Leveraging Opportunities to Apply Internet Tools to Epidemiological Studies in Diabetes

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Abstract

Background: Diabetes mellitus has risen as one of the top ten leading causes of mortality in the world. Although medical research has enhanced our understanding of how to manage and prevent this disease in its various forms, full efficacy remains difficult to achieve. The rise of the internet in the 21st century has provided researchers the opportunity to analyze information of greater complexity and scope; I explored how it could be used to specifically advance diabetes research by applying internet-based tools to two projects gathering and analyzing health-related information from end-users of epidemiological diabetes research.

Methods: For the first project, I built a Delphi survey onto an internet-based software program and administered it to healthcare professionals, researchers, and women with gestational diabetes mellitus over a six-month period to elicit opinions on a core outcome set. I appraised the literature surrounding core outcome set methodology and critically considered issues in managing Delphi results from the survey phase to consensus panel meeting phase. For the second project, I examined the activities of a private Facebook group for youth living with type 1 diabetes mellitus, then critically appraised the literature on qualitative and quantitative methodology. I developed a rigorous analysis strategy in consideration of the group as an epidemiological cohort.

Results: The internet-based Delphi survey facilitated a consensus process amongst individuals from all three stakeholder groups residing in 23 countries around the world. Survey attrition was greatest amongst women with gestational diabetes mellitus. Fidelity to the survey results was maintained during and following the consensus panel meeting. The manuscript is under review. Previous quantitative analyses of virtual patient groups include social network analysis, which evaluates each member's centrality. We incorporated this concept into our analysis protocol but adapted the centrality metric to reflect both breadth and depth of interactions, using a weighted approach drawn from economics modelling. We proposed applying multivariate linear regression analyses to relate centrality to the behaviour of offering support, captured via content analysis of qualitative data using an existing social support coding framework. We proposed to study the network as a dynamic cohort within an epidemiological person-time framework. The protocol manuscript has been revised in accordance with reviewers' comments.

Conclusions: Internet-based tools present a novel way to perform research that engages a patient population of interest; data collection is facilitated efficiently through online software, and rich interaction information can be extracted from online social network communities.

Résumé

Contexte: Le diabète sucré est devenu l'une des dix principales causes de mortalité dans le monde. Bien que la recherche médicale ait amélioré notre façon de gérer et de prévenir cette maladie sous ses diverses formes, une efficacité complète reste difficile à atteindre. L'essor d'Internet au 21e siècle a permis aux chercheurs d’analyser des informations plus complexes et plus vastes. J’ai exploré comment cela pourrait être utilisé pour faire avancer spécifiquement la recherche sur le diabète en recueillant et en analysant des informations sur la santé provenant d’utilisateurs finaux d’études épidémiologiques sur le diabète.

Méthode: Pour le premier projet, j'ai élaboré un sondage Delphi sur un logiciel Internet et je l'ai fait remplir par des professionnels de la santé, des chercheurs et des femmes atteintes de diabète sucré gestationnel sur une période de six mois afin d’obtenir leurs opinions sur un ensemble de résultats de base. Ma directrice de thèse et moi avons évalué la littérature portant sur la méthodologie des ensembles de résultats de bases et examiné les problèmes de gestion des résultats Delphi de la phase d'enquête à la phase de réunion du panel de consensus. Pour le deuxième projet, j'ai examiné les activités d'un groupe Facebook privé pour les jeunes atteints de diabète sucré de type 1, puis j'ai évalué de manière critique la littérature sur la méthodologie qualitative et quantitative. J'ai développé une stratégie d'analyse rigoureuse adaptée aux données disponibles en considérant le groupe comme une cohorte épidémiologique.

Résultats: Le sondage Delphi sur Internet a permis aux membres des trois parties prenantes, dont les membres résident dans 23 pays à travers le monde, d’arriver à un consensus. Le taux d'attrition de l'enquête était le plus élevé chez les femmes atteintes de diabète sucré gestationnel. La fidélité aux résultats de l'enquête a été maintenue pendant et après la réunion du panel de consensus. Le manuscrit est en cours de révision. Les analyses quantitatives précédentes de groupes de patients virtuels incluent l'analyse des réseaux sociaux, qui évalue la centralité de chaque membre. Nous avons incorporé ce concept dans notre protocole d'analyse tout en adaptant la métrique de centralité pour refléter à la fois l'étendue et la profondeur des interactions, en utilisant une approche pondérée tirée de la modélisation économique. Nous avons proposé d'appliquer des analyses de régression multilinéaires pour relier la centralité au comportement de l'offre de soutien, capturé via l'analyse de contenu des données qualitatives en utilisant un cadre de codage de soutien social existant. Nous avons proposé d'étudier le réseau en tant que cohorte dynamique dans un cadre épidémiologique temps-personne. Le manuscrit du protocole a été révisé conformément aux commentaires des examinateurs.

Conclusions: Les outils Internet présentent une nouvelle façon d'effectuer des études qui sollicite une certaine population de patients; la collecte de données est facilitée par un logiciel en ligne, et de riches informations peuvent être extraites des communautés de réseaux sociaux.

Preface

In this thesis, I apply internet-based tools to epidemiological studies of diabetes, illustrating ability of these tools to capture information of high complexity and scope. First, I provide a rationale for this research and outline the two main objectives of the thesis (preface 1). Chapter 2 provides an overview of epidemiology research in the age of increased internet presence, as well as a summary of the etiology and management of diabetes mellitus. In the subsequent chapters, I present the methodology and results of each objective separately.

Chapters 3 and 4 pertain to the first objective, corresponding to the first manuscript:

> Nancy Wu, Sharleen O'Reilly, Karoline K. Nielsen, Helle Maindal, Kaberi Dasgupta. Core Outcome Set for Diabetes After Pregnancy prevention across the lifespan: an international Delphi study.

Specifically, Chapter 3 details the study methodology focused on implementation of a web-based survey. This is followed by the results presented in the form of the manuscript itself in Chapter 4. This manuscript was submitted to the *British Medical Journal Open Diabetes Research & Care* in May 2020 and is under review at the time of submission of this thesis.

Chapters 5 and 6 pertain to the second objective, corresponding to the second manuscript:

> Nancy Wu, Anne-Sophie Brazeau, Meranda Nakhla, Deborah Chan, Deborah Da Costa, Geetha Mukerji, Sonia Butalia, Daniele Pacaud, Melanie Henderson, Constadina Panagiotopoulos, Elham Rahme, Kaberi Dasgupta. The Type 1 Diabetes Mellitus Virtual Patient Network (T1DM-VPN): Protocol for social network analysis and content analysis of a peer support community

Specifically, Chapter 5 details the study methodology, focusing on the synthesis of existing approaches to web-based text and activity analysis. This is followed by the results presented in the form of the manuscript itself in Chapter 6. This manuscript was submitted to the *Journal of Medical Internet Research Protocols* in June 2020; it has been reviewed with request for revisions which have been submitted.

I discuss the results of both endeavours in Chapter 7. Finally, concluding remarks are made in Chapter 8. References are provided in Chapter 9.

This thesis has been prepared according to McGill University Graduate and Postdoctoral Studies' guidelines for a "Manuscript-based Thesis".

Contribution of Authors

The first paper is a report of a core outcome set based on a modified e-Delphi method and expert consensus meeting. The original idea and design of the core outcome initiative itself was by my primary supervisor Dr. Kaberi Dasgupta, with her colleagues Dr. Sharleen O'Reilly, and Dr. Helle Maindal, with input from Dr Maindal's postdoctoral student, Dr. Karoline K. Nielsen. The initiative was funded by a meeting and planning grant (Canadian Institutes of Health Research Planning and Dissemination Grant Funding Reference #: PCS-155268; Nominated Principal Investigator K Dasgupta).

I wrote a detailed protocol for the conduct of the e-Delphi survey and submitted this to the Research Ethics Board at McGill University Health Centre, under Dr. Kaberi Dasgupta's supervision and with input from her colleagues. I executed the e-Delphi surveys, analyzed the results, and organized the consensus panel meeting in Florence, Italy, taking notes at the meetings and synthesizing the final core outcome set. I wrote the first draft and revised subsequent drafts with input from co-authors.

The second paper is a detailed study protocol that I designed to analyze a private Facebook page based virtual peer support group for youth to type 1 diabetes mellitus, initiated by my primary supervisor Dr. Kaberi Dasgupta, and her colleagues, including my co-supervisor Dr. Elham Rahme, as well as Dr. Anne-Sophie Brazeau, Dr. Meranda Nakhla, Dr. Deborah Da Costa, Dr. Geetha Mukerji, Dr. Sonia Butalia, Dr. Daniele Pacaud, Dr. Melanie Henderson, and Dr. Constadina Panagiotopoulos. The network was created through funding from Diabetes Canada and the Canadian Institutes of Health Research Planning and Dissemination *Strategy for Patient-Oriented Research (SPOR) – Patient-Oriented Research Collaboration Grant* (Nominated Principal Investigator K Dasgupta). Under my supervisors' guidance, I conducted the literature reviews in sociology and epidemiology needed to design a social network analysis approach and combined this with a content analysis approach to examination of the communication texts. I submitted the protocol for research ethics board review, with assistance from Dr. Dasgupta's research assistant Deborah Chan. I drafted the manuscript and reviewed it in accordance with comments and edits from my supervisors and their colleagues listed above.

I wrote all non-manuscript chapters of this thesis, which were then critically reviewed and revised by Dr. Kaberi Dasgupta and Dr. Elham Rahme.

Acknowledgements

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First and foremost, I would like to thank my supervisor Dr. Dasgupta and my co-supervisor Dr. Rahme for their support, not only towards this project but also towards my growth as a young scholar. I am grateful to have had Dr. Dasgupta as a mentor; her leadership and expertise, combined with humility and compassion, inspire me to become a better professional and a better person. I would be remiss if I did not also acknowledge Deborah Chan and Charlene Weight, research assistants at the MUHC, whose capabilities and eagerness to help were a constant source of reassurance.

Adding further to my motivation was the social and intellectual environment cultivated by McGill's Department of Epidemiology, Biostatistics, and Occupational Health – professors such as Dr. Lawrence Joseph who genuinely want to mentor their students; my MSc Epidemiology and MSc Public Health cohort; and my fellow trainees in the Dasgupta Diabetes Management and Prevention Research Group, Alexandra Cooke and Joseph Mussa.

Lastly, I would like to acknowledge my parents Randy Wu and Sally Lin, and my brother Alex Wu for all they have done for me. Their critical thinking and perseverance remind me of what it means to be educated, and their humility and generosity teach me what it means to be a good person.

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List of Abbreviations/Acronyms

Consolidated Standards of Reporting Trials (CONSORT)
Core Outcome Measures in Effectiveness Trials (COMET)
Core outcome set (COS)
Diabetes mellitus (DM)
Gestational diabetes mellitus (GDM)
Grading of Recommendations Assessment, Development and Evaluation (GRADE)
McGill University Health Centre (MUHC)
Outcome Measures in Rheumatoid Arthritis Clinical Trials (OMERACT)
Social network analysis (SNA)
Socioeconomic status (SES)
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Type 1 diabetes mellitus (T1DM)
Type 2 diabetes mellitus (T2DM)
Type 1 Diabetes Mellitus – Virtual Private Network (T1DM-VPN)

1. Introduction

1.1 Rationale

The World Health Organization has described non-communicable diseases to be among the greatest challenges in the 21st century. Important among these is diabetes mellitus (DM) which is one of the top ten leading causes of mortality [1]. Modern epidemiologic research has enhanced our understanding of how to manage and prevent this disease in its various forms; lifestyle behaviour change can reduce risk of type 2 diabetes mellitus (T2DM) in women with a diagnosis of gestational diabetes mellitus (GDM) during pregnancy, and insulin technology helps youth with type 1 diabetes mellitus (T1DM) the potential to live long and fulfilling lives,. Despite this knowledge, actual effectiveness in prevention and management remain difficult to achieve. The rise of the internet in the 21st century has provided researchers the opportunity to explore information of greater complexity and scope; thus, a natural question that arises is how internet tools can be leveraged to move diabetes research forward.

1.2 .Objectives

This thesis applies and thereby illustrates the ability of internet-based tools to gather and analyze health-related information from large and geogprahically-dispersed end-users of epidemiological diabetes research. In the first instance, the stakeholders are health researchers, clinicians, and women with a GDM history; they were participants in two rounds of a large, international Delphi survey conducted online. In the second instance, the subjects are youth with T1DM and the analyses presented are that of an online community. Alongside these manuscripts, I also critically consider the capacity of internet-based methods and their impact on the research process compared to their traditional counterparts.

For the first project, I aimed to identify a core outcome set (COS) for trials evaluating health behaviour change interventions for diabetes prevention following a GDM pregnancy, using a modified electronic (e)-Delphi method. In moving towards this objective, I had to address methodological issues concerning the degree of divergence a consensus panel could or should make from the e-Delphi survey findings themselves, which consist of opinions expressed by the much larger group of survey respondents. For the second project, I aimed to develop a comprehensive analysis protocol to analyze the virtual interactions facilitated in *Type 1 Diabetes Mellitus – Virtual Private Network* (T1DM-VPN), a private Facebook group that my primary supervisor and her colleagues established for youth in Canada living with T1DM. I designed the analytic approach to incorporate directed content analysis, social network analysis, and regression analysis, carefully treating the cohort as an open cohort, and thus bearing in mind the importance of person-time in analysis; previous social network analyses applied to virtual communities have often made assumptions about cohort stability that may not be appropriate.

2. Literature Review

2.1. Internet-Based Epidemiology Research

2.1.1. The field of e-epidemiology

The internet is a global network of networks. It was initially developed as a method of transferring data among several universities in the United States. Within four years of its introduction to the public in 1991, it garnered 50 million users [2]. Today, it is a ubiquitous method of communication and the number of users with devices that can interface with it is in the billions. The web is a collection of information that can be accessed via the Internet. Technologies such as email are also facilitated through the internet, but are not part of the web. This thesis predominantly makes reference to the internet, with specific use of the term “web” where intended.

The rise of the internet offers new opportunities for epidemiological research. There is the potential to reach a greater number of subjects, and to do so with greater efficiency. Novel data may be extracted from, for example, social media platforms, to understand health outcomes and behaviours, with methodological innovations to do so. Some challenges faced in traditional epidemiological methods remain, others are overcome, and a unique set of challenges arise. All of these topics may be discussed in the field of *e-epidemiology*, also termed as digital epidemiology, and defined as: the “science underlying the acquisition, maintenance, and application of epidemiological knowledge and information using digital media such as the Internet, mobile phones, digital paper, and digital TV." [2,3]. Below, I discuss two general concepts in e-epidemiology. First, I review use of the internet as a means of recruiting and executing surveys; this will be illustrated in manuscript 1. Second, I review analytic approaches to examining existing, user-generated data, as on social media platforms. This is demonstrated in manuscript 2, where I present an approach to analyze an online patient support group.

2.1.2. Internet-based tools: surveys

E-epidemiology is a relatively new concept, and frameworks are in their early stages of development. In contrast, in epidemiology as a whole, guidelines exisit for conducting and reporting specific study types (e.g., CONSORT Statement for randomized controlled trials, STROBE for observational studies) but the body of methodological papers that discuss their conduct in the context of the internet are not yet as prevalent or diverse.

The literature that *is* currently available for e-epidemiology studies focuses on an essential and common component of these studies: survey recruitment and response rate, given that these studies often use internet based communication for recruitment and assessment. It is important to bear in mind that some health data is more accurately collected with traditional methods – some studies require face to face measures of weight and blood pressure for example, even though these could be facilitated with use of remote tools. However, due to the internet's potential for reaching a large number of subjects efficiently and inexpensively, researchers in e-epidemiology have been carefully considering the benefits and drawbacks of internet-based survey recruitment and delivery, in comparison to traditional modes of recruitment and data collection such as telephone calls, paper questionnaires, and face-to-face methods. COS development is a particular area of research that has come to depend on the use of web-based surveys. As we will describe in more detail in Methodology, this was the focus of Manuscript 1.

Recruitment and response rate: The first documented mail survey took place in 1788 when Sir John Sinclair sent out questionnaires to ministers of all parishes of the Church of Scotland. The questionnaire contained 160 queries. After 23 reminders and 7.5 years, he achieved a 100% response rate [4]. Our understanding of sampling and response rate has evolved greatly since then. While some issues such as cost efficiency may be overcome with the use of web-based surveys, others such as sampling and attrition persist.

With regards to sampling, the touted advantages of using web-based surveys include efficient survey dissemination and return, and the potential to capture a geographically broad audience relative to the amount of time and money invested by the researcher [3]. For example, web-based recruitment was applied as the primary method of data collection for a large-scale cohort study of women planning a pregnancy in Denmark [5]. Researchers recruited 2500 participants over only 6 months using advertisements on a health-related website. Response rates remained high (86-90%) throughout the 12 months of follow-up. They report improved cost efficiency of using an internet approach ($160 per person) compared to a non internet-based approach (estimated $322 per person), and estimate that the gain in efficiency would be higher with an even larger sample size and follow-up time. Other studies support that in general, the benefit of using an internet-based rather than mail-in survey increases with larger sample size and volume of data collected [6]. In the early age of the internet, achieving this advantage was difficult due to the significant time and cost required to program a large web-based survey. However, the current availability of user-friendly platforms to create and manage web-based surveys have rendered survey initiation a far less resource-intensive process [2]. It has also been suggested that large-scale prospective studies that depend on telephone calls will face increasing difficulty in reaching the desired population in the face of diminishing home phone (landline) use [7].

Conversely, this brings us to a similar *critique* of web-based methods compared to traditional methods – that sampling can be skewed due to disparities in internet accessibility and internet literacy amongst a local population, and across countries. In general, populations of poorer countries have less access to the internet and its associated information and communication technologies; in 2015, access was below 40% of the population in countries concentrated in sub-saharan Africa and parts of Asia [8]. Within a country, rural areas tend to have a lower level of access to high speed internet service [9] and lower internet literacy [10] than urban areas. Fortunately, internet access has been increasing around the world, with many countries showing a statistically significant increase in just a few years [8]. In the countries that do boast high access for its population, the many benefits of internet-based research can be realised – this includes Canada, in which 94% of the population has home internet access [11].

The issue of volunteer bias in health studies – that those who choose to enrol in studies may differ in important lifestyle and health factors from non-participants – is an issue common to both web-based and traditional recruitment methods. However, there is evidence to support that the act of using health-related websites specifically may be determined by both sociodemographic and personal factors (i.e., personality traits) [12]. A study of adults in the

United States found that lower socioeconomic status (SES), older age, and male sex predicted lower engagement with seeking healthcare, health information, and self-tracking activities online compared to their counterparts [13]. This reinforces the importance of considering the specific audience captured by an internet platform when selecting an avenue to recruit participants for an epidemiological study in order to minimize, or at least recognize, the presence of selection bias.

In addition to sampling considerations, another issue is that of optimizing response rate. A meta-analysis of studies conducted prior to 2008 (not specific to healthcare) showed that mailed surveys had higher response rates than web-based surveys [14]. However, more recent studies in healthcare that directly compare response rates show that this gap is closing, especially in higher educated populations and when the method of initial recruitment is through email rather than mail [15,16].

Some barriers and facilitators of survey completion persist regardless of whether they are delivered through the internet or through paper methods; a systematic review of over 400 randomized controlled trials that used either postal *or* electronic questionnaires identified that factors such as personalizing invitations and applying incentives could increase response rate [17]. Longer surveys are also known to have lower response rates [17].

Internet-based platforms offer obvious advantages for researchers in managing the surveys themselves. This includes ease of follow-up via automated emails and editing surveys as needed throughout the study (i.e., addition of questions) [3]. This is especially useful for complex surveys such as that used in the e-Delphi method for COS development, as I illustrate in manuscript 1 and as I discuss below.

e-Delphi method in COS development: In the 1970s, the World Health Organization (WHO) brought together over 30 representatives from different cancer research groups and organizations. Over the course of two meetings, they agreed on a standard approach to collect data in cancer treatment trials, including outcomes. They proposed that their approach be accepted internationally in order for scientists to be able to properly compare their trials [18]. Their recommended set of outcomes was the first of what is known today as a core outcome set, an important development in epidemiology. Since then, over 300 COS have been published [19], and an initiative to support COS development and dissemination, called the COMET Initiative (Core Outcome Measures in Effectiveness Trials), has emerged. As we will discuss, the COS development is now importantly facilitated by e-epidemiology methods. First we provide further discussion of COS development itself.

A COS identifies the key outcomes to evaluate and report in a given field of interest. As mentioned earlier, the primary benefit of asking researchers to report the same outcomes is that it allows for systematic comparison of trial results; some studies within a field vary so extensively in reported outcomes and their associated definitions that comparison and application of results from study to study is nearly impossible. For example, a comprehensive survey of 10,000 controlled trials involving individuals with schizophrenia reported 2194 outcome scales employed in total, with one new, non-validated scale for every five trials [20]. Besides outcome *selection*, the other issue addressed by a COS is that of outcome *reporting*. Outcome reporting bias occurs when researchers do not publish their results on all of the outcomes declared at trial initiation; a 2013 systematic review of cohort studies that have assessed outcome reporting bias, including cohorts with follow-up dates ranging from 1990s to 2006, shows researchers are more likely to fully report outcomes that exhibited statistically significant change than those that did not [21]. Incomplete data prevents a full understanding of the mechanism or effectiveness of a trial intervention, and subsequently makes comparison between trials difficult. These two issues - inconsistency and lack of transparency - are mitigated with the establishment and uptake of a COS for the trials of interest. In the field of diabetes, COS have been developed for GDM prevention and treatment [22], pre-pregnancy care for women with pregestational diabetes [23], and interventions for young adults with T1DM [24], and trials in T2DM [25]. All studies used Internet reliant methods for both recruitment (i.e., emails to organizational listservs, links on Twitter and Facebook) and data collection (i.e., internet-based survey platforms) [24,26–28].

Beyond issues pertaining to research, there is an additional benefit to establishing a COS. The process of developing one represents a crucial opportunity to incorporate the perspectives of stakeholders that may have been overlooked - specifically, outcomes prioritized by the research community have not always aligned with the outcomes that patients believe are relevant [29], and researchers themselves have highlighted the need to systematically incorporate patient perspectives into decision-making in order to carry out studies of more direct value to them and their families [20,30]. For example, a COS for rheumatoid arthritis developed by the OMERACT initiative (Outcome Measures in Rheumatoid Arthritis Clinical Trials) originally included pain as the patient-centred outcome, without any patient input. However, subsequent work including a survey and qualitative interviews with patients revealed that fatigue was a prevalent, and even more important part of their experience of the illness. Further, it was an issue seldom addressed by professionals. Following further study by the OMERACT initiative, fatigue was included in the COS [31].

The COMET Initiative has emerged as the supporting organization for the development, dissemination, and research of COS in healthcare. Before designing a trial, researchers can search the *online* COMET database to ascertain whether a standard set of outcomes already exists for their field of research. Furthermore, the COMET initiative has released a handbook recommending a process for COS development [30] and reporting checklist [32]. The ideal method for developing a COS is an ongoing topic of debate and research, and there remains no standard method of assessing the quality of a COS. However, the overall process for developing a COS is established: (i) identifying candidate outcomes, (ii) eliciting views on their relative importance in a consensus process, and (iii) having a face-to-face meeting to finalize the COS.

A common method used by researchers for the consensus process in step (ii) is the modified Delphi method. The Delphi method originates in business as a systematic process for a group of stakeholders to achieve consensus [33]. The method involves asking the group to brainstorm an initial list of items, then having them participate in iterative surveys to prioritize them (in COS methodology, the Delphi step is considered "modified" because the initial list of potential outcomes is given to the panel; the list is often informed by a systematic literature review). In the first round of the survey, each individual anonymously scores their perceived importance of each item in the list. Next, the scoring results of all stakeholders are summarized and displayed for each individual to reflect upon, before a second, and potentially third round of the same survey is administered. The aim of this process is to allow survey participants to have access to the opinions of everyone in the group, to maintain an anonymous scoring system, and to encourage participants to come to a consensus. Compared to a nominal method (i.e., face-to-face meeting to discuss item prioritization), the Delphi method removes group dynamics (e.g., dominant individuals) that could unfairly bias the consensus-making process [33]. In COS Delphi processes, participants may also suggest candidate outcomes after round 1, for scoring in round 2. With the expanding capabilities of internet platforms, this multi-stage process may be facilitated online as an electronic (e)-Delphi method.

One such platform, called *DelphiManager*, has been developed by the COMET initiative. *DelphiManager* represents a customizable program that allows researchers to build and manage an e-Delphi survey on a website unique to that COS initiative. I employed in Manuscript 1 of this thesis. It allows researchers to enter all candidate outcomes and their definitions in various formats. An administrator account allows the researcher to set up a multi-round Delphi survey and send messages to participants via a built-in email system. In order to access the survey, participants must register for a unique username and password. When summarizing response data for subsequent Delphi rounds, researchers can choose to apply the system's built-in program which presents numerical data, or to download the raw data, analyze it themselves, and upload summaries in the form of visual graphs. *DelphiManager* also offers the option to customize a homepage and baseline characteristics' questionnaire.

Most COS initiatives have successfully implemented an e-Delphi method. With regards to recruitment and response rate, a systematic review of 31 COS initiatives (most of which delivered the Delphi survey online) reported that researchers were able to recruit anywhere from 9 to over 600 individuals, albeit with a response rate that varied between 45% to 100% [34]. In addition to large numbers, e-Delphi processes allow wide geographical reach: 65% of these studies recruited participants from more than one country.

A meta-analysis of surveys in COS development revealed that shorter surveys were more likely to have a higher response rate [34]. This reflects what is known about surveys in general, whether web- or paper-based [17]. The study also reported that surveys with a smaller number of respondents were also likely to have a higher response rate. The researchers note that this was likely attributable to the recruitment method, rather than the sample size itself – those studies tended to approach potential participants individually whether by email or in person, rather than invitation through an indirect call or otherwise. As previously noted, this also holds true for surveys more generally [17].

Many of the advantages conferred by a web survey prove crucial to Delphi surveys in COS development; these advantages relate directly to issues studied by the COMET Initiative group. Researchers must be able to quickly collect, summarize, and re-disseminate data between survey rounds, as longer time between initiation of survey rounds is known to increase attrition [30,34]. The preservation of anonymity is crucial, especially for patient participants whose views are traditionally dismissed in clinical decision-making [31]. In COS methodology, additional candidate outcomes may also be suggested by participants after the first round, and immediately programmed into subsequent rounds.

I have provided an introduction to e-epidemiology, described how health researchers may efficiently reach subjects by using an internet-based survey, and considered several barriers to its use. My application of the e-Delphi survey for a COS in Manuscript 1 will be detailed in Methodology. Now, I continue my review of e-epidemiology methods by describing two types of user-generated data being tracked on the internet, and the respective methods that researchers have used to analyze them. In doing so, researchers are able to gain insight into health and health-related behaviours that would be difficult, or even impossible to gain from data collected with traditional methods.

2.1.3. Internet-Based Tools: Web 2.0 data

Originally, the web consisted of platforms created by a select few users. These users created platforms containing information for other individuals to retrieve as “consumers”. Known as Web 1.0, it includes static websites such as those created by organizations and governments to share information (e.g., Diabetes Canada) as well as those offering a service (e.g., Craigslist) with limited to no opportunity for users to interact [35]. In the early 2000s however, Web 2.0 emerged as a new set of platforms enabling user interaction; these user-centric platforms rose to such prominence that they informed 2006 TIME magazine’s selection for “Person of The Year: You” [36]. Overall, the two types of data that are generated by users on Web 2.0 and tracked by their respective technologies are (i) text data and (ii) activity data.

Text data refers to the text directly generated and shared by web users. This includes posts and comments made on social media, and search queries on virtual search engines like Google. As more individuals seek information and socialize online, the health-related information that has traditionally been sought from them through interview and self-reported questionnaires can be derived from online communications and behaviour.

In 2012, a survey of Facebook and Twitter for groups related to chronic disease found 527 groups for diabetes, 216 for breast cancer, and 171 for colorectal cancer groups [37]. Many of these aimed to facilitate support for patients and their families, and many were generated by community members themselves rather a formal organization. The breadth and complexity of health-related groups is immense. Some health researchers who wish to extract and analyse text data choose to sample from a single, specific group; for example, one research group analyzed a subset of posts and comments within a single page for smoking cessation [38]. Others aim to capture the full breadth of online patient communities by searching for all groups that meet their inclusion criteria; for example, one research group analyzed a sample of data from each of 118 groups related to anorexia nervosa on Facebook [39].

While many user-centric platforms are initiated by community members, some are created by health organizations or researchers, and enrolment is controlled based on inclusion and exclusion criteria. This provides to researchers a more defined context and sample from which to extract text data, and thus allows them to draw potentially stronger conclusions about health. For example, For example, Troncone and colleagues designed an application specifically for their research study, holding regularly scheduled, virtual text chats with T1DM youth aged 12 to 18 years recruited from a diabetes care centre in Italy. They were able to code and analyze all text data from their chats [40].

Web activity (as opposed to text data) has also been used in epidemiological research. Activity refers to the behaviours of users that are tracked by the platform, but that are not explicitly displayed to users. One example of tracked behaviour is search engine queries stratified by geographic location and time. One notable study led by Ginsberg and colleagues tracked Google search patterns to predict activity of influenza-like illness in the United States, with results that were later validated by reports from established, traditional surveillance methods [41].

Another prominent example of tracked behaviour is that of interactions between social media users, which collectively give rise to entire social networks. These may be researched using social network analysis (SNA), which is a technique that stems from sociology but is applied in epidemiology to understand how network position affects health risk factors and outcomes [42]. Existing SNA of patients and their families can be *egocentric* – this involves interviewing each subject in detail to capture their subjective perspective of their immediate network. For example, one study interviewed T1DM patients and their families to understand how one's perceived support network was related to mental health status [43]. An SNA may also be *sociocentric* which, in real life, is difficult to perform because it requires capturing all subjects and data within a socially or geographically bounded network. It is not usually performed on individuals due to time-consuming and expensive data collection [44]. However, if the network of interest is virtual, then sociocentric SNA may be applied more easily because evidence of relationships and interactions between subjects is tracked [45]. This has been the case of one notable effort to examine a group of 1,700 college students who were connected on Facebook. Visual inspection of their photographs and statistical analyses determined that those who smiled in photographs were more central to the network, and on average had one extra friend, compared to those who do not smile [45].

Overall, web platforms present a novel source of health-related data that can be used to better understand patients and their families. Compared to traditional face-to-face or telecommunication techniques of exchanging and retrieving information, the web may even be the preferred medium for individuals living with stigmatized health conditions such as anxiety and depression [46]. The methods being applied to analyze data range from long-standing methods such as thematic analysis, to newer methods such as netnography, which originates in anthropology and aims to understand social interactions in an online community through observation [47]. It remains important to consider that behaviours and communications on a web platform are not necessarily generalizable to real life.

This thesis focuses on the application of these qualitative and quantitative methods in diabetes research. Thus, I provide below an overview of the three main forms of DM.

2.2. Diabetes mellitus

The two main forms of DM are type 1, resulting from destruction of insulin-producing cells due to autoimmune injury, and type 2, resulting from the body's resistance to the action of insulin. GDM is a third type of DM that is a first diagnosis of diabetes in pregnancy that resolves after delivery. Many women with GDM later develop T2DM. I discuss the types of DM in further detail below.

2.2.1. Type 1 diabetes mellitus

Definition and symptoms: T1DM is a disorder in which the beta cells of the pancreas are destroyed, rendering it unable to produce adequate insulin for glucose entry from the circulation and into the cells of the body to fuel metabolism [48,49]. The majority of T1DM cases are autoimmune-mediated [49]. T1DM differs from the general defect in T2DM, which is one of resistance to the action of insulin, often related to low physical activity and excess adiposity [48]. Uncontrolled T1DM is characterized by hypoglycemic and hyperglycemic episodes; symptoms of hypoglycemia include confusion, loss of consciousness, and even death, and hyperglycemia leads to excessive thirst, urination, and hunger, as well as fatigue, blurred vision, and in the long-term, serious cardiovascular complications [48].

Prevalence, etiology, risk factors: T1DM accounts for 5-10% of the total number of cases of DM around the world [50]. Most cases of T1DM are diagnosed in childhood and adolescence; according to 2015 Canadian Chronic Disease Surveillance System data, 24,170 children and adolescents and 84,380 young adults in Canada have diabetes [51], over 90% of which is T1DM [52,53]. Rates among youth have been on the rise around the world [54], including in Canada where the average incidence rate grew at 5.1% per year between 1990 to 1999 [55].

The cause of T1DM is thought to be multifactorial. The primary defect is immunological, with autoimmune destruction of the insulin-producing cells of the pancreas. Genetic factors include having a first-degree relative with T1DM [56] and being of northern European descent [57].

Environmental triggers that may be contributing to the increasing trend of T1DM include changes in early feeding patterns and hygiene practices [56]. Further support for environmental associations include findings of vitamin D deficiency [58,59] and viral infections [60] as possible factors in T1DM development. Obesity may also promote the development of T1DM through insulin resistance accelerating autoimmune destruction of pancreatic beta cells [61].

Management: There is currently no cure for T1DM. Individuals with T1DM administer insulin as a medication, adjusting doses in relationship to food intake and physical activity. They are required to adhere to a narrow therapeutic window of blood glucose levels, navigating a tight balance between preventing low glucose levels and high levels in order to avoid the adverse effects previously listed. Two strategies for administering insulin are either multiple daily injections using a syringe device, or continuous infusion from an insulin pump worn outside the body. Some individuals receive islet cell transplants. Advancements in pump therapy and glucose monitoring have improved the ease with which patients self-manage their condition, and innovations such as an artificial pancreas may be widely available in the near future [56].

2.2.2. Type 2 diabetes mellitus

Definition and symptoms: Compared to T1DM which is auto-immune mediated, type 2 diabetes is a metabolic disorder, the origins being a combination of the body's resistance to insulin action, and inadequate insulin secretion in response to carbohydrate intake. Untreated, the symptoms of T2DM are the same as those in T1DM (e.g., excessive thirst and urination), but their onset is more insidious. Uncontrolled T2DM in the long term leads to complications such as peripheral vascular disease, eye damage leading to impaired vision, and cardiovascular damage to organs such as the heart and kidney [48].

Prevalence, etiology, risk factors: T2DM accounts for approximately 90% of the total number of cases of DM [50], with a prevalence that has reached pandemic levels and increased incidence around the world [62,63]. According to public health data from 2013-2014, about 3 million Canadians, or 8.1% of the national population, have T2DM. The main risk factor for T2DM is overweight/obesity. Other risk factors include being physically inactive, and having a family history [48]. T2DM typically presents in middle to older adults (over 40 years of age), but it can also occur at a younger age – this is the case in Indigenous populations in Canada, where symptoms of T2DM can be seen in individuals as young as 18 years [64], and where T2DM has been formally diagnosed in youth aged 4 to 19 years [65]. There is also evidence to support that certain ethnicities are more susceptible to developing T2DM due to the interaction between genetics and an "obesity-promoting" environment in Western societies [66].

Treatment: In general, healthy behaviour interventions are recommended for all T2DM patients, and some patients are able to achieve the targeted clinical outcomes with dietary and physical activity changes alone. However, most patients need to eventually take antihyperglycemic medications, with metformin being the first line of pharmacologic treatment. If behaviour change and metformin are not successful, other medications may be added. The exact combination and formula of treatment varies depending on the severity of T2DM as established by glucose levels, measures of hemoglobin A1C, and presence of complications [67].

2.2.3. Gestational diabetes mellitus

Definition and symptoms: Gestational diabetes mellitus is defined as glucose intolerance being diagnosed for the first time during pregnancy [68]. This diagnosis is made using a glucose challenge test and/or an oral glucose tolerance test; the standard diagnostic criteria to use remains a subject of debate [67]. Because most women with GDM do not have noticeable signs or symptoms, it is recommended in Canada that all women without pre-existing diabetes be screened for GDM between 24 to 28 weeks of pregnancy. If they do occur, symptoms may include increased thirst and frequent urination. Blood sugar typically normalizes after delivery, but is a risk factor for future development of T2DM and may also be an indicator for T1DM in those who are immunologically predisposed [69].

P**revalence, etiology, risk factors**: GDM is rising in incidence around the world [70,71]. In Canada, an estimated 3-10% of pregnant women develop GDM [72,73]. Pregnancy has been conceptualized as a "stress test" on the mother's body; GDM occurs when the body cannot produce enough insulin to manage the effects of a growing baby and changing hormone levels [74]. Risk factors include obesity, family history of T2DM, a history of abnormal glycemic metabolism, polycystic ovary disease, and being over 25 years of age. GDM prevalence is also higher in Chinese and South Asian Canadians compared to white women [56,75].

Treatment: Untreated GDM leads to adverse health outcomes for both the baby and mother, such as increased size of the baby leading to birth injury and delivery difficulties [67,74]. Importantly, a diagnosis of GDM also signals a seven-fold risk for the woman to develop future diabetes compared to pregnant women without a GDM diagnosis [76]. The aim of treating women during pregnancy is to reduce these adverse outcomes. During pregnancy, diet and physical activity are recommended to achieve glycemic targets. If these are not met, then glucose-lowering medications such as insulin or metformin are used [67]. After delivery, women are advised to breastfeed, for many reasons, including reduced risk for obesity and in offspring as well as later development of diabetes in the mother and child. Maintaining good diet and physical activity behaviours also reduces the risk of T2DM development in the mother [77].

2.3 New opportunities for diabetes research

Although there are a growing number of health behaviour change trials that target women with a GDM pregnancy, effectiveness in T2DM prevention remains difficult to achieve and capture. Researchers currently measure a variety of different outcomes, which prevents systematic comparison of findings. Furthermore, the outcomes that best signal the effectiveness of a program conducted *sooner* (in the months and years) following a pregnancy, before actual potential type 2 diabetes development, have not been well-established. Thus, there exists an opportunity to develop a COS for these trials, taking advantage of the internet's capacity to engage a variety of stakeholders across the world, including patients, in a process that aims to move diabetes prevention forward. Similarly, full patient-centred effectiveness in T1DM management remains difficult to achieve, and can be importantly facilitated by the knowledge that peers with T1DM may have about living with T1DM and their ability to provide understanding and support. Therefore , many patients and families are turning to online communities for support. The rich data generated by these user interactions provides researchers with the opportunity to better understand the needs of patients with T1DM and their families as they arise in this modern context.

3. Study Methodology I

3.1. Overview

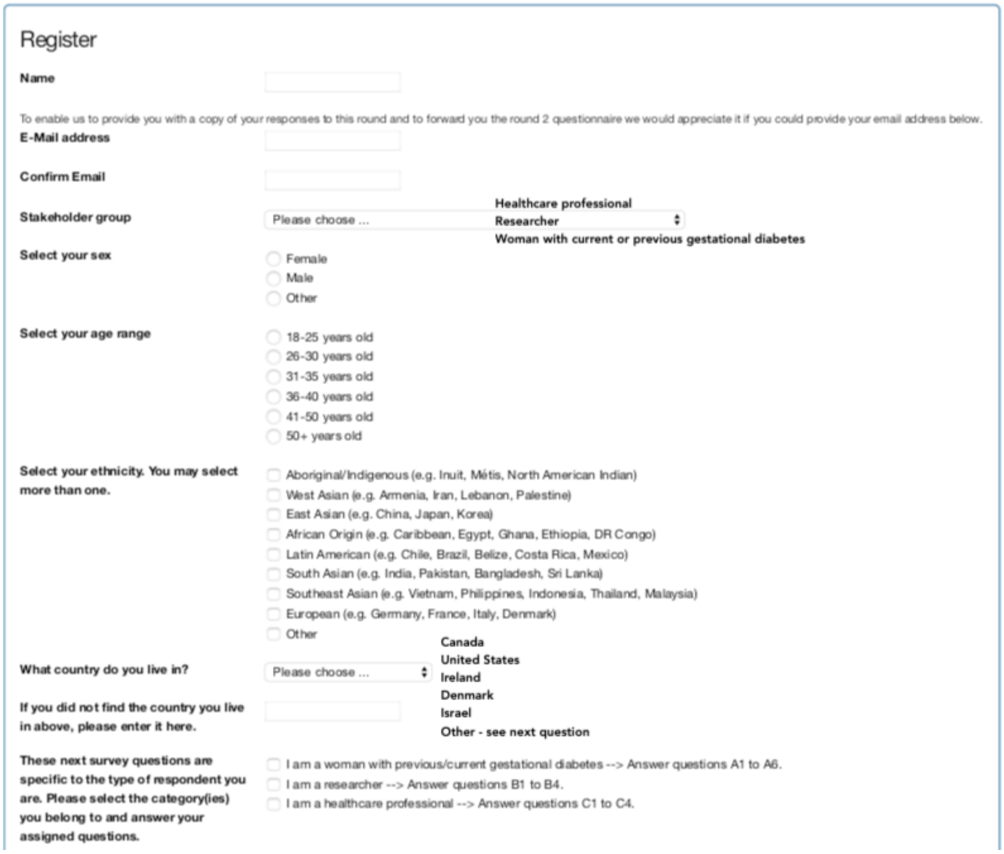
For the first project, I aimed to identify a COS for trials evaluating health behaviour change interventions for diabetes prevention following a GDM pregnancy, using a modified e-Delphi method. My thesis supervisor Dr. Dasgupta and her colleagues had already published a COS development protocol, conducted the systematic literature review to identify candidate outcomes, and held a clarification meeting to refine this candidate list [78,79]. They had also registered the project as an ongoing COS with the COMET Initiative. Over the course of several months, I set up and administered the e-Delphi survey on *DelphiManager* in several phases. I collected and analyzed these data. I worked with my supervisor and her team to organize the international consensus panel meeting. Based on the e-Delphi survey and consensus panel discussions, I organized the final COS.

3.2. e-Delphi survey

DelphiManager provided us with the website to facilitate our survey, hosted on a server in the University of Liverpool data centre. Once we confirmed the desired name for our project, they created a custom website link and provided the administrator login information (https://delphimanager.liv.ac.uk/COSDAP/Delphi, closed as of 2019) to set up our survey. The website consisted of several pages presented in a deliberately organized sequence.

The first page was a customizable homepage. The co-investigators and I provided an overview of the study, the objective of the initiative, and the multi-step process that participants could expect over the next several months. We explained that we wanted to gather input from experts, defined as: "1. People with personal experience of the condition, for example, patients, caregivers, and service users. 2. Health professionals with expertise in caring for people with the condition. 3. Researchers with expertise in designing lifestyle interventions for diabetes prevention."

The second page was a registration form with baseline questionnaire. The two fields that required a response from participants were the stakeholder field and email address. The stakeholder field helps *DelphiManager* organize scores for summarization; I asked participants to choose one of three options: healthcare professional, researcher, woman with current or previous gestational diabetes. The email was important for participants to set up their custom survey login username and password, and for me to send survey-related messages (e.g., reminder to complete survey, notifying them of opening second round). I added queries for other general characteristics such as country of origin, as well as queries specific to stakeholder type. Although the software did not allow for branching logic, which would have streamlined the questionnaire, I indicated in text which questions should be answered for each stakeholder type (Image 1).



Register

Name

To enable us to provide you with a copy of your responses to this round and to forward you the round 2 questionnaire we would appreciate it if you could provide your email address below.

E-Mail address

Confirm Email

Stakeholder group
Please choose ...
Healthcare professional
Researcher
Woman with current or previous gestational diabetes

Select your sex
○ Female
○ Male
○ Other

Select your age range
○ 18-25 years old
○ 26-30 years old
○ 31-35 years old
○ 36-40 years old
○ 41-50 years old
○ 50+ years old

Select your ethnicity. You may select more than one.
☐ Aboriginal/Indigenous (e.g. Inuit, Métis, North American Indian)
☐ West Asian (e.g. Armenia, Iran, Lebanon, Palestine)
☐ East Asian (e.g. China, Japan, Korea)
☐ African Origin (e.g. Caribbean, Egypt, Ghana, Ethiopia, DR Congo)
☐ Latin American (e.g. Chile, Brazil, Belize, Costa Rica, Mexico)
☐ South Asian (e.g. India, Pakistan, Bangladesh, Sri Lanka)
☐ Southeast Asian (e.g. Vietnam, Philippines, Indonesia, Thailand, Malaysia)
☐ European (e.g. Germany, France, Italy, Denmark)
☐ Other

What country do you live in?
Please choose ...
Canada
United States
Ireland
Denmark
Israel
Other - see next question

If you did not find the country you live in above, please enter it here.

These next survey questions are specific to the type of respondent you are. Please select the category(ies) you belong to and answer your assigned questions.
☐ I am a woman with previous/current gestational diabetes --> Answer questions A1 to A6.
☐ I am a researcher --> Answer questions B1 to B4.
☐ I am a healthcare professional --> Answer questions C1 to C4.

Image 1. Screenshot of a portion of the e-Delphi survey registration page.

The next pages included the first round of the e-Delphi survey itself. I inputted an Excel file containing the list of outcomes, domains, and definitions in a format compatible with entry into the system. The system allowed customization of certain features of the survey – for example, I elected to display outcomes by related concepts instead of displaying a set number of random outcomes per page. Participants were asked to score an outcome on a 9-point Likert scale (1-3 = not critical, 7-9 = critical). The *DelphiManager* system offers to researchers an automatic process to calculate scoring results, and present them in subsequent survey rounds as percentages stratified by stakeholder group, but I chose the alternative option of manually downloading all scoring data, analyzing it myself using *R* language and *RStudio* software, and producing data summaries in the form of bar graphs for upload and display (Figure 1). We believed that the visual graphs would help participants understand how stakeholder scores compared to one another, more easily than percentages. The last page of the survey contained an open response field for participants to suggest additional candidate outcomes.

All three Co-Principal investigators for this COS initiative, located in Canada, Ireland, and Denmark, identified groups from which participants could be recruited. I disseminated the survey to these groups through various internet platforms. Direct emails were used to reach organizations with listservs of healthcare professionals and researchers; these organization ranged from national (e.g., Diabetes Canada) to international audiences (e.g., International Federation of Obstetrics and Gynecology). We aimed to reach patients by asking these professionals to approach past participants in diabetes after pregnancy prevention studies, by sharing advertisements in Facebook groups related to motherhood, and emailing clinics requesting that they display print posters.

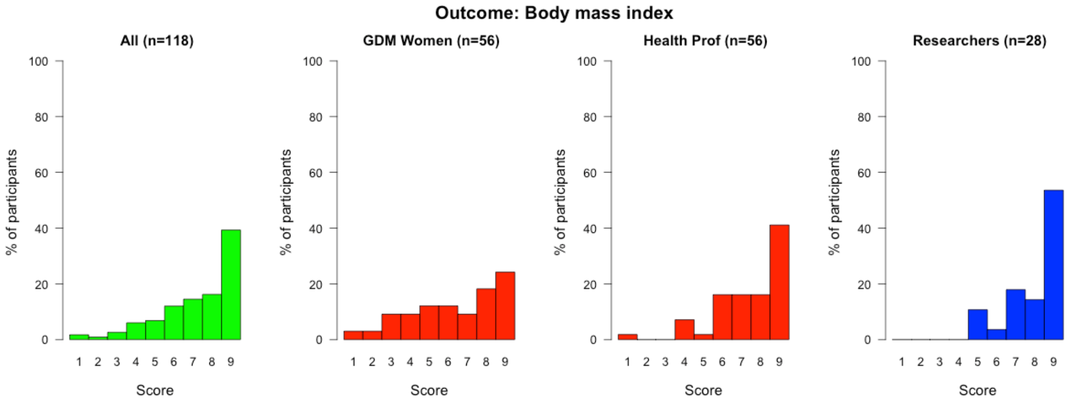


Figure 1. Sample of a bar graph summarizing round 1 survey scores for an outcome, displayed to participants in round 2.

Round 1 of the survey was open from July to September 2018. The *DelphiManager* system was able to track the registrants who had not yet completed scoring all outcomes, and by how many outcomes. This helped me to determine whom to send reminder emails. Overall, we sent reminders once every 2-3 weeks to anyone who did not fully complete the survey until the round 1 completion deadline. With the help of co-investigators who were able to verify translations of text from English, I repeated all the above processes – from homepage set up to survey completion reminders - for equivalent e-Delphi survey websites in French and Danish, to better reach local populations whose first language was not English.

It is recommended that after round 1, researchers work as quickly as possible to summarize data and set up round 2 (and round 3, if applicable) in order to minimize attrition [30,31]. Ideally, this gap between surveys should last no longer than 1-2 weeks. However, it took us 4 weeks, longer than anticipated, to initiate our second and final round due to our decision to manually download raw data from all three language surveys, combine datasets, and produce summary graphs for each outcome in each of the three languages for input. I explore the possible implications of this and available survey software features on our results in the Discussion (Chapter 7).

Round 2 of the survey was open from October to December 2018. This round included the addition of outcomes suggested by participants from round 1.

3.3. Mock consensus panel meeting

A mock consensus panel meeting between survey rounds was held in Halifax, Canada as a satellite meeting to the Diabetes Canada 2018 conference. Including the COS initiative steering members, there were 12 purposively selected healthcare professionals and/or researchers in fields of nutrition, public health, internal medicine, obstetrics and gynecology, and endocrinology. The goal was to discuss round 1 results and hold a mock vote that would be akin to the one held with a larger consensus panel following round 2 of the survey. I summarized scores for each domain of outcomes in a Powerpoint presentation and presented each slide to the mock panel. As the presenter and trainee, I was responsible for taking notes as the panel discussed each slide. At the end of the presentation, I coordinated the use of a web-based, real-time voting system for the panel to vote for the inclusion (yes), exclusion (no), or abstinence on the outcomes that were highly endorsed by the Delphi process (i.e., 70% of participants rating the outcome 7-9). Results were immediately displayed on the presentation screen once all 12 members had sent in their vote for an outcome via a link on their phone or laptop.

3.4. From e-Delphi to consensus panel meeting

There is no firm set of recommendations on how to finalize the COS following conduct of an e-Delphi process. However, there are recommendations on the principles that should guide selection of methodology. My supervisor and I reflected on the activities of the mock consensus panel and how they related to these principles. For example, the COMET initiative recommends the use of a non-voting member to "facilitate" the meeting to ensure that each consensus panel member contributes equally to the discussion [30]. To this effort, I ensured that any individual who expressed a desire to share their opinion (i.e., through body language, or through a verbal attempt to interject) was able to do so by later gathering the panel's attention to the individual without disrupting the overall flow of the conversation. This was a productive measure that we kept for the final consensus meeting as well. Given the high number of outcomes, we also kept strict track of the time spent discussing each domain. What it further means to "facilitate" a consensus meeting to achieve fair discussion is uncertain.

Importantly, I reflected on the make-up of the panel itself and whether or not, as per many existing COS initiatives, the final COS should be decided entirely by the voting members of the consensus panel. The reason for this concern is based on the notes that I took during the mock consensus panel discussion. As expected, each professional/researcher tended to be biased towards outcomes related to their own expertise. However, this had important implications in the resulting vote. For example, there were fewer experts in nutrition compared to the other fields. Reflecting this, the outcomes related to nutrition tended to be voted for exclusion (Table 1). Given the small size of most final consensus panels [34], even having a diversity of expertise may not prevent a biased COS if their representation is not equal. Moreover, the objective of a Delphi process is to systematically consider the opinions of individuals that would otherwise be overlooked. This was important for our COS scope of interest, which is prevention of T2DM using lifestyle behaviour change; this area of research is informed by a variety of fields (e.g., include obstetrics and gynecology, internal medicine, nutrition, public health, epidemiology). My supervisor and I thus concluded that even imbalance in expertise amongst a panel's voting members risked undoing the systematic consensus achieved by the Delphi process. This informed our decision to have our final consensus panel vote only on indeterminate e-Delphi outcomes, and not outcomes that already met *a priori* inclusion criteria.

Table 1. Voting results of mock consensus panel (n=12) for Delphi survey round 1 outcomes rated by 70%+ of Delphi participants as being very important (score of 7-9)

Outcome	**Yes**	**No**	**Abstain**
Diagnosis of type 2 diabetes	12	0	
Gestational diabetes mellitus recurrence	12	0	
Completion of OGTT/blood glucose/HbA1c post partum	12	0	
Attending postpartum diabetes screening test	4	8	
Healthy lifestyle behaviours	8	4	
Diabetes prevention behaviour knowledge	11	1	
Motivation to change	6	6	
Perceived diabetes risk	11	1	
Diabetes knowledge	5	7	
Oral glucose tolerance test (OGTT)	11	1	
Fasting blood glucose	5	7	
Glycated hemoglobin test	11	1	
Total energy intake	4	8	
Diet quality	8	4	
Carbohydrate intake	2	10	
Sedentary time	10	2	
Moderate to vigorous activity	10	2	
Weight	11	1	
Post-partum weight retention	10	2	
Body mass index	10	2	
Cardiovascular disease	9	3	
Diagnosis of type 1 diabetes*	2	9	
Neonatal mortality/stillbirth**	2	6	4
Quality of life	9	3	
Sleep quality	8	4	
Completion of targets/activities	11	1	
Type of health professional conducting the intervention	2	10	
Health service utilisation and cost	12	0	
Fibre intake	3	9	
Fat intake	3	9	

Glycemic load	1	11
Food group servings	9	3
Sleep quantity	5	7
Diet self-efficacy	6	6
Weight self-efficacy	4	8
Exercise self-efficacy	9	3
Perceived barriers	5	7
Health literacy	7	5
Perceived enablers or facilitators	4	8
Social support	5	7
Stress	8	4
Intervention components engaged with	11	1

*Missing one vote

**Technical difficulties experienced by 4 voting members

3.5. Consensus panel meeting

The official consensus panel meeting was held as a satellite event of the *10th Symposium on Diabetes, Hypertension, Metabolic Syndrome, and Pregnancy* held in Florence, Italy in May 2019. The 15 voting consensus panel members represented 8 countries, and were purposively selected. The meeting followed a modified nominal group format. As planned, we kept strict track of the time spent discussing each set of outcomes, and I was responsible for ensuring that every individual who wanted to contribute to the discussion was able to do so comfortably. The panel voted exclusively on indeterminate outcomes. Voting was facilitated using an online platform accessible with a link from a smartphone or laptop. Over the next several weeks, suggestions for additional outcomes as well as categorization into domains and measurement timing were discussed by the international panel over email and voted for inclusion through the online platform SurveyMonkey [80].

3.6. Final analyses

I analyzed and summarized the results of the consensus panel vote in *RStudio*. An outcome that was voted for inclusion by 70% or more of the voting members was retained for the COS. The final COS was arranged into categories by myself, my supervisor Dr. Dasgupta, and our co-investigators. I also measured degree of consensus achieved by the Delphi survey by analyzing how standard deviation of score distributions changed from round 1 to round 2.

3.7. Ethics

We obtained ethics approval from the Research Ethics Board of the McGill University Health Centre (MP-37-2019-4765).

4. Results: Objective 1

4.1. Preface

The first manuscript was submitted to the *British Medical Journal Open Diabetes Research & Care* in May 2020. The manuscript addresses the first objective of the thesis, which is to use a modified electronic (e)-Delphi method to identify a COS for trials evaluating health behaviour change interventions for diabetes prevention following a GDM pregnancy. In moving towards this objective, I had to address methodological issues concerning to what degree a consensus panel should diverge from the opinions expressed by a much larger group of e-Delphi survey respondents. I now present the results of this endeavour in the following manuscript, formatted according to the aforementioned journal's guidelines:

Nancy Wu, Sharleen O'Reilly, Karoline K. Nielsen, Helle Maindal, Kaberi Dasgupta. Core Outcome Set for Diabetes After Pregnancy prevention across the lifespan: an international Delphi study.

4.2. Manuscript 1: Core Outcome Set for Diabetes After Pregnancy prevention across the lifespan: an international Delphi study.

Title: Core Outcome Set for Diabetes After Pregnancy prevention across the lifespan: an international Delphi study.

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ABSTRACT

Introduction

Mothers with gestational diabetes mellitus (GDM) are at high risk of developing future diabetes. An active area of research is examining health behaviour change strategies in women within 5 years of a GDM pregnancy to prevent diabetes after pregnancy. We aimed to develop a core outcome set (COS) for these trials to facilitate synthesis and comparison.

Research Design and Methods

Candidate outcomes were identified through systematic review and scored for importance (1–9) by healthcare professionals, researchers, and women with prior GDM through an international two-round electronic (e)-Delphi survey. The COS includes outcomes achieving pre-specified round 2 scores, as well as outcomes with indeterminate scores that were judged important by a 15-member consensus panel. The panel organized the COS by domain.

Results

115 stakeholders participated in the e-Delphi survey and 56 completed both rounds. Standard deviation of scores decreased by 0.24 (95%CI: 0.21, 0.27) by round 2, signalling convergence. The final COS includes 50 outcomes in 19 domains. One domain focuses on postpartum diabetes screening (n=2 outcomes). Three capture health behaviours: diet (n=4), physical activity (n=2), and breastfeeding (n=2). Four address behaviour change preconditions: behaviour change theory constructs like self-efficacy (n=5), diabetes-related knowledge (n=2), health literacy (n=1), and social support (n=1). Biological effects are captured through changes in cardiometabolic risk factors (n=5), glycemia (n=3), and adiposity (n=4); as well as long-term disease development, namely: diabetes (n=3), related diseases (n=3), and complications in subsequent pregnancy (n=2). Patient-oriented outcomes deemed important are sleep quality (n=1) and quality of life (n=1). For interventions starting during pregnancy, a domain of postpartum offspring outcomes was pertinent (n=3). Finally, the COS captures two domains that inform translation of research findings: measures of program delivery (n=4) and health economic evaluation (n=2).

Conclusions

The COS includes outcomes relevant to intervention efficacy, focus for refinement, and scope for implementation.

Key words: gestational diabetes, diabetes, prevention, core outcome set, Delphi

Significance of this study

What is already known about this subject?

- Health behaviour change can reduce diabetes incidence in women who are at high risk reflected by a history of gestational diabetes mellitus (GDM). An increasing number of trials are testing interventions soon after pregnancy to accomplish this. Researchers are measuring a variety of different outcomes.

What are the new findings?

- Healthcare providers, researchers, and women with GDM specified a core outcome set (COS) that moves beyond biological measures to include behavioural, contextual, process, and economic measures.

How might these results change the focus of research or clinical practice?

- By addressing the domains highlighted by this COS, strategies can be refined iteratively to achieve approaches that are both effective and feasible to translate into programs and practice for diabetes prevention.

INTRODUCTION

Gestational diabetes mellitus (GDM) is a critical public health issue, having both a high incidence and demonstrated associations with diabetes after pregnancy (DAP) in mothers, offspring, and even fathers.[1,2] The US Diabetes Prevention Program (DPP) trial proved that DAP in mothers is preventable through health behaviour change in women whose pregnancy averaged a decade before enrolment.[3] However, most incident diabetes cases occur within 5 years of GDM.[4] We aimed to identify a core outcome set (COS) for the increasing number of trials testing health behaviour change interventions for DAP prevention sooner after pregnancy.

A COS represents the standard set of outcomes to measure for a given population, in a particular field of interest. It facilitates comparison and synthesis, and allows for iterative advancement. In October 2017, we launched the international Core Outcome Set for Diabetes after Pregnancy Prevention Trials (COS-DAP) initiative. Our focus was the development and testing of interventions that are efficacious for DAP prevention, compatible with the needs of women with young families, and feasible to be translated into programs. In accordance with Core Outcome Measures in Effectiveness Trials (COMET) guidelines, we registered and published both our COS development protocol and the systematic review from which we derived candidate outcomes.[5–7] We herein report the findings from our two-round electronic (e)-Delphi survey amongst a large international stakeholder group representing healthcare professionals (HCP), researchers, and women with prior GDM; and the final COS.

COS development is a relatively new field and, as such, is subject to methodological debate. Concurrent with our initiative, another group developed a COS with a similar target population but a more general scope of evaluating metrics to monitor following a GDM pregnancy; subsequent to their e-Delphi survey, they removed a large number of highly endorsed outcomes at a consensus panel meeting in the interest of brevity, retaining indicators of glycemia, blood pressure, and breastfeeding status.[8] In contrast, we applied *a priori* scoring criteria for inclusion based on e-Delphi results, with only indeterminate outcomes voted upon by a consensus panel. We thus present a COS that maintains fidelity with the e-Delphi survey, capturing biological, behavioural, contextual, process, and economic measures. Its comprehensive scope may permit the detection of not only biological impact, but also facilitate progress towards the ultimate goal of translating findings into real-world programs.

METHODS

We registered COS-DAP with the Core Outcome Measures in Effectiveness Trials (COMET) initiative.

Identification of candidate outcomes

As previously reported, we conducted a systematic review focused on health behaviour change (i.e., eating and physical activity) and diabetes screening intervention studies in women with previous GDM.[7] Briefly, two investigators independently screened titles and abstracts, and at least three next reviewed the full text of selected articles and extracted candidate outcomes verbatim. A face-to-face meeting amongst investigators was held in Dublin, Ireland (March 2018) for deduplication, suggestion of potentially important outcomes not identified in the review, and outcome grouping in preparation for the e-Delphi survey.

e-Delphi survey

Participants

Researchers and HCPs are knowledgeable in GDM management, risks, and diabetes after pregnancy (DAP) prevention interventions. Women with GDM can speak to the nuances of living with GDM and the experience of outcome assessments, particularly if they have participated in DAP prevention intervention studies. We recruited from all three of these stakeholder groups. As recommended for Delphi studies,[9] we aimed for 20 to 50 respondents per group. Email invitations and social media posts were disseminated through pregnancy and diabetes organizations at international (e.g., International Federation of Gynecology and Obstetrics), national (e.g., Diabetes Canada, Diabetes Ireland), and regional levels (e.g., motherhood groups). HCPs and researchers were asked to invite patients enrolled in previous GDM studies. Interested individuals were provided with a link to the survey website.

Survey

The survey was hosted on the online COMET DelphiManager system [10] in English, French, and Danish. Round 1 was open from July–September 2018 and round 2 from October–December 2018. Registration and consent were completed electronically; general characteristics were queried. Participants rated each outcome on an ordinal scale (1 = unimportant to 9 = very important) or indicated inability to score. We provided a plain language definition for each outcome. During round 1, respondents could suggest additional outcomes. All who initiated round 1 were invited to complete a second round. During round 2, participants were asked to re-rate all outcomes after considering their initial ratings and average ratings from each stakeholder group, which were displayed for each outcome. We held an investigator meeting after round 1 in Halifax, Canada (October 2018) alongside the 2018 Diabetes Canada conference to plan the consensus meeting.

Analysis

Adopting an approach described by other COS developers and COMET,[11,12] we retained outcomes for which ≥70% of participants scored 7–9 and ≤15% scored 1–3. We excluded outcomes that ≥70% of participants scored 1–3 and ≤15% scored 7–9. All others were considered indeterminate and brought forward to the consensus meeting. We analyzed the change in standard deviation (SD) of each outcome's scores from round 1 to 2, one of the approaches to quantify convergence described by the COMET initiative.[11] All analyses were performed in R version 3.5.1.

Consensus meeting

The meeting was held as a satellite event of the *10th International Symposium on Diabetes, Hypertension, Metabolic Syndrome, and Pregnancy* held in Florence, Italy (May 2019). The 15 voting consensus panel members represented 8 countries (Australia, Canada, Denmark, Hong

Kong (China), Ireland, Israel, Norway, Switzerland) and included experts in medicine (e.g., obstetrics, endocrinology, internal medicine), nutrition, public health, and epidemiology. All but one had not participated in the e-Delphi survey. Patient representatives were absent from the meeting.

The meeting followed a modified nominal group format. Panel members discussed each indeterminate outcome, then voted anonymously via FormPlus[13] to accept, reject, or indicate uncertainty on its inclusion in the COS. An indeterminate outcome was retained if ≥70% of members voted in favour of it. Panel members also discussed how to group outcomes into domains and when to measure them. Suggestions for additional outcomes were discussed over email and voted for inclusion with the same criteria through the online platform SurveyMonkey.[14]

RESULTS

The systematic review identified 172 outcomes.[7] Collapse of overlapping constructs yielded 121 outcomes that were included in the e-Delphi survey. Round 2 included an additional 33 outcomes, as suggested by participants during round 1.

One-hundred-thirty-four individuals from 23 countries registered for the e-Delphi survey. Round 1 was initiated by 115 stakeholders (HCP n=54, researcher n=27, women with prior GDM n=34). Across stakeholder groups, most were women >30 years of age and of European ethnicity (Table 1). Women with a GDM history were a median of 4 years past their last GDM pregnancy. Over half of them had ≥2 pregnancies, and 12% had developed type 2 diabetes (T2DM) in the years following the GDM pregnancy. Of the HCPs, 35% were obstetricians/gynecologists, 26% were dietitians, and 19% were endocrinologists. Over 50% of HCPs spent the majority of time on clinical activities. Amongst the researchers, 60% dedicated the majority of their time to research activities; some reported a clinical background in obstetrics/gynecology (15%), dietetics (11%), endocrinology (11%), and nursing (3.7%). Sixty-seven people initiated round 2, and 56 completed both rounds in entirety (49% of survey initiators).

Table 1: **Characteristics of survey initiators by stakeholder and survey round* (% of *n*)**

Characteristic	**Healthcare Professional**		**Researcher**		**Patient**	
	***n* = 54**	***n* = 34**	***n* = 27**	***n* = 21**	***n* = 34**	***n* = 12**
Women	75.9	73.5	77.8	76.2	100	100
Age (Years)						
<30	5.6	5.8	11.1	9.5	5.9	8.3
30-50	46.3	41.1	37	71.4	58.8	83.3
>50	48.1	52.9	51.8	19	35.3	8.3
Ethnicity						
European	61.1	61.8	63	61.9	61.8	58.3
East Asian	5.6	5.9	3.7	4.8	8.8	16.7
Latin American	1.9	0	7.4	9.5	5.9	8.3
Other**	29.5	26.4	25.9	23.8	23.5	16.7
No Answer	1.9	5.9	0	0	0	0
Country						
Denmark	14.8	17.6	14.8	19	14.7	0
Canada***	16.7	14.7	0	0	58.8	75
Australia	22.2	23.5	29.6	33.3	2.9	0
Ireland	9.3	8.8	11.1	9.5	17.6	16.7
Other†	37	35.4	44.5	38.2	6	8.3
Type of Healthcare Professional						
Obstetrician/Gynecologist	35.2	35.3	14.8	9.5		
Dietitian	25.9	23.5	11.1	9.5		
Endocrinologist	18.5	23.5	11.1	9.5		
Nurse	5.6	2.9	3.7	4.8		
Internist	1.9	2.9	0	0		
Other‡	7.3	3.1	18.5	9.5		
No answer	5.6	8.8	40.7	57.1		

*Left and right columns within each stakeholder group represent *n* in the first and second rounds of the survey, respectively. Participants who identified as researchers were not explicitly queried for a healthcare profession background.

** Indigenous, African Origin, South Asian, Southeast Asian, West Asian, or a combination of ethnicities

*** Healthcare professionals from Canada with research activity chose not to identify as researchers.

†Argentina, Austria, Brazil, Croatia, Estonia, Germany, Hong Kong, India, Iran, Israel, Italy, Mexico, Portugal, Russia, Saudi Arabia, Spain, United Kingdom, United States, Zimbabwe

‡Diabetes educator, Maternal-fetal Medicine Sub-specialist, Physician - General/Family/Primary Care, Critical Care Obstetrics

Median SD of scores in round 1 was 1.84 (IQR: 1.62–2.17) and in round 2 was 1.61 (IQR: 1.33–1.91). Mean change in SD from round 1 to 2 was -0.24 (95% CI: -0.27, -0.21). Forty-six outcomes met inclusion criteria by the end of round 2: among these, 22% related to behaviour change and context, 17% to diet, 11% to glycemia and diabetes development, 7% to physical activity, and the remainder to a variety of other concepts (Table 2). The 75 indeterminate outcomes were discussed and 8 were retained. Seven additional candidate outcomes arose from panel discussion, of which 3 were voted for inclusion (online supplementary material S1). The 57 outcomes that met COS inclusion criteria were collapsed into 50 non-overlapping outcomes. For example, "carbohydrate intake", "fat intake", "fibre intake", "saturated fat intake", and "total energy intake" were collapsed into "macronutrients". The 50 outcomes were then classified by the panel into 19 domains: diabetes (n=3 outcomes), other related diseases (n=3), complications in subsequent pregnancy (n=2), offspring outcomes (n=3), adiposity (n=4), cardiometabolic measures (n=5), glycemia (n=3), physical activity (n=2), diet (n=4), breastfeeding (n=2), behaviour change theory (n=5), diabetes-related knowledge (n=2), health literacy (n=1), social support (n=1), sleep (n=1), quality of life (n=1), program delivery (n=4), health economic evaluation (n=2), and diabetes risk screening (n=2) (Figure 1).

Table 2. **Delphi survey results for outcomes that met inclusion criteria: % of *n* participants* that rated the outcome 7-9**

Outcome	**Round 1**				**Round 2**			
	All (*n* = 115)	**HCP (*n* = 54)**	**R (*n* = 27)**	**P (*n* = 34)**	**All (*n* = 67)**	**HCP (*n* = 34)**	**R (*n* = 21)**	**P (*n* = 12)**
Diabetes								
Diagnosis of type 1 diabetes	64.3	70	59.2	57.1	77.8	85.3	73.7	60
Diagnosis of type 2 diabetes	91.8	98	92.6	80.9	96.8	100	100	80
Complications in subsequent pregnancy								
Gestational diabetes mellitus recurrence	88.7	92	88.9	76.2	98.3	100	100	90
Other related disease								
Cardiovascular disease	64	72	66.6	56.5	82.5	91.2	89.6	60
Hypertension	61	64	66.6	52.2	71.4	73.5	79	50
Cardiometabolic risk								
Diastolic blood pressure	56	58	59.2	52.1	74.6	79.3	84.3	50
HDL cholesterol	56	56	55.5	47.8	69.9	67.7	78.9	50
LDL cholesterol	57	58	66.6	52.1	74.6	79.4	84.3	50

Systolic blood pressure	56	58	59.2	52.1	71.4	73.5	84.2	50
Glycemia measures								
Fasting blood glucose	75	73.6	82.1	66.6	89.2	91.2	90	63.7
Glycated hemoglobin test	68.5	69.8	78.6	62.9	84.5	91.1	90	54.6
Oral glucose tolerance test (OGTT)	82.4	90.5	82.2	70.3	89.3	97	90	81.9
Adiposity								
Body mass index	69.5	71.4	82.2	49.9	88	91.2	100	58.4
Postpartum weight retention	70.4	71.5	85.8	58.8	79.1	79.4	95.2	50
Weight	72.8	73.3	89.3	61.8	94	100	100	66.7
Waist circumference	53.1	53.7	64.3	54.6	71.7	73.5	81	50
Dietary								
Carbohydrate intake	69.1	63.9	65.4	81	84.5	87.1	84.2	100
Diet quality	71.3	68.1	73	90.5	87.9	87.2	84.3	100
Fat intake	64.9	63.9	57.7	76.2	79.3	80.6	84.2	87.5
Fibre intake	63.8	61.7	57.7	76.1	75.9	71	73.7	87.5
Food group servings	53.1	44.7	53.8	61.9	72.4	67.7	52.7	87.5
Glycaemic load	62.7	61.7	53.9	71.4	72.4	67.8	68.5	87.5
Saturated fat intake	60.6	57.3	53.8	71.4	77.7	74.2	84.2	87.5
Total energy intake	77.6	78.7	73	90.5	93.1	93.6	94.8	100
Physical activity								
Intensity of exercise	55.4	47.8	50	60	70.6	64.5	73.8	87.5
Moderate to vigorous activity	69.6	63.1	76.9	75	81.1	71	79	100
Sedentary time	77.1	76.1	77	80	84.5	83.9	94.7	100
Quality of life								
Quality of life	63.7	60	70.3	77.3	76.2	73.5	73.7	90
Sleep								
Sleep quality	60.9	45.7	69.2	85	70.6	58.1	84.2	87.5
Knowledge								
Diabetes knowledge	76.1	73.8	65.4	95	89.5	86.7	89.5	100
Diabetes prevention behaviour knowledge	82.6	82.7	73.1	95	89.5	83.3	89.5	100
Behaviour change theory								
Diet self-efficacy	66.2	67.4	65.4	85	75.4	73.3	84.2	100
Weight self-efficacy	64.1	65.2	53.9	75	72	63.4	78.9	87.5
Motivation to change	81.5	82.7	69.2	95	89.5	86.7	94.8	100
Perceived barriers	60.8	65.2	53.8	70	73.7	70	84.2	100
Perceived diabetes risk	76.1	74	65.4	95	86	83.3	84.3	100
Healthy lifestyle behaviours	84.8	87	73.1	95	92.9	90	94.8	100
Health literacy								

Health literacy	64.2	65.2	57.7	85	72	63.3	73.7	87.5
Social support								
Social support	64.2	65.2	57.7	75	79	76.6	84.3	100
Program delivery								
Completion of targets/activities	65.2	63.1	69.2	70	87.5	80	100.1	87.5
Intervention components engaged with	57.6	63.1	57.7	42.2	76.7	73.3	94.4	100
Whether goals were set for the woman and achieved**	0	0	0	0	73.1	70.1	88.9	87.5
Offspring outcomes								
Neonatal mortality/stillbirth	57.3	59.2	65.3	38.1	75.1	75.8	89.5	75
Health economic evaluation								
Health service utilisation and cost	60.9	60.8	69.2	50	82.2	83.4	83.3	75
Risk screening interventions								
Attending postpartum diabetes screening test	85.9	84	92.6	68.2	95.2	94.1	100	90
Completion of OGTT/blood glucose/HbA1c postpartum	86.9	92	92.6	81.8	92.1	94.1	100	80

*HCP denotes healthcare professionals, R denotes researchers, P denotes patients

**This was suggested as a candidate outcome following completion of the first survey round.

The consensus panel distinguished outcomes that were relevant irrespective of time since delivery (13 domains, 34 outcomes) and outcomes pertinent to one of three specific time periods: weeks and months after delivery (4 domains, 8 outcomes), subsequent pregnancy (1 domain, 2 outcomes), and later years (2 domains, 6 outcomes) (Figure 1).

DISCUSSION

The COS-DAP initiative engaged an international group of 115 stakeholders and 15 consensus panel members. The mean standard deviation across outcome scores decreased between e-Delphi rounds, signalling overall convergence of opinion. The application of *a priori* criteria to the e-Delphi scores led to 50 outcomes. Importantly, these reflected not only disease development and physiological effects but also patient-oriented outcomes like sleep quality and quality of life; health behaviours and behavioural theory constructs; knowledge, literacy, and risk perception; participation, adherence, and process outcomes; and economic measures. The relevance of some outcomes was a function of time since delivery or intervention focus. We believe that a comprehensive approach is crucial to facilitate the development and implementation of effective DAP programs.

Disease outcomes such as incident type 2 diabetes and cardiovascular disease were endorsed, as expected. Other disease outcomes included were recurrent GDM and gestational hypertension in a subsequent pregnancy, as well as type 1 diabetes; indeed, a subset of women with GDM develop type 1 diabetes rather than type 2 diabetes in the years following pregnancy.[15] Diabetes in the offspring was also endorsed; both type 2 diabetes and type 1 diabetes in offspring are associated with GDM in the mother.[16,17]

Our stakeholders endorsed quality of life and sleep quality which are patient-oriented outcomes that are also related to diabetes risk. Lack of sleep and psychosocial stress may increase risk of insulin resistance,[18,19] and maternal sleep disordered breathing is associated with GDM development.[20] Our COS is notable for not only focusing on biological effect measures but also the behaviours that are expected to lead to these effects, namely diet, physical activity, and breastfeeding; these three domains captured outcomes such as sedentary time, macronutrients, and breastfeeding length. Complementing these were the psychological factors (e.g., perceived diabetes risk, motivation to change) that need to shift for behavioural change to occur. A systematic review of weight loss interventions determined that such factors were more strongly associated with program attrition than demographic factors.[21] Some DAP prevention studies assess these factors at baseline,[22] but their improvement over the course of an intervention may signal potential for behavioural and therefore metabolic change. Similarly, our stakeholders emphasized the importance of health literacy, diabetes knowledge, diabetes risk perception, and social support. Again, these may be not only baseline contextual factors but also factors that evolve during an intervention.

Our stakeholders also underscored program participation and program delivery outcomes. Previous DAP prevention studies have exhibited variation in both participation rates and their reporting; [23,24] this metric is crucial to justify the implementation of sustainable programs. Frameworks exist to encourage reporting of program delivery process measures,[25,26] but COS-DAP represents a mandate to employ them. Finally, this COS recognizes the importance of collecting data to ascertain costs and cost effectiveness in order to achieve real world implementation.

One main objective of the Delphi process is to be inclusive of perspectives from a variety of stakeholders.[12] It was thus important that we included three key stakeholder groups. HCPs did not endorse sleep quality highly, but researchers and women with GDM did, allowing this outcome to cross inclusion thresholds. Participation of women with GDM in the Delphi process was important in retaining ‘patient-oriented’ outcomes such as social support, quality of life, and dietary outcomes – their high endorsement of these outcomes in round 1 prompted HCPs and researchers to change their scores to similarly high numbers in round 2, or their high scoring of these outcomes pushed an otherwise lower total score past the inclusion threshold. In contrast, weight and adiposity measures were retained because of high endorsement by HCPs and researchers, but were not endorsed by women with GDM. Women’s low scores likely reflect the stigma of postpartum weight retention, which must be addressed so that inclusion of these important outcomes do not impact follow-up.

Our emphasis on inclusiveness of perspectives is also reflected by our application of *a priori* criteria following the e-Delphi survey. In contrast, as previously discussed, Bogdanet and colleagues developed a COS focusing on follow-up in women with medication-treated GDM, with an emphasis on brevity. During their consensus meeting, even outcomes with high endorsement during the e-Delphi process (≥70% of participants scoring 7–9) were considered for exclusion. A consensus panel is, by design, smaller and less diverse than a group of e-Delphi survey respondents. We argue that removing outcomes highly endorsed by the survey respondents gives the smaller consensus panel a disproportionate voice in determining what is core. Therefore, we emphasized fidelity to the e-Delphi process and comprehensiveness of the outcome set. This is important not only for this particular COS but also for COS methodology in general.

Strengths and Limitations

COS-DAP gathered perspectives in 3 different languages from 23 countries. Most came from high and upper-middle income countries, which enhances the COS' applicability in these settings. However, it may be less applicable in low or middle-income countries. Of the women with GDM, most came from Canada and had previous experience participating in diabetes prevention studies.[27,28] Although not representative of the broader target population, they had the background knowledge required to offer meaningful input.

Survey attrition was high, which aligns with reported higher attrition in surveys with greater than 50 items.[29] Our attrition was primarily among women with GDM. A COS project for epilepsy in pregnancy also reported difficulty engaging patients in the Delphi process.[30] As per ongoing discussions on COS methodology, patient input may be better captured with qualitative methods.[11] Their input was nonetheless valuable, influencing the responses of other stakeholders during round 2 of the e-Delphi survey.

We quantified convergence of opinion in the Delphi process by examining SD for each outcome's scores. This approach is similar to Brookes and colleagues' in their study of different Delphi feedback methods.[31] COS development guidelines emphasize methodological integrity if a project intends to combine perspectives from a heterogenous group of participants.[11,12] As previously mentioned, we were consistent with our published protocol and applied *a priori* survey criteria for outcome inclusion, only voting on indeterminate outcomes at the consensus meeting to avoid a COS biased towards the views of select individuals.

We acknowledge that the final COS captures a large number of outcomes, which may appear to increase participant burden. However, many are process measures and costs, captured through tracking during the intervention. Some are relevant to only specific time periods relative to pregnancy. Therefore, adopting the COS may not be as difficult as the total number of outcomes may suggest. Further, there are key potential benefits – they include identifying aspects of the strategy that may require optimization to enhance efficacy, and determining whether implementation is feasible.

COS are subject to refinement as evidence evolves. Next steps may include engagement of women with GDM in a qualitative study to better discern their priorities, as well as a COSMIN (COnsensus-based Standards for the selection of health Measurement INstruments) initiative to identify how best to measure the outcomes in COS-DAP.

Conclusion

A growing body of health behaviour change trials aim to prevent DAP in women at known high-risk of diabetes. The COS-DAP initiative executed a methodologically rigorous process to define a COS that captures not only glycemia and cardiometabolic risk factors but also behavioural, process, contextual, and economic measures. COS-DAP mandates that researchers consider a breadth of meaningful outcomes as core in this area of research. If research fails to consistently measure outcomes that are important to delivering impact on the health and wellbeing of this population, then the COS has failed to drive the change it states is at the centre of its mandate. We call on the scientific community to apply COS-DAP in future trials to build a meaningful and actionable evidence base, and ultimately improve health outcomes.

FOOTNOTES

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Some visual elements in Figure 1 were obtained through Canva. Rights to these elements belong to their respective, original copyright owner/creator.

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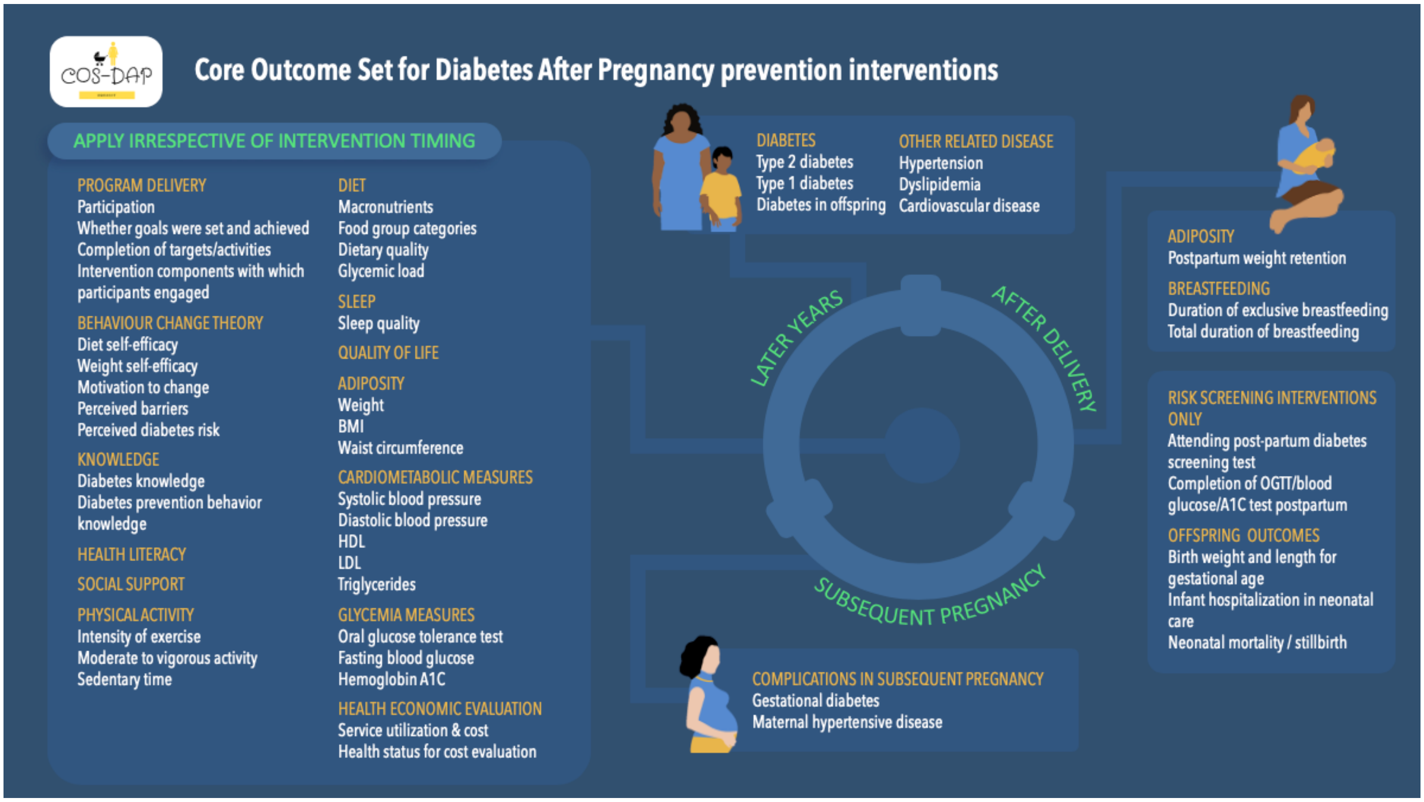
FIGURE LEGENDS

Figure 1. Core outcome set for diabetes after pregnancy prevention interventions. Fifty outcomes are grouped into 19 domains and arranged according to when they are measured relative to time since pregnancy during the intervention. Health literacy, social support, and quality of life are individual outcomes.



SUPPLEMENTARY MATERIAL

S1. **Additional outcomes voted for inclusion by consensus panel**

Outcome	**% of votes "in"***	**Rationale**
Indeterminate outcomes from the Delphi survey		
Dyslipidemia	71.4	Risk factor for cardiovascular disease and prevalent in type 2 diabetics
Gestational hypertension	78.6	Risk factor for post-pregnancy cardiovascular disease
Length of breastfeeding	100	Increases insulin sensitivity and improves glucose metabolism in the mother
Breastfeeding exclusivity	71.4	Increases insulin sensitivity and improves glucose metabolism in the mother
Infant birth weight and length for gestational age	71.4	Women with GDM are more likely to have macrosomic babies
Diabetes in the offspring	71.4	May indicate elevated risk of diabetes and CV disease in mother
Health status for cost evaluation	78.6	Cost evaluation will be important to implementation
Study participation	71.4	May help assess presence of barriers/enablers to completion of an intervention program
Suggestions from consensus panel discussion		
Maternal hypertensive disease	78.6	Includes diseases beyond gestational hypertension
Infant hospitalization in neonatal care unit	85.7	May indicate elevated risk of diabetes and CV disease in mother
Sugary beverage intake	78.6	Health behaviour associated with diabetes and CV disease

*Number of voting members differed for outcomes of each origin: n=15 for indeterminate outcomes, n=14 for consensus panel suggestions

5. Study Methodology II

5.1. Preface

The first objective of this thesis was addressed by implementing an e-Delphi method to develop a COS, gathering perspectives from a range of stakeholders around the world. The second objective of this thesis was to develop a comprehensive analysis protocol to analyze the virtual interactions facilitated in T1DM-VPN, a private Facebook group that my primary supervisor and her colleagues established for youth in Canada living with T1DM. The main aim of the network was to serve a souce of peer to peer support. Therefore, in our analytic approach, we aimed to describe the types of social support being exchanged in the group, and to determine whether being a designated peer leader predicts the type of social support offered. In developing this analysis protocol, I considered issues of data extraction and privacy. I examined available methodologies in text analysis and structural analysis of user-generated data to inform the best approach for analyzing T1DM-VPN, taking into consideration the nature of the Facebook group as an open cohort. I now present and overview of the methodology that I used to design the analytic approach, incorporating a variety of qualitative and quantitative analyses through an epidemiological lens. Specific details are described in manuscript 2, presented after this overview.

5.2. Data collection

T1DM-VPN is integrated directly into an existing social media website, Facebook. In order to analyze social media data, text and activity information need to be extracted for analysis. Some previous studies have used an Application Program Interface (API) to accomplish this. An API is a defined set of programming functions offered by an application of interest that allows others to access the application's features or data. Public information (e.g., posts on a public Facebook page, a user's number of friends) is readily accessible with the API. For example, an SNA of a public Facebook page for smoking cessation support used the services of a social media management marketing platform to download all interactions (e.g., comments, likes) through an API.[38]

There are, however, restrictions in Facebook's API that limit automatic data download. Private Facebook page data cannot be automatically downloaded; instead, content must be manually extracted to be analyzed and studied. Some researchers have performed this for private Facebook groups that they were not involved in creating. They either requested to join the group with an explanation of their research objectives to the Facebook group's administrator,[81] or received ethics board approval to create a 'faux' account to match the group's target audience, request to join, and thus access group content.[39] Other researchers, like us, are themselves founders or co-founders of the private Facebook group. This may be as part of a health intervention[82] or as a support platform, sometimes complementing a clinical program.[83] Enrolment into these groups is controlled by the researchers, and members are aware of their role in overseeing group activity. These researchers can access group content, as we will do for the proposed analyses described in Manuscript 2.

5.3. Data privacy

Internet platforms that are not under the purview of a professional institution change in structure, data-capture capability, and user policy, at a rapid rate. Much user-generated data is considered "public" and users acknowledge this when they join a platform or use their service. However, it has been debated that users do not fully comprehend the ways in which others may use this public data and are thus not making a fully informed choice. As mentioned in a brief review of e-epidemiology, it is currently up to research ethics boards to determine whether a study adequately considers the privacy rights of the study subjects [3].

T1DM-VPN was established with funding from Diabetes Canada and CIHR, and also received ethical approval and/or exemption from the involved institutions across Canada (these details are available in Results, Chapter 7). However, we decided that it was essential to seek and receive ethics approval specifically for our analysis protocol. We also collaborated with our designated peer leaders to write a transparent description of the analysis to share with members of our Facebook group, specifying what kinds of information would be extracted and de-identified before analysis. Designated peer leaders are Facebook group members who were recruited and trained by the T1DM-VPN researcher-clinician team to provide support to the other members, and to stimulate activity in the group by making posts and answering questions. More details regarding the nature of the peer leaders is provided in Results (section 6).

5.4. Analysis of User-Generated Text Data

The comments and posts shared onto an internet platform can be analysed as text data. There are many approaches to analyzing text data, but in deciding what approach was most appropriate to apply for our study, I considered two factors: firstly, the objective of our text analysis, and secondly, the nature of the text data.

YP Wu and colleagues have written a detailed commentary on qualitative research methods in medicine to help researchers determine what approach to adopt [84]. Overall, qualitative research aims to describe a phenomenon within a certain target population of interest. This is productive for forming new theories, understanding end-user perspectives and their needs, and documenting rare issues. In diabetes research, netnography has been used to understand a Twitter community of T1DM patients' and families' attitudes towards new technologies [85]; netnography applies the traditional sociological method of ethnography – which studies a community's customs and people – to virtual communities instead [47]. Researchers have applied thematic analysis to the articles and comments posted by caregivers of children with T1DM to identify barriers and facilitators in caregiving.[86] Qualitative research may have even more immediate impact when conducted with patients and their families to inform the design of interventions that would be targeted to them.

Content analysis focuses on quantifying the qualitative data. This is accomplished by interpreting the text and coding it into different categories, and then using the frequency of a category as a proxy for its significance [87]. YP Wu and colleagues propose that quantification of qualitative data fits only specific study purposes – for example, investigating the particular terms used by a group of interest in discussing a common topic. A quantitative approach is also useful if the study objective aims to understand whether certain themes are common or rare [84].

A purely qualitative approach to T1DM-VPN would be sufficient if our objective was to simply confirm or describe the existence of social support being exchanged between its members. However, our research team is uniquely positioned as the initiators of the private Facebook group; we have access to, and intend to analyze, all text data that has been generated since the group's inception over two years ago. We are able to calculate the frequencies of social support exchanges and compare our results to similar quantitative text analyses from other groups for youth with T1DM. Furthermore, we are able to perform regression analyses to achieve our objective of determining whether peer leader status predicts the type of social support offered. Thus, I decided that content analysis was an appropriate method to use for analyzing text data in T1DM-VPN.

In addition to considering the objective of our study, I also considered how the analytic method would be affected by the nature of the text data. While the posts and comments represent a form of communication, online communications cannot be treated as transcribed versions of what might be audio recordings from a real-life interview or conversation. For example, in terms of automated types of analyses, posts are arguably less useful than transcriptions which are usually generated in accordance with proper spelling and formatting; if a researcher attempts to use an automated program to either search for, or analyze text data from social media, the frequency of misspellings, colloquialisms, and other variations of language may cause the researcher to overlook or inadequately code a whole set of data.

For example, one research group endeavoured to systematically extract and code all public Facebook, Twitter, and Instagram posts about child pain and sleep [88]. The coding was accomplished manually by individual researchers. However, the data extraction was performed with an automated software program. Although the complete list of synonymous search terms for each primary concept was thorough (e.g., ' "child OR childs OR children OR childrens OR childhood OR kid OR kids OR daughter OR daughters OR teen OR teens OR teenager OR teenagers OR pediatric OR paediatric OR infant OR infants OR toddler OR toddlers OR newborn OR newborns OR adolescent OR adolescence OR "little guy" OR "little man" '), none of the lists included possible misspellings. This may have implications on the validity of the frequency of themes reported by the authors. In the case that a researcher aims to be both comprehensive in their search and quantitative in their approach, applying an algorithm [89] that includes possible textual deviations may yield more accurate results. Because of these concerns, we are not proposing to apply automated methods to transcript analysis.

Further, in the case of T1DM-VPN, manual extraction of posts and comments is necessary due to limitations in Facebook's API. As stated, I chose to code all text data manually and avoid applying any automated word analyses. This illustrated the limitations of technological tools at a particular point in time. It is important however to be cognizant of this in order to perform methodologically rigorous analyses.

The next issue to consider was which type of content analysis to perform. There are three approaches to content analysis [90]. Conventional analysis helps describe a phenomenon for which existing research literature is scarce; researchers approach text with limited preconceived categories. Summative content analysis involves interpreting the latent messages underlying text content. Directed analysis is applied when research exists about the phenomenon of interest; this prior knowledge is used to inform categories for coding. Coding frameworks already exist for our main phenomenon of interest - social support - and have been adapted to an online setting for health-specific groups [83,91]. We therefore chose to apply directed content analysis.

5.5. Analysis of User-Generated Web Activity Data

User engagement with a web platform is typically evaluated by measuring the number of virtually-enabled engagements (e.g., posts, comments, clicks, and views). When analyzing engagement on a social media platform, researchers provide absolute summary measures of these engagements; for example, the number of participants posting at least once on a Facebook page [38], or average percentage of views per post in a private Facebook group [82].

Activity between users on the other hand, has been evaluated using social network analysis; SNA has its roots in sociology. At the broadest level, it can be considered a framework for understanding social structure [92]; as a methodology, the term SNA is specific. The first step in this technique is to capture all ties among a network's members and to identify specific tie patterns. VPN is a sociocentric network in that it includes members within a (virtually) bounded community; this is in contrast to an egocentric network, which is defined based on a person's perspective of their own ties. Within a network, "nodes" (i.e., members) are connected to one another via "edges" (i.e., ties or interactions). A network can be mapped with dots and lines representing nodes and edges, providing a visual or graphical representation of its structure.

Quantitative metrics may also be generated to understand, for example, the importance of a member (centrality) and the volume of interaction within the network. A virtual network is well-suited to this type of analysis, as all interactions are documented, and thus researchers do not have to rely on participant recall and report.

The second key step in SNA is to investigate how network membership and structure are related to social behaviour and change [42]. In epidemiological studies, researchers may seek to understand how an individual's position in their network is related to their behaviour, risk exposure, or development of an outcome of interest [93]. Some studies of virtual social networks have extracted "real-life" behaviour information from direct self-report online such as public self-reports of time since smoking cessation [38], while others have inferred behaviour from particular phrases and virtual activities [94]. We chose to adopt the latter approach: namely, using phrases and virtual activities to capture the behaviour of exchanging social support.

In epidemiology, selecting an appropriate measure requires careful consideration of the nature of the phenomenon of interest, and other contextual information. As described earlier, researchers tend to calculate absolute or average measures of engagement and network interaction [82]. In cases where users have been enrolled at the same time, researchers can assume that the opportunity for a member to engage with the group is equal for all members – that is, the cohort entry, exit, and total follow-up time for everyone are the same. This is analogous to a fixed cohort. Where a user's first date of exposure to the network is unknown, and total exposure time is not clearly defined, researchers may resort to making a "steady-state" assumption – where network variables such as membership and activity are assumed to be stable [95]. Researchers have also opted to draw a random sample of users from the larger "virtual" population of the network of interest [38].

Our research team is uniquely positioned in relationship to T1DM-VPN. Firstly, we can consider T1DM-VPN members to constitute a dynamic cohort, as do most Facebook groups; users' first dates of exposure (cohort entry, in epidemiological terms) vary, as do their total exposure times. Furthermore, as the creators and administrators of the group, we have access to cohort entry time (the date that each member joined) and are also able to calculate total follow-up time. We also know how network membership has grown over time. For the few people who have left VPN of their own accord, we do not have access to the exact date that they left, but we can still track their past interactions, if any. With this knowledge, we do not have to make a tenuous assumption about the stability of our network over its 3-year history. Rather, we chose to find a way to recreate many detailed “snapshots” of the VPN network at stable points in time since its inception in June 2017.

In addition to consulting the literature for existing techniques to analyze a social network, we also consulted the T1DM-VPN peer leaders via teleconference on the proposed analysis, and invited suggestions for any analyses that they would like to see performed.

5.6. Ethics

We obtained ethics approval from the Research Ethics Board of the McGill University Health Centre (MP-37-2020-6511).

6. Results: Objective 2

6.1. Preface

This manuscript was submitted to the *Journal of Medical Internet Research Protocols* in June 2020. It addresses the second objective of the thesis, which is to develop a comprehensive analysis protocol to analyze the virtual interactions facilitated in T1DM-VPN. I designed the analytic approach to incorporate directed content analysis, social network analysis, and regression analysis, carefully treating the cohort as an open cohort, and thus bearing in mind the importance of person-time in analysis; previous social network analyses applied to virtual communities have often made assumptions about cohort stability that may not be appropriate. I now present the results of this endeavour in the following manuscript, formatted according to the aforementioned journal's guidelines:

Nancy Wu, Anne-Sophie Brazeau, Meranda Nakhla, Deborah Chan, Deborah Da Costa, Geetha Mukerji, Sonia Butalia, Daniele Pacaud, Melanie Henderson, Constadina Panagiotopoulos, Elham Rahme, Kaberi Dasgupta. The Type 1 Diabetes Mellitus Virtual Patient Network (T1DM-VPN): Protocol for social network analysis and content analysis of a peer support community

I will carry out the analysis detailed in the following manuscript over the next two months.

6.2. Manuscript 2: The Type 1 Diabetes Mellitus Virtual Patient Network (T1DM-VPN): Protocol for social network analysis and content analysis of a peer support community

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Title: The Type 1 Diabetes Mellitus Virtual Patient Network: Protocol for social network analysis and content analysis of a peer support community

Abstract

Background

Type 1 Diabetes Mellitus Virtual Patient Network (T1DM-VPN) is a private Facebook group for youth with T1DM in Canada. It is intended to facilitate peer-to-peer support. It was built on the finding that stigma is prevalent among youth with T1DM and impedes self-management.

Objective

We aim to determine if T1DM-VPN provides support as intended, and to ascertain what type of members provide support. Specifically, we will: 1) identify text consistent with any one of five social support categories, 2) describe the network by visualizing its structure and reporting basic engagement statistics, and 3) determine whether being a designated peer leader is related to a member's centrality (i.e., importance in the network) and how frequently they offer social support.

Methods

We will manually extract interaction data from the Facebook group (posts, comments, likes/reacts, seen) generated from June 21, 2017 (addition of first member) to March 1, 2020. Two researchers will independently code posts and comments according to an existing framework of five social support categories: informational, emotional, esteem, network, and tangible, with an additional framework for non-social support categories. We will calculate how frequently each code is used. We will also report basic engagement statistics (e.g., number of posts made per person-month) and generate a visualization of the network.

We will identify stable time intervals in the history of T1DM-VPN by modelling monthly membership growth as a Poisson process. Within each interval, each member's centrality will be calculated and standardized to that of the most central member. We will use a centrality formula that considers both breadth and depth of connections (*centrality = 0.8 * total no. of connections + 0.2 * total no. of interactions*). Finally, we will construct multivariate linear regression models to assess whether peer leader status predicts member centrality and the frequency of offering social support. Other variables considered for inclusion in the models are gender and age at diagnosis.

Results

T1DM-VPN was launched in June 2017. As of March 1, 2020, it has 196 patient members. This research protocol received ethics approval from the McGill University Health Centre Research Ethics Board on May 20, 2020. Baseline information about each group member was collected upon addition into the group, and collection of interaction data is ongoing.

Conclusions

This content analysis and social network analysis study of a virtual patient network applies epidemiological methods to account for dynamic growth and activity. The results will allow for an understanding of the topics of importance to youth with T1DM, and how a virtual patient network evolves over time. This work is intended to serve as a foundation for future action to help youth improve their experience of living with diabetes.

Keywords

Type 1 diabetes; youth; social network analysis; content analysis; social media

Word Count

Abstract: 441
Manuscript from Introduction to Discussion (including headings): 4446

Introduction

Type 1 diabetes mellitus (T1DM) is a chronic condition whereby one's immune system attacks the pancreas, rendering it unable to produce adequate insulin for glucose entry from the circulation and into the cells of the body, to fuel metabolism. This differs from the general defect in type 2 diabetes, which is one of resistance to the action of insulin, often related to low physical activity and excess adiposity. Patients with T1DM administer insulin as a medication, adjusting doses in relationship to food intake and physical activity. They are challenged by a narrow therapeutic window, navigating a tight balance between preventing low glucose levels and high levels. Low levels, or hypoglycaemia, can lead to confusion, loss of consciousness, and even death. Persistently high levels over time can damage blood vessels, resulting in blindness, renal injury, cardiovascular disease, stroke and a multitude of other complications. The visibility of hypoglycemic symptoms, blood glucose testing equipment, and insulin administration, among other tasks, as well as public misconceptions about T1DM may lead to stigma.

Indeed, in a previous study, we determined that approximately 65% of Canadian youth (i.e., 14-24 years of age) with T1DM experience stigma and that it is associated with greater probability of both severe hypoglycaemia and high average glucose levels (specifically elevated A1C).[1]

The Type 1 Diabetes Mellitus Virtual Patient Network (T1DM-VPN) is a private Facebook group we launched in 2017 to facilitate peer-to-peer support, allow youth to share experiences of living with T1DM, and perhaps mitigate stigma. We now aim to assess whether the Facebook group is providing the support it is intended to provide. We present herein a detailed protocol for this analysis.

We first provide an overview of T1DM management, existing web platforms for patients and their families, and the development of T1DM-VPN towards its current structure.

Barriers to T1DM Management

In Canada, 24,170 children and adolescents and 84,380 young adults have diabetes,[2] over 90% of which is T1DM.[3,4] T1DM management requires insulin pump or injection use, finger pricks for blood glucose testing, and attention to food choices, meal timing, and physical activity levels. However, youth must also manage challenges of identity development, education and career choices, and peer pressure. Managing both sets of needs can be complicated by stigma. Stigma is defined as real or perceived negative social judgement from one's surroundings or oneself.[5]

Our Canada-wide study of 380 youth determined that 65% report some degree of stigma (i.e., endorsed one or more of 3 key items on a stigma subscale).[6] Youth experiencing stigma were twice as likely to have either an HbA1c above 9% or one or more severe hypoglycemic events in the prior year. HbA1c is a measure of the average level of blood sugar over the past 2 to 3 months, and higher levels indicate greater risk of serious diabetes-related complications such as cardiovascular disease, kidney, eye, and nerve damage.[7] Severe hypoglycemia may also cause distressing conditions such as confusion, loss of consciousness, and even death.[8,9] Our study also determined that stigma was associated with a reduced sense of well-being and less self-efficacy for self-management. Most participants reported that they did not personally know anyone with T1DM and desired social support specifically from peers with T1DM.

Existing Web Platforms

Web platforms for patients with T1DM vary in reach and in purpose. On Twitter, hashtags are used by people all over the world to connect on specific topics. For example, an "#OpenAPS" hashtag is used by patients and caregivers to vocalize their experience using do-it-yourself (DIY) innovations that bridge communication between insulin pumps and glucose monitors.[10] Meanwhile, a Facebook group numbering over 27,000 members provides practical aid in using DIY programs.[11] Some caregivers of children with T1DM publish blogs in order to publicly express their experiences and feelings, with additional caregivers commenting.[12] Some youth initiate local university-based diabetes student organizations with a respective social media platform, including in Canadian towns such as Toronto and London. Other platforms are managed professionally. For example, *Beyond Type 1* is an organization that amalgamates practical resources and stories on a website, including some specific to Canada. They additionally have an application where registered adults and teenagers can socialize via public posts and comments. Social media groups may be generated by professionals as well; one clinical team in Australia created a small (34 members), private Facebook group for T1DM youth as part of a 12-week trial to support their transition to independent self-care.[13]

In this landscape, T1DM-VPN is distinguished as a joint initiative between health professional researchers and youth with T1DM. It is funded by Diabetes Canada as well as the Canadian Institutes of Health Research Grant (CIHR), specifically their *Strategy for Patient-Oriented Research (SPOR) – Patient-Oriented Research Collaboration Grants* through a grant awarded to our research group. Its core feature is a private Facebook group. Eligible members are Canadian youth (i.e., 14-24 years of age) with T1DM. Many T1DM-specific groups have been initiated organically on Facebook – however, none are known to be specific to Canadian youth, who can benefit from region-specific information and from interacting almost instantly with those who face similar everyday challenges across the country. T1DM-VPN is open only to patients, not to parents or other caregivers – at the specific request of its founding patient partners. Its three goals are:

(1) to be a community of support,
(2) to identify the issues that matter to patients, and
(3) to establish a platform for action and empowerment.

Development of T1DM-VPN

We collaborated with two patient partners to inform T1DM-VPN development – one youth with T1DM, and one adult with T1DM with experience as a certified peer leader for the chronic illness self-management program at the McGill University Health Centre called *MyToolbox*. Based on the Stanford model of chronic disease self-management, *MyToolbox* allowed individuals living with a chronic illness to engage in group discussions on self-care led by trained "peer leaders" who also live with chronic illness.[14] This program was discontinued at the MUHC but our patient partner's experience with it was important in the training of our peer leaders.

We recruited youth peer leaders for T1DM-VPN by asking our co-investigators across Canada to approach any patients who they thought would be a champion for T1DM, and by approaching patients who submitted moving testimonies from our original STIGMA study [6]. They were told that responsibilities include starting conversations in the group, and having one-on-one conversations if requested by a member.

At the 2017 Diabetes Canada conference in Edmonton, several peer leaders participated in the satellite workshop that we organized to encourage group cohesion, provide training in peer support, discuss goals, and craft community guidelines. Each peer leader receives a stipend ($25CAD/month) to support involvement in T1DM-VPN. They take an active role in initiating conversations, sharing information, and answering questions. They provide input on recruitment strategy. They reach out to our team of clinicians and researchers for information.

Some 'regular' T1DM-VPN members are recruited from among participants in our original study on stigma. Regular members are continuously recruited through the clinics of our co-investigators, and via posters displayed in clinics and posted online on diabetes-related Facebook pages and websites. Addition of members began in June 2017. As of March 1, 2020, the group has 196 youth with T1DM from over 20 towns/cities in all 10 Canadian provinces (Figure 1). An additional four are members of our research team, and one is the designated administrative account used by our research team.

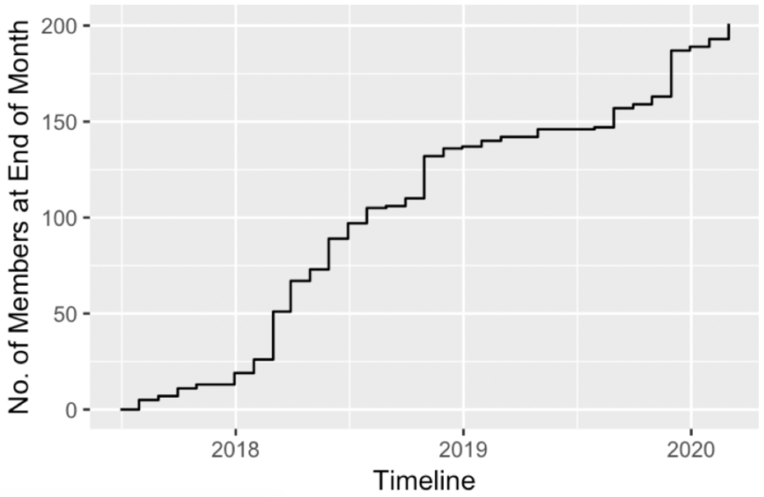

Figure 1. Number of T1DM-VPN Facebook group members from June 21, 2017 to February 4, 2020.

The administrator account is used by the research team to oversee the group. We add eligible members, help answer questions that may require professional input, and ensure that the code of conduct (e.g. no disrespectful behaviour) is followed. Fortunately, our members have only behaved in a courteous and supportive manner and we have never had to intervene. As patient membership approaches 200, we aim to determine if the project goals are being fulfilled. This will help inform strategies to strengthen and sustain the network.

T1DM-VPN members are aware that the private Facebook group was created by researchers and trained peer leaders and that communications are monitored. As we state on the Facebook group itself, T1DM-VPN is "intended to be a source of support, friendship and information. It will also be used to find out what research is important to patients like you to help guide diabetes research in Canada. As we have funding from CIHR and Diabetes Canada and have health professionals and researchers on board who will help make living with T1D easier, and will be there to answer your questions!"

Objectives

The goals of this analysis stem from T1DM-VPN's goals of facilitating social support and identifying the priorities of young Canadians with T1DM. This protocol is for an objectives-based program evaluation – a type of evaluation that ascertains that the intended activities are taking place.[15]

Our primary analysis objective is to determine whether peer leaders are (A) more central and (B) provide more social support to the group than regular members. By analyzing group members' exchanges, we also aim to achieve secondary objectives of (C) determining the existence and volume of five categories of social support and (D) identifying the issues for which informational support is requested.

Assessing the role of peer leaders has implications on the sustainability of T1DM-VPN as a program. It will help determine whether peer leaders should continue to be engaged by our team of clinicians and researchers, or if regular members can rise to become "natural" peer leaders. These findings may be of interest to professionals aiming to launch a similar initiative in another population, country, or region.

Previous Analyses of Web Platforms for Youth with T1DM

Researchers have previously performed content analysis on messages authored by youth with T1DM in an online context. One study amalgamated content from eight public T1DM forums and used an inductive coding process to categorize messages. Among the six resulting codes were "social support", "factual information", and "management". The forums were not age-specific, but they extracted data for which the user self-reported an age between 11 and 19 years old.[16] Another research group designed an application specifically for their research study, holding regularly scheduled, virtual text chats with T1DM youth aged 12 to 18 years recruited from a diabetes care centre in Italy.[17] Chats were actively moderated by researchers and/or health professionals. This study used the same social support framework that we intend to use for coding. The nature of T1DM-VPN as a private Facebook group bridges that of these two – users are enabled the spontaneity and connectivity of a public forum, but offered the privacy and peer-specific audience of the chats. T1DM-VPN users may express themselves differently because they are aware that their peers, rather than our administrative team, take the lead in answering questions and moderating discussions. Furthermore, they are aware that the group is specific to Canada and that as a result, peers may be better able to answer questions related to healthcare and insurance. Thus, it will be interesting to compare the frequency of different kinds of support offered across these different platforms.

The study in Italy also compared the frequency of social support categories from moderators vs. participants. They determined that moderators were more likely to present informational support, and participants were more likely to provide emotional support. As in this study, we will ascertain the relationship between a designated moderator status (peer leader vs. regular member?) and social support behaviour. However, the nature of T1DM-VPN differs in that the designated discussion moderators are peers, i.e., fellow youth with T1DM. As detailed in Methods, we will examine this relationship by constructing multivariate linear regression models that consider additional variables such as gender.

Shah and colleagues have previously performed social network analysis (SNA) on youth with T1DM and their parents.[18] They mapped participants' subjective network of friends and relatives through interview and found that youth with a greater number of network members providing support reported lower anxiety. Saylor and colleagues performed a descriptive, correlational study that found that T1DM youth who were members of a student-led diabetes student organization were less likely to report poor mental health related to their diabetes than youth who were not.[19] We are able to similarly capture the network positions and behaviours of youth with T1DM who actively engage with the support network (T1DM-VPN), versus those who do not. However, T1DM-VPN differs in that it provides a *virtual* network of support to members, and to our knowledge, SNA has not been applied to virtual networks of T1DM patients. Moreover, our outcome of interest is not a self-reported health status, but a measure of importance in the network, and the act of offering social support.

Overall, we are modelling T1DM-VPN as a social network for the purpose of understanding the role of different member types on this virtual platform. The interactions on a Facebook group may not reflect those that would occur between individuals outside a virtual network in their in-person social groups and settings.

Methods

Baseline information is collected upon group entry, including gender (derived from nominal information), age at diagnosis, and geographic classification (i.e., large, medium, or small population centres, rural). We will manually extract interaction data from the T1DM-VPN Facebook group feed for the period between June 21, 2017 (addition of first member) and March 1, 2020. Enrolment into these groups is controlled by the researchers, and members are aware of their role in overseeing group activity. It is essential to include all members in an SNA. While we will not seek individual-level consent, based on discussion with our peer leaders during a teleconference, we will however provide a reader-friendly description of the protocol in the Facebook group and invite members to comment, as recommended by our peer leaders. All data will be de-identified prior to analysis, replacing names with identification numbers; the document linking these numbers to individuals will only be available to members of the research team. This proposed analysis received ethics approval from the McGill University Health Centre Research Ethics Board on May 20, 2020.

Phase I: Directed Content Analysis

We will apply content analysis, interpreting the text and coding it into categories, and then using the frequency of a category as a proxy for its importance.[20] Our content analysis will be directed, applying prior knowledge to inform coding categories. Specifically, we will apply Cutrona and Suhr's typology,[21] used for online support group analysis by other researchers.[22] Its two overarching categories are *seeking* support, and *providing* support). These in turn each have five sub-categories: informational, emotional, esteem, network, tangible assistance (Appendix 1**)**. In addition, we will code and count social support facilitators (expressions of gratitude) as well as non-social support exchanges (e.g., administrative messages; Appendix 2), as adapted from Gaysynsky's directed content analysis of a private Facebook group for young clients of an HIV program.[23] After applying these initial codes to the data, any content deemed not adequately coded will be further examined and discussed to determine if new categories need to be added.

Two coders will review examples of how the social support framework has been applied in Gaysynsky and colleagues' study. First, a sample of data will be coded, analyzed for concordance between the two coders, and discussed to refine the consistency with which codes are applied. Then, all posts and comments will be reviewed to identify which code is most applicable. For a given comment, context (original post, preceding and proceeding comments) will be used to help inform coding decisions. A maximum of two codes may be applied to the same content. We will further examine the issues for which informational support is requested.

Phase 2: Social Network Analysis

Defining an Interaction

In T1DM-VPN, members interact via posts and comments. Members may additionally 'like' or 'react' to a post or comment, or vote on a poll (Table 1). Following the examples of previous SNA on Facebook [24], We will define each of these as an interaction type. We will further categorize each interaction type into a high, medium, or low engagement level (Table 1). We will also take note of who has "seen" a post and categorize this as 'low' engagement level.

Table 1. Types of Interactions

Engagement Level	Interaction Type	Definition
High	Post	Content posted by any member to the group feed.
	Comment	When a member comments on a post.
Medium	Like/react to a post	When a member likes/reacts to a post.
	Like/react to a comment	When a member likes/reacts to a comment.
	Voting in a Poll	When a member votes in a poll (type of post).
Low	Seen	When a member has seen a post (with no further interaction)

Visualizing Interactions

Based on interaction data, the social network will be visualized using programming packages specific to SNA (e.g. *sna* and *network*) (R Version 3.5.1 and RStudio Version 1.1.456.) All members (or "nodes") will be represented as dots, and any medium-high engagement level interaction between two nodes will be represented with a line connecting them (Figure 2, sample visualization).

For overall network visualization, each line between nodes will represent one or more interactions for the period of interest ('unweighted approach') rather than a separate line for each interaction ('weighted approach'). Similarly, the directionality of an interaction/line will not be indicated (undirected graph). This will render the visual representation less crowded and more interpretable. We will visualize the network both with and without peer leaders to visually appreciate their importance in driving group activity, following the example of a previous SNA evaluating the importance of a Facebook page moderator.[24] When calculating network centrality, as discussed below, we will consider both weighted and unweighted approaches.

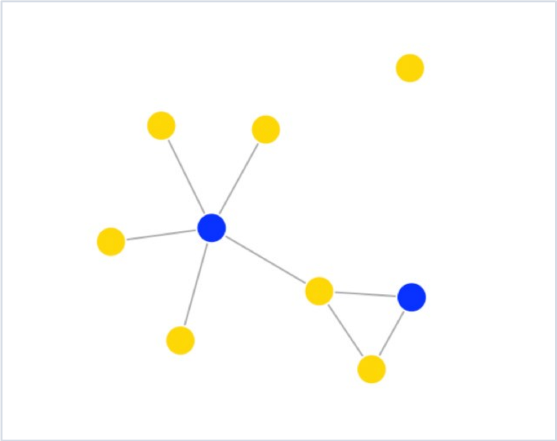

Figure 2. Sample visualization of a social network with 9 nodes. Regular members are indicated as yellow dots, and peer leaders are indicated as blue dots. Interactions are represented by connective lines.

Network Dynamics and Time in SNA

We will evaluate network dynamics over approximately a 3-year period. In epidemiological terms, this is an 'open' cohort in that members may leave or join at different times. In prior Facebook group studies, researchers have taken a data sample from what they assumed to be a stable timeframe. They then take absolute (e.g., total number of posts) or per-person (e.g., average number of posts per person) measurements.[23,25]

Instead of making assumptions about the stability of a network, we will actually identify stable timeframes by modelling monthly membership growth as a Poisson process. Any month for which the Poisson probability of observing that number falls below 50% will represent the start of a new stable interval. For several network and node attributes detailed below, we will calculate an "incident" measure for each time interval, then a summary measure across all intervals if applicable. These calculations are detailed below.

Network Attributes

Social networks can be characterized by measures of density, identification of cliques, and indicators of engagement.[26] Density is the total number of interactions divided by the total possible number of interactions. A clique is a subgroup of nodes that are directly connected to one another, with no node being connected to all in the subgroup. Quantifying engagement typically involves an enumeration of high-engagement level interactions; we will use number of posts per person-month. These three attributes will be calculated for each time interval. To summarize them, the difference in density and number of cliques from the first interval to the last will be calculated, and the mean number of posts per person-month will be taken.

Node Attributes

Just as the network may be characterized by defined metrics, nodes may also be characterized in terms of their centrality and in terms of the nature of their interactions. For each node, we will calculate the proportion of all their interactions that are categorized as high, medium, or low-engagement level (Table 1). This helps identify members who actively participate in discussion versus those who "lurk" with little direct interaction. We will also calculate the proportion of a user's interactions categorized as offering social support; this is one of the measures that will be used in the regression analysis. Because these are proportions, there is no need to additionally account for group stability.

Centrality is the other measure that will be used in the regression analysis but requires accounting for stability. Centrality refers to one's prominence in the network. In virtual SNA, prominence is calculated using virtual connections. In calculating 'degree centrality' specifically, [26,27] researchers may consider the total number of nodes with which a node is connected, or the total number of connections including repeated connections with the same node. We have developed a measure that incorporates both of these aspects. In ascertaining centrality, we will focus only on medium and high engagement-level interactions as connections. In order to capture both breadth and depth of connection in centrality, we have adapted modelling methods from economics,[28,29] creating a measure that is a convex combination of the weighted and unweighted approaches:

$$centrality = alpha * total\ no.\ of\ connections + (1-alpha) * total\ no.\ of\ interactions$$

where we choose alpha to be 0.8. Alpha is usually any number between 0 and 1, but we will be testing values between 0.5 and 1 in a sensitivity analysis. This range ensures that breadth of connections is given equal or greater weight than depth.

The centrality of each member will be calculated for each stable time interval (i.e., include interactions occurring exclusively within that interval), then standardized to that of the most central member for that interval. The resulting measures for each member will be averaged. This final mean value will be used in regression analysis.

Rather than take a direct calculation of these attributes, as existing virtual SNA have, we are adopting this approach because we appreciate that length of membership in T1DM-VPN is similar to exposure time; if a user has been involved in the group for a longer period of time, then their increased centrality may be a function of their increased opportunity to interact with others. We also understand that the number of possible connections exposed to a user a given point in time differs. Network membership increases over time, and so does the number of potential connections for a user. By taking measures of centrality from smaller, stable timeframes, we can better control for these two potential confounders.

Phase 3: Regression Analyses

We will evaluate the relationship between network centrality and designated peer leader status to determine whether those so designated are more likely to be central within the network. We will apply multivariate linear regression considering inclusion of the following variables in the model: gender, age at diagnosis, and geographic classification (i.e., large, medium, or small population centres, rural). Studentized residuals will be used to detect potential outliers. We will then calculate a BIC (Bayesian Information Criterion) for each model, where a lower BIC indicates a better model. We will also use multiple linear regression to assess whether peer leader status is correlated with their proportion of interactions offering support.

Results

T1DM-VPN was launched in June 2017 and as of March 1, 2020, it has 196 patient members. This research protocol received ethics approval from the McGill University Health Centre Research Ethics Board on May 20, 2020. Baseline information about each group member was collected upon their addition into the group, and collection of interaction data is ongoing as of May 2020.

Discussion

Peer-led virtual networks with some professional oversight/access are a promising avenue to enhance chronic disease management in general and diabetes self-management in particular. To properly understand their mechanics and impacts, traditional methods in epidemiology and social network analysis need to be adapted and applied. The proposed analytic approaches aim to do this. It will be interesting to interpret our results in the context of previous analyses of T1DM support networks that differ slightly in geographic scope, target population, and platform function.

Zhou and colleagues' have proposed a conceptual framework for social media-based health information management (SMHIM).[30] Though commonly applied to professional-patient information exchange, it may also be used to understand peer-peer interactions; health information management refers broadly to the activities that users perform in order to process health information items to fulfill their needs. This includes needs for social support. The SMHIM framework outlines processes by which users aim to improve four outcomes (4Cs).

In their framework, Zhou and colleagues focus on information processing as performed by researchers on social media data generated by users. However, we also find it useful to conceptualize T1DM-VPN members as engaging in the processes of *generating* and *retrieving* health information amongst themselves, as well as *integrating* and *applying* it in their personal lives. As a social media platform, T1DM-VPN may improve the *convenience* with which young Canadians living with T1DM exchange information with one another. The other Cs include *care*, *communication efficiency*, and *cost-effectiveness*, and are currently less pertinent to T1DM-VPN. Our aim is to understand if T1DM-VPN is providing support and stimulating engagement because it will inform how we will approach sustainability avenues. Thus far, our research team has actively invested time and resources to train the national panel of peer leaders and sustain their participation. Our team also recruits new T1DM-VPN members and moderates the community.

While growth of the network itself is indeed important, through the proposed analysis we will determine the degree of interaction within the network and the types of support offered. Demonstration of a high level of engagement and support would provide a strong rationale to develop a sustainability strategy. Another goal of our analyses is to determine whether central roles remain the purview of the selected peer leaders or whether ‘regular’ members are naturally taking on the role of peer leaders (i.e. posting often, inviting new members, offering social support). If that is the case, then there may be less need for us to recruit leaders and provide them with a stipend. The ultimate goal is for T1DM-VPN to become at least a partially self-sustaining group, with our research team transitioning from less of an active role to more of an administrative role.

We believe that our study will build evidence and provide a roadmap for the building and maintenance of virtual peer support networks in chronic disease.

Knowledge Dissemination

We will promote and disseminate our approach and findings via scientific manuscripts. We will also share findings through the Diabetes Canada website, social media, and professional conferences. In our consultation with the peer leaders to develop this analysis protocol, they expressed great interest in seeing for themselves how T1DM-VPN has developed over the years. Thus, in keeping with our participatory approach, we will share and discuss our results directly with our peer leaders. Findings may also be presented to T1D attendees of patient conferences such as *No Limits with T1D: Inspire, Empower, Connect*, held annually in Vancouver, British Columbia.

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KD, MN, DDC, GM, DP, CP, AB, and SB conceptualized and launched the T1DM-VPN project. NW grew the network further and conceptualized the analysis protocol with guidance from KD. NW and KD drafted the manuscript. All authors provided input on the analysis, critically reviewed the manuscript, and approved the final version as submitted. We would additionally like to thank the peer leaders (JM, MP, MEK, ME, AK, LL) who participated in the teleconference to inform this analysis strategy.

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Conflicts of Interest

None declared.

Abbreviations

MUHC: McGill University Health Centre
SMHIM: social media-based health information management
SNA: social network analysis
T1DM-VPN: type 1 diabetes mellitus – virtual patient network

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Appendix 1 Definitions of social support typology classifications

Social support category	**Definition**
Informational support	
1. Advice	Messages that suggest courses of action or guidance for coping with illness-related challenges and other difficulties
2. Referral	Messages that provide the recipient with a source of expertise or information (either online resources or offline professionals)
3. Situation appraisal	Messages that help to reassess or redefine circumstances, often in a manner that helps make them more positive or reveal new information that could be helpful; these messages provide a different way of looking at things
4. Teaching	Messages that provide factual information about the challenge the recipient is facing, or about the skills needed to deal with the situation
5. Other informational	Any message that provides information but does not fit into one of the categories listed above
Emotional support	
6. Relationship	Messages that emphasize closeness and love in the relationship with the message recipient
7. Physical affection	Messages that express physical contact verbally (e.g. “hugs”)
8. Confidentiality	Messages that promise to keep the recipient’s problem in confidence
9. Sympathy	Messages that express pity and sorrow for distress experienced by the recipient
10. Empathy	Messages that express understanding or emphasize the similarity of one’s own experiences to that of the recipient
11. Encouragement	Messages meant to provide the recipient with hope and confidence
12. Prayer	Messages that offer to pray for someone who is suffering or needs help

Social support category	**Definition**
13. Other emotional	Messages that express emotion or support the emotional expressions of the recipient, but do not belong into any of the other emotional support categories
Esteem support	
14. Compliment	Messages that convey a positive assessment of the recipient and/or his or her abilities
15. Validation	Messages that express agreement with the recipient's beliefs, actions, thoughts, emotions or perspective on a situation and messages that acknowledge agreement or common ground with the message sender
16. Relief of blame	Messages that aim to alleviate another's feelings of guilt or absolve them of responsibility for a situation
17. Other esteem	Messages that validate the recipient's self-concept, importance, competence or rights as a person, but do not fall into any of the previously listed esteem support categories
Network support	
18. Access	Messages that provide the recipient with access to new contacts and companions, usually because they have similar interests or concerns
19. Presence	Messages that offer to "be there" for the recipient, for example by listening to them or spending time with them
20. Companionship	Messages that emphasize the availability of companions who have similar interests or experiences
21. Other network	Messages that articulate, expand or deepen the structural connections an individual possesses, but do not fall into one of the network support subcategories listed above
Tangible assistance	
22. Loan	Messages that offer to lend a material object or money to the recipient
23. Perform direct task	Messages that offer to perform a task directly related to a stressor
24. Perform indirect task	Messages that offer to take over a task not directly related to the stressor, but which will help the recipient deal with the stressor

Social support category	**Definition**
25. Active participation	Messages that offer to join the recipient in an activity
26. Express willingness	Messages that express readiness to help, without specifying the exact nature of the assistance that will be given
27. Other tangible	Messages that provide, or offer to provide, specific material aid or services to assist the recipient, but do not fall into one of the other tangible assistance categories

Appendix 2 Definitions of codes used to classify non-social support interactions

Category	**Definition**
1. Expressions of gratitude	Messages that express thankfulness to another member of the group or the group as a whole
2. Offering congratulations	Messages that express joy or acknowledgment of the recipient's achievement or good fortune
3. Administrative/engagement in group	Messages that are related to the logistics of managing the Young Adult Program or to participating in components of the program
4. Banter	Messages that include humor or nonsense
5. Socializing	Messages that contain discussions of interacting outside the group environment, greetings (e.g. birthday or holiday wishes), invitations to events, photos and videos of the group, news about personal achievements or milestones, etc
6. Group cohesion	Messages that provide a sense of how members feel about the group
7. Negative interaction	Messages that contain disrespectful or sarcastic comments directed at other participants, statements that express being hurt, distressed, or angered by other members of the group and statements that demonstrate disagreement, tension, or antagonism
8. Community protection	Messages that aim to maintain an atmosphere of support or enforce group norms
9. Non verbal cues	Messages that express non-verbal aspects of communication, such as facial expressions and actions
10. Miscellaneous	Messages that do not fall into any one of the previously established categories

7. Discussion

7.1 Main Findings

The two manuscripts comprising this thesis applied internet-based tools to facilitate the collection and analysis of health-related information in diabetes. In the first instance, the participants are health researchers, clinicians, and women with a GDM history; they completed two rounds of a large, international Delphi survey conducted online. In the second instance, the participants are youth with T1DM and the proposed analyses presented are that of an online community. These studies illustrate the ability of e-epidemiology methods to expand the scope of research investigations, in this case, in diabetes studies.

The first project demonstrated that an e-Delphi survey delivered through *DelphiManager* was an efficient method of gathering the opinions of individuals from multiple stakeholder groups from 23 countries around the world. Such wide geographical reach would not have been feasible with conventional Delphi methods. Over the course of 6 months (July 2018 – December 2018), 115 people participated in the survey and 56 fully completed both rounds. The software design allowed us to facilitate both anonymity for the individual – which was especially important for patients, whose perspectives are often overlooked in clinical research – and visibility of each stakeholder group's perspective. Comparison of the voting scores across stakeholders and rounds, and statistical analysis of the change in standard deviation across scores, indicate that stakeholder groups influenced each other's scoring patterns. By remaining faithful to the results of the Delphi survey and only having the consensus panel vote on indeterminate outcomes, we generated a diverse and comprehensive COS for behaviour change trials aiming to prevent diabetes after a GDM pregnancy.

The second project highlights that online patient communities like T1DM-VPN may provide an existing, rich source from which to draw data from a specific group of interest, but selection of an analytic framework is not a simple matter. In developing our methodological approach to understand network structure, we applied concepts from social network analysis like centrality, to a virtual network. We created a metric of centrality that combined number of individuals with which an individual is connected and frequency of interactions, using a weighted approach drawn from concepts in economics. We proposed to study the network as a dynamic cohort within a person-time framework, a key epidemiological construct. We also proposed relate constructs like network centrality to offering support, using regression analysis. Lastly, novel insights regarding the dynamics of a closed, virtual peer network may be drawn through a regression analysis of virtual activity and user characteristics. User characteristics may be virtually derived (e.g., centrality) or derived from real life (e.g., querying of hometown, age of diagnosis). We are able to capture all interactions in a sociocentric SNA of peer-to-peer interaction in a patient group, which would otherwise be difficult or impossible through traditional data-gathering methods.

The endeavour to gather the perspectives of two different types of patient populations through two different internet-based tools allows us to consider how various epidemiological concepts apply to them. Specifically, I discuss below concepts related to sampling, selection bias, attrition, and internal validity of measurement tools.

7.2 Sampling

Sampling refers to how a study population was recruited and engaged. It is an important step in conducting epidemiological research because it informs how conclusions are drawn from the resulting data [96]. Internet-based tools have had unique implications in our efforts to engage women with GDM and youth with T1DM, and subsequently how we interpret our results.

In recruiting participants for our e-Delphi survey, we used a predominantly internet-based strategy. We disseminated the survey to relevant organizations via their email listservs of researchers and healthcare professionals. The efficiency afforded by email allowed us to capture professionals from a national and international scope. It was also important for us to reach women with past or current GDM. However, unlike professional contact information, patient listservs are rarely as accessible because of privacy considerations [3]. Thus, we encouraged professionals to share the survey by emailing women who had participated in a past GDM study. We also made an effort to post advertisements on motherhood-related Twitter and Facebook groups, and to share print posters with clinics.

Not surprisingly, researchers from our own group were the primary individuals who extended the survey invitation to women with past GDM and thus came almost exclusively from Canada. As noted in the literature review (Chapter 2), it is known that factors such as age, ethnicity, and socioeconomic status affect internet access and health-related internet use [12,13], and that these same factors affect GDM risk [56]. Thus, this convenience-based sampling strategy likely did not capture the global population of women with GDM, but rather captured those who were more closely associated to the research community to begin with, and who were more comfortable with navigating a multi-phase online survey. Despite this selection bias, their participation was still critical to informing the decisions of the healthcare professionals and researchers, even though there was important attrition, particularly in this patient group, by round 2. An internet-based Delphi survey remains an efficient avenue for patients to engage in decision-making directly alongside a large number of professionals.

Initial members of T1DM-VPN were recruited through the email list of 380 Canadian youth who participated in my supervisor's previous study of stigma related to T1DM [97]. These youth were originally recruited into the stigma study through traditional and internet-based methods including Facebook and Twitter posts coordinated with diabetes organizations as well as healthcare team outreach in diabetes clinics. The majority who participated learned of the study through social media. My supervisor and her team were able to meet recruitment targets at relatively low cost and to attract respondents from all 10 provinces from Canada. The study involved an online questionnaire and mail-in capillary blood samples. Upon questionnaire initiation, an incentive was offered to encourage its completion.

The total number recruited into the stigma study was 380; the total membership in VPN as of March 1, 2020 was 196. It should be noted that stigma study participants represent only a proportion of VPN membership. However, all stigma study participants were invited to join the network, at a time point of one to two years following their original participation in the stigma study. At the time of invitation, some would have been beyond the 24 year age limit for participation. However, it is clear that uptake was not universal and may have been related to a lower affinity for social media use, a preference for disease management in privacy, or a lack of interest in a disease-specific community. It is important to thus recognize that participants in online communities differ in some respects from the larger community of persons living with a given condition.

Recruitment into T1DM-VPN is ongoing, with each method likely attracting different groups of individuals. For example, we occasionally ask group members to directly invite eligible friends with T1DM who have Facebook. From my supervisor's study on stigma, we know that most youth with T1DM-VPN do not know personally know anyone else with T1DM. Thus, given that we have had some success recruiting additional members based on this snowball approach, it is possible that these youth and their friends already possess a support-seeking behaviour not found in non-members. Indeed, several T1DM-VPN members are active members in a local, student-initiated T1DM organizations. Some members have also reported searching for a support group themselves on Facebook. To recruit patients who may not actively seek a support group in person or online, we have been contacting healthcare teams at diabetes clinics through email and phone, and asking them to print posters and speak directly to eligible patients. We also believe that this combined traditional and internet-based approach has been valuable for engaging youth with T1DM in smaller towns, where the presence of youth with T1DM would not be high enough for a larger student-led T1DM organization to be established.

When drawing conclusions from our proposed analysis, we will be cognizant not only of T1DM youth who have not joined, but also of the different types of youth who *have* joined the group. As described in Chapter 6, T1DM-VPN peer leaders were purposively selected, then trained for social support offering behaviours. There may also be a set of "naturally" arising leaders in the group. However, relevant to attrition is the subset of members who do not regularly view discussions, and those who consistently view discussions but do not participate themselves. It is not yet known how they may differ from one another. It is important for us to reflect on the group as a forum for social support exchange as we draw our conclusions from the proposed analysis. For example, while some youth may not demonstrate explicit social support-seeking behaviours in the Facebook group, they may still be viewing the information because they find it helpful. For those who have not joined the Facebook group at all, they may still be seeking social support in real life. A thorough literature search on health-related support-seeking behaviours will be helpful once we complete the proposed analysis.

Overall, while internet-based tools are a cost-effective way to sample a geographically diverse target population, it is important to evaluate whether sampling bias may result from depending too heavily on them, and to consider additional methods of recruitment of the potentially omitted set of individuals. Our specific research objectives did not necessitate probability sampling methods, but we are careful to acknowledge possible sampling bias in drawing any conclusions.

7.3 Internal Validity

In addition to determining whether the study population is representative of the target population, researchers should also reflect on whether the indicators being collected are appropriate for the concept being studied, that is, whether the observed results are internally valid [98].

The first project of this thesis focuses on the Delphi survey. There is a vast literature on the types of survey questions and scales to employ for maximum internal validity, depending on the study objective . The scale that pertains to our study is that of the Likert scale. Across COS studies, it is the most commonly used scale in the Delphi process [30]. The *DelphiManager* system prompts participants to score each outcome on a 9-point Likert scale, indicating that 1 to 3 is “not important”, 4 to 6 is “important but not critical”, and 7 to 9 represents “critical” importance. The COMET Initiative reports that a 9-point framework has been endorsed by the (GRADE) Grading of Recommendations Assessment, Development and Evaluation Working Group for assessing the level of importance about research evidence [31].

Van Vaerenbergh and colleagues recently identified five response styles in 7-point Likert scales (e.g., extreme response style, characterized by tendency to select extreme options; mild response style, characterized by tendency to select moderate options) [99], with each style resulting in a specific systematic error. Notably, the response style may be induced by the questionnaire design itself. Thus, it is possible that labelling the 9-point Likert scale in the 3 main categories described earlier encourages a specific type of response style that we could not ascertain in our Delphi process.

It is also important to consider the validity of this scale within the broader context of a Delphi process. Consensus in a Likert scale-based Delphi process is based on whether the summation of individuals' scores passes certain thresholds [30]. In principle, the summations are only valid if individual scores are comparable to one another; to this end, researchers have extensively studied the validity and reliability of Likert scales in questionnaires, but with the assumption that the questionnaire is taken once [100]. To my knowledge, the effect of iteration on the validity of subsequent survey scores has not been studied for COS Delphi processes. The second round of a Delphi survey displays others' responses by stakeholder group. Each participant has the opportunity to change their previous score based on a change in opinion regarding an outcome's importance. However, the second round may also represent an opportunity to change a previous score in order to *calibrate* an unchanging opinion relative to their interpretation of others' scores. Therefore, any potential errors resulting from low validity and reliability in the first round of a survey may be overcome by the more *stable*, and thus potentially more valid summation of scores garnered from the second round. Indeed, this positive effect of feedback on response stabilit*y* has been demonstrated in Delphi processes for technological and business forecasting [101].

With regards to T1DM-VPN, we reflect on the validity of our text coding process. The social support framework was developed by Cutrona and Suhr to describe spousal support behaviours [91], then adapted to an online context by Braithwaite and colleagues [102]. This framework of five types of social support has since been applied to many studies of online support group interactions [40,83]. Importantly, they have considered that manifestations of real-life social support may present differently online than they would in real life. To ensure that this specificity is captured, it will be essential that the two coders (including N Wu) review previous examples of how the framework has been applied to posts and comments in an online context. For example, Gaysynsky and colleagues apply the code of physical affection to any messages that *suggest* physical contact, such as: "Muah" or "consider yourself hugged". Particular attention should also be paid to the influence of context (i.e., preceding text from other users) in interpreting a piece of text that alone, would be difficult to categorize (e.g., "yes" or "no" as provision of informational support if the preceding text is a close-ended question seeking information). To improve reliability, each of the two coders will independently code a small sample of text, then discuss and reconcile any differences in interpretation before continuing to code all text.

Given the increasingly rich types of content generated by users on social media, researchers should consider whether unique forms of social support have arisen in the "culture" of online communications, that may not be captured by a framework originating from real-life interactions. In particular, existing frameworks focus only on text data and may not adequately consider the contribution of media such as videos or images. For example, patient communities often share "memes" with one another, the nature of which has rarely been captured in scientific literature. On the internet, a meme generally refers to an image or video accompanied by a catchphrase, disseminated widely from user to user, that relays a symbolic meaning. In patient communities, memes are often altered to capture a negative experience that is experienced by all members, in a humorous light. Thus, if we apply Gaysynsky and colleagues' frameworks, the act of sharing a meme would potentially encapsulate codes of humour, emotional support, and esteem support. However, memes are not usually directed at one individual, but the entire group. This is not captured in the frameworks we will use, which focus on one-to-one exchange of social support. Thus, we may be open to the possibility of identifying new categories of social support that are unique to the complex social media environment.

7.4 Attrition

Attrition refers to the loss of participants during a study [98]. If the characteristics of those who leave differ systematically from those who remain, then the results may be biased – thus, attrition is also considered a form of selection bias [103]. As mentioned above in our discussion of sampling, our specific research objectives did not necessitate a representative sample. Nonetheless, it is important to reflect on why attrition occurred, and how it can be mitigated in future studies.

Out of the 115 individuals who participated in round 1 of our Delphi survey, 58% scored some outcomes in round 2, and 49% finished scoring all outcomes in round 2. A recent review of 31 Delphi processes for COS development reported round 2 completion rates ranging from 45% to 100% [104]. Completion rate was calculated as the number of participants who completed round

2, divided by the number of participants invited to round 2 - however, it is unclear whether "completion" was defined as scoring *some* outcomes in round 2 or scoring *all* outcomes in round 2. In either case, the completion rate observed in our study was on the lower end of the spectrum. A regression analysis revealed that for every 10 additional items in the survey, the estimated response rate dropped by 1.4 percentage points. Thus, we believe that the large number of items in our survey (121 in round 1, 154 in round 2) contributed substantially to attrition, a factor which applies regardless of paper- or internet-based delivery. With regards to the effect of survey delivery on participant response, the same review reported that the majority of COS used an e-Delphi survey (81%), with a minority using mailed paper surveys (10%) and a handful (6%) using paper surveys exclusively for patients. However, difference in response rates could not be ascertained due to the small number of studies in the latter categories.

Attrition in our survey was particularly marked for women with GDM (35% completion rate, compared to 63% for healthcare professionals and 78% for researchers.) The previously mentioned review of 31 Delphi processes reported that participant composition (multiple stakeholders vs single stakeholder) was not significantly associated with response rate (coefficient 1.44, P-value 0.598). However, the 95% confidence interval for the estimated coefficient was large (-4.15, 7.03) and their definition of multiple stakeholders includes those comprised solely of professionals from different fields. Previous studies have reported difficulty engaging patients in a Delphi process for a pregnancy-related COS [105].

One option to encourage completion is to provide incentives. However, if attrition is related to the volume and complexity of concepts being presented to patients, then a separate effort to explain the process to them would be more effective in facilitating participation. For example, researchers could supplement a text explanation of the survey process and candidate outcomes with simplified diagrams and videos.

Like other COS development processes, we chose to hold a face-to-face consensus panel meeting, taking advantage of an existing international conference to assemble experts from around the world that would be otherwise difficult to do virtually due to time zone differences, and that could decrease nuance and spontaneity in communication. However, we had difficulty establishing the logistics of how to include patient representatives at our meeting in Florence. Traditionally, consensus panel members include those who had participated in the Delphi process. From our survey data, we found that our patients were located in Canada, Ireland, Australia, and Denmark. Although we may have been able to support them in travel costs, time commitment would still be a significant barrier given that our patients are also mothers. Internet-based teleconference techniques may have enabled patients to attend the meeting, but there remains an issue of whether they would feel comfortable vocalizing their opinion amongst healthcare professionals and researchers. It has been proposed that a separate consensus panel or focus group consisting only of patients may be more effective in obtaining their input on the final COS [105]; furthermore, if not held virtually, researchers should consider selecting a meeting setting that incentivizes attendance for the targeted stakeholder (e.g., for parents, an aquarium with free admission after the meeting) [30].

7.5 Strengths and limitations

One of the key advantages of this project was our ability to directly engage the patients with diabetes for which the research is ultimately targeted, facilitated by the connectivity afforded by internet-based methods. Using an e-Delphi survey, we directly engaged women with GDM to provide their opinions, which were then shared directly with healthcare professionals and researchers around the world to inform their respective opinions on the same outcomes. The COMET Initiative has proposed that in order for a COS to be successfully integrated into future research, patients should be able to see how it was developed and feel that their perspectives were taken into account [30]. In presenting our results, we were completely transparent with the breakdown of scores across stakeholder groups, and also maintained fidelity from the e-Delphi survey to the consensus panel. In the case of T1DM-VPN, which gathers youth with T1DM across Canada into a single online community, patients have been a part of every project stage, from the establishment of T1DM-VPN and its goals to recruitment of new members. We also consulted them regarding the analysis protocol itself and how to best notify members about the study. Communication facilitated via the private Facebook page and video conferencing capabilities have played an irreplaceable role in connecting otherwise geographically and socially separated stakeholders throughout these activities. It is important to recognize that some research activities were still successfully conducted with traditional methods rather than internet-based methods, whether exclusively or in a complementary fashion. For example, the final consensus panel meeting was conducted in person, which likely allowed for the more multi-directional and richer communications required to synthesize a comprehensive COS than a video conference, which has comparatively limited audio and visual capabilities. We acknowledge that comfort with video conferencing is increasing in light of the current coronavirus pandemic.

The main limitation of this project is related to barriers in data collection and integration. As described in Methodology (section 3) regarding the e-Delphi survey, it took us longer than anticipated to initiate our second and final round due to our decision to manually download raw data from all three language surveys, combine datasets, and produce summary graphs for each outcome in each of the three languages for input. This reflects the importance of considering whether the specific functions of an internet-based platform will actually deliver the desired efficiency for conducting research. With regards to T1DM-VPN, the limitation to data collection is related to one of our strengths; while the private nature of the Facebook group allows us to capture all interactions in a closed network, the API does not permit automatic extraction of data. Overall, while the internet-based tools allow us to gather and organize a large quantity of data regarding perspectives towards diabetes prevention and care, depending on the platform and one's research needs, the resulting challenge is the labour-intensive process of data extraction and organization (in the case of T1DM-VPN) and data management (in the case of the core outcome set initiative) itself.

7.6 Areas for future research

In epidemiology, rigorous methodological frameworks have been established for certain study types and tools (e.g., CONSORT Statement for randomized controlled trials, STROBE for observational studies). Other guidelines are still in the process of being developed; the COMET Initiative has begun assembling evidence to inform COS development methodology, but the differences highlighted between our work and that of Bogdanet and colleagues reflect the ongoing debate around what constitutes a high-quality COS, and tools applied in COS development (e.g., mailed paper versus online Delphi surveys) are not standardized. In reviewing the literature on analyses of virtual patient communities, we found individual studies where researchers discuss their experience applying internet-based tools, but we did not find a summary of best practices. Current e-epidemiology research focuses on subject recruitment, data collection, survey methodology, and broader issues surrounding data privacy. Thus, an important and timely endeavour may be that of critically appraising the diversity of techniques being applied to study virtual patient networks, in order to establish a methodological framework. Given the ever-growing complexity of the internet and its tools, such a framework would help health researchers select methods that better suit their study sample and objective, and potentially yield more valid results.

8. Conclusion

Internet-based tools present new opportunities to facilitate research that engages a patient population of interest. Researchers may leverage them to efficiently reach potential subjects to collect data, or to extract existing data that can be used for health research; we were able to recruit women with GDM to participate in an e-Delphi process, and we developed a methodologically rigorous protocol to analyze existing data in a virtual social network. For patients who engage with an internet-based platform, they are able to maintain a certain degree of anonymity from one audience, while sharing their valuable perspective with another; women with GDM could comfortably contribute their opinion to the development of a COS on equal ground with healthcare professionals and researchers via the anonymous survey, and youth in T1DM-VPN can freely connect with peers across Canada for support while maintaining privacy from the general public. Making sense of the data drawn from these sources requires unique methodological considerations – researchers should consider the implications of an internet-based approach on issues such as sampling and validity. Furthermore, they should assess the capabilities of the internet-based tool to manage the potentially complex and large volume of data to ensure that they achieve the desired time and cost-effectiveness. Finally, given the complexity of the internet and the growing interest in analyzing virtual patient networks, assembling a methodological framework to guide researchers in this research may be an important and timely endeavour.

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