HEALTHCARE INEQUITY IN CANADA: EXAMINING THE FEASIBILITY OF THE PUBLIC PRODUCTION OF MEDICINES

“HEALTHCARE INEQUITY IN CANADA: EXAMINING THE FEASIBILITY OF THE PUBLIC PRODUCTION OF MEDICINES”

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LAY ABSTRACT

As the global pharmaceutical industry continues to generate significant wealth, the demand for equitable access to medicine remains at the forefront of political and grassroots agendas. In recent years, poor drug coverage coupled with unaffordable drug prices have contributed to access issues for a growing number of Canadians (Morgan et al, 2015). Although the industry cites various reasons for an increase in cost, such as high-risk research, lengthy clinical trials and significant advances in technology (DiMasi et al., 2016; Ridley, 2005), there is a growing body of research that is contradictory to the industry's reasoning for higher drug costs (Kohler et al., 2016; Siddiqui & Rajkumar, 2012; Light & Warburton, 2011).

Whereas other initiatives to date focus on drug coverage, this work proposes the Canadian Government investigate the feasibility of the public production and distribution of pharmaceuticals. Thus, the research question addresses whether successful publicly funded pharmaceutical research and development initiatives, including production and distribution, could be applicable in the Canadian pharmaceutical sector where inequity is an issue. A scoping review was conducted to draw in all relevant literature on publicly funded research models pertaining to the research and development of pharmaceuticals.

ABSTRACT

Background: As the global pharmaceutical industry continues to generate significant wealth, the demand for equitable access to medicine remains at the forefront of political and grassroots agendas. In recent years, poor drug coverage coupled with unaffordable drug prices have contributed to access issues for a growing number of Canadians (Morgan et al, 2015). Although the industry cites various reasons for an increase in cost, such as high-risk research, lengthy clinical trials and significant advances in technology (DiMasi et al., 2016; Ridley, 2005), there is a growing body of research that is contradictory to the industry's reasoning for higher drug costs (Kohler et al., 2016; Siddiqui & Rajkumar, 2012; Light & Warburton, 2011).

Whereas other initiatives to date focus on drug coverage, this work proposes the Canadian Government investigate the feasibility of the public production and distribution of pharmaceuticals. Thus, the research question addresses whether successful publicly funded pharmaceutical research and development initiatives, including production and distribution, could be applicable in the Canadian pharmaceutical sector where inequity is an issue. A scoping review was conducted to draw in all relevant literature on publicly funded research models pertaining to the research and development of pharmaceuticals.

Methods: The research undertaken for this thesis is exploratory and comprised of qualitative work that is guided by the Arksey & O'Malley (2005) scoping review methodological framework. The data collected for the scoping review was analyzed with the thematic analysis method.

Findings: Following the thematic analysis, three key themes were identified: Local Production, Public Private Sector and National Production. Although there have been some successes in low to middle income countries with regard to the local production of medicine, the likelihood of

success is contingent on whether there is a need to import active pharmaceutical ingredients (API). With regard to the public and private sector, the pre-competitive sphere serves as the typical space for collaboration. The public sector typically conducts research, whereas the private sector oversees drug development. The national production of medicine is underpinned by government intervention, which is evidenced by the varied measures taken to increase access to medicine. The preliminary literature review revealed that an Advisory Council was created to assess the viability of Pharmacare 2020. This council may be used to conduct the necessary research to assess the feasibility and strategy of publicly producing pharmaceuticals in Canada. **Conclusions:** Healthcare inequity that is linked to unaffordable medicine is exacerbated by poor drug coverage. The findings revealed that considerable investment into infrastructure, a strong civil society that pressures the government to act, and a pharmaceutical sector characterized by high prices may encourage a government to produce medicine when faced with a health crisis. Further findings revealed that API production may prevent a country from feasibly producing medicine. Considering Canada's standing as an industrialized and developed nation with access to state-of-the-art public infrastructure, in addition to a pharmaceutical market characterized by high drug prices and a strong civil society sector, the Canadian Government is in a likely position to produce medicine. However, the necessary research must be conducted to assess whether such an endeavour is feasible.

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LIST OF ABBREVIATIONS

API	Active Pharmaceutical Ingredient
CCPA	Canadian Centre for Policy Alternatives
CIHR	Centre for Innovative Health Research
CGPA	Canadian Generic Pharmaceutical Alliance
HCP	Healthcare Professional
HCO	Healthcare Organization
IMC	Innovative Medicines Canada
OECD	Organization for Economic Cooperation and Development
PBO	Parliamentary Budget Officer
pCPA	pan-Canadian Pharmaceutical Alliance
PMPRB	Patented Medicine Prices Review Board
PPP	Public Private Partnership
PSRI	Public Sector Research Institutions
R&D	Research and Development
TRIPS	Trade-Related Aspects of Intellectual Property Rights
WHO	World Health Organization

DECLARATION OF ACADEMIC ACHIEVEMENT

The following is a declaration that the research in this document has been completed by Jalal El Halabi and recognizes the contributions of Dr. Christopher J. Longo, Laura Banfield and Dr. Meridith Griffin.

CHAPTER 1: LITERATURE REVIEW

1.1 INTRODUCTION

As the cost of drug production continues to increase, governments around the world have seemingly reduced their role within pharmaceutical R&D, rather opting to support the private pharmaceutical industry through subsidies and investment (Australian Government, 2018; Caskey, 2007). In Canada, the pharmaceutical industry is dominated by private corporations ("Pharmaceutical Industry", 2018). The industry has played an integral role in the development of novel medicine; blockbuster drugs and major breakthroughs are among the most recognizable feats (Brumley, 2018). However, this past decade has been marked by scandalous headlines; from business malpractice to pricing out the most vulnerable populations, the collective call for action against the industry has become a global movement that is backed by a growing body of research and public support (Chow, 2018; Boseley, 2016; Milne & Petch. 2018; "Drug Companies", 2010). A survey conducted by Statistics Canada in 2007 found that one-in-ten Canadians did not take prescribed medicine due to cost (Statistics Canada, 2008). In a more recent survey conducted in 2015, the Angus Reid Institute found that one in five Canadian households were unable to fill a prescription due to cost (ARI, 2015). Cost related non-adherence to prescription medicine has contributed to a number of health issues, placing further strain on the healthcare system (Viswanathan et al., 2012). Further, a study conducted by Dr. Michael R. Law revealed that an estimated 730,300 Canadians forewent food, and an additional 230,000 forewent heat to pay for medicine out-of-pocket (Law et al., 2018). In light of this growing issue and the need to ensure that access to medicine is not out of reach for a high number of Canadians, alternative strategies should be investigated to assess how to reduce pharmaceutical prices. Thus, the research question sought to assess whether the success of publicly funded

pharmaceutical research and development initiatives, including production and distribution, could be applicable in the Canadian pharmaceutical sector in situations where healthcare inequity is an issue.

The choice to conduct a scoping review to address the research question is twofold; an extensive literature review can be used to draw in all relevant literature concerning publicly funded models of pharmaceutical R&D, with an analysis of the findings serving to inform the central research question, and it can be used to collect empirical research on the successes and failures of such programs. It is possible that the data collected in this thesis could be used to equip policy makers with the evidence required to promote the concept of publicly producing medicine in areas where healthcare inequity is an issue.

Prior to the scoping review, a preliminary literature review was conducted to provide an overview on the pharmaceutical industry in Canada and the number of Canadians that are affected by unaffordable medicine. Also included within this section, a proposal to increase drug coverage for all Canadians and efforts to negotiate lower drug prices with pharmaceutical companies through a national association, Pharmaceutical Pricing Alliance (PDCI, 2015).

1.1.1 The Private Pharmaceutical Industry

There are no publicly owned pharmaceutical companies in Canada (Lexchin, 2016). However, the world's top ten pharmaceutical companies research, develop and manufacture pharmaceuticals within Canada ("Pharmaceutical Industry", 2018). The Canadian Government pursues an agenda that is favourable to the industry, which is demonstrable through the lucrative work environment that the industry is provided with; first-rate academic and research institutions, a highly-skilled workforce, and hundreds of millions of dollars available in the form of subsidies and funding ("Invest in Ontario", 2018; "Canada's Pharmaceutical", 2014). Further,

there is a multitude of public private partnerships (PPPs) and collaborative initiatives scattered throughout the country that have been developed to aid industry endeavours ("Canada's Pharmaceutical," 2014). Researchers are in abundance and many of them rely heavily on private sponsorship ("Clinical Trials Ontario", 2018). Canada is known to provide the least expensive services for R&D within the fields of clinical trial administration and biomedical research amongst developed countries, while maintaining the highest ranking among the G7 countries for operational and manufacturing costs within pharmaceutical facilities (Department of Foreign Affairs, 2018).

1.1.2 Drug Access in Canada

Universal healthcare coverage is a leading point of pride for Canadians, with an estimated 90% of Canadians believing that shifting to another model would irrevocably change how Canadians perceive their country (Simpson et al., 2017). In recent years, there has been an uptick in media coverage regarding universal drug coverage, as Canada is the only developed country to provide coverage without including prescription medicine (Coletta, 2018; Ireland, 2017; Davidson, 2015). Some of the issues concerning unfilled prescriptions due to cost and poor drug coverage are presented below.

A report conducted by the Wellesley Institute contrasts outdated beliefs of the Canadian labour market concerning employer-funded drug coverage (Barnes & Anderson, 2015). Barnes and Anderson (2015) found that an estimated two-thirds of working Canadians access prescription medicine through employer-funded drug coverage or private insurance, leaving one-third without access to prescription medicine. Among the findings, the study suggests that inequitable access to medicine is based on gender, age and earnings. To further illustrate this point; one-quarter of part-time workers receive employer-provided health benefits, women are

less likely to have employer-provided health benefits and the less a person earns corresponds to how likely they are to receive employer-provided health benefit coverage (Barnes & Anderson, 2015). Non-adherence to prescription drugs that is linked to cost affects nearly 10% of the Canadian population, however, the actual percentage per province varies from 8.9 percent in Saskatchewan and Manitoba to 17 percent in British Columbia (Barnes & Anderson, 2015).

Steve Morgan is a renowned Canadian health economist that works as a full professor at University of British Colombia's School of Population & Public Health ("Steve Morgan", 2018). In a study led by Morgan, the findings revealed that Canadians are faced with some of the highest drug costs in the industrialized world, and that Canada is falling short with regard to promoting cost-conscious prescription drug utilization (Morgan et al., 2017). The report concluded this has resulted in higher prices for brand name and generic pharmaceuticals.

There has been considerable media coverage and research on the growing number of Canadians that are confronted with choosing between basic needs and medicine (Law et al., 2018; Milne & Petch. 2018; Ireland, 2017; Sawa & Ellenwood, 2017; ARI, 2015; Morgan et al., 2015; Davidson, 2015). Morgan (2015) has revealed that nearly 1 in 4 Canadian households are affected by costs associated with filling prescriptions for medicine (Morgan et al., 2015).

The Canadian Federation of Nurses has reported on what they label "a system of prescription drug coverage that is inefficient and ineffective" (Lopert et al., 2018). A recent report conducted by the federation estimates that hundreds, if not thousands of Canadians die each year due to unaffordable medicine (Lopert et al., 2018). A lead author of the report noted that to determine the exact number with precision would take years, as many categories concerning premature death overlap (Lopert et al., 2018). This report draws light on the estimated number of Canadians that have prematurely died due to unaffordable medicine.

Further, an estimated 70,000 older Canadians, aged 55+, suffer from what the report identified as "avoidable deterioration" due to cost associated non-adherence (Lopert et al., 2018).

1.1.3 A Proposal for Universal Drug Coverage

Prescription drug coverage in Canada is often referred to as a patchwork that worsens healthcare inequities (Barnes & Anderson, 2015). The literature pertaining to poor drug coverage in Canada has caught the attention of policymakers and advocates, leading to the proposal of a universal drug coverage program (Morgan et al., 2015). As part of Budget 2018, the Canadian federal budget for fiscal year 2018-2019, the government announced the creation of an Advisory Council, a non-partisan collective of individuals with expertise related to the matter at hand, to assess the viability of a national drug program with extensive coverage (Morneau, 2018; "Initial Report", 2015).

Pharmacare 2020 is a collaborative initiative that advocates for a robust national drug coverage program (Pharmacare 2020, 2018). The program follows four policy recommendations:

1. Provide universal coverage of selected medicines at little or no direct cost to patients through Pharmacare.
2. Select and finance medically necessary prescription drugs at a population level without needs-based charges – such as deductibles, coinsurance, or risk-rated premiums – on individuals or other plan sponsors (e.g., businesses).
3. Establish a publicly accountable body to manage Pharmacare, one that integrates the best available data and evidence into decisions concerning drug coverage, drug prescribing, and patient follow-up.

4. Establish Pharmacare as a single-payer system with a publicly accountable management agency to secure the best health outcomes for Canadians from a transparent drug budget (Pharmacare 2020, 2018).

Although unaffordable medicine is increasingly being recognized as a contributor to healthcare inequity, Pharmacare 2020 aims to reduce the inequity by way of increasing drug coverage for all Canadians (Law et al., 2018). The program aims to implement an extensive drug coverage plan, and in effect, reduce the number of Canadians that are unable to purchase medicine (Pharmacare 2020, 2018).

1.1.4 Estimated Savings

There has been extensive media coverage of the proposed national drug program, Pharmacare 2020, and with it, various numbers have been reported with regard to estimated savings (Lunn, 2018; Fréchette, 2017; CCPA, 2013). Conservative Health Critic Marilyn Gladu has proposed a supplementary report to address unanswered questions and costs associated with the program (Lunn, 2018). Further, Gladu, in addition to the heads of three organizations, Canadian Labour Congress, Canadian Federation of Nurses Unions and Doctors for Medicare, allege that the current government is using an Advisory Council to stall the rollout of a national pharmacare program (Blatchford, 2018).

In a report conducted by the Canadian Centre for Policy Alternatives (CCPA), it is estimated that the implementation of a national pharmaceutical plan will save nearly $11 billion in annual costs for prescription pharmaceuticals (CCPA, 2013).

However, a significantly lower figure was presented in a report conducted by the Parliamentary Budget Officer (PBO), a non-partisan federal fiscal watchdog (Fréchette, 2017). The PBO contrasted current spending with the estimated cost to implement a national

pharmacare program, which is broken down accordingly: public insurance plans, private insurance plans, and out of pocket expenses. The projected cost to implement a national pharmacare program, $20.4 billion, represents savings of $4.2 billion (Fréchette, 2017). Further, lower drug costs and expanded public drug coverage have been identified by the PBO as off-setting factors that would increase spending, as cheaper drug prices would increase aggregate consumption, and coverage for uninsured individuals would increase total consumption (Fréchette, 2017).

1.1.5 Increasing Drug Prices

The pricing of pharmaceuticals in Canada is a shared responsibility between the federal and provincial governments (Lexchin, 2015). At the federal level, the Patented Medicine Prices Review Board (PMPRB) regulates the prices of new patented medicine, while managing price increases in alignment with the rate of inflation (PMPRB, 2018). At the provincial level, the pan-Canadian Pharmaceutical Alliance (pCPA) facilitates negotiations between jurisdictions and manufacturers regarding retail pricing (Canada's Premier, 2018).

The PMPRB is an independent, quasi-judicial organization that was created by the federal government in 1987 to monitor, report on, and regulate the pricing of patented pharmaceuticals in Canada (PMPRB, 2018). If PMPRB Board Staff were to find that a drug was priced excessively without adequate reasoning following an investigation, the strongest course of applicable action falls within the bounds of a notice for a price reduction (PMPRB, 2018). The PMPRB prices pharmaceuticals according to seven comparator countries, which some critics argue has resulted in Canada paying among the highest prices for pharmaceuticals in the developed world (Morgan et al., 2017; Marwaha, 2016; Morgan, 2010). According a report

produced by the PMPRB, pharmaceutical sales have doubled from $12 billion in 2006 to $24.6 billion in 2015 (Government of Canada, 2017).

There has been extensive media coverage concerning pharmaceutical prices in Canada (TVO, 2018; Zafar, 2018; Ireland, 2017; Sawa, & Ellenwood, 2017; Davidson, 2015). Canada spends more per capita on pharmaceuticals than any other country in the world save for the United States ("About the OECD", 2018).

The report series, Generics360, was prepared by the PMPRB as part of the National Prescription Drug Utilization System to report on the latest trends concerning generic drug sales in Canada (Potashnik et al., 2018). The report found that generic drug prices in Canada are the seventh highest among members of the Organization for Economic Cooperation and Development (OECD), an organization that promotes economic and social policies to improve the livelihoods of people around the world ("About the OECD", 2018; Potashnik et al., 2018). Further, the report uncovered that efficient regulation could reduce public drug plans by nearly half a billion dollars, given generic medicine consumed by Canadians is priced according to international levels (Potashnik et al., 2018).

Among the reasons why Canada has the one of the highest drug costs among developed countries, most notably is the list of comparator countries. Critics argue that some countries, such as the US and Switzerland, should be removed given the notable differences in income, policy, and governance (Morgan et al., 2017; Lexchin, 2016). These findings have been presented to the Canadian Government, which led to the development of a proposal to amend the Patented Medicines Regulations, which is being welcomed as an innovative change to a long-standing problem (Morgan et al., 2017). With these changes, the board aims to introduce ceiling prices to curb excessive pricing by increasing the number of comparator countries to 12. The two

most expensive countries, the US and Switzerland, were dropped due to higher national per capita income and lacking a consumer protection mandate. Lastly, pharmaceutical companies will be requested to reveal the discounts and rebates granted to the various provinces and organizations across the country. This will serve to reduce the inflated market value of the drug, permitting buyers and negotiators to begin negotiations with an accurate price (Milne & Petch, 2018; "Protecting Canadians", 2018).

The pCPA is an initiative that is comprised of provincial, territorial and federal drug plans responsible for joint negotiations for brand and generic pharmaceutical pricing (Canada's Premiers, 2018). The organization was created in 2010 by the Council of Federation, a congress comprised of the premiers of each of Canada's provinces and territories, to conduct joint public drug plan negotiations. The objective is to negotiate agreements that provide greater value with regard to publicly funded drug programs (Canada's Premiers, 2018). Through the Value Price Initiative, a program that aims to reduce the cost of drugs through combined purchasing power, the pCPA has significantly reduced the prices for an estimated 80 generic drugs; an initial sale at 25% of the branded price was further reduced by 25%, thus totaling an 18% reduction (Canadas Premiers, 2018).

Although regulatory infrastructure can be used to control pharmaceutical prices, other variables, such as the costs associated with the entire pharmaceutical R&D process, in addition to technological advancements and innovative medicine, may drive costs upward (Gilman & Dowden, 2017; Grant, 2017; DiMasi et al., 2016; Roughead et al., 2007). This is evidenced by a report conducted by the Tufts Center for the Study of Drug Development (CSDD) in 2014 (DiMasi et al., 2016). The report revealed the revised cost to develop a prescription drug that gains market approval from $807 million in 2001 to $2.6 billion in 2014 (DiMasi et al., 2016).

Other researchers have called this number into question, advising policymakers to refrain from relying on cost estimates due to variation in numbers (Adams & Brantner, 2006). There are three factors that contribute to increasing national drug budgets: the price per unit of medicine, the number of users, and the average number of units per person (Dubois et al., 2000). In the previous paragraphs the focus has been on the price per unit of medicine, although the problem is compounded by the other two factors (Dubois et al., 2000). Thus, this thesis does not intend to address the other growth-related issues as the primary focus is the effects of highly priced medicine, not the total drug budget.

In an example of costs borne by the private pharmaceutical industry, Dr. Joel Lexchin, an author, medical doctor and expert in pharmaceutical policy, has written extensively on the relationship between healthcare professionals (HCP) and payments made to them by the industry (Lexchin, 2016; Morgan et al., 2015; Lexchin, 2013; Faunce & Lexchin, 2007). His findings indicate that the industry's marketing efforts aid in the aggressive expansion into the Canadian drug market. Each year, the industry spends an estimated $60,000 on marketing efforts per doctor (Butler, 2016). Drug companies and their pharmaceutical sales representatives are the first point of contact for medical doctors and in most cases the sole source of information when it comes to new medicine (Sawa & Ellenwood, 2017). Pharmaceutical sales representatives are encouraged to foster relationships with medical doctors. As a result, physicians are more likely to accept the marketed information they receive on the efficacy of the drug being advertised (Moynihan, 2003). The industry has sponsored research, conferences, clinics and other initiatives within the healthcare field (Butler, 2016). This has been linked to an increase in medical doctors in Canada that prescribe the costlier version of a drug as much as 30% of the time (Moynihan, 2003). This is exacerbated by employer-funded drug plans, as insurance

providers are complicit in accepting claims for brand medicine, even when there are multiple options available that are significantly less expensive (Cox et al., 2016).

Innovative Medicines Canada (IMC) is an organization that represents many of the pharmaceutical companies that operate within Canada (Innovative Medicines Canada, 2018). In response to the criticism concerning payments made to HCP and healthcare organizations (HCO), IMC developed a voluntary framework on the disclosure of payments. As a result, 10 of its members will publish aggregate sums of their payments to HCP and HCO (Innovative Medicines Canada, 2018). The organization revealed that HCP and HCO are paid for services rendered, such as advising, consulting, or giving speeches (Innovative Medicines Canada, 2018). A study was conducted to assess how these payments and incentive items may alter the opinions and practice patterns of HCP (Morgan, 2006). The study found that 33% of participants felt their decision to prescribe a certain medicine would likely be influenced in the event that samples or incentive items were accepted.

In another example of costs borne by the industry, the literature revealed that payments to patient advocacy groups are not uncommon, as a high number of these groups in Canada receive funding from the industry (Batt, 2017). Some coverage of this has been controversial, with journalists hinting towards a conflict of interest (Batt, 2017). Operating with a collective voice, 28 patient groups have denounced the federal government for its recent proposal to reform drug prices, citing inequity of access to certain types of medical treatments as a foreseeable issue with price reduction (CEADM, 2018).

1.2 SUMMARY & STUDY OBJECTIVES

1.2.1 Summary of the literature

The private pharmaceutical industry's dominance over the drug market in Canada is a well-documented area of study (Lexchin, 2016; Morgan et al., 2015; Morgan, 2010). The literature concerning the industry varies along a spectrum that ranges from support to vitriol (Law et al., 2018; DiMasi et al., 2016; Barnes & Anderson, 2015; Lexchin, 2015; Morgan et al., 2015; Grabowski & Hansen, 2014).

The growing number of Canadians that are unable to access medicine has become an ongoing issue that is shaping pharmaceutical discourse in Canada (Morneau, 2018; Morgan et al., 2015). Pharmacare 2020 is being hailed as a potential solution by way of securing universal drug coverage for all Canadians (Pharmacare 2020, 2018). Although there are some discrepancies in the number of dollars that will be saved by implementing a national drug program, the PBO reported a figure upwards of $4 billion (Fréchette, 2017). Unaffordable pharmaceutical prices in Canada have been linked to various factors, such as poor regulatory infrastructure, pharmaceutical R&D, marketing efforts and technological advancements, to name a few (Gilman, & Dowden, 2017; Grant, 2017; DiMasi et al., 2016). The PMPRB has been mentioned by multiple authors as a contributing factor to unaffordable drug prices, which is likely due to the perceived lack of control over the pricing of new patented pharmaceuticals (Morgan et al., 2017; Lexchin, 2016; Marwaha, 2016). Further, the estimated cost to bring a new drug to the market, which was released by the CSDD in 2014 at $2.6 billion, has been called into question by multiple sources (Grabowski et al., 2014; LaMattina, 2012; Adams & Brantner, 2006; Public Citizen, 2001). Further studies have uncovered the amount of money paid out to

Canadian doctors influences drug selection recommended to patients (Llamas, 2018; Batt, 2017; Lexchin, 2016).

The issues highlighted above provide insight into how unaffordable medicine and poor drug coverage contribute to healthcare inequity in Canada. This has resulted in a healthcare inequity that affects an estimated 10% of the population (Barnes & Anderson, 2015).

1.2.2 Study Objectives

The objectives of this thesis are:

1) To collect data on the public production and distribution of pharmaceuticals in other countries

2) To investigate whether these data could be applicable in the Canadian setting where healthcare inequity is an issue

This thesis may serve to reduce the knowledge gap on publicly funded models for the enhanced R&D of pharmaceuticals, in addition to serving as a useful set of reference material for analysts, researchers and others concerned with the pharmaceutical situation in Canada. Further, this thesis may serve to promote dialogue on the role of the Canadian Government with regard to the public production of medicine as a means to address the healthcare inequity highlighted within this thesis.

The objective of this thesis is not to propose a solution in lieu of the pharmaceutical industry nor to project the industry as maleficent. The collated data and subsequent analysis are intended to encourage dialogue between the pharmaceutical industry and governments regarding solutions around patient access to medicines. This should provide policymakers with additional evidence required to consider adding a new player within the industry, the government.

CHAPTER 2: METHODOLOGY

2.1 INTRODUCTION

The research undertaken for this thesis is exploratory and qualitative. The research question was devised upon careful consideration of keyterms that would be employed in the scoping review. To answer the research question, a scoping review was selected to examine the extent of research available on the public production and distribution of medicine in an international setting. The Arksey & O'Malley framework (2005) was selected for conducting a scoping review as the methodological framework. Arksey & O'Malley (2005) have identified four common types of scoping studies:

1. To examine the extent, range and nature of research activity: this type of rapid review might not describe research findings in any detail but is a useful way of mapping fields of study where it is difficult to visualize the range of material that might be available.
2. To determine the value of undertaking a full systematic review: in these cases, a preliminary mapping of the literature might be undertaken to identify whether or not a full systematic review is feasible (does any literature exist?) or relevant (have systematic reviews already been conducted?) and the potential costs of conducting a full systematic review.
3. To summarize and disseminate research findings: this kind of scoping study might describe in more detail the findings and range of research in particular areas of study, thereby providing a mechanism for summarizing and disseminating research findings to policy makers, practitioners and consumers who might otherwise lack time or resources to undertake such work themselves.

> 4. To identify research gaps in the existing literature: this type of scoping study takes the process of dissemination one step further by drawing conclusions from existing literature regarding the overall state of research activity. Specifically designed to identify gaps in the evidence base where no research has been conducted, the study may also summarize and disseminate research findings as well as identify the relevance of full systematic review in specific areas of inquiry. However, it is important to note that identifying gaps in the literature through a scoping study will not necessarily identify research gaps where the research itself is of poor quality since quality assessment does not form part of the scoping study remit. (Arksey & O'Malley, 2005, p.21).

This particular review was guided by the third type: to summarize and disseminate the research findings (Arksey & O'Malley, 2005). The third type closely aligned with the objectives, which consisted of the collection and investigation of data on the public production and distribution of medicine, and the intended dissemination of findings to policy makers, practitioners, and consumers who are interested in the Canadian pharmaceutical sector. However, it is noted that the review does, in a way, address some of the other types. With regard to the first type, the extent of research activity is touched upon, as the findings indicate the number of countries where the public production of medicine has occurred, which could be used to visualize the range of available material. The second type is least relevant, as a preliminary literature review revealed that little literature exists, thus a systematic review would serve little purpose. The fourth type of review demonstrated greater relevance, although the identified objective was not to identify gaps in the evidence where no research has been conducted. Thus,

the third type proved most relevant, considering the importance placed upon informing policymakers, government officials, and other relevant stakeholders involved in the Canadian pharmaceutical sector.

To ensure transparency, the research process was recorded in a Word document that was used to inform the steps taken in the study selection, in addition to the steps taken for the thematic analysis; rough notes were taken to serve as a reminder of the process as well as to guide the methodology during the write-up portion of the thesis. During the search strategy, the screening process was documented step-by-step so that the process could be repeated, as well as to contribute to an audit trail.

In accordance with the Arksey & O'Malley (2005) methodological framework, the research question, broad in nature, was designed to draw in all relevant literature, regardless of study design, excluding review articles. The scoping review was conducted in five stages: identifying the research question, identifying relevant studies, study selection, charting the data, and collating, summarizing, and reporting the results (Arksey & O'Malley, 2005).

After familiarity with the literature was gained through the completion of a scoping review protocol and search strategy, the scoping review itself was conducted. The data was charted, collated and summarized in report format.

2.2 METHODOLOGY

In order to conduct a scoping review in alignment with the Arksey & O'Malley (2005) framework, five of the steps detailed within the framework were followed. This also served to uphold transparency throughout the research process.

2.2.1 Identifying the Research Question

The following paragraphs provide the reasoning for the choices that led to the

development of the central research question. The reader may distinguish particular positions that were adopted and whether a predetermined mindset has informed this work.

During the development of the central research question, it became apparent that the research question was too broad. The initial question was framed around government capability with regard to participating in the full lifecycle of pharmaceutical innovation. Through this approach, the review would reveal what government involvement may look like, such as R&D and enhanced R&D, which may include participating in the full lifecycle, from identification of a chemical entity through to production, in addition to the manufacturing and distribution of pharmaceuticals. It was concluded this search was still too broad, hence in order to narrow the results further, the focus moved away from government capability as an area of study and towards examples of successful initiatives accomplished by governments related to the public production of medicines in an international setting. By focusing on the public production of medicine to address healthcare inequity, the goal shifted toward identifying literature that explored public production and its impact on drug pricing, and/or political factors in its success or failure. In doing so, the research question provides the reader with a greater understanding of the issue at hand and how this thesis work may attempt to develop an answer; through the examination of other governments confronted with the same healthcare inequity and how they have attempted to address the issue. Therefore, the final central research sought to address whether publicly funded pharmaceutical research and development initiatives, including production and distribution, could be applicable in the Canadian pharmaceutical setting where healthcare inequity is an issue.

2.2.2 Protocol

A protocol was used to guide the scoping review, assisting in the planning of how the

review would be conducted. Although the Arksey & O'Malley (2005) framework for conducting a scoping review was selected for this methodology, there was little information pertaining to the construction of a scoping review protocol. Thus, the Joanna Briggs Institute Reviewers' Manual 2015: Methodology for JBI Scoping Reviews, was consulted to aid in the development of a protocol (JBI, 2015). Within the guide, it states that a scoping protocol serves to:

- pre-determine the objectives and methods of the scoping review
- systematically approach the conduct and reporting of the review, while allowing transparency of process
- allow the readers to see how the results of the scoping review were arrived at
- detail the criteria that the reviewer intends on using to include and exclude studies and to identify what data is relevant
  (JBI, 2015)

The JBI guidelines highlight that any deviations of the scoping review from the protocol must be addressed and explained. Within the protocol, there are deviations from the scoping review, specifically, the title and research question (see Appendix A). The initial question that informed the protocol was: Can the Canadian Government get involved with/or participate in the full lifecycle of pharmaceutical innovation (chemical identification through to market launch)? Although this question is different than the final central research question, the purpose of the review, as indicated in the protocol, is to draw in all relevant literature and/or information on publicly funded research models pertaining to the research and development (R&D) and public production of pharmaceuticals. The title of the protocol was "Government Funded R&D of Pharmaceuticals". The title was updated to reflect the changes made to the final research question. As evidenced, the protocol serves as a useful reference tool, contributing to the audit-trail by explaining the rationale behind discrepancies, changes, or choices.

The inclusion criteria were developed within the protocol, prior to the undertaking of the scoping review. As familiarity with the literature was gained and more restricted inclusion criteria were developed, these criteria were amended to reflect this change, however, the initial search criteria, which remain unchanged, are listed below. Please see section 2.1.3 Search Strategy for the final criteria.

Sources will be considered if they address public funding for the R&D of pharmaceuticals, and or PPP approaches to R&D. To draw in greater literature, the search will not be limited to one country, however, only English-based literature will be included. To reflect a time constraint, no study published prior to January 1st, 2000 and no study published after January 31st, 2017 will be included. The timeframe was selected following an initial scan of the literature. The reviewing process consisted of one researcher, which is why studies prior to 2000 were not included – this was done to limit the amount of literature retrieved. No studies were accepted after January 31s, 2017, as this was the latest date possible to include literature prior to the analysis, which required all data to be collected into one set.

The following criteria devised assisted in basing decisions about the sources to be included in an attempt to limit literature that is non-relevant:

- initial search for relevant keywords
- include literature from pharmaceutical industry websites
- include grey literature
- include literature from academic databases
- include government data
- hand-search in the reference list of all included data

The following sources will be included in the scoping review: primary studies, websites

and online databases for grey literature from January 1st, 2000 up to January 31st, 2017 (World Health Organization, Government of Canada).

A brief scan of the literature aided in developing the following keywords:

- pharmaceutical industry
- pharmaceutical R&D
- public production
- state-owned
- pharmaceutical innovation
- public R&D

Inclusion Criteria

Any articles that referenced the full lifecycle of pharmaceutical innovation, public production of medicine, or public R&D and medicine production were of interest.

Exclusion Criteria

Articles were excluded for the following reasons: the focus was placed upon regulatory framework and regulation, controlling the production processes of pharmaceutical companies, selling off state-owned pharmaceutical assets, and government subsidies for drug development. Further, articles that focused on waning innovation and investment in R&D were excluded as the focus bore little resemblance to the central research question.

2.2.3 Search Strategy

The protocol and inclusion criteria were followed by the development of a search strategy (see Appendix B). This step served to aid in the selection of which databases to utilize and which keyterms to employ. Both the protocol and search strategy were reviewed by a committee member, LB, due to her considerable knowledge on how to conduct scoping reviews.

The search strategy is an intrinsic part of the scoping review process; hand-searching, reviewing, and citation tracking are part of the article gathering phase (Arksey & O'Malley, 2005). Without a clear strategy, the research itself may be questioned. This integral part of the thesis is where the initial Google searches were conducted, keywords were further developed and tested, and databases were selected. Through this approach due diligence may be effectively demonstrated and the strategy is demonstrative of the steps taken to draw in and collect the literature selected for this thesis.

The following databases were selected: Ovid MedLine, OECD iLibrary, Ovid EMBASE, EconLit, PubMed, and Google Scholar. Due to the nature of the topic, the databases included focused on the sciences, healthcare, economics, and policy to broaden the scope of potential data to be retrieved. Two librarians were consulted on which databases were likely to yield accurate results, L.B. and O.S. Ovid Medline is a premier database that contains biomedical journals that are published internationally. It was selected due to the focus on allied health and pre-clinical sciences. Although there is significant overlap between PubMed and Medline, both of databases were chosen because searches in PubMed could pick up articles that are deposited in PubMed Central. Further, some of these articles may be from journals that are not indexed by Medline. Similar to Ovid Medline, Ovid Embase is a biomedical database, however, it is also referenced as a pharmacological database. This database was chosen because of the focus on drug-related subjects. The OECD iLibrary contains data on the OECD, which was selected as the data has proven useful with regard to drug costs. EconLit was selected due to the economic aspect of this thesis. Although there is no economic approach, drug prices are frequently mentioned in papers related to the field of economics. Google Scholar was used during the preliminary literature review. It was selected due to the relative ease of conducting searches and broad reach. Given

that the essence of a scoping review is to be as comprehensive as possible, and that the nature of the research topic may lead to an overlap in sources within each database, databases that overlapped were searched to ensure that all measures possible were taken to effectively conduct the scoping review (Arksey & O'Malley, 2005). Further, a search on the Cochrane Database of Systematic Review was conducted to confirm whether there were any reviews related to publicly funded R&D of pharmaceuticals. In the case that a review was found, the studies identified would have been reviewed to determine whether they could be added to the dataset.

Additional keywords were added during the construction of the search strategy to enhance the search; drug industry and national infrastructure. Two librarians were consulted on keyword selection to aid in increasing the return of relevant literature. The table below displays the databases and keywords used in the search strategy.

Table 1. Search Strategy

Database	**Keywords**
Medline	((((state owned or national*) and pharmaceutical) or pharmaceutical industry) and R&D)
Medline	**1)** exp Drug Industry/ **2** pharmaceutical*.mp. **3**((drug or pharma*) adj2 (industr* or develop*)).mp. **4)** or/1-3 **5**state owne*.mp. **6)** 4 and 5 **7)** exp Drug Industry/ **8)** Technology, Pharmaceutical/ **9)** 2 or 3 or 7 or 8 **10)** national.mp. **11)** 5 or 10 **12)** 9 and 11 **13)** 5 and 9 **14)** 1 and 5
Medline	((national infrastructure and state-owned and pharmaceutical R&D) not reimbursement)
Medline	(national infrastructure and state-owned and pharmaceutical R&D)
Medline	"state-owned" or national*) and pharmaceutical R&D
Medline	"state-owned" and "pharmaceutical industry"

EconLit	((((state owned or national*) and pharmaceutical) or pharmaceutical industry) and R&D)
EconLit	"drug industry" and "state owned" or "national"
EconLit	"state-owned" and "pharmaceutical industry"
EconLit	"state-owned" or national and "pharmaceutical R&D"
OECDI	((((state owned or national*) and pharmaceutical) or pharmaceutical industry) and R&D)
OECDI	(((national infrastructure or state infrastructure) and state-owned and pharmaceutical R&D) or pharmaceutical development)
OECDI	"state-owned" and "pharmaceutical industry"
OECDI	state owne* and drug industry*
OECDI	national* and drug industry* or pharmaceutical industry*
OECDI	"national*" and "pharmaceutical R*D"
OECDI	"national*" and "pharmaceutical industry"
OECDI	"national*" and "pharmaceutical "
OECDI	"state-owned" and pharmaceutical industry" not reimbursement
OECDI	"state-owned and drug discovery"
EMBASE	**1)** exp Drug Industry/ **2** pharmaceutical*.mp. **3**((drug or pharma*) adj2 (industr* or develop*)).mp. **4)** or/1-3 **5)** state owne*.mp. **6)** 4 and 5 (27) **7)** Technology, Pharmaceutical/ **8)** national.mp. **9)** 2 or 3 or 1 or 7 **10)** 5 or 8 **11)** 7 and 10 **12)** 5 and 9
EMBASE	((national infrastructure and state-owned and pharmaceutical R&D) not reimbursement)
EMBASE	(national infrastructure and state-owned and pharmaceutical R&D)
EMBASE	(("state-owned" or national*) and pharmaceutical R&D
EMBASE	("state-owned" and "pharmaceutical industry")
EMBASE	(state owned and pharmaceutical industry and R&D

Google Scholar	(state owned and pharmaceutical industry and R&D) (drug industry and public production)

As the intent was to draw in all relevant literature pertaining to models of public production of pharmaceutical R&D, articles were included if there was a mention of the public production of pharmaceuticals or state-owned enterprise related to pharmaceuticals. Articles pulled in by the search that mentioned public private partnerships were included, as an aspect of drug development within these partnerships is considered part of public drug development. Further, articles that mentioned a strategy for public production of medicines, outlined a methodology for the public production, discussed political limitations of public production of medicine, and claimed to identify the factors that may have led to a government choosing to develop and distribute medicine without the private sector were included. Literature that focused solely on state-owned enterprise was included as this contributes to discussion surrounding public efficiency.

Articles that were not in English were excluded, in addition to the following areas of study: regulatory framework and regulation of the pharmaceutical sector, as this would have drawn in literature that would not aid in answering the research question, albeit relevant to the preliminary literature review. Literature that focused solely on regulation did not incorporate the public production of medicine, thus, it would have served little purpose if included in the dataset. Further, articles were removed upon reviewing an abstract that did not relate to the central research question. Articles that focused on government subsidies or on the local production of medicine that did not mentioning state-owned enterprise were not included, as these, too, bore little relevance to answering the research question.

2.2.4 Study Selection

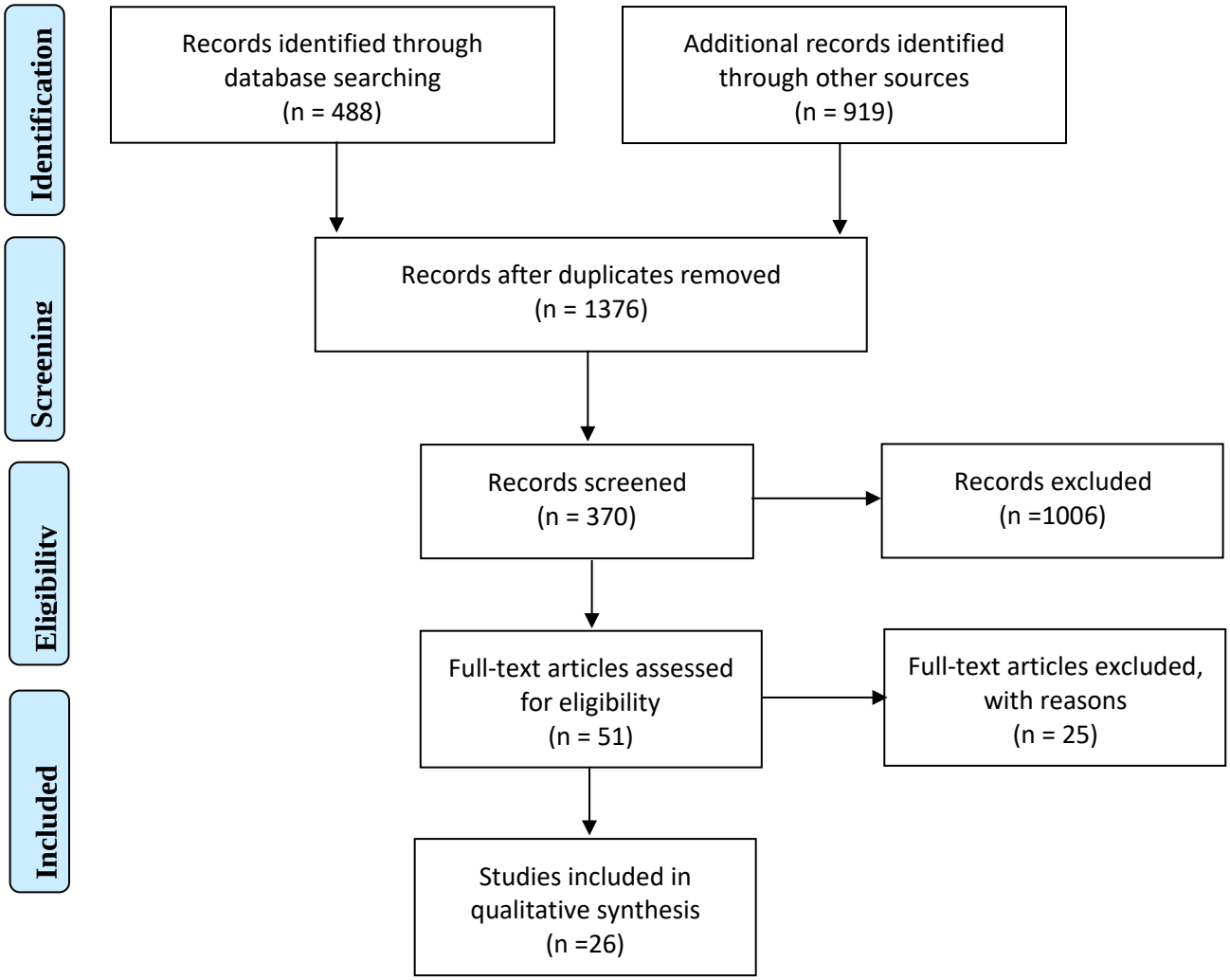
The following section details the process concerning which articles to include in the dataset. A Prisma diagram is provided at the end of this section (Moher et al., 2009).

Each article title was screened to determine whether it met the inclusion or exclusion criteria. It was then categorized as accepted, rejected or uncertain. Titles that mentioned the public production of medicine and production costs were accepted. Titles that mentioned economies of scale, regulation, government subsidies, outsourcing industry and pharmaceutical innovation were rejected. Titles that mentioned pharmaceutical prices and access, the role of the government, politics of patents, and pharmaceutical R&D were uncertain. Duplicates and media were removed.

Following the title review, the articles that were categorized as accepted or uncertain underwent an abstract review. Articles with an abstract that focused on the public production of medicine, government involvement in pharmaceutical R&D or state-owned enterprise related to pharmaceutical R&D were included in the dataset. Articles that focused on public private partnerships concerning pharmaceutical R&D and pharmaceutical production costs were categorized as uncertain. Articles that were included in the dataset underwent a reference list review.

Following the reference review, accepted and uncertain articles underwent the previously performed abstract review. Successful articles were included in the dataset. The Prisma diagram on the following page provides a visual representation of the reviewing process, displaying the number of records identified, included and excluded (Moher et al., 2009).

Figure 1. Prisma Flow Diagram



2.2.5 Charting the Results

Following the selection of the dataset, the included articles were placed into the table, *Data Extracts*. Within the table, each article was provided a number for quick reference during the thematic analysis. The table below consists of descriptive content of the 26 selected studies, with three columns; one that provides the source and reference; a second that displays data extracts selected for the thematic analysis; and a third that displays the codes generated for the thematic analysis. The table was created to facilitate the thematic analysis, as organizing the

dataset accordingly provided an organized approached when referring back to articles during the analysis.

Table 2. Data Extracts

Code(s)	Data extract(s)	Study
1. Public Private Collaboration 2. Innovative drugs	*NIH, academic medical centres and private industry have longstanding history collaborating together *Decreasing budget for R&D in both private and public sector make collaborations paramount *Decline in innovative drugs reaching those who need most	1. Leveraging Public Private Partnerships to Innovate Under Challenging Budget Times (Portilla & Rohrbaugh, 2014)
1. New drugs 2. Commercial sponsors 3. Shareholder value 4. Public health	*Publicly sponsored trials are conducted by cooperative groups sponsored by National Cancer Institute *Commercially sponsored trials are necessary to create new knowledge, improve care of patients, and develop new drugs and devices *Commercial sponsors launch trials that result in drug approval, label extension, expansion of market share and increase shareholder value *Publicly sponsored trials seek to optimize therapy for a particular disease, create new knowledge, and improve public health and can result in label extension and initial drug approval	2. Publicly Funded Clinical Trials and the Future of Cancer Care (Schilsky, 2013)
1. Innovative medicine 2. Public private partnership 3. New medicine 4. Drug discovery	*Innovated Medicine Initiative is a large-scale public-private partnership between EC & EFPIA *IMI aims to boost development of new medicine across Europe by implementing new collaborative endeavours between large pharmaceutical companies and other key actors in health-care ecosystem (academic institutions, small and medium enterprises, patients, regulatory authorities) *Strong focus on drug discovery as an ideal arena where the PPP concept of pre-competitive collaboration can rapidly deliver results *Focuses on providing proof-of-concept evidence for the efficiency of this new model of collaboration.	3. The Innovative Medicines Initiative: a Public Private Partnership Model to Foster Drug Discovery (Vaudano, 2013)
1. Manufacturing cost	*Present direct manufacturing costs and price calculations of individual antiretroviral drugs, enabling those responsible for their procurement to have a better understanding of cost structure of their production and to indicate the prices at which these antiretroviral drugs could be offered in developing country markets	4. Examining the production costs of antiretroviral drugs (Pinheiro et al., 2006)

1. Transnational cooperation	*TRANSVAC... initiated the development of a roadmap through a process of stakeholder consultation *..need for transnational cooperation and the opportunities that could be generated by such efforts *..can be achieve via the establishment of a EVRI *EVRI will support cooperation between existing R&D organizations from public and private sector and other networks throughout Europe	5. Roadmap for the establishment of a European vaccine R&D infrastructure (Leroy et al., 2014)
1. Affordable medicine 2. Pharmaceutical subsidies	*Government of Iran…has devoted considerable resources on national health, including the pharmaceutical sector *…health indicators have improved substantially over the past two decades and the availability and affordability of medicines have also been greatly improved *..order to full MOH mission in providing access to a sufficient quantity of safe, effective, and high quality medicines that are affordable for all…adopted a full generic based medicine system and local production of medicines and vaccines has become one of the main goals of the national drug policy *..investment, mainly due to lack of R&D activities and unanimous subsidies, has not been fruitful for Iran's health system *Iran's drug market has experienced a sharp growth – the market has increased annually	6. Iran Pharmaceutical Market (Cheraghali, 2006)
1. State-owned enterprise	* factors influence a Chinese state-owned enterprise's choice among alternative strategies for acquiring complementary assets * Hypotheses derived from transaction cost, resource dependency, and organizational capabilities perspectives were tested in a sample of Chinese state-owned pharmaceutical firms.	7. COMPETITION, CAPABILITIES, AND THE MAKE, BUY, OR ALLY DECISIONS OF CHINESE STATE-OWNED FIRMS (White, 2000)
1. Equitable access	* government of Iran has spent considerable amount of resources on health care services and provided a fairly equitable access for all Iranian to the health care system. health care services and provided a fairly equitable access for all Iranian to the health care system * in past three decades Iran health sector has achieved considerable success in its goals and this has substantially improved health care system indicators including life expectancy, child-mother mortality rate and access to medicines. *Ministry of Health and Medical Education (MOH) is the main policy maker and stewardship of the health care system	8. Trends in Iran Pharmaceutical Market (Cheraghali, 2017)

1. Pharmaceutical industry growth	*The pharmaceutical industry is an integral part of high technology industry. Over the past decade, the average growth of sales revenue of China's pharmaceutical industry has been the fastest among various hi-tech industries *..this paper discovers that the location distribution of China's pharmaceutical industry has evolved from the medium concentration to a dispersed state * According to the results, there are 7 regions that have brought about growth due to industry structure advantage, 6 regions that have realized growth due to competitive edge, and 5 regions that have garnered growth due to both.	9. Regional growth of pharmaceutical industry in China (Zhaohui et al., 2014)
1. Pharmaceutical market trend analysis 2. Domestic production of medicine	*Pharmaceutical market trend analysis remains one of the most useful instruments to evaluate the pharmaceutical systems efficiency. *An increase in imports of medicines, and a simultaneous decrease in domestic production prompted us to investigate the pharmaceutical expenditure structure. *On the other hand, analyzing statistics provides a suitable method to assess the outcomes of national pharmaceutical policies and regulations.	10. Trend analysis of the pharmaceutical market in Iran; 1997–2010; policy implications for developing countries (Kebriaeezadeh et al., 2013)
1. Public production of antiretroviral medicine 2. The state guaranteeing access to life-saving medicine 3. Government intervention in the pharmaceutical market	*This article examines Brazil's experience with the public production of anti- retroviral drugs (ARVs) and highlights the important role of the state in guaranteeing access to life-saving medicines and fulfilling human rights commitments. *The key to understanding the government's successful intervention in the pharmaceutical market and provision of treatment rests on the synergistic, albeit political, relationship between reform-minded public servants and civil society activists.	11. Public Production of Anti-Retroviral Medicines in Brazil, 1990–2007 (Flynn, 2008)
1. Tripartite partnerships	*The formation of tripartite partnerships among donors, AIDS officials, and nongovernmental organizations has allowed Brazil to avoid foreign aid dependency, while generating ongoing incentives for influential AIDS officials to incessantly pressure Congress for additional funding. *Given the heightened international media attention, concern about Brazil's reputation has contributed to a high level of political commitment. By contrast, the United States' more isolationist relationship with the international community, its focus on leading the global financing of AIDS efforts, and the absence of tripartite partnerships have prevented political	12. How Brazil Outpaced the United States When It Came to AIDS: The Politics of Civic Infiltration, Reputation, and Strategic Internationalization (Gómez, 2011)

	leaders from adequately responding to the ongoing urban AIDS crisis.	
1. Governmental purchasing power 2. Public laboratories 3. Domestic production and research and development 4. Large-scale production of essential medicine 5. Public private partnerships	*This article examines the use of governmental purchasing power and public laboratories to stimulate domestic production and research and development (R&D) activities in the Brazilian pharmaceutical industry. Three *Three main areas in which public laboratories can play an important role are identified: (1) large-scale production of essential medications; (2) production of strategic drugs to reduce the trade deficit in the health sector; and (3) in-house research efforts and stimulation of R&D in the private sector through public-private partnerships (PPPs) *In order for the current governmental strategy to promote industrial growth, there should be a division of tasks among public laboratories within a long-term framework, based on a stable set of priorities from the MOH.	13. The production and R&D structure of the Brazilian pharmaceutical industry: The role of public procurement and public drug production (Junior, 2012)
1. Innovating capability	*As a high-tech industry, the pharmaceutical industry in China is uncompetitive and is difficult to go further. By evaluating the innovating capability of different pharmaceutical companies, this paper attempts to find the key factors affecting the innovating ability and provides suggestions for pharmaceutical companies to improve the innovative capability.	14. Analysis on innovation capability and influencing factors in Chinese pharmaceutical industry (Song & Zhang, 2014)
1. Foreign pharmaceutical firms 2. World Trade Organization 3. Intellectual property enforcement 4. Good manufacturing practice	*China's pharmaceutical industry is undergoing tremendous positive transformations, spurred both by the government's economic and political policies and the increasing investment/ involvement by foreign pharma firms in China. *This paper will describe the three major forces driving the changes: economic, regulatory and China's entrance into the World Trade Organization. These *These changes will contribute to China's emergence in the next decade as a major force in the international pharmaceutical arena, but the speed with which this will happen is contingent on overcoming the still-existing problems of intellectual property enforcement, regulatory capabilities, innovative skills and meeting EU/US good manufacturing practice quality and compliance requirements	15. Outlook on China's pharma development—2004 (Capie, 2004)
1. Government intervention 2. Public production 3. Access to medicine	*The decision to grant the series of government use licenses was taken despite much domestic and international controversy *… there were further indications of a weakening respect for patents, as the Thai Government	16. Government Used Licenses in Thailand: The power of evidence, civil movement and political leadership

	announced decisions to issue compulsory licenses for several patended products	(Wibulpolprasert et al., 2011)
1. Local production of pharmaceuticals 2. Access to needed medicine 3. Active ingredients 4. Domestic production of medicine	*Local production of pharmaceuticals in developing countries may be seen as helping to stimulate industrial policy and/or as stimulating pharmaceutical "access" to needed medicines. However, if a developing country with manufacturing facilities is able to finish off bulk active ingredients sourced from developed or other countries at high costs, such manufacture may have no impact whatever on patient access to needed medicines. *In brief, in many parts of the world, producing medicines domestically makes little economic sense.	17. Local Production of Pharmaceuticals: Industrial Policy and Access to Medicines (Kaplan & Laing, 2005)
1. Government intervention in the pharmaceutical market 2. National pharmaceutical sector	*The Government of Seychelles considers health care a basic human right and that it should be available and accessible to the entire population. In order to ensure that this right is observed, Article 29 of the 1994 Constitution of the Republic of Seychelles allows for, among other things, that appropriate measures be taken to prevent, treat and control epidemic, endemic and other diseases *The present Seychelles National Medicine Policy was developed through a consultative process with all national pharmaceutical sector stakeholders and under the guidance of the Ministry of Health and Social Development. It	18. Seychelles National Medicine Policy ("Republic of Seychelles", 2009)
1. Local production of medicine 2. Drug production	*with particular reference to the promotion of capacity-building for local production in developing countries. *The objective of production-related industrial policy is typically to establish globally competitive and profitable industries. This is likely to generate indirect public health benefits by generally improving the local standard of living. *Efficient production of medicines often requires achieving economies of scale, and this may be difficult in smaller countries and markets.	19. Trends in Local Production of Medicines and Related Technology Transfer (Abbott, 2011)
1. Generic 2. State-owned 3. Domestic production 4. Low-cost medicine	*These programs, entitled Generic Scheme, sometimes also called the Generic Concept, formed the foundation of the new pharmaceutical system in the country. *The responsibility for the nationwide distribution of pharmaceutical products at wholesale was passed on to six state-owned companies. *According to this new definition, the government was obliged to back domestic production of pharmaceutical products and to	20.Pharmaceuticals in Iran: An Overview

	encourage the development of this sector. *It was also committed to make sufficient quantities of low-cost medicines available to the entire nation (i.e., in the most remote and deprived provinces).	(Basmenji, 2004)
1. World Trade Organization 2. Lower pharmaceutical prices 3. Cost-effective medicines	*THIS article examines the relationship between Brazil's obligations as a member of the World Trade Organisation (WTO) and its drug pricing strategy for HIV/AIDS drugs. *Brazil's strategy has been controversial though successful, insofar as they have compelled the research-based pharmaceutical industry to lower pharmaceutical prices *This paper examines why the Brazilian strategy was effective and considers the wider implications for other developing countries dealing with the HIV/AIDS crisis, pharmaceutical patent obligations and the need to provide cost-effective medicines for their populations.	21. AIDS Policy and Pharmaceutical Patents: Brazil's Strategy to Safeguard Public Health (Cohen & Lybecker, 2005)
1. Government intervention 2. Generic production	* Thailand's military-backed government on 29 November issued a compulsory licence for Merck's HIV/AIDS drug efavirenz, in an attempt to cut growing healthcare costs by encouraging the production and import of generic versions of the patented medicine * Both steps will mean increased downward pressure on drug prices, according to public health advocates, who praised the government's decision	22. Thailand Issues Compulsory Licence For Patented AIDS Drug ("Thailand Issues", 2006)
1. Collaboration 2. Local production of medicine 3. Access to medicine	* The aim of this work was to develop a framework that could bring together and guide policy-makers and others from all these relevant fields. The framework presented here provides an entry point for supporting the local production of medicines, vaccines and diagnostics in a manner that should improve access to those medical products maximizing the potential to improve public health.	23. Local Production for Access to Medical Products: Developing a Framework to Improve Public Health (WHO, 2011)
1. Government intervention 2. Access to medicine	* The literature review showed how past challenges forced changes to pharmaceutical policy in Iran. It also showed that the Iranian 'Generic Scheme'(started in 1980) was very successful in improving accessibility to pharmaceuticals, particularly in the 1980s. However,	24. Pharmaceutical policy and market in Iran: past experiences and future challenges (Davaria et al., 2011)
1. National industry 2. Government intervention	*The Iranian national drug policy is based on generic medicines, local production of generic drugs and vaccines, price control, a national industry, herbal medicine, self-sufficiency in vaccine production, licensing for locally produced and imported pharmaceutical and biological products and active good manufacturing practice (GMP) inspection.	25. Evaluation of availability, accessibility and prescribing pattern of medicines in the Islamic Republic of Iran

	*After 1979, a full generic-based drug system was adopted, with development of a national drug policy	(Cheraghali et al., 2004)
1. Public laboratory 2. Government intervention 3. Public production of medicine	*The Brazilian experience in producing HIV/AIDS drugs is based on the lawful copying of medicines patented abroad, on a health policy of universal access to antiretrovirals (ARV), and on technological learning, especially in public-sector laboratories through reverse engineering. *In 1997 the Far Manguinhos state-owned pharmaceutical laboratory was mobilized by the Brazilian health ministry to launch production of copies of medicinal drugs used to treat HIV/AIDS	26. Patents, Innovation and Public Health: Brazilian Public-Sector Laboratories' Experience in Copying AIDS Drugs (Cassier & Correa, 2003)

2.3 METHODS RELATED TO THEMATIC ANALYSIS

A thematic analysis was performed on the dataset collected for the scoping review with NVivo 12 qualitative data analysis software (QSR International, 2017). The type of analysis was selected to identify, analyze, and report on the patterns within the dataset. A step by step guide by Braun and Clarke (2006) was adhered to throughout the analysis. This recursive process is comprised of six phases that serves to familiarize the researcher with the data and in turn, generate codes, themes, and an original analysis of the dataset (Braun & Clarke, 2006). Braun and Clarke (2006) argue that the analytic method "offers an accessible and theoretically flexible approach to analyzing qualitative data and that it is a foundational method for qualitative analysis" (p.1). While other scholars, such as Ryan and Bernard (2000) argue that thematic analysis is performed within major analytic traditions, Braun and Clarke (2006) argue "thematic analysis should be considered a method in its own right" (p.2). By way of interpretation, the development of themes goes beyond semantic content as underlying ideas, assumptions, and ideologies are formed. It is through this approach that aspects related to the research question are captured (Braun & Clarke, 2006). A primary aspect of thematic analysis is the development of themes that are identified following a full review of the dataset. After revisions and refinement,

the final themes considered most relevant to the research question are upheld as the primary data to be analyzed. The following section provides detail on the steps taken within each phase, which eventually led to the development of the themes detected for analysis.

2.3.1 Collating, Summarizing, and Reporting the Results

Due to overlap, the sixth and final step of the scoping review was performed in the thematic analysis.

Phase I of the thematic analysis requires the researcher to familiarize themselves with the literature by completing a full article review - in essence, read each article in the dataset. This was completed during the reviewing process.

Phase II consisted of generating codes and selecting excerpts (data extracts) from the dataset, which were then placed into Table 2. Data Extracts. Following the full review of an article, excerpts (data extracts) that were considered representative of an article, were selected and placed into the table. As mentioned previously, each article was assigned a number for identification purposes, with separate sections designated for extracts and codes. Once a data extract(s) was created for each article from the dataset, codes were developed to capture prevalent themes reflected in the data extract(s). For example, an article that mentioned state-owned facilities that produced medicine led to the creation of the code, public production. In another example, if an article focused on collaboration between the private and public sectors, the code Public Private Partnership was employed. The same code could appear in different articles within the dataset. This was the initial generation of codes and the refinement would occur in later phases.

During Phase III the generated codes were organized by order of mention to provide an idea of how frequently certain codes appeared across the dataset. The codes were then

categorized according to potential themes, which were developed upon collating all of the generated codes into the document, *Themes. 1.0* (see Appendix C). For example, the codes, public production of medicine and public laboratory were categorized within the theme, National Production of Medicine. Following this step, the initial thematic map, *Thematic Map 1.0* (see Appendix D) was created as an accompanying visual of the initial codes and themes developed. According to Braun and Clarke (2006), "it is helpful at this phase to use visual representations to help you sort the different codes into themes" (p.13).

Phase IV consisted of refining the devised themes, ensuring they were relevant to the coded extracts from Phase II and Phase III, as well as the entire dataset. During this phase, it became evident that some themes did not belong, some could collapse into one another, and others may need to be broken down further. Following the guide to conducting a thematic analysis by Braun and Clarke (2006), it is suggested that Phase IV is segmented in two levels (steps), which is explained below.

Level One: The validity of the themes and codes were analyzed along with the data extracts. During this process, themes that did not appear relate to the extract or form a pattern were removed, whereas themes that were closely related to one another were merged. This process was also performed on the initial set of codes. This was done to ensure validity, as the initial themes devised were done so in a broad manner. The revised codes and themes were then collated into *Themes 2.0* (see Appendix E). Following this process, the initial thematic map was revised to reflect the recent changes to the themes and codes, which can be viewed in the document, *Thematic Map 2.0* (see Appendix F). Within the revised map, connections were drawn between themes and codes.

Level Two: Upon the completion of Level One, the validity of individual themes was analyzed along with the entire dataset. This differs from the prior level considerably, as themes and codes are revised according to the entire dataset as opposed to excerpts. During this process, similar codes were collapsed under similar themes. Codes that were mentioned infrequently, rarely, and/or exhibited little relevance to the research question were eliminated. Following this process, it was ascertained that the remaining themes did indeed work in relation to the dataset and that the updated candidate map accurately reflected the meanings evident in the dataset as a whole. The remaining themes were placed in a new document, *Themes 3.0* (see Appendix G) and the revised and final updated map, *Thematic Map 3.0* (see Appendix H) was created, reflecting the final themes and identified sub-theme.

Phase V involved defining and naming the final themes, ensuring that they relate to the overall story the analysis provides. During this process, the remaining themes were defined according to their make-up (codes and extracts) and named accordingly to reflect their pattern or meaning.

Phase VI, the final stage, consisted of conducting an analysis on the final themes. This analysis is presented in the section 3.1.2. Thematic Analysis. Further discussion of the final themes can be found in the discussion section.

2.4 ETHICAL CONSIDERATIONS

The Hamilton Integrated Research Ethics Board was contacted to ensure that no ethics approval was required.

CHAPTER 3: FINDINGS

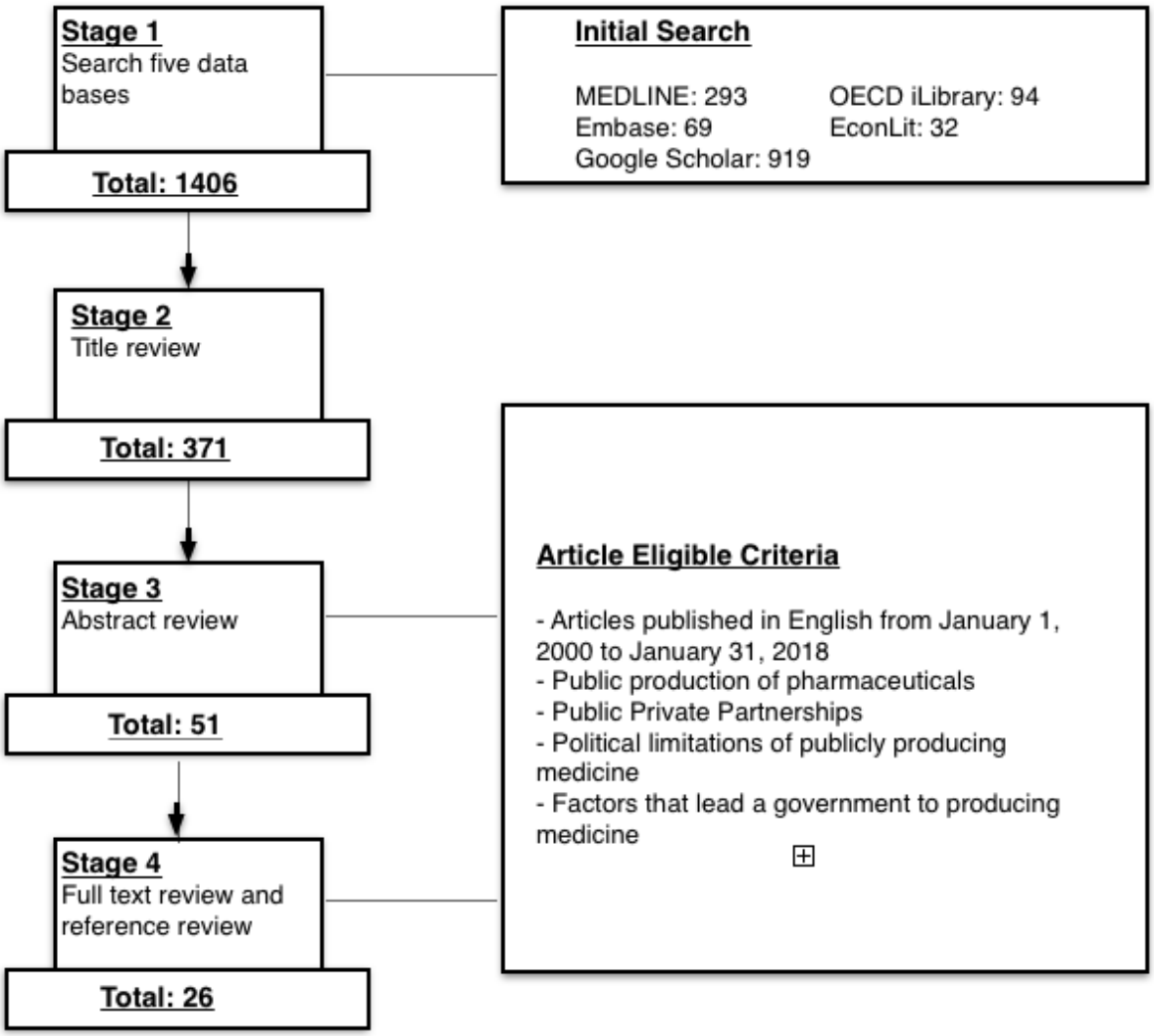
3.1.1 Preliminary Review

The preliminary literature review served to provide an overview of some of the issues facing the Canadian pharmaceutical sector, and the healthcare inequity associated with poor drug coverage and highly priced medicine. Within the review, it was revealed that a significant number of Canadians forego basic necessities in order to purchase medicine, and an even greater number of Canadians do not fill prescriptions or adhere to prescribed medicine due to cost (Law et al., 2018; Barnes & Anderson, 2015; Morgan et al., 2015). The identified healthcare inequity has spurred a collaborative approach to address poor drug coverage through the implementing implementation of national drug program, Pharmacare 2020 (Pharmacare 2020, 2018). The federal government recently announced plans to determine program viability by way of an Advisory Council, a non-partisan collective of individuals (Morneau, 2018).

3.1.2 Scoping Review

In total, there were 1406 results from the search strategy. After the review process, 26 articles were included in the dataset for the scoping review. The flowchart on the following page provides a visual representation of the results (Di Rezze et al., 2015).

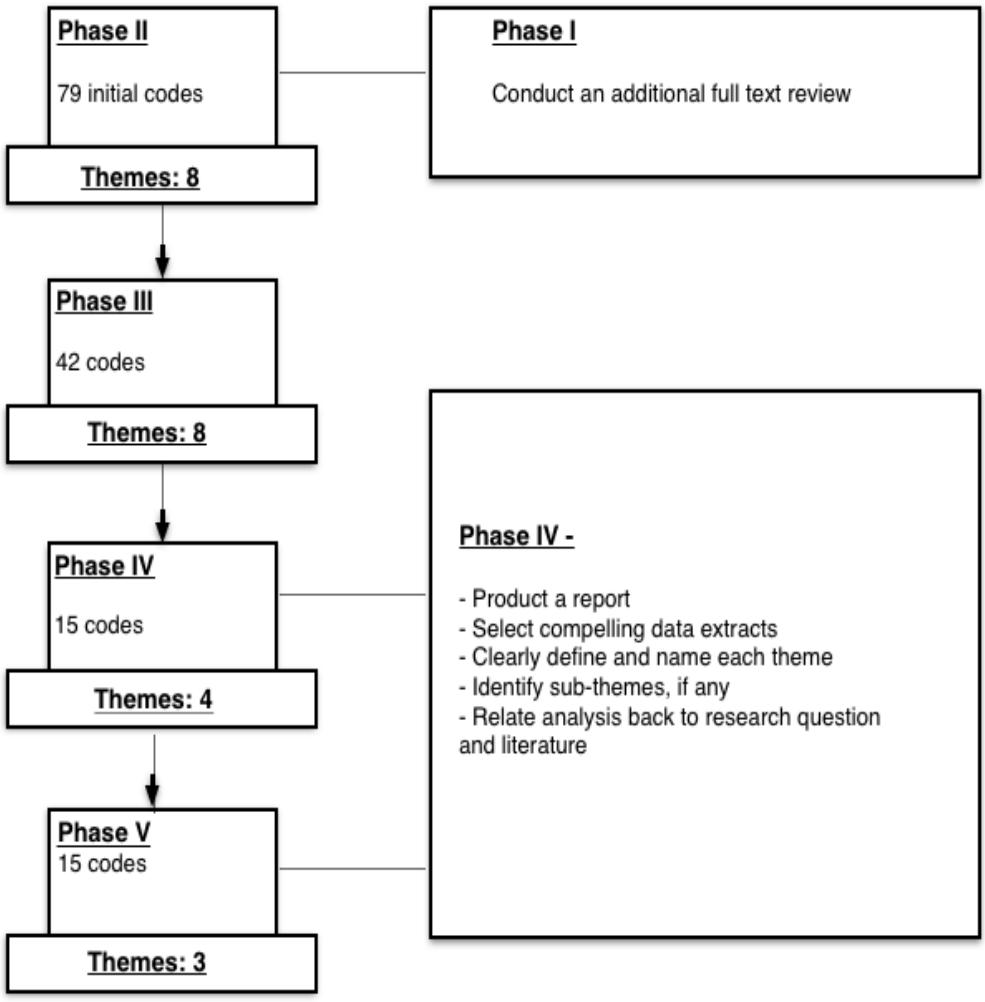
Figure 2. Flowchart of search results



3.1.3. Thematic Analysis

Following Phase V of the analysis, three major themes emerged: Local Production, Private Public Sector, National Production. The flowchart on the following page provides a visual representation of the six phases of the analysis (Di Rezze et a., 2015).

Figure 3. Flowchart depicting phases i through iv



The table on the following page contains the themes detected within the dataset and the key findings; it is an amended version of Table 1. Within each row, each article features two columns: themes and key findings. There is overlap among themes, which is why certain articles may have more than one theme.

Table 3. Key findings and themes

Theme(s)	**Key Findings(s)**	**Study**
Public Private Sector	Focus on the pre-competitive sphere and the public sector's role as a contributor to research Waning investment requires greater collaboration between the public and private sectors	1. Leveraging Public Private Partnerships to Innovate Under Challenging Budget Times (Portilla & Rohrbaugh, 2014)
Public Private Sector	Much of drug research is conducted by the public sector, whereas drug development is typically conducted by the private sector The public sector typically enhances already existing drugs, whereas the private sector typically innovates and develops novel medicine	2. Publicly Funded Clinical Trials and the Future of Cancer Care (Schilsky, 2013)
Public Private Sector	Waning innovation requires novel collaboration efforts between the public and private sector	3. The Innovative Medicines Initiative: a Public Private Partnership Model to Foster Drug Discovery (Vaudano, 2013)
National Production Local Production	The cost of API development may inhibit state or local efforts to produce ARV treatment for HIV/AIDS API costs are influenced by multiple factors, such as technology, intellectual property, novel development, and patent infringement	4. Examining the production costs of antiretroviral drugs (Pinheiro et al., 2006)
Public Private Sector	A pan-European infrastructure will contribute to a knowledge base that can be used to address public health needs with regard to vaccination efforts	5. Roadmap for the establishment of a European vaccine R&D infrastructure (Leroy et al., 2014)
National Production	Following the nationalization of the pharmaceutical sector, health indicators improved substantially, however, the Iranian Government must now focus on upgrading the sector to maintain demand and to innovate medicine	6. Iran Pharmaceutical Market (Cheraghali, 2006)
Public Private Sector	Privatization of state owned enterprise may serve to enhance competitiveness and lead to innovative drug development	7. Competition, Capabilities, and the Make, Buy, or Ally Decisions of Chinese State-Owned Firms (White, 2000)
National Production Public Private Sector	The Iranian pharmaceutical sector is expected to expand as private companies have slowly emerged over the past decade	8. Trends in Iran Pharmaceutical Market (Cheraghali, 2017)

Local Production	Chinese pharmaceutical sector growth is dependent on the region and concentration of facilities. The higher the concentration, the greater likelihood for competition	9. Regional growth of pharmaceutical industry in China (Zhaohui et al., 2014)
National Production Local Production	Under the guise of the government, the pharmaceutical market has drastically grown, however, the output of innovative medicine is low The Iranian Government is recommended to establish an environment that is lucrative for foreign investment to offset issues with the national currency	10. Trend analysis of the pharmaceutical market in Iran; 1997–2010; policy implications for developing countries (Kebriaeezadeh et al., 2013)
National Production	Three key factors influenced Brazilian state involvement in drug development; a pre-existing infrastructure of public laboratories; strong civil society pressures; a pharmaceutical sector characterized by high prices	11. Public Production of Anti-Retroviral Medicines in Brazil, 1990–2007 (Flynn, 2008)
National Production	Recognized as a condition for motivation, albeit dependent on the country, international pressure to address a public health crisis is identified as a factor that contributed to a state response in Brazil during the HIV/AIDS crisis	12. How Brazil Outpaced the United States When It Came to AIDS: The Politics of Civic Infiltration, Reputation, and Strategic Internationalization (Gómez, 2011)
National Production	Public laboratories play an integral role with regard to public drug development, negotiations with the private pharmaceutical sector, and government capability to address public health crises	13. The production and R&D structure of the Brazilian pharmaceutical industry: The role of public procurement and public drug production (Junior, 2011)
Local Production National Production	State-owned pharmaceutical companies face an issue with innovation due to waning poor investment in R&D, however, an increase in R&D may serve to correct this	14. Analysis on innovation capability and influencing factors in Chinese pharmaceutical industry (Song & Zhang, 2014)
Public Private Sector	The influx of foreign firms and multinational pharmaceutical companies has promoted growth within the pharmaceutical sector	15. Outlook on China's pharma development—2004 (Capie, 2004)
National Production	A concept comprised of three factors, knowledge generated by research, civil society, and strong political leadership led to the government's decision to infringe on ARV patents	16. Government Used Licenses in Thailand: The power of evidence, civil movement and political leadership (Wibulpolprasert et al., 2011)
Local Production	Local production of medicines may serve to increase access to medicine, however, the cost associated with development, especially APIs, may render local production as unfeasible	17. Local Production of Pharmaceuticals: Industrial Policy and Access to Medicines (Kaplan & Laing, 2005)

Local Production National Production	An objective of the policy is to encourage ongoing small scale local production to supplement health facilities	18. Seychelles National Medicine Policy (“Republic of Seychelles”, 2009)
Local Production Public Private Sector	Local production may present challenges given the importation of APIs is required to produce medicine The majority of local production of medicine is undertaken by private enterprises	19. Trends in Local Production of Medicines and Related Technology Transfer (Abbott, 2011)
National Production	The Iranian Government must invest greater resources into the pharmaceutical sector to remain innovative and to meet projected challenges with drug development, such as issues with the necessity for certain APIs	20.Pharmaceuticals in Iran: An Overview (Basmenji, 2004)
National Production	In addition to unwavering civil society pressures, considerable investment into public laboratories equipped the Brazilian Government with greater leverage come negotiation of prices for certain ARVs	21. AIDS Policy and Pharmaceutical Patents: Brazil’s Strategy to Safeguard Public Health (Cohen & Lybecker, 2005)
National Production	The Thai Government issues a compulsory license to produce ARVs without consulting and or attempting negotiations with the pharmaceutical firm Merck	22. Thailand Issues Compulsory Licence for Patented AIDS Drug (“Thailand Issues”, 2006)
Local Production	Provided a systematic approach is taken, the local production of medicine may meet access needs, however, the links between local production and improved access may not develop as rapidly as needed	23. Local Production for Access to Medical Products: Developing a Framework to Improve Public Health (WHO, 2011)
National Production	Although nationalizing the pharmaceutical sector is hailed as a success with regard to increasing access to development for the Iranian population, waning investment and an outdated strategy are hampering sector efficiency	24. Pharmaceutical policy and market in Iran: past experiences and future challenges (Davaria et al., 2011)
National Production	Following the nationalization of the pharmaceutical sector, the notable increase to access has been generally positive for the Iranian population. However, affordable pricing under the Generic Scheme has contributed to an increase in drug usage, which is having an effect on the drug expenditure. Rational drug use must be emphasized to prevent over consumption	25. Evaluation of availability, accessibility and prescribing pattern of medicines in the Islamic Republic of Iran (Cheraghali et al., 2004)
National Production	State-owned public laboratories were used to copy ARVs and in turn, effectively reduce their market price, while serving to contribute to technological knowledge acquisition. This example can be used in Southern countries facing similar problems	26. Patents, Innovation and Public Health: Brazilian Public-Sector Laboratories’ Experience in Copying AIDS Drugs (Cassier & Correa, 2003)

3.1.4. Local Production

Across the 26 articles in the dataset, six had content concerning the local production of medicine (Zhaohui et al., 2014; Song & Zhang, 2014; Abbott, 2011; WHO, 2011; "Republic of Seychelles", 2009; Kaplan & Laing, 2005). Local Production (of medicine) is a central theme that assesses the feasibility of low to middle-income countries that are exploring the concept of producing medicine locally. Warren A. Kaplan and Richard Laing (2005) are frequently mentioned within further reports concerning the local production of medicine (Abbott, 2011; WHO, 2011). Their description of local production primarily focuses on multinational corporations operating within a country (Kaplan & Laing, 2005). Therefore, local production is not synonymous with national production. The extract below displays how the WHO defines local production of medicine.

> 1. Local subsidiary of, or joint venture with, a multinational pharmaceutical company selling branded medicines in local and regional markets (i.e. Glaxo Smith-Kline, Pfizer, etc.);
>
> 2. Generic manufacturer producing medicines for the local and global markets (i.e. Ranbaxy, Cipla, etc.);
>
> 3. Generic manufacturer producing medicines for predominantly the local market; and
>
> 4. Locally–owned, small-scale manufacturers serving a portion of the domestic market. (WHO, 2011, p. 3)

Local production contains the following nodes: active pharmaceutical ingredients (APIs), manufacturing costs, generic production, affordable medicine and access to medicine. Three of the articles concerning the local production of medicine were facilitated by a global organization, the World Health Organization (Abbott, 2011; WHO, 2011; Kaplan & Laing, 2005). Locally producing medicine is identified as a means for low to middle income countries to reduce the cost of their national drug expenditure, given the country possesses the necessary infrastructure

to develop pharmaceuticals. The most informative aspect that was revealed through the analysis is how the cost of APIs can greatly impact local efforts. If a country has the pre-existing infrastructure to research, develop and produce medicine, yet there is a need to import APIs, researchers Kaplan and Laing (2005) note this may likely increase the cost of domestic production to a point so high, that the entire measure would be rendered unfeasible (Abbott, 2011; WHO, 2011; Kaplan & Laing, 2005). This finding provides a glimpse into the realities faced by low to middle income countries seeking to address healthcare inequity through the local production of medicine. The costs associated with APIs alone have dissuaded other governments from producing medicine, as evidenced in the Seychelles (Seychelles National Medicine Policy, 2009). The first extract is indicative of how likely a government would need to import APIs, given the high concentration of API production is limited to three countries. The second extract sheds light on issues faced by developing countries that seek to develop medicine locally but require the importation of APIs. The dependency on foreign ingredients may have a significant impact on local efforts to produce medicine. The last extract depicts the reasoning behind conclusive points made by Kaplan & Laing (2005) in regard to local production and feasibility.

> Global API production has also been steadily concentrating in India, China and the Republic of Korea. Around 75% of API production from China and India is exported to the rest of the world. (WHO, 2011, p. 5)

> In Latin America, a substantial part of local demand is met by local generic producers. However, these producers are predominantly reliant on supplies of active pharmaceutical ingredients (APIs) from outside the region, and this dependency presents certain

> problems. Latin American national producers express concern over access to patented technologies required for the production of newer medicines. (Abbott, 2011, p. 2)

> Nonetheless, the report concluded that, given economies of scale and technological needs required for making medicines, local production did not make economic sense for most countries. The exceptions were countries with large local markets and capacity to produce active pharmaceutical ingredients (APIs). (Kaplan & Laing, 2005, p. 7)

The high pricing of pharmaceuticals is referenced as one of the main reasons a government may explore the local production of medicine (Abbott, 2011; WHO, 2011; "Ontario Minister of Health", 2009; Kaplan & Laing, 2005). Economies of scale are cited as an additional hurdle to overcome when developing medicine locally (Kaplan & Laing, 2005). Government involvement and capability is referred to frequently throughout the literature concerning local production (Abbott, 2011; WHO, 2011; "Ontario Minister of Health", 2009; Kaplan & Laing, 2005).

Successful public endeavours are referenced by the World Health Organization (WHO) in their analysis, such as Brazil's role in securing antiretrovirals (ARVs), a cocktail of drugs to treat HIV, during the AIDS crisis and Cuba's ability to develop and manufacture pharmaceuticals while facing sanctions (Abbot, 2011; WHO, 2011; Kaplan & Laing, 2005). Within these reports, however, it was revealed that the experts in the area of study believe that the public sector is unable to operate as efficiently as the private sector in low to middle income countries (Abbott, 2011; Kaplan & Laing, 2005). The extracts below lend credence to this reasoning.

Moreover, as a state-owned laboratory, Iquego has the social responsibility to deliver products to remote areas even when the operation is unprofitable. The laboratory owns only four old trucks to deliver drugs to inhospitable places in the North and Northeast regions. A trip to remote areas in the North region, within the Amazon rainforest, takes around one month. The truck has to be loaded into a ferry boat and the trip across the Solimoes River takes approximately seven days. On top of that, Iquego usually makes small lot deliveries to these remote areas and has to cope with the high maintenance cost of the trucks due to poor road conditions. Thus, Iquego's responsibilities as a public laboratory, in terms of following the MOH's priorities, delivering drugs under unprofitable conditions, and abiding by the public procurement law, greatly reduce its ability to compete with private firm". (Junior, 2012, p. 1073)

Local production may present disadvantages compared with importation when local manufacturing cannot be undertaken reasonably efficiently, and when local procurement costs exceed costs of importation for a significant period of time. With certain possible exceptions, governments are unlikely to support uneconomic production for sustained periods. (Abbott, 2011, p. 2)

The idea that local production of medicines should be encouraged in developing countries to provide increased access is attractive since we might expect that many of the costs involved will be lower than in developed countries. It is clear, however, that investments in local medicine production will be efficient only if pharmaceuticals can be produced more cheaply locally than they can be imported on the open market. This sets up the

> inherent tension between a health policy directed to the access problem of making available low cost and quality-assured medicines and an industrial (primarily private sector) policy of optimizing profits and growth by promoting a local industry whose products may be more expensive than those on the international market. (Kaplan & Laing, 2005, p. 1)

> It should be noted that most production of medicines is undertaken by private enterprises, and government policies with respect to promotion of local production of medicines are likely to be directed at encouraging private-sector activity. (WHO, 2011, p. 50)

The cost associated with local production, in addition to responsibility borne by the government, are cited among the reasons that may reduce public sector efficiency with regard to producing and/or manufacturing medicine locally.

3.1.5 Public Private Sector

Across the 26 articles, six focused solely on the public and private sectors (Leroy et al., 2014; Portilla & Rohrbaugh, 2014; Schilsky, 2013; Vaudano, 2013; Capie, 2004; White, 2000). The theme Public Private Sector is as a pivotal part of the discussion concerning state involvement in the production of pharmaceuticals because of the role each sector plays in pharmaceutical R&D. The public sector is comprised of government owned organizations that provide services for the public. Britannica defines the public sector as:

> A portion of the economy composed of all levels of government and government-controlled enterprises. It does not include private companies, voluntary organizations, and households. The general definition of the public sector includes government ownership or control rather than mere function and thereby includes, for example, the

exercise of public authority or the implementation of public policy. ("Public Sector", 2018)

Merriam-Webster (2018) defines the private sector as "the part of the economy that is not controlled or owned by the government (Merriam Webster, 2018). Public Private Sector contains the following nodes: public private partnerships (PPPs), transnational cooperation and public vs private. The discussion concerning both sectors implicates various stakeholders within the drug development process; government agencies; the global pharmaceutical industry; pharmaceutical manufacturers; health agencies; academic institutions; patient advocacy groups; and supranational organizations (Leroy et al., 2014; Portilla & Rohrbaugh, 2014; Schilsky, 2013; Vaudano, 2013; Capie, 2004; White, 2000).

Within the literature, there was frequent discussion of the benefits of pre-competitive models, which are known to "address issues around aggregating, accessing, and sharing data that are essential to innovation, but provide little competitive advantage" (Pistoia Alliance, 2018). The pre-competitive arena is open to the public sector given the sector's contribution is limited to research. However, the most lucrative component, production, is typically granted to the private sector (Schilsky, 2013; Vaudano, 2013). Although the work conducted by the public sector during the preliminary stages of drug development is recognized as integral within the literature, the private sector is positioned as the most viable option to produce pharmaceuticals, albeit with the support of the public sector (Portilla & Rohrbaugh, 2014; Schilsky, 2013; Vaudano, 2013; Correa, 2004). Six articles in the dataset that discuss public private collaboration and/or public sector efficiency assumed a favourable tone towards the private sector (Leroy et al., 2014; Portilla & Rohrbaugh, 2014; Schilsky, 2013; Vaudano, 2013; Capie, 2004; White, 2000).

Within these articles, there is frequent mention of dwindling resources for pharmaceutical R&D. In one article, Burrill and Company reported that several drug companies sought to cut R&D expenses (Portilla & Rohrbaugh, 2014). The findings demonstrate there is a collective understanding with regard to the need for collaboration as a means to continue developing novel medicine. The below extracts provide a glimpse into the various discussions concerning cost and the need for collaboration. It was not uncommon to come across this line of reasoning within the dataset.

> The National Institutes of Health (NIH), academic medical centers and industry have a long and productive history in collaborating together. Decreasing R&D budgets both the private and public sector have made the need for such collaborations paramount [critical?] to reduce the risk of [further?] declines in the number of innovative drugs reaching the market to address pressing public health needs. (Portilla & Rohrbaugh, 2014, p. 1)

> Many pharmaceutical companies are realising that a paradigm shift in the industry's research and development (R&D) strategy is the only way of reversing the currently ongoing negative trend. Novel strategies based on an integrated and collaborative approach are required, building on innovation and leveraging on the strengths and input of all stakeholders in the health system with the shared goal of delivering effective and sustainable healthcare solutions for society. (Vaudano, 2013, p. 1)

3.1.6 National Production

Across the 26 articles, it was found that 14 focused on aspects concerning the national production of medicine (Cheraghali, 2017; Kebriaeezadeh et al., 2013; Junior, 2012; Davari et al., 2011; Gomez, 2011; Wibulpolprasert et al., 2011; "Republic of Seychelles", 2009; Flynn, 2008; Cheraghali, 2006; Pinheiro et al., 2006; Cohen & Lybecker, 2005; Basmenji, 2004; Cheraghali et al., 2004; Cassier & Correa, 2003). National Production is a major theme that is closely related to the research question; it is underpinned by the production and distribution of pharmaceuticals under the auspices of a government entity. Similar to the public sector, National Production is comprised of government owned and operated enterprise (Cheraghali, 2006). The theme contains the following nodes: state-owned enterprise, public production of medicine, public sector efficiency and public laboratories.

Within the dataset highly priced medicine is frequently mentioned as a barrier to accessing medicine for a population and this is typically followed by discussion on increasing access to affordable and quality medicine (Davari et al., 2011; Gómez, 2011; Flynn, 2008; Cohen & Lybecker, 2005; Cheraghali et al., 2004). Although unaffordable medicine was not built into the search strategy, six articles focused on issues with access due to unaffordable medicine (Junior, 2012; Gómez, 2011; Flynn, 2008; Pinheiro et al., 2006; Cohen & Lybecker, 2005; Cassier, 2003). Within these, government intervention was often utilized as a measure to secure lower prices. Various extracts below not only demonstrate the usage of government intervention, but the tone associated with such actions, which have strained relations between government and private entities. The findings reveal that through threatening actions and politicized discourse, governments have successfully secured a reduction in pharmaceutical prices or increased access to medicines.

> By periodically threatening to produce generic versions of patented medication, the government has been able to acquire medicine at more affordable prices. (Gómez, 2011, p. 334).

> These compulsory licences were the subject of a tug of war with international pharmaceutical laboratories, and the Brazilian Health Ministry used them in negotiations on the purchase price of molecules patented after 1996. In the summer of 2001 it challenged Roche with a threat to produce Nelfinavir in Brazil from 2002, until the company agreed to a substantial price reduction. (Cassier & Correa, 2003, p. 93)

> Given that Brazil possesses the manufacturing capacity to produce the drug, the threatened compulsory licence was credible and significant. (Cohen & Lybecker, 2005, p. 220)

> On 9 April 2008, the Ministry of Health decreed Tenofovir to be of 'public interest' — the first step in issuing a compulsory license. The decree was made to accelerate the process of deciding whether or not the drug will receive a patent from Brazil's patent office. (Flynn, 2008, p. 531)

The findings revealed that threatening to issue a compulsory license or commit patent infringement are among the limited responses a public entity may have in the event a private pharmaceutical entity refuse to reduce pharmaceutical prices. Thus, compulsory licensing and patent infringement have been revealed as the most commonly used interventions against the

private industry (Junior, 2012; Gómez, 2011; Flynn, 2008; Pinheiro et al., 2006; Cohen & Lybecker, 2005; Cassier, 2003).

When the discussion of benefits concerning state-owned enterprise arose, public laboratories were frequently mentioned for their utility. The extracts below demonstrate how public laboratories have been used to increase access to medicine for the treatment of HIV/AIDS.

> In Brazil, public procurement and public drug production play a central role in the health system. For some programmes, such as HIV/AIDS, the government is the only buyer of drugs, creating a monopsonic market. The public sector is also engaged in drug production through a number of public laboratories. One of these facilities, Farmanguinhos, is directly linked to the MOH, while the others are linked to local states, to universities or to the Armed Forces. (Junior, 2012, p. 1064)

> There are many benefits to state production of ARVs. The first is the access to treatment that it provides. The number of Brazilians in ARV therapy has continued to rise; in 2006 it was over 184,000, representing 83 per cent of those in the country with advanced HIV infection, according to the World Health Organization's (2006) calculations.13 Second, the provision of universal treatment reduces the amount of public resources that would have been spent on hospital care and treatment of opportunistic diseases: between 1997 and 2000, it is estimated that 234,000 admissions were avoided, representing savings of US$ 677 million. (Flynn, 2008, p. 523)

Throughout the literature, mentions of Brazil or articles that focus solely on Brazil refer to ARV access as an outstanding example of government intervention. Reduced prices and

increased access are regarded as a victory against the private industry, after negotiations to reduce prices were unsuccessful.

The data extracts below reveal some of the discussion regarding government willingness to intervene, which is demonstrative of government capability to address healthcare inequity through legislation.

> Brazil led the fight against the TRIPS ruling. The country had no tolerance for rulings that made it impossible for developing nations to ensure universal access to medicine. (Gómez, 2011, p. 334)

> Thailand has mobilized its state-run Government Pharmaceutical Organization (GPO) to supply ARVs and became the first middle-income country to issue a compulsory license to cheapen the price of medicines. (Flynn, 2008, p. 531)

> After demonstrating its capacity to provide inexpensive, quality medicines for Brazil's public health sector — especially those for neglected diseases that the private sector were not interested in — government officials and policy makers began to rely on Far-Manguinhos for help in addressing the HIV/AIDS problem. (Flynn, 2008, p. 523)

> Public laboratories have played an important role in the production of essential and strategic drugs, especially in the HIV/AIDS programme and Farmanguinhos has lately signed an agreement with the government of Mozambique supporting the construction of an ARV production facility in this African country. In addition, the MOH has been active in price negotiations and has even issued a compulsory licence to ensure the

> sustainability of Brazilian key health programmes. Although studies (Flynn 2008, p. 529) have revealed a raise in prices for ARVs in the country, Brazil's AIDS treatment model nevertheless resulted in sustained lower prices for four of the six ARVs consuming the largest percentage of Brazil's [highly active antiretroviral therapy (HAART)] budget, saving Brazil over US$1 billion from 2001 to 2005. (Junior, 2012, p. 1076)

CHAPTER 4: DISCUSSION

The preliminary literature review, scoping review, and thematic analysis have proven a useful combination to retrieve and analyze literature pertaining to the pharmaceutical sector and the public production and distribution of medicine. The scoping review was utilized to draw in literature concerning the public production of medicine, which was then analyzed via thematic analysis. The review revealed there remains a small body of literature concerning the public production of medicine. The analysis served to detect patterns within the dataset, thus revealing themes within the literature. The three themes identified will be further explored in this section. Following the discussion on themes, a key finding from the preliminary literature, which concerns the national drug coverage program, will be explored as it filters into key findings from the analysis. This is followed by the implications this type of work may have for the field of global health.

The local production of medicine was identified as a prominent theme due to the volume of literature concerning domestic production capability. The most informative aspect of the discussion arose from the findings in a report presented by Kaplan and Laing (2005) concerning the feasibility of locally producing medicine in low to middle income countries. The report revealed that the WHO believes state production of pharmaceuticals is ill advised, citing superior private sector efficiency as a key reason (Kaplan & Laing, 2005). Although the report

acknowledges successful examples of the public production of medicine, with references made towards Brazil and Cuba, there is little recognition of these successes from the international organization (Abbott, 2011; WHO, 2011). Although Cuba is highly regarded for developing some medicine under the guise of government, Kaplan and Laing (2005) make reference to compromised foreign investment and conclude that the issue is worth analyzing. However, they do not provide an in-depth analysis. Considering the report is agreeable with the findings presented from the WHO, it would prove credible if the authors properly assessed the case of Cuba prior to concluding that state owned production is ill advised – if a country could produce medicine in the face of sanctions, this may prove hopeful for other countries in the Global South with limited resources. An in-depth analysis may assess "South-South" collaboration, which consists of trade agreements between countries within the Global South (Kaplan & Laing, 2005). Abbott (2011) draws attention toward the highly concentrated number of APIs exported to the world from both India and China, which is estimated at 75 percent. Given that India and China are both burgeoning developing countries, they may play an important role in aiding countries that seek to produce medicine under state ownership, and in effect, promote the local production of medicine in low to middle income countries through trade agreements.

With regard to how the findings relate to the Canadian setting, there is a case to be made concerning the feasibility of locally producing medicine in a country that is not only developed, but one that possesses considerable resources and the necessary infrastructure to develop and distribute medicine. The Canadian Government touts the Canada's research talent and state-of-the-art infrastructure to develop medicine ("Clinical Trials Ontario", 2018; "Invest in Ontario", 2018). Thus, Canada's dependence on API importation or ability to produce APIs should be further explored. This may aid in the discussion concerning state production of medicine in the

Canadian setting. An assessment on which APIs can be produced domestically and which must be imported may serve to either strengthen or weaken the argument that the Canadian Government can feasibly produce medicine.

The Public Private Sector was identified as a key theme due to the role each sector has with regard to pharmaceutical R&D. The most informative aspect of the findings concerns how the private sector is positioned within the literature: the likely entity to produce pharmaceuticals. On the contrary, the public sector is seemingly positioned as an inefficient entity that is unable to perform at similar or greater levels than its counterpart. Although there was recognition of public sector contribution with regard to drug development, the recognition was limited to a role in research. The Canadian public sector provides support for drug development through the pre-competitive sphere. Although efficiency may be questioned in low to middle income countries, considering how integral the public sector's role is with regard to research for drug development, the Canadian Government may be able to make the case that the public sector can assume greater responsibility over drug development processes. Further, the Canadian Government may be in a likely position to propose stipulations on the private sector when collaboration occurs. The stipulations may concern the final price of a successfully developed drug or they may concern public health crises.

Although an independently operated entity is within its legal rights to decline government collaboration in Canada, it is ethically immoral to oppose collaboration in times of need. During the AIDS crisis in the early 1990's, the Brazilian government was unable to meet the demand for medicine due to excessively priced ARVs and when it turned to a private lab, Microbiologica, requesting assistance with regard to drug development, their offer was rejected (Flynn, 2008). This may lend credence to the claim that government entities should maintain public laboratories

and other infrastructure intended for drug development; in the event that a private corporation choose not to collaborate or aid a government on drug development, especially during a public health crisis, a prepared strategy for procurement or development may serve to alleviate the pressures that a health crisis may place on the government.

The national production of medicine was identified as a prominent theme throughout the dataset due to both the volume of literature concerning state involvement and the relevance to the central research question. One of the most informative aspects of the data concerns government intervention to increase access to medicine. The findings revealed that governments in low to middle income countries have either chosen to infringe patents, issue compulsory licenses, or nationalize the pharmaceutical sector. All of these reasons are seemingly linked to political motivation, which is a term used to describe acts that are carried out in the interests of a political party or particular government (Collins, 2018).

The following section will review some of the government interventions taken and whether they are applicable in the Canadian setting. The Brazilian Government threatened a pharmaceutical corporation with compulsory licensing due to high costs for HIV/AIDS treatment (Cohen & Lybecker, 2005). Considering Brazil's manufacturing capabilities, access to public laboratories and knowledge of pharmaceutical development, the threat was credible (Cohen & Lybecker, 2005). This provided Brazilian authorities with greater leverage, and in turn, served to reduce prices for some ARVs. Although this worked in Brazil and may prove successful in other low to middle income countries, this approach is an unlikely option in the Canadian setting; in 1993, the federal government eliminated compulsory licensing (Grootendorst et al., 2012). The complex legal standards since devised are intended to protect pharmaceutical intellectual property and with litigation that would ensue is a strong deterrent, thus this is no longer a

feasible option in the Canadian setting (Grootendorst et al., 2012). Further, compulsory licensing is a controversial approach that may serve to disincentivize investment into the industry and harm Canada's reputation. This form of intervention does not bode well for the relationship between the public and private sector, as it does not provide private entities with confidence in ownership.

One of the most extreme forms of government intervention overserved within the dataset concerns the Iranian Government's decision to nationalize the pharmaceutical sector following the Islamic Revolution in the 1970's (Basmenji, 2004). The government seized pharmaceutical manufacturing companies and reduced the maximal share of the private sector to 12% (Basmenji, 2004). This was followed by the implementation of centralized policy and decision-making for the pharmaceutical sector, which was administrated by six state-owned firms (Basmenji, 2004). As a result, the cost of medicine in the country has remained generally affordable and the improvement to accessibility of medicine is notable (Davari et al., 2011). However, this type of intervention is not viable in the Canadian setting, and it is seen as a violation of international trade agreements. The World Trade Organization (WTO) is a supranational organization, thus, if a member state is found in violation of the trade agreement, sanctions may be placed on the country (WTO, 2018). If the Canadian government were to nationalize the pharmaceutical industry, there consequences that would result far outweigh any perceived benefits. This approach would also serve to harm the relationship between the public and private sector.

Although compulsory licensing and patent infringement are not plausible in the Canadian setting, a key finding from the dataset that pertains to the Brazilian case of public drug production may be applicable in the Canadian setting. Flynn (2008) identified three factors that led the Brazilian government to becoming a producer of ARVs; pre-existing infrastructure,

strong civil society pressures and a pharmaceutical market characterized by high prices (Flynn, 2008). The following section will explore how these factors may be applied in the Canadian setting. The Canadian media and research community are part of a civic movement that continuously draws attention to high drug prices, poor drug coverage, and the healthcare inequity that has resulted (Law et al., 2018; Milne & Petch. 2018; Ireland, 2017; Sawa & Ellenwood, 2017; ARI, 2015; Morgan et al., 2015; Davidson, 2015). This movement has had some successes, most notably, the Advisory Council created to assess a proposal for universal drug coverage. Thus, civic engagement in Canada with regard to unaffordable drug prices appears to be an evident factor. The second factor refers to a market characterized by high prices, which is evidenced by a growing body of research that has drawn attention towards unaffordable medicine and increasing drug costs in the Canadian setting. The third factor relates to whether Canada possesses the necessary infrastructure to produce and distribute medicine. The government touts Canada as the ideal place to develop pharmaceuticals, citing state-of-the-art infrastructure, leading scientific talent and a strong research community ("Clinical Trials Ontario", 2018; "Invest in Ontario", 2018). Therefore, it is not a leap to suggest that the Canadian Government is in a likely position to produce medicine, albeit an assessment must be done to determine which kinds of medicines need to be produced to address which healthcare inequities. Further questions surrounding cost, feasibility, and areas of need are among the immediate few that arise. In the case of Brazil, the government made a decision to start producing medicine due to the health crisis. In the Canadian setting, there is no current crisis; the government has the time to determine the best approach to assessing whether the public production of medicine is a feasible measure. It is not advised to push ahead and begin with production, considering the proper research has not been conducted. Further research

surrounding medicine and areas of need must be conducted prior to any decision being made and this must be collated with other research pertaining to the public production of medicine in the Canadian setting.

The following section will explore possible strategies for moving forward, beginning with Advisory Council that has been selected to determine program viability of Pharmacare 2020. Given that the current council has been tasked with conducting an economic and social assessment in an area of study concerning pharmaceuticals, in addition to consulting experts and stakeholders, this approach may also serve as an efficient and cost-effective way to determining the viability of the public production of medicine in Canada (Fréchette, 2017). This may also serve to save time, money and to circumvent the bureaucracies associated with the creation of a counsel. An Advisory Council may be employed to conduct the necessary research to determine which kinds of medicines can be produced with readily available APIs and which ones would require importation. This will provide considerable clarity with regard to the economic analysis of such an endeavour. Further, the government may use a council to assess the documented failures and successes of public models concerning pharmaceutical production and distribution. Councils have been used across government levels on multiple occasions, in instances where the government sought counsel on how to manage key government assets and business enterprises, issues concerning mental health and addiction, and to determine the viability of Pharmacare 2020 (Morneau, 2018; Government of Ontario, 2018; Ontario Minds, 2011). A council has been identified as a fair and rigorous assessment tool, which may be the possible step required to investigate whether the Canadian Government can move forward with publicly producing and distributing medicine as a means to reduce healthcare inequity.

The interdisciplinary nature of global health fosters collaboration among various disciplines (Drain et al., 2017). As a result, research conducted within the field of global health may have far-reaching effects. The findings and subsequent analysis can be viewed as an integral part of the movement for social justice and equality. As market-forces push for less regulation and the world further globalizes, introducing price controls for pharmaceuticals may become far more difficult (Klein, 2006). As evidenced in Brazil, collective action is required to effect positive change that benefits the majority.

Through the collection of information and data relevant to the public production of medicine, the policymakers and decision-makers charged with responsibility over pharmaceutical policy in Canada may access empirical data that is rooted in evidence, not belief. Considering the evidence collected, this kind of research can be used to lend credence to the claim that government bodies around the world, given the right factors are present, could investigate whether the public production of medicines can be used to address healthcare inequity.

With regard to the limitations, due to the prevalence of bias within qualitative research, the various types of bias were examined as a measure to reduce and or prevent bias within this work (Norris, 1997).

It is recognized that the presentation of the literature concerning the pharmaceutical industry may influence the reader's view of the subject at hand. Thus, the decision to include literature that was critical of the industry is recognized as a publication bias, as it was favourable to the findings and subsequent policy options developed. However, literature that is supportive of current pricing schemes, alternative measures to addressing healthcare inequity, and supportive of the private sector were referenced to provide a more balance perspective.

Qualitative research is often criticized for lacking transparency during the analysis, thus, to limit critique and to ensure transparency, each step taken during the search strategy, as well as the thematic analysis were documented rigorously within the methodology. The intent of this was to contribute to the audit-trail, and in turn, provide an understanding of the rationale behind some of the choices made.

With regard to data collection, the dataset was formulated independently, and each article was processed through a multiple step approach. It is recognized that a second reviewer throughout the documented analysis would have served to reduce bias even greater. Thus, there is a potential for bias with regard to how the themes were interpreted.

Ideally, two independent researchers could have been employed while constructing the dataset and the review process. This may have prevented bias during the reviewing process. Due to the lack of resources this additional step was not taken. The themes were reviewed to verify a connection to the overall dataset and any themes that appeared out of place were removed.

Further, research conducted in think tanks like Fraser Institute and/or C.D. Howe Institute, which sit on opposing ends of the political spectrum, were not included in this work. This is identified as a missed opportunity, and in effect, a limitation on this thesis. The choice to exclude think tanks from this thesis is rooted in inadequacy to accurately assess the potential for political bias that seemingly influences the work developed from such research institutes.

It is possible that some of these findings are an artifact of missed steps or data that has been left out. It is likely that there is greater data available on the successes and failures of the public production of medicine. Further, if an economic analysis were conducted, it would provide greater objectivity with regard to public and private sector capability. On the other hand, the counter argument may be that despite these limitations, this thesis has what appears to be a

detailed examination of the challenges governments face with regard to addressing healthcare inequity linked to unaffordable medicine. Articles on pharmaceutical R&D that did not touch upon the public sector were excluded due to the high volume retrieved, in addition to relatability. There is a significant amount of literature concerning pharmaceutical R&D, however, it is estimated that a small fraction pertains to public production, thus, this is recognized as a limitation.

Lastly, it is probable that the public production of medicine may only be feasible for a handful of products/diseases, however, if this were coupled with some of the aforementioned recommendations, greater access to medicine for Canadians may result. That is why the leading policy option is to utilize an Advisory Council to determine which medicines are potentially available to be produced at a cost-effective rate in Canada.

5.0 CONCLUSIONS

5.1 CONCLUDING REMARKS

The growing population in Canada that is unable to access medicine due to cost or poor drug coverage are part of a healthcare inequity that continues to draw attention from many actors in society (Morneau 2018; Pharmacare 2020, 2018; Law et al., 2018).

The scoping review served as a useful research tool, drawing in literature concerning the public production of medicine. The thematic analysis performed on the literature detected patterns that have revealed key findings that may be used to lend credence to the claim that the Canadian Government is in a likely position to produce and distribute pharmaceuticals. Three key factors that led to the Brazilian Government's response to develop medicine were identified in the Canadian setting; a developed country that is among the most industrialized in the world, Canada is known to have pre-existing infrastructure capable of drug development, a strong civil

society that is engaged by the government, and a pharmaceutical sector characterized by high prices that continues to garner media attention (Canadian Parliamentary Review, 2018; "Clinical Trials Ontario", 2018; "Invest in Ontario", 2018; Law et al., 2018; Milne & Petch. 2018; Ireland, 2017; Sawa & Ellenwood, 2017). Further, the Canadian public sector is an efficient wing that continues to support drug development in a research capacity. Therefore, the Canadian Government may be poised to produce medicine considering the right conditions exists. However, it is noted that a considerable amount of further research is required prior to the government undertaking such an endeavour. An economic analysis may reveal that certain medicine production is unfeasible, or that certain APIs are unable to be produced cost effectively in Canada.

In the event the government decide to explore the public production of medicine, it may prove an efficient use of resources to utilize an assessment tool that is already in place, the Advisory Council created to assess the viability of Pharmacare 2020. The council may deem such an endeavour unfeasible, however, it may present other findings concerning investment into public infrastructure. As evidence in Brazil, maintaining public laboratories may prove as backup plan during a health crisis in the event that a private company refuse to lower drug prices. Further, a government led initiative that empowers the state through progressive solutions may serve to address knowledge gaps and in turn, increase access to medicine for vulnerable people throughout the world. This type of research may serve to promote dialogue on the role of government with regard to public drug development as a means to address healthcare inequity linked to unaffordable medicine and lead to other useful findings.

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APPENDICES

APPENDIX A: SEARCH STRATEGY

Title
The Role of the State in the Public Production of Medicine

Introduction

This search strategy has been devised with the intent to create an audit-trail, which can be used to capture the thinking-processes behind the selected searching methods. It includes the keywords, databases, and google searches conducted. The search strategy will filter into a scoping review, and ultimately, my thesis work. This way I am able to demonstrate that I have done my due diligence as a researcher via ensuring the appropriate methods were taken to draw in *all relevant literature* to answer my research question(s).

This search strategy and the information collected will be used to provide up-to-date information on countries that have nationalized portions of, and or, the entirety of R&D of pharmaceuticals. This information will then be used to support the claim that the Canadian Government should enter the pharmaceutical industry as a producer and manufacturer of medicines. I intend to extrapolate the data collected to the Canadian healthcare setting. These data will be used to serve as an effective set of reference material for analysts, researchers, policymakers, public servants, and others concerned with the exorbitant pricing of pharmaceuticals in Canada and abroad.

Lastly, this report does not attempt to comprehensively address the myriad of issues associated with medicines policy in Canada and abroad, such as **parallel trade, intellectual property rights, counterfeiting, or corporate pricing strategy, around which vigorous debate continues at both the national and international level.**

Research Question

The research question to be addressed is: Should the Canadian government get involved with/or participate in the full life cycle of pharmaceutical innovation, which may appear in the form of chemical identification through to market launch? (position myself in this with my interpretation of the data)

Original Topic

The original topic grew from a desire to address global inequality in respect to accessing medicine. To question whether the Canadian Government is able to *increase existing funding* for pharmaceutical research and development (R&D) naturally arose; specifically, whether the Canadian Government is able to allocate additional funding for researchers who have undertaken work that may result in the development of new medicines.

The Canadian Government successfully engages in the production of goods across an array of industries. Therefore, I argue that there is potential for the government to enter the pharmaceutical industry, which, up until this day, is almost entirely privatized. Public research dollars that see a project through to completion, thus resulting in the researcher maintaining greater control over ownership, would provide the researcher and the state-owned institution

(college/university) the choice to produce and manufacture pharmaceuticals, and in turn, maintain control over pricing.

Databases & Keywords

I have selected the following databases: MedLine, OECDI, EMBASE, EconLit, PubMed, and Google Scholar. Due to the nature of my topic, I found it appropriate to include databases that focus on the sciences, healthcare, economics, and policy to broaden the scope of potential data to be retrieved.

I prioritized usage of keywords such as 'state-owned' and 'pharmaceutical industry' because these terms were found throughout the most relevant literature collected via a Google Scholar search. However, I relied on other keywords, such as 'pharmaceutical R&D' and 'Drug Industry' to enhance my searches and increase the likelihood of sourcing relevant literature.

APPENDIX B: PROTOCOL

Title
Government funded R&D of pharmaceuticals: a scoping review

Objective
The objective of this scoping review is to draw in all relevant literature and/or information on publicly funded research models pertaining to the research and development (R&D) and commercialization of pharmaceuticals. This scoping review may serve as a reference point for researchers interested in developing new and/or alternative funding models for the R&D of pharmaceuticals. It is possible the findings will be used to gauge whether the Canadian government should participate in the full lifecycle of pharmaceutical innovation from chemical identification through to market launch.

Question (to be informed by the scoping review)
Whether the Canadian government can get involved with/or participate in the full lifecycle of pharmaceutical innovation (chemical identification through to market launch)

Sub questions
Whether federal funding for the Canadian Institute of Health Research (CIHR) should be increased to expand funding for the R&D of pharmaceuticals

Lines of Inquiry *(to be informed by literature)*

1) Can the research dollars currently used to develop chemical entities be increased to fund a clinical trial(s)?

2) What kind of questions arise if I invoke the debate on government ability/willingness to get involved with/participate in the full lifecycle of pharmaceutical innovation (chemical identification through to market launch)?

Background

Following my first committee meeting it was decided that a scoping review may prove as the best approach to conducting a literature review. The scoping review will serve as a means to draw in all relevant literature on publicly funded R&D of pharmaceuticals, and in turn, potentially provide an alternative perspective on how to address exorbitant pricing of pharmaceuticals in Canada. Further, as many of the claims within my proposed thesis are speculative, a scoping review may lend credence to any hypotheses made. A preliminary search has revealed that there is little research available on variance in models of publicly funded R&D of pharmaceuticals, thus, the research load should be manageable. Currently, a majority of the literature focuses on malpractice conducted under the auspices of leaders in the pharmaceutical industry, the benefits of R&D subsidies, and the relationship between pharmaceutical industry and the public sector. I seek to promote an alternative worldview that prioritizes research and development over profit by shifting the focus to what publicly funded R&D of pharmaceuticals may look like around the world. Ideally, this approach may serve to address health concerns deemed non-profitable by the pharmaceutical industry, resulting in major gaps in the

development of some drugs. Presently, the Canadian government provides a limited amount of research dollars for research concerning neglected tropical diseases and the deepening antimicrobial resistance, which typically results in little to no new medicines being produced in either field. An increase in resources would provide and/or lend greater autonomy to both the researcher and the public institution where the research is conducted. In turn, the research and/or institution responsible may be able to exert greater control over the R&D of pharmaceuticals, thus providing an atmosphere free of corporate capitalism that has historically restricted the Canadian government from pursuing new medicines, and subsequently secure greater access to medicines for both vulnerable and non-vulnerable populations.

There are not many abbreviations/terms used that require clarification. However, I will provide a brief overview of the most common terms. R&D refers to research and development. Other terms, such as drug discovery or R&D pipeline refer to newly identified chemical entities and the speed with which they are produced. I would like to clarify what is meant by discovery to market launch. In order for the government to assume total responsibility over drug development, manufacturing, and marketing, the following steps are to be taken: Pre-clinical studies, Phase I through Phase IV clinical studies, regulatory submissions, manufacturing, distribution, and sales/marketing**.** It is possible that assuming responsibility may appear in the form a public-private partnership and/or outsourcing. The politics governing which steps are outsourced may ultimately result in part ownership of a newly launched drug unless the government stipulates otherwise.

There is a significant amount of literature that substantiates the claim that subsidies to R&D boost innovation, reduce costs and increase research in unprofitable fields. Further, there is substantial literature that implicates the pharmaceutical industry in malpractice; shelving being one example. Additional literature draws linkages between profit driven R&D and biased results. Although there is a variety of literature on topics pertinent to publicly funded R&D of pharmaceuticals, including but not limited to, systematic reviews, scoping reviews, and primary research papers, this scoping review will serve to address a gap in research on publicly funded R&D of pharmaceuticals around the world. There is a strong foundation of literature that indicates increasing funding to assume the major costs of R&D of pharmaceuticals potentially has many positive outcomes. Following the successful collection of data on the varying models of publicly funded R&D around the world, I can detail the positives and negatives, and in turn, determine whether such a concept can be elaborated upon in Canada where partial funding already exists.

The following databases were used in an initial search: Google Scholar and PubMed. Upon completion, and the organizing of literature via Mendeley, I will begin to source literature from the Mendeley search system, in addition to Scholars Portal.

A search on the Cochrane Database of Systematic Review was conducted to confirm that there is no type of review on publicly funded R&D of pharmaceuticals.

Inclusion criteria

Sources will be considered if they address public funding for the R&D of pharmaceuticals, and or PPP approaches to R&D. To draw in greater literature, I will not limit my sources to one country, however, I will only use English-based literature. A deadline was set, after which it was agreed that no further studies would be included in the analysis.

The following criteria devised will assist in basing decisions about the sources to be included in an attempt to limit literature that is non-relevant:

- initial limited search for relevant keywords
- include literature from pharmaceutical industry
- include grey literature
- include literature from databases
- include government data
- search in the reference list of all hits

I will include the following sources in my scoping review: primary studies, text/opinion articles, websites and online databases for grey literature from January 1 2000 up to January 1 2017 (World Health Organization, Government of Canada).

I have already conducted citation searches in Google Scholar and PubMed for related articles from January 2000 up to January 2017. After a preliminary round of sourcing data and literature, I will conduct a secondary filter to eliminate results that are not relevant to federal funding models and or research on the benefits of federal funding pertaining to pharmaceutical R&D. Following a secondary filter, I will indicate which articles have gone through double title/abstract screening and or full-text screening. There are no participants and or studies that are relevant to this type of scoping review. I am relying on data that assesses and or addresses funding models throughout the world. Thus, the emphasis of my solicited data is placed more on the model and less on the recipient.

The core concept to be examined by this scoping review is to determine whether the Canadian government should get involved with/or participate in the full lifecycle of pharmaceutical innovation (chemical identification through to market launch). Thus, by sourcing data that solely focuses on federal funding of R&D of pharmaceuticals around the world, I can interpret whether the Canadian government can pivot from partially participating in funding the R&D of pharmaceuticals to full participation (full lifecycle of a pharmaceutical), which includes but is not limited to market launch.

Given the nature of the topic, I found it necessary to include any English based literature throughout the world. Public research dollars are a near universal concept, and although the amount provided fluctuates according to many factors (sociopolitical, economic, and cultural are to name a few), the basis for government subsidies of the R&D of pharmaceuticals is relatively similar (promote innovation, collaborate with private corporations, incentivize growth). However, if possible to note the reasons behind publicly funded R&D of pharmaceuticals per country, I will do so if it is included within the literature.

Extraction of the results

Charting the results via thematic analysis: the results can be classified under main conceptual categories, and for each category, a clear explanation will be provided.

Provide the reader with a logical and descriptive summary of the results that align with the objective and question(s) of the scoping review

A draft charting table/form including the following key information will be used:

a. Author(s)
b. Year of publication
c. Origin/country of origin (where the study was published or conducted)
d. Aims/purpose
e. Methodology/methods
f. Outcomes and details of these (e.g. how measures) (if applicable)
g. Key Findings that relate to the scoping review question/s.

Presentation of the results

Identifying the implications of the study findings for policy, practice and/or research. This may be presented as a map (given I am looking at models around the world) that links to a diagrammatic or tabular form with further description (a narrative summary that will describe how the results relate to the review objective and question/s)

APPENDIX C: THEMES 1.0

1
Public Private Collaboration
Innovative drugs

2
New drugs
Commercial sponsors
Shareholder value
Public health

3
Innovative medicine
Public private partnership
New medicine
Drug discovery

4
Manufacturing cost

5
Transnational cooperation

6
Affordable medicine
Pharmaceutical subsidies

7
Pharmaceutical system
Drug supply system

8
State-owned enterprise

9
Equitable access

10
Pharmaceutical industry growth

11
Pharmaceutical market trend analysis
Domestic production of medicine

One mention
Commercial sponsors
Shareholder value
Public health
Drug discovery
Manufacturing cost
Transnational cooperation
Pharmaceutical subsidies
Pharmaceutical system
Drug supply system
Equitable access
Pharmaceutical industry growth
Pharmaceutical market trend analysis
Tripartite partnerships
Government purchasing power
Large-scale production of essential medicine
Innovating capability
Foreign pharmaceutical firms
Intellectual property enforcement
Good manufacturing practice
Active ingredients
National pharmaceutical sector
Drug production
Pharmaceutical R&D
Cost-effective medicine
Public sector efficiency
Public vs private
Competitive models
National industry
Generic medicine

Two mentions
Innovative drugs (1, 3)
New drugs (1, 3)
World Trade Organization (17, 23)
Generic production (28, 29)
Public laboratories (14 ,31)

12
Public production of medicine
Government intervention

13
Tripartite partnerships

14
Governmental purchasing power
Public laboratories
Domestic production and research and development
Large-scale production of essential medicine
Public private partnerships

15
Public production
State-owned

16
Innovating capability

17
Foreign pharmaceutical firms
World Trade Organization
Intellectual property enforcement
Good manufacturing practice

18
Government intervention
Public production
Access to medicine

19
Local production of pharmaceuticals
Access to needed medicine
Active ingredients
Domestic production of medicine

20
Government intervention
National pharmaceutical sector

Three mentions
State-owned enterprise (8, 15, 22)
Affordable medicine (16, 22, 23)

Four mentions
Public Private Collaboration (1, 3, 14, 24)
Access to medicine (18, 19, 25, 26)

Five mentions
Public production of medicine (12, 15, 18, 31, 32)

Seven mentions
Government intervention (12, 18, 20, 26, 29, 31, 32)
Domestic production of medicine (11, 14, 19, 21, 22, 25, 32)

21
Local production of medicine
Drug production

22
Generic medicine
State-owned
Domestic production
Low-cost medicine

23
World Trade Organization
Lower pharmaceutical prices
Cost-effective medicines

24
Pharmaceutical R&D
Public funding & private investment

25
Collaboration
Local production of medicine
Access to medicine

26
Government intervention
Access to medicine

27
Public sector efficiency
Public vs private
Competitive models

28
Government intervention
Generic production

29
Government intervention
Generic production

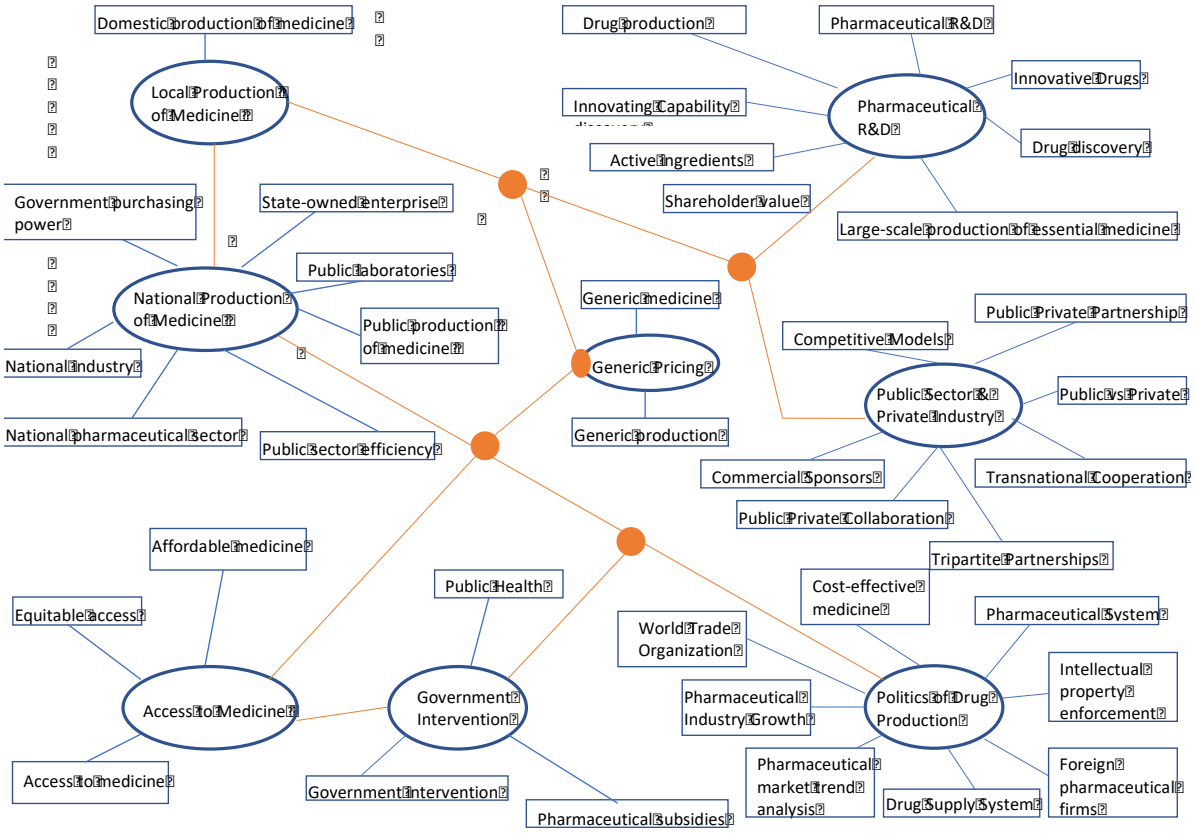
30
National production

Government intervention

31
Public laboratory
Government intervention
Public production of medicine

32
Government intervention
Public production of medicine
Local production

APPENDIX D: THEMATIC MAP 1.0



APPENDIX E: THEMES 2.0

1. Local Production of Medicine
Domestic production of medicine (11, 14, 19, 21, 22, 25, 32)

2. Pharmaceutical R&D
Pharmaceutical R&D (24)

Innovative drugs (1)
New drugs (2)
Drug discovery (3)
Innovating capability (16)

Large-scale production of essential medicine (14)
Drug production (21)
Active ingredients (19)

Good manufacturing practice (17)
Manufacturing cost (4)

Shareholder value (2)

3. Public Sector and Private Industry
Public Private Collaboration (1)
Public Private Partnerships (14)
Transnational cooperation (5)
Tripartite partnerships (13)
Commercial sponsors (2)

Public vs private (27)
Competitive models (27)

4. Generic Pricing
Generic medicine (22)
Generic production (28, 29)

5. National Production of Medicine
State-owned enterprise (8, 15, 22)
National pharmaceutical sector (20)
National industry (30)
Public production of medicine (12, 15, 18, 31, 32)
Public laboratories (31)

Public sector efficiency (27)

Government purchasing power (14) (most likely to be moved to politics of – if it happens it will be during refining of maps)

6. Access to Medicine

Equitable access (9)
Affordable medicine (6, 22, 23)
Access to medicine (18, 19, 25, 26)

7. Politics of Drug Production

Pharmaceutical system (7)
Drug supply system (7)

Pharmaceutical industry growth (10)
Pharmaceutical market trend analysis (11)

Foreign pharmaceutical firms (17)

Intellectual property enforcement (17)
World Trade Organization (17, 23)

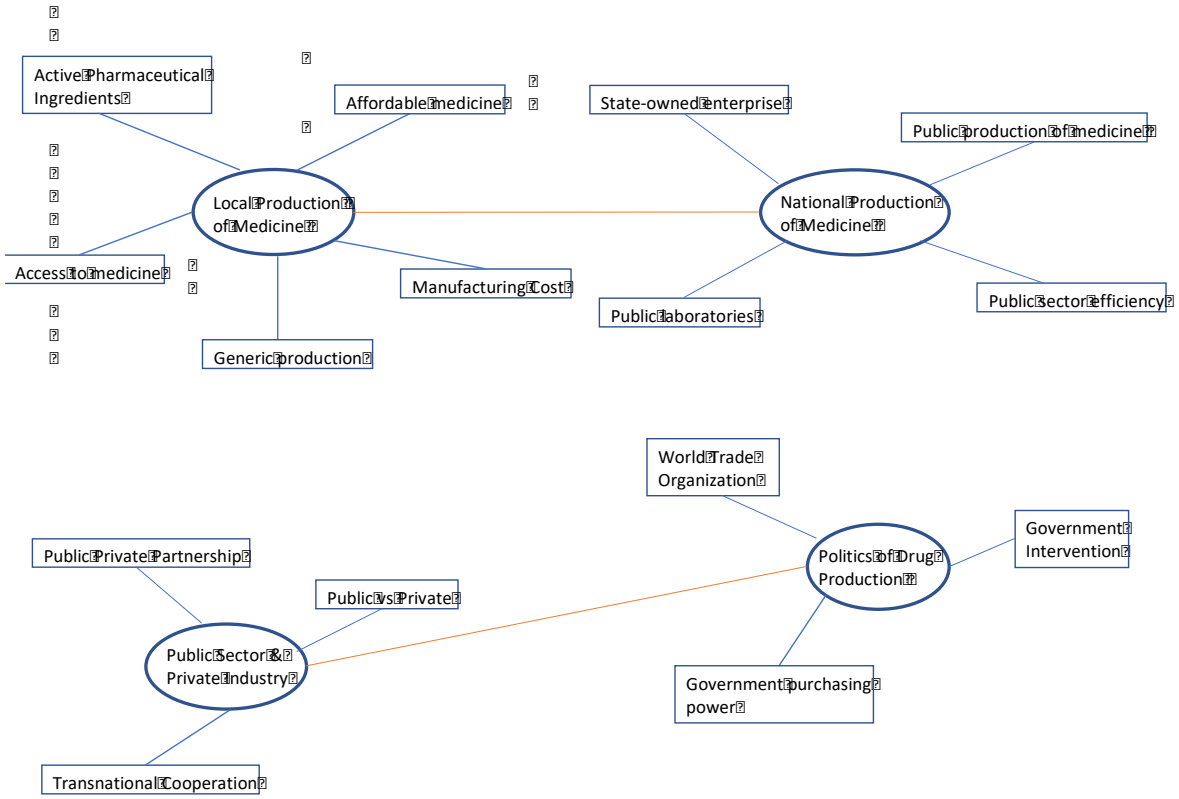
Cost-effective medicine (23)

8. Government Intervention

Public health (2)

Government intervention (12, 18, 20, 26, 29, 31, 32)
Pharmaceutical subsidies (6)

APPENDIX F: THEMATIC MAP 2.0



APPENDIX G: THEMES 3.0

APPENDIX H: THEMATIC MAP 3.0