and discounts and contingencies, is \$21.1 billion. This level of profit, he writes, is "far higher than is needed to recover the costs of development ...[and] represents excess returns for shareholders of Vertex, rather than a reasonable payment for its investment." Hollis suggests that this excess in returns for shareholders is generalizable for most orphan drugs, noting the need "for a new strategy by payers facing high-priced drugs" (p. 77).

Concerns over reasonable profit margins is compounded by the growing interest in 'orphan drugs' by the pharmaceutical industry. What was once the domain of small innovative biotechnology companies with one or two orphan drugs in their portfolio or pipeline, now, large multinational pharmaceutical giants have invested in rare diseases. Many of those small innovative biotechnology companies have now been acquired by larger companies in multi-billion dollar mergers and acquisitions, and the pharmaceutical industry has increasingly shifted its focus toward these high priced 'niche busters' (Collier 2011; Bartfai and Lees 2013). While advocates for access to rare disease drugs were previously able to make 'drop in the bucket' arguments or say that the costs for rare diseases were a 'rounding error' in drug budgets, that is not so much the case anymore, and the orphan drug market is projected to almost double by 2024 (Waters and Urquhart 2019).

In this new expensive and highly profitable orphan drug era, a new set of meanings around rare disease has had to be generated to justify these high prices. In Canada, industry and advocacy enactments and practices have centered around positing rare genetic disease patients seeking drug care as special, vulnerable, and deserving of resources—but this framing often

occurs by juxtaposing rare genetic disease with other groups who may need or seek public resources as less special, less vulnerable, and less deserving. However, often, patients and their families do not only require drug care but other welfare state provisions for the ‘collective’ as well—their bodies used within a politics that renders their access to services more precarious.

Drawing on 18 months of multi-sited ethnographic fieldwork, this ethnography tacks between different sites of social action and care: a health policy unit invested in finding policy solutions for rare disease alongside conducting health technology assessments for the provincial government, the lives of families living with and caring for ‘rare’ disease, and conferences and meetings convened by different actors such as governments, patient advocates, and the pharmaceutical industry. In addition, I conducted 50 semi-structured interviews with different social actors invested in rare disease drug access in Canada. Interviewees included patients and families, patient advocates, public drug payers, and pharmaceutical company representatives.

My analysis thus juxtaposes two types of data: the performative and practice based dimensions of meaning making in action across ‘stakeholder groups’ and phenomenological accounts and narratives of diverse rare disease patients and families. Drawing these ‘macro’ and ‘micro’ levels of analysis together helps to break apart the moral absolutes that some rare disease ‘stakeholders’ traffic in, because it shows how powerful and universalizing articulations about either individual suffering or collective sustainability overlook the contexts in which people living with rare disease live—they may be suffering but they are also very much affected by issues of collective sustainability and the distribution of resources beyond those they receive for biologically active pharmaceutical care. This deepens the conversation about high prices beyond just costs to health care systems but costs to the health care and service system that rare disease

patients need and use, and the system of deservingness, value, and worth engendered by such astronomical prices.

Linking micro and macro also demonstrates how rare disease has become configured within Canadian nation-making practices. This takes on a particular tenor as Canada is considered to be one of the ‘cradles’ of evidence-based medicine and health technology assessment. The Canadian health care system is organized around the country’s split between federal and provincial/territorial responsibilities embedded in the constitution. The 1984 Canada Health Act established a system of transfer payments to provinces, and the criteria that provincial health care systems be publicly administered, universal, portable, accessible, and comprehensive (including hospital and physician services). Provincial and territorial health care systems combine these transfer payments with internal revenues from taxation and premiums to run their health care system. However, while the system is public and universal, it has been often described as “deep but narrow” (CFHI 2014), since it covers access to general physicians and clinical care. Anything outside of this basic coverage—like pharmaceuticals taken outside of the hospital setting—needs to be covered by private health insurance benefits (usually employer provided and thus dependent on stable employment), through limited public drug programs run by provinces and territories, or paid out of pocket. This public/private arrangement is one that has long been held in tension in Canada and that gets drawn out explicitly in rare disease drug access disputes. The ways that rare disease patients are configured within these discussions is highly variable depending on which version of ‘nation’ is being enacted and from which situated position. Turning to the micro-contexts of families’ lives, we see that the ‘rare disease patient’ is not a homogenous entity but rather a range of families with different situated attitudes towards life and disease and varying stakes in these different versions of ‘Canada.’

Decision-making about drug funding in Canada's provincial and territorial public drug plans is complex, involving multiple levels of government and institutions that analyze and manage both evidence and costs. The federal regulator, Health Canada, approves drugs for marketing in Canada but regulatory approval does not mean that drugs will be available through any provincial or territorial public drug program (which rely on health technology assessments done by independent agencies like CADTH to help make evidence-based decisions). The Patented Medicines Pricing Review Board (PMPRB) works to set the maximum allowable price that can be charged for any one drug in Canada. While the pharmaceutical industry and pharmaceutical lobby organizations try to dismantle these processes by mobilizing evocative appeals to how such a complex process prevents or delays 'suffering individuals' from accessing rare disease drugs, those who manage these institutions and processes mobilize equally evocative appeals about their necessity to ensure the sustainability of the collective, a dynamic that I analyze at length in Chapter 3.

Struggles to access resources for drugs priced far beyond the ability to pay out of pocket have led to creative deconstructions of the Canadian national image as a 'caring' state (Mackey 1999), but has also provided fuel for existing and ongoing discussions about whether Canada's health care system should be semi-privatized into a two-tier system, so that resources are left over for 'the most vulnerable' who need it. In my research, those framed as the most vulnerable and the most deserving by pharmaceutical industry and some patient advocacy actors are rare disease patients prescribed expensive drugs. The movement advocating for an orphan drug policy in Canada for rare diseases and 'special treatment' for rare disease drugs in reimbursement frameworks has intersected with a parallel movement to integrate pharmaceutical coverage into the Canadian health care system for *all*. Since 2015, the 'Pharmacare' movement

has gained increasing political momentum, which would integrate universal pharmaceutical coverage into the Canadian health care system. This is a political backdrop to many of the negotiations explored throughout this dissertation as both the rare disease pharmaceutical industry and rare disease patient advocates ponder what the implications for such a system will be on the allocation of public resources towards rare disease drugs.

The particular contours of the rhetorical and conceptual binary between suffering individuals and a sustainable collective as it operates in rare disease drug access disputes is thus located within contingent political and economic sets of relationships. This helps to contextualize the absence of a rare disease drug policy in Canada. Since health policy is deeply embedded in processes of nation-building and socio-political belonging in general (Porter 1999; Mulligan and Castañeda 2018; Brotherton 2008, 2012; Cooper 2015, 2019) and in Canada in particular (see Coletta 2018; Simpson et al 2017; Sinha 2013; Crites 2005; Abelson et al 2004; Romanow 2002; Kirby and LeBreton 2002; Evans 2003), rare disease drug access discussions are betwixt and between wider public/private disputes about the Canadian health care system, and which of these versions of care is more in keeping with varying constructions of ‘Canadian’ national identity.

When people invoke ‘Canadian values’ around health care access and resource allocation, sometimes they are talking about access to innovation and the triumph of the individual over disease no matter what the costs, and other times they are talking about everyone giving up a little bit in order for everyone else to also have access to care. While ‘evidence’ has long been held as the arbiter of what should and should not be funded, the evidentiary uncertainty of rare disease drugs weakens the power of this technical solution to keep the tension between these two orientations at bay. When potentially life altering drugs are extremely expensive, the tension gets thrown into relief, putting everyone involved in some uncomfortable positions and, as I’ll

explore throughout, augments the individual/collective binary that social actors draw upon to make sense of their social commitments and infuse their version of ‘care’ with a positive moral value. Rare disease drugs sit uncomfortably in between public and private tensions in the health care system: on the one hand those selling rare disease drugs need the welfare state to pay for treatments too prohibitive to pay out of pocket, but on the other hand they need a prevailing logic of the free flow of capital and the naturalization of the profit motive to be in place to accept these high prices.

In what follows, I review the relevant literature while providing a brief background of rare disease drugs and the context of their emergence in the pharmaceutical marketplace, the difficulties of assessing rare disease drugs within the rubrics of evidence-based medicine, and the challenges rare disease drugs present to health care systems both public and private. I then move on to provide an overview of health care and drug access in the Canadian context, followed by an overview of the dissertation.

1.1 Rare disease drugs and pharmaceutical capitalism: a situated marketplace

The history of the emergence of the rare disease category and incentivizing legislations for rare disease ‘orphan drugs’ helps to situate my analytical and topical focus in this dissertation. Ways of ‘doing rare disease’ have emerged out of the contradictions of pharmaceutical development modulated by particular industrial policies premised on a belief that the ‘free market’ will solve social problems. Rare disease drugs are substances developed in the context of what Kaushik Sunder Rajan (2006) calls ‘biocapital’, a configuration of capitalist practices around the life sciences that are locally adapted in different national and scientific contexts (see also Ong and Chen 2010). This configuration is one that depends upon promissory

logics (Fortun 2001; Petersen and Krisjansen 2015; Martin 2015), ideologies of salvation through unregulated and speculative biotechnology production (Cooper 2008), the constant identification of new disease categories and ‘unmet need’ (Dumit 2012), and the restructuring of nation-state systems to push these powerful substances through (Sunder Rajan 2017; Lakoff 2005; Petryna, Lakoff, and Kleinman 2008). Since the 1970s, the pharmaceutical and biotechnology industries have been increasingly financialized, which is to say that pharmaceutical development (and pricing) is not simply the choice of a CEO and a team but dependent on venture capitalists and shareholders who see new pharmaceuticals as a ‘high risk high reward’ domain and expect massive financial returns if a drug makes it to market (Cooper 2008; Kallmeyer and Canabou 2001; Glabau 2017; Sunder Rajan 2017).

The story of rare disease drugs (and of the rare disease category itself) begins not with financialized drug development necessarily, but with drug regulation. Drug regulation involves the review of clinical trial data for safety and efficacy by like the Food and Drug Administration (FDA) in the United States, the European Medicines Agency (EMA) in the European Union, and Health Canada in Canada. If the drug passes regulation, it is then permitted to be sold and prescribed. The regulator is responsible for ensuring that private interest and profit is not privileged over the safety of the patients who take therapeutic drugs.

Throughout the 1950s and early 1960s, over 10,000 babies worldwide were born with malformed limbs and other birth defects after the drug thalidomide was prescribed widely to pregnant woman to treat morning sickness (see Klausen and Parle 2015). This spurred discussions around the need for increased drug regulation, which culminated in the 1962 Kefauver-Harris agreements in the United States. This legislation required that all drugs developed after the passage of the 1938 US Food, Drug & Cosmetics Act have proof of safety

and efficacy in order to be prescribed and used. Since undertaking an expensive clinical trial program to test a drug in a small patient population didn't strike companies as economically viable, many manufacturers opted instead to just pull the drugs off the market. These drugs were then dubbed 'orphan' or 'homeless' drugs in the 1960s, and left the people who used them without the ability to purchase treatment in the United States (Provost 1968). Patient groups formed around this problem and lobbied the FDA through the late 1970s and early 1980s to do something about it, and, after gaining support from the US congress, regulators worked with them to craft a legislation to make it happen (see Huyard 2009).

The US Orphan Drug Act (ODA) was signed into US legislation in 1983. At its core it is an incentivizing industrial policy that provides tax breaks, research grants, extended market exclusivity, and lowered evidentiary hurdles to market entry to pharmaceutical companies willing to develop treatments that affect fewer than 1 in 200,000 people in the United States. As Huyard (2009) has examined, the category of 'rare disease' itself emerged around the development of this legislation as its flexibility as a category permitted patient groups and regulators to work together towards a policy to encourage research and development on already existing drugs that were used off-label (see also Asbury 1986). Over time, other jurisdictions followed the US's lead with respect to incentivizing and regulatory pathways for rare disease: Singapore in 1991, Japan in 1993, Australia in 1997, the European Union in 1999, Taiwan in 2000, and South Korea in 2003.

The ultimate decision to put a market solution in place to the problem of 'orphan diseases' was situated in the political ethos in the United States at the time (Mikami 2017). This was Ronald Reagan's America, and there was a firm belief in the free market economy and its ability to self-regulate profits towards the social good. Adele Clarke et al (2010: 51) also theorize

this to be a time of a historical shift in the culture of medicine in the United States: “beginning about 1985 ... the nature of medicalization itself began to change as technoscientific innovations and associated new social forms began to transform biomedicine from the inside out." This change, they suggest, was marked by “a shift from medicine exerting clinical and social control over particular conditions to an increasingly technoscientifically constituted biomedicine also capable of effecting the transformation of bodies and lives” (Clarke et al 2010: 55, see also Clarke 1995). They note how this shift from clinical and social control to a new ethos of transformation through discourses of innovation also led to the production of new social, cultural, economic, organizational and institutional forms to manage these emerging technoscientific relations.

Part of these new institutional practices included trying to set definitions to contain activity and fit new forms of technoscience in within existing social and political institutions and relationships. This was certainly the case for ‘orphan drugs’: throughout the 1980s, a series of proposed amendments to the ODA sought to clarify eligibility for orphan drug status. The original version of the ODA stipulated that in order to qualify, the manufacturer just needed to provide a statement on the ‘facts and circumstances’ that make the drug unprofitable. However, those in charge of granting the orphan drug designation had no way of validating claims: the price of the product and the research and development costs were considered commercial information and not provided (Mikami: 14). After a series of negotiations, a prevalence criteria was set at 1 in 200,000 people in the United States.

While pharmaceutical and biotechnology companies were initially suspicious of the ODA (as they were of any involvement of the Food and Drug Administration in their business interests), once they realized that the ODA allowed them to draw on public funds while still

pursuing their private commercial interests, they embraced it (Asbury 1986; Mikami 2017). Pharmaceutical companies (and their investors) came to realize that the ‘blockbuster’ era of drugs for large patient populations was waning as the patents on drugs for common conditions like high blood pressure started running out. Instead, they could focus on what are called ‘niche busters’—rare diseases where there is no other treatment available and where the prices could be hiked to astronomical levels while also receiving public subsidies (Collier 2011). While neglected diseases and ‘tropical’ diseases are also included as part of the ODA, it was the rare and chronic genetic diseases that were mostly picked up by manufacturers—these patients live everywhere, including wealthy contexts that can afford drugs, and require lifelong therapy. This signaled far greater profits over time, and drug development for tropical diseases of the poor remained ‘orphaned’ (Villa, Compagni, and Reich 2009).

As understandings of genetics increased, and the biological mechanisms and pathways of extremely low prevalence genetic metabolic diseases became better understood, small biotechnology companies in partnership with academic basic science laboratories began investigating treatments for some rare metabolic diseases like Fabry Disease, Gaucher Disease, and some variants of Mucopolysaccharidosis. Pharmaceutical pipelines slowly shifted away from drug development in areas of wide public health concern and focused on drugs for chronic, lifelong, and often rare diseases (Bartfai and Lees 2013).

When drugs produced through the ODA program started emerging on the market starting in the mid 1980s, many were priced at levels considered astronomical. As Caroline Asbury asked in 1985: “should orphan drugs be developed regardless of cost? If not, who will decide where to draw the line? In either case, who will pay?” (Asbury 1985: 198). In 1990, A US National Commission on Orphan Diseases expressed significant concern “with some companies making

‘exorbitant profits’ from designated orphan drugs” (quoted in Mikami 2017:17). A 1991 suggested amendment—to put caps on profitability at an upper limit of US\$200 million—was strongly opposed by the president of the Cystic Fibrosis Foundation, the CEO of the company Genzyme, (which had amassed US\$120 million for the drug aglucerase to treat Gaucher’s disease in just 10 months), and Republican Senator Orrin G. Hatch of Utah. This opposition proved successful and no cap on profitability was set.

This new era of ‘biomedicalization’ spurred new forms of what Michelle Murphy (2017) calls ‘the economization of life’: the rise of infrastructures of calculation aimed at determining the value of life as a guide to the national economy. The general increase in the price of prescription drugs, including those for rare diseases, prompted inquiries into the value of drugs by drug payers, and the folding of cost-effectiveness and economic concerns into a process called health technology assessment (HTA). HTAs are used by drug plan managers to decide which treatments or technologies to fund. As they emerged on the market, the evidence base for rare disease drugs came under increasing scrutiny when considered in relation to their high costs. Drugs with a rare disease/orphan designation are approved in jurisdictions like the US and the EU with a special regulatory pathway in place for rare disease on the basis of less evidence and shorter trials than is required for drugs that do not have that designation. They are also frequently approved using surrogate endpoints based on biomarkers that don’t really tell much about the disease but are easy to measure and quick to show change. This leads to issues when the evidence for these drugs is critiqued from within the epistemological framework of Evidence-Based Medicine (EBM) in the processes and practices of HTA.

I build on this political and economic context to show how rare disease drug access in Canada has come to be understood through a difference in values between ‘relief of the suffering

individual’ and ‘protection of the sustainable’ collective. Social actors have developed models and frameworks and tools to deal with the material, economic, and political contingencies at hand. These practices then create and instantiate this individual/collective binary opposition by making each version into an ontological reality, making it difficult to consider policy or system transformation options outside of it. In making this claim, I build on work by anthropologists of pharmaceuticals that shows how meanings around drugs vary across contexts (Whyte, Van der Geest and Hardon 2003) and the ideologies about health in place in any locale (Nichter and Vuckovic 1994). Anthropological work has also shown how pharmaceuticals are informed by the structures of expectation and value that get formulated around them (Hardon and Sanabria 2017; Sunder Rajan 2012; Rosengarten and Michael 2009; Stockdale 1999; Hedgecoe 2004), and the contours of the illness experience deeply shaped by the biopolitical and economic dynamics of access to treatments (Petryna 2011, 2013; Petryna and Kleinman 2006; Biehl and Petryna 2011). As such, this study is analytically grounded in the understanding that the meaning system that becomes attached to pharmaceuticals is inextricable from the surrounding social and political context—pharmaceuticals both shape and are shaped by social relations and political-economic interests and concerns.

1.2 Patient advocacy: situated biosociality

The anthropological concept of ‘biosociality’ (Rabinow 1996) foregrounds the ways that genetic diagnosis and the social become entangled together in contemporary identities and communities. This has been very much present in rare disease and the incentivization of drugs for rare disease, with patients assembling together sometimes according to specific rare diagnoses or as an ‘umbrella’ group of disorders unified by rarity. Biosocial groupings of patients with rare diseases have formed to shape policy and knowledge to drive demand for those

legislations and prompt increased investment around rare disease and rare disease drug development (Huyard 2009; Novas 2006, 2008). Savvy rare disease patient advocates work within existing political and epistemic formations in order to make their case, frequently making complex linkages with other networks of actors and epistemic traditions to do so (Rabeharisoa 2003, 2006; Callon and Rabeharisoa 2003, 2008; Rabeharisoa, Moreira, and Akrich 2014; Rabeharisoa et al 2014; Aymé, Kole, and Groft 2008; Heath, Rapp, and Taussig 2007).

Biosociality is frequently understood as reflecting the political and economic configurations in which biosocial groupings emerge. Novas (2006) has pointed to rare disease advocacy as a ‘political economy of hope’, turning patients into a form of ‘biovalue’ through the valuation of patient blood, tissue, and DNA on the economic market (Waldby 2002). In the process, patients gain the power to influence political and economic relations as well as the production of knowledge. However, working alongside pharmaceutical capitalism means that advocacy can sometimes mirror the relations of their industry partners. As Novas writes: “although the dynamics of these economies are novel, the use of market solutions to achieve social objectives is troubled by the problem that has beleaguered economic theory since the 18th Century: the market only offers its luxuries to those that can afford them” (Novas 2008: 151). The politics of patient advocacy in rare disease can reflect wider structural inequalities (see Buchbinder and Timmermans 2013; Timmermans and Buchbinder 2012; Novas 2006, 2008; Best 2012; Fisher 2009; Benjamin 2013), often reflecting and refracting the ongoing neoliberalization of contemporary health care rather than its transformation into a more egalitarian world. In the US context, frequently wealthy and well-positioned parent advocates deploy affect in order to garner social and economic capital, and redirect scarce public health resources to rare diseases (Buchbinder and Timmermans 2013).

In many ways, rare genetic disease advocacy mirrors the politics of advocacy networks of HIV and AIDS¹, where the common patient advocacy practice of yoking together epistemological and ethical claims gained currency. As Epstein (1995) writes: “it mattered that these communities contained (and were in fact represented by) white, middle-class men with a degree of political clout and fund-raising capacity unusual for an oppressed group” (415). In another context, Benton’s (2012; 2015) work on AIDS in Sierra Leone shows how flows of capital distributed using neoliberal logics of care are often behind the emergence of low-prevalence diseases as a ‘priority issue’ and of defining that group as suffering in “exceptional” ways in order to rationalize the directions to which capital is allocated. Her work deftly demonstrates how this can lead to scenarios where patients of these ‘special’ disease groups adopt these qualifiers, as it is through their specialness as a disease category that they can make claims upon state and non-governmental organization resources—but these enactments have impacts upon wider pre-existing inequalities in communities.

This becomes especially tricky in genetic disease and the promissory field of personalized medicine, where ‘disease categories’ are increasingly cast into subsets of identity based on genetic profiles, which can generate forms of genetic solidarity but also forms of exclusion (see Callon and Rabeharisoa 2003; Heath, Rapp, and Taussig 2007; Navon 2011). Ideas of solidarity become murky as the radical individualism of some formulations of genetics (Fox Keller 2002) fits well within Western economic and moral liberalism at the same time as it

¹ The two movements are linked in other ways: the drug AZT for HIV/AIDS was developed through an orphan drug designation pathway, and similarly priced at astronomical levels and with dubious safety data. See Arno et al 1995.

challenges its structures of governance (Prainsack 2018; Prainsack and Buyx 2017; Reardon 2005; Zeiler 2007; Dickenson 2013).

I position rare disease patient advocacy as a set of enactments that can satisfy multiple different motives and work across different ontological realities and social orders. Positioning rare disease as ‘special’ within the political economy of hope creates a channel through which rare disease patients make claims upon the state—as we will see from some of the case studies shared in this dissertation, that channel was and is desperately needed to get any attention at all. However, it is also a pathway that pharmaceutical industry actors pave through their (often indirect) marketing and market access work, in which logics are deployed that only through drug access can a person be brought within the category of full personhood and worth implied by citizenship and only by providing drug access can the inadequacies of the state be redressed (see Ecks 2006). This then gets used to justify the deregulation or reshaping of drug approval processes, enrolling ‘the patient voice’ in support of industry logics. These ‘entangled stakes’ around the possibilities of rare disease collective identity and the motives of pharmaceutical enactments is an interplay that will surface throughout this dissertation.

1.3 Evidence-Based Medicine: a situated practice

As early work on rare genetic disease drug development proceeded in the 1980s, so too did early work on the clinical movement of what is known as ‘Evidence-Based Medicine’ (EBM). In 1983, Dr. Gordon Guyatt joined the medical faculty of McMaster University in Hamilton, Ontario, where he reconnected with his former mentor Dr. David Sackett, considered one of the ‘fathers’ of clinical epidemiology. Along with colleagues at McMaster and around the world, they developed what was considered to be a scientific medicine. According to what is

called the ‘McMaster manifesto’ published in 1992, EBM "de-emphasizes intuition, unsystematic clinical experience, and pathophysiologic rationale as sufficient grounds for clinical decision-making, and stresses the examination of evidence from clinical research" (Guyatt et al 1992: 2420). EBM holds that all available evidence should be critically appraised to weed out ineffective or inefficient procedures and tests and only integrate those procedures that are seen to be effective across populations and studies.

EBM looks at evidence according to ‘grades’ or ‘levels’ of evidence. The highest level of evidence is considered to be the randomized controlled clinical trial (RCT). An RCT can take various forms, but the ‘gold standard’ of RCTs is the double-blind randomized study. In this model, trial participants are randomized to either the intervention group or the control group, and neither the investigator or the trial participant knows whether a patient is receiving a placebo or the study drug. This model is seen to minimize potential bias and confounding factors and variables—such as a participant’s emotional attachment to certain outcomes or an investigator’s emotional attachment to particular participants. In order to get statistically significant results from this model, the sample size must be carefully calculated. As Zhong (2009: 51) writes, “even the most rigorously executed study may fail to answer its research question if the sample size is too small.” A double-blind RCT for a common disease can have a calculated sample size of upwards of a thousand participants or more. In a rare disease drug clinical trial, a trialist is lucky if they have 100 eligible participants for an RCT, and frequently have as few as a dozen participants. Rare disease trials thus require different trial models and sample size calculations and formulas, and often have a limited menu of available validated outcome measures to use. This means that rare disease drug trials are frequently ‘graded’ lower on the evidence hierarchy. Cost-effectiveness in HTA processes then measure these lower levels of evidence against the

extremely high costs of rare disease drugs, and are rarely considered to be reimbursable on that basis.

Another issue is that rare genetic diseases tend to be highly heterogeneous, both genotypically and phenotypically. While a group of people may share a seemingly specific diagnosis of ‘Mucopolysaccharidosis Type II’, how the disease manifests in each of their bodies and the rate of disease progression will be very different from person to person. The pediatric geneticist Barton Childs, who worked closely with rare metabolic diseases in his medical career, has suggested that medicine requires ‘a new logic of disease’ based on the thinking of Archibald Garrod’s understanding of the “chemical individuality”. This calls for a rethinking of the logic of disease that places all patients with the same diagnosis into a ‘type’ and investigating the type rather than the individual (Childs 1999:15). Instead, the focus should be on “each unique human [as an] open system” adapting “uniquely to a unique pattern of environments and experiences” (Childs 1999: 31). This makes the solution seem so easy. To change metrics and standards *just* for rare disease and see them as individuals rather than as members of disease groups and populations seems like a simple answer to these dilemmas. That is indeed what many rare disease patient advocates request, and part of the basis on which some patient groups have formed as collectives engaging in “evidence-based activism” (Rabeharisoa, Moreira and Akrich 2014). But as I will explore in Chapter 5, the category of rare disease is ‘wily’ due to its embeddedness in market imperatives, making a separate evidentiary track for ‘rare’ disease tricky.

Even beyond cost and level of evidence, many of my research participants voiced substantial concerns about the quality and transparency of rare disease drug trial datasets—drug payers and HTA specialists sometimes find them to be sloppy and poorly conceived, with only

the best data released to regulatory and reimbursement agencies, and other less favourable data not made available for analysis. These concerns are not altogether different from concerns about drugs for common diseases—Miller et al (2019) found that only 25% of pharmaceutical companies engage in extensive data sharing of *all* clinical trial results—but when priced at such a high cost, public drug payers noted that they are far less willing to turn a blind eye.

In this study, I position evidence about rare disease drugs as a technical lens through which social actors negotiate other things—like ethics and fair pricing and differing values about the privatization of health care and the responsibilities of the pharmaceutical industry to public health system sustainability. Issues around rare disease drug access, this dissertation will show, are only *sort of* about evidence—the actual issues stem from much deeper concerns. Indeed, as CADTH, the organization invoked in the opening passage of this chapter and which has a large influence on health system resource allocation, note in its 2018-2021 strategic plan:

Even if they prove to be genuinely effective, the increasing array of new health technologies, such as niche drugs for treating cancers and rare diseases and the imminent launch of gene therapies, will carry a fearsome price tag. The challenge for decision-makers is not new, but the scale and the pace are unprecedented. ... The choice is stark: either sound public policy and evidence-based assessment will govern the adoption and deployment of existing and new technologies, or the forces of innovation and marketing will dominate health care decision-making and dictate the allocation of resources. The stakes are huge (CADTH 2018a: 2, emphasis added).

Even if the term ‘evidence-based’ still makes an appearance here, this passage makes fairly clear that things are no longer seen as an issue of evidence per se, but as a much larger existential issue about health care systems’ viability. Yet, many fetishize evidence in rare disease, believing that if the right evidence is found there will be no problem. Hoeyer (2019) has shown a similar dynamic in the Dutch context, where a lot of the frenzy surrounding personalized medicine centers around evidence and finding new technical solutions—if we find more evidence in new

and innovative ways such as centering on the individual, the problems of uncertainty and decision-making will be solved. This has spurred the proliferation of calls for intensified and personalized data sourcing, which Hoeyer has analyzed as a form of postponement: “promises of future evidence can be used to postpone action and sidestep uncomfortable knowledge in the present” (2019: 531). Postponement avoids discussions about how there may be no public health care systems left to pay for ‘personalized’ medicine in the future at all, leaving access to treatments and life prolonging technologies increasingly the domain of not just the privileged but the ultra-wealthy (as is already the case in many parts of the world for basic medicines, see Chan 2017).

The origins of the practice of EBM run deep. As Hacking (1990) traces, causal models of truth in place in early modern Europe were slowly replaced by probabilistic models in the enlightenment period, and over time statistics came to be considered the most legitimate form of evidence. European modes of truth searching shifted from a focus on understanding human nature to understanding the ‘normal’ uncoverable through numbers—and this conception of the normal became a powerful ideological tool. Theodore Porter (1996) shows how these forms of quantification came to be seen as moral, spurring political efforts to develop a “strategy of impersonality” (xi) to gain authority through claims of objectivity. However, Timothy Mitchell’s (2002) work shows that it would be a mistake to imagine that these logics sprung from the pure and rational minds of human beings. Rather, they were often developed in response to situations. In that way, EBM is primarily an epistemological system but it also reflects an ontological and ethical orientation toward the world, embedded in the suspicion of subjectivity and emotion in Western scientific practice. This particular form of objectivity is one that requires preventing bias by removing any attachments toward any particular individual (Daston and Galison 2007).

EBM is a major consideration in health resource allocation decision-making: not only does it not make sense to provide treatments that have not been shown to ‘work,’ it also helps to resolve the tension between pharmaceutical promise and health system pragmatics that I have invoked here. The removal of bias and attachment imbricated in EBM’s epistemological orientation to the world fits well within the utilitarian calculus of consequentialist oriented moral philosophy upon which modern public health care system policies are partly based: the maxim of making decisions so as to maximize utility for the greatest amount of people is premised on the ‘greatest’ good or happiness—which in this line of ethical thinking requires a certain degree of impartiality to the individual’s plight (Mill 1998 (1863), Bentham 1961(1789); Roberts and Reich 2002; Dolan 2001). While the utilitarian maxim of ‘the greatest amount of good for the greatest amount of people’ is focused on ‘happiness’ it looks at it in an abstract sense via consequentialist thinking—some people’s happiness will be forsaken for the *greater* happiness of the common good. This liberal orientation to ethics and the minimal economically inflected threshold for social responsibility embedded in the utilitarian calculus is the political counterpoint to capitalism’s focus on the individual which is strongly appealed to in pharmaceutical marketing (see Applbaum 2009).

Thus, rare disease drugs do not only run into tensions about clinical evidence, but EBM’s entanglement with an ethics of impartiality as well. In a small sample size—and media stories of a dying individual being denied treatment—the individual never entirely disappears. Throughout my research, my rare disease patient and family research participants as well as my pharmaceutical industry research participants countered this logic of impartiality by making tales of rare disease suffering prominently visible in the news media. Principle-based approaches to bioethics have tried to deal with these types of situations by balancing the principle of

beneficence to the individual and the principle to responsibly steward resources (see Beauchamp and Childress 1994). However, a number of ethnographic examples from the chapters that follow will show how difficult this is to apply in practice (see also Friedman 1989; Hann and Peckham 2010; Keeling and Bellefleur 2016). This tension between rules and cases and principles and care (see Bassett 1996) in many ways animates discussions of evidence in rare disease.

Rare disease thus sits uncomfortably within the structuring effects of what Foucault (1997 (1976)) calls biopolitics, a form of care and governance that is concerned with the maintenance of life as the function of government, and is “directed at populations rather than individuals” (Stevenson 2014: 3) which can, whether intended or not, enable particular forms of violence through its erasure of individual context and specificity (Stevenson 2014; Lochlann Jain 2013; Bell 2016). As Foucault (1997(1976): 245-247) writes: biopolitics “deals with the population, with the population as a political problem, as a problem that is at once scientific and political.” Rare disease patients do not slip easily into logics of a population in which constants are easy or possible to establish, and thus trouble existing ethical frameworks structured around evidence.

EBM has real structuring effects in health systems (Timmermans and Berg 2003). It also plays an integral role in keeping people safe from medical harm (Davis and Abraham 2013; Lexchin 2016). Rigorous scholarship has shown how softening standards for both regulation and drug access decision-making may be cloaked in a narrative of relieving patients’ suffering but often masks a nefarious move towards increasing profits for pharmaceutical companies (Graham 2008; Lexchin 2016; Davis and Abraham 2013). As Brives, Le Marcis, and Sanabria (2016: 371) note, EBM “can be traced back to the goal of democratizing access to health care and redressing inequalities” (see also Adams 2016). At the same time, EBM has been shown to be subject to its

own gaps and tensions, particularly with respect to the ‘gold standard’ of the randomized control trial (see Deaton and Cartwright 2018) and the necessity of standardizing bodies in order to make them fit the epistemic tools of a clinical trial (see Brives 2016; Timmermans and Berg 2003; Lampland and Star 2009; Bell 2016). This has been demonstrated particularly pointedly with respect to rare diseases (Collet et al 2014; Jaggumantri et al 2015; Jaggumantri, McKellin and Collet 2016).

The ambition of EBM to separate the technical from the political has been shown to not work quite so neatly in practice (Goldenberg 2006; Lochlann Jain 2013; Solomon 2015; Moreira 2012a), its pursuit often reflecting a situated sociality of the pursuit of authority in a “political and economic climate of declining trust and growing accountability” (Lambert 2006: 2633). Universal knowledge is seen as more legitimate and actionable than the messy, context-embedded, and situated knowledge of one individual (Lampland and Star 2009). This epistemological approach necessarily deals with populations, and in its focus on generalizations across that population can be mobilized in ways that overlook the complexity of people’s lives (Lochlann Jain 2013), enabling a form of policymaking and standard setting that approaches social life as “fixed and solvable” (Knight 2015: 9). This makes it difficult to find a way between the power-laden corporate and government logics of drug access in rare disease, which are both motivated by paces of care that can sometimes be at odds with the uneven temporality and complexity of the illness experience (McGuire 2019).

1.4 Rare disease drugs within health care systems

Technologies (including pharmaceuticals) are central to the transformation of health care systems—they constantly reassemble actors around new political and ethical questions generated

by technologies and their availabilities or restrictions (Lehoux 2006; Moreira 2012b; Kaufman 2015; Rapp 1999; Koenig 1988; del Vecchio Good 2001). It is within health care systems that social actors negotiate the relationship between the state who pays for technologies and the industries who develop them. In the process, technologies change therapeutic practice as well as bodies and lives in varying ways. Rare disease drugs have not seamlessly integrated into existing health care systems. Even in jurisdictions with specific ‘orphan drug’ or rare disease policy frameworks in place, affordability and access to rare disease drugs poses significant challenges (see Weerasooriya 2019).

A national orphan drug incentivization policy does not necessarily equal actual access to drugs for rare disease. For example, the US is often lauded for its orphan drug incentivization program, but access is not so simple. Rare disease patients in the US can qualify for state funded treatment through Medicaid programs, but this varies across states. Advocates report that eligibility criteria, restrictions, and cuts to funding to the limited state programs frequently threaten access (see NORD 2018). Patients may also access through private health insurance but accessing private health insurance in the US is a challenge, and co-pays for such expensive drugs can be extremely high. In 2010, the Affordable Care Act in the United States was implemented, preventing the denial of coverage to pre-existing conditions and the imposition of lifetime limits on drug costs per beneficiary, which are quickly reached with drugs that are so expensive. However, the act is in constant threat of being repealed by the current Republican administration (Mulligan and Castañeda 2018). Manufacturers tend to launch in the US first because the absence of drug pricing regulations enables high list prices that can then be used as a comparator price elsewhere. Even limited public Medicaid programs do not use cost-effectiveness measures to help with priority setting in coverage decision-making, largely due to political backlash about

rationing, limits, and suspicion of government intervention (see Neumann 2004). Instead, rationing is done in other less systematic ways, as detailed above.

Another set of challenges exist in the European Union, where a regulatory framework to incentivize drug development was put in place in 2000. In 2009, the European Union Council recommended that member states adopt national plans or strategies for access to rare disease by the end of 2013. As of 2018, only eight recognized formal plans were publicly identifiable (Khosla and Valdez 2018: 217). Khosla and Valdez (2018) report that seven countries in the Asia Pacific region and six countries in Latin America have rare disease plans/legislations/strategies, although these do not always include provisions for access to drugs as such. The literature from the European Union demonstrates that most member states report challenges to affordability and access (Zamora et al 2019; Szegedi et al 2018; Bourdoncle, Juillard-Condat, and Taboulet 2019; Malinowski et al 2018), with the European states of Germany, the United Kingdom, France, Italy, and Scandinavia having shorter timelines between market authorization and patient access than smaller and less wealthy states of Greece, Ireland, Bulgaria, Romania, and Croatia (Deticek, Locatelli and Kos 2018). In Brazil, the right to health enshrined in the Brazilian constitution has been judicialized by patients to access rare disease drugs (Biehl and Petryna 2011; Petryna 2011; Biehl and Petryna 2013; Gibbon and Aureliano 2018). Rare disease drugs pose a challenge everywhere, but the impact on public health overall is more acute in lower income contexts even with differential pricing where manufacturers charge lower prices in lower income countries.

Some jurisdictions have put ‘special’ processes in place to account for the specificities of rare disease in an effort to recalibrate traditional understandings of pharmaceutical value in the

area of rare disease drugs². I will provide two examples here. In the United Kingdom, a special health technology assessment process for ‘highly specialized technologies’ is in place for ‘very rare’ diseases but even with different criteria and cost-effectiveness thresholds, rare disease drugs are issued denials on the basis of their costs (Woon 2017). Alternatively, a ‘risk sharing’ agreement is required, where the manufacturer and the National Health Service share the costs of the drug until value is proven in post-market trials, but these can draw on forever. In Germany, there is no special evaluation committee or process for rare disease drugs but all drugs that meet the definition of ‘orphan drug’ under the European Commission regulation are considered an ‘added benefit’ if market authorization is received. However, this provision only applies to orphan drugs whose revenues have not exceeded 50 million euros in the past 12 months—once the drug’s revenues exceed this amount, the drug is reassessed through the same HTA process as all other drugs.

Overall, the prices of rare disease drugs combined with the difficulties of producing evidence in small heterogeneous patient populations conflict with the priority setting and cost-effectiveness mechanisms used by public health care system decision-makers to maximize resources. Orphan drug policies may facilitate the development and circulation of rare disease drugs and pharmaceutical capital, but they do not solve the more existential problems to actual access caused by high drug prices. However, the capacity to assert sovereignty in drug resource allocation decision-making is narrowing, because people’s lives are frequently on the line. As

² It is out of scope to review all of these processes here, but I refer interested readers to the comprehensive 2018 environmental scan of national and international approaches to health technology assessment and decision-making processes for rare disease produced by the Canadian Agency for Drugs and Technology in Health (CADTH 2018b): https://www.cadth.ca/sites/default/files/pdf/es0326_drugs_for_rare_diseases.pdf

summarized in a Biotechnology News article on rare disease pricing and the pushback by drug payers titled ‘Specialty Pricing: Worth Risking Payor³ Wrath’: “payors are forced to reimburse high prices or let patients suffer or even die” (Bellini 2015).

1.5 ‘*A mari usque ad mare*’? Health care in Canadian nation-making

Whether the health care system is public or private, the way that health care services and provisions are structured has been shown to be core to the process of nation-making (Porter 1999). I posit throughout this dissertation that this has been the case in Canada, with that nation-making taking shape around competing political goals and ideological practices that stretch back to the origins of the Canadian colonial state: one around Canada as a nation state run through the market system and the other through Canada as a nation state run through a rationalized technocracy (see Howell 1992). Rare disease drugs have represented a form of ‘breaking point’ to these different visions as they throw into question some of the dominant narratives of both of them.

Canada’s national motto, ‘*a mari usque ad mare*’—Latin for ‘from sea to sea’—is meant to tie together the 9.98 million square kilometers that form the nation-state, incorporating ten provinces and three territories bordering the Pacific ocean to the West, the Arctic ocean (and Alaska) to the North, the Atlantic ocean to the East, and the United States to the south. This vast territory is inhabited by a mere 37 million people, in comparison to the US population of 327.2 million. Confederated in 1867 (with British Columbia joining the ‘dominion’ to complete this sea to sea vision in 1871), the motto also attempts to tie together a Canadian ‘collective’ on a

³ Industry discourse frequently uses the spelling ‘payor’, referencing the legal spelling of a health care/insurance provider, although ‘payer’ is generally used by everyone else.

land upon which centuries of violent and ongoing settler-colonialism and Indigenous genocide is the basis upon which the nation-state of Canada was developed and the basis upon which it persists today. Large swathes of the land, particularly in the western regions of the country, remain unceded to the settler state. Elsewhere, treaties were signed, but the promises made by the Crown were not only not kept but replaced with a violent structural racism in the form of the 1857 ‘Gradual Civilization Act’ and the 1876 Indian Act which is still in place today.

Most of Canada’s settler population is concentrated in cities along the southern border, and a large part of the economy is predicated on natural resource extraction, an industrial and economic focus that is becoming increasingly untenable due to climate change as well as the entanglement between northern resource extraction and violence towards Indigenous peoples. The Canadian state has a long history of treating people unequally: proximity to the white Canadian settler identity, physical and mental fitness, and level of wealth will all result in different experiences of life in Canada (Razack 2002; Vowel 2016). Yet, the narrative around Canada as an inclusive and benevolent state is strong (see Mackey 1999; McCallum 2012), even though the terms for inclusion within it have been shown to be dependent on how particular categories of ‘citizens’ meet the economic conditions of capitalism (Howell 1992; Johnston 1993; Bonnet 2003; Blackburn 2003; Chen 2003; Lux and Dyck 2016).

Nation-making practices around the health care system shift depending on who is in power federally—either the right wing Conservatives or the centre right Liberals, and whether there is a minority or a majority government. While the Conservative party tends to err towards pushing privatization either through policy or merely through sheer neglect of the public system, the Liberal party has historically supported the public/private arrangement in place—which is that the health care system is publicly funded but privately delivered, with extended health care

private insurance (usually employer sponsored) filling in the gaps of what the system does not cover (vision, dental, and pharmaceuticals taken outside of hospitals). The more left of centre party, the New Democratic Party, sometimes exercises power through supporting a minority government but always wins seats in key communities and is generally the party that articulates broader visions of universal health care. The Green party is a more recent addition to Canadian politics. This party focuses quite strongly on the environment with sometimes unclear commitments to taxing high income Canadians that is required to expand and support the health care system. The current health care system in Canada, which lacks universal coverage for pharmaceutical, dental, and home care, reflects these differences in perspectives on whether health is a right of social citizenship or a private issue that individuals should be responsible for: a difference in values that has been a core tension in the building of different health care systems around the world (see Naylor 1992; Porter 1999).

Health care as nation-making in the Canadian context is also augmented by the constitutional division of federal and provincial responsibilities that structures the Canadian political system. The Canadian health care system in its origins and its current state reflect this decentralized model of power and jurisdiction, making a ‘national’ approach to any one health issue difficult. After World War II, when universal public health care was being developed across Europe, the federal government offered provinces federally paid health care costs if they agreed to a national health insurance plan, but constitutional disputes over taxation powers curtailed the effort.

While not willing to concede provincial power to the federal government, several provinces instituted—or attempted to institute—provincial health insurance systems over the 1940s and 1950s. Most notably, the province of Saskatchewan instituted a provincial hospital

insurance system under the leadership of the provincial NDP⁴ party led by then premier Tommy Douglas in 1947. Eventually, provinces agreed to accept federal money and federal conditions and the Hospital Insurance and Diagnostic Services Act was put in place in 1957, in which the federal government reimbursed 50% of hospital costs. Efforts to later include physician services was met with intense opposition, not just from Canadian doctor's associations but American ones, too—as Picard writes (2013: 30), “they feared such an idea could spread south of the border.” Nevertheless, Saskatchewan passed the Saskatchewan Medical Insurance Act in 1961 and in 1962, the act was amended to include physician services in its public insurance scheme in 1962. All the doctors in that province went on strike for 23 days. When the strike ended, the province allowed doctors to ‘opt out’ if they wanted to and developed a well-padded fee for service model to keep doctors happy.

Over the 1960s, political momentum for national universal health care increased, as did support for more general social programs and the development of a comprehensive welfare state. Other provinces followed Saskatchewan's lead and instituted provincial health care plans. It was with NDP support (at that time Douglas had moved to federal politics as leader of the federal NDP) that a Liberal minority federal government signed the Medical Care Act in 1966, despite strong opposition from Conservative (and the now defunct Social Credit party) politicians. The Act committed the federal government to funding 50% of provincial health care costs for hospital and physician services. However, the 1966 Act fell short of the robust and broad system that the NDP had pushed for. Hospital and physician services were covered but other pivotal

⁴ At the time, the name of the NDP was the Co-operative Commonwealth Foundation (Farmer-Labour-Socialist) which united with the union movement under the Canadian Labour Congress in 1961 to form the NDP party at both federal and provincial/territorial levels.

dimensions of health care—pharmaceutical coverage, dental coverage, home care, and vision care—were left out. Fiscal crises and recessions hit in the early 1970s—the post-war economic exuberance was over. In the mid 1970s, the federal government backed out of its 50% funding commitment and established a system of ‘block transfer payments’ basically leaving the provinces to largely fund their provincial systems themselves. User fees and extra billing of patients outside the public system became common.

In 1984 the federal Liberal government passed the Canada Health Act, which included a ‘reasonable access’ clause that imposed fines for imposing user fees and extra billing (though this was rarely enforced). In addition, the Canada Health Act instilled the basic ‘principles’ of the health care system that all provinces were bound to: the system was to be publicly administered, comprehensive, accessible, portable, and universal. Although coverage for pharmaceuticals taken outside hospitals was not mandated by the Canada Health Act, provincial and territorial governments all developed limited public drug programs to fill in the gaps left by inconsistent access to private drug insurance, i.e. for low income people and seniors and children. Shortly after the passage of the Canada Health Act, however, a Conservative government was elected, which imposed cost-containment measures and substantially clawed back the federal investments in provincial health care systems. A freeze on transfer payments to hospitals was implemented and cuts were made all across the board.

It was around this time that the ODA in the US was passed, but Canada did not get involved or enact any similar legislation. There was a compulsory licensing system for medicines in place at the time, so Canadian patients were not experiencing the same issues as US patients with regards to their drugs being pulled off the market. In fact, US patients imported drugs for their rare conditions from Canada. However, in the mid-late 1980s, at the height of the Cold War

and a political climate of suspicion of ‘socialism,’ Canada also entered into free trade discussions with the United States. These negotiations led to a massive reformatting of the Canadian Patent Act through which many pharmaceuticals were copied through compulsory licensing agreements to keep costs down. Rare disease drug access issues only became an issue in Canada when the compulsory licensing scheme was scrapped in 1991, and when new drugs for rare diseases began to be developed—no longer simple chemical formulations but expensive biologics, notably the first in class enzyme replacement therapies for Gaucher Disease (a condition that largely affects white men). At first, public drug plans didn’t place too much scrutiny on these drugs—they were seen as a one off, worth the price for innovation and for the benefit they brought to the handful of patients who needed them. Many expanded their limited drug programs to include those with ‘catastrophic drug costs’ as a beneficiary of public plans.

Around this time, HTA became widely practiced by public drug plans and hospitals to decide what to place on their formularies as new drugs increasingly came to market. The organization that would later become CADTH—the Canadian Coordinating Office for Health Technology Assessment—was formed. As expensive rare disease drugs increasingly came to market in the early 2000s, they were put through the same HTA processes as common conditions, leading to the advocacy movement referenced above who strongly protested cost-effectiveness formulas applied to rare disease drugs—using those benchmarks, rare disease drugs would never be funded by public programs. The Canadian public health care system—still in frequent dispute within divergent practices of nation-making and frenzy over the ‘specter of socialism’ that came with Cold War politics and allyship with the United States, was not well equipped to really figure this out in any coherent way.

Meanwhile, the human genome was mapped, single gene disorders relatively easily targeted by therapy were identified (Jimenez-Sanchez, Childs, and Valle 2001), orphan drug development pipelines became the new focus of the pharmaceutical industry, and patients who faced barriers to accessing rare disease drugs in Canada allied with the companies developing them. People with common diseases or relatively basic health care needs—so long as they were white, able-bodied, urban-dwelling, and upper/middle-class people—settled into a public universal system that was more or less equipped to manage their needs. The health care system, despite its gaps, became a point of national pride particularly in relation to the closest ‘neighbour to the south’, the United States, where the major inequities in access to even basic care despite the high-income status of the country made Canada’s own gaps in coverage look pretty good (see Lasser, Himmelstein, and Woolhandler 2006).

As far back as the 1930s, public opinion in Canada was strongly in support of some sort of public health insurance scheme (Tuohy 1999), but what the history of the Canadian health care system makes clear is that the health care system depended upon the support of political elites to push it through despite opposition from politicians who viewed public health care as ‘socialist’ and encouraging poor quality (see Taylor 1989; Brown and Taylor 2012). However, the absence of universal pharmaceutical coverage in the Canadian system remains a source of profound inequalities in health outcomes (Persaud et al 1999). In the 2002 ‘Romanow Report’ to the Royal Commission on the Future of Health Care in Canada, the commissioner Roy Romanow noted that Canadians strongly value the universal health care system and also recommended that Canadians be protected against high drug costs. The current Liberal government has committed to building a universal Pharmacare program into the health care

system but the specifics are still unclear and pushback from the Conservative opposition is fierce.

Where rare disease drugs fit into universal Pharmacare is unclear. This is a very tender spot for rare disease patients, who fear that a stronger and more universalized pharmaceutical system will dissuade pharmaceutical companies from bringing their drugs to the Canadian market. Subtle threats that the Canadian market will be abandoned altogether if stronger drug pricing regulations are passed heighten the worry (see Ernst & Young 2019). Throughout this dissertation, and particularly in Chapters 3 and 5, I share examples of how pharmaceutical enactments subtly push privatization of the health care system or at least a push against its further universalization—lest suffering rare disease patients be left behind in favour of the wider collective. Some even suggest that the health care system be semi-privatized to a two-tier model so that public resources can go toward expensive drugs, with others left to fend for themselves.

This factors into more explicit nation-making practices in federal politics as well. In the lead up to the recent 2019 federal election, the Conservative party strongly hinted that they would scrap recent efforts toward Pharmacare and recent initiatives to strengthen Canadian drug pricing regulations. The President and CEO of the Canadian Organization for Rare Disorders publicly endorsed the Conservatives in the election, as the only party that ‘listens to patients’ and as the best party for patients with rare diseases (Wong-Rieger 2019). I mention this here to show how rare disease drug access and care has become embroiled in these individual/collective nation-making politics around the health care system, emerging, at least in some patient advocacy enactments, as being against the further universalization of the health care system—largely because nothing prevents the pharmaceutical industry from abandoning the Canadian market altogether if they do not like its health policies.

Rare disease has thus become caught within two different versions of ‘Canadian values,’ two separate directions in what Taylor-Alexander (2017) calls biomedical nationalism. These are two different modes of nation-making, both intimately tied up in ideas of who deserves care but also different relationships with the corporate side of health care. Is a person seen as inherently worthy? Or do they have to become worthy through certain actions and practices considered ‘good’ by the state? Or alternatively: are only the most suffering and most poor worthy of state resources, while everyone is lumped as having the capacity to fend for themselves? If that’s the case, who decides who is who? We will see throughout my analysis how ‘Canadian values’ can be mobilized in multiple ways: either to affirm egalitarian approaches and the idea of health care for all but with limits based on cost, or to parse populations into classes of deservingness based on their perceived level of suffering classified within constantly shifting and materially located definitions of ‘rarity.’ In the process, people with rare disease desiring high cost drugs—and whose stakes are trickily entangled with the pharmaceutical industry’s—become configured as members of the wider Canadian ‘collective’ in different ways, affecting not only access to resources but affects of deservingness and social belonging as well.

1.6 Overview of dissertation

Chapter Two is split into two parts. In the first part, I situate how I approach my data analytically. I then describe my fieldsites and methods in more detail.

In Chapter Three, I examine the ‘social life of pharmaceuticals’ (Whyte, van der Geest and Hardon 2003) by tracking how rare disease drugs travel through the ‘life cycle’ from pre-clinical research through clinical trials, and into the Canadian health care system. In the process, the range of Canadian institutions, processes, and social actors that all work to imbue rare

disease with particular but often divergent moral and financial values are introduced. I argue that one way of understanding this individual/collective tension is the way that rare disease drugs wildly shift ontological registers between development (which can focus meaning making on the relief of individual suffering) and reimbursement (which shifts the register of meaning of a rare disease drug to the implications to the collective in reimbursing such expensive drugs).

In Chapter Four, I share three case studies of patients with different types of an ultra-rare genetic disorder called Mucopolysaccharidosis and their families. These stories show how life with rare disease (and life in Canada) is different dependent on where one fits within flows of pharmaceutical capital, social positioning within wider spheres of inequality, and attachments to prolonging life at all costs. They also each show the everyday contexts of caring for disease, ones that exist in sharp juxtaposition to the politicized negotiations that take place around rare disease.

In Chapter Five, I look at how the category of rare disease gets used differently across groups of social actors in attempts to ascribe both formal and informal definitions to it. I theorize it as a ‘wily’ category, one that expands and contracts according to the pragmatic needs that social actors invest in it. I look at rare disease as a matter of prevalence, rare disease as a matter of wide public health concern, and rare disease as a matter of deservingness over other groups. The individual/collective tension changes shape around each of these enactments, demonstrating the rearrangement of political, social, and material relations that different definitions of rare disease set in motion.

In Chapter Six, I share the story of a patient with Mucopolysaccharidosis Type II and his family (particularly his mother) as they move through three different rare disease treatment modalities, struggles, and hopes: intravenous enzyme replacement therapy as standard of care, intrathecal enzyme replacement therapy as part of a clinical trial, and gene therapy as part of a

promissory narrative that up to now still has not materialized. The intensity of access struggles and the experience of being ‘rare’ fade in and out over time. As this patient, soon to be 17, ages out of the ‘dying child’ category around which much rare disease drug development and access discourse is centered, questions and intensities shift for the family.

Chapter Seven focuses on the health policy unit where I conducted part of my ethnographic fieldwork for this study. I describe two ‘citizens’ juries’ on social values in health resource allocation that they held, that focused squarely on eliciting values as to whether or not the ‘public’ supports resource allocation towards expensive rare disease drugs and under which parameters and under what circumstances. Focusing on the planning and development of the citizens’ juries by the health policy unit, I show how they worked hard to calibrate the citizens’ jury concept and the logic of ‘social values’ to develop a different ontology of the ‘collective’ in which rare disease ‘fits’.

This dissertation concludes with Chapter Eight, where I summarize the main themes that emerge in this study and their scholarly contributions, as well as reflect on the lessons that we can learn from rare disease drug access politics as the promissory era of ‘personalized medicine’ moves into view.

Chapter 2: Analytical and Methodological Framework

This chapter has two parts. In the first part, I share the analytical framework that I have used for thinking through the relationships and dilemmas introduced in Chapter 1, situating my work at the intersections of medical anthropology and feminist sciences and technology studies (STS). In the second part, I share the methodological framework that I employed for this dissertation.

2.1 Analytical Framework

The relationship between the individual and the collective is a longstanding object of anthropological and sociological analysis and moral philosophy. What binds individual persons to the social order? In social contract theory, which both utilitarian and deontological thinking draw upon, it is through tacit acceptance of the social contract that an individual becomes a part of the whole, granting the ruler legitimacy to make decisions on behalf of the collective (see Friend 2004). Emile Durkheim (1893) had a dualist understanding of individuals and collectives, in which individuals cohere into different forms of collective solidarity in different types of societies. In small scale societies where individuals are relatively homogenous and connected through kinship ties, people exhibit *mechanical* solidarity—people feel connected to one another. In more complex and industrialized societies, *organic* solidarity occurs through interdependence. Across differences in tasks, values, and interests, social cohesion happens because different sectors and people locked within the ‘division of labour’ need one another in order to function. Marcel Mauss aimed to reunite the individual and the collective which were separated into individual and collective consciousness in Durkheim’s philosophy. For Mauss (2011 [1925]), the individual and the collective exist in a dialectical and connected relationship, where the connection is less about representations than it is about rules and structures, often through

exchange, that bind people into relationships. Many other scholars have explored this line of questioning as well.

In this dissertation my goal is not to produce a totalizing analytical scheme of how individuals and collectives are related, or a universal theory of how representations become shared between individuals and collectives. Rather, my analytical approach is grounded in showing how the relationship between the individual and the collective is situationally constructed as a form of worldbuilding and nation-making, offering a new way of understanding how the value of treatments are negotiated through the tension between the individual and the collective good. This is achieved through pragmatic enactments and practices that structure and channel resource allocation and access to care. Social actors enact different versions of the individual/collective relationship to shape the moral and structural contours and responsibilities of the health care system by building practices, models, and frameworks around these different versions. These different versions articulate different modulations of the responsibility of different sectors to address problems, and the particulars of how rare disease drugs should be (or should not be) folded into the health care system. They also play with rare disease drugs' 'fluidity'—the way they travel through systems and are understood to 'work' in different contexts and bodies (see de Laet and Mol 2000; Hardon and Sanabria 2017). The categories we use to make sense of social processes—in this case, the 'turbulent tension' between the needs, wants, and aspirations of the individual and the needs, wants, and aspirations of the collective' invoked in the introductory chapter—are products of (and productive of) politics and material relations.

As Sunder Rajan (2012: 23) has noted, the anthropological task in studying the intersection between the life sciences and capitalism is to develop forms of inquiry that can best

make sense of this emergent form of social, political, and bodily ordering and how it is restructuring both health care systems and life with disease. In keeping with this, my analytical framework outlined below will describe how multiple positionalities exist in this social world, and this multiplicity enacts social processes and politics that flow through persons within pragmatic contexts and struggles to access resources in a politics around what it means to ‘care.’

2.1.1 Multiplicity and ontological politics

On the ‘macro’ level of negotiating the place of rare disease drugs within the Canadian health care system, this dissertation is concerned with how social actors put matter into motion through enactments and practices. A focus on practices is not about comparing groups or tabulating perspectives or finding the ‘truth’ of rare disease or of bodies so much as it is looking at how social actors enact different versions of rare disease care and different versions of the moral contours of resource allocation. I draw from Annemarie Mol’s (1999, 2002) framework of multiplicity and ontological politics, in which social orders become realities through practices enacted around them. As Mol (2002: 5) writes:

If practices are foregrounded there is no longer a single passive object in the middle, waiting to be seen from the point of view of seemingly endless series of perspectives. Instead, objects come into being—and disappear—with the practices with which they are manipulated. And since the object of manipulation tends to differ from one practice to another, reality multiplies.

This approach looks at practices differently than what is commonly called ‘practice theory’ in anthropology and sociology, in that my focus is not on how dispositions and representations are embodied and passed along. Instead, it is about how practices create different realities enacted through those practices, each informed by situated knowledges (Haraway 1988) and relations between them. As Yates-Doerr (2017: 145) writes, “a tenet of the practice-centered approach is

that the world is not ‘out there,’ but that worlds materialize through practices.” An acceptance of multiplicity does not aim to reconcile differences in ‘values’ into a tentative consensus or tabulate and typologize them on a spreadsheet or essentialize the ‘patient perspective.’ Instead, it asks: what different worlds are people working to build through the reality they are enacting through their practices? And how do some practices embed a world where some versions of ‘health’ come to matter over others?

If different social actors are enacting/performing different versions of the world, sooner or later ontological politics can ensue: “a politics about what is, what should, and what might be realized” (Law 2019: 10; see also Mol 1999, 2002). Analytically, this means focusing on what is produced through performance of practices and discourses and what is ‘at stake’ for social actors and the moral, epistemological, and social cases that they make for their positions in doing so. I have focused on how social actors engage in what Latour (1999: 18) calls “framing and summing up” to try to strengthen their own enactments over the enactments of others, generating possibilities and impossibilities (Law and Singleton 2014: 380), and configuring ‘bodies’ in certain ways (Yates-Doerr 2017).

In ontological politics, if one kind of reality gets pushed more than others and comes to be seen as inevitable other enactments slowly disappear from the frame of ontological politics. As Ingunn Moser (2008: 109) writes on enactments and performances in situations of controversial drug access: “multiplicity requires that we also come to terms with the complex relations and interferences between different matter-realizations, which make some of these present, visible, strong and real, while others are made absent, invisible, weak, less real or are outright excluded.” This is in keeping with Allan Young’s (1983) understanding of ideological practices, which he distinguishes from ideology and ideological knowledge: “Ideological

practices are the means by which (a) people's facts are materialized, in the sense that they are made to occur and then given the degree of unity and transcendence needed for them to enter people's consciousness; and (b) these facts are appropriated, in the sense that they are collected and selectively distributed among the people engaged in the knowledge production process" (1983: 204). When I look at ideologies around individuals and collectives in this dissertation, I am not analyzing ideology as a 'thing' but a process grounded in practices to arrange the material and social world.

Understanding the ways that stories and illness narratives get told via official and unofficial channels in drug access disputes is thus particularly important in understanding the ontological politics that animate these disputes. Buchbinder (2016) has analyzed this phenomenon through the analytic of 'scripting'. As she writes: "referring both to unwritten rules or norms for behavior and to texts to be performed, scripts are useful for thinking about how macrolevel policies meet the microlevel intricacies of routine bureaucratic encounters" (772). Throughout my fieldwork, I searched for the 'scripts' that certain social actors were trying to push through the way that they told the story around rare disease and rare disease drugs. For bureaucratic government actors and corporate industry actors alike, codified sets of 'principles' or 'values' guiding their work offered texts to be performed, and the ways that the tension between the individual and the collective good was talked about illuminated the norms for behaviour around thinking about access to treatments. As I will show in Chapter 3, a tension between affect and impartiality runs through the individual/collective tension around rare disease drugs. The pharmaceutical industry and some patient advocates push a highly affective script around rare disease drugs and access to them to delineate what I call the 'suffering individual ontology' to open the rare disease drug market. On the other hand, the bureaucratic actors who

are charged with paying for drugs through the public system attempt to diffuse this affective script and delineate the ‘sustainable collective’ ontology through impartial ways of narrating life with disease through different modes of storytelling and practices, formulas, and metrics. Both of these frames attempt to instill the script of rare disease drug access ontological politics. This requires an ethnographic sensitivity to the different ways that stories get told by powerful actors working from different situated positions, and how those stories become scripts that work to shape the ways that issues are thought about and dealt with in policy, medicine, and regulation.

It is through both practices that shape systems and particular modes of storytelling and scripting (which is of course a practice in itself) that ontological politics factors into nation-making. Drawing on Brotherton (2008, 2012), I understand state (and corporate) power “not as a monolithic function but as a proliferation of strategies that shape individual experiences... everyday practices culturally constitute the state as a dispersive network of multiple actors, institutions, and bureaucratic processes” (Brotherton 2008: 260). Similarly, as Hoag (2011: 86) has written on bureaucratic practices, they are not necessarily “the product of logics (a contextualized rational choice), orders of discourse, or superordinate powers, but as a tangle of desires, habits, hunches, and conditions of possibility.” A focus on how relationships form and are maintained within networks has been called ‘material semiotics’, which John Law (2019: 1) describes as “a set of tools and sensibilities for exploring how practices in the social world are woven out of threads to form weaves that are simultaneously semiotic (because they are relational, and/or they carry meanings) and material (because they are about the physical stuff caught up and shaped in those relations).” This entails understanding nation-making politics around health care and health care access as performative, not a thing locked into culture or fixed representations but something enacted creatively and frequently pragmatically, causing people

and other forms of matter to assemble into various relational and affective constellations of relationships (Deleuze and Guattari 1987), drawing the conditions together that allow for certain practices to happen.

I have drawn on particular analytics in the anthropology of pharmaceuticals and STS to help make relations around ontological politics understandable. In Chapter 3, I draw on Whyte, van der Geest and Hardon's (2003) analytic of the social life of pharmaceuticals which understands pharmaceuticals as gaining meaning as they become commoditized as material entities, rearranging relationships and embodiment in the process. In Chapter 5, I draw on Jensen and Morita's (2017) work on infrastructural experiments in contexts of multiplicity to demonstrate how any definition of rare disease has material and relational reverberations—it composes social actors into new configurations of assemblage. This shifts the focus from 'rational' policymaking to the rationales (and multiple interests) that underpin different definitions of 'rare disease.'

The one element I have borrowed from more traditional forms of practice theory to decipher the ontological politics around rare disease is Michel de Certeau's (1984) distinction between strategies and tactics. For de Certeau, strategies are enacted by those within large institutions or corporations and attempt to separate themselves from the environment and move the complexities and uncertainties of everyday life out of the frame. Those who engage in tactics, however, are steeped in those complexities and uncertainties—and so they work tactically within the gaps and spaces left open by strategies to reinsert spontaneous and messy aspects of life into the social world. This is a mode of making space for the 'other' amongst enactments that aim to simplify everyday life. I employ this distinction to highlight the difference between those engaged in rare disease drug access politics as 'stakeholders' as part of their job to strengthen

enactments of particular institutions, and those engaged in these disputes as a matter of living life with disease and figuring out how to manage and manipulate their institutional encounters. Strategies and tactics come out through practices as well as mobilizations of morally charged ‘values’, which, in keeping with the framework of multiplicity and following Dussauge, Helgesson, and Lee (2015: 269) I understand as “enacted, ordered, and displaced rather than as fixed and constitutive forces.” I am less interested in what social actors’ values are than I am in what particular mobilizations of values ‘do’ in nation-making practices enacted by social actors operating from different social orders and situated positions, and how they create and maintain the affective and institutionalized associations necessary to have the ‘upper hand’ in negotiating the terms around public investments in rare disease drugs.

2.1.2 The illness experience, care, and living among and across multiple social orders

On the ‘micro’ level of living with and caring for disease within families, my analytical focus is on how pragmatic enactments and practices at the macro level become part of the illness experience, as rare disease patients and their families figure out how to create meaning within their lives and/or access treatments. This entails deftly navigating what Moreira and Palladino (2005) call the regimes of truth and the regimes of hope. They do so at the same time as attending to the non-linear complexities of life with disease. As Moreira and Palladino write on these two different regimes (p. 68):

The ‘regime of hope’ and the ‘regime of truth’ differ in the way they imagine and configure the patient. In the ‘regime of hope’, actors tend to figure the patient as someone who is invested in becoming less entrapped by his or her physical condition; this patient may sometimes be desperate, but is always waiting for new solutions to his or her entrapment. In the ‘regime of truth’, by contrast, patients are configured as consumers of health care, concerned to compare the relative merits of pharmacological and surgical approaches, by taking into consideration their effectiveness, risk of harm, and cost. In their opposing configurations of the patient, the two regimes both attempt to distribute

knowledge and agency between expert and the lay public, and thus to engage, some might say to ‘interpellate’, the patient’s ‘self’ from different perspectives.

Moreira and Palladino’s distinction is relevant here: the regime of hope factors into the ontology of the ‘suffering individual’ while the regime of truth factors into the ontology of the ‘sustainable collective.’ Rare disease patients get configured within these two different ontological approaches to ‘the patient’ in various ways, and in some cases play these parts, engaging in substantial emotional labor to meet the affective and performative requirements of either configuration they are interpellated within, but are always living more complicated lives than these simplified frames imply. As the caregivers to patients with uncertain and progressive-degenerative disease, analytically I approach the parents of children with rare disease who appear in this dissertation as living across and between what Gershon (2019) calls ‘multiple and porous social orders’ in that they have to develop the repertoires to deal with and navigate the range of different enactments that formulate and instantiate versions of individual/collective politics. Tacking across the competing ontological frames of ‘the suffering individual’ and ‘the sustainable collective’ while also living everyday life requires that parents of children with rare disease engage in tactics to achieve desired outcomes in access to care while also carving out a life and a world that is meaningful to them.

Each parent’s experience of caring for their sick child is different however, calling for an analytical lens on specificity and grounded understanding rather than universalization of the ‘patient perspective.’ Differences arise due to positioning in the social world: race and class inflect the experience of disease and affective dimensions of ‘deservingness’ for resources, as do particular conditions or mutations and the configuration of treatment availabilities at any particular time. I look at caring practices for disease in families as something deeply situated in

the structural context in which individual families live, which entails looking at the illness experience at a level above individual interactions or reflexive perceptions (Metzl and Hansen 2014). The structural context for a low income family or a racialized family or a wealthy family or a well-educated family and the intersections between these different identities/forms of experience is not the same—life and the health care system is experienced differently depending on one’s complex social positioning and the social distribution of the idealized ‘parent activist’ identity (Ginsburg and Rapp 2010).

In recent years, ‘care’ has emerged as an important analytic in medical anthropology and feminist STS. As an analytic, care make visible the political, economic, and cultural work that different enactments and practices around ‘care’ have in the social world (de la Bellacasa 2011; Mol, Moser, and Pols 2010; Ticktin 2011; Taylor 2008; Kleinman 2009, 2013; Han 2012; Fassin 2011; Segal 2013). This recent work has explored care as at once a local material practice and a moral sentiment, and how the entanglement between the two can make deciphering between different articulations of ‘care’ difficult but necessary (Martin, Myers, and Viseu 2015; Smith-Morris 2018; Stevenson 2014; Povinelli 2011; Ticktin 2011; Fassin 2011). Care is something that can be subject to and channeled by different ideological/moral/ontological ‘logics’ (Mol 2008) or orientations to ethics and responsibility (Tronto 1993; Levinas 1985), something built through moral engagement with disease and striving toward the ‘good’ in varying circumstances (Mattingly 2014; Livingston 2012), something constructed in encounter to create moral meaning around tricky conditions and experiences (Buchbinder 2015), and something that can create empowerment for some within a matrix of inequalities that depends on the disempowerment of others (Buch 2015; Buchbinder and Timmermans 2013).

As such, an analysis of ‘care’ is a good companion to an analysis of multiplicity because it provides a lens on many different enactments that operate within and across social orders and social worlds. Analyzing care involves examining enactments of transactional affective-economic relation at the same time as examining moral orientations/experiences at the same time as stratification and inequality. Deciphering between different enactments of ‘care’ is vital because otherwise care is easily politicized and/or bureaucratized and/or economized for other ends. As Mol, Moser, and Pols (2010: 7) write on caring practices, “if care practices are not carefully attended to, there is a risk that they will be eroded. If they are only talked about in terms that are not appropriate to their specificities, they will be submitted to rules and regulations that are alien to them.” Thus, in imparting the illness narratives of families as they were told to me, and in portraying the banal and chronic ‘crudeness’ of the everyday (Povinelli 2011) through participant-observation data, I have aimed to restore a focus on everyday caring practices that both the affective/sensationalized script of the suffering individual ontology and the impartial/sanitized script of the sustainable collective ontology tends to diminish in the ontological politics of rare disease. It was in the disjunctures between these different scripts and ‘regimes’ to use Moreira and Palladino’s (2005) term and the lifeworlds of families that the themes around how these ontological politics function emerged most forcefully in my dataset and which has guided the ways that I have laid out the data and the chapters in this dissertation. It is in these disjunctures that we can learn about how the tension between the individual good and the collective good plays out in the social world.

In my analysis, I tack between care as a mode of experience and responsibility within families and care as a contemporary political ordering through the political role of ‘suffering’ in deservingness politics. Suffering becomes a form of capital or property that determines access to

resources in particular modes of neoliberalism (Brown 1995; Benton 2012, 2015; Ticktin 2011). This can have the effect of erasing other forms of suffering as less important or less deserving, and often this adheres to deeper and frequently racialized logics of who gets to access state resources and who does not (see Benjamin 2013; Buchbinder and Timmermans 2013). Murphy (2015) cautions against equating care with ‘positive feelings’ and calls instead for analyses that trace how hegemonic arrangements enacted under the banner of caring in technoscientific scenarios can become platforms for “the exercise of power [as it] operates through care in many divergent ways” (719). For example, ‘feel good’ feminist health activism in the late 20th century had the effect of ignoring and instantiating “persistent racisms, class privilege, colonialism, and American imperial ambitions” (ibid). Thus, critique of ‘care’ is necessary, even for practices that seem so humbly good that they self-position as beyond critique. Critiquing mobilizations of care does not mean nihilistically foreclosing it but instead troubling them, care-fully. Thus, when I highlight the displacements that some forms of care might have in the world of rare disease drug access disputes this is done in order to revive partially submerged narratives and argue for a broader and more robust vision of a health care and social service system for all those living life with chronic (and sometimes low prevalence) diseases.

There are three analytics from the anthropology and STS of care that I draw on throughout this dissertation. First, is Ticktin’s (2011) analytic of ‘regimes of care’ in which she analyzes the affective and politicized category of physiological/medical ‘suffering’ as one of the ways that refugees to France can come to ‘qualify’ for care—it is how one can become a “morally legitimate suffering body” (14). Other forms of suffering—such as poverty—are not granted a similar legitimacy for relief in humanitarian aid practices. As Ticktin notes, this focus on medical suffering can “ultimately work to displace possibilities for larger forms of collective

change” (3). This is not to say that medical suffering is not awful and deserving of action and attention, but instead that the striated valuation of different forms of bodies and lives must be pointed out and critiqued within analyses for the forms of care these practices can actually displace. This has formed part of my analytical strategy throughout this dissertation. In doing so, we see that people with rare disease who are affectively proposed as ‘deserving’ of high priced drugs also need other forms of social services as well, which are sometimes the same ones cast within rare disease drug access politics as less deserving of public resources.

Second, to highlight the particularity of these politics of care I have also built on the anthropological analytic of citizenship, which has offered a rich analytical lens into how people with different biological conditions pull themselves into the orbit of nation-state responsibility. Petryna’s (2002) analytic of biological citizenship opens understanding of how ‘citizens’ make claims upon the state based on physiology and health, whereas Nguyen’s (2010) analytic of therapeutic citizenship analyzes the absence of the state and the emergence of other structures to do the ‘state’s work’ of providing health. Both of these presume a natural role of the state that people orbit around. Rose and Novas (2005) build on Petryna with their conception of biological citizenship but argue that it is less about the state and more about biosociality: people coming to understand themselves through their biological conditions that they tie this biological identity into conceptions of personhood and citizenship held in the Western world, but is not territorially situated within nation-states. I draw on these formulations but adapt them to resource allocation disputes in a high-income setting to show how nation-making arguments for inclusion of one ‘disease group’ are built on the premise of the exclusion of others. This has the effect of deuniversalizing deservingness for care and creating different classes of citizens stratified by form and degree of suffering. This mode of activism sometimes articulated by patient advocates

and pharmaceutical industry actors has been analytically focused upon in this dissertation, while also highlighting the inadequacy of health economics logics of ‘opportunity cost’ to offer robust alternative visions of care.

Following on that note, the third and final analytic that I borrow from the scholarship on care is this formulation of ‘caring practices’ by Mol, Moser, and Pols’, focusing on their understanding of ‘care’ as a matter of ‘tinkering’ with dynamics and materialities to make possibilities for care happen. Caring practices are not only enacted by parents and families but also by other actors who recognize the fraught relationship between life with disease and the systematization of care into frameworks and processes. Some work hard to work through these tensions between principles and care, impartiality and emotion, and universals and particulars. In particular, I look at the work that the policy unit where I conducted part of my fieldwork through the lens of caring practices. Examining their work as a form of ‘policy level’ caring practice, I assert the possibilities for care within and between the more politicized versions of care that animate the tension between ‘suffering individuals’ and the ‘sustainable collective’ in rare disease.

2.2 Methodological Framework

This dissertation is based on 18 months of ethnographic fieldwork split into two phases. In the first phase, from January to June 2015, I conducted six months of in depth participant-observation at a health policy unit. This unit is housed on a university campus but largely funded by provincial grants to conduct health technology assessments to help the government decide which new technologies to fund in the public system. Except when travelling to conferences, I’d spend every business day at the unit—attending meetings, conducting participant-observation,

and following how the policy unit navigated the tensions, dilemmas, and controversies they encountered in their rare disease policy work. Throughout, I also conducted semi-structured interviews with ‘stakeholder groups’ across Canada—public drug payers, policymakers, HTA specialists, pharmaceutical company representatives, patient advocates, etcetera (covered in more detail in section 2.2.3 below). In the second phase, from July 2015 to June 2016, I conducted in depth research with families—conducting interviews and also ‘hanging out’ in everyday life. In particular, throughout that time, I followed the family of a child in a clinical trial: monthly clinical trial dose visits as well as family events, like birthday parties, enzyme replacement therapy infusions, Saturdays at the pool, and disease awareness and fundraising events the family put on in the community (with continued visits 2017-2019). Throughout my fieldwork, I attended several conferences and meetings that I approached ethnographically. I will elaborate on each of these pieces of my research design below.

This dissertation draws upon fieldwork conducted as part of my Master’s degree in anthropology (McGuire 2011), and as such is rooted in long term ethnographic engagement with families living with rare disease and with the politics that surround rare disease. One family participated in both the Master’s and doctoral research projects. For this family, informed consent was renewed for the doctoral project and the transcript of the earlier research interview revisited by the parent to ensure that they were still comfortable with the material they had shared years earlier.

2.2.1 Ethics and access

Rare disease is a small world—many patients know one another, as do many professionals working in rare disease across the ‘stakeholder’ spectrum. For this reason, I have

often been vague on certain details, and sometimes changed some highly identifying characteristics. This includes (in most although not all cases) the province or territory in which a participant lives and works. While this risks rendering invisible the impact of Canada's strong regionalism on these discussions, I did not find a major difference in the articulations of actors between regions/provinces so this was appropriate without eliminating important nuance. Still, some social actors who appear in this dissertation may still be identifiable and participants were made aware of this possibility in the informed consent process. Research primarily took place in three different Canadian provinces.

A waiver of informed consent was issued by my research ethics board for my observation of conferences and meetings. In all cases where data from those meetings and conferences have been shared, I have aimed to be respectful of speakers—if they do not generally hold a public role, I have not identified them by name. In cases where 'Chatham House Rules' were invoked or for smaller more intimate meetings I have deidentified the speaker unless they requested to be identified by name upon my contacting them. In some cases, as a researcher I did not feel comfortable sharing ethnographic material derived from these conferences and meetings as I felt it would impart disrespect to the speaker(s) and/or render them identifiable in a potentially harmful way.

I obtained consent for my research at the health policy unit from the unit's two leads, the head and the director. As the unit is located within a university an official visiting student status was granted for my time there. In the second week of my research, I gave a presentation to the unit's full staff about my project and invited them to let me know if they were uncomfortable with any portion of my research plan or if they did not wish to appear as an actor within my dissertation. No one approached me with any concerns and all were very supportive of this work,

but I have not identified any unit staff or associates directly. In the course of my fieldwork at the health policy unit, I sat in on several meetings with both government and industry representatives. In some cases, sharing ethnographic details of these meetings was not appropriate for various reasons. First, because I did not always have informed consent from the health policy unit's guests. Second, because sharing the details of confidential meetings could damage the health policy unit's working relationships with their colleagues. Third, because details could make some actors identifiable in ways that could harm them professionally. However, witnessing these meetings and the tensions navigated by participants has certainly shaped my thinking and my understanding of the ontological politics around rare disease.

In Chapter 7, I share the making of two 'citizens' juries' put on by the health policy unit. For this analysis, I have focused on the development and implementation of the citizens' juries rather than activity from the actual juries themselves. This is largely because my focus was on how the health policy unit conceived of issues and solutions, but while interested readers may wish to know more about the results of the jury experiments, the informed consent form that the participants in those experiments signed did not grant permission to possibly appear in an interloping ethnographer's work. The only instance that statements/opinions expressed by jurors are shared here is in from the opening introductory talks given by the policy unit's head, Jay, and the focus is on how he responded to and managed the questions from the audience.

2.2.2 Ethnographic participant-observation

This study's primary methodology is that of participant-observation, conducted within an ethnographic research design that placed me directly within the tensions described throughout this dissertation, summarized in Table X below.

Table 1: Sites and objects of ethnographic study

Fieldsite	Timeline	Participants
Health policy unit	January-June 2015	Health policy researchers and health technology assessment specialists; government health system managers/payers; pharmaceutical industry actors seeking advice on listing their products
Family lifeworlds	July 2015-June 2016	13 families living with ‘rare disease’ situated differently in the social world in terms of race and class.
Conferences and meetings	January 2015-June 2016 (and beyond)	Patient advocates; government drug payers; health economists and health policy researchers; representatives of the pharmaceutical industry
Texts and documents	January 2015-June 2016 (and beyond)	Carefully written texts from government, patient advocacy groups, and industry groups.

While at the health policy unit for the first six months of fieldwork for this study, I was embedded in discussions about government decision-making and the questions, conflicts, and controversies about the collective sustainability of the health care system. I was preoccupied with policies and frameworks and solutions—with patient registries and clinical trial datasets and economic modelling techniques. Once wrapping up at the health policy unit in June of 2015, I spent the next 13 months conducting research with families. While conducting fieldwork with families in the course of their daily lives and particularly the more in depth and long term work with the family participating in a clinical trial, I was embroiled in the intimate complexities of life with disease and the everyday. Whether at a family birthday party or muddling through a

long clinical trial dosage day, these system preoccupations came to feel irrelevant and I was focused on the everyday drama in front of me, the needles and the milestones and the anxieties and the tantrums and the tears and the small everyday moral decisions that parents made to keep their child safe and happy. These worlds seemed so far away from one another, and yet they are connected by the thread of policy—one, the makers of policy and knowledge, the other, those impacted by policy and knowledge. Patient advocates threaded between these two worlds conducting “research in the wild” (Callon and Rabearisoa 2003), but many of the families who participated in this study demarcate themselves and their experience from that of these ‘official’ patient advocates. So, as I’ll explain further below I hesitate to collapse the two into one biosocial ‘group.’

Another site of social action and knowledge formation in my ethnographic research design is conferences and meetings convened by different stakeholder groups. This included three patient advocacy conferences and luncheons, two industry/industry association conferences, three health technology assessment conferences, and two health services research policy meetings and roundtables. These public displays of knowledge and knowledge production were good opportunities to witness how actors engaged in practices of “framing and summing up” (Latour 1999: 16) of complexity through particular situated knowledges and positions as they had the ability to ‘set the agenda’ so to speak. That said, conferences and meetings centering around rare disease drug access and HTA in Canada are frequently attended by a variety of ‘stakeholders’, allowing for questions and contestations, forcing actors to either rationalize or waver on their materializations of issues. Sometimes there were outright vocal disagreements and sometimes tears (ironically, both times I witnessed this the tears were shed by pharmaceutical industry actors, not patients or family members). Most sessions that I attended

were recorded, as a waiver of informed consent for these spaces was part of my research ethics board approval. When attending a particularly evocative panel session or meeting, the session was transcribed and coded along with the rest of the dataset. In large part, the data from these conferences and meetings have been utilized within this dissertation as an ethnographic vignette or point of entry into a wider tension or phenomenon rather than approached analytically, although I plan to consider the function of conferences and meetings in ‘setting the agenda’ and shaping formal and informal scripts around contentious issues in future work.

Texts and documents were collected and referenced in this methodological framework. These included policy briefs, minutes from parliamentary standing committee meetings, industry white papers, and fundraising notes. These “ubiquitous features of late modern life” (Riles 2006: 5) can offer understanding of the power of controlling discourse around what the world knows about itself, often glossing over “conflict and multiplicity ... buried beneath layers of obscure representation” (Bowker and Star 1999: 47). Textual representation is a form of worldbuilding, at once “an ethnographic object, an analytical category, and a methodological orientation” (Riles 2006: 7). Carefully worded texts abound in the rare disease drug access disputes that this dissertation follows, and often as much is said in the controversies left out of certain textual framings as what is included. With this understanding in mind, I collected the documents as listed above and coded them as data.

This research was not only multi-sited (Marcus 1995) but also involved ‘studying up’ the power structure (Nader 1974), not just with one group but across different groups and forms of life. As Marcus (1995: 105) writes on multi-sited ethnography: “Multi-sited research is designed around chains, paths, threads, conjunctions, or juxtapositions of locations in which the ethnographer establishes some form of literal, physical presence, with an explicit, posited logic

of association or connection among sites that in fact defines the argument of the ethnography.” As such, this work expands upon traditional fieldsites for medical anthropology by juxtaposing different social locations, showing how what it means to care for ‘rare disease’ is not only constructed in clinics or even in families but also across multiple understandings and practices enacted by different social actors operating in diverse sites: in boardrooms, conference venues, webinars, committees, media coverage of access disputes, budget ledgers, ‘disease awareness’ marketing campaigns, policy strategy meetings, and research projects, among others.

I identify with Rayna Rapp’s (1999: 306) description of her similarly multi-sited and multivalent study of amniocentesis in the United States: “the object of investigation constantly recomposed itself in relation to the angle from which I was viewing it. And each shift of perspective brought additional aspects of the technology into focus.” This methodological design forced me to question assumptions about expensive drug access in different ways than I might have had I immersed myself in only one setting. Had I conducted in depth research only with families, I might have missed the vital importance of macrolevel negotiations and controversies and how they affect how rare disease becomes framed and enacted in high level policymaking efforts. Had I conducted in depth research only at the health policy unit, I might have missed the juxtaposition of the immanent and intense with the banality of the everyday that is central to living life with disease. Taken together, this ethnographic methodology forced me to look beyond the scripts that technoscientific controversies invoke and the easy binaries that they frequently depend upon.

2.2.3 Semi-structured interviews and participants

When necessary, I use the term often used by my interlocutors to describe themselves and other groups invested in rare disease drug access: ‘stakeholders.’ However, I do not think of these groups as existing in a rigid typology but instead as constituting fluid and heterogeneous assemblages that come to constitute ‘social worlds’ (Strauss 1978; Clarke 1991; Fujimura 1996; Garrety 1997; Clarke and Star 2008). This means that people assemble into groups “characterized by a commitment to common assumptions about what is important, and what should be done” (Garrety 1997: 731). However, this commitment is never whole, they can split and merge based on common goals, their commitments can be partial and the various social orders they participate in porous, temporal, and situational (Gershon 2019). In fact, as I’ll describe in Chapter 3, some ‘stakeholders’ are ambivalent about the ideological discourses they are expected to carry out and rationalize by virtue of their social location or employment. Additionally, social actors regularly move between and across different social orders and ontological/epistemological frames.

I conducted 50 semi-structured qualitative interviews for this project, with the range of stakeholders implicated in rare disease drug access discussions, as summarized in Table 2.

Table 2: Semi-structured interviews

Group	#interviewees
Patients and families	13
Patient advocacy group representatives	5
Public drug plan managers/employees (current and former)	8
Drug regulatory agency representative (Health Canada)	1
Provincial Minister of Health (former)	1
Pharmaceutical company representatives (all levels of company including market access, regulatory/government affairs, policy, management, clinical science)	8
Health services researchers (including health economists, HTA specialists, policy researchers)	8
Clinicians	6

Interviewee selection of those in more ‘professional/institutional’ categories was conducted via a purposive sampling method. The head of the health policy unit where I was conducting my fieldwork would review my deidentified interviewee list from time to time and recommend places where I had gaps in representation, often kindly putting me in touch with his own drug payer/government/industry contacts across Canada for an interview. In several cases, I met the interviewee in the course of my fieldwork at the health policy unit. In other cases, I requested interviews directly after meeting them at conferences or meetings or randomly just by emailing them. Interview questions for those operating in more professional/institutional roles began with general questions about a participants’ background, and were designed to elicit their understanding of the socio-material entanglements they found themselves in by virtue of their professional/institutional role and what they perceive the ‘values’ guiding rare disease drug access are and should be.

For the most part, these interviewees did not understand their professional identity or practice as socially or culturally situated—similarly to what Janelle Taylor (2003) calls medicine’s “culture of no culture” in which static and essentialist conceptions of ‘culture’ are generally applied only to patients and not to practitioners’ own worldviews. However, these professional/institutional actors, from pharmaceutical industry actors to government, were generally positioned in the world as upper to upper middle class people, with professional backgrounds and education that shaped their worldviews. Although there were exceptions, the majority of the participants in my study in these professional roles were white and/or from advantaged backgrounds. This pattern is consistent with the social stratification of racial privilege and economic and career mobility in Canada (Osberg 2008).

Interviewee selection of patients and families was conducted via a snowball sampling method. The Canadian MPS Society sent out a notice of my study and request for interviewees, and several parents contacted me directly from there. In other cases, a parent or family member already enrolled would suggest that I talk to other rare disease parents that they know, and put me in touch with them. For one family, I drew upon an earlier pre-existing research relationship from an earlier project conducted in 2010 (McGuire 2011). Interview questions for patients and families began with a request to hear their story, and were designed to elicit details on the everyday contexts of living with disease and caregiving alongside how they understand their access care to be wrapped up within wider disputes and processes. I did not elicit income levels from interviewees, but their stories and self-identified statuses place them all across the board in terms of socioeconomic/class position. Nine families were white, two families were First Nations or Indigenous, one family was mixed race (white and black), one family was of Middle Eastern descent, and one family was of East Asian descent.

In Chapter 3, I will outline where these different social actors fit into the range of practices and institutions that interact in rare disease drug access disputes, but below I briefly outline the interviewee participants in this study.

Patients and families

Parents of children with rare disease most often invited me to their homes, and interviews typically lasted from one to three hours in length. On two occasions, I met with a parent in a more neutral location like a coffee shop, on one occasion at the parent's workplace, and on one occasion, in the child's inpatient room at a children's hospital. On three occasions, teenaged/young adult patients participated in the interviews as well. In five of the 13 families interviewed, I was spending more time with them in their daily life in an ethnographic mode, and for those families interviews were often repeated usually at least two or three times.

Patient/parent advocates

While most parents and patients end up advocating either for their child or for themselves at one point or another, and are sometimes members of patient advocacy groups participating in fundraising or events, I draw a distinction between patients and families and those who take on a more formal 'official' patient advocacy role within a named organization when discussing different groups in these disputes. That said, the lines were naturally blurred because formal advocates often talked about their own experience or their child's experience as well. I draw this distinction between patients and patient advocates because the majority of families who participated in my study expressed that the world of formal patient advocacy and the work

advocates do in policy discussions was one that felt either very far away and opaque or not fully possible for them to participate in amidst their caregiving responsibilities.

Of the five patient advocates interviewed, two were representatives of rare disease ‘umbrella’ organizations and three were from condition specific organizations. Durhane Wong-Rieger, President and CEO of CORD, requested to be identified and has taken a largely public role in these disputes so deidentification would not be possible. Interviews with patient advocates were either held at their advocacy organization office or in a neutral location like a coffee shop or empty room at a conference center. Interviews were generally about one to two hours in length.

As CORD appears at several points throughout this dissertation, I will provide a bit more context of this patient advocacy organization here. First, CORD does incredible work in building and maintaining the rare disease collective identity and has helped to put rare disease ‘on the map’ in Canadian politics. Second, CORD is frequently criticized for their financial ties to pharmaceutical companies (as are many other patient advocacy organizations). This tricky set of relationships is part of what I analyze throughout in looking at the entangled stakes in different versions and visions of rare disease drug access and policy.

Government representatives

This participant category includes current and former provincial public drug plan managers and employees (8), federal drug regulators from Health Canada (1), and provincial Ministers of Health (1). As I’ll explore in Chapter 3, the political commitments and epistemic frameworks of these three different types of actors often diverge. Public drug payers are also often referred to as ‘decision makers.’ All of the participants in this category had achieved a

level of post-secondary graduate education, either doctoral or masters level. Interviews typically took place at their office or other institutional setting, with interviews lasting 45 minutes to three hours in duration—but typically, about an hour and a half.

Pharmaceutical company/industry representatives

The rare disease pharmaceutical industry is complexly situated, as are its actors. Competing in this space are ‘single product’ start-ups invested in a particular drug or disease, established pharmaceutical companies with a focus on rare disease, and large multinational pharmaceutical companies looking to cash in on the high prices and rate of return from a successful orphan drug. The financial stakes and commitments of these different types of companies are different. The objectives of a pharmaceutical industry actor also depends on their job: general managers, scientists, salespeople, and government affairs and market access specialists each have different objectives they must fulfill. All risk being ‘let go’ from their positions, or losing their own investments and stock in the company, if they do not fulfil their particular objective within the market system structure of the company. While some pharmaceutical company representatives work for companies headquartered in Canada, most are employees of subsidiary offices, meaning that their fate is decided by a head office located elsewhere. Rare disease pharmaceutical or biotechnology companies are frequently members of an organization that lobbies on behalf of their member companies’ interests. Two examples of lobbying organizations that interact in rare disease drug access politics are Innovative Medicines Canada and BIOTECanada. These organizations work with politicians and political groups, help coordinate marketing messages across companies, and release reports and white papers. These

lobbying organizations also work to ensure that the messaging around rare disease drugs is consistent with the messaging and aims of the wider pharmaceutical industry.

Participants and interviewees in this category include the full range of these actors. All had undergraduate degrees, a few had MBAs or other Master's level degrees. Two of these interviewees were interviewed in their office, but for the most part, interviews were conducted in a neutral location far from prying eyes in their offices such as a coffee shop or an empty room in a conference centre. Interviews lasted between one to two hours in length.

Health services and policy researchers and clinicians

Several health economists, HTA specialists, and policy researchers were interviewed (and also figured prominently in my interactions throughout participant-observation at the policy unit). All held advanced (PhD or Master's) degrees and either academic appointments or professional roles within public agencies. Interviews lasted between one and a half to three hours in length and usually took place in their office.

While interview data with clinicians has not figured centrally within this dissertation, I did interview different members of clinical teams that care for patients with rare disease. This included four physicians, two dietitians, one nurse, and one geneticist, all with training and education appropriate to their position. All of these interviews were conducted in their hospital/clinic offices. Interviews lasted between 45 minutes to two hours in length.

2.2.4 Data analysis

Throughout my research, I took extensive field notes. I recorded and transcribed all interviews, with the exception of two interviews where I was asked not to record. In these cases,

I took extensive notes and noted direct quotes. I uploaded all data, including fieldnotes, interview transcripts/notes, conference/meeting session transcripts, and documents to the qualitative data analysis software NVivo. I coded raw data thematically and iteratively throughout the data collection period, and generated new ethnographic questions to pursue as finer grained themes were identified. Once data collection was complete, I recoded the different themes and worked with them iteratively throughout the writing process.

Through identifying ‘themes’ and codes’, I was able to identify the scripts mobilized by both state and corporate actors that different ontological frames around life with disease and drug access depend upon, particularly the ways they work to render the issues around rare disease drugs into something “fixed and solvable” (Knight 2015: 9), creating the limited frames through which patients and families desiring access to resources can be understood. When examining my fieldnotes and interview transcripts conducted with families living with rare disease, I looked at how parents of children managed their own storytelling in such a way as to align with the narrative devices that different scripts depend upon (particularly that of the suffering individual ontology) but also the ways that their stories exceed the limited frames through which their experiences are configured within these powerful ontologies. My own storytelling as an ethnographer became a method in itself: how to show the differences and disjunctures between powerful scripts and ontological frames and the much messier and non-linear dimensions of experience and life with disease on the ground.

In my research with patients and families, I was compelled to carefully navigate my social location as a researcher. Some of my patient and family participants knew me through previous professional employment in a clinical setting, and thought me connected to and representing that world and able to help them make a clinical case for treatment access. Other

patient and family participants knew me as located at a health policy unit connected however nebulously with government, possibly with the potential to directly impact their access to care on a policy level. I sometimes found similar sets of expectations from professional actors as well, wherein people who agreed to speak with me seemed keen on me being the one to make the other stakeholders understand the difficulties and fundamental morality of their position. As Buchbinder (2009) has explored, the institutional context in which an interview is given may impact the way that people tell their narratives. They may highlight certain forms of suffering in the hopes that participating in the interview will rectify those injustices. The “pragmatic context of storytelling interactions” (109) may for example, lead to people telling stories in which they situate themselves as particular types of moral actors in the unfolding of events and processes. This is not a critique of how people tell their stories but rather an ethnographic sensitivity that necessitates a particular analytical strategy in focusing on the moral character of actors as being ‘at stake’ for them in the way that stories get told (111). In keeping with my analytical framework shared at the beginning of this chapter, I understand social actors’ storytelling as particular pragmatic enactments in a complex politics of care and multiplicity.

In the next chapter, I move to the research data portion of this dissertation. Through two ethnographic scenes as well as an extended analysis of the ‘social life’ of rare disease drugs throughout their life cycle, the socially generated and affective intensity of the ‘suffering individual’ and ‘sustainable collective’ ontologies and their politics in rare disease will become more clear. In the process, the range of institutions and social actors that interact throughout this social life, as well as what is ‘at stake’ for them, will be introduced.

Chapter 3: Research setting: what is ‘at stake’ in rare disease drug access?

This chapter is about the different practices that enact the ‘suffering individual’ ontology and the ‘sustainable collective’ ontology through the ‘life cycle’ of rare disease drugs. From invention, through research and development through regulatory approval through ‘market access,’ social actors at each step of the way put models and frameworks and practices in place to try to manage meaning around rare disease drugs. I show how in the early phases of a drug’s life cycle, the meaning can all be channeled toward the promissory and speculative potential of the drug to relieve individual suffering. In the later stages of a drug’s life cycle, on the other hand, it gets opened up to scrutiny on its effects on the sustainability of the collective health care system. It is within these contexts and practices that these competing ontologies of moral drug access are made.

Figure 1 outlines the ‘formal process for drug authorization and approval in Canada. In my exploration of the life cycle of a rare disease drug, I highlight the informal social activity and the generation (and control of) meaning at each of these formal stages. I adapt what Whyte, van der Geest, and Hardon (2003) call the ‘social life’ of pharmaceuticals. This approach illustrates how drugs do not just arrive as complete packages of neutral substance stocked on pharmacy shelves, they are “powerful substances” that are socially produced through a “complex of institutions, technologies, and practices characterized by styles of reasoning” (Whyte, van der Geest and Hardon 2003: 13). I take what Hardon and Sanabria (2017: 119) call “a process-centered approach that examines the articulations, dearticulations, and rearticulations of pharmaceutical”: drugs are entangled within and inextricable from the many meanings and practices that grant (or deny) therapeutic efficacy and social meaning to these powerful substances.

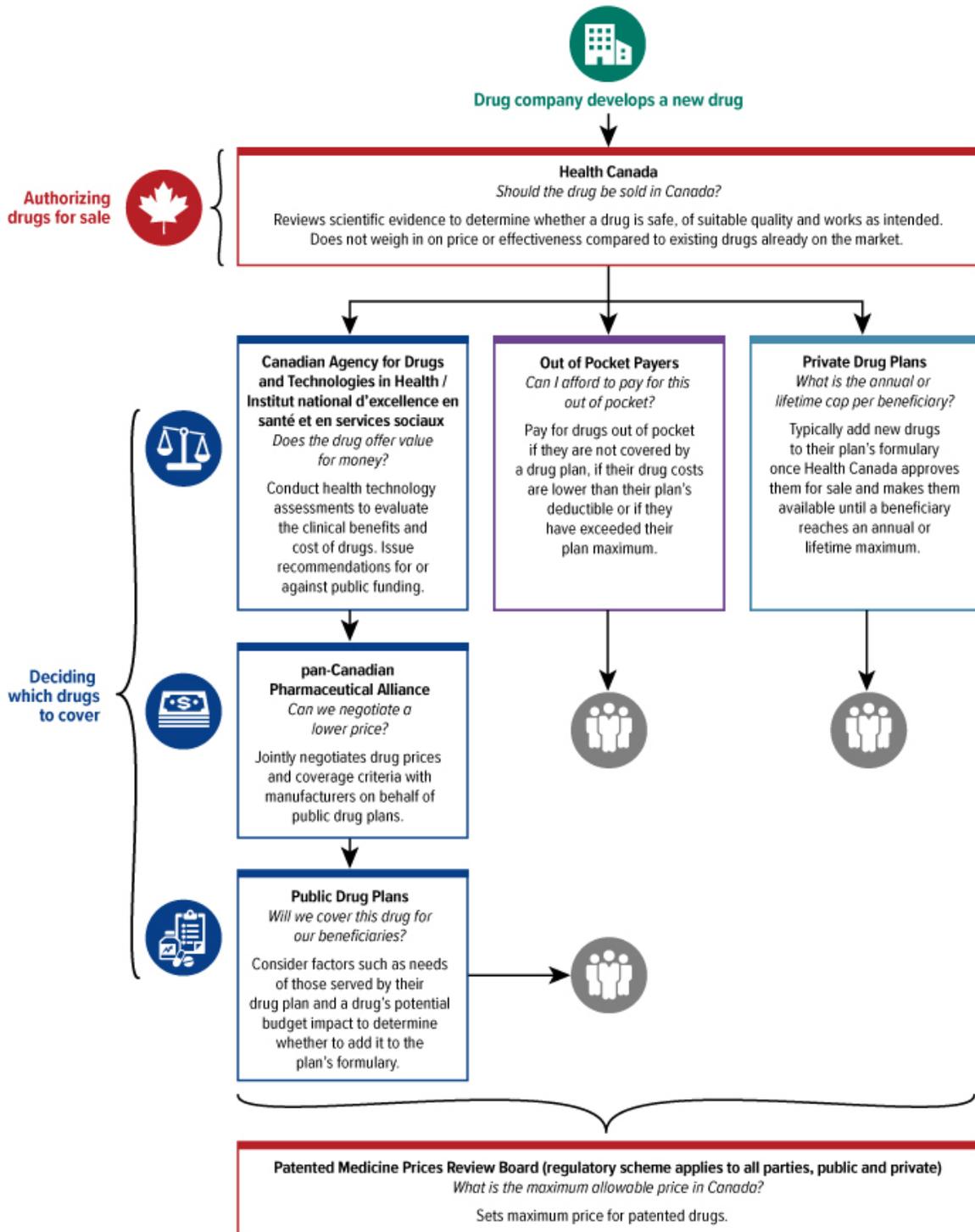


Figure 1: Drug authorization and approval process in Canada. © All Rights Reserved. *A Prescription for Canada: Achieving Pharmacare for All.* Health Canada. Adapted and reproduced with permission from the Minister of Health, 2019.

I bookend the sections on the social life of a rare disease drug with two ethnographic scenes that help to illustrate the complexities around the suffering individual/sustainable collective binary. In the opening scene, I share a scene in a hospital room. myself and the young patient and her mom are not really concerned with the clinical encounter but with the wider processes that go on outside to shape the young patient's access to a controversial expensive drug. Before I conclude the chapter, I introduce the health policy unit where I conducted part of my fieldwork, and share a scene where the unit's director, Jay, was compelled to respond to an opinion piece by the leader of a pharmaceutical policy think tank.

Taken together, the chapter serves to orient the reader to the Canadian health care and drug access system. It also theorizes the ways that social actors create a rhetorical opposition between 'suffering individuals' and 'the sustainable collective,' and build these into realities through practices. The scenes at the beginning and the end introduce the complexities of how these ontological frames—each of which simplify relationality and experience and illness to an extent—are experienced by those affected by or trying to work outside of them.

For each of the phases of social life of a rare disease drug, from drug development pipelines through regulatory mechanisms through 'indirect marketing' techniques through the reimbursement processes of the Canadian health care system, I'll ask the central question embedded in Mol's (1999; 2002) approach to multiplicity: what do practices enacted at each phase *do* in the sphere of relations they are a part of, and what is at stake for the social actors enacting them? As such, my intention in this chapter is to show, at each phase in a drug's social life, the types of relations that social actors work to highlight and imbue with meaning, and the other types they work to ignore or foreclose. I propose that we see expressions of 'values' by social actors as pragmatic enactments and performances within a particular context and historical

moment in the relationship between pharmaceutical capitalism and public health care systems. Thus, making sense of rare disease anthropologically does not mean typologizing and tabulating social actors' perspectives or values ('drug payers as a group think this', or 'the patient perspective is this' or 'pharmaceutical companies think that'). Instead, it means looking at the distinct ways that social actors build relations into drug access disputes through practices that manage the circulation of drugs within health care systems and compete for the power and legitimacy to do so.

3.1 Nora

I first met Nora and her family at a gala held by a patient advocacy group, where Nora had been selected for a youth leadership award. Nora, 12 years old at the time, wore a beautiful gown, and gave a wonderful speech. A year earlier, Nora had been the center of a very public and very drawn out and highly publicized dispute for access to a treatment called Ivacaftor (Kalydeco) for Cystic Fibrosis (CF). When Ivacaftor was first listed in 2013 at over \$300,000 per patient per year, provincial governments in Canada balked at the price—especially given that the drug did not show clinically significant increases in FEV or reductions in pulmonary exacerbations when compared to existing and cheaper treatments (O'Reilly and Elphick 2013: 933). I begin here with Nora's story because it highlights some of the dilemmas that this dissertation grapples with. It demonstrates how an extremely expensive life-altering substance catches patients and their families in a clash between health system pragmatics and pharmaceutical promise, configuring 'the patient' in different ways depending on which ontological and moral position one approaches the story with.

In order to gain access to Ivacaftor following her participation in the clinical trial, Nora and her mom had rallied outside the provincial legislature buildings, images of her 12 year old face on the front page of local and national newspapers. In the end, Nora got access to Ivacaftor through Ontario's public drug program, but only after exhausting every public relations strategy her family could think of. Nora's family is middle class and her father has an extended health care benefits package from his work that covers pharmaceutical costs not available through the public system. But since the province Nora lives in was currently in price negotiations with the manufacturer, they didn't want to pay for it either as they wanted to wait and see if the public system would pick up the tab. Negotiations over the price between the provincial drug plan and the manufacturer took a long time, and in that period Nora was in limbo and depended on community bake sales and other fundraising efforts to pay for the drug. They were supposed to be safe and provided for by the system, and here they found themselves feeling somewhat abandoned.

Ivacaftor was one of the treatments discussed in Chapter 1, which along with the combination drug of ivacaftor and lumacaftor, has a profit value of \$21 billion (Hollis 2019). It has been a site of controversy and reflection about pharmaceutical industry practice in the realm of rare disease treatments. Marketed under the brand name Kalydeco by the company Vertex Pharmaceuticals, it was developed in partnership with the Cystic Fibrosis Foundation, who sold their 8-12% royalty rights in 2013 for \$3.3 billion. CF is a progressive-degenerative genetic disease that primarily affects the lungs but also the pancreas, liver, kidneys, and intestines. CF was not always considered a 'rare disease.' It was only with the 'splicing' of the disease into different mutation variants that Vertex was able to get an orphan designation for it. Ivacaftor was developed to treat patients with the G551D mutation to the CF gene, which has a prevalence of

about 2.5-5% among cystic fibrosis patients (Fischer 2014). Ivacaftor was widely heralded as an emblem of ‘personalized medicine’ as it targets a specific gene mutation. In the years following, this drug was repurposed and combined with the protein chaperone lumacaftor for the treatment of CF patients with the F508del mutation. This was listed at a similarly high price. This raised profits but also raised precarity in patients’ access to treatment as regulatory and reimbursement agencies in Canada and around the world criticized this practice and pushed back on Vertex for the price.

A few weeks after Nora won the award at the patient advocacy gala, I went to meet with Nora and her mom Annie in a hospital room at the local children’s hospital. We had changed our plans to meet at their home outside of the city last minute: Nora had been admitted to the hospital the day before. It had been a hard winter for her, she’d had a lot of little viruses that had added up and weakened her lung function. She felt more or less fine, but she had to be there to be monitored.

While we sat in Nora’s hospital room, Annie described how for the most part, the media was sympathetic to Nora’s struggles. However, one article was published that had a different tone. “It made my blood boil!” Annie exclaimed, “I couldn’t believe it! And we still haven’t received any apology.” The article, written by a prominent Canadian science journalist⁵, argued that recent heavily publicized access struggles and subsequent funding decisions to fund the controversial drug was an example of a spurious drug advocacy tactic to put a cute young child out on display and talk about the lifesaving drug that bureaucrats are restricting access to because

⁵ To maintain Nora’s confidentiality I am not directly citing the article or naming the journalist here.

they care more about costs than for people. One of the cases referred to in the article was Nora's. Annie continued:

It was an insult to her and her integrity. How dare you slap my kid and say she was trotted out rather than say she was a brave kid that went and had to stand in front of mobs of media and be a nervous wreck! Like she never showed it, but I'll tell you when we came home at night there were often tears, where it was just so much for her.

Annie wasn't altogether that impressed with either the provincial drug plan or Vertex Pharmaceuticals and their treatment of Nora and her family, but she was *very* angry at the science journalist. The science journalist had argued that while evocative and compelling, stories like Nora's cannot be the basis of policy, a replacement for evidentiary standards, or a reason to abandon pricing controls for high cost drugs. This really pissed Annie off. How was Nora responsible for any of this? She just wanted access to the drug that she had found remarkably increased her quality of life after being in the trial. Who cares what the clinical trial data said? How was the cost of the drug her fault? The whole affair didn't make Annie feel too sympathetic to the public drug plan's concerns.

The situation that Nora found herself within, having to perform her suffering in public for access to a high cost drug, indeed was not her fault. However, she had become caught within particular political-economic dynamics that embroiled her within these dynamics. Issues around access to medicines that have long plagued the global south and other countries without public health care systems had, over the fifteen years or so, hit Canada's high-income context, and social actors living in the privileged country were left struggling for explanatory and moral frameworks to make sense of it all.

Nora's story got stuck at the center of these politics. After I got to know Nora and Annie, I started to notice how frequently Nora's highly publicized story was invoked on the slide decks

of bureaucrats, ethicists, advocates, and industry executives alike. Depending on who was doing the framing, Nora's story and image was either invoked as an example of the triumph of the moral imperative to relieve an individual's suffering or the dangers of affective storytelling to usurp important measures in place to protect the sustainability of the collective health care system. The next three sections situate this debate within the enacted practices that have shaped it and brought it to life.

3.2 'Discovery' at Phase 0: pre-clinical research and assembling a market

Clinical trials generally consist of four phases. 'Phase 0' is pre-clinical research, when the molecule or biologic is invented and/or repurposed to a particular condition. Phases 1 through 3 is where the drug is tested in clinical trials. Phase 4 is when the drug undergoes regulatory approval and, if regulatory approval is granted, hits health care systems.

The social life of a rare disease drug usually begins at 'discovery' and usually in a university laboratory, in Canada or elsewhere, where the biological and metabolic pathway of a particular genetic mutation is first identified. This identification often draws on case studies by clinicians who first identify a genetic condition in their patients and describe its natural history. Once pathways are identified, a different lab focused on targeting the mutation with a biological agent takes over. Often, rare disease drugs are complex biologics rather than small molecule drugs. Leon, an academic biophysicist explained to me in an interview that small molecules "go everywhere and hopefully they hit the target." However, when dealing with proteins and enzymes, "they have to be much more intelligent in how you deliver them" because simply inserting a foreign enzyme will be rejected immunologically by a patient.

Leon was working in a Canadian university laboratory in the 1970s, and was one of the first scientists in the world to work in enzyme replacement therapy. Using animal models, he tested the immunogenic status and targets of synthetically produced enzymes. He was working with a “glucose deficiency model that causes serious mental retardation and serious physical abnormalities, bloated liver and death.” At one point, a colleague from the US who had an infant patient with the condition called him up. He recounts the story of how he obtained ethics approval to develop the enzyme for this child by turning a corner of his university laboratory into an aseptic space in accordance with good manufacturing practice. Within six weeks of receiving the call, he shipped the enzyme to his colleague in the US, who infused the comatose infant with the compound. Within a week, the baby was awake. Two weeks later, the baby’s parents took him home: “I was on Cloud 9!”, Leon recounted. A month later, however, the baby died. They had cured the liver but not the lungs, which were extremely weak, and when the baby regurgitated one day, he died. Still, they tried, and it was an early proof of concept that showed the promise of enzyme replacement therapy, but also the complexity. Simply replacing a missing enzyme does not make the body with a missing part in the metabolism whole: the metabolism is not one part of a machine but a node of complex relationship within the body (see Childs 1999).

Prior to the 1980 Bayh-Dole Act in the US and similar frameworks in intellectual property and industry policy in Canada and elsewhere, academic basic scientists and researchers like Leon had to assign any discoveries made using public funds to the funder. However, after 1980, academics and universities were permitted to patent their discoveries and sell them to the commercial market, even if the discovery was made using public funding. This profoundly altered the influence of private property and profits in the biotechnology and pharmaceutical market (see Feldman, Colaianni, and Liu 2007; Popp Berman 2011). Many early discoveries like

Leon's are now snatched up by commercial entities rather than being developed in a less profit oriented drug development model. Commercial laboratories do basic research as well, however frequently it makes much more sense for them to purchase ideas and inventions with potential than it is for them to pay full time scientists who may or may not come up with something with potential. Small firms in Canada are also increasingly unable to keep up with the 'big fish' of large multinational companies with more infrastructure to scale up and commercialize (Gallini and Hollis 2019). Using the Orphan Drug Act (or similar incentivizing legislations), the biotech or pharmaceutical company can make use of tax breaks and research grants and other incentives to bring their newly purchased patent to market.

At this stage, the company considers whether this potential drug will satisfy the constituent to whom their primary responsibility lies: their shareholders on the financialized pharmaceutical market. Research is done on the patient population, the burden of disease, and the prices the company imagines it can fetch for the drug, which requires that patients living in wealthy countries where high prices can be charged have been identified. Direct-to-consumer marketing of pharmaceuticals is illegal in Canada and most other jurisdictions, but it does not matter because marketing is done in other more implicit ways at this stage, including funding an existing patient support group in countries to raise 'disease awareness' (or assembling a patient group if one does not exist already). In some cases, rare disease patients or their families and patient groups and advocates themselves have fundraised to finance the investment for biotechnology or pharmaceutical companies to 'de-risk' the early pre-clinical research, as we saw with the Cystic Fibrosis Foundation de-risking the early research for Ivacaftor. By now, before the drug has even been tested in humans, it has gained momentum. The promise of its ability to relieve the suffering of directly involved patients and families has been generated.

Meanwhile, clinical trialists of the research and development arm of a company, usually located in jurisdictions where they can get good tax breaks and expect good market returns on their products, work to develop inclusion criteria and primary and secondary outcome measures to be tracked in the clinical trial. These outcome measures must be validated or accepted by drug regulatory authorities like the Food and Drug Administration (FDA) in the US, the European Medicines Agency (EMA) in the European Union (EU), or Health Canada in Canada, who will later either approve or reject the drug for authorization based on its safety and efficacy profile shown in the clinical trial. Since the company wants to get the drug to market as quickly as possible, trialists frequently choose surrogate biomarkers based on two criteria. First, if they have been used before in similar types of studies, that surrogate biomarker is more likely to gain approval. Second, trialists look for biomarkers that are easy to measure and quick to show change in order to gain what is called ‘accelerated access’ (Bai et al 2013). While common diseases usually have several validated outcome measures to choose from in building their clinical trial protocol, there are generally very few for rarer diseases that will show statistically significant change from baseline. An example of a surrogate marker frequently used in enzyme replacement therapies for rare metabolic disease is the 6 minute walk distance test, which measures how much farther a trial participant can walk in 6 minutes at baseline and then at different stages while receiving the drug (see Condin 2014: 11-12).

Rare disease drug trials are also less likely to be double blinded and use an active comparator, and sometimes do not employ an RCT model at all and rather rely on uncontrolled trials using a historical control group based on data from natural history studies (Logviss, Krievens, and Purvina 2018). Manufacturers know that their trial design choices at this stage will likely lead to effectiveness and cost questions from public drug payers down the line, but as Mol

(1999: 80) notes is often the case in ontological politics, social actors work to “shift the site of the decision elsewhere: to push it along.”

A concern with clinical trial design for rare disease drugs is that with a rare disease, there is a limited pool of patients available to enroll in the clinical trial. This means that many of the identified patients end up enrolled in the clinical trial program. While manufacturers stipulate that they run clinical trials in jurisdictions where they can expect good market access returns, in rare disease where there are just a handful of patients globally they need every patient they can get. Identification of a patient for a clinical trial requires that the patient has been diagnosed in the first place, which means most patients in a clinical trial will be cared for by a biomedical health care system with resources to go beyond acute care. The patient’s clinician lets them know that a trial is in the works, and if they do not, patients or parents often find out through other patients or the internet. Most of the parents of children with rare disease that participated in my study enrolled their child in clinical trials with the aim of securing treatment, not participating in research. For them, the distinction between the two are completely collapsed. Thus, at this early stage, patients and families are primed to think of a treatment as coming—a form of ‘therapeutic misconception’ (see Henderson et al 2006) even before the trial has opened.

What do the multiple practices around a rare disease drug’s early development *do* at this phase? Practices at this stage move from witnessing disease in the clinic to working with mice in a laboratory to creating value for their shareholders (stocks are bought and sold for a company long before its product goes to trial) and creating meaning around the drug for patients. This is purely a promissory and speculative phase—but promise and speculation is extremely important to the accumulation of capital in the pharmaceutical industry (Sunder Rajan 2006). Generating a ‘buzz’ around a treatment even before the trial has started is pivotal to a rare disease drug’s

success, because that's where drug companies begin assembling their market and what some of my pharmaceutical industry research participants called the drug's 'value story.' At this phase, the drug company can focus all meaning on the potential of the drug to relieve suffering. The drug is just a concept from a regulatory point of view but a real thing in the social and political world, as parents and families start anticipating that a trial will soon open and stock values start climbing with speculation. A rare disease drug at this stage has an active social life, engaged within many (monied) relations.

3.3 'Testing' in Phase 1 to Phase 3: winning hearts and minds and bodies (and approval)

Once the decision to develop a drug has been made and the 'buzz' generated, Phases 1 through 3 are when the data is gathered that is necessary to obtain regulatory approval and 'bring the drug to market,' but a lot of other things are happening, too—particularly the instantiation of the suffering individual ontology around rare disease treatment. Substantial money is invested at this stage, and many drugs fail.

For rare disease clinical trials, clinicians at specialized hospitals in Canada and elsewhere are often recruited as 'Principal Investigators' of the trial for their hospital site and lead the clinical trial on their own patients, blurring the boundaries between research and care. Those who are not diagnosed or identified while the clinical trial is enrolling, or who don't meet the trial inclusion criteria, wait and hope for access at a later clinical trial stage or when the drug is approved on the market or try to seek compassionate access to the investigational drug (see Hyry et al 2015). By the time the drug is funneled into mechanisms for reimbursement and access, many patients have either already received the drug through clinical trial or have been "waiting desperately" to access it, to use a phrase often uttered by one of my rare disease parent research

participants. What bioethicists call the ‘therapeutic misconception’ is especially heightened in rare disease, where experimental treatments are often explicitly positioned as care rather than research (see for example Aartsma-Rus 2011).⁶

Patients access the drug through the trial, and appreciate the benefits they see and feel, if any (or at least their parents do) and access to the drug starts to be what one parent called the ‘new normal’. Depending on the trial design, and which phase of the trial a patient starts on, participation in a trial can last just a few months up to several years. Trial participants are kept up to date on the progress of the study. Meanwhile, patients and/or their families and caregivers develop their own hypotheses about how the drug is working (often noticing changes not being studied and tracked in the trial). One parent, Kelsey, has a child enrolled in a clinical trial. She emails me and close family and friends posters and datasets sent to her by the lead trial doctor letting us know which patient number has been assigned to her child of the 16 patients in the trial, so we can look for him on the graphs of preliminary trial data. Patients and/or their caregivers and families start to ask questions: what happens after the trial?

At these stages, the biggest threat to a drug’s viability and passage through the clinical trial process is safety. Several major adverse events can spell the end of a drug, though the difference between a true adverse event and the natural course of disease can be difficult to determine in a small patient sample (Sardella and Belcher 2018). It is also difficult to tell someone whose disease is killing them anyway that an experimental drug may harm them (Morel et al 2016). My research participants often commented that regulatory standards around safety

⁶ This has become a large controversy in the United States as well, particularly with the disputes around the recent implementation of Right-To-Try legislations which allows patients to bypass the FDA approval hurdle and access experimental medicines even if not part of the clinical trial.

are often considered to be more ‘relaxed’ for rare disease drugs than for other drugs, likely, they hypothesized, because the sooner a patient gets on regular treatment the sooner they can intervene in the natural course of often devastating diseases. Recently, the Food and Drug Administration in the US came under fire for an overly relaxed approach to rare disease drugs—an inquiry review of 148 drug applications found that in over 60% of cases FDA reviewers did not capture adverse event data, alongside approving drugs when there was missing information or other flaws in the application (GAO 2018).

Meanwhile, the general manager and other employees of Canadian subsidiary offices of a biotech or pharmaceutical company are continuing to generate momentum and hope around the drug’s potential through press releases about the drug’s results at each stage and close relationships with the patients and families in the trial. The company’s head office (if the company is not headquartered in Canada) decides which markets to ‘launch’ in first, usually those countries without strong pricing control mechanisms, so that they can fetch the highest price possible against which other countries’ list prices will be set. Currently, Canada is considered an ‘early launch’ country, so the process of gaining entry into the Canadian market informally begins even before the trial ends, for example through the establishment of patient support programs and relationship building with patient advocacy organizations. As one market access specialist in a large pharmaceutical company with an extensive rare disease portfolio explained to me in our interview: “the public price isn’t very heavily regulated, so Canada gets drugs launched fairly soon.” Drug prices in Canada are regulated by the Patented Medicines Pricing Review Board (PMPRB), a federal independent quasi-judicial pricing regulation agency composed of physicians, lawyers, and pharmacists who oversee PMPRB directorates. Recent

changes to drug pricing regulations in Canada aim to lower the public listing price of drug in Canada, which I'll elaborate upon later on.

Some patient advocates that I interviewed or interacted with in my research argue that a favourable regulatory launch environment in Canada will encourage more rare disease drug clinical trials to take place in Canada, and, since patients are already on the drug through the trial, will offer extra encouragement for the company to launch in Canada. However, this line of thinking has been disputed by a group of prominent rare disease clinicians who are often contracted to run rare disease drug trials in Canada (Greenberg, Mackenzie, and Sirrs 2019). Companies, they argue, need rare disease patients to make their sample size, so Canada should not be intimidated into thinking that Canadian patients will be overlooked if stronger pricing regulations are put in place. No matter who is right or wrong about this, the argument about how individuals will suffer from lack of access to (unproven) drugs if the collective system universalizes or strengthens is embedded in a powerful moral politics that intensifies at this stage.

If Canada is selected as a 'launch' country, the company begins preparing their submission to Health Canada for regulatory approval in order to gain authorization to sell the drug in Canada. They also begin their submissions for Phase 4 of the life cycle—market access and post-market monitoring. Sometimes, Canada is not selected as a 'launch country' at all, with only 48% of all new medicines launched in Canada from 2009 to 2016 (PMPRB 2019).

Besides priority review and coordinated submission standards with other regulatory agencies, one thing the pharmaceutical and biotechnology industry associations want from Health Canada is extended market exclusivity of 7-12 years after regulatory authorization as is granted to drugs with orphan designations in other jurisdictions. They argue that Canada's

current framework prevents Canadians suffering from rare diseases from accessing treatment because companies overlook the Canadian market because they will not receive large enough returns over time (see for example BIOTECanada 2015: 4). However, Canada does provide eight years of market exclusivity and has since 2006, with optional conditional 6 month renewals—but the drug has to meet the definition of an “innovative drug”, meaning a fully new chemical or biological entity. This means that a manufacturer cannot resubmit the same entity under a different indication or modify it slightly and receive renewed market exclusivity. They also cannot repurpose a drug and expect special privileges from the Canadian market. Some rare diseases are treated with simple formulations like creatine or older chemical compounds long off patent—so the Canadian market prevents market exclusivity for those formulations that then get put through trial and marketed at high prices. This type of practice has been identified as an issue in manufacturer practice around orphan drugs in other jurisdictions (Karst 2017; Feldman 2018), though whether it’s a problem or not will depend on who you ask.

In contrast to Canada’s eight years of marketing exclusivity, the EU, Japan, and Taiwan provide 10 years of market exclusivity. The US provides seven years, and Australia five years, but the product does not have to be innovative. In November 2018, the new North American free trade agreement ‘Canada United States Mexico Agreement’ (CUSMA) was signed. CUSMA extended Canada’s data protection on biological drugs from 8 to ten years, but has not yet been ratified. Beall et al (2019) estimate that the financial impact of this on Canadian drug expenditure will be an increase of \$410 million annually (range: \$40 million to \$1.4 billion) to the Canadian health care system.

The safety and efficacy data is then submitted to Health Canada for regulatory approval, a process that can take up to a year and sometimes more. Manufacturers lament this ‘lag’

because in the meantime, the ‘patent clock’ is ticking (and suffering patients waiting). If approved, the drug gets issued a Notice of Compliance (NOC) and a Drug Identification Number (DIN). This is marketing authorization only: it does not mean that the drug will actually be funded by any public body, but it may be prescribed. If a manufacturer chooses not to pursue the Canadian market, but has been issued an NOC by a similar regulatory authority in another jurisdiction, the drug can be prescribed through Health Canada’s Special Access Program (SAP), though there’s no guarantee that any public plan will pay for a drug brought in through the SAP program.

What do these practices at these stages of the social life of a rare disease drug do? These phases are about narrative and power building by drug manufacturers as much as they are about data collection. A disease that may not have had any treatment options before becomes reconfigured as something treatable through the trial (this was the case with many enzyme replacement therapies for some forms of Mucopolysaccharidosis, for example, which I turn to in Chapter 4). Along with treatability comes the accompanying narrative of pharmaceutical progress as alleviating patient suffering in profound and important ways. Pressure is put on the federal governments to structure the regulatory system to ensure that they will be an ‘early launch’ country so that Canadian patients will get access, otherwise they will be overlooked and left alone in their suffering. Biotechnology and pharmaceutical companies present themselves as the entity adopting the orphans, whereas the regulatory state is leaving them out. Being an early launch country, however, depends on turning a blind eye to monopolistic business practices. For patients in the trial, (or those hoping to access the drug as soon as possible after the trial), the drug has become intimate and personal, the possibility of it getting taken away (either by the trial

being unsuccessful or through lengthy funding delays) leads them to ally with the pharmaceutical company or advocacy group who will tangibly help them.

3.4 ‘Setting the terms’ at Phase 4: market access, collective scrutiny

Phase 4 is when drugs officially enter health care systems: in pharmaceutical industry lingo, this is called ‘market access’. In Phase 4, clinical trials are sometimes still being conducted, but these are ‘post-market’ studies that aim to gather the kind of data that payers want, such as quality of life and pharmacoeconomic data. A Phase 4 trial also extends the time that patients can access the drug while manufacturers work to make sure that public payers will pick up the tab for it at some point in the near future. Otherwise, companies also set up ‘compassionate access’ programs to provide access to patients while the price and terms of market access are being negotiated between governments and manufacturers. It is at this point that we start to see the proliferation of a different sort of strategies than those characteristic of the promissory narratives of pharmaceutical capitalism and a shift in focus to health system pragmatics. In the following sub-sections, I will show how the competing frames between ‘suffering individuals’ and ‘the sustainable collective’ become a part of the way social actors morally and pragmatically make sense of rare disease and work to redirect their meaning around the Canadian public interest.

3.4.1 Drug pricing regulation

Any new drug that passes regulatory approval in Canada must then pass through a number of processes designed to regulate their movement and pricing through the public health care system. The first of those processes is the one run by the PMPRB, which regulates drug

prices in Canada. Before the PMPRB was instituted in 1987, Canada had a system of compulsory licensing under the Patent Act, wherein individuals or corporations could apply to manufacture a drug under patent elsewhere in Canada and, after 1969, to import copies of patented drugs manufactured under compulsory licensing elsewhere, paying a fee to the patent holder. In the 1980s, Conservative Prime Minister Brian Mulroney enjoyed a close relationship with the US and was an ally in the Cold War. In the development of the Canada-United States Free Trade Agreement (CUSFTA, 1987) and the North American Free Trade Agreement (NAFTA, 1994) in the 1980s and early 1990s, the Mulroney government severely restricted the system of compulsory licensing, although they denied that substantial public pressure to do so from the US had anything to do with it (Lexchin 1993: 150-152).⁷ In 1991, the Canadian government eliminated it entirely and increased patent protection to up to twenty years. The public health care system (as described in Chapter 1 a tentative agreement between different interests and visions of Canada's future) was impacted by these global economic alliances which the health care system managers at various federal and provincial levels had to balance then and as they still do now.

In 1987, the Patent Act was altered to a system of comparative price review, along with the regulation that the price of drugs cannot increase more than the consumer price index among other measures. The PMPRB was established to manage this and uphold the Patent Act with respect to medicines. In comparative price review, the PMPRB board compares list prices of patented drugs in Canada with a 'basket' of seven countries. In an effort to increase

⁷ Canada's status as a high income country is heavily dependent on trade with the US, a major market for Canada's natural resources.

pharmaceutical investment in Canada, in 1987 the PMPRB elected to use states that pay higher drug prices as their comparison countries. The patented medicine industry lobbying organization, called RX&D at the time (a shorthand for ‘Research and Development’, now called Innovative Medicines Canada), promised to invest more pharmaceutical development in Canada for doing so. However, that promise was never realized and now, Canada pays the third highest drug prices in the world, after the US and Mexico, with what some see to be little return from industry (Morgan 2019). Opinion pieces by industry leaders and reports by pharmaceutical lobbying associations, or industry funded think tanks however, stipulate that facilitating high levels of profit is necessary for continued innovation (e.g. Tambuyzer 2010; BIOTECanada 2015; Rawson 2018)

Currently, the PMPRB’s comparators are the US, the United Kingdom, France, Germany, Switzerland, Italy and Sweden. In August 2019, new drug pricing regulations were passed to remove the US and Switzerland from the comparator basket and add seven other countries that pay lower prices for patented drugs resulting in a lower reference price—Australia, Belgium, Japan, the Netherlands, Norway, South Korea, and Spain. Increased reporting of rebates, discounts, and gifts to clinicians and patients will also be mandated, as would consideration of cost-effectiveness/cost-utility data (currently outside its purview). Industry and some patient groups lobbied strongly against these changes on the basis of claims that they will make it so that fewer drugs ‘make it’ to Canada because manufacturers will elect to forego the Canadian market altogether. A report sponsored by an industry lobbying association, Innovative Medicines Canada, threatens that “the potential for a negative impact on launches of innovative drugs in Canada is not insignificant” (Ernst and Young 2019: 25). After the new regulations were passed by the federal government in early August 2019, the Canadian Organization for Rare Disorders

(CORD, one of the major players in rare disease advocacy), released a press release stating that “new federal drug pricing regulations mean disaster for Canadians with rare diseases” (CORD 2019). The new regulations are slated to go in to effect in July 2020. On August 22nd 2019, a group of pharmaceutical companies filed a constitutional challenge against the federal government’s right to set ceiling prices for patented medications.⁸

What does drug pricing regulation do? If we’re thinking along the lines of ‘perspectives’ it depends on who you ask. A pharmaceutical company representative might say that drug pricing regulations impede innovation and restrict patient access. A drug payer might say that it allows more patients with rare disease to get treatment because it stretches the budget further. If we avoid getting mired up in ‘perspectives’ and instead focus on practices, however, we see that the industry way of ‘doing’ care for rare disease—through the development of treatments on the free market—depends on the burying of cost concerns and the restructuring of patent laws to do so. Partly this is achieved by embedding the role of intellectual property protections into a state’s national economic objectives and relationships (Gold 2013). This enactment also involves threats: to bypass, to leave behind and abandon people who are desperately ill.

⁸ Industry attempts at dismantling the PMPRB are not new. In 2015, the drug manufacturer Alexion was charged with an excessive pricing allegation for Soliris, a drug that treats two serious rare blood disorders, Paroxysmal Nocturnal Hemoglobinuria and Atypical Hemolytic Uremic Syndrome, which is estimated to cost over \$800,000/year. In retaliation, Alexion attempted to raise a judicial review of the PMPRB to contest it’s authority to regulate drug prices under the Patent Act but recently the PMPRBs allegation of excessive pricing was upheld [Alexion Pharmaceuticals Inc. v. Canada Attorney General, 2019 FC 734].

3.4.2 Health technology assessment and the Common Drug Review

The next stage in the social life of a rare disease drug is the Common Drug Review (CDR) process, which is run by the Canadian Agency for Drugs and Technology in Health (CADTH). CADTH is an independent non-profit health technology assessment (HTA) agency, but is funded by Canadian provincial and territorial governments, the federal government, and through application fees paid by manufacturers to have their product assessed. All provinces and territories pay into CADTH and will not consider a drug until it has been assessed by their drug review processes, with the exception of the province of Quebec which has its own HTA process and agency run by the l'Institut national d'excellence en santé et en services sociaux (INESSS)⁹. CADTH was founded in 1991 under another name, the Canadian Coordinating Office of Health Technology Assessment, with a modest budget of \$500,000 per year for the first three years and a focus on medical devices. In 2002, CADTH expanded its HTA activities into HTA of drugs and started the CDR. CADTH's 2018 budget was over \$30,000,000.

As described in Chapter 1, health care in Canada is delivered provincially/territorially using funding transfers from the federal government and internal revenues through taxation and/or premiums. Health care is delivered by the federal government only for some defined

⁹ While there is no one definitive answer 'why' Quebec has its own process, there are several factors that help contextualize it. In many ways, Quebec going its own way (with drug review and with some other issues related to health care as well) reflects the constitutional division in responsibilities between the federal and provincial governments. Quebec has a different colonial history and settler identity than the rest of Canada (French rather than English), and asserts itself as a distinct society. In general, the provincial government has tenuous relationship with what Quebecers call the 'ROC' (Rest of Canada) and there have been two referendums for separation. Thus, Quebec clings strongly to its constitutional provincial powers to keep its independence from the federal system at all levels of decision-making and social programs. For example, Quebec also has its own provincial pension plan that operates similarly but separately from the Canada pension plan.

populations (including war veterans and First Nations people living on reserve). The role of CADTH's CDR process is to issue recommendations to provincial, territorial, and federal drug payers. Since pharmaceuticals provided outside of hospital are not mandated by the Canada Health Act, provinces and territories have limited public drug plans for defined populations: senior citizens, cancer patients, or low income people, for example. Everyone else either relies on a private extended health care plan (usually through an employer) which funds about 36% of drug costs Canada-wide, or pays for drugs out of pocket, covering 22% of prescription drug costs in Canada. Four percent of costs are funded through social insurance policies such as worker's compensations claims (Canadian Institute for Health Information 2013). In general, a private health insurance company will not cover any drug that is available on a public formulary. Thus what does and does not get placed on a public formulary, feeds into this other sphere of dynamics, and demonstrates the financial high stakes of the rare disease space.

Before initiating the CDR process, the manufacturer is invited to arrange a 'pre-submission' meeting with CADTH to help ensure their submission includes all the relevant and required information. The submission must include clinical trial data, a pharmacoeconomic evaluation, a budget impact analysis, and an application fee. CADTH invites patient groups to provide 'patient input' on the drug in question which is then collated and summarized by CADTH staff. Once submission materials are complete, the Canadian Drug Expert Committee (CDEC) meets to review. CDEC is composed of up to 14 members, with up to 12 'technical experts' such as clinicians from various areas of medicine and pharmacists, as well as two 'community' members. 'Non-member' specialist experts, such as health economists or a clinician specializing in the disease for which a drug is indicated, may be invited to participate but do not have voting rights. CADTH (2019: 9) describes CDEC meetings as a "deliberative

framework and process” that “takes into consideration the following information when issuing recommendations and advice:

- Patient group input
- Clinical studies demonstrating the safety, efficacy, and effectiveness of the drug compared with alternatives
- Therapeutic advantages and disadvantages relative to current accepted therapy
- Cost and cost-effectiveness relative to current accepted therapy.”

The committee then issues ‘non-binding’ recommendations to provincial, territorial, and federal drug plans. The CDR process is the same for rare disease drugs as it is for common drugs, which is a point of contention for some patient and industry groups in Canada who feel that rare disease drugs should have their own process with lowered evidentiary standards and reduced consideration of cost-effectiveness.

Some also find that the CDRs requirement of effectiveness data (data on how the drug performs in the ‘real world’ on patient, provider, and system levels), in addition to efficacy data (how the drug performs in the controlled environment of the trial) should not be required for rare disease drugs as effectiveness data takes longer to collect. As Singal, Higgins, and Waljee (2014) note, however: “the distinction between these two types of trials is important but often poorly understood.” As one pharmaceutical company CEO lamented when he came to visit the health policy unit while I was conducting my fieldwork there: “the clinical trial was good enough for Health Canada, why isn’t it good enough for CADTH?” indicating that he might not fully comprehend that public drug payers require different types of data points for their decision-making. Diana, the director of the policy unit retorted: “well they wouldn’t care so much if the drug wasn’t so expensive!”

This brings us to cost-effectiveness and cost-utility analysis. One of the ways that the cost-effectiveness of a drug is determined is by looking at the quantity and quality of life derived from an intervention using the cost per 'Quality Adjusted Life Year' (QALY) formula. Health economists usually make this advanced calculation, and pharmaceutical companies are required to include this information in their submission to health technology assessment agencies who then scrutinize the industry calculations. At its simplest level, cost per QALY is the cost of the drug in relation to the rating of the estimated health of the patient while taking the drug according to what the drug has been proven to do in the clinical trial data. The 'patient perspective' is folded in as understood through population level data on patient reported 'quality of life' preferences gathered through surveys such as the EQ-5D (<https://euroqol.org>), which generates utility values according to preferences for different health states around mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Individuals elicited to provide their preferences for different health states through choosing between three levels (no problems, some problems, and severe problems) which generates different combinations of health states (245 in total, not including unconscious and dead). Using a cardinal scale of 1-0, utilities measure intervals between 'death' (being 0) and 'full health' (being 1). A calculation of less than 0 indicates a health state that is worse than death. These 'preferences' for different health states ('health related quality of life') as determined through the EQ-5D scales are then compared against what the trial data has been proven to do in actually improving the health state of the patient taking the drug. The QALY is then calculated through a distinct temporality: the amount of time spent in a health state gets multiplied by the utility score calculated through the EQ-5D. Finally, the QALY achieved through treatment is compared against the cost of the drug, creating a dollar value per QALY achieved.

Pols (2019) has explored how looking at the patient experience through utility measures is an extremely simplified (albeit extremely technical) way of understanding both ‘value’ and life with disease, which turns life with disease (which is a process) into an event that can be weighted by a preference frozen in time (Pols and Limburg 2016). However, it is embedded in a certain configuration of politics between state health care systems and industry: this simplified measure permits the value of treatments to be debated through this technical rationalized frame. It permits systems to set a ‘threshold’ for what they consider fundable—a commonly referenced though unofficial threshold in Canada is considered to be \$50,000/QALY. Rare disease drugs can be expected to cost around \$650,000 per QALY, far above this informal threshold (Neumann, Cohen, and Silver 2018). I will return to the embeddedness of this particular way of understanding and quantifying ‘quality’ around life with disease in relation to costs in the next section, and again in Chapter 7.

In recent years, CADTHs CDR recommendations have changed their tone in rare disease drug recommendations: rather than issuing a ‘Do Not List’ recommendation, unless there are glaring faults with the drug they issue a ‘List With Conditions’ recommendation, with one of those conditions being a substantially lowered price (McCormick, Berescu, and Tadros 2018). This change signals the pragmatic creativity of CADTH actors, because it shifts the narrative from ‘the drug is bad’ (which patients contest) to ‘the drug is too expensive’ (which manufacturers contest, but then the onus for lack of access is pinned on their practices).

In 2010, a new dimension to the social life of a rare disease drug was instituted: the pan-Canadian Pharmaceutical Alliance (pCPA) and which loops in to this CDR practice change. The pCPA is composed of public drug payers who have formed this alliance to negotiate a ‘bulk purchasing price’ with pharmaceutical manufacturers, effectively adding another layer of drug

pricing regulation outside of the difficult legal framework of the Patent Act. This is an especially important process for rare disease drugs: each province may have one or two patients, but if all the public drug payers (federal, provincial, and territorial) negotiate a price together for all of the rare disease patients in Canada, there is more power to lower the price. After the CDR process, and before provincial reimbursement decision-making, they negotiate. Since the costs are already ‘sunk’ for the manufacturer, so to speak, they usually do participate in the process—but it takes time. However, in the meantime, patients and patient advocates are trying to push past this system, because as one mother explained to me, “our kids don’t have a lot of time.”

What does HTA at the CDR level do? By placing ‘rare’ disease into the ‘common’ drug review, the CDR disembods data from the affectively charged enactments around the rare disease drug. HTA ‘disentangles’ the data from the affective context of its development and makes it stand for itself (Moreira 2007). The QALY calculations shift the focus away from the person with disease, and towards issues of sustainability, affordability, and ‘value for money.’ This phase of the social life of a rare disease drug refuses to favour pharmaceutical company enactments and promissory rhetoric. However, the tension comes in: what about patient enactments? What if they are the same as pharmaceutical enactments? No one knows what to do or what the implications of opening this too far and wide will be. The CDR process also does more than this disentanglement of industry-led meaning. CADTH and the CDR posits a gesture of a strong and unified nation state—a symbolic expression of public drug plan ‘togetherness’ in a country that really has fourteen separate health care systems (10 provincial, 3 territorial, and 1 federal) operating simultaneously. This centralized process within a decentralized system posits an epistemic and symbolic unity to the rationalization and standardization of the meaning of a rare disease drug before it enters the real arena of ontological politics: decision-making.

3.4.3 Drug reimbursement decision-making and market access

The CDRs recommendations are non-binding, so public drug plans often do their own evaluation of drugs before deciding how to deal with them. Because of the particular complexities of many rare metabolic diseases, where there is no ‘average’ patient to base decision-making on, many public drug plans make rare disease drug access decisions on a case-by-case basis rather than making a formulary decision for a whole population. This practice change however confronts them with a dilemma: they want to treat everyone and give everyone a chance but they also want to be consistent in their decision-making for all disease groups. Most of the public drug plan managers that participated in my study were former clinicians (usually pharmacists), and reported that rare disease decision-making and policy-making tugs at these different aspects of their professional identity. As one former public drug plan manager who had been a clinician before that reflected in our interview together:

You know, as a clinician you’re typically very focused on individual patients and what they need, and trying to manage their care and optimize the care of that individual patient. Whereas when you’re a policymaker, you’re expected to make decisions on behalf of the entire population that you’re serving, and so you end up going from sort of an n of 1 kind of an environment to an epidemiologic kind of approach to things, where by definition there are going to be people, in the tail ends of the curve, who are not going to be covered, their needs are not going to be addressed 100% of the time [...] So it’s a very different mindset, and you have to... as a policymaker the expectation is that you have to pull yourself away from what individual patients need, and deal with the entire population.

This former drug payer is indexing that there are different ontological frameworks around care in these different positions: as a clinician you focus on the individual, but as a policymaker, you have to step back and focus on the collective.

The models and metrics of HTA and cost-effectiveness/cost-utility analyses are incomplete and pragmatic solutions—but those thrust into these ontological politics find them

helpful tools to distance themselves from these double binds caused by high drug prices. In Moreira's (2012b) 'biography' of the QALY, he argues that "the QALY is both an expression and source of the epistemic and institutional debates around putting health care within an economic frame" (pp 64-5). The impetus of the normative approach of the QALY was driven by a desire to make resource-allocation decisions in a more systematic way—rather than, as one of my health economist research participants phrased it in our interview, "willy-nilly." As Moreira writes: "this way of thinking was ethical in that it provided a means through which it was possible to rise above particular interests and viewpoints and establish a level playing field in the discussion" (78). However, Moreira shows how even more integral to the uptake of the QALY in the 1990s was something else that it offered: impersonal standards. Even if proponents recognized that the QALY is methodologically incomplete or doesn't take the full complexity of the social world or inequalities into account, it allows a distancing from the emotional dimension of making a decision by turning it into a technical question.

The QALY is embedded in Von Neumann and Morgentsern's (1944) game theory, which Moreira (2012b: 72) describes as "part of a wider cognitivist approach to understanding human, social, and political behaviour." Underpinned by computational metaphors rooted in the idea of "human subjects as governed by symbolic logical processing and machines as thinking tools" (ibid.), this arm of health economics worked hard to stabilize complexity and meaning and affect by turning "a political, ethical question into a technical one ... assuming that people made decisions about health in a rational way" (Moreira 2012b: 74).

The public drug plan managers who participated in my research are well aware of the flaws of this artificial model of themselves, but the supposed objectivity and neutrality of the QALY has become an important political mediator in willingness to pay discussions with

industry. Most also appreciate the QALY because it helps them understand the consequences of funding. This ethical frame, derived from health economics, is that of opportunity cost: the idea that the true cost of something is what you aren't able to purchase because you spent the money on something else. In my research and in general in the health economics literature, some health economists take a strong view of opportunity cost and cling strongly to it, others use it more as a thought experiment, others don't think it should be used so much at all. However the framework is commonly invoked and the sanitized normativity of the framework has power to shape the terms of the discussion.

I share a scene here from a meeting that I attended to illustrate how opportunity cost figures into the sustainable collective ontology. Dr. Mike Paulden¹⁰ is now an Assistant Professor of Health Economics at the University of Alberta—at the time, he was a PhD student there. In his presentation at this meeting, he took the audience through a series of slides representing hypothetical scenarios of winners and losers. On each slide, there were two sides: the winning side, and the losing side. The winners are represented by stick figures of human beings: a man standing upright, one in a wheelchair, one using a cane—they are given form because we know who they are. They are identifiable—the rare disease patients publicly requesting access to treatment in the media. The losing side is represented by a question mark, because those people are not identifiable, they are unknown—they are not publicly requesting technology because they do not know or do not yet know that they need it. The first slide represented what he believed to be the current situation in funding expensive rare disease drugs:

¹⁰ When I contacted Dr. Paulden asking him if I could share this scene where he was presenting he consented and requested to be identified and that the image I share here from his presentation be credited.



Figure 2: “Winners and Losers.” 2015. Adapted and reproduced with the permission of Dr. Michael Paulden.

The winners win because their technology is funded. This provides health gains of 100 QALYs, which is great for them. However, this means that unidentifiable patients will have their technologies and interventions defunded. They are the losers. By virtue of their identifiability, rare disease patients win. This is ethically problematic, he argued, because true equity would mean that unidentifiable populations—ones without immediately identifying characteristics or faces—may not have things that could benefit them funded. Their health care is displaced in order to pay for the technology for the identifiable population. The only way to equitably allocate resources towards technologies within a universal system is to use an objective and impersonal formula that maintains anonymity such as the QALY.

This framework works by assuming that the impulse to care for an individual who is suffering is a switch that can be turned off by circuiting into a rationalist discourse. In his presentation, Dr. Paulden postulated that society’s main values include a preference for population health, as well as a concern for equity in resource allocation. The admittedly imperfect but only way to meet those values, he argued, is to set QALY thresholds that funded

technologies must meet. If they don't meet those thresholds, then in the interest of equity and fairness the technology should not be funded.

During the question and answer period, a clinician who treats rare disease patients raised a question: "I understand what you are saying here, I really do, but when I have a child really sick in front of me I am not really thinking about this stuff, I'm thinking about what I can do for this patient in front of me at that moment." In response, Dr. Paulden posited that decisions about whether the technology should be made available should be made before the doctor confronts the situation of the dying infant. The clinician looked dissatisfied, and as he expressed to me later: once you know about a technology that could help, you cannot un-know about it.

A number of patients and patient advocates that I interviewed had tactics that explicitly counter this position of impartiality. That is, they make themselves—and their suffering—highly visible. Take for example a patient advocate named Joey's tactics. Every time a child is diagnosed with a treatable form of the rare lysosomal storage disease called Mucopolysaccharidosis in Canada, an underground advocacy network springs into action. Journalists are asked to write news stories, Twitter and other social media accounts get fired up, and a meeting between the family requesting treatment, a clinical expert, and the provincial drug plan manager is requested. The goal, according to Joey, the leader of this advocacy process, is to draw attention to the emotional side of the case by making the patient requesting the drug highly visible—impossible to ignore. "You know what?" he said during our interview together one cold January morning, "when it comes down to it, my side wins every time, and it always will." I asked him why. He replied:

Well, because in the end, all decisions need to come down to true human emotion. No matter what. And health economists will tell you no, it's not, it's about numbers, but that's not the truth. Because in the end, they're still going and making a life or death

decision for a child for a child, an earth shattering life changing decision for a family... You have bureaucrats taking their time making decisions while that disease is ravaging a little boy when we can stop it. And if that ever goes public, who is the public going to believe? They're always going to side with that human, emotional connection that they have to people. And that's why we'll always win.

Joey is a parent of a child with a rare disease called Mucopolysaccharidosis Type VI, a progressive-degenerative genetic disorder caused by a deficiency of the enzyme arylsulfatase B that can lead to inflammation of the tissues and organs, skeletal dysplasia, cardiac problems, spinal cord compression, and premature death. His experience of fighting for access to treatment for his son led him to leave his job and pursue this advocacy pathway full time. Joey's tactic is to bypass drug decision mechanisms and work on behalf of individuals, and he does so through exposing the perceived unfairness and stinginess of the system: "for me, to be able to exploit this idea that Canada is this free and loving society and by putting the picture of beautiful little girl who's going to die without access to therapy and the only thing stopping it is dollars and cents, that's when people get afraid." Joey's mode of asserting the primacy of an individual patient's suffering over attempts to rationalize these difficult decisions is an important way that rare disease is brought into being and made to matter. He draws on Canada's national self-image as 'free and loving' to make his case.

One of the frameworks enacted manage the difficulties of priority-setting in general and the individual/collective tension in resource allocation is that of 'Accountability for Reasonableness' (A4R), developed by American philosophers Norm Daniels and James Sabin (1997). Many of the public drug payers and health policy thinkers that I interviewed or met through participant observation mentioned that they at least *try* to use this as a guiding framework in rare disease decision-making. A4R is a procedural justice framework that holds that so long as the process of coming to a decision is transparent and fair, then the decision is

legitimate. The A4R framework is derived from the philosophy of John Rawls (1971). Rawlsian moral philosophy holds that all decisions should be made from behind a ‘veil of ignorance’—by not knowing the characteristics of the individuals, the decision-maker won’t get caught up in bias or emotion and ensure equality of decision-making. Accountability for Reasonableness attempts to overcome the “impracticality of impartiality” (Friedman 1989) by filtering decisions through agreed upon procedure. Through procedure, we become ethical and do good to one another. As Daniels (2000: 1300) writes:

In pluralist societies we are likely to find reasonable disagreement about principles that should govern priority setting... In the absence of consensus on principles, a fair process allows us to agree on what is legitimate and fair... Fair procedures must also be empirically feasible. They must involve practices that can be sustained and that connect well with the goals of various stakeholders in the many institutional settings where these decisions are made.

Where in the veil of ignorance model of Rawls the decision-maker is impartial because they do not know the characteristics of the recipient of the decision, in A4R, the characteristics of the recipient of the decision are filtered through an agreed upon process, removing bias.

A4R helps public drug payers overcome discomfort with the case-by-case decision-making models in rare disease drug access. As one public drug plan manager shared with me: “you might disagree [with the decision] but at least you can see we considered all these things and we came up with this decision, there’s a lot of value in the recipients of the decision being able to say ‘yeah, you did do a fair process.’¹¹ However, public drug plan managers know that the world is not so simple. As one shared with me in an interview:

¹¹ A number of studies have queried whether Accountability for Reasonableness is acceptable or achieves its fairness objectives in the Canadian system at various levels. See for example Martin, Giacomini and Singer 2002; Martin et al 2003; Gibson, Martin and Singer 2005; Mitton et al 2006.

The challenge is in a rare disease space you have identifiable individuals whereas media about broader disease states isn't about an individual. It's much easier in a rare disease space to tell a story about the cute little girl with pigtails and that's what draws people's attention and compassion. How could possibly this big bad horrible organization that is government, which is nameless and faceless, say no to this beautiful child and deny her opportunities? [...] I wouldn't want my children on the front page of the newspaper but if it was my child with the condition I can guarantee you my child will be on the front page of the newspaper, so again it's one of those trade-offs that until you're in that situation never say never, right?

Intuition, unfairness, and emotion rub uncomfortably against this modified version of impartiality, which is partly what makes Joey's strategy so successful. If the patient's appeal goes to the media, often the Provincial Minister of Health—who is a member of the political party subject to re-election, whereas the drug plan managers are a member of the public service unaffiliated with any political party—will issue a directive from above to fund the drug. It doesn't matter what rationalized process the drug plan managers have come up with to try and decide on a particular case.

Drug manufacturers and their lobbying associations also intervene here. They are charged with making sure as many patients get access as soon as possible. For some, this is seen to be an important moral issue, as this general manager of a Canadian subsidiary office expressed in our interview: “the question really comes down to, how much do we value a life?” Canada, he said, is characterized by inertia—they want common systems to work for all. Bureaucrats operate on the unfounded fear that the system will collapse if they fund rare disease drugs, but other systems have figured it out by creating rare disease drug policies. So why can't Canada get their act together and fix it? This general manager and I had both recently attended a luncheon on rare disease drug access in Canada at a fancy hotel in downtown Toronto, well attended by industry. As we sat eating our expensive lunch, expensive linen napkins covering our laps, the opening moderator had said: ‘what we are going after here is addressing extreme human suffering.’

“Remember when the moderator said that at the luncheon the other day,” he reminded me during our interview: “That’s the sentiment I think we should be modelling.”

Others at ‘lower levels’ of the company, on the other hand, report that the pressure that drives these sorts of statements can be intense, especially in smaller companies with a lot invested in the success of a single drug product. As one market access specialist in a pharmaceutical company reflected on these high stakes in our interview, “you’ve got to try and keep everything afloat basically, and so you do push it harder than you probably should, you make claims with payers that are stretching the data more than it can be reasonably stretched.” But the point is to edge into the definition of ‘reasonable’ with drug payers. He mentioned that there is a point where they stop trying, but often they are able to find some point of negotiation: “Sometimes what you try and do is kind of work on the shadings of a decision, so sometimes the decision isn’t a no, it’s just highly restricted, so sometimes there’s some scope to work on, okay we can agree and we need to set some boundaries, could the boundaries be like that?” Another employee of a pharmaceutical company who also works in the market access department expressed that she doesn’t see these politics as sustainable, that one day things will come to a head if solutions aren’t found. As she expressed: “You know, I can sit here and say that the values that are really important are individuals and that we should be providing access to drugs that will save people’s lives... but I don’t want to be in that position, and I’m sure you wouldn’t want to be either.”

What does this phase in the social life of a rare disease drug do? It is in this stage that we see a proliferation of enactments, and a range of strategies and contestations to try to stabilize either powerful ontological and moral frame. Models of the rational choice making decision-maker and moralized and normative frameworks and languages of opportunity cost enact a version of the world that is impartial, unaffected—even if those who make these enactments

know they are more like costumes or ‘hats’ they put on to deal with the situation. These are then countered by advocacy tactics and market access strategies that slip into the cracks and emphasize partiality and emotion. Each enactment attempts to stabilize the rare disease drug in the circulation of meanings that it has for different actors. At this point in the rare disease drug’s social life, it has been socialized through this tension between opening its market through affect and closing it through impartiality. It has come to reflect the competing values between ‘relieving the suffering individual’ and ‘protecting the sustainable collective’.

3.5 The health policy unit: bypassing company lines and working through double binds

In this section, I introduce the health policy unit where part of the ethnographic fieldwork for this study was conducted. The health policy unit is located in a university, but receives grants from the government to conduct health technology assessments on new medical devices—they come in at Phase 4 of the social life/life cycle described in the previous sections. Their own unit’s work doesn’t focus so much on drugs, but their wider policy and academic work has been looking at the values questions and conundrums around rare disease drugs for several years. Most provinces have a similar set-up, where HTAs are conducted more regionally after the pan-Canadian process is complete to assess the value for money and system and budgetary impacts of a drug or technology on the actual provincial health care system (whereas CADTH’s processes take a more general view).

In 2012, Jay and Diana, the head and the director of the unit, received a five year grant from the Canadian Institutes of Health Research (CIHR) to come up with policy frameworks for sustainable innovation pathways for rare disease drugs in Canada. Not an easy task. Their way of going about it was to commit to a holistic and ‘multi-stakeholder’ approach: bring all the

different sectors together to find a different way of doing and thinking about rare disease. Some might say this is naïve, but Jay and Diana are whip smart and highly critical—as such, they know the power of relationships in policy. They are open minded, and refuse to attach to either of the easy narratives described so far—either that of the suffering individual or the sustainable collective—and push the people they work with to also look for a different way. They are highly respected by provincial drug plan managers, patient advocates, and pharmaceutical industry representatives alike. They were deeply committed to what is called ‘patient engagement’ before it became a major health policy research trend in Canada, and are pretty suspicious of the tokenism of some of the ‘patient engagement’ efforts of research and policy groups they are acquainted with.

Collaborating with different stakeholders for them isn’t always easy, and it doesn’t mean that they always agree with what people do. Jay told me to always be wary of the company line, whether it be from payers, industry, or professional advocates. When I asked him once to define company line, he replied:

Company line to me would mean defense of the status quo of the organization, and a public persona that represents that kind of formal status quo. Justifying why the company or the organization does things the way they do... Are they presenting you with a company line, are they trying to appease you? I think it’s judging those things and you may not know right away, and you may be wrong at the end of it all. Quite often the first time you talk to someone you get a sense of, you know, you’re not on the same page with this person or their objectives are different. People in industry would tell you their objective is maybe no different than mine is, which is we want to get treatments that work to the people that need them, but then you start talking about what they’re prepared to give up in order to do that? It’s then you find out whether it’s going to be someone you can trust or not. There are people in industry I would absolutely trust, but also know they are driven by other motivations, just as they would know I am. I can talk about being on the higher ground and all of that, but being on a higher ground is a subjective ground.

For Jay, working in the ambiguous spaces between ‘company lines’ is where you can actually get work done, but you have to have relationships first with people in order to do that. He’s not too interested in polarized framings around either the suffering individual ontology or the sustainable collective ontology, and doesn’t really take part in discourses about them either way. In the following paragraphs, I share a scene where Jay did feel compelled to respond to an opinion piece in a health policy journal to counter a stark rendition of a company line.

The post-it-note affixed to the print-out next to my keyboard was written by Jay: *‘Read it with a critical eye’*. The print-out was an opinion piece in *Healthcare Management Forum* and the piece, ‘Redressing the inequities in Canadian pharmacare’ was written by Dr. D. Wayne Taylor, Professor Emeritus at McMaster University and Executive Director of the Cameron Institute. In early April of 2015, when the piece was published and this event transpired, the Cameron Institute described itself as an “alternative, not-for-profit, public policy think tank specializing in the independent study of health, social and economic issues both in Canada and around the world.”¹²

In the opinion piece, Dr. Taylor argues that in trying to be public and universal, the health care system insists on mediocrity, where “the cheap, common, and easy wins over the expensive, rare, and complex” (Taylor 2015a: 50); “a manifestation of ‘bourgeois socialism’”(52). For a truly quality health care system that is patient centered, the Canadian system must “forget about the price of drugs, forget about health technology assessment, and forget about cost-effectiveness.” Dr. Taylor argued: “replacing HTA with better drug access will be a win-win-

¹² The description of the Cameron Institute has since been removed from the website. An archived snapshot of the page can be found here: <https://web.archive.org/web/20150408131817/www.cameroninstitute.org/who-we-are/>

win: A win for patients, their families, and caregivers as financial barriers to quality care are eliminated; a win for researchers who rely upon industry investment to develop novel pharmaceuticals; and a win for taxpayers with money spent improving patient health outcomes and quality of life rather than fueling agencies that do the exact opposite” (53).

Jay and the health policy unit research staff and I chatted about Dr. Taylor’s opinion piece in the health policy unit office for a little bit, and Jay decided to write a response to the piece on the journal’s blog. Jay’s response carefully parsed apart Dr. Taylor’s argument to show that HTA is only one of the inputs in drug access decision-making in the public system, but an important one: decisions can’t be based on ‘trust me’ statements from drug manufacturers alone. With the cost of new treatments for rare and common diseases alike steadily rising, the money saved by eliminating HTA would hardly make a dent in the drug costs that could quickly bankrupt the public health care system. And then how will patients get any care at all? What was ironic about this exchange was that Jay himself is critical of HTA practice. His work the past two decades has centered on finding ways to make HTA more responsive to the complexities of new treatments and on urging HTA and public drug decision-making to be more explicit and thoughtful about values. But Jay sensed the ethos of Dr. Taylor’s argument was not really about patients, but about using the evocative frame of patient suffering to raise support to dismantle the universality of the system. And so, he felt compelled to defend the ‘system’ even as he is critical of the way that some of his colleagues within it enact their relations.

Dr. Taylor’s response to Jay’s critique was swift. He accused Jay of “scare-mongering” (Taylor 2015b), agreeing that HTA “has served decision-makers well since the whole exercise of provincial government healthcare decision-makers is one of cost-containment and not of advancing the welfare of the patient.” Moreover, a public single payer system does not meet the

needs of Canadians. As Dr. Taylor writes: “The whole idea behind Canadian healthcare was the elimination of financial barriers to expensive, catastrophic healthcare—last dollar coverage in insurance terms. But with our single payor [sic] model we have first dollar coverage—all the common, cheap stuff paid for, if we were honest, much of which many of us could afford on our own.” Dr. Taylor’s goal with his framing was not to make health care more universal and robust to make sure rare disease patients are included, but to de-universalize the system so that enough money is left over to pay for high cost drugs and leaving everyone else to fend for themselves.

“Imagine, me!” Jay said with a laugh after Dr. Taylor’s response was posted, “a scare mongerer!” The scene is instructive for understanding the possibilities for politics in rare disease drug access disputes. The language that one needs to talk about these powerful value politics outside of the polarized individual/collective explanatory narratives can almost seem to be missing—as Kim Fortun (2001: 13) describes, social actors like Jay in this situation are in a ‘double bind’: “confronted with dual or multiple obligations that are related and equally valued, but incongruent.” In this double bind, to say that he cares about patients getting access to these controversial treatments would be to imply that he doesn’t care about the health care system, and vice versa—even though both of these pigeonholes are far from what he thinks. For Jay and Diana, the goal of finding ‘sustainable’ pathways toward rare disease drug development and access means finding a way to break out of the mold proffered by the individual/collective binary altogether, not reifying one or the other side or strengthening anyone’s company lines.

Jay once told me the story of how he was invited to a meeting of another CIHR funded research team. When a prominent patient advocate who works closely with industry was invoked in a student’s presentation, the whole team booed at the patient advocate’s image on the screen. Jay was pretty shocked by this: he doesn’t always agree with this patient advocate either, but is

that how you treat a colleague, booing them when they are not there? Both Jay and Diana are committed to a different way of caring about the issues than that. Instead, in their careful imperfect ways they refuse binaries and the types of relations created by them.

3.6 Conclusion

This chapter has introduced the many different contexts and practices that a drug passes through in the development, regulatory, and reimbursement phases of the ‘social life’ of a rare disease drug. I described how social actors who develop, regulate, and reimburse rare disease drugs create frameworks and models for dealing with multiplicity and ontological politics at every stage of the drug’s ‘life cycle.’ In doing so, they socialize these drugs within the dilemmas of choice-making in the complex relationships between capital-driven narratives about ‘suffering individuals’ and impartial bureaucratized approaches to care to protect the ‘sustainable collective.’ Within these phases, the drug becomes ‘socialized’ through an oscillation: between practices that shift the register of meaning between the drugs capacity to relieve individual suffering at the beginning in Phases 0-3, and then later, in Phase 4, through practices that filter this momentum through practices that focus on the sustainability of the collective system of care.

It is through these practices that the ‘suffering individual’ narrative and the ‘sustainable collective’ narrative become ontological realities in the social worlds that assemble around rare disease drugs. Many of these practices around the ‘sustainable collective’ have been developed, imperfect as they are, to try to manage the wider tension between capitalism, market-oriented reform, and access to care and services in the nation state. Canada’s health care system has been shaped by its own constitutional division between federal and provincial responsibilities as well as by global free trade and policy harmonization ideologies (that ironically foster monopolistic

practices rather than ‘free’ trade as such). However, while these models and frameworks may hang together for large population diseases, when the population in question is small or individuals are easily identifiable, impartiality is not so simply applied. Through ontological politics, the disjunctures between ways of ‘doing’ caring for disease in pharmaceutical capitalism and in health system resource allocation get thrown into relief.

The suffering individual ontology operates around practices that emphasize the role of the market in solving social problems and improving lives through profit-centered drug development—the power of this enactment is reflected in the near complete outsourcing of drug development to the private pharmaceutical industry by governments since the early 20th Century. This history and ethos is what gives the private pharmaceutical industry the power to enact practices in the first place, and instantiation of these ideological practices through historical political currents that led to market solutions to social problems like the Orphan Drug Act. However, to maintain presence and justify actions through controversy, the morally tinged ontological framework of the capacity of these arrangements to relieve the ‘suffering individual’ has been imbricated into rare disease care disputes. It is through this ontological frame that pharmaceutical enactments argue for deregulation and the reshaping of health care systems to ensure the fluid circulation of their products through rare disease bodies, health care systems, and drug budgets. This enactment configures ‘the patient’ in certain ways. In the potent links between rare genetic disease and capitalism, being worth a high price comes to symbolize a new sort of biosocial belonging, but also generates an emergent type of precarity to the whims of political and economic currents that could impact treatment availability.

The sustainable collective ontology, on the other hand, is positioned within practices that diffuse the affectively charged suffering individual enactment and funnel pharmaceuticals

through technical processes that ‘disembed’ drugs from this narrative and into an ethos of impartiality. This has been one of the central ways that publicly funded health care systems and other arms of the welfare state have pushed back against the power and money of the pharmaceutical and life sciences industries since the mid 20th Century (Moreira 2012b), but has also generated some sticky relationships between rare disease patients trying to access treatments and health care systems trying to manage their integration. This enactment constructs a rationalized and linear model of the ‘decision-maker,’ one that even decision makers know doesn’t fully represent the actual complexities they feel in these difficult positions. This enactment configures ‘the patient’ through a rationalized frame where relationships to medicines are seen as technical issues solvable through evidence and a rational economic calculus. In Canada, a strong training tradition and ethical commitment to Evidence-Based Medicine leads to some resistance to see rare disease drugs as effective, but the concerns held by social actors enacting and upholding this ontology are often less about the evidence than they are about how the public health care system will equitably distribute care in the battle between ‘winners and losers’ of resources limited public drug budgets.

The binary between the suffering individual and the sustainable collective that social actors draw on to make sense of their own social commitments is one that does political and cultural work. By this, I mean that it shapes how social actors can conceive of rare disease drugs and what it means to care for rare disease when such complexly situated technologies bring forth such difficult types of questions. Nora’s story, wherein she became the subject of a news story that criticized her as representing the ‘suffering individual’ enactment, highlights how these politics make it difficult to disentangle pharmaceutical and patient enactments. I think this was what made Nora’s story so salient to the range of social actors that picked it up and framed it

within their own ontological frameworks: it fit neatly into either narrative, crystallizing the issues for them at the same time as it cast a child as a particular type of nefarious actor, which is really what made Annie so mad. Rather than targeting the political-economic relations that generate the situation of having to make these impossible trade-offs in the first place, bodies and lives get cast into the explanatory frameworks social actors have available to make sense of the contradictions of capitalism. Similarly, Jay's experience of being accused of 'scare mongering' when he countered Dr Taylor's proposition that the health care system would be better off if we did away with protecting the collective system altogether highlights how enactments around the 'suffering individual' depend upon framing system level concerns around pharmaceutical prices as somehow morally wrong.

At the same time as these ontologies can seem rigid, in reality they are quite porous. This chapter has also shown how many social actors are ambivalent, at least to a degree, about the worlds that they are bringing into being with their enactments, dismantling the non-porous categories of types of individuals that social get placed in by virtue of their work and the social world they enact and represent (Strathern 1988, 1991). Ontologies depend on the practices that bring them into being, but practices are enacted by people who often know they are incomplete, even if they cannot always see any way outside of them.

In this difficult setting, social actors develop models and frameworks and tactics and strategies to try and stabilize these complexities into either an ontology of 'suffering individuals' or 'the sustainable collective.' Each of these ontological frames work to stabilize the meaning of drugs and drug access, but also crystallize the rare disease patient into a distinct social category. These creative and pragmatic enactments shape the medicalized subjectivities of parents with rare genetic disease in important ways—and also, on both sides, positions rare disease patients as

somehow outside of issues of collective concern. In the next chapter, I turn to three case studies of parents of children with rare disease. The three cases will also show how the practices enacted in these ontological politics inflect the “individual bodily practices” (Brotherton 2008, 2012) of the moral and phenomenological world of the illness experience. Parents of children with rare disease develop repertoires to deal with and move across ‘suffering individual’ and ‘sustainable collective’ ontologies as they grapple with life and death and access to resources from their own situated positions in the social world.

Chapter 4:

What is the ‘rare’ illness experience? Three cases of Mucopolysaccharidosis

With diagnoses of ultrarare genetic conditions increasing and our reflexive embrace of medicine’s authoritative perspective, we must wonder, who is in the position to tell the world what is true about people who are unusual and complicated?

- Kristen McConnell (2018), nurse and mother of child with a rare genetic disorder

This chapter is about the complexity and heterogeneity—biomedical and phenomenological—of the rare disease illness experience. I share the stories of three families with different types of an ultra-rare lysosomal storage disorder called Mucopolysaccharidosis (MPS). Each of these three cases will highlight how the ‘suffering individual’ and ‘sustainable collective’ ontologies are experienced differently by parents depending on where they are positioned in the social world, in terms of race, class, and availability (or non-availability) of a treatment for their child’s disorder.

In the first section of this chapter I take a closer look at Mucopolysaccharidosis so that the reader can appreciate the biochemical heterogeneity of this condition and the ways this heterogeneity, alongside the politics of rare disease care, already affect patterns of diagnosis, care, and treatment. I then turn to the three case studies. The three cases in this chapter investigate different time points in the history of ‘rare disease’: diagnosis in 1979 (before ‘orphan drugs’ and even the category of rare disease existed), diagnosis in the late 1990s (just as orphan drugs were emerging out of clinical trials and entering health care systems), and diagnosis in 2012 (when orphan drugs were already ‘big business’ and a big policy issue). I share these stories in sequence from time of diagnosis. My focus in recounting these stories is primarily simply to describe the illness experience for each of these families—to bear witness to the ways that they enact care and learn to live with disease. On a more analytical level, however, embedded in these stories is also an analysis of how parents develop repertoires for moving

across the social orders imposed by the ontological realities around the individual/collective politics that I have described.

Another dynamic these cases demonstrate is that these three families do not experience the concept of ‘rare disease’ the same way or life in Canada in the same way. These three cases include a white working class family in a rural maritime mining town, a First Nations family living on and off reserve in the pursuit of medical care, and a white middle class family living in a city with access to world class health services. They all struggle with the types of difficulties particular to low-prevalence diseases: difficult trajectories to diagnosis, progressive-degenerative symptomatology, ableism, and a lack of cultural, regulatory, and clinical awareness of the particularities of the condition. However, these cases reinsert the economic, social, and political dimensions of life course trajectories often eclipsed by narratives of rare genetic disease when ‘caring for rare’ becomes articulated largely through the lens of expensive drug access.

The understanding of MPS and the available treatments have changed over the course of the last half century. In looking at three diagnosis time points over this time period we see how MPS has shifted from being a terminal and unfortunate bodily decline to something potentially treatable, ‘fixable’ by the promissory potentiality embedded in pharmaceutical care. This confronts parents with new types of ethical and moral choices and dilemmas. The incorporation of drug care into life with chronic disease, however, is complicated and non-linear—even with gains there will still be declines. Patients and families confront both gains and declines in a different way than the canonical discourse around ‘outcomes’ and ‘benefits.’ For one of the families introduced here, treatment never did come along. I share this family’s story here to show how the mother, Abigail, has important philosophies to offer about acceptance and the

persistence of care, and how she sees that as being threatened by the frenzy over biologically active treatments in rare disease.

Treatment or no treatment, each of these three families must learn to live with chronic disease: outcomes, for them, are processes not events (Pols and Limburg 2016), an unpredictable, unstructured embodied experiment of adjusting to bodily events alongside other challenges in their lives. Part of learning to live with chronic disease is learning to navigate the structural aspects of accessing care and services—including moving across social worlds to do so. When a drug is involved in a child’s care plan, learning to tack between and navigate the ontological politics between the ‘suffering individual’ and the ‘sustainable collective’ becomes part of the illness experience. These three families develop important philosophical perspectives based on their experience within the health care system, and which are reflected in their stories and reflexive talk presented here.

The gendered dimension of caregiving in families is also important here: in these three cases as well as across the 13 families that took part in my study, it was often the mothers who take on the brunt of these complex navigations and daily caregiving. Mothers often reported a sense of responsibility and anxiety to make the right decision, connecting to a wider “culture of mother-blame” (Singh 2004, see also Rapp 1999). As has been pointed out by Baumbusch, Mayer, and Sloan-Yip (2018), there is a gender imbalance in rare disease caregiving in Canada that has not been well researched—and is yet another complex layer of the social world that rare disease treatments move within. While I don’t focus explicitly on gender here, it is important to note that caregiving is frequently a gendered phenomenon: both the everyday aspects of care and child rearing as well as the emotional labour of interpreting social orders and learning how to move within and across them effectively (Hochschild 1983).

Taken together, these three cases demonstrate how the rare disease patient that gets cast into the figure of the ‘suffering individual’ trope described in Chapter 3 is not a static entity: not biomedically, not socially, and not phenomenologically. While this may seem obvious to anthropologists and patients, much of the discourse around the ‘suffering individual’ and the ‘sustainable collective’ ontologies depend on a representation of a relatively stable version of the patient: defined entirely by their disease, explainable by their genetic mutation, always seeking drug care, and unreflectively participating in the political economy of hope (Novas 2006) or regime of hope (Moreira and Palladino 2005). These three cases undo that homogeneous assumption. While rare disease offers potent new forms of relatedness and kinship through shared experience of the medical and social world (Huyard 2012), it must not come at the expense of the erasure of the heterogeneous social and economic contexts people live their lives within. This is not to individualize experience but to maintain other dimensions of life with disease in the frame, as they are often left out in simplified narratives of drug access even though they are as important to quality of life as any biologically active treatment. Following Mol, Moser, and Pols (2010: 15) my goal in this chapter is to show how care for these three families is not about control or mastery or perfection or a perfectly healed body but about attending “to everybody’s specificities and to the relations in which we make each other be.” This requires learning to navigate and make sense of the suffering individual/sustainable collective politics that permeate rare disease politics, while also resisting them as defining frames for their everyday experience.

4.1 Mucopolysaccharidosis: heterogeneous accumulations

Biomedically, there are eight types of MPS, classified into types according to which enzyme is missing or deficient due to a deletion in the gene that codes it. These enzymes are responsible for metabolizing naturally occurring sugar molecules in the body—mucopolysaccharides—called glycosaminoglycans or GAGs. These GAGS build bones, cartilage, muscles, and tendons. When the body is done with them, they are supposed to be metabolized by the body's enzymes, and when they are not, they accumulate: in the lysosomal cells of the joints, the organs, and in some cases, the brain. The missing or deficient enzyme can be deficient or missing due to a number of different genetic mutations: refracting any one type of MPS into a number of other subtypes (Jimenez-Sanchez, Childs, and Valle 2001). MPS is but one type of condition in a wider family of 'lysosomal storage disorders' which has membership in an even wider category, called 'inborn errors of metabolism' (Garrod 1908).

Although MPS manifests differently in each affected individual, in all cases it is a multisystem and progressive-degenerative condition, meaning that symptoms get worse over time. Coarse features, skeletal abnormalities, hearing and vision loss, cervical cord compression, distorted joints, and malfunctioning organs (heart, liver, spleen) can occur. Some types of MPS cross the 'blood-brain barrier' leading to cognitive deterioration, though this may not happen with all people with the condition. Usually, people with MPS are born showing no symptoms of the condition and start showing symptoms throughout early childhood. The natural history of all of the different MPS types is not well known, and the condition manifests extremely heterogeneously among people with the same condition. Prognosis and progression of the disease cannot be predicted for any single patient, though newly diagnosed children are usually

given a prognosis of anywhere between five and twenty years old, depending on the severity of their case.

The epidemiology and incidence of MPS is poorly understood, although different types occur more frequently in different places suggesting a founder effect. While the different types of MPS were first described clinically by physicians in the 20th century, Pachajoa and Rodriguez (2014) have hypothesized that a collection of pottery from the Tumaco-Tolita people that inhabited the Pacific coast of present day Colombia and Ecuador from 300 BC to 600 AD are representations of MPS Type VI, Maroteaux-Lamy Syndrome. The figures show enlarged heads (macrocephaly), broad mouth, prominent sternum, coarse facial features, and skeletal dysplasia.

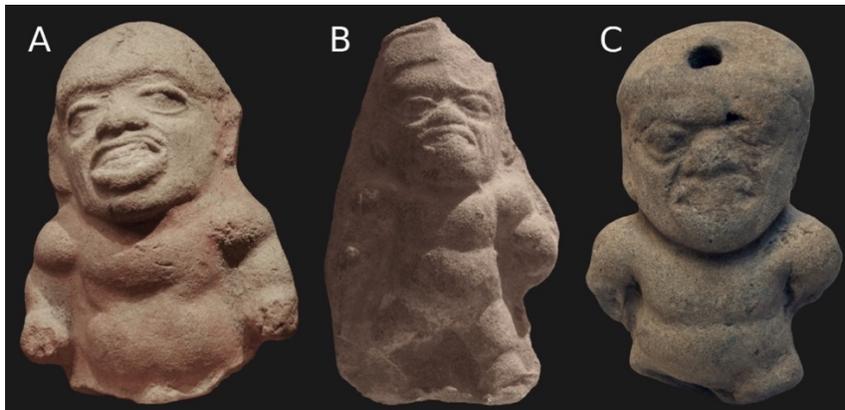


Figure 3: “Pottery samples from the Tumaco-Tolita culture representing possible cases of Maroteaux Lamy syndrome.” Image from Pachajoa and Rodriguez 2014, © 2014 Universidad del Valle. Reprinted with permission, Creative Commons license by attribution.

As Pachajoa and Rodriguez write, “It is noteworthy that the figures represented are of young people or infants, clearly suggesting that the complications experienced by people with MPS type VI as cervical cord compression may have regulated the mortality of people with this disease, because at that time there was no orthopedic spine surgery.” If correct in their

hypothesis, these pieces of art are a testament that MPS has been around a long time. But it is extremely low prevalence. Applegarth, Toone, and Lowry (2000) identified 20 cases of MPS diagnosed in British Columbia between 1969 and 1996, or 1.94 per 100,000 live births. Khan et al (2017) found MPS occurred at an incidence of 1.53 per 100,000 live births in Japan between 1982 and 2009, and 1.56 per 100,000 live births in Switzerland between 1975 and 2008. In comparison, Down's Syndrome is estimated to occur in approximately 1 in 700 live births in the United States (Parker et al 2010).

This chapter shares stories of children with three different types of MPS: MPS Type I, Hurler-Scheie, MPS Type II, Hunter's Syndrome, and MPS Type IIIa, San Filippo. Each of these types of MPS will have different patterns of care and treatment. Both MPS I and MPS IIIa are of an autosomal recessive inheritance pattern, which means that both biological parents carry the mutated gene and pass it on through their sex chromosomes (X and Y). Each of their children has a 1 in 4 chance of having the condition. MPS II is X-linked recessive, which means that the biological mother passes on the mutated gene through transmission of her X chromosome to her male child. The mother may pass the mutated gene on to a female child as well, but since females have two X chromosomes the female child will only be a carrier of the mutation except in rare circumstances and MPS II in females can occur sporadically (Scarpa 2018). MPS I can be attenuated or severe, with profound physiological challenges and joint and organ difficulties, but usually a patient with MPS I doesn't experience cognitive deterioration. A patient with MPS II may or may not have cognitive deterioration, it all depends on whether the waste travels across the blood-brain barrier or not and patients and their families just have to wait and see. MPS IIIA always has fewer and more mild physical dysmorphia than the other MPS types, but cognitive deterioration is severe.

Enzyme replacement therapy (ERT) is produced using continuous human or animal cell lines and plant cells. ERT for MPS I (laronidase) was approved in 2003, and for MPS II (idursulfase) in 2006. ERT helps with symptom management but people with MPS are still very much disabled by the condition even with expensive treatment. Intravenous enzyme replacement therapy for MPS II does not cross the blood-brain barrier to halt cognitive deterioration, but a trial experimenting with intrathecal delivery straight into the nervous system is currently underway. Enzyme replacement therapy has been shown to not be effective in MPS IIIA. Trials for gene therapy for all three of these types of MPS are currently underway.

As explored in Chapter 3, the development of a treatment also leads to the development of a biosocial disease community: in part formed organically by patients and families in the trial or seeking entry in to the trial, in part orchestrated by the pharmaceutical company in order to generate meaning and hope around the treatment. It also leads to a clinical and diagnostic infrastructure, meaning diagnosis might be more simple (though a clinician has to recognize it first in order to order the right test). In general, response to treatment is highly variable. One patient with a type of MPS may respond very well to enzyme replacement therapy, another patient may respond less well. No one knows ahead of time, so the ‘value for money’ is hard to determine or monitor according to some version of the ‘average patient’ because there is no average patient. Evidence in rare disease is always a moving target, which doesn’t fit well with the need to stabilize it for decision-making—putting everyone involved in a difficult position. In the wider spectrum of diseases classified as rare, MPS is a condition with an easily located cause (missing enzyme), and some types of MPS (I, II, IVA, VI and VII) have ERT options available. This means that it is different from many other rare diseases where the etiology of the condition is less clear or less simplistically targeted with a therapy.

4.2 Abigail and Calum, mid 1970s: diagnosis before ‘orphan drugs’ and ‘rare disease’

Calum was born in 1975 in a working class mining community in rural Newfoundland. He was Abigail and her husband Thomas’ first child, and Abigail describes him as being the perfect baby, always smiling and very affectionate. But when Calum was a toddler, he’d learn a word and then never utter it again. His nose was always dripping, his upper lip sore and inflamed. One day, he suddenly refused to eat anything but white bread and cheddar cheese slices. He couldn’t sit still. Whenever a truck drove by or a plane flew overhead, Calum would scream and scream. Abigail, knew something was up. Every time a new doctor showed up for their internship in the church run hospital in their small Newfoundland town, she brought Calum in. Each time, she was told she was being an overprotective mom. They suggested that she should try to do a better job at disciplining her bubbly, cute, and affectionate son. It was the late 1970s and getting a medical doctor from the big city to take a woman in her early twenties from a rural mining town seriously wasn’t easy.

Finally, when Calum was four, a doctor came through the town who took one look at him and said he was going to make an appointment for Calum at the Janeway in St. Johns, the only children’s hospital in Newfoundland. They went—a seven hour drive in good conditions, much longer in the snow—and the doctors there saw that there was severe scarring on his eardrum and fit him with tympanostomy tubes to drain the excess fluids behind his eardrums. They did some tests that they sent out to Halifax and Toronto for analysis and sent the family home.

Abigail received Calum’s diagnosis of Mucopolysaccharidosis Type IIIA, San Filippo, in a one-page letter from the Janeway sent to her mailbox at the post office. The letter informed her that his life expectancy was about 10 years old, but that he could very well live into his twenties though his sight and cognition would be severely affected. Later that day, she got a phone call

from the town hospital to come speak with the doctor as soon as possible. They went that evening at 5pm. When they arrived, the doctor pulled them into a private space. Abigail recounted how he told them that things didn't look good for Calum, and that he'll be a "street idiot" and they should put their son in an institution right away and move on with their lives. Abigail had been mostly silent to that point but retorted: "I didn't go to a car dealership and buy a lemon, I won't return him, he's mine!" She told me how, though it was blunt, the "street idiot" terminology helped her understand how things were going to be. She didn't need false hope.

Abigail told me this story one morning at the long term care facility where Calum had lived since 1992, ever since his brain damage made it too difficult to care for him in their home. They didn't have much money, and the monthly fee to keep Calum in care at the facility was only partially subsidized by the province. She worked very long hours as a crisis worker with at risk kids in Edmonton, but she'd still make time to visit Calum every day. During this interview, she reflected a lot on the ways she's had to fight for Calum at every step of the way. She described how when he reached kindergarten age, she was determined that he'd go:

So here I am in a little community in Newfoundland and I'm coming from a background where anybody who, I'll use the word "retarded," I don't like it but that's what they were using back then, anybody "retarded" they kind of kept them in a closet. And I said no, he's going to school! He turned five years old in 1979, and my plus was the federal government had made 1979 the year of the child and made a ruling that every child in Canada was entitled to an education, but there was no special needs classes cause all those little special needs kids were all kept at home!

Calum going to school was deeply important to her. If he was going to lose his sight, she wanted to get as much learning and experience into him as possible: "that way I can say Calum the sky is a really bright blue today, from memory he can recall what blue looks like."

The local school wouldn't accommodate Calum. The principal told her to keep him home until they figured it out. Eventually the Catholic school in town provided the space for them to

get an integrated classroom started, but didn't commit to actually building the program. Abigail rallied a public health nurse, a doctor, and a couple of other parents with special needs children to go door to door to raise money to get sensory toys and supplies for the classroom, as well as suitable toilets and parallel bars for the bathroom. That program, Abigail told me, is still running classes in rural Newfoundland today.

In 1981, they left Newfoundland for Manitoba for Thomas' job, where they stayed a year. They ended up in another city further west, where they still live today. When they left Manitoba, a doctor there pulled her aside and told her to call the university hospital when she arrived in their new city and ask for an appointment with somebody who specializes in inborn errors of metabolism. As she recounted: "I'm thinking woah, what's that! So anyway, wrote it all down, got the phone book, phoned over to the university hospital and got linked up with them." He'd had genetics doctors back in Newfoundland, but she'd never heard of this term. Calum got access to medical care, and Abigail let them do whatever research they wanted—she collected vials and vials of his urine for the researchers at the medical school, and took part in medical education by having medical residents try to diagnose him in training sessions, asking her questions like they would for any presenting patient and parent.

She enrolled Calum in school, in a program for the 'trainable mentally handicapped,' something which makes her chuckle now because Calum's condition isn't one that can be 'trained away.' He was gradually losing skills, not gaining them. Calum was super affectionate, always hugging everyone, and one of the first things the teachers focused on was getting him to stop hugging people. Abigail recounted: "I'm thinking, no I can't do that one, I can't reinforce at home that you can't hug mom and dad, I understand it's not pleasant or nice to be doing in the public but at home that's what he knows and that's what makes him happy and I'm not taking

that away!” The school also focused on trying to get him to feed himself independently. If he could feed himself independently five days in a row they could say that he had met that milestone. Abigail explained:

Well, you get one day, four days, two days, three days, but never once did you get five, and I’m thinking, like I understand that you’ve got to have five days but this is a useless task! I understand how frustrating it might be for a teacher who’s gone to school and their goal is to entice children to learn and obtain and retain that information. Here you are you’ve worked five years with this kid, who’s been toilet trained but then he loses that, he’s no longer toilet trained. You know you get a lot of teachers coming out of school and they think everything is by the textbook, well Calum don’t fit into the textbook! The textbook is your guide but you’ve got to be able to work around that and move outside the box and come up with different programs, everyone is an individual, we all do it differently.

Most of Calum’s peers were kids with Fetal Alcohol Spectrum Disorder (FASD) or Down’s Syndrome, and they all did seem to be gaining skills through their work in the classroom. She sat down with the parents thinking maybe she could learn from them and what they were doing with them, but slowly realized her journey with Calum was going to be different from theirs. As she explained, “their goals for their children was that they were going to ride the train, live independently, might not be able to handle money but be able to get their groceries and stuff like that, and I’m thinking: I’m not even going to say what my outcome is then, cause they’re going to think I’ve just given up!” But she knew what her goal was, and that was to keep Calum at home with her and Thomas for as long as possible. And that’s what Abigail and Thomas did: they kept him at home with only brief respite care until Calum’s brain damage was too severe and they couldn’t physically care for him any longer. Abigail once told me the story of the day that Calum came home after a weekend away in respite care and just laid down on the steps and couldn’t seem to move much anymore. She always knew that this would happen, or at least she had been told that it would, but it didn’t make her any more ready for it.

When Calum was a child, ‘rare disease’ as a category didn’t even exist. Calum just had a genetic disease nobody knew anything about, and for which there was no treatment. Abigail defines her life with Calum as one of acceptance, of pulling herself together and taking her feelings out of the equation when it came to making choices for Calum. For her, his well-being came first. When she’d get a call from the long term care facility that he’s upset, she’d drive over as fast as she could. She’d lay down alongside him, put her face next to his, and hum until he calmed down. She explained how “there’s times I’ve come in and said goodbye, I tell him ‘if you needs to go, you go, you don’t need to stay here for mom.’”

When Abigail and I first met in 2015, she described how the world of MPS care had changed over time: she sensed how the advent of treatments had changed the parameters of what it means to be a ‘good parent’ to a child with a rare disease, a shift that she didn’t necessarily agree with or feel a part of. At one point, she got involved with the Canadian Mucopolysaccharidosis Society: “I got involved with parents and that, but I still find, my thinking is different than a lot of people?” She explained how from the beginning, she forced herself to live in the present and she wonders if that prepared herself to be a more emotionally available caregiver for Calum. She spoke about how she knew of families who were looking for a bone marrow donation but they couldn’t find a match, so they had another child to see if the new baby would be a match. For Abigail, this was too much. As she told me: “I haven’t gone out on tangents grasping at straws, we’ve kind of accepted it as it is, and we’ve focused on Calum, it’s not about me and Thomas anymore, it’s always been about what’s best for Calum, and it’s tough, you know?” She understands how desperate that family was, but also was glad that she never felt compelled towards those desperate and risky measures. If no options existed she didn’t

have to grapple with the moral questions or the intensity or the responsibility, she could just focus on Calum.

She brought up a recent story that was all over the news, of a child with MPS whose family fought for access to treatment and won. At the place she's at in her life she's kind of glad she didn't have to make that treatment choice:

If it works for them, it works, more power to them. If in those kinds of situations, if it prolongs life for another year or so, if that's what the individual family wants then that's fine, where I've been at now and knowing what the outcome is going to be, that it's going to be like this, would I want to prolong his life any longer? I don't know. Tough calls. I guess until you've walked through it, it's hard to know how you would do it.

She knows her thoughts on this might upset some other rare disease parents. But it's her truth. Watching her child progressively decline for so long has taught her about acceptance and about suffering in ways she knows parents whose children are getting drugs are not ready to fathom. Hers is not the type of story that corresponds to the heroic medical narrative but it's her story and it's Calum's story. "My only hope is he's gone before my time comes," she told me.

Calum passed away surrounded by family in March of 2019, just six days shy of his 44th birthday. When Abigail came in to the nursing home one afternoon, she could just tell something was different with him. His arms were stiff. She called her daughter, who lives out in Newfoundland, and told her she'd better get on a plane. When Calum passed away days later, his hand in hers, she felt a deep sense of peace—she had seen him through. "It's not a sad thing for me," she told me in a message she left on my voicemail. Later, when we spoke on the phone she told me about the funeral—they'd made it a 'birthday party farewell.' They weren't sure how many people would come, or how much food to order. Enough for 50, maybe 75? In the end, 160 people came—staff and nurses from the nursing home and relatives. The crowd sang Sharon,

Lois and Brahms' song, 'Skinnamarinky-Dinky-Dink-Skinnamarinky-Doo'—one of Calum's favourite songs to sing when he was young.

Calum's story is an important part of the history of rare disease in Canada. I do not see it as an example of a tragedy of unmet need due to there not being a drug available to Calum at diagnosis, though some may read it as that. I see his story as important in far more fundamental ways. Abigail's dogged insistence on his dignity and his worth is a true story of caring for and attending to suffering, and yet, she felt out of place in patient group circles that seemed to be oriented completely around only seeing relief of suffering through the lens of pharmaceutical treatment. When it came time that Abigail and Thomas couldn't take care of him at home by themselves, they had to put him in a long term care facility—and they had to fight bitterly for that spot—but what Abigail would have liked would have been to have in home nursing care. "If I was a multi-millionaire I'd have done that," she told me with some sadness in her voice, "but I'm not!" The cost of one year's worth of enzyme replacement therapy—say, \$500,000—could have changed the course of their last years with Calum—they could have renovated their house, or moved to one better designed to care for him, and hired an aide to come in and help them. But resources aren't allocated in that way—the 'suffering individual' ontology is only focused on channeling money towards pharmaceuticals from the market system.

Abigail fought on Calum's behalf for adequate care and schooling and she and Thomas managed her son's progressive-degenerative condition in a context where progress is assumed linear towards improvement. Abigail also bore witness to the way rare disease care has changed with treatments coming on the scene. She doesn't even think of Calum or MPS in terms of 'rare disease'—the category didn't even exist when Calum was first diagnosed. That category only emerged alongside the drug incentivizing policies and treatments that came later. Abigail and

Thomas had to fight for Calum every step of the way. However, the moral questions they grappled with in making decisions on behalf of their child were not clouded with whether to pursue or not pursue a treatment. Abigail never had to engage with Canadian drug access politics or commit any of her energies to wishing and hoping that the drug development system would come through for Calum. She never had to face the question of whether she was doing the right thing for Calum by poking and prodding him with needles and tests. She just had to focus on how to make Calum as comfortable and happy as she could at every step of the way. From where she sees things, in her own way, she feels grateful for that.

4.3 Scott, Jack, and Julie, diagnosis in the mid 1990s: the ‘early days’ of access politics

By the time Scott was diagnosed with MPS Type I at 18 months in 1995, he was half deaf and half blind. He lived with his family on their small First Nations’ reserve in the north, and they’d brought him again and again to the community health centre but his symptoms were mysterious and they couldn’t figure it out. After several medevac trips between the small community and the closest city, they were sent to a major Canadian city in the south to see a specialist. The geneticist they saw there was able to diagnose him. The gold standard for MPS I is bone marrow transplant, but the prospect really terrified Julie; it sounded so dangerous. At the time, the geneticist told Jack and Julie that it was best not to pursue transplant because he was in process of, as Julie described, “coming out with a medication for these kids, not a cure, just a...” Julie trailed off looking for words. Scott piped in: “to slow it down.” Before the drug was even moved into the trial phase, they had been unofficially recruited into the trial—they just had to wait for it to begin.

Just before Scott turned five, three years after diagnosis, they received a call saying, in Julie's words, "yeah, he's going to be on the list for this special clinical trial." They told me this story in the spring of 2015 when I first met the family, and we sat together in their kitchen sipping earl grey tea. Jack and Julie sat at the table and did most of the talking, but Scott sat at a stool by the counter listening carefully and piping in with details or correcting his parents' recollection of events.

In 2000, Scott started in the clinical trial. The trial was testing an enzyme replacement therapy called laronidase (brand name Aldurazyme), and was being run by a biotechnology company called Genzyme. At first, Julie and Scott flew back and forth between their home on reserve and the trial site, but that quickly became difficult on both of them to do weekly. They decided to move to the trial city temporarily, but they didn't have much money, or more accurately as Jack described it "zero money" and the trial site was in an expensive city to live in. They couldn't afford for both Jack and Julie to be off work, so Jack took a job driving trucks for a long haul trucking company that gave him the flexibility to be back in the trial city for a couple of days so he could be there for every second infusion. Being in the clinical trial was scary: there was the expense and culture shock of the big city, and Julie experienced depression from being far away from family and dealing with the uncertainty of it all. Scott was in the trial for five long years, first in Phase 2-3 and later in a post-market trial. Once it finally received regulatory approval in Canada, the price of the drug was listed at half a million dollars a year¹³.

¹³ As detailed in the Common Drug Review report issued July 14, 2005: "The medication costs between \$100,000 and \$900,000 per year, depending on patient weight. Given the average weight of patients enrolled in the clinical trial (40kg), the average annual cost for laronidase would be \$434,720 per patient."

The family knew that moving back to their small First Nations reserve would get complicated—Scott needed to be close to a children’s hospital to receive his infusions and be monitored by pediatricians. They moved to the closest northern city from their reserve for a few years but eventually decided to move to another province when Jack’s mother got sick, so they got a small grant and loan to build a home on Jack’s ancestral First Nation’s reserve about an hour’s drive from a major city and children’s hospital. That was where they lived in 2005 when the treatment was approved by Health Canada, and where it became apparent that access to the treatment post-trial was not going to be a simple story. Not only had the treatment been deemed too expensive and not effective enough to fund, different levels of government couldn’t even agree whose responsibility it was to issue the denial. The federal government is responsible for the health care of First Nations children living on reserve, but Scott didn’t yet have status with Jack’s ancestral First Nation, so they tried to say it was the provincial government’s or the First Nations band’s responsibility. As Jack recounted:

They were saying that well he’s First Nations, so First Nations should look after it, and the First Nations are saying yes, but the federal government’s supposed to look after it, and the federal government’s saying no, it’s the provincial government because they’re living in that province!¹⁴ And so everybody kept passing the buck, but the bottom line was that they weren’t going to treat him. So I said, just bill me, just send me the bill, but you are not going to stop his treatment. If it wasn’t for him you wouldn’t have a bloody treatment, so you will treat him!

¹⁴ This jockeying back and forth between levels of government around a First Nations child’s care is not an isolated incident but a common issue in Canada. In 2005, a young First Nations child, Jordan River Anderson, died in hospital as the federal and provincial government argued over who was responsible for paying for the costs of his home care. This eventually led to the implementation of Jordan’s Principle in 2007, which holds that in disputes of this nature the care is paid for first and the particulars worked out after. However, Jordan’s Principle has been inconsistently followed and applied (see Blackstock 2016).

So, the family phoned prominent news outlets—CTV, Global, CBC, and the like—and told them to show up on the day of Scott’s appointment. Someone at the hospital had told them that they did have the drug in stock in the hospital pharmacy but someone would have to pay for it. Jack recounted: “so we showed up there and they said, well we’ve got to figure out how, who will pay for it! And I said, well, just bill me. And so they did! They billed us \$48,000.00!” Jack laughed, reflecting on the absurdity of the whole thing. “So we told them they could have our house,” referring to the small home they’d recently built on reserve using a loan from the bank and the reserve. “But we didn’t own it, the bank did, and the reserve did, we were just living there!”

At their wits end, they accepted an invitation to a conference in Toronto in October 2005 where they were told they would be able to meet with the federal Minister of Health. But when they got there, they realized that what they thought was a conference was actually just a rally in a parking garage outside of the annual Health Ministers meeting. The patient advocacy group who had invited them had flown them there to protest with them, with a group of other families holding up signs protesting the use of cost-effectiveness measures like the QALY in reimbursement decision-making.

That’s how they found themselves outside on the sidewalk in the financial district of downtown Toronto, so far away from home. Scott’s parents had rushed out of the parking garage after a prominent reporter almost stepped on Scott in a rush to get a better shot of the health ministers as they emerged from their meeting. Jack pushed the reporter out of the way and a bit of a fuss broke out. As Jack reminisced:

It just got out of hand, and it wasn’t what we thought we were getting in to! [...] Everybody was hollering at him [the federal health minister] with signs, and this wasn’t what we came here for, we’d come so far, and then that guy just about stepped on Scott when they heard the minister was coming, and we said screw this!

“Yeah, we just backed out of there,” said Julie, shaking her head. Out on the street, Jack and Julie pooled together their small change to buy Scott an order of fries from a fast food cart; Jack took his jacket off and laid it down on the sidewalk so Scott could sit down to eat his snack. They were all feeling decidedly out of place. They were also feeling used, betrayed, and dejected—Scott’s body and experience seemed secondary to the political sensationalism these drugs were generating. Jack recounted their feelings at the time: “We were thinking, what the hell did we do! We’re in Toronto now, staying at some million-dollar hotel, like they’ve got really good taste, give them credit for that!”

These were still the early days of rare disease drug advocacy and yet already massive flows of capital were being directed toward politicizing the issue so that Canadian drug payers, both public and private, couldn’t say no to them—with much of that capital going toward raising the profile of patient groups, a phenomenon that has been observed in other jurisdictions worldwide as well (see Novas 2006; Kyriakides 2015). At the time they were living paycheck to paycheck, on and off unemployment as they tried to take care of both Scott and Jack’s ailing mother, so the opulence and being brought out to restaurants by the advocacy group with \$80 pork chops on the menu was pretty surreal.

They did end up meeting the federal Minister of Health that day: two guys in expensive suits came up to them while they were sitting out on the sidewalk and told them that if they left the media behind they could meet the Minister of Health so they brought them over to him and got twenty minutes with him to tell them their story. Those twenty minutes weren’t enough, though, to solve their problems, sympathetic as the Minister of Health was to their plight.

Eventually, the treatment was funded, following a lawsuit¹⁵—the cost of the treatment is now shared evenly between the federal and provincial governments and the pharmaceutical company, Genzyme. From then on, they tried to hang low and stay out of the politics of rare disease drug access. In fact, they were ordered to: a condition of the legal ruling was that they wouldn't talk to the media about the arrangement, a condition that was lifted in 2015. Caught in the early crosshairs of rare disease drug access politics in Canada, Scott and his family were as suspicious of this particular corner of the advocacy world as they were of the excuses the federal and provincial government were making to deny access to the drug for Scott. As Jack reflected: “we tried to believe everybody when we first started and as it turns out not everybody is looking for the same thing you are.”

They backed out of the politics of ‘rare disease’ that day that they left the parkade but they stayed firmly in the world of MPS I, which brought them all over the world: to conferences and patient meet ups and all sorts of fun stuff they had never imagined. This is very different from Abigail's case, where, in the absence of a treatment, there was no such infrastructure or sociality, least of all the pharmaceutical company funding to make an MPS IIIA community happen. As we sat there together, they recalled some of their friends they had met, some of whom didn't even speak English and yet they'd managed to bond. The family adored Scott's metabolic disease doctors from childhood, they were always there to take a call, they gave the family their personal home numbers just in case they needed it. When they went in for appointments it felt like going to catch up with an old friend. But the new doctors that replaced them when they retired were, in this family's experience, not as good. “Yeah, it's very clinical

¹⁵ Citation not shared to protect confidentiality of the family.

now,” Jack said—they just want the family in and out, there’s no joking or laughter, just business.

The family is aware of the politics around these treatments, but find them ridiculous. They knew early on that both drug payers and pharmaceutical companies were both hedging their bets and blaming the other party for the problem. When it comes to disputes over the evidence for Laronidase—that the evidence isn’t good enough to justify being paid for by the public system—Jack rolled his eyes: “yeah those debates where they think it’s not helping, my god, go and see some of these kids instead of sitting in your damn office making decisions that affect peoples’ lives, go out and be a part of what they’re living.” As for disputes about the costs of the treatment, those value politics make Jack angry. As Jack said at one point: “in the very first treaty they wrote, you said you were going to look after this,” indexing how if settler-colonialism and capitalism is going to control the system, it better get its act together because rare disease drug access politics is exposing some major gaps in its seams. Governments were happy to sit back and let the drug companies do the work of treatment development, and then they complain about the exploitative system they enabled. As he shared:

Yeah, and you name one pharmaceutical company, we love Genzyme Genetics, but they’re just another multi billion dollar company who used peoples’ children as guinea pigs, and they used the doctors too, but we came up with something! And if everybody was pitching in the whole time, this stuff wouldn’t be as expensive as it is. The pharmaceutical company did it on their own, the government sat back and waited, and now we’re finally starting to try to catch up. You know that being said, if everybody did their part there wouldn’t be this huge cost. Cost should never factor into it, what is one life worth? You know, is it worth less because it’s not their son?

Scott’s story helps to foreground how rare disease drug access politics force patients and families into the middle of an ethical issue that rarely gets talked about in rare disease drug access politics, one that uses patients as guinea pigs and then tells them they don’t get the treatment they

contributed to making. Whether health care systems or manufacturers should pay for continued access to treatment for trial patients is another question, but Jack's philosophizing on the issue opens up questions that undo the property rights that are so integral to how drugs are socialized in current political economic configurations. Who really owns these biological substances?

Scott is now in his early 20s, and he has continued participating in clinical trials here and there, even one testing an intrathecal mode of delivery for Laronidase. It involves lumbar punctures that cause him immense pain because of his spinal cord compression, his vertebrae are so fused that he can feel the needle through the anaesthetic. He found out later that for the first two years of that trial he was on the placebo drug but he didn't mind, once he started receiving the actual study drug he'd feel a bit of a difference right after but nothing major. That day that I met them in their home, Julie was planning to take him over to the new grocery store opening up in town to see about a job. The family's rule was that if Scott didn't want to go to university he had to work, but he was sometimes treated badly by his coworkers and managers because he can't move super fast when given duties like sweeping floors or scrubbing toilets because of his limited range of motion. But this grocery store seemed to have a commitment to inclusion and hiring people with disabilities so they were going to give it a try.

4.4 Ella and Andrew, diagnosis in 2012: the midst of the orphan drug boom

By the time Andrew was five years old, he had received speech therapy, behavioural therapy, audiology testing, hearing aids fitted, several ultrasounds, urgent care admissions for pneumonia about once a year, and genetics testing for Smith-Magenis syndrome that, after two years of waiting for results, had come back negative. His parents, white middle class professionals with strong knowledge of the health care system, had done everything they could

for him, and the lack of answers was frustrating. That was when a teacher at his developmental preschool, who had worked with a child with MPS in Europe decades earlier, whispered to his mom, Ella, that maybe she should ask them to also test for MPS. They went to see their geneticist and had Andrew pee in a cup, and shortly after that she received a phone call from the geneticist himself at 10:30 in the morning telling them that they'd better come in for an appointment.

A couple weeks later, his diagnosis of MPS II, or Hunter's Syndrome, was confirmed. This meant that Andrew didn't just have a genetic mutation, but one that led to a progressive degeneration of his body. It meant that he didn't just have a disability, but a disability that would slowly take over his body and take him away. This was a big shift for Ella.

Ella told me this story one quiet weekday morning while her children were at school and her husband was at work. We sat around her kitchen table, the recorder between us, for almost four hours. She told me how Andrew's late diagnosis was followed by a relatively swift initiation of ERT: there were a couple of other children with MPS II in the province who had fought for and received the therapy a couple years earlier, so the public drug plan managers followed the precedent that had been set for them with little fanfare. Ella is really grateful for those parents and advocates who came before her, who helped get that precedent set. Over the first few months on treatment, the stiffness in Andrew's hands loosened a bit, his range of motion improved, his tightly spaced toes relaxed so the chronic skin problems he was having between his toes went away. At the time, they thought that his brain was fine—which was good, because the cut off for access to Idursulfase for the province was that there was no cognitive deterioration from the disease. But six months in, they did an MRI and saw that there were changes to his brain. That held stable for about two years, but then he started having seizures from his right temporal lobe.

The treatment was helping his body, but Idursulfase administered intravenously does not cross the blood-brain barrier so Andrew's cognitive functioning slowly started to decline.

Ella spoke about how “there's no job out there that's nearly as judgmental as motherhood,” referring to the strangers who would comment on Andrew's running and screaming in public. “We've had senior citizens at the library berate us for our child's behaviour, we've had a woman at the lottery counter talking loud enough for us and people at the next ten tills to hear, about our son's horrible behaviour and what kind of parents let their kids do that,” she shared. But Andrew's diagnosis changed her: she says it made her more assertive, less inclined to take that stuff personally. But it is lonely: “it's not the same as having an autistic child or a child with diabetes or things like that, where there's communities to support you.” She noted how people with a more ‘typical’ experience “often have a way of minimizing what you're going through. And who wants to open up and put everything out there as bluntly and as clearly as you can? Because, well, you're no fun to be around.” At the same time, Ella is fervent that she wouldn't change him:

And people look at us now and they think, I'm sure even amongst our close friends, people look at us now and they think ‘oh that's got to be so hard and I wouldn't want that’ and all those things. But I wouldn't give him up, I wouldn't change him, I wouldn't say, ‘take it away now’. He's resilient, he's strong, he's like it or not it's integral to who he is! And there's nothing wrong with him. That perception that people pass that in some way he is defective, or less than, and he's not! He, unfortunately, inherited a genetic trait that could have just as easily affected my two brothers! That could have just as easily been handed down to my sister and her three boys! It is luck of the draw that I got the affected X and they didn't, you know, and there's nothing wrong with him, he's not defective in any way. You know, we all carry mutations.

Ella and her husband don't take pity well, it annoys her when people look at it like a loss of some sort. She fervently pushes back on narrowly cognitive understandings of what it means to be a

full human. For her, there's nothing wrong with him—the treatment is to improve his life, not change him.

Shortly after Andrew was diagnosed, Ella took a leave of absence from her job as a nurse on an oncology ward and never went back. The family reformatted their finances and their ideas of the 'future' to just try to live day by day, and enjoy the time that they have with him. She hasn't gotten too involved with fundraising or advocacy for MPS, and sometimes she feels guilty for that, but she needs to focus on Andrew, this is a moral issue for her: "I don't want to ever think, I missed it. That was literally the best time that we were going to have with him, and we missed it... This right now could be his best time of health, he's progressive!"

This also means adjusting to Andrew's needs and the declines that happen anyway even with treatment. At one point during our interview together we turned to the family photos posted up on the wall beside the kitchen table where we sat. One photo was of Andrew in a snowsuit, looking grumpy. Ella laughed and explained that he hadn't liked skiing:

We've given up on teaching him to ski, he is not a skier! But he loves the waterslides. He's heartbroken that he's not allowed on the roller coaster or the rides anymore, but he's starting to get cervical cord compression and instability, so yeah, we said goodbye to our trampoline. But the piece of plywood in our front entry is for our new outdoor ping pong table! So we're going to paint it up green and we're going to set it up, there are other options available!

Adjusting to gains and declines with Andrew is an important part of life for the family. While biomedically cervical cord compression despite ongoing treatment is a 'bad outcome' biomedically, for families it is just another level of change to find accommodations for, to keep Andrew's life fun and interesting.

When Ella and her husband Lucas learned about a clinical trial for a new mode of delivery of Idursulfase, they were faced with a new set of choices. The manufacturer, Shire, was

experimenting with administering the enzyme intrathecally—directly into the central nervous system through the spine—hypothesized to cross the blood-brain barrier. Ella and Lucas really weren't sure of it at first. In her career as an oncology nurse, Ella had seen people pursue therapy after therapy, trading a little bit of extra time for a reduction in the quality of their last days. It was also a scary decision: in Phase I of the trial there had been a bunch of issues with the intrathecal ports, and kids getting really sick. But they had two and a half years to think about it: the trial wasn't accepting new patients at the time that Andrew started having seizures and showing gradual neurocognitive decline. When they reopened enrollment, Ella and her husband were faced with a decision, but it wasn't an easy one for this family. Ultimately, they decided to go for it, and enrolled Andrew in the trial at almost eight years old. As she shared:

I don't ever want to know, five ten fifteen twenty years down the line that the children that participated in this intrathecal trial are graduating high school, going to university, having full productive lives, and know that we didn't risk it, we weren't brave enough to try it. Either way, he will die. Everyone does. It's unavoidable. So do we allow him to progress naturally or do we take the one option out there for us?

The potential benefit of the drug outweighed her fears and concerns of overtreating, of putting quantity of life over quality. They now take a three hour flight every month to travel to the clinical trial site. For Ella, though, there's a limit. Some children have developed antibodies to the enzyme replacement therapy, causing them to reject the drug. She knows one family who has started their child on chemotherapy to suppress the immune system to minimize the antibodies. Having worked with chemotherapies, she feels that, in her words: "I don't know that that's a bridge that I'd be willing to cross." Ella and her husband are really focused on keeping Andrew's quality of life in perspective, but she knows that's in part thanks to her experience as a cancer nurse, she has become okay with letting go—though of course, it's a whole different ball game

when it's your own child. But she still knows that ultimately Andrew's body will have the last word:

There will come a time when likely you know he will have regressed to a point where we will stop what we are doing, and we will allow MPS to progress and take him. Because while I believe that this intrathecal trial has positive results and is worth doing, I don't believe that it's a cure. [...] I do imagine that there will come a point in time when we make the educated decision to stop treatment. But until then, we'll do what we can.

When Ella and I first met, Andrew had only been in the trial for a short time, a few months or so. But already she'd seen some changes: he was labeling his emotions, sleeping better, and understanding stories. But she keeps her boundaries with the treatment. She also knows that a lot of these gains are very small, and hard to measure. Having worked in the clinical world of biomedicine, she knows what that means: the benefits are too hard to measure, there aren't validated outcome measures for them, and it's all so subjective to the person experiencing or witnessing the changes.

Ella knows that a lot of this is about systems of value, and how 'society' will value pumping hundreds of thousands of dollars into a child who will never be 'typical' and will never be a 'contributing' member of society:

For how long will this society value or deem my son's life to be worth enough to continue a roughly \$6000 to \$8000 a week treatment? At what point does his treatment cost exceed his value? Because that's what it comes down to. And people look at me like I'm crazy when I say that. But it's true.

Ella is a white woman in a large city with a comfortable home and a relative sense of financial security. At the same time, she feels vulnerable as a parent of a child with MPS, she feels that social ties and senses of community are weakening. In her words: "I think that it makes our population of rare, more vulnerable. Because the more our society becomes entitled and expects that it's all about me, the less we take care of the others." She struggles with framings of 'life' as

having inherent value, because she knows how easily this slips into volatile issues of abortion or medical assistance in dying rights. But still, she feels compelled by the idea that Andrew's life is inherently worthwhile, worth saving—something that she's thrust in as a direct result of the high costs of Andrew's treatment:

There's for sure an economic cost to raising our son that far exceeds the cost of raising a traditional child, or a typical child, which worries me, especially in rough economic times. What would it take for a society's views to shift so quickly or so dramatically, and could it happen in his lifetime? I think that there needs to... we need to maintain that sense of community within our society. And it's hard right because how do you justify that, how do you justify the dollars spent?

Ella says that she never tells anyone what the cost of Andrew's weekly treatment is:

Because people would be horrified that their tax dollars are going to pay for that. You know? We have a life expectancy that is hopefully now beyond the second decade of life but how do you justify that to a population? We certainly don't share that information, because you get looks of horror. I'm spending my tax dollars on that? And that's from people that you know!

Ella thinks a lot about this: as she said, "I do lose sleep over it." She knows her family would be bankrupt within a year if they had to pay for the treatment themselves. This sense of precarity follows her, so she hopes that political currents maintain a "care for your weak, to care for your atypical, to care for your special needs" ethos. The high prices and evidence practices of the pharmaceutical companies also make her feel uneasy:

Yes the drug companies are investing a ton of money into therapies and research but this study can support my son flying down once a month, all our airfare, all our hotel, our living allowance while we're there, and still turn around and make unimaginable profits. And yes, I accept that there is a ton of research that's behind the scenes and stuff that happens, you've got to put in all that hard work and all that money to ever get lucky and hit that. But perhaps there's a way to better balance the system. Is private industry the way to go? I don't know. You do private industry you open things up to, who's funding the data? Is the data going to be skewed to support what the funder wants? You know even with his trial, it's paid for by the drug company. And so what the drug company wants is to sell drug, so will the data be skewed? It's possible to skew data, you can skew whatever statistics you want! And so you allow more free enterprise you need to look at honesty and integrity and ethics of the research and how you monitor that, you know?

It's this unevenness, this knowledge that she's playing within a rigged and unsustainable system that makes her feel precarious. She can only hope that guiding principles and ethics of the health care system value her son over the messy politics of the pharmaceutical industry. But she finds it scary—that only she can see that her son brings something to the table, something “worth more than the dollar value that government will ever invest in him.”

4.5 Conclusion

This chapter has centered on the cases of three families, bringing out not only the eventful access disputes these families become embroiled in (for drug and other forms of care) but also the everyday care practices and wider pervasive inequalities that are central to life with disease. The three cases have shown how, depending where they are socially positioned within life in Canada, the ‘suffering individual’ and the ‘sustainable collective’ ontologies are experienced unevenly and differently. In none of these three cases do either of these ontologies represent the complexities of the illness experience and caregiving in any meaningful way. Each of these three families also have different stakes in the different versions of the Canadian nation that the suffering individual ontology and the sustainable collective ontology propose. A diagnosis of MPS forced them to confront and move through health systems and inequalities that unevenly inflect life in Canada depending on where they were positioned: geographic disparities in access to tertiary care, ableism, exclusion, ongoing settler-colonialism and racism, poverty, and complex intersubjectivities of deservingness and value.

For Abigail, Calum's mom, the suffering individual ontology never did do much for her because there was never a therapy developed for Calum's type of MPS in his lifetime. The types of resources that she needed to care for her son, such as the funding to keep him at home or at the

very least not be financially stretched by paying the monthly fee for the long term care home—are not included as important in the suffering individual frame of rare disease resource allocation politics. However, her position (or non-position) within rare disease pharmaceutical development pipelines gave her distance from all of the developments around treatments for rare disease—ones that gave her significant pause as she saw them unfold. Calum was born in 1975, his MPS IIIA diagnosis came four years later in 1979. When she got involved with MPS parents in the early 2000s, she was struck by how pursuit of ‘treatment’ had subsumed the focus of the parents that she met. Abigail always tells me how her thinking seems so different from other rare disease parents, but she doesn’t see that as a bad thing. Rather, she thinks that her positioning outside of rare disease politics allowed her to care for Calum to his final days and let him go in peace.

For Jack and Julie, Scott’s parents, they found that neither the suffering individual nor the sustainable collective really served them. The suffering individual ontology tried to make Scott a poster child of the evils of the sustainable collective ontology—a First Nations child being denied access to treatment from the big bad government—but they knew that this activism wasn’t really about care for Scott. Instead, they felt tricked into the rally in that parkade that day in 2005. They didn’t want to be anyone’s poster family for either ontology, they just wanted to get Scott the treatment they felt he deserved—and that, through participating in the clinical trial, they felt was partly his. It belonged to him as much as to Genzyme Genetics. The sustainable collective ontology wasn’t really one they were going to accept either—as a First Nations family familiar with the strategies of the settler state and centuries of the violation of treaty rights under a very similar narrative, they saw through these kinds of arguments pretty swiftly. They fought back hard against it. Throughout, they struggled with poverty and other challenges, doing their best but knowing that individual/collective politics weren’t going to come through for them.

For Ella, Andrew's mom, enzyme replacement therapy was approved for Andrew pretty quickly after his diagnosis, and without a fight, which Ella is grateful for. In a way, the individual/collective politics around rare disease worked pretty well for Andrew's access to treatment, but she feels locked within a system of deservingness that could shift at any time. High drug prices leave her with a nagging sense of vulnerability and precarity about how long such an expensive treatment will be provided, and how long the 'suffering individual' ontology that supports such astronomically expensive therapies will hold power in resource allocation politics. She would never tell her neighbours how much Andrew's treatment costs, believing they might be astounded that their tax dollars are going to such an expensive treatment. And what will happen in 'leaner' fiscal times? As a medical professional, she understands and appreciates evidence, which only heightens her sense of vulnerability. She knows that statistics can be skewed, and she also knows that governments are unlikely to validate the more qualitative forms of benefits that she sees in Andrew from treatment—especially so given the costs. Ella's deliberations of whether to enroll Andrew in a clinical trial shows how the heroic narrative of drugs as lifesaving is not always straightforwardly absorbed by parents—feelings about the future, quality of life, and the non-linear teleology of their child's lives are always complex.

Pharmaceutical enactments in the suffering individual ontology work to somehow separate families like these three from issues of collective concern. After all, the pharmaceutical enactment pushes, what could be more important to families than a treatment becoming available? Yet, as we've seen with these three cases, these families are part of communities and collectives wherein resources allocated towards other domains in their lives would also be life altering. Abigail and her husband Thomas could have used more money to help keep Calum at home or to assist in a larger way with the long term care home payments. Scott and Julie could

have benefitted from a system that does not systematically deny the treaty rights of First Nations in Canada, including the federal government's responsibility for providing health care to First Nations reserve communities, perpetuating intergenerational trauma and poverty. Ella and her husband Lucas could use some peace of mind in knowing that the 'social investment' in their son is secure, so that they do not have to worry that their neighbor thinks that the drug their child receives from the public system is too expensive. On the other hand, the impartial resource allocation enactments in the sustainable collective ontology posit rare disease patients as stealing high amounts of resources from everyone else. That ontology doesn't match with the actual dynamics and difficulties of life with disease in the midst of new technologies, either.

Neither the rationalized and sanitized framings of 'the sustainable collective' or the sensationalized framings of 'relief of the suffering individual' that structure rare disease drug access discussions can capture the dignity of these three families' stories or their care practices. Both of these ontologies posit these bodies as problems to be solved. The refraction of rare disease politics into an issue of either caring for suffering individuals or the suffering collective comes at the risk of actually doing rare disease patients a disservice by taking collective problems that demand collective solutions like poverty, colonialism, and the emergent forms of precarity that revolve around high cost drugs out of the frame of what the 'rare disease patient' wants and needs.

In the next chapter, I move back into the 'macro-politics' of rare disease in looking at how different actors work to draw and redraw the boundaries of the category of rare disease according to their needs from it. Ultra-rare conditions like MPS get entangled within (and used by) desires and enactments to shape the category around a range of profit-oriented and professional motives.

Chapter 5:

What is a rare disease? The cultural, political, and economic work of a category

“What Does Rare Mean? To be rare is to be different in a special way.”

-Deborah Katz (2017), *Rare Is Everywhere* children’s book

This chapter is about how social actors work to *define* rare disease as a category, both formally in terms of a prevalence definition and informally in terms of the social and cultural significations that some would like to be attached to the category of rare disease. Certain definitions enable certain practices. As Timmermans and Buchbinder (2012: 98) write: “ontological and epistemological changes in diseases matter for the actions they facilitate,” highlighting how definitions are central to carrying out practices, enabling the instantiation of an ontology.

A definition arranged around the ‘suffering individual’ ontology is one that expands the definition of rare disease, so that it can best satisfy the market imperatives that become attached to rarity through financialized drug development. On the other hand, a definition arranged around the ‘sustainable collective’ ontology is one that narrows rare disease membership criteria, so that only the ultra-rare and the conditions that are the most debilitating get ‘special treatment’ from the system. In the meantime, what rare disease means for patients and families—a collective identity around experience of biomedicine and the health care system—gets caught up within pharmaceutical enactments in tricky ways.

These politics around the definition of rare disease assemble around both formal and informal aspects of the definition: both how rare disease will be defined in policy and public health categories as well as the more informal significations that social actors would like to be attached to ‘rare disease.’ It is in these more informal significations that we see clearly how rare disease has become caught within different versions and directions of Canadian nation-making

around health resource allocation. Recall the loaded statement from CADTH's 2018-2021 strategic plan that I shared in the introduction:

The choice is stark: either sound public policy and evidence-based assessment will govern the adoption and deployment of existing and new technologies, or the forces of innovation and marketing will dominate health care decision-making and dictate the allocation of resources. The stakes are huge (CADTH 2018a: 2).

This statement posits two different potential versions of 'Canada.' One version of Canada is based on sound and evidence-based policymaking and use of drugs and technologies in the health care system. The other version of Canada is basically controlled by industry, with resources allocated unfairly and inequitably. The definition of rare disease has become caught up in this because a narrow definition fits with the first well-regulated and rationalized version of Canada, whereas a wide definition fits within the second and more market-oriented and privatized version of Canada. Through loaded statements about what 'Canadian values' are, social actors make their case for either version of Canada—but also, what kinds of 'citizens' rare disease patients are. In the process, the version of rare disease and Canada that jives with the suffering individual ontology makes its claims through an ethos of deuniversalization and privatization. In the process, the 'deservingness' of rare disease patients for resources is constructed differently within each ontology and each version of Canadian nation-making.

In the first section of this chapter, I examine attempts, controversies and contestations over defining rare disease in terms of prevalence for any individual rare disease. I look at how social actors vie for versions of rare disease restricted to the 'ultra-rare' versus more expansive and inclusive definitions, folding in the 'not so rare.' These different forms of prevalence indicate the power of the concept of rarity as a concept to contract or expand to different types of political and economic needs and goals. In the second section, I examine attempts, controversies,

and contestations over defining rare disease in terms of an aggregate of all rare diseases, in order to demonstrate the overall impact of rare disease on the Canadian health care system. Here, a paradox emerges: rare disease is simultaneously configured as something small (a drop in the bucket of wider health budgets) and something large (a major public health concern). In the third section, venturing further into the more informal affective and political significations social actors work to attach to rare disease definitions, I examine how the high prices of rare disease drugs have also embroiled what rare disease 'is' within a deeper and wider politics of deservingness.

As different stakeholders work toward a 'Canadian rare disease policy,' rare disease takes on a 'wily' quality. By wily I don't mean devious so much as I mean opportunistic: people frame what rare disease is based on what they need the category to do for them. There are possibilities and pitfalls to this. On the one hand, defining the category of rare disease offers patients and families with a range of low prevalence diseases an opportunity to collectivize and make demands upon the state and the market, not only for drug access but also other forms of needed care. On the other hand, the particular contours of the rare disease category offers the pharmaceutical industry opportunities to open up markets and reshape regulatory and reimbursement systems in ways that may be counterproductive to other health care system needs for people with rare and common diseases alike. These two 'stakes' become entangled with one another, permitting the pharmaceutical industry to frame their profit motives and high drug prices as inextricable from the moral and ethical claims patients with low prevalence diseases make about being deserving of health resources.

The wider political backdrop of this chapter is the efforts in recent years to introduce a comprehensive and universal Pharmacare plan into the Canadian health care system, which

would create a single payer universal prescription drug coverage plan for all Canadians. This would eliminate the current system of patchwork provincial drug plans with limited beneficiary groups and the dependence of many Canadians on extended health insurance benefits through their employer, or, in the case of 15.4% of Canadians, paying for all pharmaceutical care out of pocket (CIHI 2018). The Pharmacare movement has intersected with attempts to build a Canadian rare disease regulatory and reimbursement policy. This attempt to build a system of pharmaceutical care for *all* the population has been met with a ‘counter solidarity’ formation in the dangers that such a system could pose for *rare* populations.

Across the three sections of this chapter, I identify definitions as a central conflict point within ontological politics and multiplicity. Definitions, particularly definitions for the purpose of policy or regulation are about managing multiplicity for the purpose of developing standards and infrastructure. However, a definition of rare disease is not *just* about ‘values’ about caring about complicated and unusual bodies, it is about money (a lot of it), professional identity and ambitions for social actors involved (a lot of them), and the future of a health care system (in a national and global geopolitical climate of instability and inequality). A definition is not a neutral object, it is a decision to allow some relations/actions and foreclose others (Jensen and Morita 2017). Similarly to legal decisions, definitions are established in a process of co-production and “takes a social issue that is uncertain, disordered, or contested and reorders it within a system of preordained rules and norms” (Jasanoff 2012: 162). Social actors channel their implicit and explicit values into the creation of a definition of ‘rare disease’ but it is in the process of trying to wrangle that multiplicity into a policy that the many and multiple ‘stakes’ in the wily category of rare disease become apparent.

5.1 Rare disease as a matter of disease prevalence

In this section, I examine how public drug plan managers, regulators, and patient advocates work to define rare disease through different levels of prevalence. Their different economic and political commitments result in different desires around an official definition of ‘rare.’ I begin with public drug plan managers, then move to a Health Canada representative who works on rare disease drug regulatory pathways, then to a patient advocacy group representative.

Public drug plan managers tend to put in a rather tight prevalence definition of rare disease to determine which cases should go through ‘case-by-case’ decision-making and which should get special consideration for reimbursement. Public drug plans want to focus on the ‘ultra-rare’ diseases, such as MPS. As one provincial drug plan manager explained about their case-by-case decision-making process:

We define rare disease as 1.65 per 10,000, right, so that’s really rare! As opposed to lots of other jurisdictions in other places, they’re 1 in 2000, which isn’t really *that* rare, right? So if we happen to open that umbrella, then we would certainly be taking on more patients. Could we even function as a committee to do those reviews on a patient by patient basis with so many more patients? I mean the thing about opening it up is then you get sort of more non-rare diseases, and with those you have more data on more folks. With that, you can start to develop some general guidelines as opposed to having to make specific decisions about specific patients [for ultra-rare diseases], where the data is coming from small heterogeneous groups, where the stopping rules and the outcomes might be different depending on what type of patient you have.

Thus, the larger the disease population, the more data a drug payer can expect the manufacturer of the drug to provide. If a drug for an ultra-rare disease has a clinical trial dataset based on ten patients, then a public drug payer may be willing to accept that. If a drug for a less rare disease has a clinical trial dataset based on ten patients, then the drug payer has reason to be a lot more skeptical. However, patient and industry groups often want a very wide definition of rare disease to be the basis of a rare disease policy. A drug plan manager for a different province explained

why a wider definition is a non-starter for them. It's not that this public drug plan manager is fundamentally against a special process for rare disease drugs, but instead that membership in the category of 'orphan' needs to be delimited to just the *ultra*-rare, otherwise bad market behavior might ensue:

I think maybe we just need to move away from some of the categorizing or bucketing all these drugs with some of these terms. These are the ones that I think are truly being used for a rare disease: it's a handful of patients, they are going to come with a significant price tag associated with them, they probably don't have the same level of evidence that these other drugs within that category would have... I know that puts it in to a small handful of drugs but those are the ones that probably truly require a slightly different review process because the evidence is going to be so weak... We can't be making up regulations to start excusing people from doing proper randomized control trials, it's also the excuse that if something comes up during a review they'll never go back and research it because they'll say 'well we're an orphan drug, we can't do the clinical trials on orphan drugs,' *it almost gives them an excuse not to do certain clinical studies and instead they now focus on how quickly people can get access and how do you start identifying who these patients are* (emphasis added).

In a very broad prevalence definition of rare, drugs for diseases that do not face the same challenges of accumulating evidence would receive privileges that would put profits above public health.

In contrast to the commitments of public drug payers, which is to pay for drugs, a regulator like Health Canada's concern is with authorizing the drug for the Canadian market. They are responsible for safety, primarily, and are not implicated with reimbursement as such. As a regulator involved in earlier attempts to draft new regulations for orphan drugs in Canada shared:

So the Canadian need, it isn't just a matter of taking an American system and putting it here, so we tried to assess what does the Canadian health care system need? ... So in the States it's really about prevalence mostly, it's under 200,000 in the population. When I went and looked at the European definition from a prevalence point of view it's 5 in 10,000. I was advised by both agencies [the FDA and the EMA] that you need to consider the ratio because it grows with your population. So we did select 5 in 10,000, others who

wanted you know a rare or ultra rare definition would probably prefer it to be 5 in 100,000... such as people who are involved in paying for the drugs, they want the ultra rare.

The political (and economic) commitments and mandates are different for a drug regulator like Health Canada than they are for a public drug payer, resulting in a different lens on the issue of definition. His role as a regulator in a public system, then, is to make sure that Health Canada requires drug reporting and post market vigilance to aid public drug plans in monitoring and guideline development, but he cannot structure a definition entirely around what the public drug plans might find helpful because his mandate is different. He notes how the people involved in paying for the drugs want just the ultra-rare to be included, but he cannot do anything too different from other jurisdictions, so he had to work with and choose between the prevalence definitions set in other jurisdictions like the US and the EU. Partly, this is political. Health Canada will come under fire from lobbying groups if the definition doesn't lead to many rare disease drugs 'coming to Canada' (see Chapter 3). Every year, reports go out from industry groups and think tanks calculating the percentage of orphan drugs approved in other jurisdictions that do and don't end up authorized in the Canadian market. This is used by some to shame the Canadian system—how could a country like Canada care so little about bringing new drugs to patients?

The issue of prevalence also arises as conditions are “salami sliced” into rare and ultra rare conditions in order to get regulatory approval as an ‘orphan drug.’ The regulator described how one of the things about building an orphan drug regulatory framework much later than other states (over 35 years since the Orphan Drug Act in the US and almost 20 years since the European Medicines Agency regulations) is that they've seen how orphan drug policies have

been taken advantage of by manufacturers. ‘Salami slicing’ a condition into different genomic sub-conditions and then submitting the drug for regulatory approval increases time on patent and takes advantage of the ‘perks’ of an orphan drug designation (extended patent protection, research breaks, and tax breaks etcetera) while not lowering the price.

One example of this phenomenon of ‘salami slicing’ has occurred with the drug Ivacaftor for the condition Cystic Fibrosis which is, as a whole, not considered a ‘rare disease’ unless subdivided into subsets of genetic aetiology in order to receive orphan drug designation. Ivacaftor was initially submitted for regulatory approval for patients with the G551D mutation of the cystic fibrosis gene, and received a patent from various jurisdictions to treat patients with this mutation. Over the following years, Ivacaftor was then passed through regulatory approval for other mutations of cystic fibrosis, often with a slight modifier to the drug as with the combination of Ivacaftor and Lumacaftor (Orkambi), thus receiving a new patent. The company, Vertex, has been able to accumulate massive profits through this strategy (Hollis 2019).

As ‘common’ conditions such as breast cancer become understood more through a genetic aetiology, the potential for salami slicing and taking advantage of orphan drug designations by industry becomes a larger issue (Herder 2013). Regulators such as Health Canada are in the tricky position of being charged with approving drugs based on a drug’s safety and efficacy profile and ensure important innovations reach health care systems but also having to be aware of potential ‘bad behaviour’ such as salami slicing (see Gibson and von Tigerstrom 2015). This means that Canada has the opportunity to be thoughtful about which extra ‘qualifiers’ to put in place for orphan drug status beyond prevalence, such as that the drug is for a chronic and debilitating condition for which no other treatment is available, or ceilings on the company’s overall profitability. However, again, then lobbying from industry and some patient

advocacy groups ensues, roasting the agency for not doing proper consultation and not listening to patients' needs.

He explained how one of the difficult things is that Canada is a 'subsidiary culture' in pharmaceuticals—as explained in Chapter 3, the head office is often located elsewhere. This means that subsidiary offices are very concerned about getting very relaxed regulations so that the head office does not close up shop on their Canadian subsidiary office, and they will lobby harder for the prevalence definition that their head office wants rather than being willing to think about the impacts this might have on the existing health care system. He explained how industry representatives from global head offices that he meets at international meetings “are able to be a bit more progressive, explore things a bit more freely, say let's give this a try, let's set up a pilot, so there is quite a difference, it's very noticeable actually.” However, as he went on to describe, he was on a committee that Italy led that analyzed whether EU orphan drug regulations led to better access to the actual drugs and it was more or less a “patchwork” across the EU with inconsistent access in the end, similarly to Canada.

For some patient advocacy groups, particularly 'umbrella' groups like the Canadian Organization for Rare Disorders (CORD), a very expansive prevalence definition of rare disease is desired. As the President and CEO of CORD, Durhane Wong-Rieger, shared with me in an interview on the difficulties of defining rare disease, the lack of an official definition of rare disease affects the status of rare disease on the Canadian political agenda. When I asked Wong-Rieger what actually makes a definition important for rare disease patients, she replied:

It's for practical reasons. It will practically allow drugs to be registered as orphans in the same context and that's for a very practical reason, it has no other real reason for it. There's nothing that is based in terms of the greater burden on these people, or the number of people that would create a special needs category, it has nothing really to do

with that. It really has to do with what's going to allow companies to want to register in Canada at the same time.

For her, having a prevalence definition that expands the amount of conditions that can fit in it is desired because it will encourage companies to bring the drug to Canada, which has emerged in general as the primary concern of her advocacy work. She also hopes to include rare cancers under the umbrella of rare diseases, even though some of her patient advocate colleagues in ultra rare condition specific groups or patient advocacy groups in other countries disagree. When I asked her why, she reflected:

I think it's just the fear that cancer is going to take away too many of our resources, cancer already has a big profile, and the definition based on these genetic markers where you can take big cancers and make them small cancers would dilute the definition of what a genuine rare disease is... that is, something that can be defined in terms of a genetic misalignment or something, I think that's what it is. Like geez so what, it's going to take away from our pot? So it's too bad, because you know I think it's that kind of thinking that's going to keep driving us further apart as opposed to coming together for some good solutions.

In this frame, this inclusive definition of rare disease helps bolster the public profile of rare disease, not take away from it. However, this inclusive definition does open up certain possibilities for industry—enabling them, as we saw with the public drug payer's concerns above, to pass drugs for 'less rare' diseases through a special regulatory and reimbursement pathway and benefit from lower evidentiary and cost-effectiveness hurdles to reimbursement. Thus, as we saw from the public drug plan managers' statements, including the 'less rare' diseases in the definition of rare makes a special reimbursement pathway for the 'ultra-rare' diseases less viable because it encourages bad market behaviour and raises industry profits at the expense of the public health care system.

CORD is largely funded by the pharmaceutical industry and Wong-Rieger knows that the optics of this is difficult—but she says that patients want drugs, so she feels like she is still acting with integrity on this piece: “I will say if there’s anything you see me saying or doing that does not speak to the integrity of our being the voice of the patients you let me know, because that’s not where we are.” She does feel sometimes like she’s beholden to industry but also they have given her a lot of leeway because “they know that the message will be much more legitimate if they’re not driving it. And they trust us, that we’re not going to drive it in a direction that’s going to lead them out or to really be a negative for them.” For Wong-Rieger, the patient voice and the industry voice around a rare disease definition are very well aligned. Some other patient advocates (even those within CORD’s membership) feel differently, but as President and CEO Wong-Rieger manages a lot of the relationships and sets the agenda.

In 2014-2015, CORD spearheaded the development of a rare disease ‘strategy’ for Canada. Wong-Rieger asked Jay and Diana from the health policy unit to be involved, and they said yes, and they did their part. But the way that the work got divided up, Jay recounted to me once in an interview, was all messed up. In an effort to make the strategy have multi-stakeholder and multi-sectoral representation, Wong-Rieger had different people write different parts so that they could see their interests reflected in it. However, in Jay’s view, what this resulted in was that the strategy just ended up being a tabulation of everyone’s ‘wish list’—clinicians and scientists put in their wish list for research funding and industry put in their wish list for profits and regulatory ease. Jay and Diana were supposed to represent the HTA perspective, but the HTA perspective is deeply tied to the public drug payer perspective and no provincial drug payers were willing to really take part in this strategy development exercise. Jay found it all a bit exasperating: did anyone want to actually get buy-in from the public drug payers so patients can

get access, or did they just want to get their research centres funded and their shareholders satisfied and their professional desires fulfilled?

The CORD strategy used the 5 in 10,000 prevalence marker that Health Canada had in their draft regulations at the time. CORD launched their strategy in May 2015. The province of Ontario did incorporate pieces of it into their provincial orphan drug evaluation process, but the strategy didn't really go too far. But it was a symbolic exercise: it included everyone's wish list, which in many ways is how the category of rare disease gets used by social actors. In a lot of ways, this is the dilemma that Wong-Rieger must also work within: she has to find a way to make the patient voice match various wish lists from various sectors in order to ensure the wily category of rare disease survives the realm of ontological politics—so that powerful people from different sectors will help her keep it alive. To do this, she has to tack between the suffering individual and sustainable collective ontologies, but since the industry-backed suffering individual ontology is more focused on getting drugs to patients—in effect, having the same goal as she does—she is more likely to partner with them and back up their ideological practices and ontological framing of what it means to care for rare disease and thus the prevalence definitions they'd prefer too.

From 2012 to 2017 Health Canada developed draft regulations that used the EU definition of a 5 in 10,000 prevalence to define rare disease. In 2017, the draft regulations that Health Canada had been working on since 2012 were taken off of the Health Canada website. No one really knew what to think when the draft guidelines got removed: did it mean that Health Canada was backing out of the regulations? Speaking to the National Post newspaper, Wong-Rieger called this “the kiss of death” for rare disease in Canada (Forrest 2017). It turns out that

the draft regulations got all the way to the cabinet decision-making table, but then at the last minute they got scrapped.

While substantial changes to the Food and Drug Act to fold in rare disease drugs was not going to happen, in August of 2018, Health Canada, published information about the regulatory improvements to facilitate the approval and availability of rare disease drugs in Canada. While they listed some changes to their drug review processes, what many industry and patient advocacy actors had been anticipating was how Health Canada was going to define rare disease and orphan drugs after the older draft regulations were removed. But Health Canada didn't *really* define either. Instead, the framework posted on the website stated: “there is no common definition of an orphan drug or drug for the treatment of a rare disease/condition. National regulatory authorities define ‘orphan drug’ in different ways” (Health Canada 2018). They reiterated the European definition (prevalence of 5/10,000) and the United States definition (prevalence of 1/200,000), with some added qualifying interpretations from the two different jurisdictional definitions: “life threatening, chronically debilitating condition for which no alternative treatment is available” from Europe and “a presumption of unprofitability” for a low prevalence disease from the United States (Health Canada 2018).

This nebulous cobbled together definition was not received terribly well by those who were hoping for a widely inclusive but firmly delineated definition. A week later, a blog post titled *‘Health Canada defines a rare disease – sort of’* was published on a quasi-patient advocacy/market access online platform called Zeal Access. The author, James Radke, wrote: “my main concern with the addition of ‘alternative therapies’ and ‘profitability’ is that those phrases can later be used by policy makers, politicians, ministry offices, payors [sic], and other

regulatory agencies to deny or delay the accessibility of orphan drugs. Those groups are already really good at delaying things” (Radke 2018).

In March of 2019, the federal government announced that they would be working with provinces and territories to develop a national strategy for expensive rare disease drugs, including a commitment of \$1 billion over two years starting in 2022-23, and then \$500 million per year after that. The question on many people’s minds in the absence of a clear definition, however, was: who will be included in it? Which diseases? Why? These questions still hang in the air, as it this commitment was made during an election year. The federal Liberal party was re-elected with a minority government in late October 2019, and it is yet unclear whether and how the Liberal budget will be amended post-election. The 2019 budget used a somewhat cryptic definition: “Rare diseases are life-threatening, debilitating or serious, and chronic conditions affecting a small number of patients” (Her Majesty the Queen of Right in Canada 2019: 61). How small a number of patients? Why?

5.2 Rare disease as a matter of wide public health concern

In this section, I explore another point of negotiation among social actors in ‘defining’ rare disease: how many Canadians with rare disease there are in the *aggregate*. Framing rare disease in this way allows rare disease to be understood as a public health issue, rather than just a smattering of very sick individuals spread across the country. As more single gene causes of disease are identified, there is a commensurate increase in possible targets for orphan drugs in the future. It is estimated that there are 6000-8000 ‘rare diseases’ (defined as rare based on a very broad working definition of 1 in 2000), of which there are treatments for about 6%, only 1% of

those curative (Boycott and Ardigó 2017). However, the politics in this aggregate definition of all rare diseases as they operate in the Canadian context requires disentangling.

A frequently used number in Canadian rare disease drug access disputes is that there are “1 in 12” Canadians with a rare disorder. CORD uses this figure in their publications and press reports, along with the figure that there are nearly 3 million Canadians with rare disease, with two thirds of those being children (CORD 2015, CORD 2018). CORD cites their own website as the source, which includes no rationale behind these figures (www.raredisorders.ca/about-cord/ accessed 2 September 2019). Even Health Canada uses the figure on their website outlining their current regulatory approach to rare disease drugs, stating “Some approximate 1 out of 12 Canadians has a rare disease” but does not cite the source (Health Canada 2018).

On October 25th 2018, the federal parliamentary Standing Committee on Health held a meeting on ‘Barriers to access to treatment and drugs for Canadians affected by Rare Diseases and Disorders’. This session was part of a larger investigation on rare disease drug access and measures that the state could take to improve access to treatment as the government proceeded with its plan to implement Pharmacare movement as well as proposed changes to the Patented Medicines Pricing Review Board to more strictly regulate drug prices (see Chapter 3). Thus, the committee was gathering evidence to produce a report on whether and how to take the particularities of rare disease into account if or when these system changes are made. The committee held several meetings on this topic in which witnesses were invited to provide testimonies on the matter of rare diseases. This particular session that I will invoke below however has been selected for analysis here because the 1 in 12 figure was called into question in important ways. At this meeting, the witnesses who gave statements and answered questions from the members of parliament (MPs) on the committee included a computer scientist working

on phenotypic diagnostic interfaces, an adult patient with a rare condition called Muckle-Wells Syndrome, a physician who treats patients with rare disease, a pharmaceutical policy expert, and two representatives of the pharmaceutical company Janssen Pharmaceutica (a division of the giant Johnson & Johnson), which has several rare disease products on the market and in their development pipeline.

During this session, just how many Canadians have a rare disease was a topic of confusion and dispute, as the below statements pulled from the meeting transcript in order of their parlance illustrate (HESA 118 2018):

Dr. Alex MacKenzie: The number of rare disorders is 7,000 [...] That number may well grow with time but that's our estimate right now. Roughly one million Canadians are affected. One in 12 is bandied about. We think that is an overestimate. It's closer to 2%, to 3%.

[...]

Dr. Joel Lexchin: ... This is a point that has already been made—the assumption that one in 12 people have a rare disease in Canada is unreliable and should not be used to form Canadian policy about drugs for rare diseases. Any definition of a rare disease should not just take into account how frequently it occurs, but it also needs to incorporate the element of severity. In other words, it should occur infrequently and also be severely debilitating.

[...]

Stacey Silverberg, Johnson & Johnson: In Canada, as you may be aware, we don't have a formal rare disease framework or strategy, but it is important to note the "one in 12" number that's been noted today. As well, that number comes from the Canadian Organization for Rare Disorders. One in 12 Canadians lives with a rare disorder. It is incumbent on us, as Canadians, to help this at risk population.

[...]

Raj Grewal, MP Brampton East: Dr. Mackenzie, you put the number at around one million, and everybody else, including the documents I have, puts it at about 2.8 million Canadians suffering from rare diseases. Can you elaborate on why your estimate would be one million?

Dr. Alex MacKenzie: [...] That in no way is to undermine the severity or seriousness of rare diseases. I just think we need to be as careful as we can about the numbers. If you

look at Australian, Belgian, and Italian studies, in which they have done this well, it comes in at roughly that benchmark. Given the diaspora that makes us up, there is no reason to anticipate, from a genetic point of view, that it would be any different from the 2% to 3%. I think there may be a bit more data. I tried to drill down on the one in 12 from the CORD web page, but I am unable to find the source of those numbers.

Raj Grewal, MP Brampton East: I think if you want something that everybody on the panel can agree with, identifying the number of Canadians suffering from rare diseases is probably the number one priority in order to address the problem.

The Standing Committee summarized these different framings in their February 2019 report to the Canadian Parliament. Ultimately, they implicitly gave Dr. Alex MacKenzie the last word in closing the discussion in that paragraph with his estimate of 2-3% of the population with around 1 million Canadians affected (Standing Committee on Health 2019: 8-9). In the above quotes from the meeting, however, we see that highly respected health system policy experts such as Dr. Joel Lexchin are adamant that the ‘1 in 12 Canadians’ figure is a massive overestimate.

However, even after that concern has been forcefully raised in the committee proceedings, the pharmaceutical company representative uses it anyway, noting that it comes from CORD, and stating it as a matter of fact.

What all of this ambiguity signals, however, is that the epidemiological accuracy of the “one in 12 Canadians” figure may not be as important as the social, political, and economic meanings of it. What interests are being served with this ‘1 in 12 Canadians’ definition? Which different situated enactments is it satisfying and in which ways?

In an effort to figure out the source of this figure, I sent out a number of emails to those who use it. Dr. Millan Patel¹⁶, a pediatric geneticist and board member of the Vancouver based

¹⁶ Dr. Patel requested to be identified and credited by name.

Rare Disease Foundation was the first and only to reply. The “1 in 12 Canadians” figure was posted on the Rare Disease Foundation website at the time of our communication in March 2019 (Rare Disease Foundation 2019). The Rare Disease Foundation is more focused on rare disease as a biosocial community and helping parents avoid alienation and funding small biomedical research projects than they are with drug access, but it appears that the figure originated with Dr Patel. His reply to my query was as follows (Patel 2019: personal communication):

The only source I know of is me 😊 Here is the blurb I wrote for our previous website version, it didn't make it onto the new website but hopefully I'll get it up there soon...

The statistic of 1 in 12 (or 1 in 10) people being affected with a rare disease is often quoted but its basis is rarely explained. We believe the actual chance of someone being affected with a rare disease in their lifetime (called lifetime prevalence) cannot be determined as there are not enough people trained to diagnose rare diseases and some conditions are either too severe to be compatible with life or are quite mild so are missed. There are also a large number of rare diseases waiting to be described so any estimate is likely to be an underestimate. One could even say every disease is rare because the genome, environment and lived experience of each patient form a unique constellation. With these caveats in mind, we calculate the lifetime prevalence of rare diseases at between 1 in 12 and 1 in 13 by:

1. Summing the prevalences of the 500 most common rare diseases on the [Orphanet prevalence report](#)
2. Removing all birth defects from the list.
3. Adding the prevalence of major birth defects and intellectual disability in the population (5%, range for this estimate is 2.3% to 6%).

Many people tell us they do not think that 1 out of every 12 people they know has a rare disease. We believe our estimate does not match common experience because a lot of children with rare diseases do not survive and because a lot of people who have rare diseases look completely normal to the outside observer.

In this frame, there are people with rare disease but we just do not know it either because they have not been diagnosed, because their rare disease is invisible, or because they died before they could be counted. Likely a great many of these people do not know they have a rare disease either, because this figure includes people who carry mutations but are asymptomatic *or* the

‘common’ conditions people do have just need to have their rare genetic mutation aetiology discovered—they (we) are all rare disease ‘patients in waiting’ (Timmermans and Buchbinder 2010). Birth defects are removed from the list, but then the prevalence is added back in along with the prevalence of all intellectual disabilities, folding even more people into this category. As an industry sponsored study by Auvin et al. (2018) has shown, there are very real difficulties with estimating prevalence. So, social actors like Dr. Patel do what they can to try to drum up some numbers that will put borders around the issue and also channel increased research funding to rare disease, which is a major part of Dr. Patel’s work as a clinician-scientist and with the Rare Disease Foundation.

So why would a patient advocacy organization like CORD use it so frequently? In a way, it’s a paradox. To talk about ‘rare diseases’ implies something small, infrequent, and unusual: it doesn’t happen so often, so it needs special treatment. But to talk about rare disease as being large in the aggregate, it can start to look like there are *so many* rare disease patients in the aggregate—which means that finding solutions for the ultra-rare as suggested by the public drug payers in Section 5.1 begins to look logistically impossible. Similarly to Dr. Patel’s interest in research investment, however, to be ‘larger’ is to get more attention. In order to become an epidemiological category that is seen as worthy of public health investment and expenditure, it must be more coherent than a smattering of suffering individuals across the country—one must be a delineated and strongly enough populated category that it becomes epidemiological. Recall Foucault’s analytic, which highlights the individual/population conundrum that rare disease rests within. Biopolitics is a technology of power that:

Deals with the population, with the population as a political problem, as a problem that is at once scientific and political [...] they are collective phenomena that are aleatory and unpredictable when taken in themselves or individually, but which, at the

collective level, display constants that are easy, or at least possible, to establish. (Foucault 1997(1976): 245-247).

Presenting rare disease as a collective phenomenon allows claims for recognition from the state—if biopolitics is about the collective population, then a large aggregate number of Canadians with rare diseases presents rare disease patients as a considerable *part* of that collective population.

If the ‘1 in 12 Canadians’ figure helps social actors like Dr. Patel argue for increased research funding, and patient advocates like CORD to argue for a defined population health category for rare disease so that they do not get left out of system initiatives, what does the figure do for pharmaceutical enactments? Recall that in its origins with the Orphan Drug Act in the US, ‘rare disease’ is a category with its origins in the market. Presenting rare disease as some large and ambiguous and aleatory and likely to grow in scope and cost is an important strategy of the pharmaceutical industry enactment. For one, it encourages the government to develop a policy lest it get steamrolled by new treatments coming on the market, or alternately, overlooking the Canadian market altogether, which would hardly look very good on the global stage. However, it also discourages another sort of policy: Pharmacare. It makes further universalization of the health care system look impossible. Sometimes, nebulous ambiguity invokes an affective politics of fear and threat that is good for business (Massumi 2010).

To return to the Standing Committee of Health meeting discussed in Section 4.2, Stacey Silverberg of Janssen Pharmaceutica had this to say to the committee in her summary statement (HESA 2018):

We encourage the federal government, as it develops a national pharmacare policy, to consider potential implications for Canadians with rare diseases. Coverage for new innovative medicines is essential to ensure the best care for rare diseases, but moving to a single-payer public plan may impede this. Accessing new medicines is time-sensitive for

patients with rare diseases. It is vitally important that the existing public and private mix of drug plans be maintained to ensure that the latest medicines are available for all Canadians.

A national Pharmacare system, she argued, would delay access because then the system would ration and increase its use of cost-effectiveness measures and insistence on solid evidence. This would be a ‘disincentive’ for manufacturers to list drugs in Canada, leaving rare disease patients behind. As she continued: “We are worried about our Canadians” by which, she meant, specifically those Canadians with rare diseases. Which Canadians with which rare diseases? The ultra-rare, which drug payers are willing to negotiate on? The less rare, which drug payers are a little less interested in giving special treatment to? The patients who have diseases that they think are common but may later end up being understood as rare? It is precisely this ambiguity that works well for industry: it keeps their options open, encourages favourable regulatory policy, and discourages initiatives like Pharmacare that could lead to a budgetary landslide.

Thus, the ‘1 in 12’ Canadians figure in all its ambiguity demonstrates how under the banner of ‘rare disease’ several processes are playing out here at the same time. The first is certainly the politics of numbers (see Rabeharisoa et al 2014): only one million people might not be enough people to motivate political action, so rare disease patients collectivize and present themselves to utilitarian systems as not a fringe group but part of the population. This will also encourage research funding, since public research funding should go toward matters of wide population health concern. The second, is the financial interest in a rare disease as a widely populated category—similarly to the disease prevalence issue explored in Section 5.1 above, the more diseases included within it, the more diseases will be subject to special regulatory and reimbursement frameworks as well as more special pots of research funding for rare disease. The third is the logic of privatization: if rare disease is expanded into such a large and ambiguous

problem that is so expensive, the prospect of universal pharmaceutical coverage in Canada like the proposed Pharmacare program starts to look impossible and like it will negatively impact people within the wily and ever expanding category of rare disease. The ‘largeness’ of this framing of the wily category of rare disease can be used differently by different social actors.

5.3 Rare disease as a matter of deservingness above other groups

In this section, I examine attempts, contestations, and controversies around social actors working to attach particular types of significations to rare disease: particularly, that people with rare disease are more special and *deserving* than other groups who may make claims for collective resources. Ticktin (2011) has shown how much of contemporary neoliberal politics operates around allocating resources and aid towards certain types of suffering, and overlooking others. One type of suffering that gets valued highly in neoliberalism, she notes, is *biomedical* suffering. Other forms of suffering—like poverty or addiction—do not get folded into contemporary neoliberal ‘regimes of care’ in the same way. In what follows, I show how the suffering individual ontology harnesses these care politics in order to assert that rare disease lives have a special value—more special than other groups who might need or desire resources—and argue that the health care system should be deuniversalized so that resources can be channeled toward expensive pharmaceuticals with others left to pay for themselves.

At stake in these signification politics are what kinds of biological citizens (Petryna 2003; Rose and Novas 2007) rare disease patients are. Rather than biosociality being an expansion of claims to health care upon the state by all, in this case, biological citizenship becomes ‘salami sliced’ (to borrow a term from a notorious industry practice described in Section 5.1) into

different *classes* of deservingness based on perceived specialness or suffering, opening pathways for discussions of the privatization of the Canadian health care system.

I begin this section with a scene from the 2015 CORD gala and awards ceremony that followed CORD's annual conference, where an important speaker had agreed to do the opening speech. This speaker was James Moore¹⁷, who at the time was Federal Minister of Industry for Stephen Harper's far right conservative federal government that was in power at the time. Earlier that day, before the conference wrapped up, Wong-Rieger had exclaimed with glee that this was rare disease's "big chance" to get back on the federal agenda. Moore was connected to the rare disease world because his young son Spencer, born in 2012, has a rare skeletal dysplasia. This was his first time speaking publicly about his personal experience and his role as a 'rare disease dad.'

During his speech, Moore exclaimed: "As CORD has noted, nearly 3 million Canadians are affected by over 7000 rare diseases, many of them kids." He continued:

"The job of any government on the left or the right is to improve the quality of life of constituents. We're not gonna do that on things like rare diseases if we don't listen to organizations like CORD. That's why I'm so thrilled that you moved forward on a new policy to move this forward [referring to the CORD strategy discussed in Section 5.1]. As Minister of Industry and as a dad, you put forward a truly pan-Canadian effort so we can move forward. It's all part of all this learning and keeping the family together."

This feel good speech by Moore, however, is somewhat blurred by the context of an earlier public statement he had given previously. In December of 2013, a journalist had asked Moore at a press conference on what the federal government was going to do about the high rates of child

¹⁷ As an elected political figure at the time of this speech, Mr. Moore has been identified by name rather than pseudonym.

hunger and poverty in Canada. “Is it my job to feed my neighbour’s child? I don’t think so!” he had said with a dismissive laugh (Smith 2013). Yet here he was in front of a group of rare disease patients and advocates affirming himself as part of the rare disease ‘family’ and tying this in with his political role.

This contrast of Moore’s statement on the imperative to improve the quality of life for people with rare disease and the non-imperative to address child hunger and poverty that he uttered in another context is invoked here because it indexes how particular groups are attributed value and worth over others by imagining them as part of a (deserving) community, or in Moore’s terms, a family. Yet, as we saw in Chapter 4, people with rare disease also live in poverty, or find other dimensions of a social safety net that they could use for their care or their child’s care either lacking or missing completely. However, their biomedical needs and strategies to address them are granted *more* deservingness by social actors like Moore than their needs for say, a pan-Canadian poverty strategy, which was and is severely lacking.

Invoking a group of people as kin, Melinda Cooper (2017) has shown, is a common neoliberal strategy to imply and enforce sameness—often in moral opposition to those ‘other’ groups who present a threat or a violation to the boundaries of the family. If we accept the 1 in 12 figure discussed in Section 5.2 that puts the number of Canadians living with rare disease at almost 3 million, there are also 4.9 million people living in poverty in Canada (<http://www.cwp-csp.ca/poverty/just-the-facts/>, accessed May 17 2019). Children living in poverty, however, are “the neighbour’s kids”—not part of the ‘family’ in Moore’s politics. Which initiatives get accorded value by certain actors and which ‘citizens’ become valued in an unequal settler-colonial state like Canada is rife with politics.

This scene has been shared here to begin this section because it highlights how rare disease requires a critical politics of care capable of dissecting the striated terrain upon which people are accorded value. This is in no way to discount the suffering of people with rare disease—instead, what this data highlights is how the experiences of people with rare disease become *used* in ways that can end up increasing the vulnerability and precarity that rare disease patients face in their lives. It also creates a rationale for privatization of the health care system in the name of the suffering rare disease patient, as I'll explore below. As Chen (2003) has shown of the Canadian context, invoking the figure of the 'child victim citizen' as in need of protection has been a longstanding strategy of conservative politics to privatize and/or marginalize.

In order to frame people with rare disease as deserving of such high amounts of resources, some pharmaceutical industry actors and patient advocates and even some patients argue that the allocation of resources should be striated based on fault. As one rare disease pharmaceutical company general manager averred in our interview together: "Why not allocate funds to genetic diseases first," he asked, "where the person didn't do anything, they have a disease that's not their fault!" He used the example of the obesity epidemic. A lot of funds go to that, he asserted, but obesity is likely their own fault. Another pharmaceutical company general manager that I met with for an interview later that same week used a similar example: heart disease. Heart disease medications are cheap and can be absorbed the individual, and plus, heart disease is often caused by poor lifestyle choices. Why does the public system care for them, and yet deny care to suffering rare disease patients?

Several parents of children with rare disease who I interviewed and/or encountered throughout my fieldwork pick up this logic as well, asserting that their child's suffering is more deserving of scarce health resources than other groups. They compared their child's situation

with like people living with health consequences of ‘lifestyle choices’ like alcoholism, addiction, or smoking. As one mom averred in our interview together, “I’m not saying that they don’t deserve it, however how about they move a little bit down the line, because these kids don’t have a choice!” These politics of deservingness and worth as they get picked up by patients and families is a response to the precarity that emerges for families in these high stakes politics of care. As another parent shared with me, having a child with rare disease makes her feel compelled to say and think things that she never thought she would say—the worry that the rare disease pharmaceutical industry can just “back out” and medicines get taken away causes her such great anxiety that she finds herself doing whatever she can to make sure the political and economic conditions supporting development and reimbursement of treatment remain. The current configurations of pharmaceutical capitalism may have brought her child a drug, but it also roped her into this system of impossible trade-offs and feelings of division.

Some pharmaceutical industry representatives invoke the special ‘rare disease’ experience of suffering as rationale to fundamentally change and privatize the public health care system. This was the argument of a policy and governmental affairs manager of a pharmaceutical company with a large rare disease drug portfolio. As he shared:

So I mean a health care system exists to help people who are sick, and the vast majority of people will have common illnesses [that aren’t as expensive to treat] ... So in an ideal world, and I don’t know how this happens, I would rather people direct their own resources to looking after diseases that are kind of within the realm of the average person able to kind of afford it, and well, this is going to sound very communist, but people should pay according to what they can pay so that there’s more funding left over to cover things like rare diseases, which I mean people really are kind of stuck. In this frame, the health care system would redirect the large amounts of resources spent on ‘common diseases’ in order to keep all of the public funds for rare diseases, where people are *more* ‘stuck.’ Average people have common diseases and the average person can pay their own

way. In order to make the system equitable for rare disease patients, the universality of the system must be fundamentally altered so that more resources can be directed towards them. But if the Canadian system de-universalizes—leaving those with ‘common’ and cheap diseases to care for themselves—who will decide if the average and common diseased person is not *also* stuck? Will it be means/income tested? Determined based on perceived individual responsibility for causing the disease? What if this common disease is shown one day to have a genetic etiology that is rare?

These politics of deservingness and resource allocation also figure into the divergent nation-making practices around the suffering individual and sustainable collective ontologies. The suffering individual ontology frequently picks up the ‘rule of rescue’ as a matter of ‘Canadian values,’ though only for people with diseases that are not their ‘fault.’ For example, Joe is a market access strategist and invoked the rule of rescue in our interview together: “my bias is I strongly believe, and I think it’s a Canadian value, that we don’t want to see people left behind.” Pulling an example from his home province of Newfoundland, he spoke about how many fishermen there don’t even bother to learn how to swim because if the boat capsizes, there’s no point in trying to swim to shore because you’ll die of hypothermia within minutes. He compared this to drug care: “But if you’ve got the right survival suit then you’ve got a chance at survival!” Joe thinks that when health economists or drug payers invoke concepts like ‘opportunity cost’—the idea that the true cost of something is what you’re giving up in order to purchase it—they’re missing the point: “that’s not health policy it’s politics. That’s making sure that I can spread the benefit to the most people so they’ll like me.”

When I countered his statement about ‘Canadian values’ with the fact that many people do get left behind under the auspices of ‘Canadian values’—for instance, people living in

poverty, Indigenous people living on reserves with no access to clean water, missing and murdered Indigenous women, refugees being denied entry to Canada—he replied, “well you know I think that’s public relations more than anything else,” suggesting that those groups should then work to get a better public image and maybe they’d be conceived of as valuable and worthy of care too. This indexes how worth and deservingness is dependent on being attributed a positive moral value and deserving of special citizenship rights in the public sphere. That (rare genetic) biomedical pain and suffering has better ‘public relations’ than other groups ties back in to the individual responsibility and deservingness trope that powerful framings of rare disease facilitates, even as it renders life with rare disease more precarious at the same time.

These types of framings are not without their counter-framings about Canadian national identity from the sustainable collective ontology. While good intentioned, however, these counter-framings heighten the intensity of this politics of deservingness: the only other model there seems to be is a late liberal economy of abandonment (see Povinelli 2011). Take, for example, the statements of a health economist named Edward, who I interviewed one cold winter afternoon in his Canadian university campus office. Edward frequently consults for public drug payers, and he sees the goal of his work with them as delineating the ‘decision problem’ such that the politics and emotions of drug access do not dominate their decision-making. For him, the equity issues of rare disease have already been addressed through incentivizing legislations like the Orphan Drug Act—when it comes to reimbursing them, if the pharmaceutical companies are choosing to gauge, that’s the company’s problem, not the public drug payer’s. Edward refuses to accord rare disease any ‘special’ status more deserving than any other disease group and he was direct with his statement: “I would not have society be willing to pay more to treat my common cold because actually mine is a rare cold with exactly the same

symptoms.” He sees this normative position as fundamentally important to the future of the Canadian health care system.

Our conversation turned toward the very public access struggles that play out in the newspapers. I asked him if he thinks that rare disease patients seeking access to drugs have shifted or challenged the premises of the decision problem as he frames it. Our exchange illustrates his position:

Edward: Yeah, I mean the reality of politics, especially in provincial politics is if you can get to the minister and get on the front page of the newspaper you can work around the system. Have they truly changed the nature of the decision problem? No!

Marlee: So they’ve just skirted it?

Edward: They’ve just skirted it and claimed an unfair share of the pie. And I mean it’s their right as individuals to attempt to do that. I think it’s in contravention of their responsibilities as a member of society, but that’s fine.

In contrast to all of the framings of rare disease patients as deserving, Edward sees them as bad citizens—in contravention of how they should be approaching their plight not as disease sufferers, but as Canadian ‘members of society.’ At stake in both Joe and Edward’s framings of the proper ‘Canadian’ way to care is whether people with rare disease should receive special treatment rather than being subject to measured standards. The simplicity promised by both of their somewhat reductive approaches is alluring, but both bypass situated engagement with the intersections between bodies and benefit and meaning. Deservingness is a wily and shapeshifting quality as well, which is perhaps why it fits so well in the politics of rare disease.

5.4 Conclusion

In this chapter, I have analyzed how social actors work to define rare disease in formal and informal ways. The category either expands or contracts in prevalence, impact, and signification as it moves between different frames. And the category encompasses many

different material, political, and economic goals enacted by these different groups: patients' needs for a collective platform as a way to make claims upon the state for resources, public drug payer's needs for a manageable scope of work and drug budget expenditure, the pharmaceutical industry's goals for profit and market supremacy, among others. These different enactments do not always exclude each other—sometimes stakes are intertwined, and sometimes they are not: “belonging marks relations based on continuities of identity” (Strathern 1996: 531) but the ‘rare disease identity’ is neither continuous nor fixed. Thus, the category of rare disease is wily: it expands and it contracts depending on the pragmatic needs and professional desires that many have invested in different contours of ‘rarity.’

In the first section of this chapter, I explored how setting a prevalence definition of rare disease is not a simple task. A very narrow definition of rare disease—restricted to the ‘ultra orphan’—as desired by the public drug payers, would ease the passage of drugs for ultra rare diseases through the system. They’re more willing to negotiate for that. Drugs for ‘less orphan’ diseases? Not so much. They are not willing to let industry off the hook for producing strong evidence and charging reasonable prices when the population is ‘not so rare’. Some patient groups for ultra rare disorders also want this more restricted definition, though they worry that doing as such will lead the pharmaceutical industry to pull out of the orphan drug market altogether, so they feel caught. A very wide definition of rare disease—as industry and some ‘umbrella’ advocacy organizations like CORD desire—would be worth holding out for because it would increase rare disease’s financial viability and profits from the Canadian market in the long run, and perhaps the continued focus on orphan drug pipelines by the pharmaceutical industry. The regulatory agency Health Canada sort of meddles in between, but a definition in this high stakes environment is an ontological experiment in the management of complex

relations and commitments so there's been some waffling back and forth. The definition of rare disease prevalence is one that wavers between public and private voices and performances with the 'patient voice', highly dependent on who articulates it, saddled precariously in between.

In the second section, I explored a paradox in the definitional politics of rare disease: presenting rare disease as something small at the same time as it is something large, affecting '1 in 12 Canadians.' 'Rare' implies small and infrequent, but when put into the aggregate of all rare diseases in this (highly contested) way, rare takes on a paradoxical largeness. Rare disease oscillates from being enacted as small and rare, just a 'drop in the bucket' of wider spending, to something enacted as large and foreboding, certain to grow, too big for public health care systems to handle in a universal single payer model of Pharmacare. At the same time, the 1 in 12 Canadians figure offers people with rare disease the opportunity to present themselves as an important group in a utilitarian framing of public health. This enacted 'largeness' of rarity however spins a new set of relations into the politics of care over Pharmacare and a rare disease policy—suddenly rare disease is too big for any government to possibly take care of so governments must choose: take care of the rare or take care of the common but both will not be possible. In this '1 in 12 Canadians' formation, disparate bodies are drawn together (even more disparate than the bodies around which the rare disease category was originally invented) in a way that could, if more 'disease genes' are discovered, eventually include every human body in need of (expensive) treatment and cure (Timmermans and Buchbinder 2010; Dumit 2012).

In the third section of this chapter, I examined the tricky politics of deservingness that social actors work to attach to rare disease. This is a more informal part of defining rare disease—Health Canada will not be putting it into their regulatory definition, for instance, even if it is implicitly in any definition—but informal definitions circulate in ways that restrict the

ability to talk about and delineate the issue at hand. As Ticktin has shown, biomedical suffering is accorded more value in humanitarian ‘regimes of care’ than other forms of suffering—in this case, the regime of care is even further stratified into *rare and genetic* biomedical suffering. The long neglect of rare genetic disease by utilitarian and population health directions certainly inflects this politics, and if patients had not rallied they may still be neglected by the pharmaceutical industry. However, the flows of capital and interest accorded toward low prevalence diseases can in some cases operate to create new forms of privilege, division, and deservingness that strengthen the individual/collective binary through use and reification rather than taking it apart (see also Benton 2012, 2015).

The process of defining rare disease in formal and informal ways also figures into the competing forms of nation-making around public/private visions of the health care system that has animated health care system politics in Canada. Who gets to set the definition gets to set the terms, and a ‘narrow’ definition of rare disease has become attached to the sustainable collective ontology, whereas a wide and aleatory definition of rare disease has become attached to the suffering individual ontology. I have shown in this chapter how those enacting the suffering individual ontology attach a rationale of privatization to the category of rare disease, wherein common diseases (particularly those that people ‘bring their condition upon themselves’) should fend for themselves so that resources are left over for high cost rare disease drugs. The principle of universality in the Canadian health care system comes to be framed not as an ideal to continue to strive for, but as something to be dismantled and sliced into different classes of deservingness. Those enacting the sustainable collective ontology, on the other hand, have no other tools in their ethical toolbox than to frame rare disease patients as ‘bad citizens’ stealing more than their fair

share of the pie from the collective. In the meantime, patients get thrust into these deservingness politics and competing visions and enactments of the proper shape of the health care system.

Attention to these shifting and contingent boundaries helps make visible how the category of rare disease does cultural, political and economic work within the health care system. The oscillation between public and private, rare and common, deserving and undeserving is *part* of the market oriented category of rare disease, not an unfortunate political side effect. In its ambiguity and unstable contested qualities, this oscillation also works upon the illness experience, as patient and family stakes become intertwined with those of other powerful social actors in ways that offer patients and families certain possibilities but also certain pitfalls.

In the next chapter, I turn to an extended case study of a family, who, over the course of 13 years since the child received a diagnosis of MPS II, shift between standard of care treatment, experimental treatment in a clinical trial, and a promissory world of gene therapy. In this case, the mother develops repertoires to live among and across the competing ontologies of ‘care for rare,’ with the various evidentiary, biopolitical, and deservingness politics discussed in this chapter shaping her experience as a caregiver in particular ways.

Chapter 6: What does it mean to ‘be rare’? Rare disease, treatment possibilities, and the politics of care

“Affective experiences do not circulate along the same channels as other facts: you have to try them out for yourself”

-Chloe Silverman (2012: 380).

This chapter is about how a woman named Kelsey has learned to navigate the ontological politics around the suffering individual/sustainable collective binary opposition across three different kinds of treatment possibilities and hopes for her son, Erik, who has MPS II. I focus on three dimensions of experience at play in this family’s life over the past decade. First, how Kelsey experiences these eventful access issues alongside the everyday. Second, how evidence and benefit is experienced as a phenomenon that occurs in an individual life, rather than something that occurs within a disease population. Third, how ‘rare’ as a concept and category and frame of experience fades in and out of focus for Kelsey and the family over time as different treatment options and potentials enter (and exit) Erik’s life.

Erik is in a clinical trial for the intrathecal delivery of idursulfase, testing the ability of this mode of delivery for halting or reversing his cognitive decline. Erik also receives weekly infusions of the enzyme replacement therapy idursulfase, paid for by the provincial public drug plan. In recent years, Kelsey has also become involved in fundraising for gene therapy, though it didn’t really go as she had hoped. As Kelsey navigates these different treatments across different social orders (interacting with governments, pharmaceutical companies, and researchers), the fact that her child’s disease is ‘rare’ only means something to her insofar as it helps her to navigate rare disease treatment access politics. She has learned to inhabit and perform the part of

the parent of the ‘suffering individual’ when she needs to press for treatment access. However, as her child ages, however, and as rare disease treatment pipelines and politics move away from her child on to the ‘younger ones,’ questions around resource allocation and distribution and the striated valuation of bodies and lives begin to shift for her. Meanwhile, the family learns to live in the space in between the little everyday benefits they see emerging from treatment, potential futures opened up by other potential treatments, and being caught within systems of evidence and measurement.

In the first section of this chapter, I share Kelsey’s narrative of securing access to intravenous idursulfase treatment for Erik shortly after his diagnosis. I then move to the clinical trial of intrathecal idursulfase in sections 2 and 3. In section 4, I describe Kelsey’s work with other MPS II families fundraising for the gene therapy trial. However linear these sections are laid out over time as they occurred, the experience has not been linear for Kelsey and Erik or the rest of the family. Throughout these sections, I point toward how what ‘rare disease’ is to Kelsey shifts depending on how well the concept serves her in making her claims for resources and care as Erik’s body gets drawn into national resource allocation politics and international research and clinical trial infrastructures.

Juxtaposed with the more system-level entanglements of defining rare disease shared in Chapter 5, looking at the experience of a family over 13 years of living with these national and global drug development and access politics demonstrates how parents develop tactics to work within them—but doing so is not easy on families. Kelsey’s way of knowing and caring for Erik is informed by an ethical orientation toward caring for and helping her child—as Kelsey shared with me once, “it’s an experiment really, to keep him from progressing.” For her, the perceived efficacy of the drug is intimately tied to the range of possible futures that a drug can facilitate.

Having the possibility to explore that future taken away is experienced as a form of violence for Kelsey, whether or not a drug has been proven to ‘work.’

As new treatments come into view, new regimes of qualification and precarious access do too. As Erik’s body and future become increasingly situated within material, economic, and medical practices, Kelsey became, as Rapp (1999: 306) has written on amniocentesis, “at once [a] conscript to technoscientific regimes of quality control and normalization, and [an] explorer of the ethical territory its presence produces.” For Kelsey, who has done the majority of system and treatment navigation on Erik’s behalf while her husband worked a demanding job with long hours, rare disease is not a ‘thing’ or an ‘object’ or a policy problem to be solved but a platform from which to articulate moral claims so that treatment possibilities are kept open for Erik. That the treatments are so expensive and so entangled in controversy and billion dollar stakes is secondary to Kelsey, but it is through having to navigate those politics that ‘rare disease’ comes to mean anything to her at all. The intensity of articulations of ‘rare disease’ as a special frame of experience is produced *through* the complex interaction between moral experience, utilitarian public health discourses, and market system control of these powerful and meaningful substances.

At the same time, Erik’s body is not a bare blank unsocialized body waiting to be known in its pure state. As all bodies, his is cultivated within and through economic, political, and cultural practices and relationships (Lock 1993). So too, is Kelsey’s positionality as a parent and advocate for her child. Her ability to even contemplate alternative futures for Erik is embedded in wider relationships of power and money: living in a high income country, and having the ability to advocate for and gain access to resources. Contemplating a certain type of ‘future’ for one’s self or one’s child (or at least being in the social position of having it provisionally

granted) is something that is unevenly distributed across race, gender, and class (Benjamin 2013; Ginsburg and Rapp 2010). Bodies and lives are always situated somewhere.

However, even as this family enjoys certain forms of privilege, they are not immune to the violence of pharmaceutical profit regimes and accompanying deservingness politics. Traveling across three different forms of treatment potentialities over time demonstrates that the way that Erik has been valued by pharmaceutical politics in the past may not be the way he will be valued in the future in neoliberal regimes of care and value. At 16 years old, he is on the cusp between a social category that motivates action and compassion—the innocent and deserving dying child—and an undervalued social category that is notoriously under resourced in Canada—the intellectually disabled adult (see Ouellette-Kuntz 2005; Ombudsman Ontario 2016). Linking with the stories shared in Chapter 4, this adds another dimension to the individual/collective theme that runs through this dissertation. Another parent whose child ‘aged out’ of the category of the highly valued dying child described to me the feeling as one of having been “chewed up and spit out” by rare disease value politics. Where one fits within the value to relieve the ‘suffering individual’ is not constant, it can shift, it depends on how you become valued within current neoliberal regimes of value and care.

6.1 Diagnosis and treatment access: intravenous idursulfase

I first met Kelsey on a sunny coffee shop patio in 2010, when she was noticeably apprehensive at our first meeting. “How much of the story and what part of the story?” she asked me, as we sat down and her children played nearby. I know now that she was reading me: the past years had been hard, she’d had to talk to the media several times, and people’s motives are not always clear. In rare disease politics, you’re forced to tell your story over and over again, to

perform your suffering, and for what? Eventually, we settled in, developed the beginnings of trust, and she told me the story below.

As readers of this dissertation know by now, signs of genetic metabolic diseases like MPS II often creep up slowly. Erik's head was big, that was the first clue. Kelsey and her husband Brady both have small heads, and Erik's even looked bigger than some other babies his age. He wasn't babbling like babies do; he was diagnosed with hearing loss and had tubes put in. He stopped breastfeeding somewhat suddenly. It was at that point that a pediatrician suggested that they do some genetic tests. Kelsey and Brady were called in for a meeting at the metabolic disease clinic at their local children's hospital. Kelsey refers to that day as the day life changed forever. MPS II, Hunter Syndrome, a scary diagnosis, a potentially terminal disease, a disease they'd never even heard about before.

A few months later, an enzyme replacement therapy called Idursulfase (brand name Elaprase) manufactured by a rare disease drug company called Shire Human Genetic Therapies was approved by the Food and Drug Administration in the US, and by Health Canada several months after that. Idursulfase is a recombinant version of the idonurate-2-sulfase enzyme, manufactured from a human cell line. The treatment 'replaces' the missing enzyme in the body. Kelsey had learned about the drug shortly after Erik's diagnosis, and had been following it through regulatory channels. As soon as it was approved, Kelsey approached her local children's hospital, the drug company, and her provincial drug plan for access to the drug. She was denied by all three. She requested a phone call with the manager of her province's public drug plan. Kelsey explained how on the day of their scheduled call the drug plan manager said 'We need to come up with a federal plan before we can treat Erik, it's not fair to all the other kids in Canada if we treat just him.' She recalled her reply: "I said, 'well you haven't had a federal policy ever,

you've been working on one for 15 to 20 years, and I'm not going to wait another 15 to 20 years for you to come up with a plan while I watch my child die!"

After threatening to go to the media, Kelsey's request for access to the treatment was finally approved by her provincial drug plan. At just over 3 years old, Erik received his first dose of enzyme replacement therapy, and has received it weekly ever since for the past 13 years. Kelsey can't imagine life without this treatment.

At the time of his diagnosis, the concept 'rare disease' was new to her but she learned how to use it to throw the sustainable collective logics thrown at her right back by highlighting the different way Erik would be treated if he had a common disease:

Yeah so because it's a rare disease, you know we had to deal with a diagnosis and then we had to deal with the fact that it's rare and we don't know if anybody thinks Erik's life is really worth saving! And other families who go to the Children's Hospital, cancer is the best example they don't have to deal with that! But the cancer probably costs the hospital and government a lot more money than rare disease drugs do.

The low evidence base of idursulfase and its high costs (CEDAC 2007) didn't really matter to her. As she said: it's not Erik's fault or my fault that it's expensive, I don't know enough about the ins and outs of it all but why should he be denied treatment if he had had cancer they would have been doing everything they could!" Kelsey and Brady took videos of him before and after he started on the treatment and she said "before he started ERT you could tell that he had Hunter's Syndrome, so it's like helped his features tremendously his joints gained range, I think things were starting to progress, but his joints reversed."

"I know families who stockpile this stuff" Kelsey once told me when we were standing in her kitchen, as she held up an empty 6mg vial of a drug called idursulfase, about the size of her thumb. "Not in Canada, they're too strict here, but in the US. They order extra from the hospital

pharmacy saying they dropped one or punctured the IV bag by accident” she explained. “You do that every once in a while and you have a little stash for a week or two, just in case.” Each week, Erik receives treatment via an intravenous port surgically implanted in his chest. Kelsey, or sometimes a home infusion nurse, arranges all of the tools onto a disinfected tray, disinfects the skin around his port, fills the IV bag with the enzyme, clips the IV into his port, and tucks the IV bag into a small blue backpack for the four hours it takes to infuse into his bloodstream. It’s a part of family routine, a temporal anchor point in the week. The drug company provides the funding for these infusions to be done at home rather than in the hospital, further enabling the treatment to become part of the ordinariness of the everyday.

In 2007, idursulfase went through the CDR process described in Chapter 3. The CDR drug expert committee issued a negative recommendation based on the 96 patient clinical trial.

They listed three reasons why (CEDAC 2007: 1-2):

1. While idursulfase has been shown to have a biologic effect and improve some outcomes in patients with Hunter Syndrome, the clinical significance of its effects are not established. For example, idursulfase improves distance walked in 6 minutes (6MWD) but the average improvement is less than 10% above baseline values. Idursulfase has not been shown to improve clinically relevant outcomes such as quality of life, pain, rates of hospitalization, or the resources required for home care support.
2. It is unlikely that idursulfase enters the central nervous system and therefore, it is not expected to improve the neurological complications of Hunter syndrome.
3. Idursulfase costs \$4,215 for a 6mg vial and the cost for treatment of a 35 kg patient (the average weight of patients in the clinical trial reviewed by the Committee) is \$675,000 per year. The Committee did not feel that the high cost was justified given the lack of evidence of improvement in clinically important outcomes.

The report also pointed towards some safety concerns, including infusion reactions, cardiac arrhythmia, pulmonary embolism, cyanosis, and respiratory failure. They closed their report with the words: “reimbursement of idursulfase would raise questions about equity, since drugs that

have not been shown to be cost effective for other diseases are not generally reimbursed.” Kelsey and I discussed this report during our first interview together and she noted with dismay: “these people who don’t even know the families or what life is like for the child with MPS make all these Godly decisions!”

The province did not move to take Erik off the drug after this report was released, but Kelsey was well aware that Erik’s access to idursulfase was contested. Kelsey and I kept in touch after that first interview in 2010. In 2013, Kelsey’s provincial drug plan manager sent her a waiver, and told her she had to sign it. The waiver included the following release:

I agree that, during the period for which the Province provides funding for my treatment with the Product, I will undergo evaluations and assessments as required to obtain the information necessary to determine whether I have met the criteria established by the Province for continued funding.

They didn’t tell her what the criteria would be, only that the evaluations and assessments were set by the province. The criteria would certainly not take into consideration anything pinpointed as of value by Kelsey or the rest of the family, the people who live with Erik every day. Kelsey refused to sign.

“Why would I ever sign something that could legally let them do something like that?” she said with exasperation. She told me how she asked a friend of hers, a lawyer, if she had to sign it, and her friend said no, she’s not under any obligation to sign anything. So she ignored it. In early 2014, they sent it to her again: ‘our records indicate that you have not returned this form to date [...] Thank you for your cooperation.’ Access to the drug for Erik is too important to her to mess around, and she still has not signed the waiver. She doesn’t like the idea of him being monitored by the province, she has no confidence that they appreciate the particularities of rare disease. What if they find some excuse to take the treatment away?

When we first met in 2010, it didn't look like Erik had a severe form of MPS II with neurocognitive impairment. As Kelsey explained during our first encounter: "apparently he's not in the severe category because otherwise he'd be dropping 10 IQ points a year." He had a bit of a speech delay but thought that was due to the scarring in his ears, so they had him fitted with hearing aids. But shortly after we met, Kelsey and Brady began to notice, uncertain, as Erik slowly lost developmental skills. Intravenous idursulfase prevents further physiological decline: it helps his body metabolize the accumulated sulfates but only in his joints and organs—the synthetic enzyme administered intravenously does not cross what is called the 'blood brain barrier.'

By pushing and performing the part of what she calls the 'fire breathing Dragon Mom', Kelsey secured and maintained access to intravenous idursulfase for Erik. Caught in the clash between health system pragmatics and pharmaceutical promise, she leveraged the epistemological and policy gaps in provincial and federal drug access mechanisms to make sure her son would get access and that it would be maintained. She was fortunate to be well situated in a particular social position to do so. She knew how to communicate so that the public drug plan manager didn't just ignore her requests to talk. Her social position as a relatively privileged white woman ensured that the public drug plan manager knew that her threat to go to the media had teeth: an innocent white child's suffering would make a compelling media story. She had a lawyer in her personal network who could give her advice on her options, and as she didn't have to work outside the home to feed her family she had the time to fight back. She knew, as an educated white Canadian woman, that she could refuse to sign a government waiver and face few consequences.

6.2 The clinical trial: intrathecal idursulfase

In this section, I describe how Erik came to qualify for a clinical trial that is testing the administration of idursulfase intrathecally. Kelsey already knew about the trial because as one of forty or so MPS II patients in Canada, Erik was already on registries run by the manufacturer, Shire, and they'd already checked in on the family to see if Erik could be in the trial. But on their first check, he was not in the severe category—it didn't seem that his brain was affected. It was extremely overwhelming to suddenly be in the 'severe' category of MPS II. As Kelsey described to me:

So we get his diagnosis and we don't know if his brain's been affected or not and for 4 ½ years we were hoping and praying his brain would be okay. We were told his brain would be okay! And then all of a sudden it's not okay. And it was interesting because we'd been down [to the trial center in North Carolina] to be assessed for the trial numerous times and the first time we were assessed, I guess Erik would have been five, and Dr. Stoller [the lead trial doctor] told us his brain was okay, go home, don't come back, he won't need this trial... I remember it was the summer, it would have been probably June or July. And then it was probably six months later, well less than a year but probably more than six months after that, I got in touch with Dr. Stoller, and I said look, I can't tell if it's because I've been so scared for so long or if there actually is something going on, but can we just come back, for one more assessment?

On that next trip to North Carolina they learned that Erik did in fact have neurocognitive impairment. Kelsey was in despair. By five years old he was supposed to be safe: neurocognitive issues usually show up a little earlier than that. An affected brain meant Erik would slowly forget words, memories, and his siblings' names, he'd gradually lose the ability to swallow and move on their own. For Kelsey, deciding to enroll Erik in an experimental clinical trial testing idursulfase through an intrathecal mode of delivery was a "no brainer" to use her words—she doesn't consider the trial to be research, but desperately needed treatment. As Kelsey recounts of that time:

I remember being up at [the family's lake cottage] and I was drinking too much and I was taking sleeping pills and I was a mess. [...] I couldn't get out of bed, because it was the difference between life and death. It was like, okay, my kid is now dying! Fortunately, there was the trial and it was open, and so once I dragged myself... once I got out of the depths of my hole it was like, alright, now I have to fight for this drug.

Since the drug was in clinical trial, fighting for it meant doing everything in her power to make sure Erik fit the narrow inclusion criteria. To be included in Phase I of the intrathecal trial, patients had to have an IQ below 77. Erik's IQ was actually too high, but Kelsey tried whatever she could to get him in range:

So Erik got a 78 or a 79, in order to qualify for Phase I you had to have a 77, so Erik didn't even qualify, he just did in my mind! So we had to wait for him to come back in [for another assessment], I let him stay up really late so he was tired and foggy the next day, I did everything I could to get him to qualify, probably didn't feed him breakfast too or something, and so he qualified and we were next in line [to have the CSF pressure tested].”

Qualifying with an IQ below 77 was just the first hurdle—the other criteria was that he had to have a cerebrospinal fluid (CSF) pressure of <30.0cm of H₂O. But unlike keeping Erik up late and not feeding him breakfast so that he'd score low on the IQ test, there were no little everyday tricks that she could use to try to make sure his CSF pressure was within eligibility levels. Kelsey and Brady ran through all of their options to make sure Erik's pressure was within inclusion range without it getting back to the clinical trial doctor. They couldn't ask Erik's pediatrician to test his pressure; it would be against both clinical and research codes of conduct. They looked into getting a lumbar puncture done privately to test the pressure, but any hospital would have had to log the procedure; they might be found out. At their wits end, they considered getting Erik a subscription for Diamox, a drug used in mountain climbing to reduce pressure at high altitudes. As Kelsey recounts:

We could not get this fricking Diamox without questions, you know. So we ordered it online. And this drug shows up. And we didn't even know, we had no idea if it's even going to show up. And then this drug shows up, it's from Glasgow, we ordered it from some random website, and we're like, so how do we know if it's actually Diamox?

Ultimately, even after testing the pills by taking them themselves, they decided against giving it to Erik—it was too risky. But, Kelsey affirms: “I fully would have, I would have, and I've talked to other parents who would too, like you do anything for your kid right?”

Kelsey grappled with the slow pace of waiting to see if he would qualify, without any control over the outcome. She recounted: “But the waiting? Like I was psychotic, probably literally I would have been certifiable crazy.” She described sitting in the waiting room to find out whether he qualified:

I've never been so close to having a panic attack, I was shaking, and I couldn't stop shaking and I was sweating and I thought I was going to throw up, and I literally had a garbage can near me because I didn't know if I was going to be able to keep it together and then he came in and he was like, 'he qualified.' And I was crying.

At 7 years old, Erik was enrolled in the trial. Since 2011, the family has oriented their life around making sure Erik gets his monthly dose of what Kelsey calls 'liquid gold'. In the trial, idursulfase is administered intrathecally (directly into the cervical spine). As she described: “I mean IV ERT made some changes but IT [intrathecal] it's kind of like the superdrug.”

The process was hard on Kelsey, though. For the first years, she went back and forth to the trial site in North Carolina with Erik. She described the disorientation she felt:

Going to North Carolina, it was hard to come back. It was like, they *got* me, and they know me, and I know them, and there are other MPS parents and they get you too and I get them. And then I get home and my neighbors are talking about 'oh I'm trying to potty train my kid and they're not doing it' and 'we had this fight about finances' and I just wanted to be like fuck your finances! So I felt like I had no connection at home, I was angry at everybody that talked about stupid things. So every time I got home from North Carolina, every time, I couldn't sleep, I just would cry for hours. And I think I probably cried myself to sleep every night for the first 6 months of the trial... And then, Erik was

learning again! And he was doing well. And then it just became normal, going to North Carolina. Slowly it became routine, and expected, and we knew what to do. I was always packing or unpacking or booking hotels or flights or childcare, every month. And so it was busy in that way, but it became our normal, and Erik was slowly gaining skills. We still didn't know what it would look like, it probably took about a year or two years to know what to expect with Erik and from Erik, but he wasn't dying. And he didn't die.

Eventually, she convinced the trial doctors to let her get the trial doses at her local Children's Hospital, so they only have to travel to North Carolina a couple times a year. The eventfulness of the experimental treatment slowly moved into the everyday, and it was in that everyday that the treatment's efficacy came to mean something to her. As well, her own endurance and willingness and ability to fight for her child becomes a part of the narrative of Erik triumphing over disease (see also Wainer 2015), leading her, as she told me once, to sleep better and rest easier knowing that she's done everything that she can for her child.

One thing that Kelsey finds difficult is that she does not quite trust that the clinical trial is measuring the areas where she is seeing changes in Erik as a result of receiving the trial treatment. One scorching summer's day in 2015, Kelsey and I sat on the dock outside of her extended family's shared lakefront cottage, chatting about this and that: tattoos and traffic patterns and our families. Erik and her other two children played nearby in the fresh warm lake water. Suddenly, Kelsey trailed off on the conversation, her gaze focused on Erik. He'd been splashing around in the shallow water just a few feet away from the dock. Kelsey exclaimed: "Look! He's not losing skills anymore, he's gaining them." Erik, 11 years old at the time, was playing with a toy called a water blaster. We watched as he immersed it fully underwater, and filled up the barrel. He then raised the toy out of the water, aimed it a few feet in front of himself, and pushed the lever through the barrel. Water shot out in a steady stream, back into the lake. He

laughed joyously, deep from his belly, and looked over at us, grinning. He dipped the water blaster under the water to fill it up and try again.

As we continued to watch Erik play in the water, Kelsey turned to me, shaking her head: “I tried to teach him how to use that thing for years! It’s the intrathecal, I know it,” referring to the trial therapy. “It’s so frustrating to me that this kind of stuff isn’t part of the clinical trial!” Kelsey said, shaking her head. “They’re just measuring his IQ and I fill out a questionnaire every once in a while, there’s no space to say ‘hey, Erik can do these things that he was never able to do before the intrathecal! Notice it!’ It’s only by spending time with him, by knowing him, that you can see the difference.”

Whether the endpoints chosen in the clinical trial prove the drug’s efficacy for regulatory approval or not, Kelsey is certain the drug works for Erik because of the things no one is bothering to measure: he sleeps better, he can understand consequences more, he relates more with his siblings, and he’s learning to play with toys that previously were just meaningless plastic objects to him. She’s not sure if he was ever on placebo, but the differences in him after receiving the trial treatment were so noticeable that she really doesn’t think so. He even asked Kelsey one time when they arrived in North Carolina for a trial dose: “mom, where are the other boys like me?” Kelsey thought it was amazing that he put that together and attributes it directly to the drug. Drug benefit derives from the myriad little ways she sees it changing Erik’s disease course over time. After we discussed the difficulties of collecting evidence for a small study sample trial as we sat on the dock that day, she exclaimed: “yeah, rare disease sucks!”

Kelsey’s approach to drug benefit is quite different from the way that drugs are proven to work in the framework of the randomized clinical trial, the supposed ‘gold standard’ of Evidence-Based Medicine (EBM). In EBM, different forms of evidence are considered to exist

within a hierarchy, where at the top of the hierarchy is randomized, double-blind, placebo-controlled trials of a large study sample. Observational data produced within the daily life of family interaction—like Kelsey’s—does not even make it on to the pyramid. This gold standard of evidence is produced through a rigorous methodology, wherein a drug passes through four phases of study to prove that it works across a population of study subjects. Endpoints are chosen, and if those endpoints are proven—the drug is seen to ‘work’. This is tricky for rare disease because of the small patient population and the heterogeneity of the condition. It’s also tricky because while evidence might be good enough for regulatory approval, but reimbursement and access is a whole other thing. Kelsey knows that, and has her game plan prepared for when the trial ends:

I think it will be a lot harder to take a drug away from a child than it would be to get him on it in the first place. So I feel like I have at least, well, I have more protection right now than I did when I was trying to get Erik IV [referring to intravenous idursulfase]. So yes, Shire could say sorry, Shire could take it away. I mean the trial could shut down, so I don’t feel protected for sure, completely. And yeah, the province could say no we’re not giving drug, or IT, or Canada could, but I feel like I have more protection. Like if I went to the media, if I went and got lawyers, I feel like I have more protection right now than I did when I was waiting for Erik to get IV.

Getting in to the clinical trial didn’t only get Erik treatment, it also got Kelsey into a good position to advocate if she has to. She is fully ready to perform the part of the ‘suffering individual’ on Erik’s behalf if she needs to—she knows that it works and has currency, and she’ll do everything in her power to ensure that the treatment is denied based on cost or evidence level. That said, intrathecal idursulfase might not have an easy time when it goes through the regulatory and reimbursement phases of its life cycle: if the trial is successful, it will be indicated to be used alongside intravenous idursulfase, compounding costs to health systems. It is not an ‘innovative’ drug in Canada’s definition, since the substance itself already exists and already has

a patent. Intrathecal idursulfase is not any different from intravenous idursulfase in its properties, it's really just a matter of mode of delivery. The allure of testing a new mode of delivery for an existing drug for a manufacturer is so that they can renew their marketing exclusivity and profit yield. This means it will likely not get extended marketing exclusivity in Canada under current rules—so the drug company, which is now Takeda after Shire was acquired by the pharmaceutical giant in 2018, may not choose to enter the drug into the Canadian market. But Kelsey is hopeful that she knows the game enough by now. At least she doesn't have to do the waiting like she had to do for intravenous idursulfase, and like she sees other parents of children with MPS II having to do because they didn't make it into the trial in time.

Not all children got in to the trial like Erik did, and some MPS II parents across North America have formed tight communities, so they know who got in to the trial and who didn't. These exclusions have really impacted Kelsey and how she thinks about stuff like clinical trial design. On the day at the lake cottage, I also asked Kelsey for an update on her friend's son, Adam, who was one such case. Adam receives weekly intravenous idursulfase infusions but his cognitive degeneration is leading to physiological degeneration that the enzyme replacement therapy in his bloodstream could not fix. Kelsey is part of a small group of (largely wealthy and white) mothers of children with MPS II scattered around North America who call themselves the 'Dragon Moms.' They had recently asked the pharmaceutical company, still Shire at the time, to let Adam receive the experimental therapy on compassionate grounds, but Shire refused. Most recently, they had written a personal letter to the CEO. Kelsey rolled her eyes: "well, Pornskov won't do anything! He doesn't care at all!" using the group's nickname for Shire's CEO, Flemming Ørnskov. Shire was not going to put their neck on the line for one kid whose condition had progressed so far. Not only would it cost them money (without the payback of Adam's data),

it would also potentially jeopardize the drug's safety profile if Adam, whose condition had gotten worse in recent years, were to have a bad reaction to treatment. Treating Adam was too high of a risk. That there are no protections in place for patients like Adam alarms her:

I think it's so messed up that there isn't a governing body for big pharma, like the World Health Organization, that would cover the whole world, that could say and look at it objectively, like not from a parent perspective, not from a pharma perspective, but say yes, this drug is working, this kid should get it, and that protects pharma. So if Adam died on it, because yeah, he hasn't gotten drug he is more severe and he's got more medical issues, pharma could still get their drug approved. But as a result, now it's getting harder and harder for anybody to give Adam drug because he's getting more complicated and there is a higher risk of him dying on it. If they'd just have given it to him in the first place he would have been doing well like Erik! But anyways, it would protect pharma so if Adam died it wouldn't hurt their approval... But who is going to look after the Adams of the world and the Eriks of the world when big pharma draws a line in the sand and says no? Like who is going to look out for humanity I guess... I don't understand how we've been humans and living and doing, like there's been big pharma for this many years, but it's been, but we're killing people, we're letting, not killing, we're letting people die when they don't have to.

What made Kelsey so mad about this particular denial was because the pharmaceutical company was always so magnanimous and 'caring' in other ways. As far as Kelsey sees it, the clinical trial for intrathecal idursulfase isn't research it's treatment, and Pornskov was really pushing it by denying their requests for Adam. For her, it doesn't matter what the data says or what's inclusion and exclusion criteria are written in the trial protocol: the drug is working, whether the benefit is being measured properly or not, and she's certain that Adam would have flourished on the drug had he been given the chance.

Of course, Kelsey's position is a situated one. Her incredulity at the lack of institutional or legal capacity to ensure access is partly due to her positionality. As a relatively privileged white woman living in the global North, it wasn't until she had a child with disability and genetic condition that it became apparent to her that a world exists where improving a given individual

child's life chances isn't always sufficient cause for action. Children all over the world die all the time for lack of medicines, basic ones, and lack of clean water and other basic necessities too. Still, she's on to something with her critique: why isn't there a global governing body of the pharmaceutical industry? Who should get to make these decisions and according to which principles?

6.3 Clinical trial days: the lived experience of evidence production

In this section, I look at clinical trials as sites of meaning making that expand far beyond whatever datasets are produced by the trial in the end. As data collection takes place, clinical trial treatments become part of the everyday context of experience for parents like Kelsey and children like Erik who participate in the clinical trial. To illustrate, we travel to the medical day unit of Kelsey and Erik's local children's hospital, where Erik receives his monthly dose of intrathecal ERT for the trial. In exploring the temporality, materiality, and intensity of a clinical trial day, we see how attachment to a drug is made long before the 'proof' emerges in clinical trial datasets. The purpose here is to show how part of what it means for a drug to 'work' is the way it blends into lives and narratives and routines, where the anticipatory space of the clinical trial for a family is not seen as research but instead as treatment. Erik is not a passive actor in this story, however: as his neurocognitive capacity gets measured and his body poked and prodded he has a lot to say, too.

6.3.1 Early morning

I arrive at Kelsey's home at 7:00am, one of the many days I accompanied her and Erik and his brother and sister to the hospital where the clinical trial procedure takes place. We need to be at the hospital by 8:00am, ideally a bit before, and we have a whole city's worth of rush

hour traffic to get through. Kelsey is rushing to get ready to go with the precision of an air traffic controller. She acknowledges my arrival by saying, “Hey Marlee! EMLA?” referencing the numbing cream we needed to put on Erik’s chest port, which would be accessed at the hospital in order to give him the anaesthetic. I nodded and after washing my hands, find Erik sitting on the couch with his shirt off, looking annoyed. I help Erik’s little sister smear the cream gently over the spot on his bare chest, and then cover the creamed up area with a large clear plastic bandage. Everyone brushes their teeth, wrangles their stuff into backpacks and cloth grocery bags, we hop in to the car, and we go.

Upon arrival at the hospital, we are ushered into a room in the medical day unit where Erik would be monitored and tested before and after the procedure. The research coordinator is there waiting for us. Erik is not allowed to eat until the trial procedure is over, so his siblings who accompany him also don’t eat breakfast out of solidarity, and everyone is a little on edge. The nurse comes in to weigh him, but he doesn’t want to go to the room where the scale is. He hates taking off his shoes, and he knows he’ll have to. “Come on Erik!” his little sister said, “I want to watch cartoons and we can’t until this is done!” Erik relents, pushes his shoes off, and shuffles to the room with the scale. His height and weight are measured and recorded. He shuffles back, and before heaving himself back on to the mobile stretcher to watch cartoons, puts his shoes back on.



Figure 4: Corner of Medical Day Unit room, where Erik is monitored before and after the clinical trial dosage. © All Rights Reserved, Marlee McGuire.

6.3.2 Mid-morning

About 20 minutes before Erik is to be called to the operating room for the trial procedure, the clinician acting as Principal Investigator of the trial for the drug manufacturer came by to conduct a neurological exam. Erik is happy to see her, but he also knows what is coming: he's going to be asked to take off his shoes again.

Part of the neurological exam is to monitor his gait as he walks up and down the coordinator. The way he walks is taken as an indicator of neurological function, so the clinician needs to be able to see whether he walks flat on his foot or on the ball of his foot, which can be hard to tell with big sneakers on. "Can you take off your shoes, Erik?" she asks gently. "No!" he said. Erik's little sister saved the day yet again: "it's okay Erik! Marlee and I are also going to walk in the hallway without our shoes," and she looks at me, signaling. We both slip off our

shoes and walk out into the hallway, gesturing at Erik to come with us. He shook his head, but did follow us, though he still refused to take off his shoes. Kelsey and the physician looked at each other, silently saying ‘okay, this is the best we are going to get today.’ We all walked together along the corridor, but he’d only do it once before he decided he’d had enough. The clinician wrote down the details she could get into the data collection form. These moments are tense in a small population clinical trial: a consistent streak of poor results is more likely to shape the dataset in a small trial than it would in a large one, potentially making it look like the drug doesn’t work. Datasets are made with the assumption of compliant and submissive bodies in mind, not an almost teenager, hungry and annoyed. The clinician completed her form, and said goodbye.

Shortly after the test, Erik is called to radiology for the procedure. We all make the journey, down the elevator down the hallway, through the secured locked doors, where we wait for the anesthesiologist in the waiting room. Kelsey wanted to talk to the anesthesiologist. When Erik had first started the trial, he’d had a port implanted at the base of his spine that allowed access to Erik’s central nervous system so the dosage could be made that way. That port is also part of what’s being tested in the trial. Shortly after the port surgery, there had been an issue with it. He’d gotten a big infection, his central nervous system fluid leaking everywhere. Kelsey had ordered it removed—she didn’t trust the evidence on it so far, other kids had had issues with the port too—but now that means that this procedure must be done surgically each month. She wanted to discuss with the anesthesiologist if it’s okay—to be put under anesthesia each month. He comes by, they discuss it, he assures her that it’s quite likely okay, the impact on him cognitively and physiologically is likely no worse than if he were to drink a light beer once a month.

Once this discussion is complete, and the anesthesiologist has briefed Kelsey on the plan for the anesthesia, we enter the dimly lit room where the procedure takes place. The pediatric surgeon, the surgical nurses, the clinical trial research coordinator, and myself wrap ourselves in lead garments: skirts tied around our waists, vests around our torsos, zipped to our necks. Erik laid down on the operating table. Kelsey punched the password into the iPad she keeps queued with Erik's favorite cartoons for this occasion. She pulls one up on the screen, presses play, arranges herself beside Erik at the top of the operating table, holding the iPad up by Erik's face so he can watch the cartoon as the anesthesiologist does their work. After a minute or so, Erik's eyelids become heavy and close, his body goes limp. Kelsey says "Okay, he's out". She kisses him on the forehead: "see you soon bud, I love you". She is escorted out of the room—she's not allowed to stay, in case something goes wrong and she gets upset and in the medical team's way. The anesthesiologist does one last check of Erik's breathing and also departs.

The surgical team moves quickly. They tape Erik's eyelids shut just in case they flutter open during the procedure. They gently prop Erik on to his left side, so that his back is facing them. They place the blue surgical sheets upon him, isolating the surgical area on his lower back by leaving it bare. The research coordinator nervously looks at the clock, writes down the time on her procedure log. The nurse swabs his lumbar region with a disinfectant that stains his white skin a reddish brown. The monitor above the table shows the surgeon the image of what lies beneath Erik's skin, helping him to find the exact point where to make the lumbar puncture. The surgeon positions the needle between Erik's vertebrae. "OK, 1-2-3" he says, everyone braces. "Go", and he pushed in the needle. Erik's lumbar spine has been accessed. The surgeon draws out cerebrospinal fluid, caps off the vial, hands it to the research coordinator. He then attaches a vial of the experimental drug to the needle: a mix of saline and idursulfase. It takes less than a

minute for the drug to leak in to Erik's cervical spine. "OK" says the surgeon, and the team gets to work, retrieving the needle, removing the blue sheets, taking the tape off his eyes, placing a band-aid on the place where the needle had been inserted for the spinal tap.



Figure 5: Erik after the trial dosage, still under an aesthesia on the operating room table. © All Rights Reserved. Marlee McGuire.

The research coordinator fills out her log, the procedure is complete in less than five minutes. A porter arrives, and the clinical team helps shift Erik onto a wheeled stretcher bed. I follow along with the porter and the research coordinator to the anaesthesiology recovery room, where Erik's breathing would be monitored for an about an hour, and he would slowly wake up from his chemically imposed slumber. When he starts to stir, the recovery room nurse comes and checks his breathing. He likes the nurse, but he doesn't like waking up from the anaesthesia. "Leave me alone! She can't tell me what to do" he says, swatting at her, and nestling into his pillow. The nurse laughs, "okay, well if you have that much energy you're good to go."

6.3.3 Late morning to early afternoon

When Erik gets wheeled back to the medical day unit from the recovery room, everyone can finally eat breakfast. Kelsey sets him and his siblings up with some food she brought from home and the cartoons are turned on. The research coordinator and the staff nurse monitor his vitals, every hour, noting them on the study datasheet. Everything looks fine, but we have to wait until a set time after the procedure to make sure he's in the clear. Kelsey thinks the doctor in charge is too cautious, but there have been adverse events from intrathecal idursulfase, serious allergic reactions. The Children's Hospital has a therapy dog program, and a therapy dog comes to visit for a little while, hanging out with Erik and his sister on the gurney.



Figure 6: Therapy dog on clinical trial dosage day. © All Rights Reserved. Marlee McGuire.

Time passes, we give the kids their lunch, and we wait. Kelsey's grandmother comes to pick up Erik's sister to bring her to gymnastics class. Finally, around 2:30pm, we are discharged. We gather up the bag of empty food containers, a bag containing a change of clothes for Erik and the

iPad, say goodbye to the nurses, and make our way to the elevator that would bring us to the underground parking lot. Erik's little brother chatted with Erik about the kind of sushi he wanted—every month, after the clinical trial day, the family orders a big platter of sushi, Erik's favourite, for dinner. We reenter the world outside of the experiment.

6.3.4 The social life of experiment

This ethnographic section has shown some of the lived experience behind the clinical trial dataset. The frustrations, the drives across the city, the long days, the fraught and controlled activity of the operating room are the real life contexts that a clinical trial dataset does not encompass. Kelsey is forced her to reconcile her attachment to her hope that the drug will work—and her observational claims that it is working—with how Erik's access to the treatment after the trial will be dependent on how it fares within the various systems of measurement it will pass through in regulatory and reimbursement channels. The dataset anonymizes, it removes the observational world of moral experiment that Kelsey lives in from the world of truth and places it in to the world of inconsequential anecdote. For Erik, on the other hand, the procedure is a somewhat unpleasant routine, made slightly better with access to usually forbidden cartoon watching and sushi for dinner.

For drug companies, evidence is a site of potential profit and deregulation through political and scientific individualization. For public drug payers, evidence is a stable artifact around which legitimate decisions can be made. For parents like Kelsey, evidence is something that takes all of these complexities and sanitizes and anonymizes them into numbers that will determine her child's life course. She knows that the clinical trial isn't studying Erik as a whole

being and just measuring some outcomes that he may or may not experience, or that may or may not show up as statistically significant across all the subjects in the clinical trial.

In mid-December of 2017, I opened up Facebook and saw a post written by Kelsey on her public page dedicated to MPS II research fundraising. She wrote: “I don’t have a lot of words right now, but this news shakes my world.” Kelsey’s post was linked to a press release on Globe Newswire (2017), which outlined:

The study did not meet either its primary or its key secondary endpoint. The primary endpoint evaluated the difference in cognition between the SHP609-treated and control groups, as measured by change from baseline in General Conceptual Ability (GCA) scores in children with Hunter syndrome after 12 months of treatment. The key secondary endpoint evaluated the difference between the SHP609-treated and control groups as measured by the change from baseline in Adaptive Behavior Composite (ABC) score.

The press release reported that the trial wasn’t closing despite these dismal first results, and that ongoing analysis and subset analyses of the full data set may have other conclusions.

Nevertheless, it sounded major alarm in the MPS II community that this drug that families desperately believed was working and working extremely well may not make it out of the trial phase. As Kelsey posted later on: “What I do know without a doubt is that this drug works and I will go to jail before I see this drug get taken away.”

Shortly after receiving the news of these disappointing early results, Kelsey told me about how one of her US based Dragon Mom friends collaborated with MPS II parent advocates in the UK and Canada to put together a research grant proposal. Their goal was to correct what they felt were some massive oversights in the clinical trial design. They didn’t think that the Phase II/III trial was long enough to show difference between the treatment and control groups, and the extension study that Shire was doing didn’t have controls at all—they worried that this would lead to the FDA and other regulatory agencies saying that the dataset didn’t show a clear enough

difference. So they wanted to fill in some gaps. Shire indicated that such a parent led study would be well received, and they met with the FDA and put together a research proposal. They asked for donations and ultimately set up a survey on toileting: a consistent thing that parents were reporting across the trial was that children's toileting skills were improving. The parent who led the study thinks it's going to make the trial, Kelsey isn't so optimistic but thinks it probably can't hurt. In any case, these parents were taking things into their own hands—if the manufacturer wasn't going to make sure the trial data wasn't ambiguous and eventually lead to problems with the FDA and other regulatory agencies, they would. Their children were subjects in the clinical trial and that led them to claim a sense of ownership over the dataset, and the directions in which it would lead the drug through its social life and into bodies as standard of care.

The trial wrapped up in September of 2018—as of September 2019, trial subjects are still receiving dosages and should still do so for at least a year or so. Data is still being gathered but the dataset for regulatory approval has been closed. Kelsey has been told that intrathecal idursulfase will probably be submitted to regulatory agencies with an indication of children under six, because it turns out that it was the data on the older kids—like Erik—that was making the endpoints look statistically insignificant. So older kids will have to be prescribed the drug 'off label' and she knows this will make a tougher access case.

In January of 2019, Shire, a relatively small but lucrative rare disease pharmaceutical company was acquired by the Japanese company Takeda Pharmaceuticals for \$62 billion USD. The acquisition gave Takeda entry to the lucrative North American market and Takeda became one of the 10 largest pharmaceutical companies in the world. Takeda and another company, AbbVie, had been trying to take over Shire for years, and Takeda swooped in and convinced

shareholders that it was a good idea because their confidence (and stock prices) were a little bit lower than usual because of the disappointing top line results on the intrathecal trial. Takeda (or some other pharmaceutical giant) would likely have eventually succeeded with the acquisition anyway had the intrathecal top line results not been poor, but this moment of vulnerability helped it to happen when it did.

MPS II parents believe that Takeda is still proceeding with submitting the data to regulatory agencies rather than just withdrawing the drug, but time will tell. Kelsey also told me a rumour that she heard that Takeda bought out another drug for MPS II that was in its early phases of development that was supposed to also cross the blood-brain barrier to protect their interests with intrathecal idursulfase. She imagines that means they're planning on going ahead with intrathecal idursulfase since all the clinical trials have been done, otherwise why would they buy out their competition like that? Still, she thinks, it kind of sucks that this other drug won't get made, what if it could help too? But Takeda needed to protect its market, they couldn't have another drug come on the market that could undercut the intrathecal idursulfase. For now, Kelsey isn't getting too wrapped up in worries about it, she's trying to move forward and live life, but she's ready to pull out her rare disease Dragon Mom persona if she needs it.

Taken together this section has shown the immense investment—of time, money, affect, worries—that parents and families invest into a product in a clinical trial. Parents develop 'narratives of efficacy' (Condin 2014) and also feel a sense of ownership of the drug, they take matters into their own hands when it comes to producing data that could help the drug along. However, this section has also shown that behind the lived experience of evidence production the drug is subject to its other economic entanglements as well. The fate of intrathecal idursulfase is not only in whether the dataset is good enough for regulatory approval, but also whether Shire's

investment in the clinical trial for intrathecal idursulfase makes it through the \$62 billion acquisition by Tekada and can compete with other products in its new owner's development pipelines. Intrathecal idursulfase being brought to market is also entangled in competitive business strategies in which other products in development pipelines that threaten to undercut it will be nipped in the bud—competition eliminated and monopoly increased. From what Kelsey understands, the plan for regulatory submission is to only include data on the younger research subjects for whom the data looks more promising, leaving older patients like Erik to try to get it off-label. As Erik and the family spend long dosage days at the hospital each month, getting poked and prodded and petting therapy dogs, the drug is working through multiple other channels in its social life. For parents like Kelsey, that the disease is 'rare' fades in and out of focus depending on whether and how she needs to fight for the drug and for Erik. The rest of the time it's just regular life.

6.4 The technoscientific beyond in search of a cure: gene therapy

For a time, intrathecal idursulfase's status as 'liquid gold' or a 'superdrug' was somewhat displaced for Kelsey. In early 2017, the potential for an even better and more definitive cure appeared as a possibility: gene therapy, with a promise that such a therapy could 'cure' the faulty gene.

Gene therapy hasn't been without controversy. In 1999, a 17 year old patient named Jesse Gelsinger died of multiple organ system failure after being injected with a dose of experimental gene therapy as part of a trial for ornithine transcarbamylase deficiency. Jesse had been relatively healthy prior to the trial, his condition was well controlled with a low protein diet and medication. This unfortunate case caused significant controversy because while at first it was

presented as random and unforeseeable, it was soon found out that other patients and mice had gotten sick from the vector. It was also found that the lead scientist in charge had a serious financial conflict of interest in the success of the trial. Subsequently, the FDA halted all 257 gene therapy trials in place at the time until safer gene delivery technologies were found. In recent years, a handful of clinical trials have been initiated investigating gene therapies for rare diseases, and two have been approved by the FDA in the US. Gene therapies as one might expect by now are expensive, and have been controversial. Zolgensma for Spinal Muscular Atrophy was approved in May 2019. The price is around \$2.1 million USD. In August of 2019, it was found that company scientists manipulated data and that there was faulty record-keeping and poor quality data collection on mice, leading some to wonder if gene therapy will be able to surpass manufacturing issues and the dark shadows of gene therapy's history (Hughes 2019).

In the spring of 2017, researchers in the US that an MPS II advocacy organization had been supporting with research grants had some success with developing a vector for the IDS gene, and it showed some promising results in mouse models (Fu et al 2018). The MPS II community got pretty excited and decided to band together. The goal was to raise \$2.5 million USD so that MPS II parents could de-risk the early development for the researchers and help them build a facility to produce the vector on a larger scale sufficient for clinical trials. Kelsey sent out an email to her research fundraising mailing list:

*I have to "go there" a bit in order to share this information and save my child, but I don't want to and I'm not diving in. I am doing this for Erik. Human clinical trials for gene therapy in MPS II Hunter Syndrome are around the corner. We could begin next year. *IF* we raise \$2.5 million dollars. Right. That.*

Along with a few other MPS II parents, I spoke with our gene therapy researchers a couple weeks ago. Mice with MPS II start dying around 7-months of age. When they treated their mice that made it to 9-months old with double the dose of what they give their younger mice, these 9-month old mice came back. They normalized (to be clear, I

don't want Erik as anybody other than who he is, but avoiding an early death, surgeries, hospital trips, and letting him be as independent as he can and wants to be would be my dream). I don't know how many months old my Erik mouse would be, but can you imagine? I don't even know what that would look like. Erik as a typical 13-YO kid? I won't. I can't. Not yet. It's too scary. The letdown would be too monumental. Even writing this I'm choking back tears and emotions. Shove them back down. For now.

BUT, I do believe it is possible. WITH YOUR HELP. The thing is, with a rare disease, we NEED your help raising awareness. Nobody knows about MPS II Hunter Syndrome but us and in order to raise \$2.5 Million dollars, we need people to know.

With gene therapy SO close, our MPS II community has banded together. We've organized teams. If each team raises \$10,000, we'll reach \$1 Million. I think we can do better. Our runs raise \$10,000 each year without a cure on the horizon. Our Food Truck event raised \$20-40,000. Our gala raised \$80,000. \$10,000 is attainable. Let's beat \$10,000. \$10,000 to see an Erik who has no physical or cognitive limitations?? For real. [...]

So what can you do? You can share a link to our fundraising page and ask your community to donate. Tell them why they should donate. Tell them how close we are to human clinical trials. Tell them how you know Erik and how MPS II Hunter Syndrome affects him. Tell them how MPS II Hunter Syndrome affects you.

THANK YOU. If you have questions, ask. I'm a mom on a mission to save her kid's life. I'll do anything. The fire-breathing dragon has been mostly sleeping for the past few years, but she's being called back out... it is time.

In the year leading up to gene therapy looking like a possibility, Kelsey had told me about how she felt like with the trial going well and nothing major on the horizon or any access struggles in her near future she was learning to appreciate the uneventfulness of life. She had mentioned gene therapy before but it was an abstract concept, something about vectors, and it seemed pretty far off. When the gene therapy researchers that she references in the email above had success with the mice, all the lights turned on, and Kelsey summoned the “fire-breathing dragon” up from sleep. As in the text above, Kelsey started to imagine Erik actually being cured, a life for him without limitation. She loves him as he is, she was careful to point out in the email, it wasn't that

she wanted to change him but gene therapy could offer a better life for *him*. Intrathecal idursulfase came to seem like just a stopgap, a bridge to this actual cure.

‘Rare’ as a concept gained salience in her life again because it helped her frame to her family and friends what was special about Erik’s disease and this gene therapy potential—kids with common diseases have a whole society around them who see their condition and want to help them, but Erik depends on you to raise that awareness on his behalf. Over the next year or so, Kelsey threw herself into organizing fundraising runs and community events to help towards this \$2.5 million goal, drawing together all her family and friends (and her anthropologist, me) to help.

The researchers working with the MPS II parents were not the only ones working on an MPS II gene therapy. In the meantime, a clinical scientist who had been involved with the intrathecal idursulfase trial moved over to a biotechnology company working on another gene therapy model for MPS II, separate from those researchers that the parents were raising money for. Kelsey was a bit annoyed about that, but also curious to see if Erik could get into that trial since it was already recruiting. She got in touch with the clinical scientist who knew Erik and Kelsey well from earlier days in the intrathecal idursulfase trial and the clinical scientist told them they should probably come down to her center in Pittsburgh to do some tests to look into it. Kelsey said yes, but then it became apparent that their travel to Pittsburgh and the tests would not be funded by the company, and Kelsey would have to foot that bill herself. “Isn’t a pharma company doing this, shouldn’t they be paying for that?” Kelsey asked. “Well, no, this is just some testing to see,” was the response. Kelsey managed to secure some funding from an advocacy organization—the cost of the testing alone was \$18,000—and the family traveled down to Pittsburgh. The clinical scientist did all the tests and then said “well, Erik is too old, this

trial is not for you.” Kelsey was surprised and not surprised—somehow she knew that Erik was being used as a datapoint for this clinical scientist and that she was not serious about enrolling Erik in the trial. But, she told me, she had to try, just in case.

Gene therapy hasn’t turned out to be so close after all. The MPS II parents did end up raising the \$2.5 million, but then there was some sort of contamination with the vector so suddenly the researchers needed some more money. Kelsey doesn’t know too much about it—the whole process kind of divided some of the MPS II parents. Some of them got really secretive and protective and there are a bunch of non disclosure agreements and Kelsey’s not on the board of the advocacy organization overseeing things so she’s not sure what’s happening now. But she can’t get too wrapped up in it. “Erik’s old now,” she told me recently. All the new treatments are going to be tested on and indicated for the little ones. The zeal around treatment development for MPS II is all about saving the ‘MPS II boys’ but even though intellectually Erik is a child, physiologically he’s almost a man now.

Kelsey and several other parents who participated in my study have talked about how a lot of the discourse around rare disease drug access in general centers on saving ‘the kids.’ If adults are seeking expensive therapy, it’s usually about how drugs will let them go back to work, be productive members of society, parent their own kids. That progress narrative is likely not in Erik’s future, unless he somehow gets gene therapy and it in fact works miracles, but when? How? There is another researcher in the UK who also says he’s working on vector, but Kelsey is cautious. She’ll help to fundraise, probably, but it’s too easy to lose all equilibrium. She needs to focus on making sure Erik gets sustained access to intrathecal idursulfase now that the trial is over and it will soon begin moving through the next stages of its socialization through the life cycle. One step at a time.

6.5 Conclusion

This chapter has presented how one family has moved through three different treatment hopes in securing rare disease drug care over the past 13 years: first, intravenous idursulfase, then, intrathecal idursulfase, and finally, gene therapy. These three treatment modalities exist in different spheres: intravenous idursulfase in ordinary everyday standard of care, intrathecal idursulfase in a liminal experimental mode of a clinical trial, and gene therapy in a promissory world of potential. Each promise to do different things—to open up different forms of moral possibility and selfhood for Kelsey and for Erik. In the process, different dynamics of family care practices, drug benefit, rare disease, and living life with MPS II become visible.

For each of these three treatment possibilities and hopes, Kelsey drew upon the repertoires that she has developed for managing care for her child in between the suffering individual and sustainable collective ontologies. For intravenous idursulfase, she pushed against the sustainable collective ontology by threatening to make the issue highly visible and going to the media. She secured access to that treatment for Erik, and has maintained it by carefully navigating the politics of evidence around it, such as when she refused to sign the waiver to permit the province to collect outcome measures on him that could lead to them stopping the treatment. For intrathecal idursulfase, she tried to manipulate the evidentiary regime around the trial protocol to make sure that Erik qualified. When the trial is over, she is fully ready to pull out her ‘fire breathing Dragon Mom’ persona and fight for his continued access, by highlighting how he is suffering and needs the treatment no matter what the evidence says or what the costs are. For gene therapy, she drew her community into fundraising by highlighting Erik’s ‘rarity,’ in the process learning new things about the cutthroat world of rare disease therapeutic development like when she traveled to Pittsburgh to see about a clinical trial only to learn that the researcher

knew in advance that Erik would not qualify due to his age, but wanted to collect some data on his disease progression nonetheless.

What does it mean for a drug to ‘work’? At the level of this family, evidence operates as a messy, empirical, and deeply felt process: little benefits from treatment that emerge in the context of everyday life. Whether and how the drug is ‘working’ is also inextricably tied up in the possibilities for a future that a drug has embedded within it—as with Kelsey’s framing of gene therapy, this is even applied to a potential drug that hasn’t gone through any human trials yet. This however does not mean that parents like Kelsey are ‘irrational’ or do not understand evidence and science. Kelsey is a keen assessor of evidence, as her decision to not use the intrathecal port shows, and makes choices based on risks and benefits balanced within an ongoing context of moral experiment and possibility that operates in everyday life not in a dataset.

What does it mean for your child to have a ‘rare disease’ as opposed to any other type of devastating pediatric disease? For Kelsey, ‘rare’ is not an a priori quality of Erik’s disease but something that Erik’s disease becomes in interaction with inadequate biomedical knowledge, health system pragmatics, and capitalist market system dynamics. Being ‘rare’ offers her a frame of speaking and articulating Erik’s plight that motivates action, that throws the contradictions of both rationalized and sensationalized frames into relief, to make sure that the conditions supporting Erik’s treatment aren’t pulled away.

Overall, the suffering individual ontology has worked well for Kelsey so far—she thinks that the pharmaceutical industry is a bit messed up, but the language around biomedical suffering around rare disease has helped her to push back against the sustainable collective ontology. However, as Erik is getting older, she is starting to notice that he’s no longer fitting into the

innocent dying child trope, and his resource needs are going to rise beyond just what he needs for biopharmaceutical care as he ages into a different social category—the intellectually disabled man. Watching Erik grow from a child into a teenager has raised questions for Kelsey. “He’s old now,” as she said—he’s no longer the desired subject for clinical trials and treatments will increasingly be indicated for the ‘young ones.’ As rare disease drugs transform formerly terminal conditions into treatable diseases, prolonging the lives of individuals who previously might not have survived through childhood, the subjects of deservingness politics focusing on the ‘suffering individual’ as described throughout this dissertation are coming to collide with other categories of persons who are not accorded such value in neoliberal regimes. To harken back to the stark ‘winners and losers’ formulation of the health economist in Chapter 3, we see that while Erik may be a ‘winner’ of resources now, he may be a ‘loser’ in resource allocation politics later, as he gets older. In these politics, one can be a ‘morally legitimate suffering individual’ (Ticktin 2011) in some ways, and outside of it in other ways.

In the next chapter, we move back to the health policy unit and Jay and Diana’s attempts to find a way to break apart the power politics that structure treatment access on the ‘micro’ level, enacting their own care practices through research in an attempt to find a way to repair these difficult questions. They understand how these politics of care affect families like Kelsey’s, and so they aim to develop a new ontological framework for nation-making around resource allocation outside of the suffering individual/sustainable collective binary opposition. However, moving beyond these politics of care is not simple or easily enacted.

Chapter 7: **What does the public think? Making a collective in which rare disease fits**

In this chapter, I focus on the health policy unit to look at how Jay and Diana, head and director of the health policy unit, tried to take apart some of the politics that structure rare disease drug access disputes through two ‘citizens’ juries’ that they designed and implemented in the Spring of 2015. Unsatisfied with both the ‘suffering individual’ and the ‘sustainable collective’ ontologies, they designed the citizens’ juries as a way to bring stakeholders and the ‘lay public’ together to, they hoped, develop a new ontology around rare disease—to collect ‘values’ as social facts that could make room for a collective in which rare disease fits.

Jay and Diana are motivated by stories like the families shared in this dissertation. They have ‘engaged with patients’ long before ‘patient engagement’ was a health policy research trend, and in listening to patient stories and taking them seriously, know the types of difficulties and precarities faced by parents like Kelsey as they navigate treatment access in Canada are real. The deservingness politics around rare disease drug access disturb them, and so too do the sanitized and sensationalized frames of the suffering individual/sustainable collective binary opposition. Working in policy, they know the power of ‘values’ in the process of nation-making, and they wanted to articulate and enact a version of Canadian ‘social values’ through the juries that forced a new way of approaching the politics around rare disease drugs.

In this chapter, I show how they worked creatively *with* the tension between values to relieve the suffering individual and protect the sustainable collective to try to make the citizens’ juries intervene meaningfully within these politics. In making the findings actionable to policymakers and rare disease legible to jurors while also playing with the boundaries and margins of individual/collective logics, Jay and Diana enacted a form of policy level caring

practice from within the tricky entangled politics of pharmaceutical capitalism, health system rationing, and heterogeneous bodies.

A citizens' jury is an exercise where a small group of 'lay' people (conceptualized as jurors as in a court trial) are educated on a particular contentious policy issue and then engage in a deliberative process about it together. Citizens' juries are mobilized by governments and researchers in difficult policy areas where many competing interests are at play, such as environmental regulation and health resource allocation. The health policy unit's citizens' juries focused squarely on rare disease, and aimed to elicit whether the 'public' thinks that resource allocation toward expensive rare disease drugs is reasonable and fair.

My focus in this chapter is on the way Jay and Diana and their colleagues in the research team imagined the social values collected from the jurors as a potential solution to the tensions around rare disease. They had to work hard to calibrate the citizens' jury concept and the tools that are available for systematically collecting values to meet their goals. Additionally, the 'citizens' called into being as jurors had to be educated, and their values collected, in careful and particular ways. Thus, this chapter is concerned with the conceptualization, planning, and development of these juries rather than the data on the values elicited from the actual juries themselves. This is a pragmatic caring practice: they cannot 'reinvent the wheel' in terms of how things are done (at least not if they want their work to have any impact) but they can come at issues from a different angle, neither fetishizing the suffering individual in need of relief nor rationalizing and sanitizing the moral dilemmas of rare disease through logics of the sustainable collective. Instead, they work to hold the two in tension and find solutions from there.

Throughout this dissertation so far, we have seen that 'rare disease' is caught within multiple stakes, materialities, and situated knowledges: public drug budgets, pharmaceutical

company shareholder values, scientific knowledge, experiential knowledge, randomized controlled trial datasets, and powerful symbolically charged drugs. In the last chapter, Kelsey's story of shifting through three different treatment possibilities shows that relationships with treatments shift over time and benefit is entangled in a range of affective, physiological, and moral complexities that aren't quite captured by any of the above. Public drug plan decision-makers are expected to satisfy all of these different stakes in their allocation of resources, but as Rabeharisoa (2017: aq) notes, "institutions are not a priori equipped to absorb and maintain multiple realities in a generous tension." The terms of reference for these citizens' juries, then, was to come up with values and preferences of the 'ordinary public' to help find a more 'neutral' reality to guide them in doing so. Jay and Diana are well connected with government and highly respected—if they produce something, provincial drug payers may not necessarily act on what they suggest, but they will likely read it and consider it. If results were strong, the juries data could encourage a shift in provincial HTA practice and decision-making committee principles. Whether or not the juries shaped things at the policy level, however, they hoped that results from a thoughtfully framed citizens' jury could balance out some of the 'noise' around rare disease drug access in Canada and urge a different way of engaging with the matter.

In the first section of this chapter, I will briefly review the history of the citizens' jury concept and explore the meaning of its use to resolve health and health resource allocation issues in the Canadian context. I'll also situate these particular juries in the politics around rare disease the year that the health policy unit's juries were conducted, when it seemed somehow that values were "in the air." In the second section, I look at the different hopes that Jay and Diana and the health economist on the citizens' jury project team had surrounding the capacity of the juries to smooth the tensions and polarities around rare disease. In a dispute about whether the juries

should be about opportunity cost or about working outside of that logic, the importance of framing for how rare disease becomes understood by others is apparent. In the third section, I will describe some of the tensions and issues encountered in the design of the juries and the selection of the tools, expert witnesses, and exercises to appropriately collect ‘social values.’ In the fourth section, I will share how jurors were ‘made’ through the juror recruitment and selection process and how rare disease was ‘made to matter’ to them through the opening talk Jay gave to both sets of juries.

Writing on the use of public deliberation processes like the citizens’ jury by UK Labour politicians of the ‘Third Way’ in the 1990s, Rose (2000: 1395) notes that public participation is a particular “way of visualizing political problems, a rationality for rendering them thinkable and manageable, and a set of moral principles by which solutions may be generated and legitimized.” Rose notes how in the UK context, public participation processes fit well within the UK national aspiration for a co-existence between individualism and collectivism: in this imaginary, people can be free and autonomous individuals and also govern one another through community and citizenship and collective belonging (1404). I can’t speak for other citizens’ juries in Canada, but in the case explored in this chapter, I argue that these particular juries play on a similar tension between individualism and collectivism—but centered less on autonomy and more precisely on moral responsiveness in difficult times where competing values and visions between ‘stakeholders’ feel intractable. How should we, as a nation (or at least a province), respond to rare disease drug access dilemmas?

I theorize the citizens’ juries as an enactment of care through taking a “practical position in a controversy” (Moser 2008: 106), trying to find a way to care meaningfully for rare disease even within the contradictions of capitalism. To do so, Jay and Diana must satisfy all

‘stakeholders’ and represent all of the tensions and stakes involved in rare disease drug access dilemmas while pointing towards the spaces available for caring in between those tensions. In enacting care in this way—rather than taking one symbolically charged position or the other within the individual/collective tension—they destabilize the symbolic power of those ontologies while also still meeting their expectations as rigorous and respected researchers and participants in the policymaking process.

7.1 Citizens, stakeholders, and nation: in search of the elusive common good

In this section, I first review the history and theory of the citizens’ jury concept. I then move to an analysis of what citizens’ juries and other public participation processes index in the Canadian health care system. A review by Street et al (2014) found that between 1995-2010, 66 juries demonstrating deliberative inclusive methods in health-related areas were published. Of those 66, 36 occurred in Canada, 16 in the United Kingdom, seven in Australia or New Zealand, three in the US, one in Brazil, and one in Italy. The concentration of juries in Canada indicates a fixation on ‘values’ and deliberation in health related issues in the country. It is out of scope to review all of the public participation and citizens’ jury efforts that have taken place in Canada here, but in this section I will focus on two divergent reports on Canadian ‘values’ about health care. These two reports help to situate these citizens’ juries within debates about Canadian nation-making surrounding the health care system and whether and how rare disease fits in.

The history of the citizens’ jury concept helps to illustrate the centrality of ‘social values’ in the politics of nation-making around divisive issues. The citizens’ jury concept was developed

through the 1970s and 1980s by researchers at the Minneapolis based Jefferson Center.¹⁸ In the United States, citizens' juries are trademarked by the Jefferson Center—allowing close control over their design and inclusivity methods. Elsewhere, they have been conducted using a variety of different methodologies and designs (Wakeford 2014). Moreira (2012b) has argued that the development of the citizens' jury concept at the Jefferson Center stemmed from an attempt to rethink the way that the relation between 'elites' and the 'ordinary public' had been conceptualized in the second half of the 20th Century. Ned Crosby, a researcher at the Jefferson Center and the primary architect of the citizens' jury concept, was profoundly influenced by the political scientist Robert A. Dahl, "who had proposed that competition between group interests remained the engine of democratic life" (Moreira 2012b: 115 on Dahl 1956). Dahl firmly believed in the potentials of deliberative democracy to maintain and manage the relationship between economies and people and be moral beings in doing so.

Much of Dahl's writing, Moreira analyzes, was in response to the 'elitist theory of democracy' proposed by the sociologists C. Wright Mills and Martin Lipset—who believed in the conceptualization of 'complex society' upheld by theorists such as Max Weber (1922) that elites control centralized bureaucracies and eliminate the need for public participation. Both Mills (1956) and Lipset (1963) held that the worldviews of 'elites' and 'ordinary people' are so significantly different that democratic processes are mainly driven by elites, divorced from the everyday life of 'the people'. Dahl's refutation of this was that society is in fact 'made' by these plural perspectives of the world, and that together, they could build new structures and forms.

¹⁸ Named after former US president and 'founding father' Thomas Jefferson who was an advocate of the trial by jury model in settling legal disputes.

Crosby and his colleagues at the Jefferson Center tried to crystallize Dahl's vision of pluralities and progress in the citizens' jury model, so that plural perspectives could be accounted for, not through 'lobbying' by interested stakeholders but instead through a "constrained setting where the passions, beliefs, and interests that were at the root of citizen disengagement and partisan politics could be superseded by procedures and rules" (Moreira 2012b: 118). Other ways of gathering 'public opinion' such as opinion polls and focus groups are seen as less rigorous and legitimate than a full jury, because those methods for eliciting public opinion enable 'off the cuff' uneducated, and potentially unrepresentative opinions, whereas the citizens' jury involves education, representative and inclusive sample selection, and deliberation over mere opinion. Deliberation—finding a way in between polarities through educated discussion—is pivotal.

Thus, citizens' juries have evolved as a way to neutralize partisan polarities and move forward in the face of intractable dilemmas. However, as Rose (2000) has critiqued, public deliberation processes depend upon certain framings of citizenship and citizens. If ordinary citizens are to help diffuse polarized perspectives between stakeholders, they must be constructed as ethical beings that are outside of relations of power and will work towards the common good rather than towards their own selfish interests. Ethical beings outside of the realm of interested power are configured as not having an 'axe to grind' or a particular interest to promote—which means that they can be neutral and rational in ways that involved stakeholders (like patients and industry and payers) can't be. Through a process of education on the issues at hand, these ordinary people made into citizens *become* culturally neutral and apolitical, able to take a clear 'perspective' on the stable world that stakeholders with interests or axes to grind cannot see.

Citizens' juries appeal to the complexities of Canadian "biomedical nationalism" (Taylor-Alexander 2017) in key ways. Part of the nationalist narrative of what is called 'Canada' has long been one of peaceful rational unity, an identity partly built on self-articulated contrasts to the 'neighbour to the south', the United States (Mackey 1999). This is perceived as a certain kindness and compassion and politeness, institutionalized in the social service and publicly funded universal health care system. However, the principles of the Canadian health care system enshrined in the Canada Health Act—publicly administered, comprehensive, accessible, portable, and universal—believe a heterogeneous set of expectations and beliefs about how exactly that system should be managed. The imperfectness of the system is often proposed as a rationale for its dismantling and privatization in the name of 'other Canadian values' such as competition, innovation, and the right to seek private health care. In the Canadian context, public participation processes have been used in the health care context for the past three decades—roughly coinciding with the advent of health technology assessment, the restructuring of the Patent Act in the course of free trade agreement negotiations, and rising health care costs in the face of new drugs and technologies. 'Social values' became imagined as a way to manage the tensions and contradictions between these competing visions—ones often articulated through, as we have seen, articulations of the imperative to relieve the 'suffering individual' (through the free circulation of pharmaceutical drugs and capital) and the 'sustainable collective' (through the need to efficiently and accountably allocate resources based on solid evidence as a form of care).

Two oft cited reports about the Canadian health care system help illustrate this situated tension, and the importance of cultivating 'social values' to support either vision: the 2002 Kirby Report, and the 2002 Romanow Report.

In 1999, Liberal Senator Michael Kirby led the development of a report by the Senate Standing Committee on Social Affairs, Science, and Technology on the challenges faced by the Canadian health care system. Kirby's conclusions, based on the statements by 400 'witnesses', stipulated that publicly administered health care (as stipulated by the Canada Health Act) is not 'patient centered.' Instead, the publicly administered requirement of health care in Canada (which essentially bans two-tier health care) is instead "the means for achieving the ends to which the other four principles are directed" (Kirby and LeBreton 2001: 41). The rationale of that view is that since patients sometimes have to wait for services in a publicly administered system, the 'collective' is put before the needs of the patient. Kirby's committee questioned if Section 7 of the Charter of Rights and Freedoms—that Canadians are guaranteed the right to life, liberty, and security of the person—wasn't violated by the inability to purchase health care services privately. This report was widely seen as subtly encouraging the privatization of the Canadian health care system, and the development of a parallel private system alongside the public one available to those who can afford it—although Kirby strongly refuted that, stipulating instead that the health care system should just be reformed and health care premiums of 50 cents to \$4 per day collected from citizens (Kondro 2002).

Concurrently, former New Democratic Premier of Saskatchewan, Roy Romanow, had been commissioned to do a Royal Commission on the Future of Health Care in Canada. Romanow's 2002 report on how Canadians value the health care system in this royal commission were based on a series of twelve 'dialogue groups' held across the country and followed a US based values elicitation method called ChoiceWorks dialogues trademarked by the California company Viewpoint Learning. In total, 489 participants were randomly selected to represent cross-sections of the Canadian population. These twelve groups were asked to ponder scenarios

for the reform of the health care system, develop their own vision of what they would like the health care system to look like in ten years time, and ponder the trade-offs and choices that would have to be made to realize their vision (see Maxwell, Rosell and Forest 2003). The research group in charge of collecting these values reported that these dialogue groups had produced “a new health care contract... anchored by the traditional values of a healthcare scheme provided by the state-universal coverage and access based on need—while adding new economic values of efficiency and accountability” (Maxwell, Rosell and Forest 2003: 1033).

Romanow’s report repeatedly grapples with the infiltration of private interests and the ethos of privatization in Canadian health care promoted by some organized groups (like industry), and he refutes them strongly as having no evidence of better outcomes or a stronger health care system. In his introduction to the final report to the Canadian Royal Commission on the Future of Health Care in Canada, Romanow wrote (2002: xxi):

Canada’s journey to nationhood has been a gradual, evolutionary process, a triumph of compassion, collaboration and accommodation, and the result of many steps, both simple and bold. This year we celebrate the 40th anniversary of medicare in Saskatchewan¹⁹, a courageous initiative by visionary men and women that changed us as a nation and cemented our role as one of the world’s most compassionate societies. ... Medicare is a worthy national achievement, a defining aspect of our citizenship and an expression of social cohesion. Let’s unite to keep it so.

Inspired by these citizen dialogues, in his report Romanow “redefined the role of the citizen, from passive consumer of healthcare services to active participant in the governance of the health

¹⁹ A public medicare plan was first instituted in 1947 by the Cooperative Commonwealth Federation government (today known as the center-left New Democratic Party) in the province of Saskatchewan under the leadership of Tommy Douglas, a movement that would over time become nationally adopted through the 1960s (see Chapter 1).

system” and established that public participation should be part of the health care covenant with regular reruns of these dialogues (Maxwell, Rosell and Forest 2003: 1033).

These two reports were profoundly different framings of the virtues and vices of a universal health care system. They were also profoundly different values elicitation methods. Since framings of ‘Canadian values’ are so important in Canadian nation-making, this is important. Kirby’s report was based on 400 statements by “many witnesses who appeared or sent submissions to enlighten us on the history of publicly-funded health care in Canada, the changing health status of Canadians, the challenges we face now, and what can be done to improve our health care system in the future” (Kirby and LeBreton 2001: v). Romanow’s report was based on an established method for eliciting values systematically by deliberately representing ‘cross-sections’ of the population (apart from health care professionals, who were excluded) and on trade-off exercises. These methods generate very different publics, and highlight the politics of representation and method in framing—and coming to some sort of conclusion—about an issue.

Both of these reports were written before rare disease drug access was recognized as a health policy issue in Canada. Were these inquiries to be conducted in 2019, there would be no choice but to attend to the challenges presented by rare disease drug access. The system never did include everyone—as both Kirby and Romanow’s reports attest—but the exclusion of rare disease can no longer so easily be justified through appeals to rationality and scientific authority. In this context, ‘social values’ gained a new urgency.

Pharmaceutical enactments in rare disease work to highlight rare disease as an issue of values—the public health care system is cast as backwards at best and fundamentally unethical and caring more about costs than about people at worst. This is a powerful framing because it

makes the public health care system look illegitimate and run by bureaucrats who do not *care* about people's suffering. This has prompted an attempt (through citizens' juries and other public participation processes) to prove that resource allocation is not about *public payer* values but it definitely can't be about pharmaceutical industry values either. Patient values about resource allocation are seen as somewhat unhelpful—as one economist once shared with me in an interview: “I mean if you ask a patient how much should the government be willing to pay for your care, the answer is all the money it has! That's not a very useful perspective for me.” At the end of the day, decisions have to be made—but on what principles? How? In the face of these intractable incompatibilities presented by rare disease, the values of the *public* came to be seen as the only legitimate way out of this ethical quagmire. However, as will be seen in the sections that follow, the precise way that a public is engineered as having values to be elicited, and the precise mechanics of their elicitation is not a straightforward process.

7.2 “My hope for the juries is that...”: ethical investments in the citizens' juries

On my first day of fieldwork at the health policy unit, after they'd set me up in the desk they'd assigned me in the open office space of their policy research lab, I met with Diana and Jay to discuss the work the unit would be carrying out over the coming months. They were a bit worried about my stay not meeting my needs as a researcher. A month before my arrival, the price of oil had crashed substantially. The health policy unit is located in the province of Alberta—Canada's 'oil country'—where much of the provincial revenues come from oil extraction, primarily from the notorious tar sands in the north of the province. The conservative provincial government hadn't saved any surplus revenue, and also squandered all of the province's savings, so there was nothing left to see the province through 'thin' times. So, they

had implemented a freeze on spending in the province. This meant there would be no new medical technology acquisitions and thus no need for HTAs to be conducted for the projected future—and besides their research activities, conducting HTAs for the provincial government is a core part of the health policy unit's work. I explained that I was much more interested in the different relationships they have to manage, and the logics they employ in doing so, than I was in the HTA products themselves. Besides, seeing the conversations that come up about health resource allocation in the midst of an oil price crash would be interesting for me. Somewhat bewildered by this but open to the idea, they told me about the things they had planned for the next year and that I could conduct ethnographic participant-observation on, including the citizens' juries.

Diana was clear that the citizens' juries were an opportunity for reimagining the ethical principles that she felt structure thinking about rare disease. "My hope for the juries is that we can complicate the utilitarian ethics that people always zone in on in rare disease," Diana explained. By 'people' she meant Canadian public drug plan managers but also some policy researchers and health economists. She was hopeful that by showing that the citizen jurors don't necessarily think that people with rare diseases should be left behind because of the cost of their treatments, they could convince their government colleagues to develop more well-rounded decision-making processes that take into account the specificities of rare disease.

In an interview with Jay a couple days later, we came back to this topic of drug prices and the citizens' juries. The drug prices are astronomical, yes, but what if the public is in fact okay with them? Jay reflected: "I would like to understand more about the pricing of drugs. Is it just something that we're picking up on as an excuse [to not fund the treatment]? If for some reason we all actually consider it to be fair, then let's get that off the table and deal with that, but

we get muddied up and price gets in the way.” That way, the conversation could shift back toward whether the drugs help rare disease patients or not, rather than getting ‘muddied up’ about willingness to pay. Jay has worked in HTA a long time—in fact, he was the founding director of the organization that is now known as CADTH, back in 1990. Before that, he worked in HTA for hospitals. He remembers the days of HTA before the economic part was added on—when it was just about systematic reviews of the evidence—and how HTA has as a result become more complicated and more political. He remembers how pharmaceutical industry people used to come into his office and ask him to not use the term ‘cost-effectiveness’ saying it would make more sense to use the term ‘cost-consequence analysis’ instead. Comparing costs with effectiveness controlled the narrative in ways that didn’t fit with their business interests, whereas consequences are less tethered to tangible outcomes. He’d been negotiating these kinds of dynamics for a long time.

Jay was also hopeful, though, that the juries could bring up some social values statements from jurors that could force the companies to reflect more openly on their pricing practices and their return on investment: “would it make a difference [to the jurors] if a company says we’re making a 15% return on investment here, because we have seven years to collect this money back, or if they say we’re making a 60% return on our investment. Would people [jurors] react differently?” he asked in one of our interviews together. Pharmaceutical companies don’t open their books to the payers or to the public—it’s very unclear how much profit they make on a drug compared to how much they invested in its development, or how much of that profit gets reinvested in research and development for new treatments. It is considered confidential business information. Basically, Jay was hopeful that the social values of the ordinary public would force conversations like that. But if this ‘cross-section’ of the public actually accepts the prices as they

are—“if people in the public see that generally the only way these things can be produced, and made available, is at this price, and they accept the reasons, then the conversation becomes different,” he explained. Doing so through a ‘non-reactive’ and deliberative process with a sample of ordinary citizens, for him, was one way to find a way to at least talk about prices, and resolve the issue. The direction that the conversations about pricing would take would ultimately be dependent on what the public said their values were. He wanted to take himself and his values—and those of health economists and drug payers and other stakeholders too focused on the price issue as a result of their own bias—out of it.

Jay and Diana’s vision for the juries was that they could open up new pathways of conversation around rare disease drugs and force the stakeholders out of their stubborn positions. If done well, industry could no longer say that the bureaucrat’s values were guiding things and government could no longer say that industry terms were driving the discussion. Patients could not level either claim. Rather, the neutral apolitical ‘public’ set those guiding values, not any of these interested parties. No fingers could be pointed because the direction gone in was the will of the collective.

Another member of the research team, a health economist, felt exactly the same way about the importance of the neutrality of the public voice but wanted the juries to be firmly situated in the logic of opportunity cost. For him, all of the exercises conducted with the jurors should ask them whether they would support taking resources away from an unidentified group in favour of an identifiable person with rare disease. Early in the planning of the juries in January 2015, he sent around an email attesting to this. I didn’t see the email personally, but I did see Jay and Diana thoughtfully discuss a measured response. Ultimately, as the research leads of the citizens’ jury team, Jay and Diana were the ones to decide and the health economist left the

majority of the planning and development to them. So long as the methodology was rigorous and followed standard health economics reasoning of trade-offs and the methodology of discrete choice experiments (discussed in the next section), he was satisfied.

A couple weeks later, I interviewed the health economist in his office. He outlined how he finds it extremely troubling that people with rare disease might get more resources allocated to them than other disease groups because they are identifiable: through evocative media stories and the low numbers of people with the disease, a face can be put to the resource demand, whereas other groups in need of health resources—who we can't name or know simply because they are not yet identified—don't have that privilege. This is how sustainable collective enactments stand up against the evocative suffering individual enactments. However, in many ways this normative enactment of morality ends up strengthening pharmaceutical industry enactments that promise to uphold all of the affective dimensions of illness and care. As he opined: “I think it is inequitable and inconsistent with a population health starting position for our decision making, to privilege the values of the beneficiaries just because we can identify them.” It was then that he explained his hopes for the citizens' juries:

Therefore, a second best state of the world, is to use society's values because they are indifferent, they are equally poor estimates of the values of the beneficiaries and those who lose as a result of the decision, so we're maintaining the principle of treating people equally except when we get direction that we should treat people unequally. So from that position, it goes from a pragmatic recognition that we almost certainly won't know who bears the opportunity cost. So, okay, if equity is a founding value, one of the founding values of the health system, then how we address that problem, how we incorporate values into the decision making should be coherent with that equity, and we should not privilege one set of values because they happen to be identifiable.

In this health economist's view, society is 'indifferent'—unlike all of the other stakeholder groups with vested interests. Indifference is the only pathway to a rational system. He truly

believed that the citizens' jury was necessary to direct conversations around rare disease drug resource allocation. If the public is okay with treating people unequally because they are identifiable, then fine, the decision-makers can do so with the knowledge that they are acting legitimately as representatives of the will of the people. He doesn't think this is a perfect solution—as he notes, it is “a second best state of the world”—but in the presence of politics and interests, where people insist on acting against the interests of equality, their best bet is to collect the values of the public—so long as they “actually have a deeper appreciation of the issues” and aren't “driven just by our intuitive response to the question.” Citizens' juries offer a way to encourage values statements that are more rational and understanding of opportunity cost than those of a comments section of a newspaper story about the government withholding a lifesaving drug from a young child.

In the end, Jay and Diana and their health economist colleague were saying more or less the same thing: that the public's values should be deferred to over those stakeholders with a vested interest or a budget to manage or an axe to grind—or worse, their own values as policy researchers and academics. But the approach to the issue—and their hopes around what the values will show—were different. Jay and Diana hoped that the juries would show that utilitarian framings are not only harming people with rare disease, but also heightening the intensity of the value politics around these treatments. They hoped to open the conversation to other lines of inquiry and questioning between industry and payers, rather than reducing the issue to whether patients ‘deserve’ the treatment or not. The health economist hoped that the juries would show that the public does not support privileging identifiable groups—making them into winners—if it means that other unidentifiable groups without such evocative stories would become the losers and not get health resources. It's not that he doesn't support rare disease patients per se, but that

he finds the pricing practices of the companies so egregious and the emotional politics around rare disease so uninformed that just funding the drugs (and taking resources away from others) is irresponsible “from a population health starting position for our decision making,” to use his words.

At stake in this disjuncture is the way that rare disease would be framed in the elicitation of people’s social values. As Diana noted during one of our chats together in her office, “however you pitch this, you can get entirely different answers!” If they came on strong about the cost of treatments, jurors would get ‘sticker shock’ over the million dollar price tags and not think about the individuals living with disease. If they didn’t talk about cost at all, the jurors would not fully consider the dilemmas that funding rare disease drugs pose to collective sustainability. The values as collected just wouldn’t be reflective of the complexity of the issue and would be dismissed by their colleagues So, Jay and Diana knew they had to tread carefully in designing the juries, and particularly so during an oil price crash, when public opinion becomes entangled in an affective anxiety about budgets, scarcity, and collective futures.

Jay and Diana are extremely sympathetic and collaborative colleagues, so they did their very best to make sure that the health economist’s views and desired methods were supported and reflected to a certain extent. But still, had the health economist held the reins, the issues may have been pitched to the jurors in a completely different way. Policy researchers and decision-makers may want to take their values out of it in an effort to make their end products and policy recommendations less biased, but being truly ‘value-free’ in research design is not possible. So, the citizens’ juries team relied on methodological rigour as a proxy for the unbiased elicitation they are searching for here. However, the politics inherently embedded in knowledge making practices are never far from the research design. I take this up in the next section.

7.3 Values by design: trade-offs and collecting social values the right way

Jay and Diana's ultimate goal with the juries was to turn values into social facts so that 'decision-makers' can use them as a moral guide. In this section, I describe the challenges and tensions faced in designing 'the exercises' that the jurors would complete, wherein they would have to select between choices presented to them. These 'objective' measures of assumed stable 'standard preferences', however, were carefully balanced with an attempt to ensure the jurors understood the full range of the affective and moral complexities of such high stakes resource allocation dilemmas.

The first challenge was defining the 'attributes' that would make up the exercises that the jurors would do. As a researcher named Natalia said when she walked into the meeting room one early winter morning very early in the development of the citizens' jury project: "You're going to kill me. I had to cut down the categories, by a lot." Natalia was referring to the attributes of the many possible ways that the categories of benefit to a patient, caregivers, and society at large could be said to benefit from a drug. Natalia was a visiting PhD student from an elite US university and her supervisor had sent her to work on the juries so that she could have some empirical content in her PhD thesis. A few days before, Natalia and two researchers at the health policy unit and I had spent a long afternoon in the health policy unit's meeting room and drawn up a list of all of the ways that pharmaceuticals can be considered to benefit patients, caregivers, and society, and particularly so for rare disease where pharmaceuticals are often the first in an area of 'unmet need'. We had brainstormed long and hard, thinking through some of the more intangible dimensions of drug benefit, and came up with a very richly textured set of things to

think about. Natalia was worried the team would be upset, because it almost felt like a kind of violence to have to take some of these dimensions of experience out.

The reason that Natalia had to cut down the list so much was because the categories and attributes were to be used as the basis of the ‘discrete choice experiments’ (DCEs) that would be conducted on the jurors. A DCE involves presenting people with hypothetical scenarios made up of different combinations of attributes (‘choice sets’) that the person (or small group of persons) has to choose between. The theoretical assumptions behind DCEs are similar to the theoretical assumption of the rational choice decision-maker using the QALY described in Chapter 3. As Amaya-Amaya, Gerard, and Ryan (2008: 13-14, emphasis added) write on DCEs:

The choice sets comprise two or more alternatives, which vary along several characteristics or attributes of interest, and individuals are asked to choose one alternative... DCEs assume... that individuals’ preferences (as summarised by their utility function) are revealed through their choices... The theoretical underpinnings of DCEs contain many elements of the standard economic theory of *consumer behaviour*. As with consumer theory, it is assumed that participants in DCEs are *rational decision makers* and they seek to maximise *innate, stable preferences*. That is, when faced with a set of possible consumption bundles of goods, they assign values (preferences) to each of the various bundles and then choose the most preferred bundle from the set of affordable alternatives.

In this logic, choices are a direct representation of preferences. That the choices are determined in advance delimits the selection problem, making sure that experiments are standardized across groups. If the juror had anything to say that fits outside of the choice sets as presented, they could say them in the course of their small group deliberations, but those would form the ‘qualitative’ portion of the study in which the transcripts would be analyzed thematically and mined for ‘social value statements’. That part could handle more complexity and emotion and experience—but for the DCEs, the jurors had to be cast into the role of the rational choice making consumer with innate and stable preferences.

If the researcher adequately understands and describes the selection problem to those being tested, and variability among individuals (education, health state, income) controlled for then the assumption of the DCE method is that the preferences that respondents come to through deliberation and select as their choice will be “most akin to the decisions that individuals make in real life” (Amaya-Amaya, Gerard, and Ryan 2008: 17). Care must be taken to identify and refine the attributes so that they are easily interpreted and not ambiguous. Interaction effects between attributes must be minimized, but too few attributes will be too linear—there needs to be just enough (usually about three) to detect complex non-linear relationships, but not so many as to increase the possible combinations for respondents to choose between and risk not only too much complexity but also cognitive overload. Natalia had been charged with paring down the attributes and fitting them into the software that had been chosen for the DCE analysis, called Sawtooth. To do so, she had had to remove a lot of the more intangible and affective dimensions of drug benefit that we had brainstormed, and that experiences like Kelsey’s shared in Chapter 6 demonstrate.

When we had initially been assigned the task of defining the categories and assigning attributes to them, Jay had urged us to make sure that the categories were as simplified as possible. Diana disagreed: brainstorming first is important, to make sure everything’s there, and we can simplify later. Otherwise how was the team supposed to come up with anything different and more interesting? Jay acquiesced but reminded us that policymakers aren’t interested in these multidimensional things—context changes decisions, and limiting the purview makes life easier. Diana said: “so what’s the point of the jury then!” and we laughed but also looked to Jay for his answer. His response was that the point was to show the incongruence between the public’s concerns and those of decision-makers, but it had to be realistic. The point here wasn’t

to “reinvent the wheel,” Jay later said in another meeting, but to build on what has already been done to look at social values about drug benefit on a more granular level—but not too granular. The trade-off exercises would be more effective if we focused on concrete categories, and didn’t introduce too much complexity. Upon reviewing the revised list of categories, a student health economist on the project looked at them and said “oh, perfect, this is pretty much just like the EQ-5D!” referring to the standardized instrument used to measure health-related quality of life for use in QALY calculations. One of the research associates on the team groaned, she finds the EQ-5D a bit thin and assumption-laden. But the bright side for the team was that complexity had been more or less tamed and the DCEs wouldn’t turn into an exponential morass.

Ultimately, the team came up with a series of exercises for both juries that they hoped would meet their ethical and research goals. One such exercise was a ‘tipping point’ exercise to get jurors to deliberate on whether rare disease should get ‘special treatment’ in drug coverage decision-making because of the severity of many rare diseases. This was an attempt to figure out if the jurors supported the use of cost-effectiveness as a guiding principle in decision-making, which requires impartiality across disease groups and a calculus for determining rights to resources—or if severity of disease changed their view on that.

The exercise presented jurors with the element of severity—and the associated loss of opportunities and quality of life—which would require some degree of partiality in decision-making, to see if the jurors supported a practice of paying more QALYs for some lives than others. The jurors would be provided with sheets defining ‘severe’, ‘moderate’, and ‘mild’ states of disease and asked to rank 15 disease states described on index cards, from most severe to least severe. Then, they’d be asked to imagine that there are two groups of patients with the most severe disease as ranked by the jurors. One of the groups has 100 patients, the other 10,000

patients, and only one group could be helped. The team expected the jurors would choose the large group. In that case, they would bring the next scenario in: choose between a large group of 10,000 patients with the second most severe disease as ranked, and a small group of 100 patients with the most severe disease as ranked. If the jurors chose the large group again, they'd continue to be proposed scenarios where the small group always had the most severe disease, and the large group having the less severe disease from the disease ranked third onwards. The exercise would be complete when a 'tipping point' would be found—the point at which social values indicated that a small group with a more severe disease should get resources before a large group with a less severe disease. After that, with the tipping point in mind, the jurors would be asked to make trade-offs between the disease states and population sizes with the age of onset of the condition across the lifespan.

Most of the exercises followed along this vein and using a similar logic: some looked at severity, some introduced the element of uncertainty of benefit into the equation, some at improvement to quality of life versus survival, and so forth. In all cases, the jurors were asked to make difficult decisions that made them think about rationing and choosing one group over another. While the research team planned to qualitatively analyze transcripts of the exercises to understand the social value judgments uttered as jurors deliberated, the DCEs were seen as the best way to quantitatively assess how consistent their answers were between different interactions of factors. Concrete and relatively uncomplicated attributes were best for this task. They are also understood as the most neutral and apolitical. Having the jurors make trade-offs between concrete and tangible and easily explained 'choice sets' would make the results more actionable.

Another matter for the team to work out was which expert witnesses to invite to teach the jurors about the issue at hand. If their findings were to have any legitimacy at all, they would have to demonstrate that the jurors had been educated and ‘stakeholder’ perspectives adequately represented. Otherwise, the juries might be criticized as biased or illegitimate because the jurors weren’t adequately ‘primed.’ Much of what citizens’ juries aim to do is provide decision-makers with accountable and reasonable principles to base decisions on—much like the Accountability for Reasonableness framework described in Chapter 3. However, as Daniels writes on Accountability for Reasonableness, for procedures to be fair, they “must involve practices that can be sustained and that connect well with the goals of various stakeholders” (Daniels 2000: 1300). This was one of the reasons why the jury research team ultimately decided to invite a very fulsome panel of ‘expert witnesses’ to speak to the jurors, including a clinician, a public drug payer, a health care delivery manager, a parent of a child with a rare disease, an adult with a rare disease, and a representative of a pharmaceutical company marketing rare disease products.²⁰ That way, they could say that the jurors had been educated on all the complexities and no one stakeholder group could complain that their perspectives hadn’t been heard. The health economist on the team disagreed with having an industry representative—he expressed at a meeting that the only perspective they could provide was the cost of drug production, which he felt shouldn’t bear any role in decision-making. Jay and Diana disagreed. Jurors may very well value the benefit to society that pharmaceutical innovation and economic productivity brings,

²⁰ Two stakeholders who were clearly missing are 1) a child with a rare disease—imagined to be represented by their parent who may have desires for the extension of their lives that are different from their own; and 2) a person with a ‘common’ disease not imagined to be within the special fold of rare disease.

whether the health economist thinks it should be important or not. They overruled, and the pharmaceutical industry representative was invited.

Having all the different ‘stakeholders’ there would also help to manage the jurors’ own interpretation of the issues at hand and help keep their expressed social values manageable. During one of our office chats, Diana and I discussed what perspective the industry representative would provide that could be helpful for the jurors. The following exchange illustrates how questions around the current institutional and economic arrangements must be carefully managed in the citizens’ jury context:

Diana: Well, I would have him [the industry representative] there to justify, because I know someone will say well, just get them to lower their price. Well, the price isn’t going to get lower...

Marlee: It’s just not going to happen?

Diana: It’s not going to happen, I mean unless you, I think this is the case where unless you nip it in the bud early on by not letting it go into the private market system, you’re never going to get that.

While a lot of the basic research that leads toward drug development is conducted in public universities or laboratories, the cost and risk involved in drug development means that most of the time those public discoveries are sold and commercialized by the private pharmaceutical industry. Thus, for Diana, if we want any drugs at all—unless we are going to ‘nip it in the bud’ and not let drug development move to the private market—the pharmaceutical industry must be considered a stakeholder and given a voice. Allowing too many discussions in the jury to center around a simplified narrative of “just get them to lower their price” wouldn’t lead to much change or actionable results that could tangibly help rare disease patients right now. Instead, the issue had to be tackled from within, with all voices represented at the table so that changes could

be negotiated. Policy research—and even sincere attempts to ‘care differently’—cannot stray too far from the constraints of the situation at hand if that policy research wants to have any actionable effect at all.

It was in the activities outside of the DCEs that Jay and Diana were able to do the real interpretive and ethical organizational work of pulling apart some of the ethical principles that guide rationing. The expert witnesses that the research team invited to represent the different ‘stakeholders’ all did remarkable jobs. Not only did they present the different ‘perspectives’ they also did role playing exercises and completed choice set exercises too, and then were asked to justify their decisions to the jurors. In these activities, values were not stabilized, sanitized and standardized into choice sets like in the DCEs, rather, the ‘at stake-ness’ of rare disease care for Canada was constantly articulated by the expert witnesses and by Jay and Diana as the moderators. This iterative and relational process of negotiating what is at stake may not show up in the statistical configuration of peoples values in the study results (although it may have influenced jurors’ choices in the DCEs, it’s hard to say), but it was an integral part of how the juries and rare disease were made meaningful in these two juries.

7.4 Making citizens and making rare disease matter

Developing the exercises and inviting the expert witnesses was one thing, but the research team also needed jurors to *do* these exercises for them. To build their sample of jurors, the HTA unit worked with Canada Post to make a regional and socio-economic distribution model of Northern Alberta by postal code. Canada Post then mailed out a letter developed by the research team inviting interested citizens to get in touch with the research team if they were interested in being a juror. This Canada Post service, also used to distribute junk mail and

advertising, stratifies populations by statistical information on average salary, ethnicity, and education level. The research team sent out 3000 letters, and received 225 responses. The text in the letter included the following explanation and purpose:

New health technologies need to be carefully examined before the Government of Alberta or Alberta Health Services can decide whether they should be paid for and used to treat patients. Because there are so many new technologies, it is not possible to fund all of them. Someone has to choose which ones are the most important. Until now, the public has not been involved in making these decisions. The purpose of this project is to try out a new way to involve the public in health policy decisions. It is called a Citizens' Jury.

If interested, prospective candidates were asked to sign a consent form for the research team to contact them by telephone. Potential jurors were then telephoned by the research team and screened. Jay and Diana extended offer letters to those chosen amongst the options to show the widest distribution of different social factors (age, annual income, education level, region, gender, and ethnicity) that loosely mapped onto demographic statistics in Northern Alberta, until they had 16 jurors confirmed for each of the two juries, with 32 jurors in total. The first jury would be held in April, and the second in early June. In this way, a representative sample of 'the public' was called into being. Participants were paid \$400 for their participation in the juries, which began on Friday evening and were adjourned late Sunday afternoon. Their travel and accommodation and any childcare costs incurred were also paid.

Once the team had their 'public' all set up, they needed to introduce them to the jury exercise and educate them on the issue they'd be deliberating on over the course of the weekend. For both juries, as the jurors filed in to the budget hotel conference room on Friday evening and piled their plates with the dinner items from the hot buffet at the back of the room, it was clear many were happy to be there if a little bewildered. They'd agreed to the task and been given some cursory background information but many still seemed unsure what this university group

were doing and why they were paying this diverse group of people \$400 each to do it. So, after dinner, Jay gave presentations to help orient them. In these presentations, Jay had to highlight the value of the perspectives they'd provide, and why their participation in this citizens' jury exercise matters. But it was more than just explaining, this was a process of moral subject and identity building.

Jay opened the presentation for each jury by telling them a bit about what a citizens' jury is, and why this method is more rigorous than others, while also making the jurors feel comfortable giving opinions even if they're not experts on the topic—even if they've never heard of rare disease before. This quote from the June jury presentation is an example of affirming their importance while also letting them know that a lack of expertise is not a bad thing:

It's one thing if you get robocalls, or if you just talk to a street surveyor where you just give a gut reaction. That is not what we want. We want informed discussion and some conclusion on the basis of that, and listening to other people of society. But we want you to raise your opinions instead of testing you on what you know and how much you know, and see what people think over the course of a couple days. ... And hopefully through what comes out here, provide advice to policymakers, and I don't mean in a belittling way, but from ordinary people, which is what you represent.

He explained that it was precisely this ordinariness that they were looking for: "you're not intended to represent any particular group, you bring what you bring! And we can't take that away from you or stop you, we're not looking for you to represent a profession or a society or a cause." And not everyone in the jury group has to agree, but they do have to deliberate: "several answers are fine, as long as you can explain why, so we understand the reason. The decision is not important to us, but how you got to that." In this, Jay was trying to set the jurors up to meet the mixed methods goals of the study: the decisions they made were in fact important for the quantitative analysis of the DCEs, but they also wanted jurors to go beyond choices and express 'social values statements' and deliberations that they could then analyze qualitatively and

thematically. Here, ordinariness had to be affirmed as simultaneously extremely important to political governance but also as a mix of uninformed and informed, biased and objective. What matters is how they think, as people who lay outside of relations and unsullied by power and vested interests. As Jay put it in the April jury presentation: “if there was a king of the world, what do you think the king of the world should think about?”

Jay then had to explain rare disease and make it legible to the jurors as a problem that matters. Jay’s presentation was not a simple task: how to educate this “engineered public” (Moreira 2012b: 113) on the complexities of rare disease drug access. He did so by appealing to a narrative they already knew well. The image on one of his slides was of two cartoon human figures pulling on a rope in opposing directions:

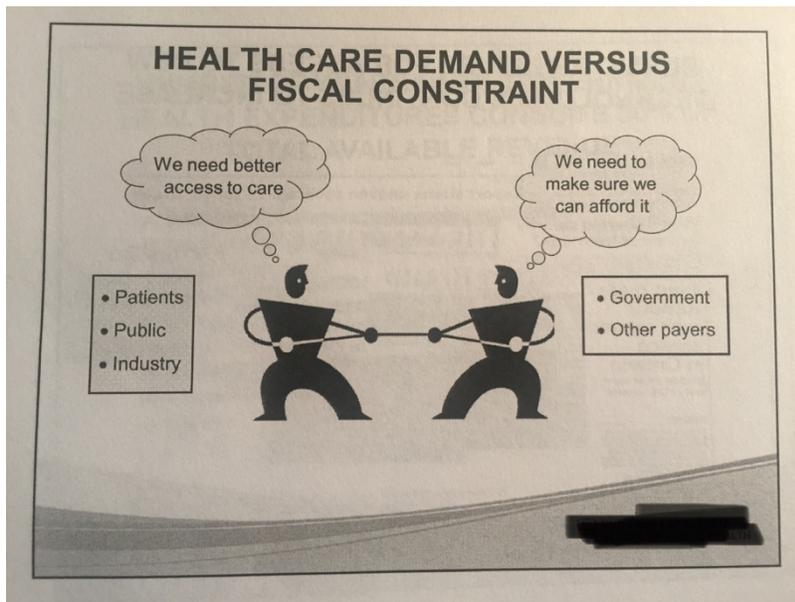


Figure 7: Slide from Citizens’ Jury opening presentation handout, April & June 2015.

One side of the rope—composed of patients public, and industry—desires and demands better access to care. The other side—composed of government and other payers—is concerned about affordability and sustainability. Jay explained: “so the situation we have is a tussle between patients, the public, and industry who say we need better access to care. And on the other side, government and other payers saying we need to make sure we can afford to pay for it!” Jay continued before he switched his slide: “a perfectly legitimate position for everyone to take, really! I mean, you may be on the government side as part of your job. If you happen to be a patient who needs it, your view might change!”

At the same time as making rare disease into a legible category for these jurors, he had to make the jurors into the type of citizens who might care about rare disease. Jay framed the issue as a fiscal challenge: health care spending per capita is rising every year, many provinces are spending huge portions of their total available revenue on health care, and other budgets—like education and infrastructure—have to make do with what is left over. He explained how Ministries of Health are often seen as the ‘bad guy’ by other ministries because they take up so much of the available revenue. Yet there are so many new medical advances, and increased public pressure for access to these new technologies too. And then, there is what Jay termed a “new kid on the block”, rare diseases. He showed a series of newspaper headlines about patients petitioning governments for expensive treatments, and how the policy response had been essentially to cover rare disease drugs on case-by-case one offs. He explained how since the patient population is so small, the companies have to charge a lot to make a profit—“and we can argue about what it ought to be,” he said—but in order to make drugs for people with rare diseases available, there are going to be these high costs. “And that’s why, because of the cost

issue, you see these stories in the media, because patients don't have any other recourse to deal with it," he explained.

After seeing all the graphs Jay presented on rising health care costs, a juror in the April jury questioned whether it wouldn't be more efficient to have private health care. Jay called on one of the expert witnesses in the audience, a former government drug payer, to explain to the jurors that Canada's system *is* sort of private: it's privately delivered, clinicians work for themselves and aren't civil servants—they just bill the system, which is publicly funded. He went on to explain: "the other option would be to be privately run and privately funded, so where the money comes out of your pocket. But which is cheaper?" and gave the juror some comparisons between Canadian spending and that of what he called "our neighbours to the south," the United States, showing that their spending per capita and percentage of GDP spent on health care is in fact much higher. Jay jumped in:

And the counterargument is that there are 40,000,000 uninsured people in the US. So the question is, from a societal perspective, and this is too big to discuss here, but do you want a system that takes care of most people to the best extent that can happen, or do you want the best to be available to a small part of the population but large parts of the population don't have it? And again, I'm simplifying it, but that's the choice we have.

In this comparative frame, Jay and the expert witness worked to bring the juror back to both current institutional realities as well as back to the moral argument for publicly funded health care in the first place. The question can't be let's not spend money on others' health care at all. Instead, the question Jay wanted the jurors to think through was: how can we make decisions the best we can and preserve the Canadian system of making "taking care of most people to the best extent that can happen"? Plus, private systems cost more anyway, because they don't have the same regulatory and pricing mechanisms vis-à-vis the market dimensions of health care services and technologies as are in place in Canada.

The system can't afford everything, so how should decisions be made? What should the principles be? The following quotes from Jay's presentation from each jury highlighted the incompleteness of utilitarianism and rational economic calculus to help us in these situations:

Jury 1 opening presentation: So, this is what this weekend is about. What do we value? Do we value the greater good meaning most people under all circumstances? And that's fine, in some places most of it is done that way. But is that we value as a society? So you're going to be starting with these exercises. You'll be challenged by these kinds of things. And you will have to defend the choices.

Jury 2 opening presentation: And the idea that we in society, want no person left behind, is that a value we share? Should we leave someone behind because for this particular disease there are 10,000 people, for the same amount of money, you want us to help these 50? So we leave these people behind? Because they were born with a disease? Not easy questions to answer.

Jay explained how one of the ways that people have approached decision-making is through evidence, but there is too much uncertainty attached to rare disease drugs—and perhaps even all drugs—to try to restrict this to a technical decision. As he explained: “There's uncertainty. You don't even know in fact how well something works for an individual, even a population, you know? A drug can work for some people, not for others.” Jay then broached the topic of industry: “And there are industrial policies, this is not just about health, society requires to grow, innovation has to be supported... you want to encourage development.” Jay also had to satisfy and explain the logic of health economics and budgetary realities by bringing the discussion back to current actionable institutional frameworks: “the other thing in health is very often you're making trade-off choices, you can't do everything. So you have to remember a key term, opportunity cost... you can only spend a dollar once, basically.” In this way, Jay was educating these jurors to be able to do what a lot of the ‘stakeholders’ in rare disease drug access disputes

aspire to but don't always succeed in doing: "absorb and maintain multiple realities in a generous tension" (Rabeharisoa 2017: aq).

At this point of the presentation in the April jury, a juror exclaimed: "well maybe the government should go to the heritage fund to get some more money!" referring to Alberta's savings fund created in 1976 where surplus oil revenues were supposed to go. When the price in oil had crashed, it was discovered that the progressive conservative government in power over the past 44 years who had developed the fund in the first place had later squandered it. Jay laughed, "well, I think the heritage trust fund is running out!" One of the health policy unit's research associates and I gave each other a quick look—just that morning she had discussed her worries with me that the jurors' perspectives might be clouded by the austerity politics around the oil price crash that was all over the news. Jay went on to explain "with these decisions here, you've got a finite budget. And right now, with the oil prices coming down, this is what Alberta is facing all of a sudden, and you've got to make much tougher decisions. You can't keep adding unless something else goes." He explained how if the jurors decide that we need more funding for health, that may be the case—but they need to keep in mind that they will then have "folks coming in and saying, what about the schools you promised to build!"

Opportunity costs, moral ideals, waning budgets, uncertainty, hope, desperate patients, an innovating but profit-oriented drug industry—it was in these tensions that Jay constructed and made rare disease into a legible category and an important ethical dilemma in these presentations. He worked to draw together all of the different desires that stakeholder groups exploit in the story about rare disease drugs and in the wily category of rare disease, and asked citizen jurors to provide input so that, as he put it in the second jury, "the decisions are not made in a black hole with big lobby action from every possible sector." Jay presented these tensions as

difficult but not insurmountable, thanks to the power of social values as a contrast to the values of those with powerful interests:

So how do you reduce tensions? We believe that everyone has to be in the room talking. And what decision-makers have said, the decisions about what to fund and what not to fund through the public purse require value judgments. ... But their question to themselves and others, is whose values? Is it mine? ... But if you [as a decision-maker] want your values to represent the values of the public that you are speaking for, or working for, then you need to know what the value judgments are. And the problem is, they don't know! And we don't know, what the public and society values.

The citizens' juries helped the health policy unit and their wider research team to imagine a decision-making framework that took all of these competing tensions into account in all of their complicated and contradictory moral frames, and find a set of principles that a legitimate and accountable and reasonable decision-making framework could be structured around. The 'public' and 'society' were not enacted here as morally neutral or apolitical beings. Instead, they were enacted as people who could understand and deliberate around the symbolically and morally charged individual/collective tension and grapple with the complex socio-material entanglements of rare disease.

7.5 Conclusion

In designing the juries, Jay and Diana and the research team hoped to show, or at least make space for the possibility to show, that the social values of 'ordinary Canadians' are more complex than imagined by decision-makers and the health economists who support them. This involved finding ways to cater to and yet also cut through the politics of rare disease drug access, and develop a new ontology outside of the suffering individual/sustainable collective binary opposition by working creatively within it. Faced with the task of representing rare disease to the 'public' while also maintaining their position (and ability to actually have an impact) as high

caliber researchers embedded in government decision-making networks (with associated methodological expectations), Jay and Diana and the research team carefully navigated the implicit political agendas that structure rare disease drug access.

Jay and Diana's savvy working of rare disease and health system politics in the development and execution of the citizens' juries highlights how policy research—like HTA more generally—is firmly situated within complex networks of relationships. No one is 'outside' of politics. Instead, as shown throughout this chapter, both an 'unbiased' research product and an 'unbiased' sample of citizens is socially produced through a series of fine-grained and very political decisions. At the same time, Jay and Diana harnessed the citizens' juries as an opportunity to rethink and rearticulate discussions of how to 'care' for rare disease in new ways. Their thoughtful calibration of utilitarian ethics and concerns of collective sustainability as enabling some forms of political good but shutting out multiple others indexes an attempt to make sure that logics of opportunity cost or QALYs, useful as they may be, do not completely shadow out questions of individual suffering. Doing so does not mean, however, handing the reins over to pharmaceutical enactments of suffering individuals—their presentations to the jurors remained fully concentrated on challenges to the health care system. Of course, they have their own values—and those show through their words and actions—but I see their careful methodical ways as pragmatic enactments to reduce the power of other enactments to take hold of the narrative. This was a general principle that I saw as structuring their work in my time with them during my fieldwork: cutting through rhetoric, maintaining relationships, and finding ways to enact caring practices at the policy and research level.

At stake here is the future of rare disease care, but also Canadian nation-making via politicized framings of 'social values.' Citizens' juries in this case are a particular form of

nation-making, as the ‘social values’ of the jurors are imagined as a way to find better principles for action between public and private visions of health care, and for finding a way through the ‘suffering individual’ ontology that exists in dialectical tension with the ‘sustainable collective’ ontology. The type of national problem that rare diseases are made out to be, and the type of citizens that both people with rare disease seeking resources and the jurors are made out to be, will influence the current of the discussions.

What kind of a cultural formation is this figure of ‘social values’? Moreira (2012b) asserts that public participation processes like the citizens’ jury are best understood as choreographies “that is to say, as the outcome of the ‘coordinated action of many ontologically heterogeneous actors in the service’ of a collective undertaking” (112, quoting Cussins 1996:600). Rose (2000) understands them as ‘political technologies’ developed to soothe the tensions of pluralism in a context where “the uniform social citizenship that was the objective of the citizen-forming and nation-building strategies of the 19th and 20th centuries is now challenged by diverse forms of identity and allegiance that are no longer deferential to such a territorialized image of national and civic culture” (1401). Here, I have shown how social values are certainly choreographies and certainly seen as antidotes to pluralism, but ones that are firmly situated in finding ways to make the contradictions of capitalism ‘work’ by forging new ontologies for caring relations.

I have closed this dissertation’s data chapters with the citizens’ juries because they highlight in many ways how politics and social orders backed by powerful ontological frames and the practices that create and stabilize them constrain us. These shape our imaginations about the actions that we can take within systems—and yet despite it all, social actors still work hard to imagine a world otherwise. During one of the citizens’ jury exercises, one of the expert witnesses

providing the ‘lived experience’ perspective on rare disease and I were seated against the wall, observing the activity taking place in the middle of the room. As the jurors were asked to choose between different trade-off options between disease groups, a research assistant placed coloured dot stickers on a flip chart to record their decisions. At one point, while the jurors deliberated, the expert witness nudged me and whispered “geez, what if we found a way to take care of all these diseases, what about that?” Is there a way of caring around the tensions generated by expensive new technologies? I turn to this and other questions that rare disease drugs present us with in the conclusion of this dissertation.

Chapter 8: Conclusion

Is a collective the sum total of a number of individuals added together, or can we only understand what individuals are if we first learn about the – various – collectives to which they belong?

-Annemarie Mol, *The Logic of Care* (2008: 57)

In early summer 2017, I ran in a local charity race in support of Kelsey's small fundraising charity for MPS II. For this charity race, sponsored by a bank, any non-profit organization has the option to sign up a running team and collect donations. Since Erik was diagnosed, Kelsey has tried to hold a fundraising event every year or so and donates the proceeds to organizations looking into research towards a 'cure' for MPS II. That year, Kelsey had focused her efforts on this charity race, and all the proceeds were to go to the \$2.1 million needed to de-risk early gene therapy trials. She had teamed up with another rare disease organization to have t-shirts made that could be worn by runners in similar fundraising races across Canada. They were bright orange technical fabric, and emblazoned on the t-shirt was the name of the charity organization and the words 'The Only Thing Stronger Than Love Is Hope.'

Kelsey and some of her relatives were cheering us on and waiting near the finish line. Erik was walking the five kilometer race with his dad—as well as a group of documentary filmmakers who were filming footage for a documentary on MPS II. I ran the five kilometer race with Erik's two younger siblings.

At one point, about a third of the way into the 5 kilometer loop, a man ran up beside me and Erik's little sister. Erik's brother was running several feet ahead of us in an effort to catch up with his cousins and aunt who were also running the race. I strained to make sure I didn't lose sight of him as the man initiated us in conversation. He asked us in a friendly but searching tone: "What does that mean, on your shirt? What are you running for?" We kept a steady pace as I

gestured towards Erik's sister and explained how it's for research into a gene therapy cure for a very rare genetic disease that her older brother has. He squinted skeptically and replied, "Right! Gotta feed the medical industrial complex, huh!" and then ran off. I looked over at Erik's little sister to see if she had heard but she was concentrated on running, and appeared to have stopped listening to the exchange.

I was familiar with this man's argument, and admittedly sometimes felt the pull of it myself as I was writing this dissertation. Of all the tragedies and forms of suffering in the world, why channel energy, money, and care into diseases that affect a relative handful of people worldwide? From *his* shirt, I knew that the man who had offered this unsolicited commentary was running for a refugee relief organization—raising funds for people fleeing desperate and protracted violence from war in places like Syria and Yemen and people whose homes are becoming increasingly uninhabitable due to climate change. There are more pressing issues facing the world than rare disease drug development, and the 'medical industrial complex' as the man had said, garners a lot of money and attention. Besides, what is the point of developing new drugs, if large swaths of the world's population do not have access to essential medicines that already exist? As I completed the race that day, hand in hand with Erik's little sister, I recalled a long interview I had conducted with a prominent biochemical genetics clinician, during which she had shared the anguish she sometimes felt over this question. She had volunteered in a famine stricken war zone after medical school, and sometimes, when part of a group of highly paid clinicians in a state of the art Canadian hospital all discussing one rare disease patient's case during rounds, she couldn't stop thinking of the distended bellies of the starving children she had tried to help.

As an outsider, the man at the race sees the skewing of social priorities and resources toward tales of medical heroism, while people who do not have resources and camera crews documenting their evocative story suffer in the shadows. Kelsey, on the other hand, as an insider of her own unfolding story, sees her role as a profoundly moral journey where she is tasked not only with caring for her son but also making sure that progress toward a cure for MPS II does not slip off the social, political, and economic agenda before Erik reaches an age where he'll be left behind by the medical industrial complex altogether. But does it matter? How much can individual families' experiences of suffering and grief matter in the setting of collective priorities and agendas? And who determines which forms of suffering are accorded value and get to be on that agenda?

My goal in this dissertation has been to show how the ontological politics around access to costly drugs for rare disease in Canada center around a sticky tension between competing enactments of values around the imperative to care for suffering individuals versus the imperative to put in place impartial standards and frameworks to protect the sustainability of the collective public health care system. Through the practices that are enacted around this individual/collective tension, each side of the binary opposition operates as an ontology: the 'suffering individual' ontology and the 'sustainable collective' ontology, each with their own formal and informal scripts (Buchbinder 2016) that shape how stories are told and the patient experience is configured. By juxtaposing these ontologies and their scripts as they shape the 'macro' setting of policy around rare disease with the much messier and less linear lifeworlds of families, I have troubled both of these powerful ontological frames and offered a way of understanding how tensions between the individual and the collective good operate through powerful configurations of the patient experience and frames around life with disease. However,

I have also shown that these configurations and frames and scripts are embedded in a politics around money, power, and care. The relationship between the individual and the collective, at least in this setting, is not a cultural dynamic so much as it is a mediated material semiotic one, constituted by practices of tacking between capital and budgets and the impossible double binds and trade-offs that the current drug development and pricing system presents us with. The ethnographic data shared throughout the chapters of this dissertation has shown how public drug payers, pharmaceutical company representatives, policymakers and researchers, patients and families, and patient advocates all draw on this individual/collective tension in different ways, to make sense of their social commitments and also make sense of rare disease.

The meanings of rare disease and of rare disease drugs do not hold stable across the different groups of social actors that I have explored within this dissertation, largely because of the multiplicity of different material and political stakes invested within this wily category. I have used the methods of ethnography to juxtapose ‘macro’ contexts of negotiating the contours of rare disease drug access (and rare disease itself) in Canada’s publicly funded health care system with the ‘micro’ moral worlds of families living with and caring through devastating progressive-degenerative diseases that happen to be ‘rare.’ In doing so, I have shown that the boundaries of the individual/collective tension that social actors enact through practices around drug development and access collapses when considering how these practices are generating new kinds of precarities and new classes of deservingness. The individual/collective tension is not a natural ‘thing’ but an enacted set of relationships dependent on the practices that bring it into being. Rare disease patients (or their parents) learn to tack between these different ontological frames of the moral world, developing repertoires necessary to perform the ‘suffering individual’ identity in order to secure access to treatment. However, the ‘suffering individual’ ontology

pushed by the pharmaceutical industry does not fundamentally challenge the system or argue for better care and a stronger service and support system for people living with chronic disease and disability. It's primary function is to channel capital towards pharmaceuticals.

In the introduction to this dissertation, I noted that my central research questions for this study were: 1) what do practices around high drug prices *do* to the relations they draw from and the relations they create? 2) What are the different politics of care performed in rare disease drug access disputes? 3) How do pragmatic enactments and practices at policy, government, industry, and advocacy levels affect and inflect the experience of being 'rare' for patients and families?

First, this dissertation has shown how high drug prices do much more than line the pockets of pharmaceutical company CEOs and shareholders, or even, as in industry articulations, allow for continued research and development into the vast area of unmet need that is 'rare disease.' In Chapter 3, I showed how high drug prices amplify the intensity of the range of practices that aim to filter the symbolic meanings and attachments to rare disease drugs through impartial frameworks and formulas designed around a rational economic calculus. This puts patients in a sticky position, as with Nora's story, when a newspaper article included her story as an example of how patients demanding resources are eroding the health care system's ability to make evidence-based decisions and negotiate drug prices.

In Chapter 4, I showed how high drug prices have forced patients and families through access struggles that can amplify and augment the colonial violence imbricated in Canada's responsibility to Indigenous peoples, as with Scott's story, where as a First Nations child who had participated in the clinical trial that led to the drug, he got bounced around by different levels of government as they tried to avoid paying for the treatment. I also showed how for a relatively privileged white middle class family, high drug prices generate anxieties of deservingness and

worry that the political currents will shift, as with Ella's story from Chapter 4, where she shared that she loses sleep at night about how long her child will be considered worthy of such a huge amount of resources. I continued this analysis in Chapter 5, where I looked at how, in negotiations over the formal and informal contours of defining the rare disease category, high drug prices necessitate that rare genetic disease patients be framed as extremely deserving—more deserving, perhaps, than other disease groups who 'brought their condition upon themselves.' In sum, high drug prices amplify the individual/collective tension explored here, increasing the intensity of 'trade offs' between individual and collective forms of care. One may even wonder if high drug prices depend on this tension and the oscillations between inclusion and exclusion that place bodies and lives at the center of disputes over deservingness and value.

Second, this dissertation has taken an approach to the politics of care that understands care as something that is performed within contemporary politics through practices, enactments, and articulations—care, like knowledge, is always situated somewhere. As Povinelli (2011: 22, 160) writes:

We get nowhere within neoliberalism arguing whether this or that person did or didn't care about the vulnerable or that this or that social welfare program was or was not a failure. Instead, we need to start asking what are the measures of failure, the arts of failure ... the arts of caring for others always emerge from and are a reflection on broader historical material conditions and institutional arrangements ... In the first instance, the question is, what do we believe care to consist of, such that when we experience a form of relating to one another socially, we experience that form of relating as a form of caring for others?

Here, Povinelli points us toward the understanding that what people imagine 'care' to be reflects the broader contexts and situated positions in and from which care is enacted. My analysis of the different politics of care performed in rare disease drug access disputes has shifted between the pragmatic practices of different groups of social actors trying to make things work in the

conditions of possibility bestowed upon them. The practices that enact care become ontological realities—in this case, at the ‘macro’ system level, two competing ones—that each configure patients, families, illness and deservingness in particular ways. Thus, looking at the disjunctures between these macro level framings and the actual unfolding of the everyday practices of care at the micro level becomes vital for ensuring the ‘patient voice’ does not become overly eclipsed within powerful frames.

For public drug payers, care consists of practices that can be understood as reasonable from a rationalized position of evidence. This is necessary, to them, within this complex domain of uncertainty and pharmaceutical capitalism, because their task is not only to care about individuals but about the collective health care system as well. Impartial frameworks and formulas for decision-making, imperfect as they are, help them to do this. For pharmaceutical company representatives, care consists of getting medicines to these suffering individuals with rare disease, so long as the profit-based system of drug development remains in place, and health care systems are willing to arrange themselves around making that happen. For patient advocates, whose enactments often trickily entangle with pharmaceutical industry actors, care consists of practices around pushing back against the impartial frameworks and formulas of public drug payers, ensuring the narrative stays focused on the suffering individual as a more important onus of decision-making than the sustainability of the collective.

For all of these groupings of actors, these enactments of the politics of care are frequently marked by ambivalence—the worlds they are enacting is imperfect, and they know it, but for whatever reason they must play the game. Caring practices like Jay and Diana’s through the health policy unit’s citizens’ juries, attempt to move beyond polarities and binaries to find a way to ask different sorts of questions, but the tools they have at their disposal to do so have this

individual/collective conceptual binary imbricated within them.

My third and final research question was: how do pragmatic enactments and practices at policy, government, industry, and advocacy levels affect and inflect the experience of being ‘rare’ for patients and families? Running through all of these chapters has been this line of analysis. In Chapter 3, I explored how the movement from a focus on pharmaceutical promise to relieve individual suffering in Phases 0-3 of the social life of a rare disease drug oscillates to a focus on health system pragmatics and the sustainability of the collective in Phase 4—generating confusion and the “dearticulation of pharma-matter” (Hardon and Sanabria 2017: 119) that had in earlier phases been strongly articulated and rearticulated through its potentialities. In Chapter 4, I looked at how rare disease has *become* a category salient to families over time, in the process, however, so too have the moral questions around caring for a desperately ill child shifted as new treatments offer new possibilities but also new vulnerabilities that intersect with where a family is positioned socially in a country marked by ongoing and deepening inequality. In Chapter 5, I looked at how the attempts to widen the category of rare disease to meet market imperatives has in fact increased the precarity of patients with ultra-rare diseases as social actors play ‘hard ball’ and use rare disease as a professional wish list for what kind of world they’d like to see around them, for professional and personal reasons. The stakes of patients and their families, trickily intertwined but in no way identical with the stakes of the pharmaceutical industry become refracted through deservingness and attempts to privatize the Canadian health care system. In Chapter 6, Kelsey’s story of moving through three different treatment hopes and access struggles shows how ‘being rare’ is something that fades in and out over time, dependent on how the category can meaningfully contribute to her moral experimentation in caring for her son Erik. In Chapter 7, I looked at how, while perhaps unbeknownst to patients and families, the

way their plight and their identity as citizens seeking health resources depends on how the figure of ‘social values’ gets framed, and publics holding and enacting those values are engineered.

Taken together, these three research questions have shown rare disease drug access in Canada to be embroiled within a tricky ontological politics, where a lot is at stake for all of the social actors introduced in this dissertation. By looking at rare disease drug access as imbricated within different versions of Canadian nation-making, I have theorized rare disease drug access disputes as part of a much deeper politics of care. Canadian nation-making around the health care system has long centered around this tension between a more privatized vision of health care and competing visions that aim to make the public system more robust. In order to survive the conditional citizenship of privatized health care, being ‘important’ and ‘valuable’ to society becomes a competition of sorts, a contest over whose suffering is more special and deserving of redress and resources (see Brown 1995; Ticktin 2011; Benton 2015). This is a game that one can be winning one day and losing the next—or winning in some ways but deeply losing in other ways, troubling the starkly dichotomous formulation of ‘winners’ and ‘losers’ used by some health economists introduced in this dissertation to justify withholding access to treatment. One may get access to an expensive treatment but have other needed social services defunded or pushed off the policy agenda or the health care system de-universalized by elite interests so your child can get free access to a controversial drug but have to pay or take out private insurance for that same child’s carpal tunnel syndrome surgery.

As such, suffering individuals are not in some way separate from wider questions of collective concern, but the ontological politics of rare disease drug access often neatly delineates ‘suffering individuals’ and the ‘sustainable collective’ into separate conceptual categories. The focus on the materialities of rare disease drugs in macro and micro contexts that I have taken in

this dissertation, however, has shown that ‘suffering individuals’ are in fact deeply affected by issues of collective concern and the robustness (or lack thereof) of the service system.

Ethnographically, opportunity cost and trade-offs and QALYs are thus less about who wins and who loses in terms of different competing disease populations so much as it is about the way that these practices feed into pharmaceutical enactments to refract ‘solidarity’ into multiple competing versions with different models of care imbricated within them.

The multi-billion dollar question, of course, is whether things can realistically be done any other way. Health care systems, to a degree at least, depend on systematization—and in this dissertation my goal has not been to discount or deny the fact that difficult decisions in the allocation of resources must be made. However, the stories and practices shared within this dissertation open up space for a rethinking of the conceptual categories and relations used to make sense of rare disease drugs. We have seen how the intensity of experience and life with disease and moral experiments of care rub uncomfortably against practices of impartiality and distancing embedded in the processes and frameworks of drug access decision-making. It is within this gap—and the promise to care for the suffering individuals left behind by the ‘big bad government’—that pharmaceutical enactments and pricing practices actually gain power.

If we understand the generative powers of the individual/collective tension described here not as an uncomfortable side effect of pharmaceutical capitalism but a relation its practices depend upon, we see how the ethico-political project of universal publicly funded health care needs to grapple with problems far deeper than just how to make evidence-informed decisions. Astronomical drug prices are no longer an issue isolated to rare disease and the evocatively titled category of ‘orphan drugs’—rather, drugs for all treatments are becoming more and more expensive, with the practice of arbitrary and sudden price increases operating to no abandon

(Hernandez et al 2019). People who can afford these prices pay, people who are covered by a universal public health care system receive access until the drug gets taken off the formulary, while others in less secure situations globally suffer and die for lack of access to increasingly expensive insulin and epi-pens and asthma pumps. Rare disease has operated as a testing ground for pushing these limits, for seeing how far these types of pricing practices can go.

The scene at the five km charity race with which I opened this conclusion chapter indexes that these national health care system politics are part of a much wider global politics of different forms of suffering and deep inequalities. The power of enactments around scarcity and the limited good, performed by private and public social actors alike, forces a constant ‘choosing between,’ such that it feels impossible to ‘care’ for everyone and everything. I’ve thought a lot about this interaction with the man at the five km charity race since it occurred. In the end, we were both running a race sponsored by a bank, our attempts to do ‘good’ implicitly partaking in systems of practices that tie into networks of power and money and violence that I’m sure both of us would disagree with, even as the relatively comfortable lives we lead are complicit within them. Is there any way out, or are we always and irredeemably caught in a politics of care and suffering that attributes worth (financial and otherwise) to some bodies while others die with no attention?

Rare disease has been considered a ‘model’ for the promissory world of personalized medicine (i.e. see Tabor and Goldenburg 2018). The small patient populations with high levels of uncertainty demand different ways of understanding disease and drug benefit, and a willingness and capacity to live with and manage uncertainty. This will be a reality of personalized medicine as well, since even ‘targeted’ treatments work variably in complex bodies shaped not only by genes but by interactions with environment as well. The deeper concerns

pointed to in this dissertation, however, lie not necessarily with evidence and benefit but with the ways that bodies and lives and drug prices and inequalities in access to care will be framed in the ontological politics that will inevitably accompany personalized medicine. Who will have access and who will not? How will other existing inequalities be redressed or exacerbated by personalized medicine? I suggest a politics of care that does not simply focus on ‘evidence’ and whether an intervention works on the individual body or not but how relations assemble and fragment around the flows of power and money towards technoscience. This is related to, but embedded in a slightly different relationality, than framings of opportunity cost.

The question that rare disease offers personalized medicine and Pharmacare and other efforts toward health system improvement is this: if the world is not a stable entity that social actors have competing perspective on, and rather something enacted through practices, what practices would permit drug access to be enacted from within a novel politics of care? Rare disease offers the opportunity for future research to look at creative solutions to drug development and access and the entanglement of stakes between those living with rare disease and those profiting from it. Following the philosophical thinking of the parents of children with rare disease who appeared in this dissertation: who really owns these complex biologic substances? Why isn't there a governing body that oversees pharmaceutical industry strategies to deny and overlook and abandon the sick if systems don't restructure according to their desires? Is private industry the way to go? How do the intensities of access around new treatment potentialities put parents into desperate situations of grabbing at straws, and how can we instead help parents work on acceptance and allowing for narratives of caring in the face of decline to be important too? On an everyday level, these questions ask: how can we put practices in place that do not feed into the suffering individual/sustainable collective binary, but rather collapse it?

In the end, the tension between the collective good and the individual good can only be managed, not overcome. What this dissertation has shown is that the anxieties about being in the epidemiological ‘tail ends of the curve’—the ‘rare’—are real within the lives of families trying to access resources and care. This dissertation has also shown how these anxieties are manipulated by a particular form of pharmaceutical market-making that is centering upon these gaps. There is a lack of formal and legal state capacity to regulate industry in order to manage this tension, which augments worries and fears among patients and their families. This leads patients and families to be so worried about ensuring that the conditions supporting treatment remain that they align with ontologies and scripts pushed by the global pharmaceutical industry even as those ontologies and scripts partition their care needs into valued and less valued forms of care, which threatens to dismantle and privatize the very service system that they depend upon in order to flourish in favour of channeling budgets entirely toward expensive on-patent drugs. The government can manage this by strengthening the protections that support both the individual and the collective good.

In December of 2019, the Canadian Prime Minister issued a parliamentary mandate letter to the federal Canadian Minister of Health, the honourable Minister Ms. Patty Hadju. The letter mandated that the federal Minister of Health proceed with instituting Pharmacare and an accompanying rare disease strategy. Thus, based on this ethnography, I have three suggestions for the honourable Minister Ms. Hadju.

First, reinstating compulsory licensing as part of the Patent Act could both strengthen the government’s position in pricing negotiations with industry and, in the event of economic downturns or other forms of collapse (with climate collapse a distinct possibility), offer a legal

pathway for the breaking of patents in order to ensure that needed pharmaceutical care is available and patients are not left behind.

Second, pushing back against the rhetoric that pharmaceutical care is the only form of care that these uncommon and unusual bodies need can be achieved only by applying a disability justice lens to rare disease. This would require a different set of conversations about how health budgets are managed and bodies cared for. A mandatory disability justice fund could be instituted that requires that pharmaceutical companies generating profits from the Canadian health care system pay a percentage of the price of the drug into that fund and the money dispersed towards projects that focus on accessibility and augmenting the voices and concerns of people living with disabilities and chronic disease across the life course. It is imperative that this fund be managed independently of the pharmaceutical industry in order to ensure that pharmaceutical access discussions do not eclipse discussions about other forms of needed care.

Third, there has been some vocal disagreement mobilized by some patient advocates against the use of subsequent entry biologics, or ‘biosimilars,’ essentially generic versions of biologic drugs. However, Health Canada (2019) and the International Coalition of Medicines Regulatory Authorities (2019) has determined that they are confident that biosimilars following strict regulatory processes are as safe and effective as the original biologic. What is needed is a critical ethnographic exploration of these disagreements (one that goes beyond technical debates of evidence which will forever forestall into differences in ‘perspectives’) in order to understand the substance of these tensions. Along with ensuring that rare disease regulatory pathways are not taken advantage of in this new era of pharmaceutical market-making, how generic versions of biologics will be integrated into health care systems will determine the future viability of universal health care systems.

Anthropologically, this dissertation contributes to understanding how the contradictions of capitalism as they play out in the pharmaceutical and life sciences industries are shaping both systems of governance and everyday life. It shows how individualization, neoliberalization, and privatization occur in context, through the manipulation of the tension between the individual and the collective good—pitting individuals against the collective and vice versa. As such a number of tensions operate in rare disease drug access disputes and thus through the rare disease body that are obscured when speaking through technical frames like evidence and cost-effectiveness. There is very little anthropological work on pharmaceutical resource allocation within public health care systems in high-income contexts, which has left the much lauded phenomenon of ‘universal health care’ vastly undertheorized in its actual particularities, controversies, and complexities. As pharmaceuticals—and the new regimes of valuation and pricing that increasingly come with them—intervene in bodies and communities, so too do they intervene in intersubjectivities of deservingness and worth. In disambiguating the different ontologies of care that operate in a controversy, and how these get experienced and navigated by diverse families, this dissertation has developed a framework for understanding the different meanings and enactments that circulate in a world where the ‘welfare state’ is increasingly under siege. This threat comes both through direct intervention (i.e. through free trade agreements or other harmonizations of social policy) or indirectly, as in rare disease care politics, where the publicly funded health care system—and questioning and resistance of high drug prices—are framed as morally wrong. These are the mechanisms through which privatization (and public support for it) occurs. Yet, this research has also pointed toward the need to imagine care differently than it is done in liberal framings of impartiality, and imagine a more transformative politics in which an ‘ethics of care’ (Tronto 1993) or a ‘logic of care’ (Mol 2008) could flourish.

As Barbara Prainsack (2017) asks: what kind of world would it take to be able to have ‘personalized medicine’ but without the inequalities in access that pervade it?

This study is a fine grained ethnographic engagement with various social actors which has led to a deeper understanding of how power operates through configuring the patient experience and the meaning systems of life with disease. Through practices and scripts, different ontologies form which have system shaping effects. While this fine grained ethnographic engagement led to these insights and a deeper understanding of how power operates upon and through bodies, lives, and systems, this strength is also a limitation of the study. In many ways, rare disease is a small community, so ethnographic work and storytelling risks making social actors identifiable and/or subjects me as the researcher to certain non-disclosure expectations. This has limited the ability to share and present some ethnographic data. While I as a researcher had high levels of access to powerful social actors as they went about their work, a limitation of this study is that I have had to keep large amounts of data confidential. This also made the writing process exceedingly difficult as some forms of ‘evidence’ could not be directly shared. Instead, I had to factor my ethnographic understanding into the ways that I reconstructed the issues for readers in somewhat less direct ways.

This study could also have been strengthened through a greater engagement with the role that affect plays in arranging these relations, as well as a greater engagement with the gendered dimensions ‘orphan drugs’ and rare disease resource allocation and caregiving. Beyond that it is mostly women identifying people who take on the brunt of care and moral, interpretive, and emotional labour in navigating rare disease access politics, a number of gendered tropes animate rare disease drug access politics. For example: subtle mobilizations of ‘hard’ scientific evidence as ‘male’ and ‘soft’ qualitative evidence as ‘female,’ which can either be a virtue or a vice

depending on who is doing the framing. These frames permeate the mobilization of different types of data in ‘post-truth’ debates. There are also many patriarchal overtones in discursive framings of industry ‘adopting’ poor orphans while the state acts as a much maligned ‘bad mother’ in denying care. Greater engagement with how these entangle with ideas of self-interest and morality could have enriched my findings here. These were all general subtle themes that operated at the surface of my data but which I did not pursue. Additionally, far more engagement with the material dimensions of ‘making’ the medicines—in laboratories and factories and other dimensions of the rare disease drug supply chain—would have added more depth to the meaning systems and materialities of medicines that is lacking here.

Future research will pick up on some of the themes identified above and also look more directly at resistances to pharmaceutical capitalism by patient communities. Specifically, I plan to study the patient led ‘drug buyers’ clubs’ that are forming around expensive personalized and rare disease medicines in the United Kingdom, Canada, and the United States. These nascent activist groups are working across and within state borders to demand the breaking of patents, ‘hacking’ treatments, or purchasing generic medicines from states where a drug does not hold a patent. Do the ‘suffering individual’ and ‘sustainable collective’ ontologies operate similarly in those politics? How will the politically charged ‘patient voice’ get treated when making demands that call into question intellectual property regimes? If anything at all, this dissertation has pointed toward a need to give space to the transformative potential of ‘the patient voice’ and the illness experience outside of the situated enactments that seek to channel it in any particular direction.

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