Perspectives and experiences of Canadian pediatric rare disease researchers in collaborative research with industry: a mixed methods study

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PREFACE

Approvals

Approval to conduct the thesis as part of the requirements for my Master's degree in Epidemiology was obtained from the School of Epidemiology and Public Health (SEPH) at the University of Ottawa. This study obtained approval from the University of Ottawa's Research Ethics Board (Appendix 1).

Contributions

Charlena Degen (CD) was the primary investigator and led all components of the study, which was co-authored by Dr. Ian Graham (IG) and Dr. Beth Potter (BP) as co-supervisors and thesis advisory committee member Dr. Kym Boycott (KB). This study was conceived by CD, IG and BP. CD was responsible for planning the methods and creating study instruments under the guidance of IG and BP, with critical expertise contributed by KB. CD collected the data. CD analyzed and interpreted the study results with feedback from IG, BP, and KB. CD also drafted the thesis and manuscript, with guidance and critical edits from IG, BP, and KB. All authors reviewed the results and approved the versions of the thesis.

ABSTRACT

Objectives: We investigated pediatric rare disease researchers' experiences and perspectives with research collaborations involving industry partners.

Methods: This mixed methods study included a cross-sectional survey of academic/hospital-based Canadian pediatric rare disease researchers which informed semi-structured interviews with a subsample of survey participants. We analyzed survey data descriptively and interview data thematically, integrating findings narratively.

Results: Of 126 survey respondents, 59 (47%) reported research collaborations with industry; we interviewed 10 of these researchers. Important benefits to collaborations with industry reported by survey participants and interviewees included access to funding and resources, while disadvantages stemmed from perceptions that partners had different motivations. Interviewees provided advice for future researchers including careful selection of an industry partner, relationship building, clear expectations, and utilizing supportive institutional structures.

Conclusion: Our findings provide insights into the experiences of pediatric rare disease researchers and offer suggestions on how to conduct successful collaborative research with industry.

Key Words: Collaborative Research, Pediatric Rare Disease, Industry, Partnership, Industry- Academia Relationships

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LIST OF ABBREVIATIONS

CHEO: Children's Hospital of Eastern Ontario

CIHR: Canadian Institute for Health Research

IKTRN: Integrated Knowledge Translation Research Network

IND Application: Investigational New Drug Application

IP: Intellectual Property

MTA: Material Transfer Agreement

R & D: Research and Development

CHAPTER 1

As part of my job working for an industry consultant, I became interested in relationships between academic researchers and private companies in the biomedical or pharmaceutical industries (hereafter, referred to as industry). In my role I am often responsible for profiling key opinion leaders in a disease area, and I began wondering how the profiling of researchers I do for industry might influence their interactions with researchers. Early in my MSc in epidemiology, I applied for a stipend from the Integrated Knowledge Translation Research Network (IKTRN). This network studies partnerships between researchers and those who are not researchers. A criterion for the stipend involved focusing on research partnerships and my interest in industry-researcher relationships was a perfect fit. Having observed differences between academia and industry through my work, I wondered how these sorts of research collaborations come about and work to produce high quality and relevant research. In discussion with my MSc co-supervisors, my work supervisor and doing some of my own research, I landed on pediatric rare diseases as the focus for my partnership research. The field of pediatric rare diseases was particularly interesting to me because it is not a large field in Canada which meant I could probably survey a large portion of researchers in this space. This is also a very active area of research and drug development that has experienced rapid growth in recent decades due to policies to advance rare disease drug development globally, and advances in technology giving greater ability to identify and develop novel therapeutics [1–4].This is how my MSc research journey began.

Before proceeding, I would like to clarify some terminology. By the term academic researchers, I mean individuals who are employed by universities or university-affiliated hospitals or research institutes. In this thesis the terms university and academia are used interchangeably to describe “the part of society, especially universities, that is connected with studying and thinking, or the activity or job of studying.” [5]. By the term industry I am referring to the for-profit organizations that are involved in the healthcare sector such as pharmaceutical, biotechnology, life science tools and services, healthcare equipment and

suppliers, and healthcare technology [6]. The terms partnership and engagement are used interchangeably with collaboration throughout the thesis.

1.1 Background

1.1a What is collaborative research?

Bansal et al. [7] defined collaboration in research as "research involving coordination between the researchers, institutions, organizations, and/or communities" (p. 137). In the context of scientific research, Sonnenwald [8] defined collaborative research as "interaction taking place within a social context among two or more scientists that facilitates the sharing of meaning and completion of tasks with respect to a mutually shared, superordinate goal" (p.645). To the best of my knowledge, there is no international or even national consensus on the formal definition of collaborative research. Furthermore, the concept has been referred to by terms such as: joint research, research co-production, integrated knowledge translation, and participatory action research. Hara et al. [9] interviewed scientists from a research centre focused on chemistry and chemical engineering and found descriptions of collaboration generally contained a common goal and sharing of knowledge. Katz & Martin [10] have suggested that collaborators (or partners) are defined by their contributions, responsibilities, and inclusion in the original research proposal.

1.1b Collaborative Research Between Academia and Industry

Over the last 30 years there has been considerable growth in the attention paid to collaborative research and development (R&D) between universities and industry [11]. This growth may be due to factors that have led to collaborative research being increasingly prioritized by both private industry and public research funders.

From the industry perspective, Rafols et al. [12] and Wang et al. [13] have suggested that increased engagement in collaborative research may have resulted from a shift by many healthcare firms from internal models of R&D to external or open innovation models in response to reduced productivity. External models of R&D include individual university-researcher partnerships, organizational university-

industry partnerships, academic centres of excellence, innovation centres, open crowdsourcing, and biotech creation [13]. Some have proposed that reduced industry productivity could be the byproduct of high development costs and time, strengthened regulations and requirements, and patent expiration of many drugs [14–16]. Wang et al. [13] argue that external models of R&D, including collaborations, can bolster industries' productivity. Optimizing productivity in drug development is an area of vital importance to the pharmaceutical industry, as the development of a drug can be extremely expensive, ranging from US$161 million to 14.54 billion per product [15, 17].

From a public funding perspective in Canada, collaborations between universities and industry are becoming a priority for research funders. For example, the Government of Canada has previously implemented many university-industry initiatives such as the Centres of Excellence for Commercialization of Research, and The Business-led Networks of Centres of Excellence program [18]. Organizations such as the Canadian Institute for Health Research (CIHR), the National Research Council and Genome Canada all directly work with industry to advance research [18].

As there are many forms of relationships between academia and industry, it is important to distinguish collaborative research as its own form of relationship. Perkmann et al. [19] offer a taxonomy of relationships between industry and academia (Table 1). Perkmann et al. [20] further distinguish between commercialization activities and academic engagement activities. Commercialization activities include patents, licensing, and academic entrepreneurship of the researcher's knowledge [20]. Whereas academic engagement involves academic researchers and non-academic organizations cooperating in knowledge transfer including collaborative research, contract research and consulting [20]. Perkmann et al. [19] define collaborative research as "research jointly pursued by university and industrial partners- commonly with public funding." Collaborative research emphasizes the cooperation of industry and academic partners, while other forms of academic engagement including contract research and consulting are application-oriented research carried out by the university or the academic and funded by industry [19, 20].

Table 1. Types of University-Industry Relations

Commercialization Activities	
Licensing	Contractual assignment of university-generated intellectual property (such as patents) to external organizations
Academic entrepreneurship	Development and commercial exploitation of technologies pursued by academic inventors through a company they (partly) own
Academic Engagement Activities	
Collaborative research	**Research jointly pursued by university and industrial partners – commonly with public funding**
Contract research	Application-oriented research and development activities carried out by university – commissioned and funded by industry
Consulting	Application-oriented research and development activities or advice provided individually by academics – commissioned and funded by industry

From Perkmann M, King Z, Pavelin S. Engaging excellence? Effects of faculty quality on university engagement with industry. Res Policy. 2011;40(4):539–52. (Reproduced with Permission)

1.1c Potential Advantages and Disadvantages of Collaborative Research with Industry

Studies have revealed that collaborations between academia and industry can be beneficial to an industry's R&D and productivity, as such collaborations can have a positive impact on the movement of drugs into the next phase of the research process and can also influence the success of drug approvals [21, 22]. Potential benefits for academic researchers collaborating with industry include creation of new opportunities, increased treatment options for patients, personal intellectual stimulation, participation in higher quality research, and financial rewards [23, 24]. Furthermore, collaborations with industry have been shown to be appealing to those working in academia given that many institutions and researchers lack the infrastructure, knowledge and resources needed to progress research from the lab into the clinic [25]. Wang et al. [13] note that those who work in industry have expertise in regulatory processes and

have the resources necessary to move products through the drug development pipeline, making them ideal partners for research collaborations [13, 26].

While these advantages may be appealing to some, many researchers are reluctant to enter into a relationship with industry. Collaborations in general require additional time to create relationships, time to negotiate expectations, and require giving up complete independence [27–30]. When collaborating with industry there are additional concerns about ethical issues such as conflicts of interest, as well as, reproducibility and validity of the research [23, 31]. Nevertheless, academics are still deciding that collaborating with industry is a beneficial avenue for research and ensuring their success is an important opportunity for investigation.

1.1d Factors Influencing the Success of Research Collaborations

While there does not appear to be any published blueprint or framework to guide or describe how collaborations between the biomedical or pharmaceutical industry and academic researchers should be undertaken to foster success (i.e., to realize benefits and minimize risks), general guiding principles for research partnerships tend to emphasize such things as: building relationships based on trust, respect, dignity, and transparency; including all perspectives; shared decision-making; open, honest, and responsive communication; recognizing, valuing, and sharing diverse expertise and knowledge; flexibility and tailoring of the research approach; mutual benefit of the partnership or reciprocity; and addressing ethical considerations [32, 33]. There are, however, guidelines for interactions between patient advocacy organisations and industry that focus on how a patient group can engage with biopharmaceutical companies to promote trust through thoughtful, responsible, and ethical interactions [34]. Presumably, using principles to guide partnerships can be considered a factor contributing to successful relationships.

Several authors have reviewed or studied the factors or influences that may impact the success (or lack of success) of relationships between academic and industry partners. We have grouped factors into three broad categories: factors predisposing the development of relationships, factors related to the relationship, and contextual factors that can impact the relationship. Some factors promote successful

partnerships while others hinder them. Additionally, some factors have been identified as both facilitators of success when present and barriers to successful collaborative research when absent. The determinants of research partnership success identified in previous studies are:

Table 2. Factors Impacting the Success of Relationships

	POTENTIAL FACTORS PREDISPOSING THE DEVELOPMENT OF RELATIONSHIPS	POTENTIAL FACTORS RELATED TO THE RELATIONSHIP	CONTEXTUAL FACTORS THAT CAN IMPACT THE RELATIONSHIP
FACILITATOR	• Previous experience conducting collaborative research [31, 35, 39, 40]	• Managing confidential information and conflicts of interests [23, 31, 36, 46] • Commitment to and adaptability of the relationship [31, 36, 38]	
BARRIER	• Time required to develop relationships [23, 27, 29, 31]		• Turnover of industry personnel and acquisitions of companies [44]
FACILITATOR OR BARRIER:	• Potential to access funding or other industry resources [27, 29–31, 35–38] • Geographic proximity of partners [35, 38, 39] • Personal Characteristics [20, 41] • Individual, institutional, and industry standing (reputation, previous performance, connections, size) [35, 37]	• Common goals, alignment of interests [37–39, 42, 43] • Compatibility of cultures and motivations of industry and academia [20, 26, 27, 29–31, 35, 38, 40, 43] • Negotiating and establishing agreements, expectations and rights [27, 30, 31, 37–39, 42, 44, 45] • Trust [29, 37–40, 44, 47] • Mutual benefit or perceived value of partnership [29, 39, 43, 44] • Frequency and quality of communication between partners [23, 29, 31, 37, 40, 43, 44] • Different knowledge bases and compatible capabilities [29, 37, 40, 43]	• Policy and legislative setting (legal restrictions, government supports, Health technology assessment organization) [20, 35, 38, 45] • Supportive university/institutional processes and structures (e.g. tech transfer offices, industry liaison offices, REB review process, guidance on conflicts of interest) [20, 23, 29, 35, 38, 39, 42, 45]

Several studies have recommended behaviours that a researcher can employ to increase the likelihood of a successful partnership. For instance, a breakout session among conference participants at the Clinical and Translational Science Awards Industry Forum in 2010 suggested that to be successful, industry-researcher collaborations in the development of diagnostic tests should establish early on agreements on intellectual property (IP), publication, and data sharing [45]. Stewart [44] has suggested that engaging in short term projects when initially engaging with industry will provide an avenue for determining partner compatibility. Frequent face-to-face meetings have been suggested to ensure adequate communication between partners [43, 44].

The literature on the determinants of successful collaborative research remains limited. The research that has been conducted has tended not to focus on collaborative health research. Furthermore, even less is known in the field of rare diseases regarding factors related to the nature of success or lack of success of biotechnology or pharmaceutical academic-industry research collaborations, despite multistakeholder partnerships being proposed as a method to improve rare disease research [48].

1.1e Pediatric Rare Diseases

Before discussing collaborative research in the area of pediatric rare diseases, it is important to first provide some context about pediatric rare diseases and why this area of research is a useful one in which to study collaborative research.

Rare diseases are a group of conditions that individually affect a small number of people in the population. Rare diseases are typically defined based on their prevalence in the population, but specific definitions vary across jurisdictions. In the United States, to be considered a rare disease a condition must affect fewer than 200,000 people in the country [49]. In Europe rare diseases are considered to be those that affect no more than 1 in 2000 people [50]. Richter et al. [51] conducted a systematic review that included a review of rare disease definitions. They found that on average, a rare disease was defined as

having a prevalence of 40 or fewer cases per 100 000 individuals, equivalent to 1 in every 2500 people. Although these diseases are individually rare within the population, thousands of rare diseases have been identified. Nguengang Wakap et al. [52] estimated that rare diseases collectively affect 263–446 million persons globally. Furthermore, rare diseases significantly impact the pediatric population, as approximately 70% of rare diseases have a pediatric age of onset [52]. In Canada, the Canadian Organization for Rare Disorders estimated that rare diseases impact approximately 1 in every 12 Canadians, with children making up two thirds of those affected [53].

Over 90% of rare diseases do not have any available disease-modifying treatments [54]. Some key differences between rare disease research and other clinical/health research are the greater involvement of patient advocacy groups, smaller patient populations, extremely high drug costs, and limited funding for research [55]. The small sample sizes of individuals with rare diseases are an important factor in drug development as clinical trials are often discontinued due to lack of patient accrual [56].

In recent years there has been increasing growth in research in the rare disease space. The orphan drug market has seen a compound annual growth rate of 12%, which is over twice the growth of the non-orphan drug market [1]. The orphan drug market here consists of products given orphan designation by regulatory bodies in the United States, Europe, and Japan; and meet additional criteria EvaluatePharma [1]. Many countries have implemented initiatives to encourage companies to invest in the development of drugs specifically for rare diseases, in recognition of the important unmet needs among patients with rare diseases and the small market for such drugs (due to the inherently small patient populations). These initiatives often include incentives such as: extended market exclusivity, tax credits and reduction in fees [2]. Policies that streamline the regulatory process for rare disease drugs, or that are designed to support decisions about covering the costs of expensive orphan drugs, have also been implemented in some jurisdictions. For example, in March of 2023, the Minister of Health announced $1.5 billion investment into Canada's first National Strategy for Drugs for Rare Disease aiming to increase access and affordability of rare disease drugs [57]. A portion of this investment is allocated to research, with $32 million directed

to CIHR to fund primary research and another $20 million allocated to Canadian Agency for Drugs and Technologies in Health and the Canadian Institute for Health Information to support approaches to the collection and use of real-world evidence needed to inform decisions about access to orphan drugs [58].

In sum, companies engaged in drug development for rare diseases experience unique challenges related to the lower potential for profits, difficulties in accessing high-quality data needed to inform the drug development process, and difficulties with the regulatory process [59]. Denton et al. [48] have suggested that collaborations between industry and academic researchers may be a way to address some of these challenges. Learning about researchers' experiences conducting collaborative research with industry in the pediatric rare disease space as well as identifying the factors that facilitate and/or hinder the success of such collaborations will provide insights for researchers and academia contemplating, or already working, with industry.

1.1f Collaborative Research in Pediatric Rare Diseases

Some academic researchers who have engaged in industry collaborations within pediatric rare disease research settings have published about their experiences, providing some insight into potential characteristics and influences on the success of such collaborations in the rare disease field. For example, Gaillard et al. [60] described a collaboration between industry, academia and patient organizations on research to evaluate a new treatment formulation for the rare disease nephrotic cystinosis which they considered a success due to obtaining market authorization by the regulatory authorities needed to place their product on the market in France. Berry et al. [61] described the interactions with industry experienced by the Urea Cycle Disorders Consortium, an National Institutes of Health funded multi-stakeholder research consortium. Some of the principles that governed these interactions included, for example, transparent and equitable policies and processes, a requirement that interactions must benefit patients and families, establishing agreements surrounding confidentiality and IP, and a commitment that the Consortium would not profit from its research activities [61]. Challenges to collaborations mentioned by Berry et al. [61] were issues of conflict of interest, conflicting confidentiality agreements, and

companies trying to include a small cohort of patients in multiple clinical trials. Additionally, these authors briefly mentioned that differences in motivations between partners and industry could be challenging, even though they shared a common agenda [61]. Mavilio [62] described an alliance between GlaxoSmithKline and a charity-funded Telethon Institute of Gene Therapy; their descriptive paper described the mutual benefits that the partners received by allowing for a cultural exchange. Salkeld [63] also discussed the value of collaborative research in rare disease; commenting that a disadvantage to such collaborations was the time required to create contracts. Further exploration is needed to determine what promotes or hinders the success of potential collaborative relationships between academic researchers and industry in rare disease research specifically given the involvement of patient advocacy groups, smaller patient populations, extremely high drug costs, and limited funding resources in this space [55].

In the literature, establishment of agreements, transparent processes, and differences in motivations are all areas of concern that appear in both the general research related to academic-industry collaborations, and in academic-industry collaboration in pediatric rare disease. Collaborations that benefit patients and consortia ought not profit from research seem to be greatly emphasized in the academic-industry interactions. As there is limited research on academic-industry relationships specific to pediatric rare diseases, we do not know which of the factors that influence the success of relationships in the general research apply to our population or if there are any additional factors influencing their success.

1.2 Summary of Rationale

There has been a growing shift toward collaborative partnerships between industry and academic researchers in the field of biomedical research generally and drug development specifically [1,11]. This shift aligns with the priorities of industry toward “external” approaches to research to reduce risk and increase productivity, and the priorities of public research funders in Canada and elsewhere, presumably to increase the funds available to support health research [12, 13, 18].

Perkmann et al. [19] define collaborative research (as distinct from other types of academic-industry relationships) as “research jointly pursued by university and industry partners, commonly with public funding.” There are no well-established guidelines for successful academic-industry collaborations, but several reviews and studies have identified potentially important factors for researchers to consider (e.g., related to factors that can predispose the development of a collaborative relationship, factors related to the relationship, and other contextual factors that can impact the relationship), which broadly align with principles for research partnerships/co-production more generally [32, 33].

Rare diseases are inherently uncommon individually but collectively impact a large number of individuals, particularly children [52]. In part due to policies and programs implemented by governments in several countries, combined with scientific and technical advances, there has been a large growth in recent decades in the interest of private companies in developing drugs for rare diseases, and the number of such drugs being developed, evaluated, and made available to patients [1].

Similar to the trend for biomedical research as a whole, several authors have recommended that collaborations between industry and academics may be valuable for rare disease research. Some have even argued that such collaborations could help to address some of the specific challenges that are acknowledged as barriers to rare disease drug development (e.g., related to high development costs, lower potential for profit due to small markets, and a scarcity of high-quality data) [55, 59].

Despite this argument that collaborative research may be valuable for pediatric rare disease, there is very limited evidence about what unique challenges and opportunities there may be in this research area, related to academic-industry partnerships. The recommendations of researchers in this area that have published their own experiences with such collaborations seem to echo what we know about academic-industry collaborations in general: that there is a need to study this more systematically.

1.3 Objectives

The overall aims of the thesis were to determine the frequency and nature of the research relationships that Canadian academic or hospital-based pediatric rare disease researchers have with industry, to describe their experiences with collaborative research specifically, and to understand their perceptions of what promotes or hinders the success of such relationships with industry.

To determine the frequency and nature of relationships between researchers and industry, we conducted a cross-sectional online survey study to answer the following research questions:

1) What types of research relationships do Canadian pediatric rare disease researchers have with industry?

2) How common are the different types of relationships with industry?

3) What is the nature of collaborative research being conducted?

4) Are the characteristics and perspectives of researchers related to their experiences of collaborative research with industry?

To describe researchers' experiences with collaborative research and understand their perceptions of what promotes or hinders the success of such research relationships, we conducted a qualitative study to answer the following research questions:

1) How do Canadian pediatric researchers in the field of rare diseases describe their experiences with collaborative research?

2) How do collaborative research projects come about?

3) What makes a successful research collaboration?

4) From a researcher's perspective, what are the perceived advantages and disadvantages of engaging in collaborative research?

5) What tips do researchers have for developing and maintaining positive collaborative research projects?

1.4 Structure of Thesis

This thesis is in a thesis-by-article format. The research was designed as a mixed methods study comprised of a cross-sectional online survey of Canadian pediatric rare disease academic researchers which informed a subsequent qualitative one-on-one interview study of a purposeful subsample of survey participants who had collaborated with industry in the area of pediatric rare diseases. The thesis contains one manuscript prepared for submission to a journal (Chapter 2), presenting the combined results from the mixed methods study. Chapter 3 integrates the findings with current literature, offers suggestions for future pediatric rare disease researchers who may wish to engage in collaborative research relationships with industry, and makes suggestions for future research on collaborative research.

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CHAPTER 2

Preface

Chapter 2 consists of a manuscript titled "Perspectives and experiences of Canadian pediatric rare disease researchers in collaborative research with industry: a mixed methods study" which aims to address all objectives of the study. The research was designed as a mixed methods study comprised of a cross-sectional online survey of Canadian pediatric rare disease academic researchers which informed a subsequent qualitative one-on-one interview study of a purposeful subsample of survey participants who had collaborated with industry in the area of pediatric rare diseases. This manuscript contains an introduction section including background and study objectives. The majority of study methods are presented here within chapter two. Additional methods can be found in the appendix. Relevant appendices will also be noted throughout the article. Results of both the quantitative study and qualitative interviews are presented here followed by a discussion of findings in the context of the literature.

Authors' contributions: CD, IG, and BP conceived of the study and planned the methodology with expert input form KB. CD collected and analyzed the data and drafted the manuscript. CD, IG, BP, and KB contributed to interpreting the data. All authors provided critical feedback and revisions to the manuscript and approved the final version.

Publication: This manuscript has been prepared for submission to *Orphanet Journal of Rare Diseases* and follows the formatting guidelines from this journal. To facilitate reviewing by examiners of this thesis, the version of the manuscript included here includes additional details and is therefore longer than the version that we will eventually submit to the journal.

Ethics: Obtained approval from the University of Ottawa's Research Ethics Board. (Appendix 1)

Title Page

Perspectives and experiences of Canadian pediatric rare disease researchers in collaborative research with industry: a mixed methods study

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Abstract

Introduction: Collaborative research between academic researchers and industry partners may be a strategy to increase research productivity in the field of pediatric rare disease but little is known about how researchers view and experience such collaborations. We aimed to understand research collaborations between pediatric rare disease researchers and industry, what facilitates and hinders the success of these collaborations.

Methods: In this explanatory sequential mixed methods study, we first identified Canadian pediatric rare disease researchers based in academic or hospital settings using literature searches, an environmental scan, and snowball sampling, and invited them to complete a cross-sectional online survey about their experiences in research partnerships with industry. The survey findings informed qualitative semi-structured interviews with a purposeful subsample of survey participants who had collaborated with industry, to understand their perspectives and experiences in greater depth. We analyzed survey data descriptively and interview data thematically. We integrated the quantitative and qualitative findings narratively.

Results: From 126 individuals who completed the survey, we interviewed a subsample of 10 participants. Of the 59 survey participants who reported conducting one or more collaborative research projects with industry partners, 41 reported such experience specifically in pediatric rare diseases. Half of these researchers assigned a rating of 90 or higher to their most recent collaborative experience on a scale of 0 (not positive at all) to 100 (extremely positive). Important benefits to collaborations identified from both the survey and interview findings included access to funding and resources and translation of knowledge. Differences in motivations between academic researchers and industry partners were perceived as important disadvantages or barriers to collaborating. Interviewees provided advice for future researchers to help them engage in successful collaborations, which fell under four categories including: (i) selection of partner/project; (ii) relationship building opportunities; (iii) clear expectations; and (iv) supportive institutional structures.

Conclusion: Collaborations with industry may enhance research in pediatric rare diseases. Our findings provide insights into the experiences and views of pediatric rare disease researchers and offer suggestions on how to conduct successful collaborative research with industry. Research is needed to investigate industry partners' experiences working in collaboration with pediatric rare disease researchers.

Key Words: Collaborative Research, Pediatric Rare Disease, Industry, Partnership, Industry- Academia Relationships

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2.1 Introduction

2.1a Background

There has been an increase in focus in recent decades on rare disease research, as many countries implement strategies or policies to streamline or support the regulatory review and provision of new treatments that are rapidly being developed for these disorders [1–4]. Despite this increased interest and investment, over 90% of rare diseases do not have any available disease-modifying treatment [5]. A number of authors have recognized that challenges to drug development and challenges related research for rare diseases may contribute to this high unmet need among individuals who have rare diseases. These challenges include the lower potential for profits from therapies in a small market, despite US and European policies that incentivize industry investment; difficulties with regulatory processes; and difficulties in generating robust evidence to evaluate treatments [3, 6, 7].

Collaboration between academic researchers and industry partners has been advocated as a means of bolstering research productivity in the field of rare diseases [8], potentially addressing some of the challenges that researchers face. Collaborative research, sometimes called joint research, can be defined as "research jointly pursued by university and industrial partners- commonly with public funding (p.540) [9]." Collaborative research emphasizes the cooperation of industry and academic partners. This distinguishes it from other forms of academic-industry engagement, such as contract research and consulting, which are application-oriented projects typically carried out by academic researchers and funded by industry [9, 10] (Appendix 2). Collaborations between academia and industry can be beneficial and have a positive impact on the movement of drugs into the next phase of the research process and on the success of drug approvals [11, 12]. Additionally, collaborating with industry can create more opportunities for researchers, increase treatment options for patients, be intellectually stimulating, produce higher quality research, and result in financial rewards [13, 14]. However, disadvantages or risks associated with academic collaborations with industry have also been identified, with a major concern being ethical considerations such as conflicts of interest [13].

To the best of our knowledge, there is no formal blueprint or framework in the literature to guide or describe how collaborations between academic researchers and partners in biomedical or pharmaceutical industries should be conducted. However, there have been some suggestions of factors that may influence the success of such collaborations. These include factors predisposing the development of a relationship (e.g., access to resources, geographic proximity of partners, previous experience conducting research, time required to develop relationships, personal characteristics and standing) [10, 13, 15–25], factors related to the relationship itself (e.g., alignment of interests and capabilities, compatibility of cultures and motivations, establishing expectations and agreements, managing confidentiality and conflicts of interest, trust and commitment, perceived value, communication, complementary capabilities) [10, 13, 15–19, 21–24, 26–32], and contextual factors that may impact the relationship (e.g., supportive organizational processes and structures, policy and legislative setting, turnover of industry personnel) [10, 13, 15, 16, 18, 22, 27, 29, 32].

Much of this research into academic-industry relationships does not consider the unique needs of rare disease researchers. The limited research specific to rare diseases indicates that in order to promote successful collaborations between academic and industry partners may need to focus on the establishment of agreements, transparent processes, cultural exchange, collaborations that benefit the patient, and initiatives that do not directly financially profit from research [33–35]. While these factors are similar to those identified for collaborations in health research more broadly, the challenges and unmet needs in the rare disease field underscore the need to more specifically understand research collaborations in this context.

The overall aims of the study were to determine the frequency and nature of the research relationships that Canadian academic or hospital-based pediatric rare disease researchers have with industry, to describe their experiences with collaborative research specifically, and to understand their perceptions of what promotes or hinders the success of such relationships with industry. Investigating how these rare disease researchers consider and experience collaborations with industry partners will

provide insights about challenges and opportunities that may guide researchers to engage in future successful collaborations.

2.1b Study Objectives

To determine the frequency and nature of relationships between researchers and industry, we conducted a cross-sectional online survey study to answer the following research questions:

1) What types of research relationships do Canadian pediatric rare disease researchers have with industry?

2) How common are the different types of relationships with industry?

3) What is the nature of collaborative research being conducted?

4) Are the characteristics and perspectives of researchers related to their experiences of collaborative research with industry?

To describe researchers' experiences with collaborative research and understand their perceptions of what promotes or hinders the success of such research relationships, we conducted a qualitative study to answer the following research questions:

1) How do Canadian pediatric researchers in the field of rare diseases describe their experiences with collaborative research?

2) How do collaborative research projects come about?

3) What makes a successful research collaboration?

4) From a researcher's perspective, what are the perceived advantages and disadvantages of engaging in collaborative research?

5) What tips do researchers have for developing and maintaining positive collaborative research projects?

2.2 Study Methods

2.2a Study Design

We used an explanatory sequential mixed methods research design [36]. In this design, quantitative methods are first implemented, followed by a qualitative component that is informed by and seeks to help to explain the quantitative findings [36]. This mixed method design was appropriate for our study as it allowed the data collection and analysis methods of qualitative and quantitative approaches to be incorporated into one study as neither would be sufficient on their own [37–39]. In our study, the quantitative component was a cross-sectional online survey (administered from March-June 2022); the qualitative component was a set of semi-structured interviews with a subsample of survey respondents (conducted from July-November 2022). The survey included a sample of Canadian pediatric rare disease researchers and was used to determine the frequency and nature of the relationships between researchers and industry, focusing particularly on collaborative research, and researchers' perspectives on advantages and disadvantages of collaborating with industry partners. The survey results informed the subsequent purposive sampling and collection of data for the qualitative interviews, which focused on a subsample of researchers with experience of collaborative research with industry partners in pediatric rare disease, capturing their perceptions of what promotes or hinders the success of such relationships. We report our study here following the Journal Article Reporting for Mixed Methods Article Reporting Standards [40]. (Appendix 3)

2.2b Quantitative Survey Methods

Survey Sample

The target population for the survey was Canadian academic or hospital-based researchers with an interest in pediatric rare diseases. As there is no existing sample frame for this population, we had to develop one using three methods: 1) We conducted a formal search of the literature to identify and extract contact information for corresponding authors with Canadian affiliations from studies related to rare diseases in pediatrics published between 2019 and 2021, assisted by a health sciences librarian and

using the SCOPUS database (Appendix 4); 2) We conducted an environmental scan of websites from Canadian rare disease pediatric groups, networks, and organizations (extracting researcher names and affiliations from public information), identified by research team members and by informal web searching; and 3) We used snowball sampling methods, asking survey participants to identify names of other pediatric rare disease researchers they believed may be eligible for the survey.

Survey Recruitment and Administration

We were guided by Dillman et al.'s [41] tailored design method for administering internet surveys. All potential participants from the sampling frame were contacted by personal email to invite their participation (sample correspondence, Appendix 5). The email invitation contained information describing the study, the estimated time commitment for survey completion, the link to the survey, and C.D.'s contact information. We sent up to five reminder emails to non-responders: one reminder three days after the initial invitation and subsequent reminders approximately a week apart.

Survey Data Collection

Participants were asked to complete a single (one-time) online questionnaire through SurveyMonkey (Appendix 6). Participants were screened in the initial questions of the survey to determine eligibility: we asked whether they had an interest in the field of pediatric rare disease research, were an independent researcher (defined as a researcher with autonomy regarding their research activities), had an academic institution or hospital research institute or other research organization appointment, and were eligible to receive peer-reviewed grant funding. If the participant answered no to any of these questions, they were considered ineligible, received a thank you message and were removed from the sample. After confirming eligibility, participants were taken to the remaining survey questions, which were aligned with the study objectives and informed by previous literature.

The questionnaire was developed by C.D., I.G., B.P. and reviewed by the research team. Beyond the screening questions described above, the questionnaire included sections covering professional characteristics, industry-researcher relationships, pediatric rare disease collaborative research, project

characteristics, interest in future collaborations with industry, advantages/benefits and disadvantages/barriers to collaboration, and demographic characteristics. The survey included closed-ended questions (e.g., multiple choice, yes/no), and open-ended short answer questions. We asked participants about their experience with research projects involving any of the industry-research relationships outlined in a taxonomy provided by Perkmann et al. [9], including the number of research projects within each type of relationship. Participants who indicated that they had experience as an investigator in at least one previous collaborative research project with industry in the field of pediatric rare disease answered more detailed questions about their experience with their most recent such project. All participants were asked about the extent to which they agreed or disagreed on a 5-point Likert scale (strongly disagree to strongly agree) with seven potential advantages/benefits and seven potential disadvantages/barriers to collaborating with industry; and whether they would consider future collaborative relationships. Finally, we asked a series of demographic questions and closed the survey by asking participants if they would be willing to participate in a follow-up interview.

Survey Data Analysis

We analyzed survey data using R version 4.0.3. Questionnaire data from individuals who did not complete at least 50% of the survey were removed and these individuals were considered non-respondents. All questions were analyzed descriptively using frequency tables with proportions for categorical variables and means with standard deviations and/or medians with lower and upper quartiles for continuous variables. We presented descriptive findings in graphical format when appropriate. Demographic data and data characterizing participants' ratings of advantages and disadvantages of research collaborations with industry were stratified by self-reported participation in such collaborations. For demographic data we used standardized differences (effect sizes between groups [42]) to compare differences between groups stratified by self-reported participation in collaborations with industry. However, no statistical hypothesis tests were conducted in this descriptive analysis given that we had no a priori hypotheses about differences between groups.

2.2c Qualitative Interview Methods

Interview Sample and Recruitment

Individuals were selected for interviews using purposive sampling from the survey respondents who agreed to be contacted for this purpose; we were specifically interested in interviewing researchers who indicated that they had collaborative research experience with industry in pediatric rare diseases. The email invitation for the interviews explained the purpose of the study and expectations, and included the consent form and C.D's contact information (sample correspondence, Appendix 7). A total of 3 emails were sent to individuals inviting them to participate in an interview.

Interview Data Collection

The interviews were guided by interpretive description concepts [43] with the purpose of capturing themes and patterns of what makes an excellent collaborative research relationship with industry. Thorne et al. [43] defined the foundation of interpretive description as the "investigation of a clinical phenomenon of interest to the discipline for the purpose of capturing themes and patterns within subjective perceptions and generating an interpretive description capable of informing clinical understanding (p.5)." This method allowed us to describe and interpret the phenomenon of collaborative research with industry through the shared experiences of researchers; we aimed to generate findings that can be used to promote the success of future research collaborations [44].

The interviews were semi-structured and were informed by the survey responses. Prior to initiating the main interview questions, the interviewer (C.D.) reviewed the taxonomy of industry-research relationships by Perkmann et al. [9] to highlight the definition of collaborative research relationships with industry as the topic for the remainder of the interview. The Interview guide (Appendix 8) included questions asking participants to describe their collaborative research experience with industry in general, any particularly positive or negative experiences they might have had, their perceptions about advantages/ disadvantages of collaborative research (informed by their individual responses to the survey questions on these topics), additional information about their last collaboration with industry, what

defines a successful collaborative research project and any tips they may have for those wishing to conduct successful collaborations with industry. Interviews were conducted by C.D. using Zoom. Each interview lasted approximately 45 minutes. Sessions were audio recorded and transcribed verbatim, with initial transcription by Zoom's automated program and verification by C.D. to ensure accuracy. Transcripts were de-identified prior to analysis.

Interview Data Analysis

We followed the thematic analysis process described by Braun & Clarke [45]. Given our interpretive description approach, there were no pre-existing codes and C.D. inductively created codes from the data [46]. The transcripts were read and re-read by C.D., with initial impressions and notes taken. I.G. and B.P. also read each transcript and added notes. To create themes and subthemes, initial codes were created by C.D and reviewed by the I.G and B.P. Initial subthemes or themes were then presented and discussed by C.D, I.G and B.P. Refined subthemes and themes were presented to the entire research team to ensure applicability and credibility. (Appendix 9).

Strategies to Ensure Methodological Rigor

Strategies to ensure rigor and trustworthiness included triangulation of data by integrating different data sources [47], producing a thick description of collaborative research from the perspectives of academic/hospital-based researchers [47], seeking and receiving research ethics board approval [47], and declaration of the position of the researchers [47]. C.D was also the interviewer and the transcriber to avoid transcription error [48], and transcripts were verified, read and re-read with initial impressions and notes taken. Team members with different disciplinary perspectives and experiences participated in the analysis and interpretation of the findings.

2.2d Integration of Methods

We integrated the quantitative and qualitative findings using a connecting and building approach [36]. Quantitative and qualitative aspects of the study were linked through the sampling frame where the sample for the interviewees was generated from survey respondents. The survey findings also informed

interview content by identifying key areas for further exploration with researchers and we asked interviewees to expand on their specific responses from the survey. Integration at the interpretation and reporting level was done through a narrative approach by weaving both the quantitative and qualitative on a theme-by-theme basis into a single report [36].

2.2e Ethical Considerations

This study was reviewed and approved by the University of Ottawa's Research Ethics Board (Appendix 1). The survey and interviews were conducted in English. Consent for survey participants was obtained by their indication to consent using a checkbox on the first page of the survey. Interviewees provided written informed consent.

2.2f Reflexivity of Authors

C.D was the primary investigator on this project as part of her MSc in Epidemiology thesis project at the University of Ottawa. All of the researchers we surveyed and interviewed were aware of this as part of the consent process. C.D works for an industry consultant where her primary role was to conduct desk market research on key opinion leaders. Ian Graham was the supervisor of this project and is the Director of the IKTRN, a Senior Scientist in the Clinical Epidemiology Program of the Ottawa Hospital Research Institute and Distinguished Professor in the School of Epidemiology and Public Health at the University of Ottawa. He is interested in understanding how engaging stakeholders in the research process works and the impact it produces. Beth Potter was a co-supervisor on this project. She leads a research network in the field of pediatric rare diseases and is a Professor in the School of Epidemiology and Public Health at the University of Ottawa. She is interested in generating evidence to improve health care and outcomes for children with rare genetic diseases and has had previous experience conducting collaborative research with industry. Kym Boycott is a leader of Canada's national genome-wide sequencing platform for rare disease, Care4Rare Canada, a Medical Geneticist at the Children's Hospital of Eastern Ontario (CHEO), Chair of the Department of Genetics (CHEO) Senior Scientist at the CHEO Research Institute, and Professor

of Pediatrics at the University of Ottawa. She has conducted collaborative research with industry in the area of rare pediatric diseases.

2.3 Results

2.3a Participant Characteristics

Survey Participant Characteristics

After removing duplicates, invalid or bounced emails, we distributed the survey invitation to 679 individuals by email. Of these, 58 individuals did not meet the eligibility criteria for completing the survey, 34 declined to participate, and 461 were non-respondents. A total of 126 individuals who identified as being independent researchers with an interest in pediatric rare diseases were included in the survey analysis, representing a response rate of 20% (126/621) (Appendix 4). The average time to complete the survey was 7 minutes.

Survey participant characteristics are shown in Table 1, for the overall sample and stratified by self-reported participation in collaborative research with industry based on Perkmann et al's [9] researcher-industry relationship taxonomy. Participants were distributed across Canada, with the highest proportions residing in Ontario (38%) or Alberta (22%). Approximately 79% were aged 45 years or older, 61% self-identified as a man or male, and 20% identified as a racialized person. Most participants had either a professional degree or had earned a doctorate. The sample was distributed across workplace settings with 36% based primarily in a hospital setting, 28% based at a hospital-based research institute and 29% at a university. A variety of positions were held by the researchers, with professors of all ranks (98%), clinicians (67%), and industry consultants (21%) among the most widely endorsed roles (not mutually exclusive). The majority of participants had eleven or more years of experience as an independent researcher (62%) and on average dedicated 46% (sd: 26) of their time to research. The most common types of research that participants reported conducting were clinical (52%) and biomedical (49%). Sixty-eight percent of survey respondents reported receiving a pediatric rare disease research grant in the last 5 years.

Table. 1 Characteristics of Survey Participants, Overall and Stratified by Self-Reported Experience of Collaborative Research with Industry *(n=126)*

	Overall n=126 n (%)	Collaborative Research Experience n=59 n (%)	No Collaborative Research Experience[a] n=67 n (%)	Standardized Differences n=126
Province/ Region of Residence				0.345
British Columbia	10 (8.3%)	6 (10.7%)	4 (6.2%)	
Alberta	26 (21.7%)	12 (21.4%)	14 (21.9%)	
Saskatchewan	4 (3.3%)	2 (3.6%)	2 (3.1%)	
Manitoba	8 (6.7%)	3 (5.4%)	5 (7.8%)	
Ontario	45 (37.5%)	18 (32.1%)	27 (42.2%)	
Quebec	20 (16.7%)	11 (19.6%)	9 (14.1%)	
Atlantic Canada	6 (5%)	3 (5.4%)	3 (4.7%)	
Outside of Canada	1 (0.8%)	1 (1.8%)	0 (0%)	
Prefer not to answer/ missing	6	3	2	
Age				0.417
35-44 years old	25 (21%)	9 (16.3%)	16 (25%)	
45-54 years old	49 (41.2%)	20 (36.4%)	29 (45.3%)	
55-64 years old	32 (26.9%)	17 (31%)	15 (23.4%)	
65 years or older	13 (10.9%)	9 (16.3%)	4 (6.3%)	
Prefer not to answer/ missing	7	4	3	
Gender or Sex[b]				0.319
Woman or Female[c]	43 (39.1%)	15 (30.6%)	28 (45.9%)	
Man or Male[d]	67 (60.9%)	34 (69.3%)	33 (54.1%)	
Prefer not to answer/ missing /non-valid response	16	10	6	
Racialized Persons				0.231
Yes	23 (20%)	8 (15.1%)	15 (24.2%)	
No	92 (80%)	45 (84.9%)	47 (75.8%)	
Prefer not to answer/ missing	11	6	5	
Education				0.538
Bachelor's Degree or below	2 (1.6%)	1 (1.7%)	1 (1.5%)	
Professional Degree (e.g., medicine, dentistry, law)	72 (58.5%)	31 (53.5%)	41 (63.1%)	
Master's Degree	4 (3.3%)	0 (0%)	4 (6.2%)	
Earned Doctorate	45 (36.6%)	26 (44.8%)	19 (29.2%)	
Prefer not to answer/ missing	3	1	2	
Primary Workplace Setting				0.049
Hospital	45 (35.7%)	21 (35.6%)	24 (35.8%)	
Hospital-Based Research Institute	35 (27.8%)	17 (28.8%)	18 (26.9%)	
University	38 (29.4%)	17 (28.8%)	20 (29.9%)	
Other (e.g., Private Clinic, Academic Hospital)	9 (7.1%)	4 (6.8%)	5 (7.5%)	
Positions (select all that apply)				
Professor (all ranks)	123 (97.6%)	57 (96.6%)	66 (98.5%)	0.123
Clinician	84 (66.7%)	39 (66.1%)	45 (67.2%)	0.023
Department Head (e.g., hospital, university)	14 (11.1%)	7 (11.9%)	7 (10.4%)	0.045
Industry Consultant	26 (20.6%)	16 (27.1%)	10 (14.9%)	0.303
Executive of Professional Organization/Society	12 (9.5%)	8 (13.6%)	4 (6%)	0.258
Government Advisor/Consultant	17 (13.5%)	13 (22%)	4 (6%)	0.476
Patient Organization Advisor/Consultant	23 (18.3%)	15 (25.4%)	8 (11.9%)	0.351

	Overall n=126 n (%)	Collaborative Research Experience n=59 n (%)	No Collaborative Research Experience[a] n=67 n (%)	Standardized Differences n=126
Other (e.g., Manager, Entrepreneur, Medical Director)	18 (14.3%)	9 (15.3%)	9 (13.4%)	0.052
Years Worked as Independent Researcher				0.553
Less than 1	1 (0.8%)	0 (0%)	1 (1.5%)	
1-3	9 (7.1%)	3 (5.1%)	6 (9%)	
4-5	9 (7.1%)	1 (1.7%)	8 (11.9%)	
6-10	29 (23%)	12 (20.3%)	17 (25.4%)	
11+	82 (61.9%)	43 (72.9%)	35 (52.2%)	
Percentage Time Dedicated to Research (0-100)				0.525
Mean (SD)	46.1 (26.0)	53 (26.1)	39.8 (24.5)	
Median (Q1, Q3)[e]	50 (20,75)	50 (31,75)	30 (20,50)	
Prefer not to answer/ missing	1	0	1	
Primary Research Type				0.284
Biomedical	50 (39.7%)	26 (44.1%)	24 (35.8%)	
Clinical	66 (52.4%)	28 (47.5%)	38 (56.7%)	
Health Systems and Services	6 (4.8%)	3 (5.1%)	3 (4.5%)	
Social, Cultural, Environmental and Population Health	1 (0.8%)	0 (0%)	1 (1.5%)	
Other (e.g. all of the above, clinical and biomedical)	3 (2.4%)	2 (3.4%)	1 (1.5%)	
Pediatric Rare Disease Research Grant, Last 5 Years				0.027
Yes	84 (68.3%)	40 (69%)	44 (67.7%)	
No	39 (31.7%)	18 (31%)	21 (32.3%)	
Prefer not to answer/ missing	3	1	2	

[a] no collaborative research: all participants who reported 0 collaborative research projects with industry (n=52) or who did not respond to the survey question asking how many collaborative research projects they had contributed to with industry (n=15)
[b] question asked to participants: How would you describe your current gender identity? By gender, we mean your self-identified gender, which may differ from the sex assigned at birth or from the one entered in legal documents; many participants responded with their sex (male, female, intersex) instead of their gender identity (woman, man, non-binary, etc.) and thus we have labelled this variable "gender or sex" here
[c] includes responses of female, women, she/her
[d] includes responses of male, man, cis male, m, male with additional descriptors
[e] Q1= Quartile 1 (25th percentile); Q2=Quartile 3 (75th percentile)

Survey Participants' Frequency and Types of Relationships with Industry

Survey participants were asked how many research projects they had contributed to within each type of academic-industry relationship from the taxonomy [9]. Ninety-two participants (75%) reported contributing to at least one research project involving any of these industry relationships, with 27 individuals reporting having contributed to at least one project in a licensing relationship, 29 to an academic entrepreneurship project, 59 to a collaborative research project, 56 to a contract research project, and 51 to consulting (Table 2). Of the 59 participants reporting at least one collaborative research project with industry, 31 indicated contributing to 1-3 such projects, 17 contributed to 3-6 projects, 6

contributed to 6-9 projects and 5 contributed to 10+ projects (Table 2). Of these same 59 respondents who reported collaborative research relationships, 41 reported collaborative research experience with industry in pediatric rare disease specifically (not shown).

When we stratified survey participant characteristics by self-reported collaborative research experience (Table 1, no statistical hypothesis tests conducted), among the 59 who did have collaborative experience with industry relative to those who did not report such experience (n=67), higher proportions did not reside in Ontario (33.1% vs 42.2%, standardized difference for province: 0.345); were aged 65 years or older (16% vs 6%, standardized difference for age: 0.417); self-identified as a man or male (69% vs 54%, standardized difference for gender: 0.319); reported a role as an industry consultant (27% vs 15%, standardized difference: 0.303), executive of a professional society or organization (14% vs 6%, standardized difference: 0.258), government advisor or consultant (22% vs 6%, standardized difference: 0.476), or patient organization advisor or consultant (25% vs 12%, standardized difference: 0.351); had an earned doctorate (45% vs 29%, standardized difference for education: 0.538); reported their primary research type as biomedical (44.1% vs 35.8%, standardized difference for primary research type: 0.284) and reported eleven or more years of independent research experience (73% vs 52%, standardized difference for independent research experience: 0.553). In addition, those reporting collaborative research experience with industry reported a higher median proportion of time dedicated to research than those without such experience (50% vs 30%, standardized difference for time dedicated to research: 0.525).

Table. 2 Frequency of projects by academic-industry relationship for survey respondents *(n=126)*

	Overall n=126 n (%)	**Collaborative Research Experience n=59** n (%)	**No Collaborative Research Experience[a] n=67** n (%)
Any Relationship			
Yes	92 (74.8%)	59 (100%)	33 (51.6%)
No[b]	31 (25.2%)	-	31 (48.4%)
Prefer not to answer/missing	3	-	3

Licensing			
0	84 (75.7%)	38 (67.9%)	46 (83.6%)
1-3	22 (19.8%)	13 (23.2%)	9 (16.4%)
3-6	1 (0.9%)	1 (1.8%)	0 (0%)
6-9	3 (2.7%)	3 (5.3%)	0 (0%)
10+	1 (0.9%)	1 (1.8%)	0 (0%)
Prefer not to answer/missing	15	3	12
Academic entrepreneurship			
0	78 (72.9%)	31 (57.4%)	47 (88.7%)
1-3	21 (19.6%)	17 (31.5%)	4 (7.5%)
3-6	5 (4.7%)	4 (7.4%)	1 (1.9%)
6-9	2 (1.9%)	1 (1.85%)	1 (1.9%)
10+	1 (0.9%)	1 (1.85%)	0 (0%)
Prefer not to answer/missing	19	5	14
Collaborative research			
0	52 (46.9%)	0 (0%)	52 (100%)
1-3	31 (27.9%)	31 (52.5%)	0 (0%)
3-6	17 (15.3%)	17 (28.8%)	0 (0%)
6-9	6 (5.4%)	6 (10.2%)	0 (0%)
10+	5 (4.5%)	5 (8.5%)	0 (0%)
Prefer not to answer/missing	15	0	15
Contract research			
0	60 (51.7%)	19 (34.55%)	41 (67.2%)
1-3	35 (30.2%)	19 (34.55%)	16 (26.2%)
3-6	14 (12.1%)	11 (20%)	3 (5%)
6-9	5 (4.3%)	4 (7.3%)	1 (1.6%)
10+	2 (1.7%)	2 (3.6%)	0 (0%)
Prefer not to answer/missing	10	4	6
Consulting			
0	59 (53.6%)	17 (30.9%)	42 (76.4%)
1-3	24 (21.8%)	16 (29.1%)	8 (14.5%)
3-6	14 (12.7%)	11 (20%)	3 (5.5%)
6-9	8 (7.3%)	6 (10.9%)	2 (3.6%)
10+	5 (4.6%)	5 (9.1%)	0 (0%)
Prefer not to answer/ missing	16	4	12

[a] In further analyses, participants who answered 0 (n=52) or who did not respond to the survey question about the number of collaborative research projects they conducted with industry (n=15) were considered to have no such collaborative research experience

[b] Participants who answered 0 to all types of relationships (n=29) or who did not respond to the survey question about the number of projects they had conducted with industry but had indicated no participation in any relationship with industry on a previous question (n=2) were considered to have no experience

Interviewee Characteristics

Of those surveyed, 41 individuals agreed to participate in a follow-up interview. Of these, 16 reported having participated in collaborative research with industry in pediatric rare disease research, 15 of whom provided valid email addresses and were invited to participate. Ten interviews were conducted, representing an interview participation rate of 66%.

Interviewee characteristics are shown in Table 3. Interviewees resided in British Columbia (1), Alberta (2), Manitoba (1), Ontario (3) and Quebec (3). All were over the age of 45, 7 self-identified as a

man or male, 2 self-identified as a racialized person, half had a professional degree and half had earned a doctorate. The primary workplace setting of interviewees included hospitals (30%), hospital-based research institutes (30%), and universities (40%). A variety of positions were held by those we interviewed, for example professors at all ranks (100%), clinicians (50%), industry consultants (40%), and patient organization advisors or consultants (40%). All had worked at least 6 years as an independent researcher. The interviewees dedicated a median of 69% (Quartile 1: 50, Quartile 3: 75) of their time to research. Seven conducted their primary research in the biomedical field, two in the clinical field and one in the health systems and services field. All had received a grant in the last five years to study pediatric rare disease. Among those interviewed, from their survey responses, four interviewees reported contributing to 1-3 collaborative projects with industry, four interviewees 3-6 projects and two interviewees 10+ projects.

Table. 3 Characteristics of Interview Participants *(n=10)*

	n (%)
Province/ Region of Residence	
British Columbia	1 (10%)
Alberta	2 (20%)
Manitoba	1 (10%)
Ontario	3 (30%)
Quebec	3 (30%)
Age	
45-54 years old	1 (11.1%)
55-64 years old	6 (66.7%)
65 years or older	2 (22.2%)
Prefer not to answer/ missing	1
Gender or Sex[a]	
Woman or Female[b]	3 (30%)
Man or Male[c]	7 (70%)
Racialized Persons	
Yes	2 (22.2%)
No	7 (77.8%)
Prefer not to answer	1
Education	
Professional Degree (e.g., medicine, dentistry, law)	5 (50%)
Earned Doctorate	5 (50%)
Primary Workplace Setting	
Hospital	3 (30%)
Hospital-Based Research Institute	3 (30%)
University	4 (40%)
Positions (select all that apply)	
Professor (all ranks)	10 (100%)

Clinician	5 (50%)
Department Head (e.g., hospital, university)	2 (20%)
Industry Consultant	4 (40%)
Executive of Professional Organization/Society	2 (20%)
Government Advisor/Consultant	3 (30%)
Patient Organization Advisor/Consultant	4 (40%)
Other (e.g., Manager, Entrepreneur, Medical Director.)	4 (40%)
Years Worked as Independent Researcher	
6-10	1 (10%)
11+	9 (90%)
Percentage Time Dedicated to Research (0-100): Median (Q1, Q3)[d]	69.0 (50,75)
Primary Research Type	
Biomedical	7 (70%)
Clinical	2 (20%)
Health Systems and Services	1 (10%)
Pediatric Rare Disease Research Grant in the Last 5 Years: Yes	10 (100%)
Number of Collaborative Research Projects	
1-3	4 (40%)
3-6	4 (40%)
10+	2 (20%)

[a] question asked: How would you describe your current gender identity? By gender, we mean your self-identified gender, which may differ from the sex assigned at birth or from the one entered in legal documents; we have labelled this variable "gender or sex" here

[b] includes responses of female, women, she/her

[c] includes responses of male, man, cis male, m, male with additional descriptors

[d] Q1= Quartile 1 (25th percentile); Q2=Quartile 3 (75th percentile)

2.3b Overall Experience, Nature of Collaborations and Initiation of Collaborations with Industry

Overall Experience and Satisfaction with Industry Collaborations

Survey participants who reported that they had collaborative experience with industry on a pediatric rare disease research project (n=41) were asked to rate their experience on their last such collaborative project on a scale from 0 to 100, where 0 was not positive at all and 100 was extremely positive. The median score was 90 (Quartile 1: 70, Quartile 3: 96)(Figure 1). All but three individuals assigned a score of 50 or above; 8 participants out of 41 responding to the question gave their experience a score of 100.

We also asked interviewees to share their experiences collaborating with industry; they collectively described a range of positive, negative, and mixed experiences.

> *"Well on a very high level it's been for me probably one of the most productive, meaningful aspects of my academic research and clinical career...I think for me my interactions with industry were irreplaceable I don't think I would have accomplished as much academically or now in the biotech translational world and the development of a small company that's in the diagnostic business just would not have gone there without meaningful interaction with industry."(5966)*
>
> *"So honestly this was a very challenging experience mostly...because of the paperwork that we have to do inside the University and getting the MTA [Material Transfer Agreement] agreement...but to be honest the industry side was much more collaborative than the University side" (6401)*
>
> *"I could easily rate the companies I deal with on a scale of one to ten and there would be some ones and there'd be some tens in there. So, my experience has been very mixed." (1763)*

Despite the variation in their specific experiences, in general most interviewees described collaborating with industry as a win-win that advantages both the researcher and the industry partner.

> *"So all in all it was a very very productive collaboration...it was a balanced sort of quid pro quo where we each got sort of what we were looking for." (6189)*

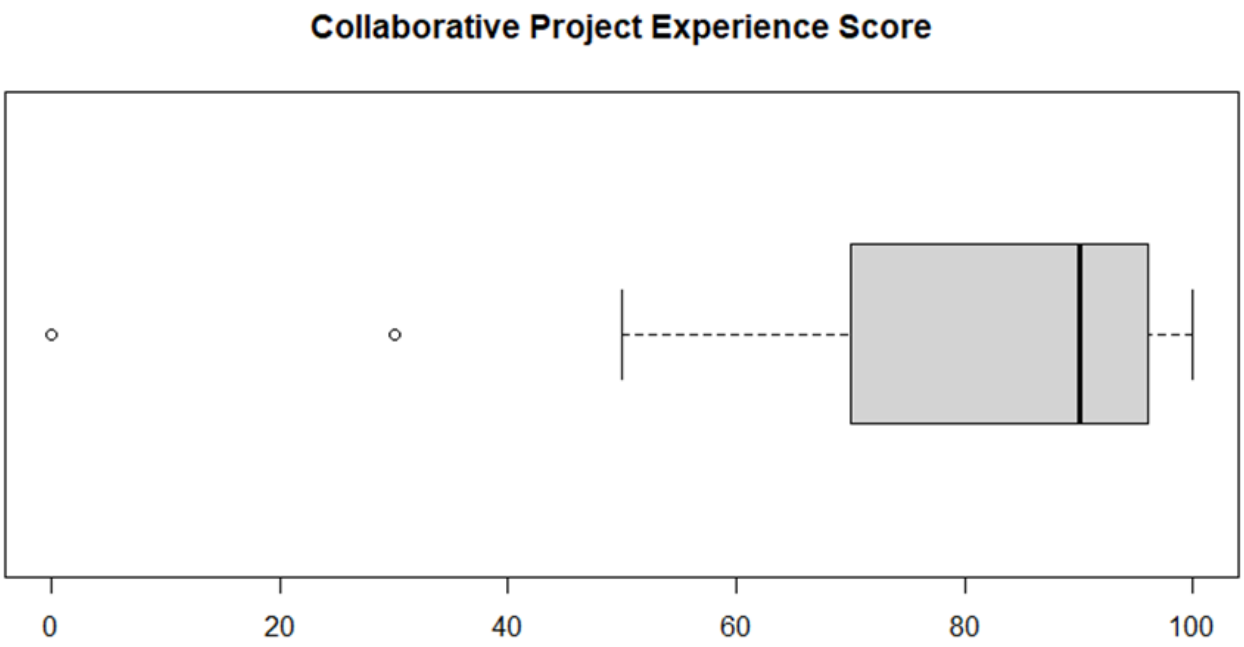

Figure 1. Collaborative Project Experience Scores *(n=41)*
Among survey participants who had experience collaborating on pediatric rare disease research projects with industry, distribution of satisfaction ratings (from 0 as least positive to 100 as most positive) for their most recent experience. The box shows the interquartile range (IQR), the dark line within the box displays the median value, the "whiskers" indicate the range of points within IQR x1.5 from the median, and the individual points are individual ratings that fell outside the whiskers.

Nature of Collaborative Projects, Including Involvement of Researchers and Industry Partners

Survey participants who had a collaborative relationship with industry on at least one pediatric rare disease research project were asked about the characteristics of their most recent such project (Table 4). Collaborative projects were reported to be most commonly in biomedical (42%) and clinical (42%) fields; and funded in part or fully by industry (63%), government-based research funders (46%), or academic institutions (32%). Industry partners were most often from the pharmaceutical (61%) and/or biotechnology (34%) sectors. Over 60% of respondents reported that they themselves participated in all phases of the research project, with the exceptions of developing or applying for resources (54%) and the development of the dissemination process (49%). However, respondents reported much smaller proportions of industry partners participating in each aspect of the research; the only aspects of the study

to which at least 50% of respondents reported the industry partner having contributed were developing the study agenda (56%), refinement of the research question (56%) and developing or applying for resources (51%). From responses to an open-ended question, 15% of survey participants commented on other aspects to which their industry partner contributed that were not listed in the response choices provided, for example, managing the drug approval process.

Interviewees also discussed their, and their industry partners', level of participation in one or more collaborative research projects. About half of the interviewees described industry partners' general involvement in projects as "hands-off" or separate from the actual research being done. In many of these cases, there was a separation of roles where the researcher acted as the scientist doing the experiment or trial, and the industry partner acted as the funder or as the expert in moving the product through the approval or regulatory steps.

> *"Investigator initiated but industry funded projects which the industry partners were hands off in the sense that they didn't tell me what to do or how to do it but we reported back to them frequently and they had a great interest in what we were doing" (2595)*

The remaining researchers we interviewed described varying degrees of industry participation in their collaborative research projects where some described the industry partner as involved "right off the bat" in multiple aspects of the research, some noted instances where industry acted as a scientific advisor for the research, and some indicated that the degree of industry partner involvement was project dependent.

> *"The products that we create eventually some of them right off the bat we're doing in partnership with let's say firms that really know about website design app development" (0606)*

Table. 4 Survey Participants' Descriptions of a Most Recent Collaborative Research Project with Industry *(n=41)*

	n (%)
Research Project Category	
Biomedical	17 (41.5%)
Clinical	17 (41.5%)
Health systems and services	5 (12.2%)

Other (diagnostic biomarkers, efficacy and drug side effects)	2 (4.9%)
Funding (check all that apply)	
Academic Institution	13 (31.7%)
Government Research Funding Agency	19 (46.3%)
Government Department	3 (7.3%)
Health Charity	9 (22.0%)
Patient Group	6 (14.6%)
Private Industry	26 (63.4%)
Other (e.g., venture capital)	2 (4.9%)
Industry Partner Sector (check all that apply)	
Healthcare Equipment and Supplies	1 (2.4%)
Health Provider Services	2 (4.9%)
Health Technology	6 (14.6%)
Biotechnology	14 (34.1%)
Life Science Tools and Services	5 (12.2%)
Pharmaceuticals	25 (61.0%)
Other (clinical trial, in vitro diagnostics, none)	3 (7.3%)
Survey Participant's Contributions to the Project (check all that apply)	
Idea Generation	30 (73.2%)
Study Agenda: scope, priorities, objective(s)	26 (63.4%)
Refinement of Research Question	32 (78.0%)
Design of Study Methodology (approach)	30 (73.2%)
Design of Methods (e.g., selection of outcome measures)	30 (73.2%)
Develop/Apply for Resources (e.g., funding applications/grant proposals)	22 (53.7%)
Research Ethics Board Review	27 (65.9%)
Data Collection	34 (82.9%)
Data Analysis	29 (70.7%)
Development Dissemination Process	20 (48.8%)
Dissemination of Findings	30 (73.2%)
Reporting of Findings (e.g., article, report, conference presentation)	33 (80.5%)
Other (beta testing biomarkers)	1 (2.4%)
Industry Partner's Contributions to the Project (check all that apply)	
Idea Generation	17 (41.5%)
Study Agenda: scope, priorities, objective(s)	23 (56.1%)
Refinement of Research Question	23 (56.1%)
Design of Study Methodology (approach)	19 (46.3%)
Design of Methods (e.g., selection of outcome measures)	16 (39.0%)
Develop/Apply for Resources (e.g., funding applications/grant proposals)	21 (51.2%)
Research Ethics Board Review	3 (7.3%)
Data Collection	8 (19.5%)
Data Analysis	15 (36.6%)
Develop Dissemination Process	11 (26.8%)
Dissemination of Findings	18 (43.9%)
Reporting of Findings (e.g., article, report, conference presentation)	16 (39.0%)
None of the above	3 (7.3%)
Other (e.g., funding, supply of drug, approval processes)	6 (14.6%)
Collaboration Initiation	
Researcher	21 (51.2%)
Industry partner	10 (24.4%)
Researcher and Industry Jointly	9 (22.0%)
Other (expectation from government funded was that there would be industry partners)	1 (2.4%)

Initiation of Collaborations

Survey participants who self-identified as having previously participated in collaborative pediatric rare disease research with industry were also asked about who initiated their most recent collaborative project (Table 4): most were initiated by the researcher (51%), with a smaller proportion initiated by the industry partner (24%), or the researcher and industry partner together (22%). Similar to the survey, interviewees reported partnerships with industry initiated by the researcher, industry or jointly. When discussing researcher-initiated collaborations, the interviewees mentioned that they would begin communications through applications to the company, industry-sponsored peer review grant application cycles, or by reaching out to the companies directly.

> *"We talked to them and we'd say 'we've got this project are you interested in hearing about it?' They say "sure" you know it doesn't hurt to send in an application and we send in an application, and they turn around and say "yep this is something we can support" and it happens very easily and quickly, and often I can talk to senior people in the company about that." (1763)*

Industry-initiated collaborations were often perceived as arising due to the researcher's reputation as an expert.

> *"Biotech already have maybe seen a publication or seen something you've done and then they think ohh I have a tasty drug that maybe could be used towards that. I wonder could you test it in your system, to see if that works." (3001)*

> *"I would say as a general rule these companies do their homework. They will seek out the expert in the community, so in my area I guess it's based on your know your publication record based on attending meetings, based on your specialty and they send a lot of probes and what they do is they make you know advisory boards which is a kind of disguised way to pay you money to listen to them...but we've been using that a lot for giving...[our] patients access to these drugs." (2656)*

Participants suggested that the type of industry and how well-known a researcher is may be factors influencing who initiates the collaborative relationship.

> *"If we're trying to touch [base] with the pharmaceutical it's usually us to go out after them but for the biotech they come after us, is typically what I'm seeing." (3001)*

> *"As a younger person when I was less well known in the kind of research that I do it would be me looking for potential research partners in industry...As I've got a little bit more senior and a little better known in some of these fields every now and then you'll be working with folks I just knew in the industry often academics who then went over to industry...and say you know our company is really interested in this...kind of research I know you're interested in we'd love to support you if you have a project in mind." (2595)*

In the interviews, most participants discussed multiple collaborative experiences with industry and with different types of initiations. Whether a relationship was initiated by the industry partner, the researcher, or together, common themes we identified from the interviewees' descriptions of how these collaborative projects began included shared interests aligning, and previous relationships that facilitated continued interactions.

> *"And this happens a lot right in this kind of relationship, is [that] we would apply for a grant with a research question in mind then the industry partner would say that's aligned with our interest we'd like to fund your research." (2595)*

> *"Where I had relationships [a previous relationship] with industry that said 'okay we have discovered this novel biomarker you know are you interested or not?' and invariably they would say 'we will look at it and evaluate it' and so if they became interest[ed] then they moved it through the regulatory hurdles where they had the expertise....And so in doing that that became sort of the lead in for my collaboration and consultation...with industry because invariably they would have somebody else or some other organization come to them with a unique innovative diagnostic or therapeutic and they then knew of my expertise in the area and asked me to serve as a consultant for them over the years" (5966)*

Additionally, third parties sometimes facilitated collaborative relationships. The researchers reported that occasionally they had colleagues or personal connections who were already involved in a project, had previously worked with a company, or now worked in industry themselves, aiding the industry partner and the researcher in forming a collaborative relationship. Other organizations like patient groups, granting agencies and research support organizations also assisted in creating collaborative research relationships.

> *"One of the physicians who had already been involved with them right from the beginning had said 'Listen if you really want to push this forward you need to contact me' because he himself doesn't have information." (0606)*

> *"We were looking for other opportunities for this research...I was approached by [Research Organization 1] to continue this work and to develop a pilot project with a company that could help us get pilot data for a potential [Research Organization 1] competition looking at personalized medicine for different disorders" (6189)*

When asked about why they chose a collaborative approach when forming a relationship with industry, interviewees provided a variety of reasons including greater opportunities for success, the only possible approach due to patented compounds or funding needs, seeing the value of the project, and development and improvement of the drug.

"They have a patent on this compound and it is the only way that I could approach and I have funding from [the] University on this project right and this is the only way that I could approach them." (6401)

2.3c Advantages and Benefits to Collaboration with Industry

All survey participants were asked about their degree of agreement or disagreement with seven statements about potential advantages or benefits to collaborating with industry on research projects (Figure 2). The majority agreed or strongly agreed that all seven were potential benefits: access to funding, translation of knowledge, knowledge sharing, access to non-financial resources, opportunities for advanced research, shared responsibility, and maximization of outputs. Overall, agreement with these potential benefits ranged from a low of 56% of participants somewhat agreeing or strongly agreeing that shared responsibility was a benefit, to a high of 95% of participants somewhat agreeing or strongly agreeing that access to funding was a potential benefit. Noteworthy differences in agreement between those who had previously participated in collaborative research with industry and those who did not are described below and are shown in Figure 2. We did not conduct hypothesis tests to statistically evaluate these differences.

We asked interviewees to expand on their survey responses about the potential benefits of collaborating with industry, or to share additional benefits they might identify or have experienced. We identified five of the seven benefits asked about on the survey as major themes in the interviews, including access to funding, translation of knowledge, knowledge sharing, access to non-financial resources, and opportunities for advanced research. Additionally, interviewees discussed potential benefits not mentioned in the survey including advancement of the research team, industry culture and

patient advocacy.

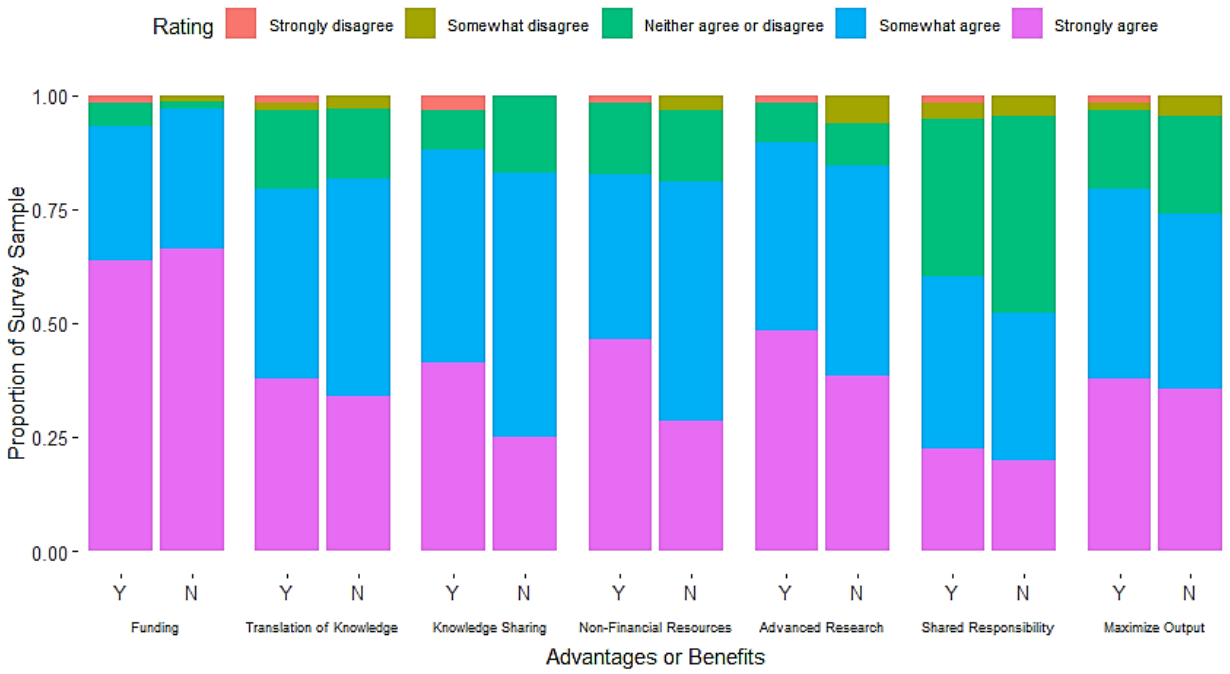

Figure 2. Survey Responses to Potential Benefits to Collaboration with Industry (*n=121-123*)
Survey participants' degree of agreement or disagreement with statements of potential advantages of collaborative research with industry, stratified by whether they had previous experience with such collaboration.
Y=Yes, the researcher had prior experience with collaborative research with industry
N=No, the researcher did not have prior experience with collaborative research with industry

Access to Funding

As noted above, almost all of the survey participants (95%) somewhat agreed or strongly agreed that access to funding was a benefit to collaborating with industry; this was the case regardless of their previous collaborative experience (Figure 2). Funding was also highlighted by the interviewees, as several discussed industry filling the gap in the research ecosystem left by traditional funding agencies and addressing not only the scope of funding but also the speed of said funding.

> *"The magnitude of the funding is much much higher...much greater opportunity for success than going through a standard research based grant...for which the funding is like at a level of embarrassment...But to try and get the funding that we've got by traditional granting mechanisms...get some small grants that are helpful like the Community University Engagements... that's been useful but it's small funding like really it contributes a spit in the bucket." (6198)*

> *"Big advantage is that they have the funds available there's no delay in writing grants looking for the money" (4786)*

Interviewees discussed that sometimes industry funding supported direct project costs, while other times it went to the researcher or trainees in the form of stipends. Some interviewees also mentioned industry providing in-kind contributions and performing pro-bono work.

> *"They [industry partner] supported my research, through gifts in-kind in other words providing me with diagnostic materials free of charge to do other innovative research and that sort of thing." (5966)*

Translation of Knowledge

Most survey participants somewhat agreed or strongly agreed that translation of knowledge was a potential benefit to collaborating with industry (81%), again with no major differences in ratings when stratified by previous collaborative experience (Figure 2). Several interviewees also discussed how working with industry was an important way to translate knowledge gained from research into clinical practice.

> *"For our discoveries in the lab to be translated towards the clinic and eventually impact patients' care and lives we don't have the means to do that... I would also say that being a basic scientist that we lack the expertise in how to translate, how to do drug development, how to prepare the research so that it can eventually form part of an IND [Investigational New Drug] application or Health Canada application" (6988)*

> *"It's been the most enjoyable part of my work as an academic and as a clinician to have that freedom to offer technologies and diagnostics that aren't otherwise available and making them meaningful for families and helping them, and helping them and helping their child" (6189)*

Some interviewees spoke about the benefit of translation of knowledge not solely as a reflection of industries' strengths in research partnerships, but also as a reflection of the flaws within academia. These perceived flaws were related to the slow pace of academia, and lack of expertise needed to develop products and move them through the regulatory process. Additionally, some felt that academia lacked awareness or drive to pursue opportunities for advancement through collaborative partnerships with industry, which they saw as hurting academia's ability to innovate.

> *"They have the in-house expertise, and the pace is different because, the earlier this medication gets into patients the earlier they can make profits...in academia the pace is really pedestrian...for me as a clinician it's very frustrating" (4786)*

Knowledge Sharing

Of the 122 survey participants who shared their views on the statement, 104 (85%) somewhat agreed or strongly agreed that knowledge sharing was a potential benefit to collaborating with industry. A higher proportion of those who reported previous participation in collaborative research with industry "strongly agreed" that this is a benefit (41%) relative to those who had not participated in collaborative research (25%) (Figure 2). Some survey respondents also proposed additional benefits to industry collaborations in response to an open-ended question, and some of these responses were connected to knowledge sharing (e.g., networking and relationships, and benefiting from different perspectives).

The ability to share knowledge with industry was also appealing to many of the interviewees. They discussed how coming together to share their skills and expertise with one another allowed for truly collaborative discussions.

> *"Very very good experience from industry because they are always giving me proper feedback and if I need any scientific consultation regarding the compound that we are in agreement to use for our cancer they always provide good information and we have some meeting with the industry and the partner, sometimes to discuss the result and it's very good actually I was surprised how they how collaborative they are" (6401)*

Although several interviewees emphasized industry expertise as an advantage to collaborating, it was also mentioned by some that those in industry were not content experts. This seemed to arise when participants discussed working with small biotechnology companies that have limited staff and resources, as well as when working with the commercialization teams that do not have scientific expertise.

> *"Many companies we're dealing with are small biotechs that are marketing the product and therefore they're not content experts. They're there to market their product and obviously make money out of it." (2656)*

Access to Non-Financial Resources

Most survey participants (82%) somewhat agreed or strongly agreed that access to non-financial resources was a potential benefit to collaboration with industry. The proportion who "strongly agreed" was higher among those who had previously experienced collaborating with industry (47%) compared to those who had not collaborated with industry (29%) (Figure 2). Non-financial resources were also noted as a benefit to collaboration by interviewees. These resources included access to products, drug

development programs, technologies, consultants, industry infrastructure, industry's previous work and access to industry's time.

> *"One of the big advantages [is that] they have the medications and they have the...programs that's developing these medications." (2595)*

Additionally, many of our interviewees emphasized that working with industry allowed for access to their expertise particularly their regulatory and product knowledge.

> *"They knew what was required by [the] FDA [U.S. Food and Drug Administration]...they knew what was required up front...they knew how many barriers or how many hoops had to be crossed before you get to even submitting...and they often had in place the collaborations with others, or internally they had developed a system that could move a product through those tubes" (5966)*

Opportunity for Advanced Research

Among survey participants, the opportunity to conduct more advanced research was perceived as an advantage to collaborating with industry, with 87% either somewhat agreeing or strongly agreeing with this statement. A slightly higher proportion of those who had participated in collaborative research with industry strongly agreed with this potential advantage (48%), compared to those who had not (39%) (Figure 2). Some survey respondents also wrote about innovation, discoveries, and new treatments to improve outcomes in response to an open-ended question about additional benefits of collaboration with industry. This idea was echoed throughout the interviews, as researchers expressed that working with industry allowed them to do new and exciting work that benefited science overall and accelerated the innovation cycle.

> *"Our result was also very promising...very close to a very important discovery for one of the deadliest child cancer...we published in a very good journal, and now we are taking it to the next level actually and hopefully, to be successful." (6401)*

> *"The push pull...relationship [is] where to get things done you need more than academic push you need some industry at the other end that's pulling it along saying we're interested we've got skin in the game so to speak." (5966)*

One interviewee stressed that the collaboration with industry allowed them to produce work that was not just innovative scientifically, but also relevant and wanted by the community, which related to both the

opportunity to advance research and the translation of research knowledge into practice as potential advantages of industry collaboration.

> *"It's also giving patients and families access to information they want to know about as well. So there's a whole community level component to this...to make sure we're delivering something to the autism community that they want as well and that they want to see" (6189)*

Advancement of Research Team

Although not asked about in the survey, the advancement of the researchers' teams featured in many interviews as a benefit of collaborating with industry, particularly for the trainees involved on those teams. The rewards that trainees may receive included the availability of funds, as well as the opportunity to gain experience working in an industry setting and learning what is involved in developing a drug or product.

> *"You have the students or some people in your team that...see firsthand what's really involved with the drug development the trials and tribulations of working with the company so you involve them...it's not very often that you'll have...something developed in the lab where it's going to go right working with the industry so I think it's an amazing experience for the trainees to be able to see that." (3001)*

Industry Culture

Advantages related to industry culture also emerged during the interviews as a potential benefit to collaborating with industry. Many interviewees discussed a range of characteristics that they attributed to industry and perceived as assets to collaborating. These included frankness, focus, straightforwardness, quick learning, and being organized.

> *"[Industry] tend to call a spade a spade they tend to be very honest they're not going to beat around the bush, because they've got the skin in the game after all" (5966)*

Patient Advocacy

A small number of interviewees also identified advocacy as a benefit of collaborating with industry, asserting that collaborations allowed for a unified voice, greater influence on government and regulations, and the chance to advocate for their patients.

"My main interest with industry now is to raise awareness, public advocacy for these patients, access medication." (2656)

2.3d Barriers and Disadvantages to Collaboration with Industry

We asked survey participants to what extent they agreed or disagreed with seven statements about potential barriers or disadvantages to collaborating with industry on research projects (Figure 3). The majority somewhat agreed or strongly agreed that 6 of the 7 listed were indeed possible disadvantages: differences in goals, conflict of interest, communication, ethics, IP rights, and regulatory considerations. Lower agreement was seen for scheduling issues, with 39% of participants agreeing or strongly agreeing that this was a barrier. Similar to our findings regarding agreement about benefits, when the results for barriers and disadvantages were stratified by self-identified experience in collaborative research with industry, there appeared to be some potential differences, which are shown in Figure 3 and described below.

In the interviews, participants provided further perspectives on the possible disadvantages or barriers to collaborating with industry on research projects. Four of the seven barriers that we asked about on the survey were identified as major themes in the interviews: differences in goals, conflict of interest, communication, and ethical concerns.

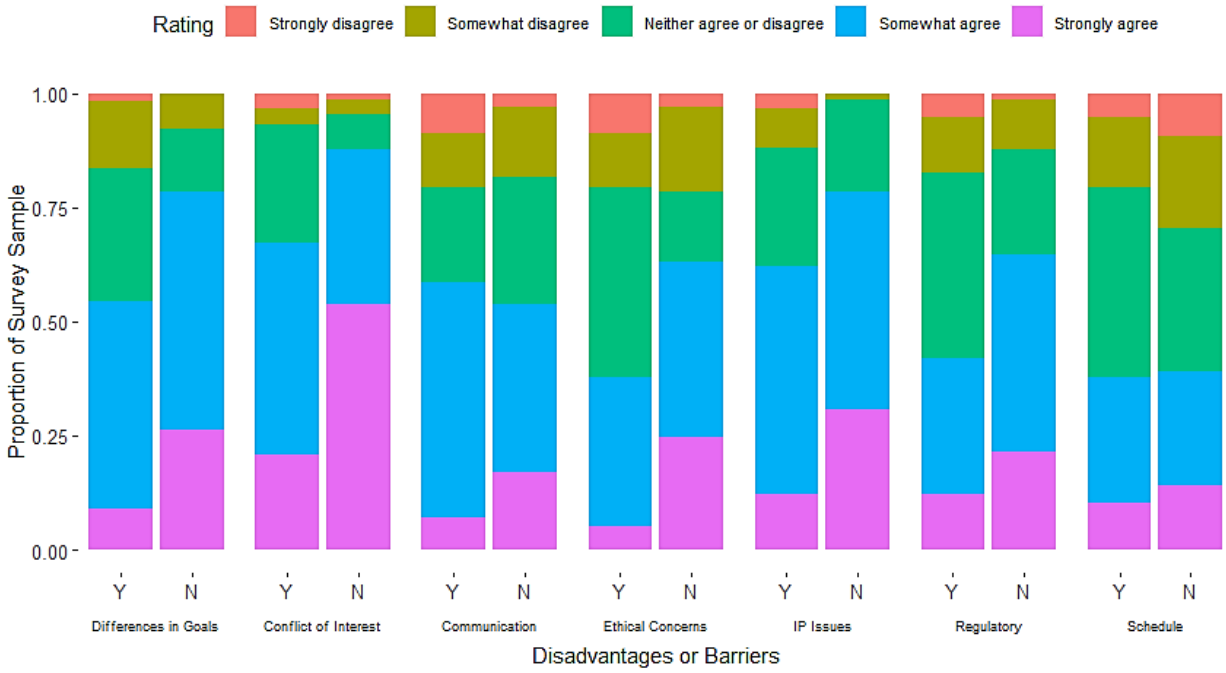

Figure 3. Survey Responses to Potential Barriers to Collaboration with Industry *(n=120-123)*
Survey participants' degree of agreement or disagreement with statements of potential disadvantages of collaborative research with industry, stratified by whether they had previous experience with such collaboration.
Y=Yes, the researcher had prior experience with collaborative research with industry
N=No, the researcher did not have prior experience with collaborative research with industry

Differences in Goals

Overall, 68% of survey participants somewhat agreed or strongly agreed that differences in goals was a potential barrier or disadvantage of collaborating with industry (Figure 3). We observed a lower proportion strongly agreeing this was a barrier among those who had participated in collaborative research (9%) compared to those who had not participated in collaborative research (26%). As well, respondents had the opportunity to provide additional comments about barriers in response to an open-ended question on the survey, and one participant noted, *"Timelines and respect for deadlines are critical to industry, not so much in academia – (the) differing mentality is a challenge" (5471).*

Differences in goals featured prominently in the interviews, as many participants described differences in motivations, cultures, and practices between the world of the researcher in academia and the world of the industry partner. For example, many interviewees noted that they perceived the motivations to conduct the research as fundamentally different between the two, where industry is

motivated by profit and researchers are motivated by the desire to help patients or the desire to advance their research. Their perceptions about the profit motivations of industry made several of the interviewees feel distrustful or suspicious. Some interviewees suggested that this lack of trust and suspicion is something that appears frequently in academia, resulting in some feeling "scared" to collaborate with industry.

> *"The primary focus is of course to make money, whereas for the scientists the main interest maybe helping patients or having their research advance. And you can feel that duality they say that they want to help patients but the primary goal clearly is to make money because otherwise their company wouldn't exist right." (4786)*

> *"I think a lot of them [academic researchers] are scared to death of it [collaborating with industry], thinking that it somehow breaks the sacrosanct science, the purity of the science in some way, that oh, partnering with industry...all they want is money they're going to steal our research or they're not going to do things ethically" (6189)*

Some interviewees also noted that the profit goals of industry were a particular challenge to collaborating for researchers working in the field of rare diseases, as small cohorts of patients do not allow for large market value, reducing an industry's motivation to do the research in this area.

> *"The frustration for me was also sometimes dealing with repurposing it with rare disease because there's millions of drugs which are sitting in the large pharmaceutical cohorts...but because they don't see the market big enough they won't open it up" (3001)*

Interviewees discussed how these differing goals were associated with different priorities for academic researchers versus potential industry partners, for example, scientific understanding versus product development. This was connected to a contrast in speed and pace of each environment, with industry seen as a fast-paced environment compared to academia, which was seen as slow. The difference in pace led to many voicing frustrations with academic processes causing lengthy delays or even resulting in the loss of an industry partnership, including bureaucracy related to ethics approvals, agreements, and general paperwork.

> *"My mindset is discovering the mechanism going deep inside the mechanism...answering some questions. This type of things is not at all important in the industry...they are looking at the big picture" (6401)*

> *"That required working with Academic Institution Industry Office to get things sorted out as far as the ethics around that. That's been I'd say the biggest stumbling block for working with industry I*

hate to say it. An enormous challenge to try and get things through there because of very rigid rules that are age old I think and not sort of keeping up with the current, environment of working with industry" (6189)

On the other hand, some participants also criticized industry's need to rush, as they believed that it could result in harmful outcomes for patients.

"You have seen several times that they release some medication and after a few years they have to have recall for this medication and stop that or give warning to the people who take this medication...Why it is happening because always they are rush to give the products to, the patients." (6401)

Conflict of Interest

The majority of survey participants (78%) somewhat agreed or strongly agreed that conflicts of interest were a potential barrier or disadvantage to collaborating with industry. A notably lower proportion of participants who had previously participated in collaborative research strongly agreed conflicts of interest was a potential barrier (21%) compared with those who had not previously participated in collaborative research (54%) (Figure 3). Interviewees discussed conflict of interest as a potential barrier or disadvantage to collaborating with industry, but multiple participants described it as something to be aware of and managed, not as a roadblock to entry into collaborative relationships. Several researchers we interviewed believed that conflict of interest was not an issue specific to industry but appears in all areas including the academic setting.

"Everybody's conflicted even having a CIHR [grant]...can be a conflict...because you want to renew the grant, publish papers and keep your job so it's eyes wide open. Because, everyone is conflicted in one way or the other...I reject the notion...that just because it's industry it's special or different because I also have a financial stake in my CIHR grant if I don't renew it I'll lose my job" (6988)

Researchers we interviewed sometimes stated that they believed themselves to be at less risk for conflict of interest than other researchers working in the rare disease space. For example, some researchers who did not oversee patient care or those who did not engage in clinical research expressed the belief that their research was less risky with respect to conflicts of interest.

"I don't have much, financially to gain off of this stuff right...In the end I'm trained as a nurse so...I can't receive a pharmaceutical trial right, I don't get little kick backs because I have enrolled so many patients and I am over seeing the medical case of a child so I could be more of a neutral person." (0606)

Communication

Of 123 survey participants who answered the question, 54 (44%) somewhat agreed and 15 (12%) strongly agreed that issues with communication was a potential barrier or disadvantage to collaborating with industry. Those with previous experience with collaborative research were less likely (7%) to strongly agree that communication was a barrier compared to those without collaborative research experience (17%) (Figure 3). Similar to the survey findings, communication issues were identified in the interviews as challenges for researchers when collaborating with industry. For example, two interviewees expressed concerns about their industry partner's lack of communication, lack of consultation and lack of follow-through.

Beyond but related to communication, many interviewees spoke about concerns with some industry partners' apparent attitudes, as reflected in their behaviours when interacting with the academic researcher. This seemed to play an important role in distinguishing whether an experience was positive or not for an interviewee. Specifically, when interviewees described negative collaboration experiences, they sometimes described feeling used or exploited, and used terms such as "*pushy*", "*dishonest*", and "*difficult to deal with*" to describe the partner.

> *"There's been some difficulties on route because sometimes,...especially biotech companies who will reach out and try to form a partnership with you, ...actually want to use you, which you don't know about to later that they want to use you as a way of helping them get credibility, more, so they can then actually get better finance from the bank...they basically wanted your name attached so they could go to the bank and say oh there's an expert in such and such that I you know to proof of principle that our drug is working well." (3001)*

Additional Ethical Concerns

Of 123 survey participants who answered the question, 51% either somewhat agreed or strongly agreed that ethical concerns were a barrier to collaboration with industry (Figure 3). There was a lower proportion of those who strongly agreed (5%) among survey participants who had collaborative experience with industry compared to participants who had no collaborative experience (25%). Multiple interviewees spoke of experiences where they believed an industry partner in research conducted

themselves in an unethical way. For example, they described instances where partners lied to them, withheld information, put a spin on results, tried to go beyond a clinical indication for a product, tried to remove property, and "*stole ideas*".

> *"The world isn't...full of altruism that's for sure I mean...I've had examples of where I would say industry stole my ideas" (5966)*

Industry Turnover and Acquisition

An additional barrier to successfully collaborating with industry that was identified in the interviews but not asked about on the survey was changes to industry's structure, staff, or governance during the collaboration. Many researchers we interviewed noted shifts in ownership (particularly when working with a small company), size, personnel and direction of focus of their industry partner, which often impacted their collaborative experience in a negative way, although in at least one case a change in ownership revitalized the project.

> *"These companies have changed hands multiple times...been taken over by larger conglomerates which makes it very complicated to kind of follow the trail of who's in charge of what." (2656)*

> *"When she [additional researcher] retired she donated her app to a not for profit ...It sat there but then... [the not for profit] got bought out...shifted over to a startup company that does digital health innovations...I actually have a meeting with him next week" (0606)*

Barriers Endorsed on the Survey but not Identified in Interviews

Overall, the majority of survey participants somewhat agreed or strongly agreed that issues related to IP rights (71%) and regulatory issues (54%) were potential barriers or disadvantages to collaboration with industry. A lower proportion of individuals strongly agreed that IP was a potential barrier among those who had previous experience collaborating with industry (12%) compared to those that did not have previous collaborative experience (31%) (Figure 3). As previously noted, scheduling issues was the only potential barrier with which only a minority of survey respondents agreed (39%) and we did not observe major differences in agreement between those with and without prior collaborative experience.

2.3e Ingredients for Successful Research Collaborations

The interviewees were asked, from their perspective, what makes a collaborative research project with industry successful and to provide any tips they may have for creating, and then maintaining positive research relationships with industry. This topic was not specifically addressed in the survey. In summarizing suggestions from the interviewed participants within the following section, we draw both from explicit advice they provided for other researchers and from the participants' reflections on their own experiences.

Outputs of a Positive Collaboration

When asked how they would define a successful collaboration, interviewees discussed research results (e.g., published work, advancement of research, innovation, or proving a hypothesis), the translation of knowledge of the research results aimed at impacting patients (e.g., adoption of a product, giving back to the community), and building collegial relationships.

> *"Well, it depends on the project you know with this immune deficiency project it will be a success if we're able to prove our hypothesis...so that would be the most successful and then we get it published...that would be the measure of success that I would be looking for." (1763)*

> *"I want to see this impact the lives of patients. So we think that we could add ten years of life of ambulation to these patients, perhaps longer. And even if it's a couple of years that'll have a big impact...and change the standard of care for these patients. That's really what it's all about." (6988)*

> *"The collegiality and you make a lot of friends that way." (5966)*

Selecting an Industry Partner and Project

The researchers we interviewed stressed how choosing the right partner can lead to a positive collaboration. Industry culture was an important aspect of partner selection and included elements such as: the goals or motivation of the partner, whereby a genuine interest in the patients or disease was considered a strength; a potential partner's views about working with academia; and compatible working style, with interviewees expressing different views about whether a 'hands-off' or involved style might work best.

> *"Importantly...hearing from them about the interest in the patients am I hearing from them they have a genuine interest in this disorder, that makes me more likely to work with them." (3001)*

"And to this day I think our relations are not very good with that group...I think it just reflects they had a really adversarial attitude towards how to work with academia." (6988)

"Because the company was very supportive...they were supportive to get the project done but they weren't pushy from the point of view of what the results were looking like. You know they didn't want to micromanage the project" (1763)

Interviewees also highlighted the importance of liking the people one works with and the need to use caution, look for warning flags, and to trust their gut if they feel that a situation is undesirable. In the case that a situation or relationship is negative, some researchers recommended walking away from it when possible.

"Don't work with people that you end up not liking, that's really important it, sounds so simple but it's absolutely true" (6189)

"Now seriously I mean if you if you don't like the person or have you know your radar is tingling...feelings are really important you have to have a rapport with the person and the trust. Now of course if they're a psychopath and they could fool you initially and things could change, so I mean you certainly have to be prepared to walk." (6988)

In addition to selecting the right partner when collaborating with industry, interviewees recommended the project be mutually beneficial and incorporate multidisciplinary teams to assist in creating a positive collaboration.

"It was done respectfully, collaboratively, equally, there were benefits that were equal, you know to both parties it was definitely a mutually beneficial you know a basis and for me what that means is that it's going to offer some help to my patients and their families" (6189)

Building Positive Collaborative Relationships Based on Mutual Trust

Throughout the interviews, the notion of relationship building appeared frequently. The researchers we interviewed suggested that good collaborative relationships were built on mutual trust, openness, and transparency.

"I think what's really important is rapport, relationships, trust, all those things are important you have to like the people you're working with and both parties have to get something out of it...a lack of trust a lack of transparency lack of communication that can all be toxic for collaboration." (6988)

"Not sort of you know oh what's the catch kind of attitude, we have to be open and honest with each other and communicating why we would possibly come together, you know what we each expect from each other, and how we can also share in the benefits" (6189)

However, one interviewee did caution researchers to avoid disclosing to the industry partner all of the researcher's information up front and another recommended starting with small deliverables as a way to test drive the relationship as a precursor to being more open and building trust.

> *"A lot of times juniors, people will basically discuss and they'll tell everything in the first meeting. Never do that. Never never do that." (3001)*

> *"Be careful about over promising. You know there's a thing in life you should under promise and over deliver. And I think that's true...don't say you're gonna go for the moon if you can't...propose an incremental sort of approach and if it goes better and faster than you'd anticipate that's great but don't over promise." (1763)*

Participants also discussed the strong interpersonal skills needed to create positive collaborative relationships with an industry partner, such as good communication, leadership, negotiation skills, and problem-solving skills.

> *"If you demonstrate a capacity to work as a team, to lead a team to be a team player, to be okay to be the loser, to know how to be the winner but to always be supportive then that's a really good starting point" (0606)*

Interviewees discussed mutual understanding of the perspectives of both partners and to tailor interactions to best fit all needs. For instance, industry is a fast-paced environment that might require researchers to adjust their approach to ensure a positive collaboration.

> *"Based on my experience the industry wants fast and effective result. Even it is negative it doesn't matter but it should be very timely because they are in a competition right. So, if you are fast on time and you respect their deadline, it is the most important thing for them and they will approach you again" (6401)*

Planning, Setting Goals, Expectations, and Governance

Several interviewees placed a strong emphasis on the planning stage prior to the start of a collaborative project with an industry partner. There was a focus on setting goals and expectations up front, specifically surrounding responsibilities, collaborative involvement, rules and regulations, timing, and who controls publishing and licensing rights. Some interviewees specifically mentioned the need to establish academic freedom in relationships, which included financial independence, publishing independence and to stay at arm's length from the industry partner.

"Realistic expectations on the two sides. So that it's well discussed well planned, everybody is aware of the limitations of what you know what the experiments on both sides will be, what the deliverables on both sides would be, and also taking into account the timeframe of when everything will be." (3001)

"My experience always been very positive largely because, as we said, the industry partners have been hands off, they gave us free academic reign, they're not trying to influence the results that I publish the way I publish...So it's been a very positive relationship, and not one that I felt there were any strings attached in any way." (2595)

Using Available Supports

Many participants we interviewed advised using resources provided either by the university with which the researcher is affiliated, or by including intermediary organizations, in the form of innovations and liaison offices, or from commercial research organizations who assist in facilitating and funding industry-researcher collaborations such as Mitacs (Mitacs is a nonprofit national research organization funded by the government that "has assisted organizations in reaching their business goals, has funded cutting-edge innovation, and has created job opportunities for students and postdocs"[49])

"A successful collaboration I think requires trust, they require transparency, I should also say that tech transfer office... excellent in terms of drafting these agreements and protecting the interests of the institute and the investigator. That's also another important element. The contract can't have things in it that can put the investigator and institute in a difficult position. So that's a really important element is what that contract actually says." (6988)

"When you are working with the industry, if you have Mitacs on board they could be a great facilitator in negotiation. You can ask [for] funding for your students, for your trainee and your project. You know they give you much funding right, if you convince the industry that funding you for example ten thousand dollars then Mitacs will give you fourteen thousand on top of it to work on it. So, this is it is very, very, very good so this is something that it could be very helpful." (6401)

As well, many interviewees highlighted the potential value of being aware of and open to the opportunities that a collaborative relationship with industry can bring. This includes making a researcher's institute aware of how they can become involved in commercial projects.

"I think we should always be pushing the other funding bodies that we liaise with like the Research Institutes we work within, the faculty of medicine in which our department exists...to become aware and supportive of these things and advertise them...I don't think some of our own home institutions are aware enough of the opportunities out there." (6198)

Lastly, a participant advised others to seek mentorship from those who have experience with industry-academia collaborative relationships.

"Another advice is to talk with lots of people that were already, that have already had these relationships or experience with industry because, just with mentorship it's always important to get the insight from people who have already done what you would like to do so that you can avoid mistakes and anticipate issues." (4786)

2.3f Future Collaborations

We asked survey participants if they would consider collaborating with industry in the future and the vast majority (90%) indicated that they would consider such a collaboration. A few researchers we interviewed mentioned their feelings on future collaborative relationships with industry. Several were supporters of these collaborations and felt that the future is in private-public partnerships. However, a few highlighted that changes need to be made in how academia interacts with industry for such collaborations to be successful.

"I'm a very strong supporter of that [collaborations] I think that's where the future lies...in private public partnerships, it's the only way to get technology out there" (6189)

"Time for the company is very important...totally different from University...So if they [the university] want to stop the research one year for an MTA they [industry] don't like it, so they [industry] do their own research because they have money they have their own scientists...they are faster and again this will be a loss for the University at the end and for us at the end right. And you know, hopefully your research and your analyzes in the end could help....the policymaker reads it and hopefully they make some changes." (6401)

2.4 Discussion

We investigated the experiences and perceptions of academic pediatric rare disease researchers in Canada regarding their research collaborations with industry. We were interested in the frequency and nature of these relationships, perceived benefits and disadvantages or barriers, and factors that promote or hinder their success. Of 126 pediatric rare disease researchers we surveyed, 59 indicated that they had previous experience with collaborative research with industry of which 41 indicated their experience was in pediatric rare disease. Overall, survey participants who had engaged in collaborative research with industry in pediatric rare disease had positive experiences (e.g., half rated their most recent experience as 90 or higher on a scale of 0 out of 100) and the vast majority (90%) would consider collaborations with industry in the future. Several benefits to collaboration were endorsed or described by both the survey participants and the interviewees; access to funding and improved translation of knowledge were among

the mostly highly endorsed benefits. However, survey respondents and interviewees also endorsed and discussed several disadvantages or barriers to collaborating with industry, including differences in goals and motivations between industry and rare disease researchers. The stated motivations of many rare disease researchers interviewed were aimed at helping patients, whereas they perceived industry was profit motivated. In order to maximize benefits and reduce the risk or impact of disadvantages, interviewees provided advice for future researchers to help them engage in successful collaborations with industry. Suggestions tended to fall under four categories including: (i) careful selection of partner/project; (ii) engaging in relationship building opportunities; (iii) establishing clear expectations and governance practices; and (iv) advocating for and using supportive institutional structures.

Our findings regarding potential advantages and disadvantages to collaborations with industry are consistent with the literature specific to the pediatric rare disease environment. For example, access to funding as a benefit was important to both the survey participants and the interviewees, which is not surprising as the rare disease research space has historically been challenged by limited funding [6]. This benefit is particularly unique to collaborations with industry as other collaborative partners such as policy makers, patients or other academic collaborators may struggle to find funding [50]. The translation of evidence into practice as a potential benefit of collaborating with industry was a major theme we identified from our interviews; this is consistent with the stated benefits of collaborative research generally [51]. Similarly, differences in goals and motivations between academia and industry was identified as a key disadvantage or barrier to collaboration with industry in our study, which has also been documented in previous studies both within the rare disease environment and generally [10, 16–18, 23, 24, 33]. The stated motivations of several rare disease researchers we interviewed included helping patients and advancing science, whereas they often perceived that industry was more profit-motivated. When van Rijnsoever & Hessels [14] investigated the motivations of researchers (not specific to the pediatric rare disease context), they found that many were motivated by scientific output, curiosity, and career benefits, but they did not identify altruism as a motivating factor, unlike our interviewees. This

difference in findings may be due to the professional roles of our interviewees, given that 50% were health care providers and likely closely connected to rare disease patients' unmet needs. Conflict of interest has historically been an important concern about collaborations with industry [21, 30]. While a majority of survey participants in our study who had not previously collaborated with industry strongly agreed that conflict of interest was a potential barrier to industry partnership (54%), this proportion was much lower among those who had previously collaborated with industry (21%). Participants we interviewed, all of whom had collaborative experience with industry, discussed the importance of managing conflicts of interest, but did not typically see it as a major barrier and some expressed that it was not a problem specific to working with industry. Previous experience with industry may impact views about conflict of interest and, in turn, views about conflicts of interest may influence researchers' decisions about whether to collaborate.

In order to maximize the potential benefits of industry collaborations in research, and to reduce the impact of barriers and disadvantages, researchers we interviewed provided advice for future researchers that we grouped into four broad categories. First, interviewees advised researchers to carefully select a partner and project. This involves choosing a partner that you actually like; entering into relationships with caution; seeking out mutually beneficial collaborations; and incorporating multidisciplinary expertise on the collaborative team. Second, interviewees advised engaging in relationship building opportunities to establish mutual trust such as practicing open communication and transparency; understanding perspectives of each partner; and conducting incremental projects with small deliverables to test drive the relationship. Third, interviewees advised establishing clear and transparent agreements and governance practices by discussing and establishing expectations for each other prior to finalizing the partnership. These expectations should cover such things as: responsibilities, roles, regulations, time horizons, publishing and licensing rights. Finally, interviewees advised advocating for and using supportive structures by taking advantage of intermediary groups, either within the researcher's institution or externally who can assist researchers in collaborations; and reducing

bureaucratic roadblocks within the institution that hinder collaborative relationships with industry. These findings are consistent with previous literature as building trust has been seen as an essential part of good collaborations generally [52, 53] and collaborations with industry specifically [16, 18, 21, 22, 24, 31, 32, 50]. The lack of trust in industry that some academic researchers hold could possibly explain why some researchers we interviewed advised others to enter into relationships with caution; and may also have been based on their own less positive experiences. Many of the tips from our interviewees were related to the potential enablers and barriers to collaborative academic-industry relationships suggested in the literature, for example, institutional structures such as institutional supports [10, 13, 15, 16, 18, 22, 27, 29], quality communication [13, 16, 19, 21, 24, 26, 32], establishing contracts and expectations [17–19, 21–23, 27, 29, 32, 33], compatible industry and academic culture, [10, 15, 19, 24, 28, 34, 35] and mutually beneficial collaborations [16, 22, 26, 32, 33]. Despite some interviewees advising researchers to seek support from academic institutions in their collaborations, their own experiences with academic processes and structures intended to support industry collaboration varied. Some authors argue that the roadblocks in academic institutions to collaborating with industry are hurting academia's chances of impacting the development of disease treatments, as industry partners may be able to contribute infrastructure, knowledge or resources that are otherwise unavailable to academic institutions [54].

Our study had some limitations. For example, our literature search strategy used to develop a sampling frame for the survey required individuals to be published or have information in the public domain, and our eligibility criteria required individuals to be independent researchers. This could have led to our survey sample being relatively older in age and with more extensive research experience, which could have led to selection bias if the views of older and experienced researchers are different from those who are younger or less experienced. We are unable to determine whether our survey sample was reflective of the underlying population of Canadian pediatric rare disease researchers as there was no previous enumeration of this population for comparison. There was relatively little overlap in the lists of potentially eligible individuals derived from each of the three sources that made up our sampling frame

(Appendix 4), indicating that each source was likely to have been relatively incomplete and supporting the need for multiple sources. Additionally, survey results may have been impacted by non-response bias given the response rate of 20%, although this response rate was likely an underestimate as we were not able to determine the eligibility of individuals who did not respond to the survey invitation. Individuals with experience in partnering with industry may have been more likely to participate in the survey and those with more positive experiences may have been more willing to be interviewed. We also asked participants to recall and self-report on past events and experiences, which may impact the validity of our findings to the extent that such events may not have been recalled accurately. Furthermore, we were unable to ascertain the perspectives of industry partners due to the scope of our project, and as a result we need to be careful to avoid over-interpreting findings related to researcher speculations about industry partners' goals and motivations. Future research should aim to gain industry perspectives directly.

Despite these limitations, our study had important strengths. For example, we used three sources to create a unique sample frame of Canadian rare disease researchers and received 126 responses from a relatively diverse group of participants in terms of industry experience, province, primary workplace setting, positions, and research type. We were able to capture rich descriptions of the collaborative research experiences with industry from the Canadian pediatric rare disease researchers we interviewed, which has not been done before. We also used multiple strategies to ensure the use of rigorous methods, which are listed in section 2.2d. To the best of our knowledge, there has been little research focus on understanding collaborative relationships between pediatric rare disease researchers and industry in Canada. Our research was able to capture the experiences and perceptions of pediatric rare disease researchers who have, and those who have not, collaborated with industry. The new knowledge we have generated may be useful to future researchers considering potential relationships with industry partners. For example, considering the benefits/advantages and barriers/disadvantages that previous researchers have encountered may help researchers to make more informed decisions about whether to collaborate, and about selecting industry partners and managing the relationship. The suggestions provided by

interviewees based on their experiences may also help future researchers to maximize benefits and avoid pitfalls when establishing industry collaborations. More research is needed to determine how our findings may apply beyond pediatric rare disease research. Future research could also analyze different institutional processes and structures to determine how academic organizations can best facilitate successful collaborative research with industry and mitigate against potential disadvantages or barriers for pediatric rare disease researchers in Canada.

2.5 Conclusion

Collaborative research between pediatric rare disease researchers and industry has the potential to have a positive impact on the success and innovation of treatments in pediatric rare diseases. This study focused on the perspectives of pediatric rare disease researchers in Canada, including some who have previous collaborative experience with industry. Participants provided several tips for future researchers and the academy on how to increase the chances of positive collaborations with industry, which included careful selection of partner/project; engaging in relationship building opportunities to establish mutual trust; establishing clear expectations and governance practices; and advocating for and using supportive institutional structures. Our study focused on only one of the partners involved in collaborative research which is an important starting point to gain a comprehensive understanding of collaborative research with industry. Similar research needs to be done to investigate industry partners' experiences working collaboratively with researchers.

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APPENDICES

Appendix 1: Ethics Certificate

15/11/2022

Université d'Ottawa
Bureau d'éthique et d'intégrité de la recherche

University of Ottawa
Office of Research Ethics and Integrity

CERTIFICAT D'APPROBATION ÉTHIQUE | CERTIFICATE OF ETHICS APPROVAL

Numéro du dossier / Ethics File Number	H-11-21-7230
Titre du projet / Project Title	WHAT MAKES A SUCCESSFUL RESEARCH COLLABORATION BETWEEN INDUSTRY AND ACADEMIC RESEARCHERS IN THE FIELD OF RARE DISEASES? A MIXED METHODS PROPOSAL
Type de projet / Project Type	Thèse de maîtrise / Master's thesis
Statut du projet / Project Status	Renouvelé / Renewed
Date d'approbation (jj/mm/aaaa) / Approval Date (dd/mm/yyyy)	02/12/2021
Date d'expiration (jj/mm/aaaa) / Expiry Date (dd/mm/yyyy)	01/12/2023

Équipe de recherche / Research Team

Chercheur / Researcher	Affiliation	Role
Charlena DEGEN	Département d'épidémiologie et santé publique / Department of Epidemiology and Public Health	Chercheur Principal / Principal Investigator
Ian GRAHAM	Département d'épidémiologie et santé publique / Department of Epidemiology and Public Health	Superviseur / Supervisor
Elizabeth POTTER	Département d'épidémiologie et santé publique / Department of Epidemiology and Public Health	Co-superviseur / Co-supervisor
Kym Marie BOYCOTT		Co-chercheur / Co-investigator

Conditions spéciales ou commentaires / Special conditions or comments

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Université d'Ottawa

Bureau d'éthique et d'intégrité de la recherche

University of Ottawa

Office of Research Ethics and Integrity

Le Comité d'éthique de la recherche (CÉR) de l'Université d'Ottawa, opérant conformément à l'*Énoncé de politique des Trois conseils* (2014) et toutes autres lois et tous règlements applicables, a examiné et approuvé la demande d'éthique du projet de recherche ci-nommé.

L'approbation est valide pour la durée indiquée plus haut et est sujette aux conditions énumérées dans la section intitulée "Conditions Spéciales ou Commentaires". Le formulaire « Renouvellement ou Fermeture de Projet » doit être complété quatre semaines avant la date d'échéance indiquée ci-haut afin de demander un renouvellement de cette approbation éthique ou afin de fermer le dossier.

Toutes modifications apportées au projet doivent être approuvées par le CÉR avant leur mise en place, sauf si le participant doit être retiré en raison d'un danger immédiat ou s'il s'agit d'un changement ayant trait à des éléments administratifs ou logistiques du projet. Les chercheurs doivent aviser le CÉR dans les plus brefs délais de tout changement pouvant augmenter le niveau de risque aux participants ou pouvant affecter considérablement le déroulement du projet, rapporter tout événement imprévu ou indésirable et soumettre toute nouvelle information pouvant nuire à la conduite du projet ou à la sécurité des participants.

The University of Ottawa Research Ethics Board, which operates in accordance with the *Tri-Council Policy Statement* (2014) and other applicable laws and regulations, has examined and approved the ethics application for the above-named research project.

Ethics approval is valid for the period indicated above and is subject to the conditions listed in the section entitled "Special Conditions or Comments". The "Renewal/Project Closure" form must be completedfour weeks before the above-referenced expiry date to request a renewal of this ethics approval or closure of the file.

Any changes made to the project must be approved by the REB before being implemented, except when necessary to remove participants from immediate endangerment or when the modification(s) only pertain to administrative or logistical components of the project. Investigators must also promptly alert the REB of any changes that increase the risk to participant(s), any changes that considerably affect the conduct of the project, all unanticipated and harmful events that occur, and new information that may negatively affect the conduct of the project or the safety of the participant(s).

Safaa LAMHOUJEB
Coordonnateur de l'éthique / Ethics Coordinator
Pour/For **Daniel LAGAREC** Président(e) du/ Chair of the **Comité d'éthique de la recherche en sciences de la santé et sciences / Health Sciences and Sciences Research Ethics Board**

Appendix 2: Table of Types of Academia-Industry Relationships

Commercialization Activities	
Licensing	Contractual assignment of university-generated intellectual property (such as patents) to external organizations
Academic entrepreneurship	Development and commercial exploitation of technologies pursued by academic inventors through a company they (partly) own
Academic Engagement Activities	
Collaborative research	**Research jointly pursued by university and industrial partners – commonly with public funding**
Contract research	Application-oriented research and development activities carried out by university – commissioned and funded by industry
Consulting	Application-oriented research and development activities or advice provided individually by academics – commissioned and funded by industry

From Perkmann M, King Z, Pavelin S. Engaging excellence? Effects of faculty quality on university engagement with industry. Res Policy. 2011;40(4):539–52. (Reproduced with Permission)

Appendix 3: Checklist for the Journal Article Reporting for Mixed Methods Article Reporting Standards (MMARS)

Table 3

Mixed Methods Article Reporting Standards (MMARS): Information Recommended for Inclusion in Manuscripts That Report the Collection and Integration of Qualitative and Quantitative Data

Paper section or element	Description of information to be reported	Recommendations for authors to consider & notes for reviewers
Title page		
Title	• See the JARS–Qual and JARS–Quant Standards.	• *Authors*: Refrain from using words that are either qualitative (e.g., *explore*, *understand*) or quantitative (e.g., *determinants*, *correlates*), because mixed methods stands in the middle between qualitative and quantitative research. • *Authors*: Reference the terms *mixed methods* or *qualitative and quantitative*.
Pg. 21		
Author note	• See the JARS–Qual and JARS–Quant Standards.	
Abstract	• See the JARS–Qual and JARS–Quant Standards. • Indicate the mixed methods design, including types of participants or data sources, and analytic strategy, main results/findings, and major implications/significance.	• *Authors*: Specify the type of mixed methods design used. See the note on types of designs in the methods research design overview section below. • *Authors*: Consider using one keyword that describes the type of mixed methods design and one that describes the problem addressed. • *Authors*: Describe your approach(es) to inquiry and, if relevant, how intersecting approaches to inquiry are combined when this description will facilitate the review process and intelligibility of your paper. If your work is not grounded in a specific approach(es) to inquiry or your approach would be too complicated to explain in the allotted word count, however, it would not be advisable to provide explication on this point in the abstract.
Pg. 22		
Introduction		
Description of research problems/ questions	• See the JARS–Qual and JARS–Quant Standards.	• *Authors*: This section may convey barriers in the literature that suggest a need for both qualitative and quantitative data. • *Reviewers*: Theory or conceptual framework use in mixed methods varies depending on the specific mixed methods design or procedures used. Theory may be used inductively or deductively (or both) in mixed methods research.
Pg. 23-25		
Study objectives/ aims/research goals	• See the JARS–Qual and JARS–Quant Standards. • State three types of research objectives/aims/goals: qualitative, quantitative, and mixed methods. Order these goals to reflect the type of mixed methods design. • Describe the ways approaches to inquiry were combined, as it illuminates the *objectives* and mixed method rationale (e.g., descriptive, interpretive, feminist, psychoanalytic, postpositivist, constructivist, critical, postmodern or constructivist, or pragmatic approaches).	• *Reviewers*: A mixed method objective, aim, or goal may not be familiar to reviewers. It describes the results to be obtained from using the mixed methods design type where "mixing" or integration occurs (e.g., the aim is to explain quantitative survey results with qualitative interviews in an explanatory sequential design). For instance, the goal of a qualitative phase could be the development of a conceptual model, the goal of a quantitative phase might be hypothesis testing based upon that model, and the goal of the mixed methods could be to generate integrated support for a theory based upon quantitative and qualitative evidence.
Pg. 25-26		
Method		
Research design overview	• See the JARS–Qual and JARS–Quant Standards. • Explain why mixed methods research is appropriate as a methodology given the paper's goals. • Identify the type of mixed methods design used and define it. • Indicate the qualitative approach to inquiry and the quantitative approach used within the mixed methods design type (e.g., ethnography, randomized experiment) • If multiple approaches to inquiry were combined, describe how this was done and provide a rationale (e.g., descriptive, interpretive, feminist, psychoanalytic, postpositivist, constructivist, critical, postmodern or constructivist, or pragmatic approaches), as it is illuminating for the mixed method in use. • Provide a rationale or justification for the need to collect both qualitative and quantitative data and the added value of integrating the results (findings) from the two databases.	• *Reviewers*: Because mixed methods research is a relatively new methodology, it is helpful to provide a definition of it from a major reference in the field. • *Reviewers*: Mixed methods research involves rigorous methods, both qualitative and quantitative. Refer to the JARS–Qual standards (qualitative) and JARS–Quant standards (quantitative) for details of rigor. • *Reviewers*: One of the most widely discussed topics in the mixed methods literature would be research designs. There is not a generic mixed methods design, but multiple types of designs. At the heart of designs would be basic, core designs, such as a convergent design, an explanatory sequential design, and an exploratory sequential design. Although the names and types of designs may differ among mixed methods writers, a common understanding is that procedures for conducting a mixed methods study may differ from one project to another. Further, these basic procedures can be expanded by linking mixed methods to other designs (e.g., intervention or experimental trial mixed methods study), theories or standpoints (e.g., a feminist mixed methods study), or to other methodologies (e.g., a participatory action research mixed methods study).
Pg. 26		

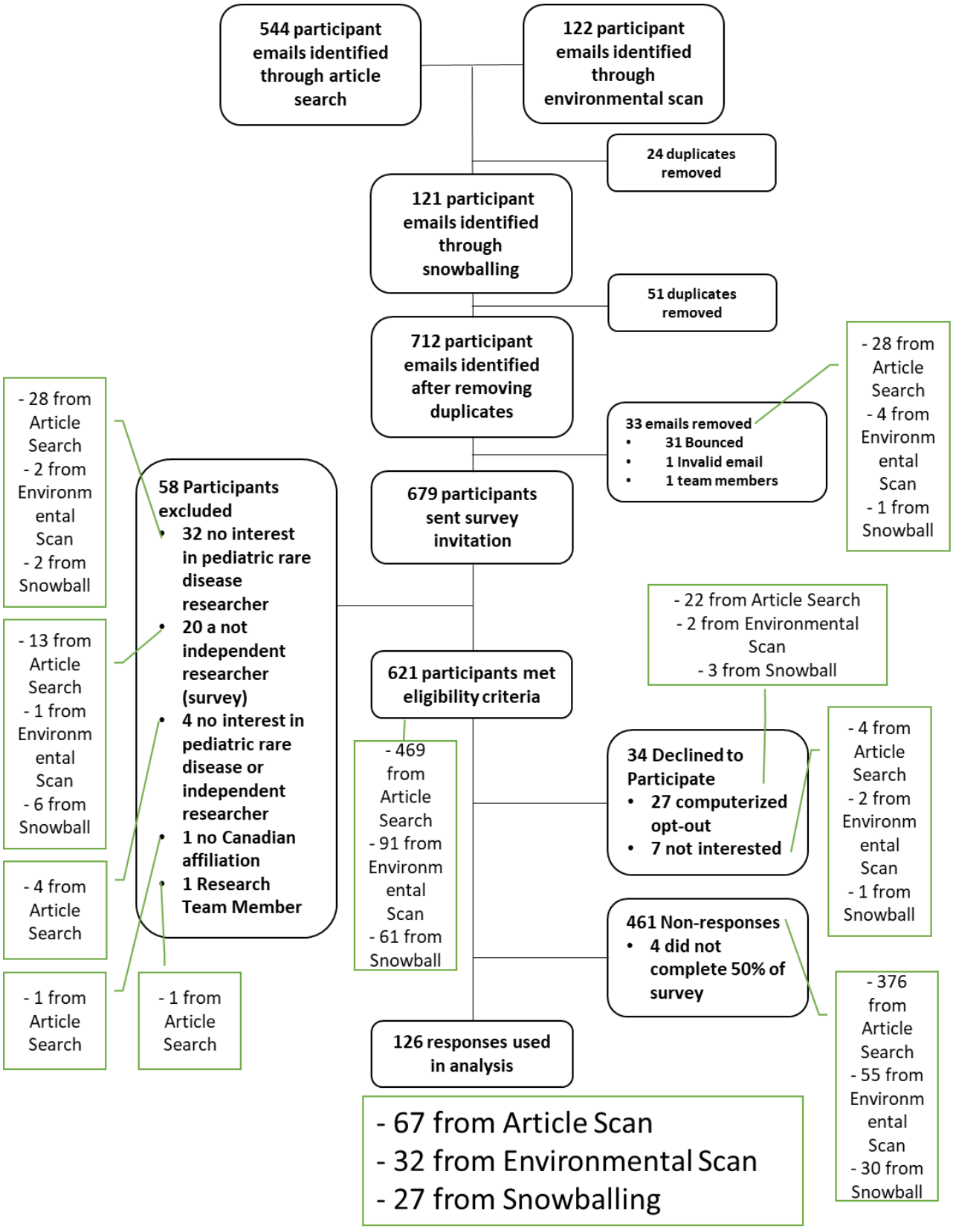
Table 3 (*continued*)

Paper section or element	Description of information to be reported	Recommendations for authors to consider & notes for reviewers
Participants or other data sources Pg. 26-27, 29	• See the JARS–Qual and JARS–Quant Standards. • When data are collected from multiple sources, clearly identify the sources of qualitative and quantitative data (e.g., participants, text), their characteristics, as well as the relationship between the data sets if there is one (e.g., an embedded design). • State the data sources in the order of procedures used in the design type (e.g., qualitative sources first in an exploratory sequential design followed by quantitative sources), if a sequenced design is used in the mixed methods study.	• *Authors*: Because of multiple sources of data collected, separate descriptions of samples are needed when they differ. A table of qualitative sources and quantitative sources is helpful. This table could include type of data, when it was collected, and from whom it was collected. This table might also include study aims/research questions for each data source and anticipated outcomes of the study. In mixed methods research, this table is often called an *implementation matrix*. • *Authors*: Rather than describe data as represented in numbers versus words, it is better to describe sources of data as open-ended information (e.g., qualitative interviews) and closed-ended information (e.g., quantitative instruments).
Researcher description Pg. 31	• See the JARS–Qual Standards.	• *Reviewers*: It is helpful to establish in a publication the researchers' experiences (or research teams' experiences) with both qualitative and quantitative research as a prerequisite for conducting mixed methods research. • *Authors*: Because mixed methods research includes qualitative research, and reflexivity is often included in qualitative research, we would recommend statements as to how the researchers' backgrounds influence the research.
Participant recruitment		
Participant sampling or selection Pg. 26-29	• See the JARS–Qual and JARS–Quant Standards. • Describe the qualitative and the quantitative sampling in separate sections. • Relate the order of the sections to the procedures used in the mixed methods design type.	
Participant recruitment Pg. 26-29	• See the JARS–Qual and JARS–Quant Standards. • Discuss the recruitment strategy for qualitative and quantitative research separately in mixed methods research.	
Data collection		
Data collection/ identification procedures Pg. 27-30	• See the JARS–Qual and JARS–Quant Standards.	
Recording and transforming the data Pg. 27-30	• See the JARS–Qual Standards.	
Data analysis Pg. 28-30	• See the JARS–Qual and JARS–Quant Standards. • Devote separate sections to the qualitative data analysis, the quantitative data analysis, and the mixed methods analysis. This mixed methods analysis consists of ways that the quantitative and qualitative results will be "mixed" or integrated according to the type of mixed methods design being used (e.g., merged in a convergent design, connected in explanatory sequential designs and in exploratory sequential designs).	
Validity, reliability, and methodological integrity Pg. 30-31	• See the JARS–Qual and JARS–Quant Standards. • Indicate methodological integrity, quantitative validity and reliability, and mixed methods validity or legitimacy. Further assessments of mixed methods integrity are also indicated to show the quality of the research process and the inferences drawn from the intersection of the quantitative and qualitative data.	

Table 3 (*continued*)

Paper section or element	Description of information to be reported	Recommendations for authors to consider & notes for reviewers
Findings/Results		
Findings/Results subsections Pg. 31-62	• See the JARS–Qual and JARS–Quant Standards. • Indicate how the qualitative and quantitative results were "mixed" or integrated (e.g., discussion, tables of joint displays, graphs, data transformation in which one form of data is transformed to the other, such as quantitative text, codes, themes are transformed into counts or variables).	• *Authors*: In mixed methods research, the findings section typically includes sections on qualitative findings, quantitative results, and mixed methods results. This section should mirror the type of mixed methods design in terms of sequence (i.e., whether quantitative strand or qualitative strand comes first; if both are gathered at the same time, either qualitative findings or quantitative results could be presented first). • *Reviewers*: In mixed methods Results sections (or in the Discussion section to follow), authors are conveying their mixed methods analysis through "joint display" tables or graphs that array the qualitative results next to the quantitative results (e.g., categorical or continuous data). This enables researchers to directly compare results or to see how results from the quantitative and qualitative strands.
Discussion		
Discussion subsections Pg. 63-68	• See the JARS–Qual and JARS–Quant Standards.	• *Authors*: Typically, the Discussion section, like the Method and Findings/Results, mirrors in sequence the procedures used in the type of mixed methods design. It also reflects upon the implications of the integrated findings from across the two methods.

Appendix 4: Search Strategy for Survey Participants



Survey Participation Flow Chart 1

A search strategy was developed with the assistance of a librarian from the University of Ottawa Library for the electronic database, SCOPUS, using medical subject headings (MeSH) related to pediatrics and rare diseases, and a search term specifying that an author had to have a Canadian affiliation. 50 of the articles were title and abstracted screened to determine relevance of search strategy with 78% seeming to be relevant to pediatric rare disease. The corresponding authors' names, affiliations and email addresses were extracted and put into excel. Each was scanned to determine that they met the eligibility criteria, had a valid email address and duplicates were removed. The environmental scan was conducted looking at pediatric rare disease research groups, networks and organizations by searching websites of academic institutions for departments, researchers or research groups with a focus on rare disease, searching patient organizations websites related to pediatric rare disease, and general google searches for networks and researchers with an interest in pediatric rare disease. Examples of these include the Canadian Pediatric Neuromuscular Group, Canadian Neuromuscular Diseases Network, the rare disease group at BC Children's Hospital Research Institute, Rare Neurological Diseases Group at The Neuro, etc. Anyone who indicated an interest in rare disease, was labeled as a researcher and had some Canadian affiliation was eligible. Names, email addresses and affiliations were extracted from the if given on initial discovery or searched for on an academic profile and put into excel. The two lists were combined, and duplicates were removed. Additionally, the survey incorporated snowball sampling methodology by asking individuals to identify names of other pediatric rare disease researchers and contact information was obtained from the public domain.

Appendix 5: Sample of Survey Email Correspondence

- **FROM:** Charly Degen Email via SurveyMonkey
- **SUBJECT:** University of Ottawa Study on Rare Disease Research with Industry Survey Invitation

Dear Dr. [LastName],
I am writing to request your participation in a survey about partnerships between rare disease researchers and industry as part of the research MSc thesis project at the University of Ottawa: What makes a successful research collaboration between industry and academic researchers in the field of rare diseases? a mixed methods study.

A goal of the survey is to determine the types of research relationships Canadian Pediatric academic/hospital-based researchers have with industry in the field of rare disease. The graduate student Charlena Degen, is a candidate in the MSc epidemiology program. Charlena is working with Dr. Ian Graham, Dr. Beth Potter, and Dr. Kym Boycott. She is interested in hearing from both those that have previously worked with industry as well as those who have not to map the landscape of industry-researcher relationships. For individuals who have previously worked with industry, she is especially interested in learning researchers' experiences.

You have been identified as an individual who works in the area of pediatric rare diseases and have been selected to complete a brief questionnaire about your experiences as a researcher.

The questionnaire is short and should take approximately 15 minutes or less to complete. To begin the survey, click on the link below:
[SurveyLink]

This survey is confidential, and your participation is voluntary. You may stop at any time or skip any questions that you prefer not to answer. All information will remain confidential and no identifying information will be reported or published.

If you have any questions or concerns, please contact Charlena Degen, Principal Investigator for this project at the University of Ottawa. It is important to know that the University of Ottawa Research Ethics Board has approved the ethical components of the project. If you have any questions regarding the ethical conduct of this study, you may contact the Office of Research Ethics and Integrity via email (ethics@uottawa.ca) or telephone (613-562-5387).

We appreciate your help with this survey.
Many Thanks,
Charlena Degen
Charlena Degen (Principal Investigator/Graduate Student)
MSc Epidemiology Candidate
School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa

Appendix 6: Survey Questionnaire

You have been invited to participate in the survey component of the thesis project: What makes a successful research collaboration between industry and academic researchers in the field of rare diseases? A Mixed Methods Study.

Before agreeing to participate in this study, it is important that you read and understand the following information.

Who is conducting the Study?

Charlena Degen (Principal Investigator/Graduate student),

Dr. Ian Graham (Supervisor/Co-Investigator)

Dr. Beth Potter (Co-Supervisor/Co-Investigator)

Dr. Kym Boycott (Co-Investigator)

What is the purpose of the study?

The purpose of the study is to determine the types of research relationships Canadian pediatric academic/hospital-based researchers have with industry in the field of rare disease. We are interested in hearing from those who have both worked with industry and those who have not. All responses are important to the research project.

What does my participation consist of?

Participation will consist of completing an online questionnaire through SurveyMonkey about the types of research relationships you have had with industry in the field of rare disease. It will take approximately 15 minutes to complete. The survey will include closed-ended, multiple choice, yes/no, and short answer items. You will be asked questions related to your perceptions and experiences with research with industry with a focus on collaborative research. You will also be asked demographic information to help us better interpret the survey findings.

What are the risks of participating?

There are no known risks to participating in the questionnaire. You can skip any questions or stop at anytime. All the information you provide will be kept confidential. No identifying information will be revealed in subsequent publications of the survey findings.

What are the benefits of participating?

There are no benefits from participating other than knowing you are contributing to Ms. Degen's MSc thesis research and to generating knowledge about the collaborative research experiences that Canadian Pediatric academic/hospital-based researchers have with industry in the field of rare disease.

What about confidentiality and my privacy?

All information you share will remain confidential. The questionnaire results will be used only for this research project and will not be shared with any third parties. No identifying information will be published or shared. To minimize the risk of security breaches and to help ensure your confidentiality, we recommend that you use standard safety measures, such as signing out of your account, closing your browser, and locking your device when you are no longer using it/when you have completed the study. The data collected (survey data set, contact information, and consent forms) will be kept in a secure manner. It will be stored on a secure server housed at the University of Ottawa Faculty of Medicine and destroyed after 10 years. It will only be accessible to the research team.

Is my participation voluntary?

Your participation is voluntary. You are under no obligation to participate and if you choose to participate, you can withdraw from the survey at any time and/or decline to answer any questions, without suffering any negative consequences. It is important to note that once the survey is submitted, you will be unable to withdraw your responses from the study as the researchers will be unable to retrace individual datasets.

If I have any questions?

If you have any questions about the study, you may contact the researcher or their co-supervisors. It is important to know that the University of Ottawa Research Ethics Board has reviewed and approved this study. If you have any questions regarding the ethical conduct of this study, you may contact the Office of Research Ethics and Integrity via email (ethics@uottawa.ca) or telephone (613-562-5387).

The University of Ottawa Research Ethics Board recommends that you (keep/print/save) a copy of this consent form for your records.

By pressing the NEXT button, you are consenting to participate in this research study. If you do not wish to participate, you may exit the page at this time.

Thank you for considering whether to participate in the survey.

1. Do you have an interest in the pediatric rare disease field?

- ◯ No
- ◯ Yes, please describe in the comment box below what your primary topic area or disease of interest is.

2. Are you an independent researcher? (By independent researcher we mean you are autonomous regarding your research activities; and have an academic institution or hospital research institute or other research organization appointment; and are eligible to receive peer-reviewed grant funding)

- ◯ Yes
- ◯ No

3. Which of the following best describes your primary work setting?

- ◯ Hospital
- ◯ Hospital-based research institute
- ◯ University
- ◯ Government
- ◯ Industry
- ◯ Other (please specify)

4. Please select all roles that apply:

- ☐ Professor (all ranks)
- ☐ Clinician
- ☐ Department Head (Ex. hospital, university, etc.)
- ☐ Industry Consultant
- ☐ Other (please specify)
- ☐ Executive of Professional Organization/Society
- ☐ Government Advisor/Consultant
- ☐ Patient Organization Advisor/Consultant

5. How many years have you worked as an independent researcher?

- ◯ Less than 1
- ◯ 1-3
- ◯ 4-5
- ◯ 6-10
- ◯ 11+
- ◯ N/A

6. What percentage of your time is dedicated to research?

0 50 100

7. How would you categorize your primary research?

- ◯ Biomedical
- ◯ Clinical
- ◯ Health systems and services
- ◯ Social, cultural, environmental and population health Other
- ◯ (please specify)

8. Have you ever contributed to a research project where any of these industry-research relationships occurred? (Check all that apply)

[by contributed we mean you were a lead investigator, co-investigator, or close collaborator]

Perkmann, M., King, Z., & Pavelin, S. (2011). Engaging excellence? Effects of faculty quality on university engagement with industry.

Research Policy, *40*(4), 539-552.

- ☐ **Licensing** = Contractual assignment of university-generated intellectual property (such as patents) to external organizations
- ☐ **Academic entrepreneurship** = Development and commercial exploitation of technologies pursued by academic inventors through a company they (partly) own
- ☐ **Collaborative research** = Research jointly pursued by university and industrial partners – commonly with public funding
- ☐ **Contract research** = Application-oriented research and development activities carried out by university – commissioned and funded by industry
- ☐ **Consulting** = Application-oriented research and development activities or advice provided individually by academics – commissioned and funded by industry
- ☐ I have not participated in any relationship with industry
- ☐ Other (please specify)

9. How many research projects have you contributed to within each type of academic- industry relationship?

	0	1-3	3-6	6-9	10+
Licensing = Contractual assignment of university-generated intellectual property (such as patents) to external organizations	○	○	○	○	○
Academic Entrepreneurship = Development and commercial exploitation of technologies pursued by academic inventors through a company they (partly) own	○	○	○	○	○
Collaborative Research = Research jointly pursued by university and industrial partners – commonly with public funding	○	○	○	○	○
Contract Research = Application-oriented research and development activities carried out by university – commissioned and funded by industry	○	○	○	○	○
Consulting = Application-oriented research and development activities or advice provided individually by academics – commissioned and funded by industry	○	○	○	○	○

Based on the definition:

Collaborative research = Research jointly pursued by university and industrial partners – commonly with public funding

10. Were any of your collaborative research projects with industry in pediatric rare disease?

- ◯ No
- ◯ Yes, please provide the what topic(s)/disease(s) of focus in the comment box below:

Please answer the following questions based on your most recent (ongoing or completed) collaborative research project in pediatric rare disease with industry:

11. At what stage is your collaborative research project in pediatric rare disease with industry currently at?

- ◯ Project is Completed
- ◯ Idea Generation
- ◯ Study agenda: scope, priorities, objective(s)
- ◯ Refinement of Research Question
- ◯ Design of Study Methodology (approach)
- ◯ Design of Methods (e.g. selection of outcome measures)
- ◯ Develop/Apply for Resources (e.g. funding applications/grant proposals)
- ◯ Research Ethics Board Review
- ◯ Data Collection
- ◯ Data Analysis
- ◯ Development of Dissemination Process
- ◯ Dissemination of Findings
- ◯ Reporting of Findings (e.g. article, report, conference presentation)
- ◯ Other (please specify)

  [ ]
- ◯ None of the above

12. From the list below, please select the position that best describes your previous or current role related to the collaborative research project in pediatric rare disease with industry:

- ◯ Principal Investigator (PI)
- ◯ Co-PI
- ◯ Co-Investigator
- ◯ Research Coordinator
- ◯ Collaborator
- ◯ Key Personnel
- ◯ Other (please specify)

  [ ]

13. Based on your collaborative research project in pediatric rare disease with industry, who were/are the other members on the research team (e.g. co-investigators, collaborators, advisors): (check all that apply)

- ☐ Basic Scientists
- ☐ Clinical Scientists
- ☐

Health Services Research and Policy Scientists

Population and Public Health Scientists

Clinicians

Industry Employees Government

Employees Patient Partners

Other (please specify)

14. How is/Was the collaborative pediatric rare disease project with industry funded? (check all that apply)

- [ ] Academic Institution
- [ ] Government Research Funding Agency
- [ ] Government Department
- [ ] Health Charity Patient
- [ ] Group Private Industry
- [ ]
- [ ]

Other (please specify)

15. What was/is the research area of the collaborative pediatric rare disease project with industry?

- ◯ Biomedical
- ◯ Clinical
- ◯ Health systems and services
- ◯ Social, cultural, environmental and population health ◯

Other (please specify)

16. What sector was/is the industry collaborator(s) from related to the collaborative research project in pediatric rare disease with industry? (check all that apply)

- [ ] Healthcare Equipment and Supplies
- [ ] Health Provider Services
- [ ] Health Technology
- [ ] Biotechnology
- [ ]
- [ ] Life Science Tools and Services
- [ ] Medical Insurance Pharmaceuticals
- [ ]

Other (please specify)

17. Based on the collaborative research project in pediatric rare disease with industry, who initiated the collaborative relationship with industry?

- ◯ Reseacher

- ◯ Industry partner
- ◯ Researcher and Industry Jointly Other
- ◯ (please specify)

18. What areas of the collaborative research project in pediatric rare disease with industry did you/do you plan to participate in? (check all that apply)

- [ ] Idea Generation
- [ ] Study Agenda: scope, priorities, objective(s)
- [ ] Refinement of Research Question
- [ ] Design of Study Methodology (approach)
- [ ] Design of Methods (e.g. selection of outcome measures)
- [ ] Develop/Apply for Resources (e.g. funding applications/grant proposals)
- [ ] Research Ethics Board Review
- [ ] Data Collection
- [ ] Data Analysis
- [ ] Development Dissemination Process
- [ ] Dissemination of Findings
- [ ] Reporting of Findings (e.g. article, report, conference presentation)
- [ ] Other (please specify)

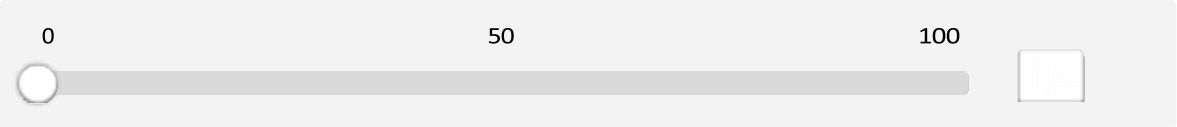
- [ ] None of the above

19. What areas of the collaborative research project in pediatric rare disease with industry did the industry partner participate in? (check all that apply)

- [ ] Idea Generation
- [ ] Study Agenda: scope, priorities, objective(s)
- [ ] Refinement of Research Question
- [ ] Design of Study Methodology (approach)
- [ ] Design of Methods (e.g. selection of outcome measures)
- [ ] Develop/Apply for Resources (e.g. funding applications/grant proposals)
- [ ] Research Ethics Board Review
- [ ] Data Collection
- [ ] Data Analysis
- [ ] Develop Dissemination Process
- [ ] Dissemination of Findings
- [ ] Reporting of Findings (e.g. article, report, conference presentation)
- [ ] Other (please specify)

- [ ] None of the above

20. How positive was your experience working collaboratively with industry? (rate on a scale 1-100 where 100 is extremely positive and 0 is not positive at all)



Based on the definition:

Collaborative research = Research jointly pursued by university and industrial partners - commonly with public funding

21. Would you consider participating in a collaborative research project with industry in the futute?

◯ Yes, I would consider participating in a collaborative project with industry ◯ No, I would not participate in a collaborative research project with industry

◯ I don't know if I would consider collaborating with industry on a research project

22. To what extent do you agree or disagree that the following are potential benefits to collaborating with industry on research projects? If you feel there is a additional benefit please specify under other.

	Strongly agree	Somewhat agree	Neither agree or disagree	Somewhat disagree	Strongly disagree
Knowledge sharing	◯	◯	◯	◯	◯
Access to funding	◯	◯	◯	◯	◯
Access to non financial resources	◯	◯	◯	◯	◯
Shared responsibility	◯	◯	◯	◯	◯
Translation of knowledge into practice	◯	◯	◯	◯	◯
Maximize outputs	◯	◯	◯	◯	◯
Opportunities for advanced research	◯	◯	◯	◯	◯

Other (please specify)

23. To what extent do you agree or disagree that the following are potential barriers/challenges to collaborating with industry on research projects? If you feel there is a additional barrier and/or challenges please specify under other.

	Strongly agree	Somewhat agree	Neither agree or disagree	Somewhat disagree	Strongly disagree
Conflicts of interest	○	○	○	○	○
Intellectual property rights issues	○	○	○	○	○
Ethical concerns	○	○	○	○	○
Differences in goals	○	○	○	○	○
Communication differences	○	○	○	○	○
Regulatory difficulties	○	○	○	○	○
Time/Schedule differences	○	○	○	○	○

Other (please specify)

24. Please enter the name of any Canadian pediatric rare disease researchers that you feel should receive this survey?

25. In which province or territory do you primarily reside?

- ◯ British Columbia
- ◯ Alberta
- ◯ Saskatchewan
- ◯ Manitoba
- ◯ Ontario
- ◯ Quebec
- ◯ New Brunswick
- ◯ Other (please specify)
- ◯ Nova Scotia
- ◯ Prince Edward Island
- ◯ Newfoundland and Labrador
- ◯ Northwest Territories
- ◯ The Yukon
- ◯ Outside of Canada Prefer not to answer

26. What is your age?

- ◯ 18-24 years old
- ◯ 25-34 years old
- ◯ 35-44 years old
- ◯ 45-54 years old
- ◯ 55-64 years old
- ◯ 65 years or older

27. How would you describe your current gender identity? By gender, we mean your self- identified gender, which may differ from the sex assigned at birth or from the one entered in legal documents.

28. Do you identify as a person with a disability?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

29. Do you identify as an Indigenous person?

- ◯ Yes
- ◯ No

◯ Prefer not to answer

30. Do you identify as a racialized person (member of a visible minority in Canada)?

◯ Yes

◯ No

◯ Prefer not to answer

31. What is the highest degree, certificate or diploma you have obtained?

- ◯ University certificate or diploma below bachelor level
- ◯ Professional Degree (e.g. medicine, dentistry, law, veterinary medicine, physical therapy)
- ◯ Bachelor's degree
- ◯ Master's degree
- ◯ Certificate or diploma above bachelor level
- ◯ Earned doctorate

32. Have you received a research grant in pediatric rare disease in the last 5 years? If yes, what topic(s)/disease area(s)?

- ◯ No
- ◯ Yes

33. Would you be willing to participate in a follow-up interview regarding your experiences with collaborative research with industry?

- ◯ No
- ◯ Yes (please provide contact information)

34. If you would like to receive the results of the survey please provide your email below:

Appendix 7: Sample of Interview Email Correspondence

From: Charly Degen
Subject: Rare Disease Research with Industry Interview Invitation

Dear Participant Name,

On behalf of the research team, I would like to thank you for completing the Rare Disease Research with Industry Survey and indicating your willingness to participate in the interview portion of this study.

We would like to invite you to tell us your experiences working with industry on collaborative research projects in an interview with a team researcher. Your input will help us to get a rich understanding of collaborative research experiences with industry from the perspectives of Canadian Pediatric academic/hospital-based researchers in the field of rare disease.

Participation will consist of a Zoom interview and will last no longer than 30-45 minutes. The interview will involve general questions relating to your experiences working with industry and your perceptions of factors that influence successful collaborations, challenges/barriers to working collaboratively with industry, benefits to working with industry and development of partnerships between industry and researchers.

This interview is confidential, and your participation is voluntary. You may stop at any time or skip any questions that you prefer not to answer. All information will remain confidential and no identifying information will be reported or published.

If you decide to participate, please review the attached consent form and provide us with some timeslots that will work for you.

If you have any questions or concerns, please contact Charlena Degen, Principal Investigator for this project at the University of Ottawa. It is important to know that the University of Ottawa Research Ethics Board has approved the ethical components of the project. If you have any questions regarding the ethical conduct of this study, you may contact the Office of Research Ethics and Integrity via email (ethics@uottawa.ca) or telephone (613-562-5387).

We appreciate your help with this project.

Many Thanks,

Charlena Degen
Charlena Degen (Principal Investigator/Graduate Student)
MSc Epidemiology Candidate
School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa

Appendix 8: Interview Guide

*Please note that prior to this interview, the research staff will have already provided the participant with the informed consent form, provided sufficient time for the participant to review the consent form and have their questions answered, and obtained the participant's signature on the consent form.

Pre-Recording

Thank you for agreeing to speak to me today and for previously completing the survey. We are very interested in hearing about your experiences working with industry in a collaborative way. This interview is part of the qualitative portion of my research project, in which, similar to the survey, I'm interested in research collaborations between industry and academic researchers in the field of rare diseases.

During this conversation I am interested in learning more about what you have previously experienced when you work with industry. We will be discussing:

- How the partnership developed
- Factors that influence the success of a collaboration with industry
- What the challenges may be working collaboratively
- The benefits of working collaboratively with industry
-Any advice you might have for people for who may participate in collaborative projects in the future

This should take approximately 30 to 45 minutes. As mentioned in the consent form, this will be audio recorded and transcribed but all identifying information will be removed by the research team and will not be published. Direct quotes may be used but any identifying information will be removed. You can stop the interview at any time or choose not to answer any question I might have.

Do you have any questions before we start?

Are you comfortable with starting the interview?

I would now like to start the recording are you okay with this?

Recording

Collaborative Research Generally

[bring up table] In the survey you mentioned that you have participated in "*x typed of relationships with industry*". Today I wanted to talk about the times you worked collaboratively, which is Research jointly pursued by university and industrial partners – commonly with public funding.

1. In general, how would you describe your experience working jointly with industry on research projects?

Probes:
How do your collaborative research projects with industry usually come about?
Who and how are they initiated?
In the survey you mentioned that industry worked with you on "*X (Example starting with defining the research question, drafting a research proposal, deciding on study design, methods, outcome measures, collecting data, analyzing data, interpreting finding, disseminating findings)"* Is this typical of the involvement of industry during collaborative research projects?

2. (if had multiple collaborative projects) Can you tell me about any particularly positive or negative experiences you have had conducting collaborative research projects with industry?

Probes:
What aspects made the project positive or negative for you?
How was this project different or stand out from others you have conducted?

3. In the survey you told us that you agreed that "*X (ex. Dissemination of findings, etc)*" was an important advantage when working collaboratively. Can you tell us more about why you feel this is a benefit to working collaboratively with industry?

Probe: What was the most important factor to working collaboratively?

4. In the survey you told us that you agreed that "*X (ex. Conflict of interest, etc)*" was a draw back when working collaboratively. Can you tell us more about why you feel this is a draw back when working collaboratively with industry?

Last Collaboration and Success

In the survey you answered several questions about your last collaborative pediatric rare disease research project. You indicated you were a (*name role*) on the project about (*Name disease area/topic*). You told us the project was (*stage of project*) where you worked collaboratively with industry from (*name sector*). The next set of questions are about that project to help us better understand your experiences.

5. You indicated that *X* initiated the project, can you tell me more on how that came about?

6. What made this project interesting to you and your industry partner?

Probe: Why did you decide that a collaborative approach would be best for this project?

7. What was the goal of this project?

Probe: Did you and industry align with what you wanted as an outcome of the project overall?

8. In the survey, you gave the project a X in terms of your experience. What made you give it this score?

Probes:
What do you think caused your collaboration on this research project to be successful/not successful?
What worked well? What did not?

Advice for Future Success

Thank you for sharing your experiences on your last project. I have some final questions about collaborative research.

9.In your opinion, what do you think makes a collaborative research project successful?

10. What tips for researchers do you have about how to create and then maintain positive collaborative research relationships?

Probe: what tips do you have for avoiding an unsuccessful collaboration with industry?

11. Do you have any other comments or anything you think is important about collaborative research with industry?

Appendix 9: Qualitative Theme Creation Steps

To create themes and subthemes, initial codes were created by C.D and reviewed by the I.G and B.P. Initial subthemes or themes were then presented and discussed by C.D, I.G and B.P. Refined subthemes and themes were presented to the entire research team to ensure applicability and credibility. In the table below, we presented codes that were aggregated into subthemes, and/or themes. For example, the initial codes: filling funding gap, speed, magnitude funding recipient and knowledge of sources were initially coded from the data. These codes were then grouped to form the subtheme Access to Funding, which became part of the larger theme, "Advantages or Benefits to Collaborating with industry." This method was used to create the themes presented in Chapter 2.

Codes	**Subthemes**	**Theme**
Negative Experience, Positive Experience, Mixed Experiences, Politically Complicated, Meaningful, Career Impact, Integral Interactive, Collegial, Productive, Open, Close Collab, No Drawbacks Encountered, Complex Feelings, Long-Standing, International, Eye-Opening, Diverse	Descriptions of Experience	Overall Experience with Industry
Industry Involvement, Frequency of Contact, Collaboration Involvement, Years Experience, Clinical Trial Experience, Regulatory Trial Experience, Stakeholders, Researchers Role, Contributions, Regulatory Requirements, Phase, Researcher Approach, Process, Compassionate Use, Reporting Obligations, Power Dynamics, Academic Institute Contract Involvement, Industry Expectations, President's Office Involvement, Canada Unique Landscape, Diagnostic Vs Therapeutic, Therapeutic Pathway Challenges, Diagnostic Landscape, Healthcare Landscape, Patient Registries, Clinical Trial Vs, Government Challenges	Collaborators Participation	Nature of Collaborations with Industry

Industry Funded, Researcher Common Interests, Grant Application, Application to Company, Reaching Out, Access to Drug, Engaging with Industry, Timing, Communication, Reaction to Initiation, Industry Expertise, Previous Relationship, Academic Entrepreneurship, Pharma	Researcher Initiated	Initiation of Collaboration with Industry
Researcher Expertise, Rare, Previous Relationship, Industry Common Interests, Clinical trials, CDTS Subcontract, Biotech, Proof of Principal, Credibility, Researcher Developed	Industry Initiated	
Previous Relationships, Merge Expertise, Both Common Interests, Scientific Meeting	Jointly	
Colleague, Personal Connection, Granting Competition, Granting Organization, Support Organizations, Patient Organizations	Third Party	
Push Pull Dynamic, Only Possible Approach, Patent Compound, Funding, Value of Project, Integration of Patient Experience, Drug Improvement, Drug Development, Means to End	Collaborative Approach	
Age/Experience, Bio vs Pharma, Company Culture	Determination of Type of Initiation	
Viability of Profit, Researchers Scared to Initiate	Engagement Challenge	
Filling Funding Gap, Speed, Magnitude, Funding Recipient, Knowledge of Sources,	Access to Funding	Advantages or Benefits to Collaboration with Industry

Translation Into Clinic	Translation of Knowledge	
Knowledge of Product, Regulatory Knowledge, Translation of Product, In-House Experts	Industry Expertise	
Advances Research, Innovation, Accelerated Innovation Cycle, Industry Interests	Advances Research	
Knowledge sharing, Network Creation, Troubleshooting	Collaboration Characteristics	
Access to Products, Drug Development Programs, Previous Work Done, Infrastructure, Technologies, Access to Consultants	Non-Financial Resources	
Honest, Straightforward, Focused, Quick-Learners, Well-Organized	Industry Characteristics	
Good for Trainees, Team Travel	Team Advancement	
Unified Voice, Advocacy for Patients, Influence Government and Regulations	Advocacy	
Industry Ease, Convenience	Industry Ease	
Different Motivations, Different Priorities, Differences in Pace/Speed, Industry Rush Product, General Administrative Bureaucracy, Ethical Bureaucracy, Academia Lack of Knowledge Translation, Difficulties to Engage, Different Regulations, Different Language, Approvals/Agreements, Rules and Regulations, Bad Contract, Behind Times, Academic Delay, Barrier to Trainee, Missed Opportunity, Academia View on Partnership, Ulterior	Differences in Goals & Motivations	Barriers and Disadvantages to Collaboration with Industry

Motives/Specious, University Researcher Relationships		
Lack of Communication, Lack of Consultation, Lack of Follow-Through	Communication	
Users, Know-it-all, Self-Importance, Money Hungry, Different View on Collaboration, Naïve, Dishonest, View of Academia, Exclusionary, Difficult to Get Along, Underestimate Researcher, Pushy, Unwilling to Reciprocate, Marketing, Care Salesman	Industry Attitude	
Change in Company Size, Change in Direction, Change in Ownership, Change in Personnel, Company Size	Industry Turnover & Acquisition	
Work Not Publishable, Reluctance to Publish, Spin	Publishing Difficulties	
Ethical Conduct, Confidentiality, Go Beyond Indication, Steal Ideas, Remove Property, Data Ownership	Additional Ethical Issues	
Licensing	Licensing	
Conflict of interest, ethical double standard, ethical conduct, academic kickbacks	Conflict of Interest	
Too Specialized, Non-Content Experts, Users, Reluctance to Publish	Biotech Issues	
Produce Results, Publish, Publish Trainee, Prove Hypothesis, Discovery, Innovation, Advances Research	Results	Outputs of a Positive Collaboration
Impacts Patients, Give Back to Community, Adoption of Product	Translation of Knowledge	

Collegial Relationships	Collegial Relationships	
Patient or Disease Motivated, View of Academia, Not Influence Results, Hands Off, Not Pushy, Supportive, Management Style	Alignment of Culture and Motivations	Careful Selection of Partner and Project
Like Colleagues, Don't Tell All, Intuition, Look for Warning Flags, Consider Benefit to Industry, Caution, What's the Catch, Double Check, Prepared to Walk Away	Choose Partner Carefully/ Caution	
Cross Over Disciplines, Plays to Strengths, Mutually Beneficial	Includes Different Knowledge Bases	
Mutually	Mutually Beneficial	
Academic Freedom, Publish Independently, Stay Arms Length, Financial Independence, Plays to Strengths, Philosophy Alignment, Common Vision, Common Will, Common Interests,	Fits Resource Needs	
Trust, Equal, Honesty, Respect, Confidentiality, Openness and Transparency, Relationships	Components for Positive Collaboration	Engaging in relationship building opportunities to establish mutual trust
Understand Audience, Work Fast, Clear Discussions	Sharing and Understanding	
Relationship Building First, Communication, Negotiation Skills, Resolve Problems Quickly, Collaborative Effort, Team Player and Leader	People Skills	
Under promise, Small Deliverables, Test Drive	Test Drive with Small Deliverables	
Personal Ethics, Check/Manage COI, Institute Oversight, Licensing Awareness, Ethics Considered	Ethical Considerations	Establishing clear expectations, agreements and governance practices

Expectations, Well-Planned, Awareness of Publication Needs, Rules and Regulations	Well Planned	
Mitacs, Work with Innovation Offices, Use Organizational Resources	Use Intermediary Organizations	Advocating/using supportive institutional structures
Continue Learning, Mentorship	Mentorship	
Open, Opportunity Awareness, Make Institute Aware	Awareness of Opportunities	
Changes to System, Two Communities, Academic Environment, Research Ecosystem, Academic Institutes contract improvements	Advocate for Supportive Structures	

CHAPTER 3

3.1 Summary of Findings

3.1a Survey Participant & Interviewee Characteristics

We surveyed 126 Canadian pediatric academic/hospital-based researchers about their experience conducting collaborative research with industry. Our samples mainly consisted of more experienced researchers who had either a professional degree or had earned a doctorate. The majority of participants were over 45 years of age (79%) and self-identified as male or a man (61%), and a fifth self-identified as a racialized person. Participants were distributed across Canada, with 60% residing in Ontario (38%) and Alberta (22%). They held a variety of positions including professor at all ranks (98%), clinician (67%), and industry consultant (21%). Of the 126, 59 survey participants (47%) had previous experience with collaborative research with industry (as defined by Perkmann et al.[1]), and 41 (69%) of those had experience in collaborative research with industry in pediatric rare disease.

The interview sample consisted of 10 of the 41 survey participants who had experience in collaborative research with industry in pediatric rare diseases. All were over the age of 45, and more than two-thirds self-identified as a man or male, 2 self-identified as a racialized person, half had a professional degree and half had earned a doctorate. From the survey responses among those that were interviewed, four reported contributing to 1-3 collaborative research projects with industry and six reported having contributed to more than 3 collaborative projects with industry.

3.1b Collaborative Experiences with Industry and Levels of Participation in the Research Life Cycle

Survey participants rated their collaborative experience with industry in pediatric rare disease positively (median score of 90 on a scale of 0-100, with 100 meaning “entirely positive”). Though there were a variety of experiences described by the interviewees, in general most interviewees described

their collaborations with industry as a win-win that advantages both the researcher and the industry partner.

Survey participants described their participation and their industry partner's participation in the stages of the research process. Interviewees described a range of participation levels in the research process by the industry partner. There was more participation by the researchers in all areas of the research process compared to their industry partner. Industry partners mostly contributed to the study agenda, refinement of the research question, and the developing or applying for resources stages of the project. Some partners were involved in almost every stage of the research and others were "hands-off" or removed from the research being done. In many of the cases where the industry partner was removed from the research, the industry partner was responsible for moving the product through the regulatory hurdles once research was complete.

3.1c Advantages/Benefits and Disadvantages/Barriers of Collaborative Research with Industry

Nearly all survey participants agreed or strongly agreed that potential advantages/ benefits of collaborating with industry included access to funding, translation of knowledge, knowledge sharing, access to non-financial resources and opportunity for advanced research. There was less consensus between the individuals who had collaborative experience with industry compared to those who had no collaborative experience with industry about potential disadvantages/barriers to collaboration with industry. Those with collaborative research experience with industry were less likely to identify differences in goals, conflict of interest, and communication as barriers to conducting collaborative research compared with respondents who had no industry experience.

Similar to the survey findings, advantages such as access to funding, translation of knowledge, knowledge sharing, access to non-financial resources and opportunity for advanced research were also described in the interviews. Interviewees also discussed disadvantages/barriers such as differences in

goals, conflict of interest, and additional ethical concerns. While not asked about in the survey, interviewees described other advantages/benefits to collaborating with industry including advancement of the research team, industry culture, and patient advocacy. Disadvantages/barriers described only in the interviews were industry turnover and acquisition.

3.1d Tips for Researchers

Interviewees provided tips for researchers about how to create, and then maintain, positive collaborative research relationships. These tips fell into four main categories: (i) careful selection of partner/project; (ii) engaging in relationship building opportunities to establish mutual trust; (iii) establishing clear expectations, agreements and governance practices; and (iv) advocating/using supportive institutional structures.

3.2 Discussion

Considering the increase in the number of new therapies being developed for rare diseases and investments in research in this field in recent years, it is important to understand how academia can best collaborate with industry including advantages, disadvantages, and strategies to promote success from a researcher's perspective. This is essential as both academia and industry play an important role in aspects of R&D. In Chapter 1 we categorized factors identified in the literature as influencing success and experience of academic-industry relationships into 3 groups: 1) factors predisposing the development of academic-industry relationship, 2) factors related to the academic-industry relationship, and 3) contextual factors that impact the relationship. In the remaining section we will discuss how the suggestions and guidance that the interviewees provided relates to the reported benefits/ barriers discussed by our study participants and the factors that influence success in the wider literature.

3.2.a Careful Selection of Partner and Project

Our interviewees highlighted the importance of choosing the appropriate industry partner and project when deciding to collaborate with industry. The majority of interviewees identified their prime motivation for partnering with industry was the opportunity to access funding and other non-financial resources (industry expertise, products, etc.) they did not have access to. Access to industry funding and other resources is also identified in the literature as a predisposing factor in developing an academic-industry relationship [2–9]. Even though some interviewees advised financial independence from the industry partner, the overwhelming majority in both the survey and the interviews indicated that access to funding was an advantage to collaboration with industry and many interviewees said that funding provided by industry is filling in the gap in the rare disease research ecosystem. Given that rare disease space historically has had limited funding resources and opportunities, this advantage that industry provides may be why many decide that collaboration is the best option for their goals [10]. Selecting the most appropriate partner that can enhance one's financial and resource needs is an important starting point.

Another partnership selection criteria from our findings relates to the potential for mutual benefit for both partners in the collaboration. Our participants' experiences revealed that when both partners benefit from the partnership, the collaboration is more successful. Seeking mutual benefit or perceived value in the partnership is an important factor in the success of a potential collaborative relationship that is also reported in the general literature [4, 11–13]. In the rare disease literature, Berry et. al [14] noted that considering joint benefit from the relationship went beyond benefits for just the researcher and industry partner but also included patients and families. Though our interviewees did not explicitly say that projects must benefit patients and families, they did emphasize the importance of finding a collaborative partner that was motivated by the patients or addressing the disease of interest,

which shows the importance of taking into account potential benefits of the collaborative research for the patient in rare disease collaborations with industry.

Related to the concept of mutual benefit, interviewees also spoke of specific considerations that influenced their (and their industry partner's) decisions to collaborate. They spoke about academia and industry bringing different knowledge bases, expertise, and strengths to the relationship that were synergistic and needed to complete the project. This could include things like industry having expertise in obtaining drug regulatory approvals that researchers lacked and researchers having scientific expertise or reputations that industry wanted to access. In our study, interviewees pointed out that a good collaboration consists of a multidisciplinary team that plays to the strengths of those involved. Strengths of academia and industry can be complementary as academia are experts in basic research activities such as disease and pathway knowledge whereas industry are experts in the regulatory processes and have the resources necessary to move products through the drug development pipeline [15, 16]. That academia and industry have different knowledge bases and strengths has been acknowledged in the literature [4, 8, 13, 17]. Dilling et al. [8] found that a new cell therapy platform was able to be developed due to complementary capabilities of the researchers and industry partners. For the relationship to be a good one, all partners must bring skills to the table that would result in everyone receiving benefit from joining forces.

Participants recognized successful partnerships were ones where there was general alignment in culture and motivations of the partners and the importance of recognizing the commonalities and differences in cultures that might positively or negatively affect the relationship. Interviewees revealed that industry culture and motivations can either be a benefit or barrier to collaboration. Industry was characterized as being focused, straightforward, and organized which was seen as advantageous when collaborating but differences in motivations can fester frustration and distrust. Sixty-eight percent of our survey participants strongly or somewhat agreed that differences in goals was a potential barrier to

collaboration. Elaborating on some of the possible cultural differences, interviewees perceived industry to be motivated by generating profit which was amplified by small cohorts of patients in rare disease making engagement challenging. Differences in motivations was observed in the rare disease literature as Berry et al. [14] found that the motives of decision making were not aligned despite having a shared agenda. When searching for the best partner, interviewees advised others to focus on choosing an industry partner whose culture best fits with their needs. Characteristics of a good industry collaborator include being motivated by improving patients' wellbeing, not viewing academia as an adversary, having a well-suited work style, and including people who the researcher genuinely likes. They also suggested looking for warning flags when entering a relationship and walking away from the relationship when necessary. These suggestions by interviewees on how to select a good collaborative partner target many factors noted in the literature as potentially influencing the success of academic-industry relationships including, compatibility of cultures and motivations [2–7, 13, 16, 18], and alignment of interests [7, 8, 11, 13, 19]. As previously mentioned, we found that many of these factors can be beneficial to collaboration or become barriers to successful collaborations if ignored. By selecting the appropriate partner that fits the needs of the researcher this may aid in ensuring that these influences become beneficial to collaboration.

Both the potential benefits/barriers described by the survey participants and the interviewees, and the suggestions made by the interviewees provide a glimpse into the rationale behind choosing an industry partner. We found that the choice of industry partners and projects are generally based on the resources needed to complete the project, mutual benefit that will arise from conducting the proposed project, compatibility with industry culture, and ensuring complimentary capabilities and synergies of partners' strengths, knowledge, and expertise. Careful selection of the right industry partner is necessary but not sufficient to guarantee a successful collaborative research project, partners must engage in trust building opportunities.

3.2b Engaging in Relationship Building Opportunities to Establish Mutual Trust

Strategies suggested by our interviewees for establishing trust among partners conducting collaborative research included: sharing and understanding legal and organizational regulations and policies governing each partner's conduct, practicing transparent and open communication, and test-driving relationships by working together to achieve small deliverables thereby incrementally building trust in each other. An interviewee also highlighted why establishing trust was so important by noting that early career researchers should not prematurely disclose all their ideas and plans to potential industry partners until they have established a trusting relationship, as their prospective partners may run off with their ideas. In the rare disease literature, Salkeld [20] acknowledges that in order to collaborate data sharing is necessary, making trust an important element of building a collaborative relationship. When researchers and industry partners are able to build trust, collaborations are more likely to be productive, but when there is a lack of trust collaborations can crumble [7, 11, 17, 21]. Some academics identify lack of trust stemming from researchers' concerns about the potential for unethical behaviour of industry [4]. Our interviewees spoke of instances where industry conducted themselves in an unethical way such as lying to the researcher, withholding information, putting a favorable spin on results, making generalizations not supported by the data, trying to remove researchers notes from their research lab and stole the researcher's ideas. Pediatric rare disease researchers inherently work with vulnerable populations (children, many of whom have severe chronic conditions and unmet needs), which may have contributed to the emphasis on trust among those we surveyed and interviewed.

Interviewees noted that people skills such as good communication, leadership, problem-solving skills, and negotiation skills can have a positive influence on relationships with industry partners which may be advantageous when building relationships. Good communication between the partners was noted by our participants to be critical to building trust. Fifty-six percent of our survey participants identified communication issues as a barrier to collaborations with industry. This sentiment was echoed

in our interviews; two researchers had difficulties with their industry partners' lack of communication and when interviewees had negative interactions, they often described the industry partner involved as pushy and dishonest. One suggestion in the literature for how to enhance communications in collaborative research is frequent face-to-face meetings [4, 12, 13].

3.2c Establishing Clear Expectations, Agreements and Governance Practices

Our interviewees emphasized the establishment of clear governance practices and expectations particularly in the planning stage by checking/managing potential conflict of interest; and setting expectations prior to initiating the project about responsibilities, collaborative involvement, rules and regulations, timing, publishing and licensing rights. Establishing expectations in terms of publishing rights is an important factor for the success of the collaborations since industry partners may be reluctant to publish as noted in the literature [5, 22]. Publishing research regardless of the findings is important to academic researchers as a component of scientific integrity. A few interviewees also suggested a priority should be ensuring academic freedom is included in the partnership agreement and that this needs to be addressed in the early stages of the collaboration. Expectations are specific to the research and project but interviewees who had experience with collaborative projects in rare diseases with industry recommended that transparency and communication of expectations can help create and maintain positive collaborative relationships. These findings are generally consistent with previous literature that has also described multiple factors that potentially influence academic-industry relationships including: managing confidential information and conflicts of interest [2, 8, 23, 24]; and negotiating and establishing agreements, expectations and rights [2, 5–8, 11, 12, 19, 25]. In the rare disease literature, Berry et al. [14] found that issues of conflict of interest, conflicting confidentiality agreements and companies trying to include a small cohort of patients in multiple clinical trials were concerns when collaborating with industry. Strategies to address these potential issues are early participation of legal

teams [19], mitigation of conflict of interest issues through creation of guidelines [14]; and early agreements on rights and data sharing [25].

3.2d Advocating/Using Supportive Institutional Structures

Researchers we interviewed described how initiation of many of their collaborative projects was facilitated by third party individuals or organizations. Colleagues, personal connections, patient organizations, granting agencies, and research support agencies all assisted in finding and enabling collaborative relationships with industry. The helpfulness of this support resonated with many as interviewees who suggested researchers seek out the aid of intermediary organizations either within the academic institution or externally when collaborating with industry. Academic institution structures and organization can play a significant role in the collaboration experience of researchers. This has also been observed in the literature [3, 4, 7, 11, 18, 19, 24, 25]. Researchers we interviewed spoke about how their technology transfer offices, research and innovation offices, and industry liaison offices within their organizations are "excellent at drafting agreements and protecting the interests of the institute and investigator" while others described how their university bureaucracy caused delays in their research. Researchers working with industry have also reported lack of sufficient guidance and support from their institutions on working with industry [24]. Differences in our researchers' experiences in the support received with their own university/institutions highlights the need for supportive structures within the academic institution to better assist those wanting to enter into collaborative relationships with industry.

3.3 Limitations and Strengths

Our study has some limitations. As there was no previous enumeration of Canadian academic/hospital-based researchers conducting collaborative pediatric rare disease research, our recruitment strategy for the survey relied on identifying researchers who were either published or had information about their research accessible in the public domain. This may have resulted in an incomplete sample frame and led to participant selection bias if those in the sampling frame are

systematically different from our intended target population of Canadian rare disease researchers based at academic/hospital settings. Furthermore, the survey response rate was 20%, raising further issues of potential selection bias due to non-response. For example, individuals with industry experience may have been more likely to participate in the survey. The study sample was relatively large (n=126) and diverse, although we were not able to compare responders to non-responders to identify any systematic differences there may have been between these groups. Those with more positive experiences may also have been more willing to be interviewed.

Social desirability could be of concern in the interview data as interviewees may have exaggerated the benefits/barriers in an attempt to provide responses they believed the interviewer was interested in hearing. While a concern, our participants with experience with collaborative research not only reported positive experiences with industry, they also spoke candidly about negative experiences as well. In both the survey and interviews, we asked participants to recall and self-report on past events and experiences, which may impact the validity of our findings to the extent that such events may not have been recalled accurately. Finally, as this study only surveyed and interviewed academic/hospital-based researchers, it did not capture the viewpoint of industry. This was a pragmatic decision related to the need to limit the scope of the thesis to the timeframe and resources available to conduct an MSc thesis. Additional research should be conducted with industry participants to learn their perspective on what constitutes good collaborative research and partnership with academic/hospital-based researchers conducting research into pediatric rare diseases.

Our study has multiple strengths. First, to the best of our knowledge we are the first to study Canadian pediatric rare disease academic/hospital-based researchers' experiences collaborating with industry. We believe that our search strategy led to a sampling frame including a fairly large and comprehensive cross-section of individuals invited to participate. Second, our mixed methods approach allowed us to incorporate both quantitative and qualitative methods into our research which captured

both the frequency of different types of academic-industry relationships of the researchers, characteristics of collaborative projects with industry in pediatric rare diseases, and also provided an in-depth look into these collaborative relationships with industry. Third, our study asked interviewees to provide tips to prospective researchers which can serve as a starting point for potential industry partnership guidance. Finally, we incorporated several methods to ensure rigor and trustworthiness including triangulation of data by converging different data sources, producing a thick description of successful collaborative research from the perspective of academic/hospital-based researchers, receiving research ethics board approval, declaration of positionality of the researchers, and inclusion of investigators on the research team that have experience with collaborative research with industry and other non academic partners.

3.4 Conclusion and Implications for Future Research

In summary, to the best of our knowledge we are first to document the relationships that Canadian pediatric rare disease researchers have with industry and undertake an in-depth exploration of their collaborative research experiences with industry. We found that Canadian pediatric rare disease researchers often had positive experiences collaborating with industry and many would consider collaborating with industry in the future. They identified many benefits to collaboration including access to funding, translation of knowledge, knowledge sharing, and advancement of the research team. Collaborations with industry could address the funding needs of many in the rare disease space [10]. Researchers' perceived industry to often be driven by profits, which is a challenge for rare disease researchers as small cohorts make industry less willing to enter into rare disease research due to viability of profit. Perceptions about different motivations between academic researchers and industry partners were also mentioned as contributing factors to negative collaborative experiences. However, interviewees also revealed that to make a partnership viable, there needs to be a common goal focused on the well being of the patients. Tips for researchers to increase the likelihood of positive collaborative

relationships involve careful selection of the industry partner, engaging in trust building opportunities, establishing clear governance practices, and using/advocating for supportive institutional structures. Suggestions provided by our interviewees can serve as a starting point for researchers interested in guidance on conducting collaborative research and also identify areas for future research on how to initiate and maintain fruitful collaborative relationships with industry. Research is needed to elicit industry partners' experiences and perspectives working with academic pediatric rare disease researchers.

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