COMPLEMENTARY, ALTERNATIVE, AND INTEGRATIVE MEDICINE, NATURAL HEALTH PRODUCTS, AND MEDICAL CANNABIS: PATIENT PREFERENCE AND PREVALENCE OF USE, QUALITY OF PATIENT HEALTH INFORMATION, AND SAFETY AND EFFECTIVENESS CONCERNS

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A Thesis Submitted to the School of Graduate Studies in Partial Fulfilment of the Requirements for the Degree Doctor of Philosophy

Abstract

The thesis is comprised of three separate studies that each relate to one of the aforementioned therapy types: complementary, alternative, and integrative medicine (CAIM), natural health products (NHPs), and medical cannabis. Parallels can be drawn across these therapy types in general including patient preference and prevalence of use, quality of patient health information, and safety and effectiveness concerns. Knowledge of these parallels both informed the development of these three studies and emerged across findings. Chapter 1 provides a comprehensive introduction to these parallels in the context of CAIM, NHPs, and medical cannabis. Chapter 2 comprises a cross-sectional survey determining NHP use disclosure to primary care physicians among patients attending a Canadian naturopathic clinic. Chapter 3 comprises a qualitative interview study identifying attitudes towards medical cannabis among family physicians practicing in Ontario, Canada. Chapter 4 comprises a sentiment analysis of Twitter data to understand how CAIM is mentioned during the COVID-19 pandemic. Lastly, chapter 5 serves as the conclusion of this thesis, and summarizes the most important findings, addresses study strengths and limitations, and discusses future directions from this work.

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"I may not be there yet, but I'm closer than I was yesterday" was the guiding philosophy that I adopted on the day that I began my PhD studies. It motivated me to appreciate the journey, as opposed to unnecessarily long for the destination, which at the time seemed immensely distant. Each day I made a promise to myself that at the very least I would make an attempt to chip away at my tasks at hand, regardless of whether those attempts were successful, and despite the amount of progress made. At times, the journey was incredibly trying, and filled with both the mental and physical exhaustion and ailments that are married to the goal of creating knowledge, yet other moments were filled with elation provided through the opportunities to share my findings emerging from such a dynamic and complex field with the world. Nonetheless, completing a PhD has been an incredible privilege that has been afforded to me, and for that I am, and forever will be, grateful.

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List of Abbreviations

API: application programming interface

AUC: area under the ROC curve

CAIM: complementary, alternative, and integrative medicine

CAM: complementary and alternative medicine

CBD: cannabidiol

CCNM: Canadian College of Naturopathic Medicine

CI: confidence interval

COREQ: consolidated criteria for reporting qualitative research checklist

COVID-19: coronavirus disease 2019

DTM: document term matrix

EBM: evidence-based medicine

MD: medical doctor

NCCIH: National Centre for Complementary and Integrative Health

NHP: natural health product

NLP: natural language processing

NRC: National Research Council Canada

OR: odds ratio

ROC: receiver operator characteristic

RSNC: Robert Schad Naturopathic Clinic

SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

THC: tetrahydrocannabinol

Declaration of Academic Achievement

I declare that the PhD thesis contained herein is my own work. This document has been prepared in the format of a "sandwich thesis" whereby it contains three individual studies prepared for publication in scholarly, peer-reviewed journals. At the time of writing, the first two studies have been accepted for publication or published, Chapter 2 in *Complementary Therapies in Clinical Practice*, and Chapter 3 in *CMAJ Open*. The third study, while completed, has yet to be published but has been preprinted. The citations for all three studies can be found below. With the guidance received by my primary supervisor, Dr. Jason Busse, and my two committee members, Dr. Mitchell Levine and Dr. Cynthia Lokker, I contributed to all three projects as follows: designing and conceptualizing the studies, collecting and analysing data, drafting the manuscripts, giving final approval of the manuscript versions and submitting them to the journals, addressing the peer-reviewed feedback received on the manuscript submissions, and proofing manuscripts accepted for publication. To varying extents, my co-authors on the manuscripts, assisted with the following tasks: collecting and analysing data, critically revising the manuscripts, and giving final approval of the manuscript versions to be submitted to the journals. The studies comprising this thesis were conducted between September 2018 and January 2021.

Thesis Study Citations:

- Study 1: Ng JY, Garber A, Luong M, Cooley K, Busse JW. No improvement in disclosure of natural health product use to primary care medical doctors in the last 15 years: A survey of naturopathic patients. Complementary therapies in clinical practice. 2020 May 1;39:101106. https://doi.org/10.1016/j.ctcp.2020.101106.

- Study 2: Ng JY, Gilotra K, Usman S, Chang Y, Busse JW. Attitudes toward medical cannabis among family physicians practising in Ontario, Canada: a qualitative research study. CMAJ open. 2021 Apr;9(2):E342. https://doi.org/10.9778/cmajo.20200187.
- Study 3: Ng JY, Abdelkader W, Lokker C. Tracking Discussions of Complementary, Alternative, and Integrative Medicine in the Context of the COVID-19 Pandemic: A Month-by-Month Sentiment Analysis of Twitter Data. Research Square. [Preprint] https://doi.org/10.21203/rs.3.rs-352428/v1.

Chapter 1

Introduction

Chapter 1: Introduction

Complementary, alternative, and integrative medicine (CAIM), natural health products (NHPs), and medical cannabis represent three categories of therapies which contain a number of overlapping characteristics relating to patient preference and prevalence of use, quality of patient health information, and safety and effectiveness concerns, from which parallels can be drawn. The definitions and importance of each are first defined in this introductory chapter, followed by three research studies that each contribute to these parallels. This thesis ends with a conclusion chapter which summarizes the most important findings, addresses study strengths and limitations, and discusses future directions from this work.

Complementary, Alternative, and Integrative Medicine, Natural Health Products, and Medical Cannabis: Definitions and Importance

Complementary and alternative medicine (CAM) is generally defined as a group of diverse medical and healthcare interventions, practices, products or disciplines that are not considered as part of conventional medicine [1]. Specifically, the National Center for Complementary and Integrative Health (NCCIH) defines “complementary” as a non-mainstream practice used together with conventional medicine, whereas “alternative” refers to a non-mainstream practice used in place of conventional medicine [2]. In contrast, “integrative health” is defined as the coordinated delivery of conventional and complementary approaches together [2]. For the purpose of this thesis, these therapies will be referred to collectively as CAIMs hereafter. Most CAIMs can generally be categorized into one of the following: whole medical systems (i.e. naturopathy, homeopathy); mind-body medicine (i.e. biofeedback, meditation); biologically based practices not usually used in conventional medicine (i.e. botanical medicine,

chelation therapy); manipulative and body-based practices (i.e. chiropractic, massage); and energy medicine (i.e. acupuncture, tai chi) [3]. CAIM is perceived to be of value by its proponents for its emphasis on a holistic, patient-focused approach to healthcare, which include mental, emotional, functional, spiritual, economic, and social aspects [2,4].

Natural health products (NHPs) are defined by Health Canada according to the following six categories: probiotics; herbal remedies; vitamins and minerals; homeopathic medicines; traditional medicines such as Chinese medicines; and other products like amino acids and essential fatty acids [5]. Some NHPs are considered CAIMs (i.e. the use of herbal products outside of mainstream conventional care), while others comprise conventional medical practices (i.e. the use of a given vitamin for vitamin deficiency) [6]. Furthermore, while many NHPs are used as therapeutic agents themselves, others have been used to develop pharmaceutical medications [7]. For example, aloe vera is used topically for acne, skin rash, burns, and is also used orally for weight loss, diabetes, and hepatitis [8]. Metformin, a common drug used to treat type 2 diabetes, is derived from French lilac (*Galega officinalis*), which itself was historically used as the remedy dating back to the Middle Ages [9]. Beyond serving as the starting material for pharmaceutical medicines, NHPs hold importance due to the fact that they are relied upon by up to 80% of the world's population as a source of healthcare and traditional medicine [10].

Cannabis refers to a flowering plant in the family Cannabaceae; while the exact number of species within the genus is disputed, the following three are generally recognized: *Cannabis sativa*, *Cannabis indica*, and *Cannabis ruderalis*. The cannabis plant contains about 540 chemical substances [11], and over 100 of them are classified as cannabinoids, of which tetrahydrocannabinol (THC) is primarily responsible for the plant's psychoactive effects [11,12]. The term "marijuana" refers to the parts of or the products from the cannabis plant that contain

THC, while industrial hemp refers to plants that have minimal THC [11]. Cannabidiol (CBD) is the prominent cannabinoid that is of particular interest to healthcare researchers and clinicians, as this specific compound is responsible for cannabis' purported therapeutic value [13]. In this context, medical cannabis is considered both a CAIM and an NHP, although this is not universally agreed upon by experts. It should also be noted that under Health Canada's updated Natural Health Products Regulations, certain parts of the cannabis plant can be included in NHPs provided that they do not contain more than 10 parts per million tetrahydrocannabinol, or phytocannabinoids that have been isolated or concentrated [14]. Cannabinoids are known to affect cell receptors in the brain and body, changing how they behave and communicate [12]. Cannabinoids may serve as a promising therapy in treating and/or managing epilepsy, nausea and vomiting induced by cancer chemotherapy and weight loss, loss of appetite associated with HIV AIDS, chronic pain, and muscle spasticity associated with multiple sclerosis [11].

Three major parallels can be drawn across CAIMs, NHPs, and medical cannabis, with respect to their context in healthcare. These relate to the following: 1) patient preference and prevalence of use, 2) quality of patient health information, and 3) safety and effectiveness concerns. Each parallel is described in the paragraphs to follow.

Patient Preference and Prevalence of Use

Many patients use CAIM, NHPs, and/or medical cannabis in conjunction with, and a minority in lieu of, conventional care. The use of CAIM is highly prevalent globally, with 88% of World Health Organization member states (170 countries) having acknowledged their use of CAIM (including NHPs), having, for example, formally developed policies, laws, regulations, programs and offices for CAIM [15,16]. The prevalence of CAIM use among many Western

countries is high; for example, among Canadians it is approximately 80% [16]. The use of CAIM is also known to be highly prevalent among patients living with wide-range of diseases/conditions; in cancer patients, as many as 90% report using some form of CAIM [17,18, 19]. Various reasons motivate patients to use CAIM, including symptom relief, improved quality of life, to augment conventional therapy, support one's philosophical orientations towards health, and achieve a sense of control over one's care [20,21,22]. Increasingly, many patients and practitioners have recognized the value of integrative medicine (the combination of complementary and conventional therapies) [23,24], and sub-specializations of integrative care for specialized diseases/conditions have been established, such as integrative oncology [25,26]. Health Canada has reported that 71% of Canadians have used NHPs [5]; some studies have reported even higher rates, including a cross-sectional survey in British Columbia, Canada, which identified that 85% of patients were taking one or more NHPs [27]. Furthermore, approximately half of the respondents believed that NHPs were safer than prescription medications [27]. This aligns with the 70-95% of the global population that rely on traditional medicines, including NHPs [28]. While the change in global prevalence of medical cannabis use may be more difficult to ascertain, many countries in the Western world have in recent years moved to legalize its use [29]. Canada was the second country in the world to legalize cannabis for all purposes in October 2018 [30, 31], and reported users of medical cannabis have increased dramatically since this time [32]. The number of medical client registrations with federally licensed sellers grew from 345 520 in October 2018 to 377 024 in September 2020. Additionally, the number of individuals registered with Health Canada for personal and designated cultivation of cannabis for their own medical purposes increased from 25 945 in October 2018 to 43 211 in September 2020 [32]. Patients report using cannabis for a wide-range of conditions, which

include pain relief, anxiety, and depression [33, 34], and many believe that medical cannabis should be integrated into conventional healthcare settings [34]. Similar to the motivations for CAIM use, patients using medical cannabis cite their beliefs that it is natural and therefore safer than prescription medicine, provides symptom relief, and improves their quality of life [35].

Quality of Patient Health Information

The quality of publicly available health information surrounding CAIM, NHPs, and medical cannabis has been found to be variable depending on the source; more concerningly, it has been found that some sources contain information that are misleading or inaccurate, and therefore, pose a potential risk to patients' health. Apart from consulting their healthcare providers directly, patients tend to seek CAIM information offline (i.e. magazines, newspapers), and more increasingly common, online (i.e. health blogs, social media) [36-40]. Patients are at a high risk of encountering false and unfounded information [38], coupled with the fact that they also may not disclose their information-seeking behaviours to their healthcare providers [39]. Furthermore, the variable quality of information online presents additional challenges to patients [38,39,40]. With regards to how information on the labels of NHPs impact consumer decision making, it has been found that most consumers did not regularly read product labels, nor did they understand the information on them [41]. Furthermore, evidence of NHP companies making claims on product labels for ingredients known not to be safe, and NHP mislabeling whereby the chemical contents did not match the ingredients listed on the label has been found [42,43]. More recent efforts have been made to create databases that provide greater transparency surrounding NHP labelling and contents for the benefit of researchers, healthcare practitioners, and patients alike [43,44,45]. Consumer health information about medical cannabis has also suffered from

similar issues. Studies evaluating the accuracy and quality of medical cannabis claims online have found that a large proportion of claims made are inaccurate and based on low-quality evidence [45,46]. Another study found that edible cannabis products sold in metropolitan areas did not comply with pharmaceuticals' basic label accuracy standards. They found that more than 50% of the analyzed products contained significantly less cannabinoid content than labelled, with certain products having negligible quantities of THC [47]. Information regarding CAIM, NHPs, and medical cannabis, may not necessarily always be true, accurate, or reliable.

Safety and Effectiveness Concerns

Similar safety and effectiveness concerns exist with respect to CAIM, NHPs, and medical cannabis. All three therapy types generally tend to be under-researched in comparison to conventional therapies such as pharmaceuticals and surgery. While some CAIMs (including NHPs) have undergone more careful examination and have been found to be generally safe and effective, such as meditation and yoga [48,49], others have not been adequately researched to determine their effectiveness, and some have been found to be potentially harmful or interact adversely with conventional medicines [49,51-53]. A well-documented, common belief among patients is the idea that “natural means safe and better” [54], however, this is untrue as, for example, many herbal NHPs can be harmful when taken in large quantities. It has also been documented that at therapeutic doses certain weight loss and bodybuilding supplements for example, can result in hepatotoxicity or even hepatic failure [55].

On a national and international scale, systemized pharmacovigilance of CAIMs is poorly coordinated, and NHPs are generally not regulated to standards as high as that of pharmaceutical medicines with respect to quality, effectiveness or safety [51]. Patients taking cannabis for

medical purposes containing high THC levels may be at risk of increased mental illness and cognitive impairment, or risk of developing psychotic disorders later in life [56-58]. Furthermore, medical cannabis is known to negatively interact with certain pharmaceutical medicines when taken together [59]. The use of medical cannabis can also result in transaminase elevations, sedation, sleep disturbances, infection, and anemia [59].

These concerns are compounded by the fact that patients do not tend to disclose their use of these therapies to their conventional healthcare providers, the latter of whom have received little if any training and education on these topics. One meta-analysis of 86 observational studies reported that patients only disclosed their CAIM use to their physicians 33% of the time [43]. The reasons for non-disclosure include conventional healthcare providers not asking about CAIM use, fear of provider disapproval, perception that disclosure is unimportant, and beliefs that providers lacked CAIM knowledge or time, as well as beliefs that CAIM use is safe [43,44]. Patients are more likely to disclose CAIM use if they are asked by their primary physician, however, such discussions rarely occur [60-63]. These findings largely also pertain to patient disclosure of NHPs [64,65]. While medical cannabis itself is derived from an NHP, an added layer of stigma is attached to it by both healthcare providers and patients alike as a result of its long and complex history as an illicit substance. A study of 221 healthcare providers found that increased positive attitudes toward the use of medical cannabis was associated with lower stigmatization of patients who used it [66]. Among patients using cannabis for medical purposes, approximately one-third do not disclose their use to their physician [67,68]. Not surprisingly, patients living in jurisdictions where medical cannabis use is illegal are even less likely to disclose their use to their physician [67], and even among those using it legally, they may hide this information to avoid judgement [68].

One of the primary reasons why conventional healthcare practitioners fail to inquire about CAIM, NHP, or medical cannabis use, however, is simply because they lack the knowledge and training on these topics themselves. One study involving 1247 health professionals found that most respondents did not feel prepared to address patient questions regarding CAIM [69]. It is also documented that healthcare practitioners admit to having little if any educational training on the topic of CAIM [70-72]. Despite their widespread use, healthcare professionals also possess varied training or knowledge regarding herb toxicology and adverse drug-herb interactions [73-76]. In some countries with deeply rooted cultures of traditional medicine, the healthcare providers trained in conventional medicine may have adjunct training in their country's traditional medicine system (i.e. traditional Chinese medicine in China or Ayurveda in India) [4,77], but this knowledge is not standardized across different regions of the world. Additionally, physicians lack the training and knowledge surrounding the safety and effectiveness of medical cannabis [79-81]. More promisingly, however, is that healthcare practitioners who lack knowledge of CAIM [69], NHPs [73-76] and medical cannabis [80-84], are increasingly open to the potential value of these interventions and generally express positive attitudes towards gaining education on this topic.

Identified Parallels and Relationship to Thesis Studies

This thesis is comprised of three separate studies that each relate to one of the aforementioned therapy types: CAIM, NHPs, and medical cannabis. Parallels can be drawn across these therapy types in general, as outlined in Chapter 1, including patient preference and prevalence of use, quality of patient health information, and safety and effectiveness concerns. Knowledge of these parallels both informed the development of these three studies and emerged

across findings. Chapter 2 reports a cross-sectional survey determining NHP use disclosure to primary care physicians among patients attending a Canadian naturopathic clinic. Chapter 3 details a qualitative interview study identifying attitudes towards medical cannabis among family physicians practicing in Ontario, Canada. Chapter 4 provides a sentiment analysis of Twitter data to understand how CAIM is mentioned during the COVID-19 pandemic. Chapter 5 serves as the conclusion of this thesis, and summarizes the most important findings, addresses the studies' strengths and limitations, and discusses future directions from this work.

Study Designs and Theoretical Underpinnings

As this thesis is comprised of three studies each informed by a different research methodology, it is worthwhile to briefly discuss the theoretical underpinnings considered, as all research is, to some extent, social. Three major theoretical underpinnings include positivism, constructivism, and realism. Positivism can be described as a philosophical system that is premised on the belief that there is a truth to be discovered and a real world that can be observed, analyzed, and understood [85]. In contrast, constructivism reflects a belief that there is no single, specific, nor certain truth, but instead that truth is socially constructed and historically situated [85]. Realism falls between these two aforementioned philosophical systems whereby individuals' (i.e. researchers') interpretations of that truth are shaped by a variety of social and interpersonal forces [85]. By this definition, it can be acknowledged that the cross-sectional study design is an example of a positivist research methodology, as is the sentiment analysis. Qualitative interviews, in contrast, can be informed by any or all of these philosophical systems, however, in the present study we adopted a realist approach whereby we took practitioners' reports at face value assuming they would report truthfully about their beliefs and attitudes.

Chapter 1 References

[1] Ventola CL. Current issues regarding complementary and alternative medicine (CAM) in the United States: Part 1: The widespread use of CAM and the need for better-informed health care professionals to provide patient counseling. Pharmacy and Therapeutics. 2010 Aug;35(8):461. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2935644/.

[2] National Center for Complementary and Integrative Health (NCCIH). [Internet]. Complementary, Alternative, or Integrative Health: What's In a Name?; 2018 [cited 2021 Jan 14]. Available from: https://www.nccih.nih.gov/health/complementary-alternative-or-integrative-health-whats-in-a-name.

[3] Merck Manual [Internet]. Types of Complementary and Alternative Medicine; 2018 [cited 2021 Jan 14]. Available from: https://www.merckmanuals.com/professional/special-subjects/integrative-complementary-and-alternative-medicine/types-of-complementary-and-alternative-medicine.

[4] World Health Organization. WHO Traditional Medicine Strategy 2014-2023. Geneva: World Health Organization; 2013. 76 p. https://www.who.int/medicines/publications/traditional/trm_strategy14_23/en/.

[5] Health Canada. [Internet]. About Natural Health Products; 2016 [cited 2021 Jan 14]. Available from: https://www.canada.ca/en/health-canada/services/drugs-health-products/natural-non-prescription/regulation/about-products.html.

[6] Wieland LS, Manheimer E, Berman BM. Development and classification of an operational definition of complementary and alternative medicine for the Cochrane

collaboration. Alternative Therapies in Health and Medicine. 2011 Mar;17(2):50. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3196853/.

[7] Bernardini S, Tiezzi A, Laghezza Masci V, Ovidi E. Natural products for human health: an historical overview of the drug discovery approaches. Natural Product Research. 2018 Aug 18;32(16):1926-50. https://doi.org/10.1080/14786419.2017.1356838.

[8] National Center for Complementary and Integrative Health (NCCIH) [Internet]. Aloe Vera; 2020 [cited 2021 Jan 14]. Available from: https://www.nccih.nih.gov/health/aloe-vera.

[9] Witters LA. The blooming of the French lilac. The Journal of Clinical Investigation. 2001 Oct 15;108(8):1105-7. https://doi.org/10.1172/JCI14178.

[10] Ekor M. The growing use of herbal medicines: Issues relating to adverse reactions and challenges in monitoring safety. Frontiers in Pharmacology. 2014 Jan 10;4:177. https://doi.org/10.3389/fphar.2013.00177.

[11] National Center for Complementary and Integrative Health (NCCIH) [Internet]. Cannabis (Marijuana) and Cannabinoids: What You Need to Know; 2019 [cited 2021 Jan 14]. Available from: https://www.nccih.nih.gov/health/cannabis-marijuana-and-cannabinoids-what-you-need-to-know.

[12] Health Canada [Internet]. About Cannabis; 2018 [cited 2021 Jan 14]. Available from: https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/about.html.

[13] Harvard Health Publishing [Internet]. Cannabidiol (CBD) - What we Know and What we Don't; 2018 [cited 2021 Jan 14]. Available from:

https://www.health.harvard.edu/blog/cannabidiol-cbd-what-we-know-and-what-we-dont-2018082414476.

[14] Government of Canada. [Internet]. Health Products Containing Cannabis or for Use with Cannabis: Guidance for the Cannabis Act, the Food and Drugs Act, and Related Regulations; 2020 [cited 2021 Jan 14]. Available at: https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/guidance-cannabis-act-food-and-drugs-act-related-regulations/document.html.

[15] World Health Organization. WHO global report on traditional and complementary medicine, 2019. Geneva: World Health Organization; 2019. 226 p. https://www.who.int/traditional-complementary-integrative-medicine/WhoGlobalReportOnTraditionalAndComplementaryMedicine2019.pdf.

[16] Esmail N. Complementary and Alternative Medicine: Use and Public Attitudes 1997, 2006, and 2016. Vancouver: Fraser Institute; 2017. 87 p. https://www.fraserinstitute.org/sites/default/files/complementary-and-alternative-medicine-2017.pdf.

[17] Savas P, Robertson A, Beatty L, Hookings E, McGee M, Marker J, et al. Patient preferences on the integration of complementary therapy with conventional cancer care: Complementary therapy and cancer preferences. Asia-Pacific Journal of Clinical Oncology. 2016 Jun;12(2):e311-8. https://doi.org/10.1111/ajco.12226.

[18] Begbie SD, Kerestes ZL, Bell DR. Patterns of alternative medicine use by cancer patients. Medical Journal of Australia. 1996 Nov;165(10):545-8. https://doi.org/10.5694/j.1326-5377.1996.tb138639.x.

[19] Adams M, Jewell AP. The use of complementary and alternative medicine by cancer patients. International Seminars in Surgical Oncology. 2007 Apr 30;4(1):10. https://doi.org/10.1186/1477-7800-4-10.

[20] Astin JA. Why patients use alternative medicine: results of a national study. JAMA: The Journal of the American Medical Association. 1998 May 20;279(19):1548. https://doi.org/10.1001/jama.279.19.1548.

[21] Kristoffersen AE, Stub T, Musial F, Fønnebø V, Lillenes O, Norheim AJ. Prevalence and reasons for intentional use of complementary and alternative medicine as an adjunct to future visits to a medical doctor for chronic disease. BMC Complementary and Alternative Medicine. 2018 Dec;18(1):1-8. https://doi.org/10.1186/s12906-018-2179-8.

[22] McCaffrey AM, Pugh GF, O'Connor BB. Understanding patient preference for integrative medical care: Results from patient focus groups. Journal of General Internal Medicine. 2007 Oct 12;22(11):1500-5. https://doi.org/10.1007/s11606-007-0302-5.

[23] Snyderman R, Weil AT. Integrative medicine: Bringing medicine back to its roots. Archives of Internal Medicine. 2002 Feb 25;162(4):395-7. https://doi.org/10.1001/archinte.162.4.395.

[24] Maizes V, Rakel D, Niemiec C. Integrative medicine and patient-centered care. Explore. 2009 Sep 1;5(5):277-89. https://doi.org/10.1016/j.explore.2009.06.008.

[25] Society for Integrative Oncology. [Internet]. What is Integrative Oncology? [cited 2021 Jan 14]. Available from: https://integrativeonc.org/knowledge-center/what-is-integrative-oncology.

[26] Yun H, Sun L, Mao JJ. Growth of integrative medicine at leading cancer centers between 2009 and 2016: A systematic analysis of NCI-designated comprehensive cancer center websites. JNCI Monographs. 2017 Nov 1;2017(52). https://doi.org/10.1093/jncimonographs/lgx004.

[27] Barry AR. Patients' perceptions and use of natural health products. Canadian Pharmacists Journal / Revue des Pharmaciens du Canada. 2018 Jul;151(4):254-62. https://doi.org/10.1177/1715163518779409.

[28] Robinson MM, Zhang X. Traditional Medicines: Global Situation, Issues and Challenges. The World Medicines Situation, 3rd Ed. Geneva, Switzerland: World Health Organization, 2011:1–14. http://digicollection.org/hss/documents/s18063en/s18063en.pdf.

[29] World Health Organization. WHO Expert Committee on Drug Dependence Pre-Review Cannabis Plant and Cannabis Resin Section 5: Epidemiology. Geneva: World Health Organization; 2018. 82 p. https://www.who.int/medicines/access/controlled-substances/Section5.CannabisPlant.Epidemiology.pdf?ua=1.

[30] Government of Canada. [Internet]. Cannabis Act; 2018 [cited 2021 Jan 14]. Available from: https://laws-lois.justice.gc.ca/eng/acts/c-24.5/

[31] The Canadian Encyclopedia. [Internet]. Cannabis Legalization in Canada; 2019 [cited 2021 Jan 14]. Available at: https://www.thecanadianencyclopedia.ca/en/article/marijuana-legalization-in-canada.

[32] Data on Cannabis for Medical Purposes. [Internet]. Health Canada; 2020 [cited 2021 Jan 14]. Available from: https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/research-data/medical-purpose.html.

[33] Kosiba JD, Maisto SA, Ditre JW. Patient-reported use of medical cannabis for pain, anxiety, and depression symptoms: Systematic review and meta-analysis. Social Science & Medicine. 2019 Jul 1;233:181-92. https://doi.org/10.1016/j.socscimed.2019.06.005.

[34] Lintzeris N, Driels J, Elias N, Arnold JC, McGregor IS, Allsop DJ. Medicinal cannabis in Australia, 2016: The cannabis as medicine survey (CAMS-16). Medical Journal of Australia. 2018 Sep;209(5):211-6. https://doi.org/10.5694/mja17.01247.

[35] Piper BJ, Beals ML, Abess AT, Nichols SD, Martin M, Cobb CM, et al. Chronic pain patients' perspectives of medical cannabis. 2018;14. https://doi.org/10.1097/j.pain.0000000000000899.

[36] Zhao Y, Zhang J. Consumer health information seeking in social media: A literature review. Health Information & Libraries Journal. 2017 Dec;34(4):268-83. https://doi.org/10.1111/hir.12192.

[37] Breckons M, Jones R, Morris J, Richardson J. What do evaluation instruments tell us about the quality of complementary medicine information on the internet? Journal of Medical Internet Research. 2008;10(1):e3. https://doi.org/10.2196/jmir.961.

[38] Bianchini C, Truccolo I, Bidoli E, Mazzocut M. Avoiding misleading information: A study of complementary medicine online information for cancer patients. Library & Information Science Research. 2019 Jan;41(1):67-77. https://doi.org/10.1016/j.lisr.2019.02.006.

[39] Holmes MM, Bishop FL, Calman L. "I just googled and read everything": Exploring breast cancer survivors' use of the internet to find information on complementary

medicine. Complementary Therapies in Medicine. 2017 Aug;33:78-84. https://doi.org/10.1016/j.ctim.2017.06.007.

[40] Brauer JA, El Sehamy A, Metz JM, Mao JJ. Complementary and alternative medicine and supportive care at leading cancer centers: A systematic analysis of websites. Journal of Alternative and Complementary Medicine. 2010 Feb;16(2):183-6. https://doi.org/10.1089/acm.2009.0354.

[41] Boon H, Bozinovski N. A systematic narrative review of the evidence for labeling of natural health products and dietary supplements. Journal of Alternative and Complementary Medicine. 2019 Aug;25(8):777-88. https://doi.org/10.1089/acm.2018.0533.

[42] Dwyer JT, Coates PM. Why Americans need information on dietary supplements. Journal of Nutrition. 2018 Aug 1;148(suppl_2):1401S-1405S. https://doi.org/10.1093/jn/nxy081.

[43] Navarro V, Avula B, Khan I, Verma M, Seeff L, Serrano J, et al. The contents of herbal and dietary supplements implicated in liver injury in the United States are frequently mislabeled. Hepatology Communications. 2019 Jun;3(6):792-4. https://doi.org/10.1002/hep4.1346.

[44] Durazzo A, Camilli E, D'Addezio L, Piccinelli R, Mantur-Vierendeel A, Marletta L, et al. Development of dietary supplement label database in Italy: Focus of FoodEx2 coding. Nutrients. 2020 Jan;12(1):89. https://doi.org/10.3390/medicina56070336.

[45] Boatwright KD, Sperry ML. Accuracy of medical marijuana claims made by popular websites. Journal of Pharmacy Practice. 2020 Aug;33(4):457-64. https://doi.org/10.1177/0897190018818907.

[46] Kruger DJ, Moffet IM, Seluk LC, Zammit LA. A content analysis of internet information sources on medical cannabis. Journal of Cannabis Research. 2020 Dec;2(1):1-6. https://doi.org/10.1186/s42238-020-00041-1.

[47] Vandrey R, Raber JC, Raber ME, Douglass B, Miller C, Bonn-Miller MO. Cannabinoid dose and label accuracy in edible medical cannabis products. JAMA: The Journal of the American Medical Association. 2015 Jun 23;313(24):2491-3. https://doi.org/10.1001/jama.2015.6613.

[48] National Center for Complementary and Integrative Health (NCCIH) [Internet]. Safe Use of Complementary Health Products and Practices; 2021 [cited 2021 Jan 14]. Available from: https://www.nccih.nih.gov/health/safety.

[49] Cramer H, Lauche R, Langhorst J, Dobos G. Yoga for depression: A systematic review and meta-analysis. Depression and Anxiety. 2013 Nov;30(11):1068-83. https://doi.org/10.1002/da.22166.

[50] Saeed SA, Antonacci DJ, Bloch RM. Exercise, yoga, and meditation for depressive and anxiety disorders. American Family Physician. 2010 Apr 15;81(8):981-6. https://www.aafp.org/afp/2010/0415/p981.html.

[51] Bellanger RA, Seeger CM, Smith HE. Safety of complementary and alternative medicine treatments and practices. In: Side Effects of Drugs Annual 2019 Jan 1 (Vol. 41, pp. 559-571). Elsevier. https://doi.org/10.1016/bs.seda.2019.06.004.

[52] Pratt M, Wieland S, Ahmadzai N, Butler C, Wolfe D, Pussagoda K, et al. A scoping review of network meta-analyses assessing the efficacy and safety of complementary and alternative medicine interventions. Systematic Reviews. 2020 Dec;9:1-25. https://doi.org/10.1186/s13643-020-01328-3.

[53] Rossi EG, Bellandi T, Picchi M, Baccetti S, Monechi MV, Vuono C, et al.. Patient safety in complementary medicine through the application of clinical risk management in the public health system. Medicines. 2017 Dec;4(4):93. https://doi.org/10.3390/medicines4040093.

[54] National Center for Complementary and Integrative Health (NCCIH). [Internet]. Natural Doesn't Necessarily Mean Safer, or Better; 2021. [cited 2021 Jan 14]. Available from: https://www.nccih.nih.gov/health/know-science/natural-doesnt-mean-better

[55] Navarro VJ, Khan I, Björnsson E, Seeff LB, Serrano J, Hoofnagle JH. Liver injury from herbal and dietary supplements. Hepatology. 2017 Jan;65(1):363-73. https://doi.org/10.1002/hep.28813.

[56] Bossong MG, Niesink RJM. Adolescent brain maturation, the endogenous cannabinoid system and the neurobiology of cannabis-induced schizophrenia. Progress in Neurobiology. 2010 Nov;92(3):370-85. https://doi.org/10.1016/j.pneurobio.2010.06.010.

[57] Lubman DI, Cheetham A, Yücel M. Cannabis and adolescent brain development. Pharmacology & Therapeutics. 2015 Apr;148:1-16. https://doi.org/10.1016/j.pharmthera.2014.11.009.

[58] Camchong J, Lim KO, Kumra S. Adverse effects of cannabis on adolescent brain development: A longitudinal study. Cerebral Cortex. 2016 Feb 23;bhw015. https://doi.org/10.1093/cercor/bhw015

[59] Brown J, Winterstein A. Potential adverse drug events and drug-drug interactions with medical and consumer cannabidiol (CBD) use. Journal of Clinical Medicine. 2019 Jul 8;8(7):989. https://doi.org/10.3390/jcm8070989

[60] Foley H, Steel A, Cramer H, Wardle J, Adams J. Disclosure of complementary medicine use to medical providers: A systematic review and meta-analysis. Scientific Reports. 2019 Dec;9(1):1573. https://doi.org/10.1038/s41598-018-38279-8

[61] Sirois FM, Jiang L, Upchurch DM. Use and disclosure of complementary health approaches in US Adults with cardiovascular disease. The American Journal of Cardiology. 2018 Jul;122(1):170-4. https://doi.org/10.1016/j.amjcard.2018.03.014

[62] Connor J, Buring JE, Eisenberg DM, Osypiuk K, Davis RB, Wayne PM. Patient disclosure of complementary and integrative health approaches in an academic health center. Global Advances in Health and Medicine. 2020 Jan;9:216495612091273. https://doi.org/10.1177/2164956120912730

[63] Sanford NN, Sher DJ, Ahn C, Aizer AA, Mahal BA. Prevalence and nondisclosure of complementary and alternative medicine use in patients with cancer and cancer survivors in the United States. JAMA Oncology. 2019 May 1;5(5):735. https://doi.org/10.1001/jamaoncol.2019.0349

[64] Jennifer R. G, Debora A. P, Yihang L, Derjung M. T. Factors related to disclosure and nondisclosure of dietary supplements in primary care, integrative medicine, and naturopathic medicine. Journal of Family Medicine and Disease Prevention . 2019 Aug 8 [cited 2021 Jan 14];5(4). https://doi.org/10.23937/2469-5793/1510109

[65] Ben-Sasson M, Levy I, Ben-Arye E, Attias S, Schiff E. Dietary and herbal supplements use among patients hospitalized in internal medicine departments. Complementary

Therapies in Medicine. 2020 May;50:102345. https://doi.org/10.1016/j.ctim.2020.102345

[66] Melnikov S, Aboav A, Shalom E, Phriedman S, Khalaila K. The effect of attitudes, subjective norms and stigma on health-care providers' intention to recommend medicinal cannabis to patients. International Journal of Nursing Practice. 2020 Mar 31;e12836. https://doi.org/10.1111/ijn.12836

[67] Azcarate PM, Zhang AJ, Keyhani S, Steigerwald S, Ishida JH, Cohen BE. Medical reasons for marijuana use, forms of use, and patient perception of physician attitudes among the US population. Journal of General Internal Medicine. 2020 Jul;35(7):1979-86. https://doi.org/10.1007/s11606-020-05800-7

[68] Leos-Toro C, Shiplo S, Hammond D. Perceived support for medical cannabis use among approved medical cannabis users in Canada. Drug and Alcohol Review. 2018;37(5):627-36. https://doi.org/10.1111/dar.12823.

[69] Aveni E, Bauer B, Ramelet A-S, Decosterd I, Ballabeni P, Bonvin E, et al. Healthcare professionals' sources of knowledge of complementary medicine in an academic center. Nardini C, editor. PLOS ONE. 2017 Sep 29;12(9):e0184979. https://doi.org/10.1371/journal.pone.0184979.

[70] Pedreira-Robles G, Vasco-Gómez A, Martínez-Delgado Y, Herrera-Morales C, Junyent-Iglesias E. Traditional and complementary medicine in a nephrology department: Practitioner knowledge and advice. The British Journal of Nursing. 2020 Apr 9;29(7):426-30. https://doi.org/10.12968/bjon.2020.29.7.426.

[71] Gyasi RM, Abass K, Adu-Gyamfi S, Accam BT. Nurses' knowledge, clinical practice and attitude towards unconventional medicine: Implications for intercultural healthcare.

Complementary Therapies in Clinical Practice. 2017 Nov;29:1-8. https://doi.org/10.1016/j.ctcp.2017.07.001.

[72] Clevenger SF. Knowledge and attitudes towards utilizing complementary and alternative medical (CAM) treatments by mental health practitioner from various disciplines. Journal of Traditional and Complementary Medicine. 2018 Sep. https://doi.org/10.1016/j.jtcme.2017.08.015.

[73] Suchard JR, Suchard MA, Steinfeldt JL. Physician knowledge of herbal toxicities and adverse herb-drug interactions. European Journal of Emergency Medicine. 2004 Aug;11(4):193-7. https://doi.org/10.1097/01.mej.0000134721.72356.f7.

[74] Taing M-W, Clavarino AM, McGuire TM. Australian community pharmacists' knowledge of popular herbal/nutrient weight-loss complementary medicines. Journal of Pharmacy Practice and Research. 2017 Dec;47(6):463-70. https://doi.org/10.1002/jppr.1313.

[75] Ung COL, Harnett JE, Hu H, Desselle SP. Barriers to pharmacists adopting professional responsibilities that support the appropriate and safe use of dietary supplements in the United States: Perspectives of key stakeholders. American Journal of Health-System Pharmacy. 2019 Jun 18;76(13):980-90. https://doi.org/10.1093/ajhp/zxz079.

[76] Harnett JE, Ung COL, Hu H, Sultani M, Desselle SP. Advancing the pharmacist's role in promoting the appropriate and safe use of dietary supplements. Complementary Therapies in Medicine. 2019 Jun;44:174-81. https://doi.org/10.1016/j.ctim.2019.04.018.

[77] Patwardhan B, Warude D, Pushpangadan P, Bhatt N. Ayurveda and traditional Chinese medicine: A comparative overview. Evidence-Based Complementary and Alternative Medicine. 2005 Dec 1;2(4):465-73. https://doi.org/10.1093/ecam/neh140.

[78] Zolotov Y, Vulfsons S, Zarhin D, Sznitman S. Medical cannabis: An oxymoron? Physicians' perceptions of medical cannabis. International Journal of Drug Policy. 2018 Jul;57:4-10. https://doi.org/10.1016/j.drugpo.2018.03.025.

[79] Takakuwa KM, Mistretta A, Pazdernik VK, Sulak D. Education, knowledge, and practice characteristics of cannabis physicians: A survey of the society of cannabis clinicians. Cannabis and Cannabinoid Research. 2019 Aug 23;can.2019.0025. https://doi.org/10.1089/can.2019.0025.

[80] St. Pierre M, Matthews L, Walsh Z. Cannabis education needs assessment among Canadian physicians-in-training. Complementary Therapies in Medicine. 2020 Mar;49:102328. https://doi.org/10.1016/j.ctim.2020.102328.

[81] Takakuwa KM, Mistretta A, Pazdernik VK, Sulak D. Education, knowledge, and practice characteristics of cannabis physicians: a survey of the Society of Cannabis Clinicians. Cannabis and Cannabinoid Research. 2019 Aug 23. https://doi.org/10.1089/can.2019.0025.

[82] Balneaves LG, Alraja A, Ziemianski D, McCuaig F, Ware M. A national needs assessment of Canadian nurse practitioners regarding cannabis for therapeutic purposes. Cannabis and Cannabinoid Research. 2018 May;3(1):66-73. https://doi.org/10.1089/can.2018.0002.

[83] Sideris A, Khan F, Boltunova A, Cuff G, Gharibo C, Doan LV. New York physicians' perspectives and knowledge of the state medical marijuana program. Cannabis and Cannabinoid Research. 2018 May;3(1):74-84. https://doi.org/10.1089/can.2017.0046.

[84] Ricco J, Danner C, Pereira C, Philbrick AM. The times they are a-changin': Knowledge and perceptions regarding medical cannabis in an academic family medicine department. PRiMER: Peer-Review Reports in Medical Education Research. 2017 Sep;1. https://doi.org/10.22454/PRiMER.2017.593677.

[85] Alvesson M, Skoldberg K. positivism, social constructionism, critical realism: Three reference points in the philosophy of science. Reflexive methodology: New vistas for qualitative research. 2009:15-52. https://www.sagepub.com/sites/default/files/upm-binaries/28039_02_Alvesson_2e_Ch_02.pdf.

Chapter 2

Study 1: No Improvement in Disclosure of Natural Health Product Use to Primary Care Medical Doctors in the Last 15 Years: A Survey of Naturopathic Patients

Chapter 2: No improvement in disclosure of natural health product use to primary care medical doctors in the last 15 years: A survey of naturopathic patients

Abstract

Background: The use of natural health products (NHPs) is common in North America. In 2003, we found that 42% of NHP users had not disclosed this information to their primary care medical doctors (MDs). We repeated our survey in 2018/2019 to explore if the rate of NHP use disclosure had improved.

Methods: From November 2018–February 2019, a 21-item survey about NHP use and disclosure was administered to adult patients who visited the Robert Schad Naturopathic Clinic in Toronto, Canada.

Results: Almost all patients surveyed were using NHPs (99%), and 46% were using NHPs and prescription medication concurrently. Consistent with our 2003 findings, 42% of respondents who used NHPs did not disclose this information to their MD.

Conclusion: Disclosure of NHP use to MDs by naturopathic patients is limited and remained unchanged over the past 15 years. Future research should explore primary care MDs' hesitancy to inquire about patient NHP use.

Background

Natural health products (NHPs), which include vitamins and minerals, herbal remedies, homeopathic medicines, traditional medicines, and probiotics, are used by 80% of people worldwide [1]. Individuals using NHPs often report the belief they are safe because they are natural [2-4]. However, NHPs used in excess or in conjunction with certain drugs have the potential to cause toxic effects or, in rare cases, death [2-8]. For example, usnic acid (promoted for weight loss) can cause severe acute hepatitis or liver failure [2], St. John's Wort increases the risk of stroke or heart attack when used with digoxin [9], and a third of NHP users who are on warfarin therapy are at risk for excessive bleeding [3]. It is therefore desirable for medical doctors (MDs) to be aware of their patients' NHP use.

Despite the high prevalence of NHP use, anywhere between 20%–90% of patients do not disclose use to their MD [3,8-14]. Lack of disclosure has been associated with patients' fear of judgement from MDs and belief that disclosure is unnecessary [3,4,9-13,15]. In 2003, we surveyed 198 Canadian naturopathic patients (88% response rate) and found that while 93% of respondents used NHPs, 42% did not disclose use to their MD [15]. The single factor most strongly associated with disclosure of NHP use was whether or not the patient's primary care MD asked about NHP use. In the Province of Ontario, Canada, it should be noted that “naturopathic doctors” (i.e. NDs) and “medical doctors” (i.e. MDs) comprise two separate healthcare professions. In this study, we repeated our study, 15 years later, at the same naturopathic college clinic to explore if patients' rate of NHP disclosure rate to their MDs had changed.

Methods

From November 15 to 24, 2019 and January 24 to February 2, 2019, all adult patients (18+ years) who visited the Robert Schad Naturopathic Clinic (RSNC) were given the opportunity to participate in our study. The RSNC is a naturopathic teaching clinic located at the Canadian College of Naturopathic Medicine (CCNM) in Toronto, Canada. This was the same clinic that we surveyed in 2003 [16]. A consecutive sampling technique was used, meaning that on days when the surveys were administered, members of our study team approached each patient attending the clinic. A verbal, scripted invitation was used alongside signs that advertised that a survey on NHP disclosure was being conducted. Patients who provided informed consent were given a 21-item questionnaire to complete that inquired about demographics, health care (including use of NHPs and prescription medication), and disclosure of NHP use to their primary care MD. The participant information letter and informed consent form is provided in **Appendix 1**. As per the survey's instructions and informed consent, participants were allowed to skip or not answer any questions that they did not wish to or feel comfortable answering. This questionnaire is available in **Appendix 2**. Questionnaires were completed anonymously, and once completed, participants deposited their questionnaire directly into a secure box. Ethical approval for this study was provided by the CCNM Research Ethics Board.

As participants were permitted to skip or not answer questions, missing values were present and only data that was reported were included in analyses. Frequencies were generated for all collected data. We compared respondent characteristics between the 2003 and 2019 surveys using an unpaired *t*-test for age and a chi-squared test for dichotomous and categorical factors. We created univariable and multivariable logistic regression models to explore factors associated with: (1) patient disclosure of NHP use to their primary care MD and (2) MD inquiry

about NHP use. Independent variables were: (1) age, (2) sex, (3) level of education, (4) length of time attending RSNC, (5) number of visits per year to RSNC, (6) patient concern regarding NHP-drug interaction and for NHP disclosure only, (7) whether or not their MD asked about NHP use. Results are presented as odds ratios (OR) with 95% confidence intervals (CI). An OR greater than 1 indicates an increased association. All analyses were two-tailed and statistical significance was defined as $p < 0.05$. All analyses were performed using IBM SPSS Statistics software, version 24.

Results

A total of 25% of patients approached completed the questionnaire (277 of 1112). The mean age of respondents was 40.5 years (range 16–84) and most were female (77%, 211 of 274) employed (54%, 140 of 258), white (48%, 131 of 270), and had a university degree (68%, 185 of 273) (**Table 1**). Compared to the 2003 survey, respondents were similar in age, sex and employment status, but less likely to be white and more likely to report higher levels of formal education (**Appendix Table 1**). Only 7% of respondents (19 of 273) had been referred for naturopathic care by their MD, and 54% (148 of 275) had attended the RSNC for more than one year. Forty-percent (107 of 271) visited the naturopathic clinic at least 11 times a year, whereas most (62%, 168 of 272) saw their primary care MD 0-3 times a year.

Almost all respondents (99%, 274 of 277) used NHPs, 46% (126 of 274) used NHPs and prescription drugs concurrently, and 54% (148 of 274) used NHPs alone. Patients reported use of the following NHP categories: vitamins and minerals (87%, 240 of 276), herbs (59%, 164 of 276), probiotics (51%, 141 of 276), homeopathic remedies (25%, 69 of 276), traditional Chinese medicines (15%, 42 of 276), and medical cannabis (9%, 25 of 276). The most common NHPs

included vitamin D (68%, 187 of 276), magnesium (55%, 151 of 276), and omega-3 fatty acids (50%, 138 of 276) (**Table 2**). The most commonly used prescription medication types were thyroid hormone (17%, 21 of 121), anti-hypertensive agents (16%, 19 of 121), birth control (15%, 18 of 121), and anti-depressants (13%, 16 of 121) (**Table 3**).

Disclosure of NHP Use to Medical Doctors

Forty-two percent (114 of 269) of respondents did not disclose NHP use to their primary care MD. Yet, 78% (209 of 268) discussed prescription drug use with their naturopathic doctor, and only 27% (72 of 268) were concerned about potential interactions between prescription medications and NHPs. The most common reasons provided for not disclosing NHP use were: (1) MDs do not approve of complementary and alternative medicine use (21%, 27 of 131); (2) MDs would not understand (21%, 27 of 131); (3) patients were uncomfortable talking about NHP use (5%, 7 of 131); and (4) it was not relevant (5%, 6 of 131).

In the adjusted model, the only factor associated with disclosure of NHP use to MDs was whether the latter asked about NHP use (OR 5.27, 95% CI 2.57 to 10.78; $p < 0.001$) (**Table 4**). However, 75% (201 of 268) of respondents stated their MD did not ask about NHP use. None of the independent variables explored showed a significant association with whether primary care MDs inquire about patients' NHP use (**Table 5**).

Discussion

Our survey of naturopathic patients found that almost all reported use of NHPs, but less than half (42%) disclosed use of these products to their primary care MD. The most common reason for non-disclosure was concerns that MDs would not approve. MD inquiry about NHP

use was strongly associated with disclosure, but the majority of MDs did not instigate such discussions. Almost half of the patients we surveyed combined prescription medication with NHP use, but only a quarter were concerned about interactions.

Similarities and Differences to Survey Administered 15 Years Ago

The characteristics of survey respondents were relatively similar to that of the survey administered 15 years ago. The mean age was significantly higher 40.5 (SD=17.2) in 2019 vs. 37.3 (SD=14.7) in 2003 (p=0.04), and comprised of more females (77.0% vs. 71.8%) although not significantly (p=0.26). Participants in the recent survey were significantly more multi-ethnic than 15 years ago, though still predominantly White (48.3% vs. 76.8%) (p<0.001). Education level was relatively similar across both surveys. A significantly lesser proportion of participants were employed in the recent survey (54.3% vs. 66.5%) (p=0.01). Generally speaking, more participants in the recent survey attended the CCNM clinic for a longer period of time. Number of visits to the CCNM clinic per year as well as number of visions to primary care family doctor were relatively similar across both surveys.

While we added a number of additional NHPs to the recent survey, in terms of those listed in both surveys, we found that vitamins, garlic, echinacea, chamomile, and licorice remained the most commonly taken NHPs. A considerably larger proportion of patients in the recent survey reported using omega-3 fatty acids (50.0% vs. 1.9%), probiotics (44.2% vs. 2.5%; though only written as *Lactobacillus acidophilus* in the 2005 version), and iron supplements (24.3% vs. 1.2%), compared to the survey 15 years ago. A number of participants in the recent survey, similar to the first survey, reported taking kava kava (*Piper methysticum*) (2.9% vs. 3.1%) and St. John's Wort (*Hypericum perforatum*) (5.8% vs. 5.0%), despite the fact that Health

Canada has issued advisories on both regarding safe use and potential for drug-herb interactions. In a scenario of optimal safe consumption, disclosure rates ought to mirror use of NHPs that have more significant safety considerations.

In regards to medication use reported by survey respondents, medications used for thyroid disease (17.4% vs. 11%), hypertension (15.7% vs. 6%), birth control (14.9% vs. 20%), depression (13.2% vs. 13%), and hyper-cholesterol (12.4% vs. 4%) remained as the six most common categories of prescription medications across both surveys.

Implications and Importance of the Current Survey

Prior studies have reported NHP nondisclosure rates ranging from 15% to 74%, with the reasons for nondisclosure being lack of inquiry from MDs, lack of time, belief that their MDs would not know about NHPs, patients' fear of being judged, and patients perceiving disclosure as irrelevant because NHPs are safe [3,11,17-20]. Yet, patients' failure to disclosure NHP use to a healthcare provider makes it difficult to recognize or report drug-herb interactions or adverse events, which occurs with increasing likelihood with long-term use and polypharmacy [21]. This study allowed us to evaluate a unique population that almost entirely uses NHPs of some sort (i.e. 99%), which is considerably higher than other populations that have been studied in the literature including Health Canada's report that that 71% of Canadians used NHPs [22].

The 42% NHP nondisclosure rate we found is identical to results at the same naturopathic clinic 15 years earlier [16]. Among the general population, a recent study found that most respondents would prefer to take an NHP versus a prescription drug and that half of respondents believe that NHPs are safer [21], despite the literature finding otherwise whereby in some cases even serious harm can arise from taking NHPs, such as hepatotoxicity or heavy metal poisoning

[23,24]. Considering misleading health claims and lack of information about NHP-prescription drug interactions, there is merit in patients involving their MD in decisions to initiate or continue NHP use [4,25,26]. For instance, one study of 1118 patients found that 59% concurrently used NHPs and prescription drugs, which increased their risk 6.4 times for experiencing severe bruising, cardiac arrest, seizures, and shallow breathing [27]. Some NHPs can increase perioperative patient risk of bleeding (i.e. garlic), hypertension (i.e. ginseng, ephedra), or prolongation of anaesthetic effects (i.e. kava kava, ginseng) [28]. NHP use is common among cancer patients where there is a potential risk of adverse events [29]. Aside from providing such information, MDs who are aware of their patients' NHP use can report adverse events to Health Canada to help inform removal of unsafe products or modifications to safety information [25].

Particular to this study, certain adverse effects and drug interactions are known among NHPs commonly taken by our patient population. More than half of all patients took one or more vitamin supplements in our study. In recent years, the consumption of multivitamins has increased globally and the common assumption among patients is that they are generally safe, even if not necessarily effective [30]. Patients taking high dosages of vitamin C can experience osmotic diarrhea and gastrointestinal upset [31] while overdosing on vitamin A can result in hypervitaminosis and hepatotoxicity [32,33], as examples. Nearly 30% of patients surveyed took turmeric which can cause gastrointestinal issues [34-36]. Green tea was also another commonly taken NHP, and while generally safe, in large quantities can lead to hepatotoxicity [37]. It is also known that green tea contains compounds that have the potential to alter absorption and metabolism of other substances which may result in adverse interactions between catechin and prescribed drugs [38]. Concerns also exist surrounding NHPs that have been associated with serious health risks identified by Health Canada; notably, we asked survey participants to report

whether they took St. John's Wort and kava kava, to which approximately 6% and 3% responded "yes" respectively. Advisories regarding both have been issued by Health Canada in the past (St. John's Wort in 2000, kava kava in 2002). In the advisories, it was warned that St. John's Wort may interfere with medications taken for HIV infection, heart conditions, blood clots, asthma, depression and migraines [39], and kava kava was banned in August 2002 over concerns of hepatotoxicity [40], as well as uncertainty of how to extrapolate evidence from various populations and forms of consumption (e.g. as a tea, standardized extract, traditional preparations) [41]. Ultimately, the ban on kava kava was lifted in Canada and in other jurisdictions, with the provision of label warnings regarding the potential for drug-herb interactions, and directions to consult a health care provider if pregnant, lactating, or suffering from liver disease or epilepsy.

Standards associated with NHP manufacturing, packaging, labelling, licensing and regulation continue to develop and evolve in recognition of gaps and opportunities for improvement [42]. For example, there is ongoing debate regarding how to manage competing types of evidence from both scientific and traditional sources with respect to health claims [43]. Uncertainty arises stemming from issues in the global NHP market regarding product quality including findings of inconsistency in ingredients (presence of fillers, adulterants, contamination or inaccurate undeclared constituents) or inaccurate labels based on contents or claims [44-46]. Although these issues, and others, are not necessarily unique to NHPs, there is some convergence with the regulation, and regulatory issues, of pharmaceutical products while acknowledging the differences in accessing these products [47-49]. Patients who disclose their NHP use, may be able to receive help from their healthcare provider in navigating these complexities and make an informed decision, as well as access quality products they can trust.

Patients often rely on family, friends, or the internet for information regarding NHPs, rather than their MD(s) or other healthcare providers [49-52]. As our study found, patients more frequently disclose NHP use to their naturopathic doctor in comparison to their MD. As these patients have all actively sought out naturopathic care, however, it could be inferenced that they have greater trust in naturopathic doctors in comparison to the general public. The majority of MDs, pharmacists, and nurses have minimal, if any, training in complementary medicines, including NHPs [53]. Providing MDs with a live tutorial can significantly improve their knowledge of complementary medicine [54] although the viability of this approach remains uncertain amidst existing resources and expertise in alternate providers. Future research should explore healthcare practitioners' reasons for not inquiring about patients' NHP use, identify strategies to encourage inquiry, and facilitate decision-making with patients.

Strengths and Limitations

Use of a previously validated survey strengthens our findings, as does the use of a consecutive sampling technique to reduce sampling bias. There were a number of limitations to our study, including a modest response rate of 25%, reliance on self-report for NHP use, and restriction of our sample to a single naturopathic teaching clinic. Thus, our results may not be generalizable to other patient populations using NHPs.

Conclusions

The use of NHPs is common among patients in North America, and these products can interact with prescription medications and cause adverse effects. Disclosure of NHP use provides MDs with the opportunity to educate patients on NHP-drug interactions. It is therefore important

for MDs to be aware of patient NHP use. Almost all naturopathic patients in our survey used NHPs, but less than half disclosed this information to their primary care MD. The low rate of disclosure in the population we surveyed has remained constant over the past 15 years. Patient disclosure is strongly associated with MD inquiry; however, most do not ask. Future research should explore strategies to encourage MD inquiry regarding NHP use and how best to ensure productive discussions following disclosure by patients.

Ethics approval and consent to participate: Approval for our survey was granted by the CCNM Ethics Review Board. All participants were provided with a letter of consent to participate prior to completing their survey.

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Chapter 2 References

[1] Parasuraman S, Thing GS, Dhanaraj SA. Polyherbal formulation: Concept of Ayurveda. Pharmacognosy Reviews. 2014;8(16):73-80. http://doi.org/10.4103/0973-7847.134229.

[2] Seeff LB, Bonkovsky HL, Navarro VJ, Wang G. Herbal products and the liver: A review of adverse effects and mechanisms. Gastroenterology. 2015;148(3):517-532.e3. https://doi.org/10.1053/j.gastro.2014.12.004.

[3] Chang HY, Chang HL, Siren B. Exploring the decision to disclose the use of NHPs among outpatients: A mixed-method study. BMC Complementary and Alternative Medicine. 2013;13(1);319-319. https://doi.org/10.1186/1472-6882-13-319.

[4] Leung VW, Shalansky SJ, Lo MK, Jadusingh EA: Prevalence of use and the risk of adverse effects associated with complementary and alternative medicine in a cohort of patients receiving warfarin. Annals of Pharmacotherapy. 2009, 43 (5): 875-881. https://doi.org/10.1345/aph.1L631.

[5] Ben-Arye E, Samuels N, Goldstein LH, Mutafoglu K, Omran S, Schiff E, et al. Potential risks associated with traditional herbal medicine use in cancer care: A study of Middle Eastern oncology health care professionals. Cancer. 2016;122(4):598-610. https://doi.org/10.1002/cncr.29796.

[6] Block KI. Significance of NHP interactions in oncology. Integrative Cancer Therapies. 2013;12(1):4-6.

[7] Conte-Schmidt N, Cruz-Rivera O. Concurrent use of herbal supplements and prescription drugs in northeastern Puerto Rico. Journal of Pharmaceutical Health Services Research. 2018;9(1):53-58. https://doi.org/10.1111/jphs.12208.

[8] Kew Y, Chia YL, Lai SM, Chong KY, Ho XL, Liew DW, et al. Traditional and complementary medicine (TCM) among study population with cardiovascular risk; Use and substitution for conventional medicine in Pahang, Malaysia. Medical Journal of Malaysia. 2015;70(2):86-92. http://www.e-mjm.org/2015/v70n2/traditional-medicine.pdf.

[9] Sirois FM, Jiang L, Upchurch DM. Use and disclosure of complementary health approaches in US adults with cardiovascular disease. The American Journal of Cardiology. 2018;122(1):170-174. https://doi.org/10.1016/j.amjcard.2018.03.014.

[10] Farooqui M, Hassali MA, Shatar AKA, Farooqui MA, Saleem F, Haq NU, et al. Use of complementary and alternative medicines among Malaysian cancer patients: A descriptive study. Journal of Traditional and Complementary Medicine. 2016;6(4):321-326. https://doi.org/10.1016/j.jtcme.2014.12.008.

[11] Davis EL, Oh B, Butow PN, Mullan BA, Clarke S. Cancer patient disclosure and patient-doctor communication of complementary and alternative medicine use: A systematic review. The Oncologist. 2012;17(11);1475-1481. https://doi.org/10.1634/theoncologist.2012-0223.

[12] Johny AK, Cheah WL, Razitasham S. Disclosure of traditional and complementary medicine use and its associated factors to medical doctor in primary care clinics in Kuching Division, Sarawak, Malaysia. Evidence-Based Complementary and Alternative Medicine. 2017 Jan 1. https://doi.org/10.1155/2017/5146478.

[13] Leng JCF, Gany F. Traditional Chinese medicine use among Chinese immigrant cancer patients. Journal of Cancer Education. 2014;29(1):56-61. https://doi.org/10.1007/s13187-013-0542-5.

[14] Tuna S, Dizdar O, Calis M. The prevalence of usage of herbal medicines among cancer patients. Journal of the Balkan Union of Oncology. 2013;18(4):1048–51. https://jbuon.com/archive/18-4-1048.pdf.

[15] Farooqui M, Hassali MA, Shatar AKA, Shafie AA, Farooqui MA, Saleem F, et al. Complementary and alternative medicines (CAM) disclosure to the health care providers: A qualitative insight from Malaysian cancer patients. Complementary Therapies in Clinical Practice. 2012;18(4):252–256. https://doi.org/10.1016/j.ctcp.2012.06.005.

[16] Busse JW, Heaton G, Wu P, Wilson KR, Mills EJ. Disclosure of NHP use to primary care physicians: A cross-sectional survey of naturopathic clinic attendees. Mayo Clinic Proceedings. 2005;80(5):616-623. https://doi.org/10.4065/80.5.616.

[17] Jou J, Johnson PJ. Nondisclosure of complementary and alternative medicine use to primary care physicians: Findings from the 2012 National Health Interview Survey. JAMA Internal Medicine. 2016;176(4):545–546. https://doi.org/10.1001/jamainternmed.2015.8593.

[18] Saxe GA, Madlensky L, Kealey S, Wu DP, Freeman KL, Pierce JP. Disclosure to physicians of CAM use by breast cancer patients: Findings from the Women's Healthy Eating and Living Study. Integrative Cancer Therapies. 2008;7(3):122-9. https://doi.org/10.1177/1534735408323081.

[19] Foley H, Steel A, Cramer H, Wardle J, Adams J. Disclosure of complementary medicine use to medical providers: A systematic review and meta-analysis. Sci Rep. 2019;9(1):1573. https://doi.org/10.1038/s41598-018-38279-8.

[20] Health Canada. [Internet]. About Natural Health Products; 2016 [cited 2021 Jan 14]. Available from: https://www.canada.ca/en/health-canada/services/drugs-health-products/natural-non-prescription/regulation/about-products.html.

[21] Barry AR. Patients' perceptions and use of natural health products. Canadian Pharmacists Journal / Revue des Pharmaciens du Canada. 2018 Jul;151(4):254-62. https://doi.org/10.1177/1715163518779409.

[22] Government of Canada. [Internet]. About Natural Health Products; 2016 [cited 2021 Jan 14]. Available from: https://www.canada.ca/en/health-canada/services/drugs-health-products/natural-non-prescription/regulation/about-products.html.

[23] Navarro VJ, Barnhart H, Bonkovsky HL, et al. Liver injury from herbals and dietary supplements in the U.S. Drug- Induced Liver Injury Network. Hepatology 2014;60:1399-408. https://doi.org/10.1002/hep.27317.

[24] Budnik LT, Baur X, Harth V, Hahn A. Alternative drugs go global: Possible lead and/or mercury intoxication from imported natural health products and a need for scientifically evaluated poisoning monitoring from environmental exposures. Journal of Occupational Medicine and Toxicology. 2016 Dec;11(1):1-6. https://doi.org/10.1186/s12995-016-0139-0.

[25] Health Canada. [Internet]. 2017 Report on Compliance Monitoring: Natural Health Products; 2019. [cited 2021 Jan 14]. Available from: https://www.canada.ca/en/health-canada/services/inspecting-monitoring-drug-health-products/compliance-monitoring-reports/2017-reporting-compliance-monitoring-natural-health-products.html.

[26] Health Canada and the Public Health Agency of Canada. [Internet]. Evaluation of the Natural Health Products Program 2010-2011 to 2014-2015; 2016. [cited 2021 Jan 14].

Available from: https://www.canada.ca/content/dam/canada/health-canada/migration/department-ministere/health-sante/transparency-transparence/corporate-reporting-rapports-gestion/evaluation/2016-2017/natural-health-products-produits-sante-naturels/alt/nat-health-prod-eng.pdf.

[27] Necyk C, Tsuyuki RT, Boon H, Foster BC, Legatt D, Cembrowski G, et al. Pharmacy study of natural health product adverse reactions (SONAR): A cross-sectional study using active surveillance in community pharmacies to detect adverse events associated with natural health products and assess causality. BMJ Open. 2014;4(3):e003431. https://doi.org/10.1136/bmjopen-2013-003431.

[28] King AR, Russett FS, Generali JA, Grauer DW. Evaluation and implications of NHP use in preoperative patients: A retrospective review. BMC Complementary and Alternative Medicine. 2009;9:38. https://doi.org/10.1186/1472-6882-9-38.

[29] Jermini M, Dubois J, Rodondi PY, Zaman K, Buclin T, Csajka C, et al. Complementary medicine use during cancer treatment and potential herb-drug interactions from a cross-sectional study in an academic centre. Scientific Reports. 2019;9(1):5078. https://doi.org/10.1038/s41598-019-41532-3.

[30] Hamishehkar H, Ranjdoost F, Asgharian P, Mahmoodpoor A, Sanaie S. Vitamins, are they safe? Advanced Pharmaceutical Bulletin. 2016 Dec;6(4):467. https://doi.org/10.15171/apb.2016.061.

[31] Institute of Medicine (US) Panel on Dietary Antioxidants and Related Compounds. Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids. Washington (DC): National Academies Press (US); 2000. https://doi.org/10.17226/9810.

[32] Penniston KL, Tanumihardjo SA. The acute and chronic toxic effects of vitamin A. The American Journal of Clinical Nutrition. 2006 Feb 1;83(2):191-201. https://doi.org/10.1093/ajcn/83.2.191.

[33] Russell RM. The vitamin A spectrum: From deficiency to toxicity. The American Journal of Clinical Nutrition. 2000 Apr 1;71(4):878-84. https://doi.org/10.1093/ajcn/71.4.878.

[34] Sharma RA, McLelland HR, Hill KA, et al. Pharmacodynamic and pharmacokinetic study of oral Curcuma extract in patients with colorectal cancer. Clinical Cancer Research. 2001;7:1894-900. https://clincancerres.aacrjournals.org/content/7/7/1894.long.

[35] Kuptniratsaikul V, Thanakhumtorn S, Chinswangwatanakul P, Wattanamongkonsil L, Thamlikitkul V. Efficacy and safety of Curcuma domestica extracts in patients with knee osteoarthritis. The Journal of Alternative and Complementary Medicine. 2009 Aug 1;15(8):891-7. https://doi.org/10.1089/acm.2008.0186.

[36] Carroll RE, Benya RV, Turgeon DK, et al. Phase IIa clinical trial of curcumin for the prevention of colorectal neoplasia. Cancer Prevention Research. 2011;4:354-64. https://doi.org/10.1158/1940-6207.CAPR-10-0098.

[37] Mazzanti G, Di Sotto A, Vitalone A. Hepatotoxicity of green tea: An update. Archives of Toxicology. 2015 Aug 1;89(8):1175-91. https://doi.org/10.1158/1940-6207.CAPR-10-0098.

[38] Roth M, Timmermann BN, Hagenbuch B. Interactions of green tea catechins with organic anion-transporting polypeptides. Drug Metabolism and Disposition. 2011 May 1;39(5):920-6. https://doi.org/10.1124/dmd.110.036640.

[39] Wharry S. Health Canada sounds warning over St. John's wort. CMAJ: Canadian Medical Association Journal. 2000 Jun 13;162(12):1723. https://www.cmaj.ca/content/162/12/1723.3.

[40] Mills E, Singh R, Ross C, Ernst E, Ray JG. Sale of kava extract in some health food stores. CMAJ: Canadian Medical Association Journal. 2003 Nov 25;169(11):1158-9. https://www.cmaj.ca/content/169/11/1158.

[41] Kuchta K, Schmidt M, Nahrstedt A. German kava ban lifted by court: The alleged hepatotoxicity of kava (Piper methysticum) as a case of ill-defined herbal drug identity, lacking quality control, and misguided regulatory politics. Planta Medica. 2015 Dec;81(18):1647-53. https://doi.org/10.1055/s-0035-1558295.

[42] White J, Reid G. A suggestion for evolution of Canada's health regulatory system. FACETS. 2018 Jan 25;3(1):45-60. https://doi.org/10.1139/facets-2017-0049.

[43] Dwyer JT, Coates PM, Smith MJ. Dietary supplements: Regulatory challenges and research resources. Nutrients. 2018 Jan;10(1):41. https://doi.org/10.3390/nu10010041.

[44] Newmaster SG, Grguric M, Shanmughanandhan D, Ramalingam S, Ragupathy S. DNA barcoding detects contamination and substitution in North American herbal products. BMC Medicine. 2013 Dec;11(1):222. https://doi.org/10.1186/1741-7015-11-222.

[45] Abe AM, Hein DJ, Gregory PJ. Regulatory alerts for dietary supplements in Canada and the United States, 2005–13. American Journal of Health-System Pharmacy. 2015 Jun 1;72(11):966-71. https://doi.org/10.2146/ajhp140574.

[46] Job KM, Kiang TK, Constance JE, Sherwin CM, Enioutina EY. Herbal medicines: Challenges in the modern world. Part 4. Canada and United States. Expert review of

Clinical Pharmacology. 2016 Dec 1;9(12):1597-609. https://doi.org/10.1080/17512433.2016.1238762.

[47] Farooqui M, Hassali MA, Shatar AK, Farooqui MA, Saleem F, Haq NU, et al. Use of complementary and alternative medicines among Malaysian cancer patients: A descriptive study. Journal of Traditional and Complementary Medicine. 2015;6(4):321-326. https://doi.org/10.1016/j.jtcme.2014.12.008.

[48] Almuzaini T, Sammons H, Choonara I. Quality of medicines in Canada: A retrospective review of risk communication documents (2005–2013). BMJ Open. 2014 Oct 1;4(10). https://doi.org/10.1136/bmjopen-2014-006088.

[49] Cheung RY, Goodwin SH. An overview of Canadian and US approaches to drug regulation and responses to postmarket adverse drug reactions. Journal of Diabetes Science and Technology. 2013 Mar;7(2):313-20. https://doi.org/10.1177/193229681300700205.

[50] Raj N, Fernandes S, Charyulu NR, Dubey A, GS R, Hebbar S. Postmarket surveillance: A review on key aspects and measures on the effective functioning in the context of the United Kingdom and Canada. Therapeutic Advances in Drug Safety. 2019 Jul. https://doi.org/10.1177/2042098619865413.

[51] Frawley JE, Anheyer D, Davidson S, Jackson D. Prevalence and characteristics of complementary and alternative medicine use by Australian children. Journal of Paediatrics and Child Health. 2017 Aug;53(8):782-7. https://doi.org/10.1111/jpc.13555.

[52] Pike A, Etchegary H, Godwin M, McCrate F, Crellin J, Mathews M, Law R, Newhook LA, Kinden J. Use of natural health products in children: qualitative analysis of

parents' experiences. Canadian Family Physician. 2013 Aug 1;59(8):e372-8. https://www.cfp.ca/content/59/8/e372.short.

[53] Awad A, Al-Shaye D. Public awareness, patterns of use and attitudes toward natural health products in Kuwait: a cross-sectional survey. BMC Complementary and Alternative Medicine. 2014 Dec;14(1):1-1. https://doi.org/10.1186/1472-6882-14-105.

[54] Aveni E, Bauer B, Ramelet AS, Decosterd I, Ballabeni P, Bonvin E, et al. Healthcare professionals' sources of knowledge of complementary medicine in an academic center. PloS one. 2017 Sep 29;12(9):e0184979. https://doi.org/10.1371/journal.pone.0184979.

[55] Mikail CN, Hearney E, Nemesure B. Increasing physician awareness of the common uses and contraindications of herbal medicines: utility of a case-based tutorial for residents. The Journal of Alternative & Complementary Medicine. 2003 Aug 1;9(4):571-6. https://doi.org/10.1089/107555303322284866.

Chapter 3

Study 2: Attitudes towards Medical Cannabis among Family Physicians Practicing in Ontario, Canada: A Qualitative Research Study

Chapter 3: Attitudes towards Medical Cannabis among Family Physicians Practicing in Ontario, Canada: A Qualitative Research Study

Abstract

Background: Medical cannabis has been legally available in Canada since 2001, but the benefits and harms remain uncertain. We explored attitudes toward medical cannabis among Ontario family physicians.

Methods: Between January and October 2019, we conducted a qualitative study of Ontario family physicians through semi-structured telephone interviews. We applied thematic analysis to interview transcripts and identified representative quotes.

Results: Eleven physicians agreed to be interviewed, and 3 themes regarding medical cannabis emerged: (1) reluctance to authorize use, (2) concern over harms, and (3) lack of practical knowledge. Participants raised concerns about the limited evidence, and their lack of education, to guide therapeutic use of cannabis; particularly as this relates to harms associated with neurocognitive development, exacerbation of mental illness, and drug-interactions in the elderly. Some physicians felt medical cannabis was overly accessible and questioned their role following legalization of recreational cannabis.

Interpretation: Despite increasing availability, family physicians expressed reluctance to authorize medical cannabis due to lack of knowledge and concerns regarding harms. Family physicians may benefit from guidance and education that addresses concerns they have surrounding medical cannabis.

Introduction

Cannabis has been legally available for select medical conditions in Canada since 2001 [1]; however, use by patients has been limited until recently as initial regulations made access difficult. Licensed healthcare practitioners can provide authorization for patients to acquire medical cannabis, who can then register with Health Canada to produce a limited amount of cannabis for personal use, designate another individual to produce their medical cannabis, or acquire cannabis for medical purposes through a licensed producer [2]. On October 17, 2018, the Cannabis Act came into force legalizing the sale and use of recreational cannabis across Canada [3]. The number of Canadians authorized to use medical cannabis increased from 23 930 in June 2015 to 303 221 by June 2020 [4]. Increased use of medical cannabis was likely the result of easing of regulations [5-7], greater availability through growing numbers of producers and cannabis clinics [8-10], and reduced stigma around use of cannabis for therapeutic purposes [11-14]. One online patient resource now lists 100 medical cannabis clinics in Ontario alone [15].

Market data from 2017 to 2019 shows that Ontario ranks the highest among all provinces regarding the amount of medical cannabis sold to clients and the total number of client registrations [16]. Patients increasingly seek guidance from physicians regarding benefits and harms of therapeutic cannabis; however, the evidence for medical cannabis is limited and often conflicting [17,18]. For example, the most common indication for medical cannabis is chronic pain [19]. The National Academies of Sciences, Engineering, and Medicine concluded that patients treated with cannabis are more likely to experience a clinically significant reduction in pain symptoms [20]; however, the National Institute for Health Care and Excellence has made a strong recommendation against use of cannabis for chronic pain [21]. Physicians receive minimal education regarding cannabis during their training and in 2019 the Canadian Medical

Association issued their policy on medical marijuana stating that while cannabis may offer patients relief when conventional therapies fail, a lack of evidence surrounding the risks and benefits of its use makes it difficult for physicians to properly advise patients [22]. The purpose of this qualitative study was to investigate attitudes toward medical cannabis among Ontario family physicians.

Methods

Study Design

We contacted family physicians with the intention to stop recruitment once data saturation was achieved. We conducted a descriptive qualitative research study [23] and used thematic analysis [24] to explore attitudes toward medical cannabis among family physicians. We followed the consolidated criteria for reporting qualitative research (COREQ) checklist in reporting our findings [25]. The participant information letter and informed consent form provided to all participants in the study is found in **Appendix 1**.

Participant Sampling and Recruitment

Interview transcripts were reviewed after every interview was conducted, and recruitment was stopped after data saturation was reached. Family physicians practicing in Ontario, Canada, were eligible for our study and recruited between January and October 2019. We acquired our participants through snowball sampling [26]. This process began with one of us reaching out to a family physician to provide contact information of colleagues that held variable views toward medical cannabis. We then asked physicians who agreed to participate for contact information of their colleagues we could approach to interview. This continued until we interviewed enough

physicians to achieve saturation of themes and subthemes on perspectives regarding medical cannabis [27]. Prior to being interviewed, each participant was sent an information letter and a consent form outlining the purpose of the study and how confidentiality would be maintained.

Data Sources

Participant interviews were facilitated with an interview guide (**Appendix 2**) consisting of open-ended questions; we developed and tested our guide in accordance with McGrath and colleagues' (2019) method, which provides 12 recommendations for conducting qualitative research interviews (**Appendix 3**) [28]. Furthermore, we consulted qualitative studies on related topics to inform our interview guide [29-32], and engaged a family physician to review our interview guide for clarity/completeness. For each participant, we collected demographic information including gender, age, specialization, years of practice, location of medical school training, location of residency training and site of practice (urban or rural). We also asked participants to state whether they authorized or prescribed medical cannabis.

Data Analysis

After providing consent, each physician was interviewed by phone; all interviews were audio-recorded. JYN has training in qualitative interviewing and provided supervision/training to two research assistants. We stopped recruitment when 3 members of our team agreed that saturation of themes had been achieved. Transcripts were not returned to participants and no follow up interviews were conducted. The two research assistants transcribed all audio-taped interviews verbatim. We ensured participant anonymity by replacing names with an identification number in all transcribed documents/interview notes. We analyzed all interview

data applying inductive thematic analysis, which has been shown to be effective in investigating and describing a range of experiences [33]. We adopted a realist approach whereby we took practitioners' reports at face value assuming they would report truthfully about their beliefs and attitudes [34]. Two of us read the interview transcripts and notes several times. Next, the same individuals coded and aggregated transcribed text into meaningful themes/subthemes and labelled constructs. We used an open coding process to establish the primary categories of information from each transcript, independently and in duplicate, and then connected the categories to derive main themes/subthemes. Any disagreements were resolved by discussion. Based on the codes generated from the analysis, the same 2 individuals generated a set of theoretical propositions, independently and in duplicate, and achieved consensus. Lastly, all team members reviewed the results and confirmed the main themes/subthemes of our study findings, which were accompanied by supporting quotes. Both manual coding and NVivo 12 Software (QSR International) were used.

Ethics Approval

The Hamilton Integrated Research Ethics Board approved our study (project no. 5458).

Results

We contacted a total of 21 family physicians in total; eight declined to participate, and 2 were found to be ineligible (not actively practicing), while the remaining 11 agreed to participate in our study. We did not continue recruitment after interviewing these 11 physicians as data saturation was reached. Our participants included 6 men and 5 women, who had been in practice for a median of 3.5 years (range = 1-33). Eight attended medical school in Canada, 3 abroad, and

all had completed their family medicine residency in Canada. One participant held additional specialization in public health and preventive medicine (**Table 1**). The average interview time was approximately 30 minutes.

Main Themes

We identified 3 main themes: (1) reluctance to authorize medical cannabis, (2) concern over harms associated with medical cannabis, and (3) lack of knowledge surrounding administration of medical cannabis. Each theme contained 4 subthemes; participant quotes supporting thematic analysis are shown in **Table 2**.

Theme 1: Reluctance to Authorize Medical Cannabis

Subtheme: Lack of Evidence

Eight physicians felt the evidence supporting the use of cannabis for medical purposes was limited. Specifically, they perceived that clinical trials were often poorly designed, followed patients for short time-periods and did not inform long-term effects, and benefits in trials demonstrating statistical significance was typically modest. Two physicians felt more research on effectiveness was needed before cannabis should be offered to patients. Respondents noted evidence gaps regarding cannabis harms among children, emerging adults and the elderly, cannabis effects on driving capacity, and whether the net benefit-to-harm ratio was favourable for management of mental illness (e.g., post-traumatic stress disorder, anxiety).

Subtheme: Indications for Therapeutic Use

All participants felt that cannabis may be helpful for managing chronic pain, particularly neuropathic pain. Five perceived a therapeutic role for anxiety, 4 for insomnia, and individual physicians endorsed multiple sclerosis, relief from chemotherapy-induced nausea/vomiting, and appetite stimulation as indications. Medical cannabis was not participant physicians' first line of treatment for any condition and was considered only after other treatment options had failed, or on request by patients.

Subtheme: Discomfort with Therapeutic Use of Cannabis

Six physicians avoided authorizing medical cannabis altogether, and 2 prescribed synthetic cannabis (i.e., Nabilone). Physicians that supported therapeutic use of cannabis reported a lack of knowledge regarding what cannabis type should be used and how to pursue dosing and optimal monitoring; they preferred to instead refer patients to colleagues with an interest in cannabis.

Subtheme: Openness to Emerging Evidence

Despite the perceived lack of evidence and reluctance to authorize medical cannabis, 3 participants noted it was important to keep an open mind. They were willing to consider that cannabis may have a role in healthcare, acknowledged that patients were increasingly asking about medical cannabis, and were aware of the need to address their own biases when engaging in discussions.

Theme 2: Harm Associated With the Use of Cannabis

Subtheme: Effect on Neurocognitive Development

Four physicians raised concerns about the effect of cannabis on neurocognitive development and queried whether cannabis use among adolescents/young adults may predispose them to mental illness. Some physicians felt that setting the legal age for use of recreational cannabis at 18 may give the impression that therapeutic use was safe at this age.

Subtheme: Harms in the Elderly

Two physicians raised concerns about cannabis use among the elderly, including the potential for drug interactions given the common occurrence of polypharmacy in this population. They also raised concerns regarding adverse events associated with cannabis use, such as dizziness and sedation, and how this may affect elderly patients' quality of life, ability to drive, and capacity to care for themselves.

Subtheme: Exacerbation of Mental Illness

Three physicians expressed concern over the impact of cannabis use on individuals with pre-existing, or at high risk for, mental illness. Participants noted that cannabis use may exacerbate patient's symptoms of depression/anxiety or interfere with sleep, and acknowledged evidence to implicate cannabis use in early onset psychosis among emerging adults.

Subtheme: Concerns Regarding Cannabis Clinics

Although physicians largely referred patients who were interested in pursuing medical cannabis to practices that focused on this therapy, 3 raised concerns about the quality of care

provided through cannabis clinics. There was a perception that very few interested patients were denied cannabis, and that most patients were not provided with a detailed explanation of possible harms. One physician highlighted their experience that patients with co-morbid mental illness, including substance use disorder, found it easy to access medical cannabis though these clinics.

Theme 3: Knowledge about Medical Cannabis

Subtheme: Inadequate Training

Five physicians described their knowledge of medical cannabis as insufficient in regard to clinical indications, dosing, or monitoring. Older physicians were not exposed to information on medical cannabis in medical school or residency, while more recent graduates encountered some lectures but were not well-versed on the topic. Our participants felt that acquiring training in the use of medical cannabis required them to seek out online courses and conferences.

Subtheme: Continuing Education

Nine physicians expressed an interest in receiving education regarding medical cannabis. When asked what kind of training/education they wished to receive, answers were mixed and often related to their patient population. Some physicians expressed an interest in general topics, such as clinical indications for cannabis and dosing.

Subtheme: Physician's Role Regarding Medical Cannabis

Two physicians expressed frustration regarding their role with medical cannabis due to the atypical nature of the intervention and the limited impact of their involvement. Specifically, medical cannabis does not have to be dispensed by a pharmacist, authorizing cannabis does not

lower the cost for patients, and physicians cannot control the composition of cannabis used for therapeutic purposes. One physician felt that there was no role for the medical profession to remain involved in therapeutic cannabis following legalization for recreational purposes.

Subtheme: Recreational Versus Medical Cannabis

Six physicians raised the issue of how legalization of recreational cannabis affected its therapeutic use. Ten participants felt there was merit to preserving a separate stream for medical use, due to the higher likelihood of more rigorous regulation for medical cannabis: specifically, more consistent products adhering to higher safety standards.

Interpretation

Family physicians in our study were reluctant to authorize medical cannabis due to perceptions of limited supporting evidence, uncertainty regarding clinical indications, and associated harms. Those willing to consider use of medical cannabis typically referred interested patients to clinics that focused on this therapy but were concerned that such clinics may provide cannabis indiscriminately without comprehensive discussion of the possible benefits and harms. One participant questioned whether there remained a role for medical cannabis after legalization for recreational purposes, but most physicians acknowledged that medicinal cannabis would likely adhere to more rigorous quality standards. This belief requires confirmation through formal study. Participants were largely supportive of both research and continuing education to inform the role of medical cannabis for their patients.

Our findings are similar to other published studies that found physicians lack a consolidated perspective regarding whether cannabis is a medicine, and have concerns regarding

the limited evidence base for medical cannabis [19-22,30,35,36]. Regardless, many participants stressed the importance of keeping an open mind and considering patients' values/preferences. We found that physicians had multiple concerns associated with patients' medical cannabis use, and there is evidence to suggest possible harms regarding neurocognitive development [37-39], drug interactions particularly among elderly users [40-44], exacerbation of mental illness [44,45], and lack of standards and quality of care provided through cannabis clinics [46,47]. Physicians felt their training in medical cannabis was lacking, and their interest in continuing medical education in this area is consistent with other surveys [29,30,32,35,48-51]. Of note, some observational data has suggested cannabis may be substituted for prescription medication, including opioids, anxiolytics/benzodiazepines, sedatives, and antidepressants [52,53], however, this issue was not raised by our participants.

One of our participants questioned whether physicians should remain involved with medical cannabis after legalization of recreational use; however, the Canadian Federation of Medical Students has released a position statement calling for increased cannabis education during medical training [54]. The increasing use of cannabis by Canadians suggests that family physicians should continue to address the challenge of discussing use of medical cannabis with interested patients [55]. Open discussions may promote shared decision-making and provide opportunities to assist patients in differentiating evidence from hyperbole [56].

Our study highlights the importance of addressing family physicians' knowledge gaps and concerns surrounding medical cannabis. Further research should further investigate needs of family physicians, as well as medical students and residents, regarding cannabis education [35,57]. Increased knowledge of the evidence for benefits and harms of medicinal cannabis may

improve physicians comfort with discussing this topic with interested patients and reduce reliance on cannabis clinics which may not always provide impartial advice [58-60].

Limitations

We interviewed a modest number of physicians to inform our qualitative study; however, we sampled to saturation and only stopped recruiting new participants when no additional themes emerged in our last interview. We used snowball sampling to recruit physicians, which is prone to sampling bias [61], and we only captured the views of physicians practicing in urban settings. Few of our participants authorized medical cannabis, and those against physicians authorizing medical cannabis may have been overly represented in our sample. Participants may have censored their answers in order to appear as 'good participants' (social desirability bias); however, many physicians we spoke with were forthcoming regarding their concerns about medical cannabis. We did not implement member checking to verify our findings. To ensure trustworthiness and rigor of our study results, 2 members of our team who are familiar with qualitative research methods conducted open coding and theme generalization independently and in duplicate. No members of our study team have used medical cannabis or have any financial or intellectual conflicts of interest in this area and had no motivation to encourage positive or negative answers.

Conclusion

Family physicians in our study were uncertain regarding the therapeutic potential of medical cannabis, except for chronic pain and particularly neuropathic pain for which all felt the evidence supported effectiveness. Most physicians did not provide therapeutic cannabis to their

patients and expressed uncertainty regarding harms and appropriate use. Family physicians may benefit from guidance and education that addresses concerns they have surrounding medical cannabis.

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Chapter 3 References

[1] Government of Canada. [Internet]. Cannabis for Medical Purposes under the Cannabis Act: Information and Improvements; 2020 [cited 2021 Jan 14]. Available from https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/medical-use-cannabis.html.

[2] Health Canada. [Internet]. Medical Document Authorizing the use of Cannabis for Medical Purposes under the Access to Cannabis for Medical Purposes Regulations; 2018 [cited 2021 Jan 14]. Available from https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/licensed-producers/sample-medical-document-marihuana-medical-purposes-regulations.html.

[3] Lametti D. Cannabis Act. House of Commons Canada: Government of Canada; 2020. 128. S.C. 2018, c. 16 https://www.canlii.org/en/ca/laws/stat/sc-2018-c-16/latest/sc-2018-c-16.html.

[4] Health Canada. [Internet]. Data on Cannabis for Medical Purposes; 2020 [cited 2021 Jan 14]. Available from https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/research-data/medical-purpose.html.

[5] Rogin J. Her Majesty the Queen v. J.P. (a young person). Ontario Superior Court of Justice: Criminal Lawyers' Association; 2003. 11. 03-CR-00002 http://cannabislink.ca/legal/rogin.htm.

[6] Borenstein J. Her Majesty the Queen v. Long. Ontario Court of Justice: Criminal Lawyers' Association; 2007. 21. 88 O.R. (3d) 146 https://www.canlii.org/en/on/oncj/doc/2007/2007oncj340/2007oncj340.html.

[7] McLachlin CJ and Abella, Cromwell, Karakatsanis, Wagner, Gascon and Côté JJ. Her Majesty the Queen v. Owen Edward Smith. Supreme Court of Canada: Criminal Lawyers' Association; 2015. 19. 36059. https://scc-csc.lexum.com/scc-csc/scc-csc/en/item/15403/index.do.

[8] CBC News. [Internet]. Medical Marijuana Middlemen: How Specialty Clinics Cash in on Legal Prescriptions; 2017 [cited 2021 Jan 14]. Available from: https://www.cbc.ca/news/business/medical-marijuana-prescription-clinics-1.4086351.

[9] Kahan M, Srivastava A, Clarke S. Cannabis industry and medical cannabis clinics need regulation. Can Fam Physician. 2019 Dec;65(12):864-868.

[10] Marijuana Business Daily. [Internet]. Canadian Marijuana Industry Snapshot; 2017 [cited 2021 Jan 14]. Available from: https://mjbizdaily.com/wp-content/uploads/2017/11/CanadaReportFINAL.pdf.

[11] Lashley K, Pollock TG. Waiting to inhale: Reducing stigma in the medical cannabis industry. Administrative Science Quarterly. 2020;65(2):434-482. https://doi.org/10.1177/0001839219851501.

[12] Harvard Health Blog. [Internet]. Older adults and medical marijuana: Reduced stigma and increased use; 2020 [cited 2021 Jan 14]. Available from: https://www.health.harvard.edu/blog/older-adults-and-medical-marijuana-reduced-stigma-and-increased-use-2-2020040119321.

[13] Aranda AM, Conti R, Wezel FC. Distinct but not apart? Stigma reduction and cross-industry evaluative spillovers: The case of medical marijuana legalization. Academy of Management Journal. 2020. https://doi.org/10.5465/amj.2018.1460.

[14] Marijuana Med Info. [Internet]. Medical Marijuana Assessment Clinics in Canada; 2020 [cited 2021 Jan 14]. Available from: https://www.marijuanamedinfo.ca/clinics/

[15] Health Canada. [Internet]. Market Data under the Access to Cannabis for Medical Purposes Regulations; 2018. [cited 2021 Jan 14]. Available from https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/licensed-producers/market-data.html.

[16] Health Canada. [Internet]. Information for Health Care Professionals: Cannabis (marihuana, marijuana) and the Cannabinoids; 2018. [cited 2021 Jan 14]. Available from: https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/information-medical-practitioners/information-health-care-professionals-cannabis-cannabinoids.html#chp71.

[17] Allan MG, Finley CR, Hauptman R, Beahm NP. Missing 'high' quality evidence for medical cannabinoids for pain? Alberta College of Family Physicians, Tools for Practice. 2017 https://acfp.ca/wp-content/uploads/tools-for-practice/1510681044_tfp199mmandpainfv.pdf.

[18] Boehnke KF, Gangopadhyay S, Clauw DJ, Haffajee RL. Qualifying conditions of medical cannabis license holders in the United States. Health Affairs. 2019 Feb 1;38(2):295-302. https://doi.org/10.1377/hlthaff.2018.05266.

[19] National Academies of Sciences, Engineering, and Medicine. 2017. The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research. Washington, DC: The National Academies Press. https://doi.org/10.17226/24625.

[20] NICE Clinical Practice Guidelines Expert Committee. Cannabis-based medicinal products. NICE. 2019 Nov 11. https://www.nice.org.uk/guidance/ng144.

[21] Canadian Medical Association. [Internet]. CMA Policy on Medical Marijuana; 2019 [cited 2021 Jan 14]. Available from: https://www.cma.ca/cma-policy-medical-marijuana

[22] Sandelowski M. What's in a name? Qualitative description revisited. Research in Nursing & Health. 2010 Feb;33(1):77-84. https://doi.org/10.1002/nur.20362.

[23] Vaismoradi M, Turunen H, Bondas T. Content analysis and thematic analysis: Implications for conducting a qualitative descriptive study. Nursing & Health Sciences. 2013 Sep;15(3):398-405. https://doi.org/10.1111/nhs.12048.

[24] Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. International Journal for Quality in Health Care. 2007 Dec 1;19(6):349-57. https://doi.org/10.1093/intqhc/mzm042.

[25] Miles MB, Huberman AM: Qualitative Data Analysis: A Sourcebook of New Methods. 2nd ed. Thousand Oaks, CA: Sage, 1994. https://us.sagepub.com/en-us/nam/qualitative-data-analysis/book246128.

[26] Ando H, Cousins R, Young C. Achieving saturation in thematic analysis: Development and refinement of a codebook. Comprehensive Psychology. 2014 Jan 1;3:03-CP. https://doi.org/10.2466/03.CP.3.4.

[27] McGrath C, Palmgren PJ, Liljedahl M. Twelve tips for conducting qualitative research interviews. Medical Teacher. 2019 Sep 2;41(9):1002-6. https://doi.org/10.1080/0142159X.2018.1497149.

[28] Zolotov Y, Vulfsons S, Zarhin D, Sznitman S. Medical cannabis: An oxymoron? Physicians' perceptions of medical cannabis. International Journal of Drug Policy. 2018 Jul 1;57:4-10. https://doi.org/10.1016/j.drugpo.2018.03.025.

[29] Islam DA. Investigating the Clinical Decision-Making Process of Physicians in Rural Ontario: The Perspective and Attitudes on Medical Cannabis. Guelph, Ontario: 2019. 153 p. https://atrium.lib.uoguelph.ca/xmlui/handle/10214/17364.

[30] Zolotov Y, Vulfsons S, Zarhin D, Sznitman S. Medical cannabis: An oxymoron? Physicians' perceptions of medical cannabis. International Journal of Drug Policy. 2018 Jul 1;57:4-10. https://doi.org/10.1016/j.drugpo.2018.03.025.

[31] Braun IM, Meyer FL, Gagne JJ, Nabati L, Yuppa DP, Carmona MA, et al. Experts' perspectives on the role of medical marijuana in oncology: A semistructured interview study. Psycho-oncology. 2017 Aug;26(8):1087-92. https://doi.org/10.1002/pon.4365.

[32] Braun V, Clarke V. Using thematic analysis in psychology. Qualitative Research in Psychology. 2006;3(2):77-101 https://doi.org/10.1191/1478088706QP063OA.

[33] Hayes N. Doing psychological research: Gathering and analysing data. Open University Press; 2000. https://psycnet.apa.org/record/2003-88287-000.

[34] Shahi A, Allain S, Turner S, Bailey K. Cannabis therapy knowledge study: Toward establishing a pedagogical tool. University of Ottawa Journal of Medicine. 2018 Nov 15;8(2):19-22. https://doi.org/10.18192/uojm.v8i2.3672.

[35] Szaflarski M, McGoldrick P, Currens L, Blodgett D, Land H, Szaflarski JP, Segal E. Attitudes and knowledge about cannabis and cannabis-based therapies among US neurologists, nurses, and pharmacists. Epilepsy & Behavior. 2020 Aug 1;109:107102. https://doi.org/10.1016/j.yebeh.2020.107102.

[36] Lubman DI, Cheetham A, Yücel M. Cannabis and adolescent brain development. Pharmacology & Therapeutics. 2015 Apr 1;148:1-6. https://doi.org/10.1016/j.pharmthera.2014.11.009.

[37] Bossong MG, Niesink RJ. Adolescent brain maturation, the endogenous cannabinoid system and the neurobiology of cannabis-induced schizophrenia. Progress in Neurobiology. 2010 Nov 1;92(3):370-85. https://doi.org/10.1016/j.pneurobio.2010.06.010.

[38] Camchong J, Lim KO, Kumra S. Adverse effects of cannabis on adolescent brain development: a longitudinal study. Cerebral Cortex. 2016 Feb 23;27(3):1922-30. https://doi.org/10.1093/cercor/bhw015.

[39] MacCallum CA, Russo EB. Practical considerations in medical cannabis administration and dosing. European Journal of Internal Medicine. 2018 Mar;49:12–9. https://doi.org/10.1016/j.ejim.2018.01.004.

[40] Abuhasira R, Schleider LB-L, Mechoulam R, Novack V. Epidemiological characteristics, safety and efficacy of medical cannabis in the elderly. European Journal of Internal Medicine. 2018 Mar;49:44–50. https://doi.org/10.1016/j.ejim.2018.01.019.

[41] Brown JD, Winterstein AG. Potential adverse drug events and drug–drug interactions with medical and consumer cannabidiol (CBD) use. Journal of clinical medicine. 2019 Jul;8(7):989. https://doi.org/10.3390/jcm8070989.

[42] Antoniou T, Bodkin J, Ho JM. Drug interactions with cannabinoids. CMAJ: Canadian Medical Association Journal. 2020 Mar 2;192(9):E206. https://doi.org/10.1503/cmaj.191097.

[43] Lowe DJ, Sasiadek JD, Coles AS, George TP. Cannabis and mental illness: A review. European archives of psychiatry and clinical neuroscience. 2019 Feb 1;269(1):107-20. https://doi.org/10.1007/s00406-018-0970-7.

[44] Hill KP. Cannabis use and risk for substance use disorders and mood or anxiety disorders. JAMA: The Journal of the American Medical Association. 2017 Mar 14;317(10):1070-1. https://doi.org/10.1001/jama.2016.19706.

[45] Lucas P, Walsh Z. Medical cannabis access, use, and substitution for prescription opioids and other substances: A survey of authorized medical cannabis patients. International Journal of Drug Policy. 2017 Apr 1;42:30-5. https://doi.org/10.1016/j.drugpo.2017.01.011.

[46] Fitzcharles MA, Shir Y, Häuser W. Medical cannabis: Strengthening evidence in the face of hype and public pressure. CMAJ: Canadian Medical Association. 2019 Aug 19;191(33):E907-8. https://doi.org/10.1503/cmaj.190509.

[47] Sagy I, Peleg-Sagy T, Barski L, Zeller L, Jotkowitz A. Ethical issues in medical cannabis use. European Journal of Internal Medicine. 2018 Mar 1;49:20-2. https://doi.org/10.1016/j.ejim.2018.01.016.

[48] Pierre MS, Matthews L, Walsh Z. Cannabis education needs assessment among Canadian physicians-in-training. Complementary Therapies in Medicine. 2020 Mar 1;49:102328. https://doi.org/10.1016/j.ctim.2020.102328.

[49] Karanges EA, Suraev A, Elias N, Manocha R, McGregor IS. Knowledge and attitudes of Australian general practitioners towards medicinal cannabis: a cross-sectional survey. BMJ

[50] Open. 2018 Jun 1;8(7):e022101. http://doi.org/10.1136/bmjopen-2018-022101.

[51] Ziemianski D, Capler R, Tekanoff R, Lacasse A, Luconi F, Ware MA. Cannabis in medicine: A national educational needs assessment among Canadian physicians. BMC Medical Education. 2015 Dec 1;15(1):52. https://doi.org/10.1186/s12909-015-0335-0.

[52] Corroon Jr JM, Mischley LK, Sexton M. Cannabis as a substitute for prescription drugs–a cross-sectional study. Journal of Pain Research. 2017;10:989. https://doi.org/10.2147/JPR.S134330.

[53] Piper BJ, DeKeuster RM, Beals ML, Cobb CM, Burchman CA, Perkinson L, et al. Substitution of medical cannabis for pharmaceutical agents for pain, anxiety, and sleep. Journal of Psychopharmacology. 2017 May;31(5):569-75. https://doi.org/10.1177/0269881117699616.

[54] Hartman M, Lasry D, Khan AU, Wu H, Kassam S, Wong A, et al. Canadian Federation of Medical Students Position Statement on Recreational Cannabis Legalization. Halifax, Nova Scotia: Canadian Federation of Medical Students. 2018 Mar 10. https://www.cfms.org/files/meetings/sgm-2018/resolutions/CFMS-position-paper-on-cannabis.pdf.

[55] Ng JY, Garber A, Luong M, Cooley K, Busse JW. No improvement in disclosure of natural health product use to primary care medical doctors in the last 15 years: A survey of naturopathic patients. Complementary Therapies in Clinical Practice. 2020 May 1;39:101106. https://doi.org/10.1016/j.ctcp.2020.101106.

[56] PharmOut. [Internet]. FDA Crackdowns on False Claims Made by Cannabis Advertisers; 2019 [cited 2021 Jan 14]. Available from: https://www.pharmout.net/fda-crackdowns-false-claims-cannabis-cbd-medicine-advertisements/.

[57] Ziemianski D, Capler R, Tekanoff R, Lacasse A, Luconi F, Ware MA. Cannabis in medicine: A national educational needs assessment among Canadian physicians. BMC Medical Education. 2015 Dec 1;15(1):52. https://doi.org/10.1186/s12909-015-0335-0.

[58] Kansagara D, Morasco BJ, Iacocca MO, Bair MJ, Hooker ER, Becker WC. Clinician knowledge, attitudes, and practice regarding cannabis: Results from a national veterans health administration survey. Pain Medicine. 2020 Nov;21(11):3180-6. https://doi.org/10.1093/pm/pnz322.

[59] Zylla D, Steele G, Eklund J, Mettner J, Arneson T. Oncology clinicians and the Minnesota Medical Cannabis Program: A survey on medical cannabis practice patterns, barriers to enrollment, and educational needs. Cannabis and Cannabinoid Research. 2018 Oct 1;3(1):195-202. https://doi.org/10.1089/can.2018.0029.

[60] Philpot LM, Ebbert JO, Hurt RT. A survey of the attitudes, beliefs and knowledge about medical cannabis among primary care providers. BMC Family Practice. 2019 Dec;20(1):17. https://doi.org/10.1186/s12875-019-0906-y.

[61] Sedgwick P. Snowball sampling. BMJ: British Medical Journal. 2013 Dec 20;347(dec20 2):f7511–f7511. https://doi.org/10.1136/bmj.f7511.

Chapter 4

Study 3: How is Complementary, Alternative, and Integrative Medicine Mentioned during the COVID-19 Pandemic? A Sentiment Analysis of Twitter Data

Chapter 4: How is Complementary, Alternative, and Integrative Medicine Mentioned during the COVID-19 Pandemic? A Sentiment Analysis of Twitter Data

Abstract

Background: Coronavirus disease 2019 (COVID-19) is a novel infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Despite a paucity of evidence, various complementary, alternative and integrative medicines (CAIMs) have been being touted as both preventative and curative. We conducted sentiment and emotion analysis with the intent of understanding CAIM content related to COVID-19 being generated on Twitter.

Methods: Tweets relating to CAIM and COVID-19 were extracted from the George Washington University Libraries Dataverse Coronavirus tweets dataset from March 03 to June 10, 2020. We trained and tested a machine learning classifier using a large, pre-labelled Twitter dataset, which was applied to predict the sentiment of each CAIM-related tweet, and we used a natural language processing package to identify the emotions based on the words contained in the tweets.

Results: Our dataset included 17528 English-language Tweets. The highest CAIM-related tweet count was during the 2nd to 3rd week of May followed by the period around late March. Most tweets (n=9344, 54.6%) were classified as positive, 30.6% were neutral (n=5242) and 14.8% were classified as negative (n=2529). The most frequent emotions expressed across tweets were trust, followed by fear, while surprise and disgust were the least frequent.

Conclusion: The use of sentiment and emotion analysis of Twitter data provides insight into the kinds of information being disseminated. Our findings warrant further qualitative investigation of

the identified emotions in the analysed tweets, which could be used to combat misinformation and improve public health strategies surrounding the use of social media information.

Background

Coronavirus disease 2019 (COVID-19) is a novel infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. In December 2019 it was first discovered, having originated from Wuhan, China, and has since rapidly spread across the globe, with 220 countries reporting cases. As of December 10, 2020, over 68.1 million cases and 1.55 million deaths have been reported [2]. Common symptoms associated with COVID-19 include fever, tiredness, and dry cough, but can also include aches and pains, nasal congestion, runny nose, sore throat or diarrhea. While some patients infected with the disease do not exhibit symptoms, COVID-19 is of great concern to global public health as approximately 5% of people who are infected will become seriously ill and develop difficulty breathing [1]. Certain health precautions such as frequent and thorough hand washing, social distancing, wearing masks, and self-isolation have been shown to reduce the spread of COVID-19 [3]. There are no proven drugs to prevent or cure COVID-19 [4,5], and newly approved vaccines are just becoming available in certain countries [6,7]. Despite this, some complementary, alternative, and integrative medicines (CAIMs) are being touted as the solution [8].

According to the National Centre for Complementary and Integrative Health (NCCIH), complementary and alternative medicine is defined as “health care approaches that are not typically part of conventional medical care or that may have origins outside of usual Western practice”. “Complementary” refers to care in combination with conventional medicine, whereas “alternative” refers to care in place of it. “Integrative medicine” refers to bringing conventional

and complementary approaches together in a coordinated way [9]. While the use of CAIMs in the context of some diseases have been shown to be effective or promising, it is also well-documented in the research literature that CAIM is sometimes promoted as a remedy for which the evidence-base is lacking [10,11]. This is further compounded by the fact that many patients assume that CAIM is both safe and effective, even though both CAIM therapies and practitioners are generally subject to less regulation [12]. There is a growing movement of conventional and CAIM practitioners working together to support the safer and more effective uses of CAIM therapies, but concerns remain about misinformation circulated online [13,14,15]. Of particular interest is social media, as the body of literature that has considered its impact and growing significance as a source of health information for the general public has grown over the recent years [16,17,18]. Emerging methodologies that have been employed to study social media content include the utilization of natural language processing (NLP), which is defined by Liddy as "a theoretically motivated range of computational techniques for analyzing and representing naturally occurring texts at one or more levels of linguistic analysis for the purpose of achieving human-like language processing for a range of tasks or applications" [19]. One of the subfields of NLP is sentiment analysis, which automatically classifies text according to the polarity (positive to negative) of the sentiments expressed therein [20]. A positive and negative sentiment can be defined as a favourable and unfavourable expression towards a subject, respectively, while a neutral sentiment represents an expression that is neither favourable nor unfavourable.

In the context of recently past pandemics, such as influenza-A (H1N1), NLP analyses of social media content (i.e. Twitter) served multiple purposes, including monitoring, predicting, and tracking levels of infection, and identifying the kinds of information circulated, distilled into content categories [21,22,23,24].

To our knowledge, a very limited amount of research has been conducted at the intersection of CAIM and social media [25,26], while no studies have ever investigated what information surrounding CAIM is communicated across social media during any pandemics that have occurred since the inception of the Internet. In the present study, we conducted a sentiment analysis with the intent of understanding what kind of CAIM content related to COVID-19 is being generated on Twitter during the pandemic. We identified Twitter as our social media platform of choice since it is easy to use, cheap, and accessible, and the data can be easily collected in comparison with other platforms that have more restrictive privacy policies [20]. As the first study of its kind, our findings provide insight into a previously unexplored environment in the context of CAIM, that is both popular and free to patients, yet rife with quickly and continuously generated information of unassessed quality.

Methods

Approach

We used a supervised machine learning approach, in which the machine algorithm is given labelled data—a dataset that has been classified—to be used for predicting the classification of the targeted unlabelled data, in our case CAIM-related tweets [27]. Overall, our approach consisted of the following 2 phases: 1a) training and testing a machine learning classifier using a large, pre-labelled Twitter dataset, 1b) using the trained classifier to predict the sentiment class of each tweet, and 2) utilizing an NLP package to identify the emotions based on the words contained in the tweets. We first searched for CAIM-related tweets from within a set of COVID-19-filtered tweet dataset using CAIM-related search terms. All Tweets analysed in this study, therefore, contained at least one CAIM-related word/term and at least one COVID-19-

related word/term. We then obtained the training dataset; a large dataset of tweets that have been pre-labelled based on positive and negative sentiments created by Go et al. [28] and made publicly available through the Sentiment140 website [29]. In short, a sentiment can be defined as a "positive or negative feeling", and thus training data hand-labeled by humans can be subject to a great degree of subjectivity. The use of Sentiment140 training data mitigates this to an extent, however, as it consists of tweets with emoticons. For example, ":)" in a tweet indicates that the tweet contains positive sentiment and ":(" indicates that the tweet contains negative sentiment. We used two supervised machine learning approaches to conduct both a sentiment analysis (using the GLMnet trained classifier [30]) and an emotion analysis (using Syuzhet NLP package in R [31]) of our CAIM-tweets dataset. Study steps are detailed in the following sections and depicted in a flowchart in **Figure 1**.

Development of Search Strategy

Preliminary searches of Twitter-related sentiment analyses yielded no consistent nor standardized method for identifying search terms. In preparation for conducting searches across a large dataset of tweets, we first searched the Twitter platform using a number of CAIM-related and COVID-19-related terms to identify the most frequently used terms. Commonly used COVID-19-related terms were relatively simple to identify, as most Twitter users used the terms "COVID", "coronavirus" or "COVID-19. Given the lack of consensus on a complete or comprehensive operational definition of CAIM [32], we browsed MeSH headings on MEDLINE and selected the most commonly used terms to refer to CAIM [33], and common CAIM systems and their respective practitioners (i.e. "homeopathy" vs. "homeopath", etc.) [9].We excluded highly specific or specialized types of CAIM that would not typically be used by the general

public (i.e. “electroacupuncture” as opposed to “acupuncture”, the specific genus and species of herbs as opposed to a generic term such as “herbal medicine”, etc.). A shortlist of 44 CAIM-related terms were combined with the 3 COVID-19-related terms, resulting in 132 unique Twitter searches. After applying these searches to Twitter, we looked at the recency of the use of terms to identify those most relevant to include in our final search strategy. Based on this approach, our final CAIM search strategy included the following terms: “Ayurveda”, “Ayurveda medicine”, “dietary supplement”, “herbal”, “herbal medicine”, “herbal supplement”, “herbal therapy”, “herbalism”, “herbs”, “homeopathy”, “homeopathic”, “natural medicine”, “natural medicines”, “natural therapies”, “natural therapy”, “naturopathic medicine”, “naturopathy”, “traditional medicine”, “traditional medicines”, “vitamins”, and “vitamin”.

Data Collection

To collect tweets at the intersection of COVID-19 and CAIM, we applied our CAIM search strategy to a COVID-19 filtered tweets dataset made available by the TweetSets website [34,35]. TweetSets is an open-source online platform from the George Washington University (GWU) that archives Twitter datasets for research purposes. GWU Dataverse is part of the Harvard Dataverse, a free data repository open to all researchers from any discipline, both inside and outside of the Harvard community [36]. TweetSets allows users to select, generate, and download tweet IDs from publicly available filtered tweets datasets by allowing for querying on keywords, hashtags, mentions, users, embedded media, and type of tweet (original, retweet, quotes, or reply). Through TweetSets, we accessed the Coronavirus dataset, created by Kerchner and Wrubel [37], which contained 239 613 930 COVID-19 related tweets from March 03, 2020 to June 10, 2020, as of June 27, 2020. GWU compiled the tweets by applying the keywords

#Coronavirus, #Coronaoutbreak, #COVID19 using the post statuses/filter method of the Twitter stream application programming interface (API). We applied our CAIM-related search strategy to filter the Coronavirus dataset, thus identifying tweets containing both CAIM and COVID-19-related content. We limited tweets to original English-language tweets that included one or more of the CAIM-related search terms.

The TweetSets output was a condensed series of tweet IDs relating to the identity of each included tweet. To extract the text of the tweet, date of posting, user account identifiers, and tweet metadata (i.e. location coordinates, hashtags, tweets URL, retweet status, and language code), a "Hydrator" software [38] was used. This software allowed us to extract the tweet details from the tweet IDs in our search results. The output dataset was a comma-separated values (csv) file that was imported into Microsoft Excel for data cleaning and analysis, which is described in further detail below.

Sentiment Analysis of CAIM-related Tweets

Contextual polarity sentiment analysis involves determining the polarity of the opinion resulting in an output of positive, neutral, and negative values [39]. Sentiment analyses of the collected tweets was performed in Rstudio software. The contextual polarity sentiment analysis was conducted using the GLMnet package [39] for the classifier and theText2Vec package [40], an R package which provides a framework for text analysis and NLP. We used a supervised machine learning approach whereby the learning capabilities of the model was determined by a labelled training dataset. For this training, we used the Sentiment140 tweets dataset [29], which is a labelled dataset of 1.6 million twitter messages created by Go et al. [28] using machine learning to classify tweets into positive and negative based on their sentiments. The training

dataset, Sentiment140, contained the targeted correct attributes (sentiment) from which the learning machine algorithm found patterns that mapped the input data attributes to the target (sentiment e.g., positivity, neutrality, negativity). The machine learning model functions by analysing the input (our tweet dataset) based on knowledge acquired from the training set, and then returning a predicted value related to the sentiment of each identified CAIM-related tweet. The training dataset was split into training and testing (evaluation) datasets in an 80:20 ratio. Words in the training dataset were tokenized using the itoken() function in Text2Vec Package, a process of reducing a text into phrases or words called tokens. The aim of this process is to identify meaningful words in a given sentence since textual data is a stream of characters [41]. Prior to the tokenization, we applied some text pre-processing procedures to the training and testing datasets: each word was converted to lowercase, and symbols, numbers, and non-words were removed.

N-grams was used as our feature selection (i.e. the process of selecting a subset of relevant features (words, variables, attributes, or predictors) for use in model construction. N-grams is a space reduction method that selects a subset of the dataset to identify more relevant features from the pre-processed text to improve classification quality and reduce computational complexity. N-gram is the sequence of a given number of words (N), and it is a probability model to predict the most probable word that might follow a certain sequence while preserving the word locality information and we have used bi-grams which is the sequence of two words [42,43]. For the machine to understand the text within our dataset, the text had to be vectorized in a process called text vectorization; in other words, this process transformed text into an array of numbers (vectors) to make it understandable by the machine [44]. Vectorized bi-grams were organized in a document-term matrix (DTM) —a mathematical matrix that describes the

frequency of terms in a collection of texts [45]. A machine learning classifier, the algorithm for prediction of the target class label, was fit to the created DTM for training. The classifier output was set to generate fitted probabilities values for each tweet, with a score ranging between 0 and 1 (0 tending towards the most negative, 1 tending towards the most positive, and values between 0.35 and 0.65 being considered neutral [46]). We selected the regularized generalized linear model, GLMnet, as our classifier; this is an extension of the generalized linear model with built-in variable selection making them helpful in real world datasets. To decrease bias in the results of the classifier, we have used the 5-fold cross validation. To evaluate the performance of our machine learning model as applied to the evaluation dataset, we determined the receiver operator characteristic (ROC) curve and area under the ROC curve (AUC).

Emotion Analysis of CAIM-related Tweets

To further identify the emotions relayed within our tweet dataset, we used the Syuzhet R package, which is capable of extracting sentiment and sentiment-derived plot arcs from text using a variety of sentiment dictionaries within the package [31]. Syuzhet employs a lexicon dictionary of emotions based on the National Research Council Canada (NRC) Emotion Lexicon [47,48]. This lexicon was created by manual annotation of a list of English words and their associations with eight basic emotions (anger, fear, anticipation, trust, surprise, sadness, joy, and disgust) and two sentiments (negative and positive) accomplished by crowdsourcing. IBM SPSS version 25 was used for the statistical analysis and visual representation of the results in terms of frequencies, means, time series and count summaries for the eight emotions.

Results

Tweet Dataset

With our search terms, we identified 25 191 original tweets, of which 17 528 (69.6%) were posted in the English language. The most commonly used CAIM-related hashtags were #vitamin followed by #ayurveda. "Vitamin" was overwhelmingly the most common CAIM-related term followed by "herbal" and "Ayurveda", as shown in **Table 1**. The number of CAIM-related tweets during our study period peaked between the second and third week of May 2020 followed by the period around late March 2020; the fewest CAIM-related tweets were collected during the fourth week of May 2020 followed by the period around mid-April 2020 (**Figure 2**).

Sentiment Analysis

Our sentiment analysis algorithm using the GLMnet classifier for direction of the tweet sentiments had an AUC of 0.894 as shown in **Figure 3A**, which indicates a good ability for our classifier to distinguish between different classes. Sentiments across all tweets analysed were classified as positive (54.6%, n = 9344), neutral (30.6%, n = 5242), and negative (14.8%, n = 2529), as shown in **Figure 3B**.

Emotion Analysis

When applying the algorithm employing the emotion lexicon to our tweet dataset, we were able to crosslink these emotions with text words within the tweets. The most prevalent emotion identified in the tweets was related to trust, which was associated with a total of 13 575 words as shown in **Table 2**. This was followed by fear, and sadness. Anger, disgust, and surprise were the least represented emotions in our dataset. **Figure 4** is a word cloud that depicts the most

common words found across our subset of tweets analysed categorized by emotion, whereby the larger the size of the word, the more frequently it was used across all tweets. It is important to note that the emotions are reflective of a word itself, and not a tweet. In **Table 3**, we provide illustrative examples of tweets with a positive, neutral, and negative sentiments.

Discussion

Over recent years, social media has become an increasingly popular generator and source of data that has interested a wide range of researchers [49]. The use of internet (including social media) data in studies, such as content and sentiment analyses, overcome some of the limitations of traditional social science research methods that rely on time-consuming, costly, retrospective, time-lagged, and small-scale approaches that rely on surveys and interviews [24,50,51]. In the context of pandemics, some research has even found that social media can be used to predict and detect one [52,53,54]. Further to this, once a pandemic has been identified, social media data can also be used to track public perceptions of the disease in question [22,24,55,56]. One topic in the context of a pandemic, which has not been well-studied across social media, is the mention of CAIM. Yet, this topic is arguably of great interest given that a wide variety of CAIMs are being touted as preventative or curative against COVID-19 [57,58,59]. In fact, WHO Director General Tedros Adhanom Ghebreyesus at the Munich Security Conference on February 15, 2020 is quoted saying “We’re not just fighting an epidemic; we’re fighting an infodemic” in reference to the rampant spread of misinformation, most notably across social media platforms [60].

In the present study, we conducted a sentiment and emotion analysis of Twitter data to explore what is said about CAIM in the context of COVID-19. To our knowledge, this is the first study to provide insights into the sentiments expressed by Twitter users at the intersection of

CAIM and COVID-19. The majority of the tweets we identified and analyzed carried a generally positive sentiment. This was reflected in the emotional representation of "trust" with the highest word count in the dataset, an emotion that is frequently considered positive. We need to note the difference between the sentiment analysis of a tweet and the lexicon analysis using the Syuzhet package, as sentiment analysis is a whole tweet representation while the emotion lexicon is a word-based analysis. The latter algorithm compares words in the dataset to the NRC Sentiment and Emotional Lexicon, and it correlates words to eight standard emotions (anticipation, trust, joy, surprise, fear, sadness, anger, and disgust). From these patterns, the CAIM-related content being shared via Twitter would indicate support for CAIM interventions for COVID-19. This is in line with a plethora of published research studies that have found that the general public, across a number of different countries, tend to view CAIMs favourably and their usage continues to increase [61,62,63,64,65]. From **Table 1** and **Figure 4**, as well as the illustrative tweets in **Table 3**, we see a focus on vitamins for prevention and treatment, which is also not entirely surprising given that across various surveys vitamins are the most commonly used CAIMs [66,67]. In fact, the 2012 National Health Interview Survey found that across all types of CAIM, natural health products (including vitamins) were the most commonly used among Americans [68].

To date, a limited but growing number of studies involving social media data have been published relating to COVID-19. Some of these provide a more generalized overview of public COVID-19 discussions. Xue et al. [69] used unsupervised machine learning, qualitative analysis, and sentiment analysis to understand Twitter users' discourse and psychological reactions to COVID-19, finding that while information relating to treatments and symptoms were not prevalent topics, fear of the unknown nature of the disease was dominant across all identified

themes. Hung at al. [70] also applied machine learning methods to analyze data collected from Twitter including to identify the social network's dominant topics and whether the tweets expressed positive, neutral, or negative sentiments. They identified 5 main themes including: health care environment, emotional support, business economy, social change, and psychological stress. Of approximately 900 000 tweets analyzed, their sentiment analysis classified 48% of tweets as having a positive sentiment, 21% as neutral, and 31% as negative. Abd-Alrazaq et al. [71] leveraged latent Dirichlet allocation (a type of NLP) for topic modelling to identify topics discussed in the tweets relating to the COVID-19 pandemic, in addition to conducting a sentiment analysis. They identified four main themes associated with their subset of included tweets including: origin of the virus; its sources; its impact on people, countries, and the economy; and ways of mitigating the risk of infection. They also found that the mean sentiment was positive for 10 topics and negative for 2 topics (COVID-19-caused deaths and an increase in racism). Based on their findings, they noted that a more proactive and agile public health presence on social media is warranted to combat the spread of misinformation.

Other studies have focused their objectives on identifying types or prevalence of misinformation. Mackey et al. [72] used NLP and deep learning to detect and characterize illicit COVID-19 product sales using Twitter and Instagram data. They identified a few hundred tweets and posts, respectively, containing questionable immunity-boosting treatments or involving suspect testing kits, as well as a small number of posts about pharmaceuticals that had not been approved for COVID-19 treatment. Kouzy et al. [73] conducted searches on Twitter-related to COVID-19, then summarized and assessed individual tweets for misinformation in comparison to verified and peer-reviewed resources, ultimately concluding that medical misinformation and unverifiable content were being propagated at an alarming rate. In contrast, Singh et al. [74] also

analysed COVID-19-related Twitter content but found that while discussions surrounding myths and links to poor quality information did exist, their presence was less dominant than other crisis-specific themes. Lastly, Krawchuk et al. [75] conducted a descriptive study which detailed Twitter activity regarding spinal manipulative therapy and claims that it increases or boosts immunity. They found that misinformation linking spinal manipulation and increased immunity increased dramatically at the onset of the COVID-19 crisis.

Future Directions

Several future directions could be followed, based on the present study as well as emerging research in this topic area. As misinformation surrounding the COVID-19 pandemic is both rampant and pervasive on Twitter, among other social media platforms, several researchers have begun developing tools to track such misinformation. Sharma et al. [76] designed a dashboard to track misinformation on Twitter, which aims to identify false, misleading, and clickbait contents from collected tweets. Al-Rakhami et al. [77] has proposed an ensemble-learning-based framework for verifying the credibility of a vast number of tweets, which classifies tweet information based on tweet- and user-level features into two categories, either "credible" or "non-credible". Tools such as these can be applied to Twitter datasets containing information at the intersection of CAIM and COVID-19 to both compare with and validate our findings. Additionally, while our sentiment and emotion analysis provides us with insight into the polarity of sentiment and the emotions expressed in our dataset, a qualitative content analysis could identify: specific themes pertaining to this intersection of topics, trending topics, ideas most commonly linked in the text, and characterize who is generating and sharing related tweets.

Strengths and Limitations

We extracted a large number of Tweets that were posted at the height of the first wave of the COVID-19 pandemic between March 03, 2020 and June 10, 2020 inclusive and applied two different methods to analyze the tweet dataset. We employed a supervised machine learning approach utilizing the Text2Vec package for our sentiment analysis. The purpose of this method was to acquire generalizable results built on labelled data which provided results for each tweet as a whole based on the combination of words (respecting their locality and relation to each other), rather than a lexicon-based analysis which treats each word as a separate entity. Using the highly-cited Sentiment140 dataset for training our sentiment analysis model is a strength as the dataset contains 1.6 Million machine-labelled tweets into positive and negative. Finally, the Syuzhet package in R is considered a good machine learning technique to provide an emotion representation of the words within the tweets based on the NRC emotion lexicon database. We applied a fair amount of rigor in developing our search strategy by consulting reviews of CAIM, MeSH terms, and conducting trial searches within Twitter to ensure that we identified the most relevant and used terms.

Limitations include the fact that we did not account for all CAIMs, as they represent a dynamic and wide range of therapies. This was mitigated by the preliminary searches of Twitter for the CAIMs most commonly mentioned in tweets that informed our decision on what terms to include. A further limitation is that sentiment has been classified along the continuum of positive to negative, without additional approaches to detect such linguistic elements as sarcasm, context, and complex emotions or sentiment, which are evident in the tweets illustrated in Table 3 [78]. On balance, our algorithm had an AUC of .89 which is considered a good performance for a classifier. During the initial phases of the study we relied on the Twitter rest/standard API, which

does not allow a tweet retrieval past a certain time. Due to this limitation within the Twitter API, we relied on the Harvard Dataverse COVID-19 dataset, which had not been updated past June 10, 2020 at the time of study completion. As such, we have a narrow window of time reflected in the analyzed tweets. If a new dataset becomes available, we could apply our methods to discern how the sentiments and emotions in tweets have evolved as the pandemic has progressed. We limited our tweets to originals and in English; given the global nature of the pandemic and the regional differences in CAIM treatments, tweets posted in other languages undoubtedly also contain information of value that was omitted from our analysis. Future research on the amplification of messaging via retweets could also lead to new insights into the spread of CAIM-related content in the context of this pandemic.

Conclusions

We conducted a sentiment analysis with the objective of understanding what was being mentioned about CAIM in the context of the COVID-19 pandemic on Twitter. A total of 17 528 English-language tweets were analyzed. The most common CAIM-related hashtag used was #vitamin followed by #ayurveda. Most of the tweets, 54.6%, were classified as positive, followed by neutral (30.6%) and negative (14.8%). The most frequent emotions expressed across tweets was trust, followed by fear. Social media continues to be an important source of data that provides a range of advantages over traditional data sampling techniques, such as surveys and interviews. The use of sentiment analysis on Twitter data at the intersection of CAIM and COVID-19 provides insight into how such data is being disseminated. Our findings warrant further qualitative investigation of the emotions identified across tweets analysed, which could

be used to combat against misinformation and inform improved public health strategies surrounding the use of social media information.

Chapter 4 References

[1] World Health Organization (WHO). [Internet]. Coronavirus Disease (COVID-19); 2020. [cited 2021 Jan 14]. Available from: https://www.who.int/news-room/q-a-detail/q-a-coronaviruses.

[2] World Health Organization (WHO). [Internet]. Coronavirus Disease (COVID-19) Pandemic; 2020. [cited 2021 Jan 14]. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019.

[3] Chu DK, Akl EA, Duda S, Solo K, Yaacoub S, Schünemann HJ, et al. Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: A systematic review and meta-analysis. The Lancet. 2020 Jun 1. https://doi.org/10.1016/j.jvs.2020.07.040.

[4] WHO Solidarity Trial Consortium. Repurposed antiviral drugs for COVID-19—interim WHO SOLIDARITY trial results. New England Journal of Medicine. 2020 Dec 2. https://doi.org/10.1056/NEJMoa2023184.

[5] Simonovich VA, Burgos Pratx LD, Scibona P, Beruto MV, Vallone MG, Vázquez C, et al. A randomized trial of convalescent plasma in COVID-19 severe pneumonia. New England Journal of Medicine. 2020 Nov 24. https://doi.org/10.1056/NEJMoa2031304.

[6] Lurie N, Saville M, Hatchett R, Halton J. Developing COVID-19 vaccines at pandemic speed. New England Journal of Medicine. 2020 May 21;382(21):1969-73. https://doi.org/10.1056/NEJMp2005630.

[7] Peiris M, Leung GM. What can we expect from first-generation COVID-19 vaccines?. The Lancet. 2020 Nov 7;396(10261):1467-9. https://doi.org/10.1016/S0140-6736(20)31976-0.

[8] National Center for Complementary and Integrative Health (NCCIH). [Internet]. In the News: Coronavirus and "Alternative" Treatments; 2020 [cited 2021 Jan 14]. Available from: https://www.nccih.nih.gov/health/in-the-news-coronavirus-and-alternative-treatments.

[9] National Center for Complementary and Integrative Health (NCCIH). [Internet]. Complementary, Alternative, or Integrative Health: What's In a Name?; 2018 [cited 2021 Jan 14]. Available from: https://www.nccih.nih.gov/health/complementary-alternative-or-integrative-health-whats-in-a-name.

[10] Bianchini C, Truccolo I, Bidoli E, Group CI, Mazzocut M. Avoiding misleading information: A study of complementary medicine online information for cancer patients. Library & Information Science Research. 2019 Jan 1;41(1):67-77. https://doi.org/10.1016/j.lisr.2019.02.006.

[11] Murdoch B, Zarzeczny A, Caulfield T. Exploiting science? A systematic analysis of complementary and alternative medicine clinic websites' marketing of stem cell therapies. BMJ Open. 2018 Feb 1;8(2):e019414. https://doi.org/10.1136/bmjopen-2017-019414.

[12] Cancer.org. [Internet]. Why are complementary and alternative therapies harder to evaluate?; 2020 [cited 2021 Jan 14]. Available from: https://www.cancer.org/treatment/treatments-and-side-effects/complementary-and-alternative-medicine/complementary-and-alternative-methods-and-cancer/why-cam-is-hard-to-evaluate.html.

[13] Chen AT, Taylor-Swanson L, Buie RW, Park A, Conway M. Characterizing websites that provide information about complementary and integrative health: Systematic

search and evaluation of five domains. Interactive Journal of Medical Research. 2018;7(2):e14. https://doi.org/10.2196/ijmr.9803.

[14] Sharma V, Holmes JH, Sarkar IN. Identifying complementary and alternative medicine usage information from internet resources. Methods of Information in Medicine. 2016;55(04):322-32. https://doi.org/10.3414/ME15-01-0154.

[15] Mazzocut M, Truccolo I, Antonini M, Rinaldi F, Omero P, Ferrarin E, et al. Web conversations about complementary and alternative medicines and cancer: Content and sentiment analysis. Journal of Medical Internet Research. 2016;18(6):e120. https://doi.org/10.2196/jmir.5521.

[16] Korda H, Itani Z. Harnessing social media for health promotion and behavior change. Health Promotion Practice. 2013 Jan;14(1):15-23. https://doi.org/10.1177/1524839911405850.

[17] Chou WY, Hunt YM, Beckjord EB, Moser RP, Hesse BW. Social media use in the United States: Implications for health communication. Journal of Medical Internet Research. 2009;11(4):e48. https://doi.org/10.2196/jmir.1249.

[18] Moorhead SA, Hazlett DE, Harrison L, Carroll JK, Irwin A, Hoving C. A new dimension of health care: Systematic review of the uses, benefits, and limitations of social media for health communication. Journal of Medical Internet Research. 2013;15(4):e85. https://doi.org/10.2196/jmir.1933.

[19] Liddy ED. Natural language processing. Encyclopaedia of library and information science [Internet]. 2nd ed. New York: Marcel Decker, Inc.; 2001. [cited 2021 Jan 14]. Available from: https://surface.syr.edu/cnlp/11/.

[20] Gohil S, Vuik S, Darzi A. Sentiment analysis of health care tweets: Review of the methods used. JMIR Public Health and Surveillance. 2018;4(2):e43. https://doi.org/10.2196/publichealth.5789.

[21] Signorini A, Segre AM, Polgreen PM. The use of twitter to track levels of disease activity and public concern in the US during the influenza A H1N1 pandemic. PloS One. 2011;6(5). https://doi.org/10.1371/journal.pone.0019467.

[22] Szomszor M, Kostkova P, St Louis C. Twitter informatics: Tracking and understanding public reaction during the 2009 swine flu pandemic. 2011 IEEE/WIC/ACM International Conferences on Web Intelligence and Intelligent Agent Technology; 2011 Aug 22; Vol. 1, p. 320-3; IEEE. https://doi.org/10.1109/WI-IAT.2011.311.

[23] Kostkova P, Szomszor M, St. Louis C. # swineflu: The use of twitter as an early warning and risk communication tool in the 2009 swine flu pandemic. ACM Transactions on Management Information Systems. 2014 Jul 1;5(2):1-25. https://doi.org/10.1145/2597892.

[24] Chew C, Eysenbach G. Pandemics in the age of twitter: Content analysis of tweets during the 2009 H1N1 outbreak. PloS One. 2010;5(11). https://doi.org/10.1371/journal.pone.0014118.

[25] Delgado-López PD, Corrales-García EM. Influence of internet and social media in the promotion of alternative oncology, cancer quackery, and the predatory publishing phenomenon. Cureus. 2018 May;10(5). https://doi.org/10.7759/cureus.2617.

[26] Marcon AR, Klostermann P, Caulfield T. Chiropractic and spinal manipulation therapy on twitter: case study examining the presence of critiques and debates. JMIR Public Health and Surveillance. 2016;2(2):e153. https://doi.org/10.2196/publichealth.5739.

[27] Talabis MRM, McPherson R, Miyamoto I, Martin JL, Kaye D. Chapter 1: Analytics defined. In: Information security analytics. Elsevier; 2015. p. 1-12. https://doi.org/10.1016/B978-0-12-800207-0.00001-0.

[28] Go A, Bhayani R, Huang L. Twitter sentiment classification using distant supervision. CS224N project report, Stanford, 1(12), 2009. https://www-cs.stanford.edu/people/alecmgo/papers/TwitterDistantSupervision09.pdf.

[29] Sentiment140. [Internet]. General Information; 2021 [cited 2021 Jan 14]. Available from: http://help.sentiment140.com/.

[30] Stanford University. [Internet]. Glmnet Vignette; 2014 [cited 2021 Jan 14]. Available from: https://web.stanford.edu/~hastie/glmnet/glmnet_alpha.html.

[31] The Comprehensive R Archive Network. [Internet]. Introduction to the Syuzhet Package; 2017. [cited 2021 Jan 14]. Available from: https://cran.r-project.org/web/packages/syuzhet/vignettes/syuzhet-vignette.html.

[32] Cochrane Complementary Medicine. [Internet]. Operational Definition of Complementary Medicine; 2011 [cited 2021 Jan 14]. Available from: https://cam.cochrane.org/operational-definition-complementary-medicine.

[33] Ng JY, Boon HS, Thompson AK, Whitehead CR. Making sense of "alternative", "complementary", "unconventional" and "integrative" medicine: exploring the terms and meanings through a textual analysis. BMC Complementary and Alternative Medicine. 2016 Dec 1;16(1):134. https://doi.org/10.1186/s12906-016-1111-3.

[34] George Washington University. [Internet]. TweetSets. Twitter datasets for research and archiving; 2020 [cited 2021 Jan 14]. Available from: https://tweetsets.library.gwu.edu/.

[35] Zenodo. [Internet]. gwu-libraries/TweetSets: Version 1.1.1; 2018. [cited 2021 Jan 14]. Available at: https://doi.org/10.5281/zenodo.1289426.

[36] Harvard University. [Internet]. Harvard Dataverse; 2020 [cited 2021 Jan 14]. Available from: https://dataverse.harvard.edu/.

[37] Harvard University. [Internet]. Harvard Dataverse. Coronavirus Tweet Id]; 2020 [cited 2021 Jan 14]. Available from: https://doi.org/10.7910/DVN/LW0BTB.

[38] Documenting the Now. [Computer Software]. Hydrator; 2020 [cited 2021 Jan 14]. Available from https://github.com/docnow/hydrator.

[39] Muhammad A, Wiratunga N, Lothian R. Contextual sentiment analysis for social media genres. Knowledge-Based Systems. 2016 Sep 15;108:92-101. https://doi.org/10.1016/j.knosys.2016.05.032.

[40] The Comprehensive R Archive Network. [Internet] Text2Vec: Modern Text Mining Framework for R; 2016 [cited 2021 Jan 14]. Available from: https://CRAN.R-project.org/package=text2vec.

[41] Verma T, Renu R, Gaur D. Tokenization and filtering process in RapidMiner. International Journal of Applied Information Systems. 2014 Apr;7(2):16-8. https://doi.org/10.5120/ijais14-451139.

[42] Houvardas J, Stamatatos E. N-gram feature selection for authorship identification. In: Euzenat J., Domingue J, editors. Artificial intelligence: Methodology, systems, and applications. AIMSA 2006. Lecture Notes in Computer Science, vol 4183. Berlin, Heidelberg: Springer; 2006. https://doi.org/10.1007/11861461_10.

[43] Järvelin A, Järvelin A, Järvelin K. s-grams: Defining generalized n-grams for information retrieval. Information Processing and Management. 2007 Jul 1;43(4):1005-1019. https://doi.org/10.1016/j.ipm.2006.09.016.

[44] Sueno HT. Converting text to numerical representation using modified Bayesian vectorization technique for multi-class classification. International Journal of Advanced Trends in Computer Science. 2020;9(4):5618-23. https://doi.org/10.30534/ijatcse/2020/211942020.

[45] Madsen RE, Sigurdsson S, Hansen LK, Larsen J. Pruning the vocabulary for better context recognition. In: Proceedings of the 17th International Conference on Pattern Recognition, 2004. ICPR 2004. 2004 Aug 26 (Vol. 2, pp. 483-488). IEEE. https://doi.org/10.1109/IJCNN.2004.1380163.

[46] Nimirthi P, Krishna PV, Obaidat MS, Saritha V. A framework for sentiment analysis based recommender system for agriculture using deep learning approach. In: Social network forensics, cyber security, and machine learning; 2019. p. 59-66. Singapore: Springer. https://doi.org/10.1007/978-981-13-1456-8_5.

[47] National Research Council Canada. [Internet]. The Sentiment and Emotion Lexicons; 2020. [cited 2021 Jan 14]. Available from: http://sentiment.nrc.ca/lexicons-for-research/.

[48] Mohammad SM, Turney PD. Crowdsourcing a word–emotion association lexicon. Computational Intelligence. 2013 Aug;29(3):436-65. https://doi.org/10.1111/j.1467-8640.2012.00460.x.

[49] Kapoor KK, Tamilmani K, Rana NP, Patil P, Dwivedi YK, Nerur S. Advances in social media research: Past, present and future. Information Systems Frontiers. 2018 Jun 1;20(3):531-58. https://doi.org/10.1007/s10796-017-9810-y.

[50] Mavragani A. Infodemiology and infoveillance: Scoping review. Journal of Medical Internet Research. 2020;22(4):e16206. https://doi.org/10.2196/16206.

[51] Eysenbach G. Infodemiology and infoveillance: Tracking online health information and cyberbehavior for public health. American Journal of Preventive Medicine. 2011 May 1;40(5):S154-8. https://doi.org/10.1016/j.amepre.2011.02.006.

[52] Samaras L, García-Barriocanal E, Sicilia MA. Comparing social media and Google to detect and predict severe epidemics. Scientific Reports. 2020 Mar 16;10(1):1-1. https://doi.org/10.1038/s41598-020-61686-9.

[53] Al-garadi MA, Khan MS, Varathan KD, Mujtaba G, Al-Kabsi AM. Using online social networks to track a pandemic: A systematic review. Journal of Biomedical Informatics. 2016 Aug 1;62:1-1. https://doi.org/10.1016/j.jbi.2016.05.005.

[54] Ritterman J, Osborne M, Klein E. Using prediction markets and Twitter to predict a swine flu pandemic. 1st International Workshop on Mining Social Media; 2009 Nov 9; Vol. 9, p. 9-17. https://www.research.ed.ac.uk/en/publications/using-prediction-markets-and-twitter-to-predict-a-swine-flu-pande.

[55] Jain VK, Kumar S. An effective approach to track levels of influenza-A (H1N1) pandemic in India using twitter. Procedia Computer Science. 2015 Jan 1;70:801-7. https://doi.org/10.1016/j.procs.2015.10.120.

[56] Lampos V, Cristianini N. Tracking the flu pandemic by monitoring the social web. 2010 2nd International Workshop on Cognitive Information Processing; 2010 Jun 14; p. 411-16; IEEE. https://doi.org/10.1109/CIP.2010.5604088.

[57] Caulfield T. Pseudoscience and COVID-19-we've had enough already. Nature. 2020 Apr 27. https://doi.org/10.1038/d41586-020-01266-z.

[58] Desta TT, Mulugeta T. Living with COVID-19-triggered pseudoscience and conspiracies. International Journal of Public Health. 2020 Jul;65(6):713-4. https://doi.org/10.1007/s00038-020-01412-4.

[59] Larson HJ. Blocking information on COVID-19 can fuel the spread of misinformation. Nature. 2020:306-. https://doi.org/10.1038/d41586-020-00920-w.

[60] Zarocostas J. How to fight an infodemic. The Lancet. 2020 Feb 29;395(10225):676. https://doi.org/10.1016/S0140-6736(20)30461-X.

[61] Klein SD, Torchetti L, Frei-Erb M, Wolf U. Usage of complementary medicine in Switzerland: results of the Swiss health survey 2012 and development since 2007. PloS one. 2015 Oct 29;10(10):e0141985. https://doi.org/10.1371/journal.pone.0141985.

[62] National Center for Complementary and Integrative Health (NCCIH). [Internet] Statistics on Complementary and Integrative Health Approaches; 2020. [cited 2021 Jan 14]. Available from: https://www.nccih.nih.gov/research/statistics-on-complementary-and-integrative-health-approaches.

[63] Esmail N. Complementary and Alternative Medicine: Use and Public Attitudes 1997, 2006, and 2016. Vancouver: Fraser Institute; 2017. 87 p. https://www.fraserinstitute.org/sites/default/files/complementary-and-alternative-medicine-2017.pdf.

[64] Lobera J, Rogero-García J. Scientific appearance and homeopathy. Determinants of Trust in complementary and alternative medicine. Health Communication. 2020 Apr 16:1-8. https://doi.org/10.1080/10410236.2020.1750764.

[65] Islahudin F, Shahdan IA, Mohamad-Samuri S. Association between belief and attitude toward preference of complementary alternative medicine use. Patient Preference and Adherence. 2017;11:913. https://doi.org/10.2147/PPA.S132282.

[66] O'Brien SK, Malacova E, Sherriff JL, Black LJ. The prevalence and predictors of dietary supplement use in the Australian population. Nutrients. 2017 Oct;9(10):1154. https://doi.org/10.3390/nu9101154.

[67] Moore J, McClain A, Hong MY. Dietary supplement use in the United States: Prevalence, trends, pros, and cons. Nutrition Today. 2020 Jul 1;55(4):174-81. https://doi.org/10.1097/NT.0000000000000402.

[68] Clarke TC, Black LI, Stussman BJ, Barnes PM, Nahin RL. Trends in the use of complementary health approaches among adults: United States, 2002–2012. National Health Statistics Reports. 2015 Feb 10(79):1. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4573565/.

[69] Xue J, Chen J, Chen C, Zheng C, Li S, Zhu T. Public discourse and sentiment during the COVID 19 pandemic: using latent Dirichlet allocation for topic modeling on Twitter. PloS One. 2020 Sep 25;15(9):e0239441. https://doi.org/10.1371/journal.pone.0239441.

[70] Hung M, Lauren E, Hon ES, Birmingham WC, Xu J, Su S, et al. Social network analysis of COVID-19 sentiments: application of artificial intelligence. Journal of Medical Internet Research. 2020;22(8):e22590. https://doi.org/10.2196/22590.

[71] Abd-Alrazaq A, Alhuwail D, Househ M, Hamdi M, Shah Z. Top concerns of tweeters during the COVID-19 pandemic: Infoveillance study. Journal of Medical Internet Research. 2020;22(4):e19016. https://doi.org/10.2196/19016.

[72] Mackey TK, Li J, Purushothaman V, Nali M, Shah N, Bardier C, et al. Big data, natural language processing, and deep learning to detect and characterize illicit COVID-19 product sales: infoveillance study on Twitter and Instagram. JMIR Public Health and Surveillance. 2020;6(3):e20794. https://doi.org/10.2196/20794.

[73] Kouzy R, Abi Jaoude J, Kraitem A, El Alam MB, Karam B, Adib E, et al. Coronavirus goes viral: quantifying the COVID-19 misinformation epidemic on Twitter. Cureus. 2020 Mar;12(3). https://doi.org/10.7759/cureus.7255.

[74] Singh L, Bansal S, Bode L, Budak C, Chi G, Kawintiranon K, et al. A first look at COVID-19 information and misinformation sharing on Twitter. arXiv preprint arXiv:2003.13907. 2020 Mar 31. https://arxiv.org/abs/2003.13907.

[75] Kawchuk G, Hartvigsen J, Harsted S, Nim CG, Nyirö L. Misinformation about spinal manipulation and boosting immunity: an analysis of Twitter activity during the COVID-19 crisis. Chiropractic & Manual Therapies. 2020 Dec;28(1):1-3. https://doi.org/10.1186/s12998-020-00319-4.

[76] Sharma K, Seo S, Meng C, Rambhatla S, Liu Y. Covid-19 on social media: Analyzing misinformation in twitter conversations. arXiv preprint arXiv:2003.12309. 2020 Mar 26. https://arxiv.org/abs/2003.12309.

[77] Al-Rakhami MS, Al-Amri AM. Lies Kill, Facts save: Detecting COVID-19 misinformation in Twitter. IEEE Access. 2020 Aug 26;8:1559 61-70. https://doi.org/10.1109/ACCESS.2020.3019600.

[78] Sarsam SM, Al-Samarraie H, Alzahrani AI, Wright B. Sarcasm detection using machine learning algorithms in Twitter: A systematic review. International Journal of Market Research. 2020 May 28. https://doi.org/10.1177%2F1470785320921779.

Chapter 5

Conclusion

Chapter 5: Conclusion

The thesis is comprised of three separate studies that relate to CAIM, NHPs, and medical cannabis. Parallels can be drawn across these therapy types in general, as previously outlined in Chapter 1, including patient preference and prevalence of use, quality of patient health information, and safety and effectiveness concerns. Indeed, knowledge of these parallels both informed the development of these three studies and emerged across findings. This conclusion chapter first summarizes the most important findings and addresses the strengths and limitations of each study. This is followed by a discussion of future directions and the associated methodological challenges of conducting research relating to CAIM, NHPs, and medical cannabis.

Contributions to the Health Research Literature

The first study comprises a descriptive cross-sectional survey determining NHP use disclosure to primary care physicians among patients attending a Canadian naturopathic clinic and is detailed in Chapter 2. In contrast to analytical cross-sectional studies, which involve the collection of data for both exposures and outcomes at a specific point in time in order to compare outcome differences between exposed and unexposed participants, the objective of a descriptive cross-sectional study is to characterize the prevalence of a health outcome in a select population [1,2]. Conducting this survey at a naturopathic clinic provided an opportunity to study a patient population with a high prevalence of NHP use (99%). This provided a clear picture of how this population uses NHPs and discloses this use to their healthcare providers. The study was conducted on the premise that misleading health claims and a lack of information about NHP-prescription drug interactions are rampant, and that patients often rely on family, friends, or the

internet for information regarding NHPs, rather than their MD(s) or other healthcare providers [3-6]. The non-disclosure rate was found to be 42% which was nearly identical to a study conducted at the same clinic 15 years prior [7]. Reasons for non-disclosure included the following: MDs do not approve of complementary and alternative medicine use (21%, 27 of 131); MDs would not understand (21%, 27 of 131); patients were uncomfortable talking about NHP use (5%, 7 of 131); and it was not relevant (5%, 6 of 131). Numerous safety and effectiveness concerns surrounding NHPs were also brought to light through conducting this survey, as a subset of patients, albeit small, reported using a number of herbal therapies that were issued consumer advisories by Health Canada in the past, namely kava kava and St. John's wort [8,9]. One value of a cross-sectional study is that it is relatively inexpensive and less time-consuming than other types of studies, such as those with an experimental design [1,2]. The administration and collection of surveys proved to be relatively straightforward, as an organized team of staff at the naturopathic clinic ensured to verbally invite each patient attending the clinic to participate in the survey. Furthermore, cross-sectional studies allow for data from a comparatively-large pool of participants to be collected and compared, allowing for numerous characteristics to be viewed all at once (age, gender, etc.) [1,2]. Cross-sectional studies are not without their methodological limitations, however, as they only capture data from a single point in time, and therefore, cannot be used to analyze behaviour over a period of time or establish long-term trends [1,2]. Though not necessarily applicable to descriptive cross-sectional studies, it is also worth mentioning that it is difficult to establish cause-and-effect relationships between variables based on this research method [1,2]. Furthermore, in cross-sectional studies, participants are susceptible to recall bias [1]; in other words, the findings are dependent on their self-reporting of NHP use (among other items collected) and are based on the assumption that

previous events or experiences were remembered and reported accurately. Limitations specific to this research, included a moderate response rate of 25%, and the restriction of the participant sample to a single naturopathic teaching clinic. As a result, these findings might not necessarily be generalizable to other patient groups using NHPs. In the survey, patients were asked to explicitly respond to questions which included the term "family physician" which may be perceived as a limitation, as some patients may not have had a family physician, or instead may have consulted another healthcare provider such as a nurse practitioner or pharmacist. In terms of future research, it would be worthwhile to investigate the reasons why healthcare practitioners do not ask about the use of NHP in patients, identify methods to promote inquiry, and facilitate decision-making with patients. Nevertheless, while some studies have investigated the rate of NHP use disclosure to primary care practitioners, this work provides updated findings specific to the Canadian naturopathic patient population.

The second study comprises a qualitative interview study that identified attitudes towards medical cannabis among family physicians practicing in Ontario, Canada and is presented in Chapter 3. A qualitative interview can be defined as a research method that resembles a conversation with a study participant, and is characteristically designed to allow respondents to share information in their own words. This method is particularly useful for gathering detailed information and understanding social processes (i.e. attitudes, opinions, perceptions of a given topic) [10-12]. In speaking with physician participants, it was revealed that their patients were increasingly inquiring about medical cannabis, with some patients disclosing use even prior to consulting with their physician. This was a cause of concern for many physicians interviewed, based on their beliefs that more research on medical cannabis is warranted before they would feel more comfortable in recommending it to their patients. Physicians also expressed concern

that they were being placed in a difficult situation, whereby, if they did not authorize it, their other option would be to refer their patients to cannabis clinics, yet they felt that such clinics provided patients with medical cannabis too liberally and without advising them in enough detail about the potential risks associated with its use. Other safety and effectiveness concerns highlighted by the physicians interviewed included the potential for interactions between medical cannabis and pharmaceutical medications as well as stand-alone adverse effects, potential harms specific to youth (i.e. brain development) and the elderly (ability to drive, capacity to care for themselves). Physicians felt that they lacked the necessary knowledge/training to counsel patients effectively on medical cannabis and expressed desires to learn more about the topic.

One major advantage of the qualitative interview study design is that it allows for the collection of highly-detailed information. Researchers are afforded the opportunity to explore topics in great depth through qualitative interviews, as participants elaborate on the details of their lived experiences, which cannot be captured by other methods which ask participants to "fit" their perspectives into the limited response options provided by the researcher (i.e. multiple-choice survey) [10-12]. Qualitative interviewing also provides the researcher with the opportunity to make observations beyond the participant's oral responses; for example, the respondent's vocal tone, delivery, and emphasis [10-12]. Although we interviewed a small number of physicians, sampling was conducted until saturation and recruitment of new participants was stopped when no additional themes appeared. To ensure the reliability and rigour of study findings, open coding and theme generalization were conducted by two experienced researchers independently and in duplicate, which reflects two strengths specific to the present study.

General disadvantages associated with the qualitative interview method include recall bias, and the fact that many steps comprising this type of study, including recruiting and interviewing participants, transcribing and reviewing transcripts, and coding data, can be time-intensive and costly [10,11]. Though not necessary pertinent to this study, it should also be noted that qualitative interviews involving sensitive or taboo topics and/or vulnerable populations, may also be emotionally taxing or even pose a safety risk to both the interviewers and interviewees [10,13,14]. Limitations specific to the present study included the fact that participants were recruited using snowball sampling which is prone to sampling bias. In addition, this study only captured the views of physicians working in urban settings and results may not be generalizable to rural physicians. Few participants approved medical cannabis, and therefore, this view may have been over-represented in our study. Participants may have censored their responses to report answers that would be perceived as more socially desirable, however, many of the physicians expressed their concerns about medical cannabis. Future research should explore the needs of family physicians, among other healthcare practitioners such as nurse practitioners and pharmacists, with respect to medical cannabis education. Increased awareness of the evidence of the benefits and harms of medical cannabis may allow physicians to feel more comfortable in discussing this issue with interested patients, and reduce their reliance on cannabis clinics, which may not always provide unbiased advice.

The third and final study comprises a sentiment analysis of Twitter data to explore how CAIM is mentioned in the context of the COVID-19 pandemic and is described in Chapter 4. A sentiment analysis can be defined as the examination of the polarity (i.e. positive, neutral or negative) of opinions and emotions contained in free-text natural language (i.e. words and symbols) [15,16]. Sentiment analyses have multiple applications and are commonly used in

business marketing to better understand consumers' opinions of a product [15,16]; however, their applications in the context of health-related topics discussed on social media have also gained popularity [16, 17]. The present sentiment analysis study was initiated based on the premise that there is not only a large patient preference for CAIM and a high prevalence of use of these therapies, but that sentiments surrounding such activities are being disseminated across Twitter in high volumes. Furthermore, it is known that social media is a common avenue to circulate (mis)information to many individuals rapidly, effectively, and with ease. Of 17 528 tweets analysed, the most popular hashtag related to CAIM used was #vitamin followed by #ayurveda. Most of the tweets were rated as positive (54.6%), followed by neutral (30.6%), and negative (14.8%). The most frequent emotions expressed through tweets were confidence, followed by fear. These findings indicate support for CAIM interventions for the prevention/treatment of COVID-19, despite the fact that none of these therapies have yet to demonstrate effectiveness for this disease. The use of sentiment analysis on Twitter data at the intersection of CAIM and COVID-19 offers insight into how these data are disseminated. The usefulness of the sentiment analysis research method is that it helps researchers to understand the conversations and discussions taking place between individuals on a given platform (i.e. Twitter) [17,18]. This can enable researchers to identify the spread of misinformation and understand how patients feel about their healthcare experiences, which can be used to identify gaps in patient/public perceptions of health-related topics and implement corrective measures [19-24]. Sentiment analysis also has the capability to overcome some of the limitations of traditional social science methods that rely on time-consuming, costly, retrospective, time-lagged, and smaller-scale approaches (i.e. surveys and interviews), which achieving similar if not equivalent results [25-27].

The disadvantages associated with sentiment analyses primarily revolve around limitations of machine-learning. In most cases, sentiment analyses cannot completely replace the need for a researcher to read (at least a subset of) the free-text natural language being analyzed. Often, useful nuances in sentences themselves exist which fail to be captured by sentiment analysis [15,28]. Furthermore, the expression of sarcasm, irony, jokes, and exaggerations, are often challenging to capture by programs designed to carry out sentiment analysis; failing to recognize or account for these can skew study results [15,28]. Study-specific limitations include the fact that not all CAIMs could be accounted for, however, this was mitigated by conducting preliminary searches of Twitter for the CAIMs most mentioned in tweets that enabled informed decision-making on what terms to include. A further limitation is that sentiments were classified along the continuum of positive to negative, without additional approaches to detect linguistic elements such as sarcasm or context, among other complex emotions or sentiments. On balance, the algorithm had an AUC of .89 which is considered a good performance for a classifier. Tweets were collected from the Harvard Dataverse COVID-19 dataset, which had not been updated past June 10, 2020 at the time of study completion. Lastly, included tweets were limited to original material posted in English.

As misinformation about the COVID-19 pandemic is both rampant and pervasive on Twitter, among other social media platforms, several researchers have begun creating tools to track misinformation. Tools such as these can be applied to Twitter data containing information at the intersection of CAIM and COVID-19 to both compare with and validate this study's findings. In addition, while this sentiment and emotion analysis provides insight into the polarity of thoughts and emotions reflected in our dataset, a qualitative content analysis could further

identify specific themes pertaining to this intersection of topics, trending topics, ideas most commonly linked in the text, and characterize who is generating and sharing related tweets.

Field-Specific Future Directions and Challenges

The global popularity of CAIM, NHPs and medical cannabis have all increased considerably over the past decades [29-32], with Canadians having been no exception [33,34]. Along with this surge in interest, the evidence-base surrounding these types of therapies has been increasingly scrutinized, and calls have been made to demonstrate their safety and efficacy. In comparison to many conventional medical therapies, limited research has been conducted on CAIM, NHPs, and medical cannabis. Several factors exist which impede this research [35-37], such as negative attitudes towards such therapies [38], a lack of dedicated funding (more specifically with regards to CAIM and NHPs) [39], and even disagreement within the practitioners of, and research community studying, these therapies as to what constitutes best research evidence [40,41]. In addition to the challenges shared in researching CAIM and NHPs, the study of medical cannabis is further complicated by the fact that its use is mired by a long history of stigma and politicization, and it is regarded by many, even today, as an illegal recreational drug [44-46].

The conduct and application of research about these types of therapies face a number of unique challenges, primarily because the very cultural and philosophical underpinnings differ fundamentally between proponents of CAIM (inclusive of NHP and medical cannabis) therapies versus conventional healthcare [47-55]. While evidence-based medicine (EBM) has been discussed in the medical literature for many decades and is widely-regarded and accepted as the golden standard approach among conventional healthcare practitioners [56], the integration of EBM into the training and education of CAIM providers is comparatively more recent. This has

been the case because proponents of CAIM have historically favoured empiricism as the basis of obtaining knowledge and skills [47-55]. Differences in fundamental theories, philosophies, and cultures, have culminated in many CAIM stakeholders altogether opposing the EBM movement [52]. This inability of CAIM proponents to collaborate and agree with the dominant medical system has ultimately resulted in continued skepticism of both CAIM therapies and practitioners by those representing conventional healthcare [56-58]. Although the identification of EBM has been growing inside CAIM communities [59,60], this has been limited by a lack of credible, reliable and varied sources of evidence for research [61,62].

Beyond informing the development of the three studies comprising this thesis, knowledge of the parallels that can be drawn across CAIM, NHPs, and medical cannabis, can also be used to inform field-specific future directions based on the studies' findings. Across the three studies, data was captured from three key stakeholder groups, as follows: patients (study 1), physicians (study 2), and the general public (study 3). Despite the application of different research methods across these studies, the collective findings highlight that further research is warranted with respect to patient preference and prevalence of use, quality of patient health information, and safety and effectiveness concerns. The cross-sectional study of NHP use disclosure highlights a select patient population with a high prevalence of NHP use, combined with a willingness to consume products that may lack an evidence-profile for safety and efficacy. The qualitative interview study of family physician's attitudes towards medical cannabis identified that while interest in this therapy among patients is high, many physicians are hesitant to authorise cannabis due to perceived lack of clinical evidence. The sentiment analysis study exploring the polarity and emotions of text containing mention of CAIM and COVID-19 found on Twitter, suggests

that the public perceives CAIM therapies favourably, based on a proportionately higher quantity of positive sentiments and feelings expressed.

With these findings in mind, future research should target the exploration of information literacy and training/education surrounding CAIM, NHPs, and medical cannabis. The need for research investigating the development and implementation of CAIM, NHPs, and medical cannabis-specific training and education for conventional healthcare practitioner is necessary [60, 63-68], given the high patient preference and prevalence of use of these therapies. While some initiatives have taken root in more recent years [70-74], the standardization of such curriculum across medical schools, even across a single country such as Canada, is far from achieved [75]. At present, a need also exists to ensure that actively practicing conventional healthcare practitioners are aware of, and are provided with, the necessary resources to acquire the knowledge they require to counsel a patient on these therapy types. More recently, a number of eHealth tools, including signal detection systems [76-78], clinical decision support tools [79-80], and personal digital assistants [81-82], have been developed to incorporate aspects of CAIM, NHPs, and medical cannabis. Despite this, little research has explored how the delivery of these resources can be ameliorated by eHealth, which therefore comprises a warranted future direction.

Based on the findings that patients and the general public actively express positive interest in using, or at least considering, CAIM, NHPs, and medical cannabis, further research is justified in the area of understanding patient health literacy with respect to these types of therapies. In fact, typical characteristics of patients who actively choose to incorporate these types of therapies into their medical care include being well-educated (i.e. have earned a university degree) and having made attempts to educate themselves about the therapies they are

considering using [83,84]. The demographics of this patient population are often difficult to reconcile with the fact that the research evidence-base surrounding the safety and efficacy of CAIMs, NHPs, and MC are well-documented to be much less than that of conventional medicines (i.e. pharmaceuticals, surgery) [61,62]. While there has been considerable research that has been conducted that identified the reasons for using these therapies [85-87], there have been fewer studies that have investigated whether or how a patient could be guided to make evidence-informed decisions around these therapies [88-91], and even less research verifying whether such strategies are effective. For example, it remains to be seen which strategies developed to persuade a patient against taking a potentially harmful therapy, are effective. Lastly, proponents of CAIM, NHPs, and medical cannabis (i.e. CAIM practitioners) are philosophically in conflict with stakeholders in conventional healthcare [47-55]. Views held by opposing groups differ at the most fundamental levels, whereby some proponents of CAIM outright reject the scientific method (and therefore, disagree on the very definition of what constitutes “safe”, “efficacious” or “effective”), let alone the processes of preventing, diagnosing, treating or managing disease [47-55]. To address this fundamental barrier, arguably the most important future directions involve not only understanding relationships between stakeholders from both groups, but also exploring how they can be improved to first generate, then facilitate continuous and respectful dialogue. Fortunately, a trend towards the achievement of this goal appears visible as conventional healthcare providers are increasingly being taught to approach these therapies, their traditions, and their practitioners with respect [92-94]. Further, many CAIM practitioners are embracing the integrative medicine movement that combines their care with that of conventional healthcare practitioners [95-98]. In conclusion, it must be acknowledged that CAIM, NHPs, and medical cannabis differ from conventional medical

practices with respect to history, culture, and philosophy, therefore, a continuing need exists to develop improved and mutually-agreed upon methods for studying these therapies.

Chapter 5 References

[1] Wang X, Cheng Z. Cross-sectional studies: Strengths, weaknesses, and recommendations. Chest. 2020;158 Suppl 1:S65-71. https://doi.org/10.1016/j.chest.2020.03.012.

[2] Cummings CL. Cross-sectional design. In: Allen M, editor. The SAGE encyclopedia of communication research methods. Thousand Oaks, CA: SAGE Publications; 2018 [cited: 2021 Jan 14]. Available from: https://doi.org/10.4135/9781483381411.

[3] Raj N, Fernandes S, Charyulu NR, Dubey A, Ravi GS, Hebbar S. Postmarket surveillance: A review on key aspects and measures on the effective functioning in the context of the United Kingdom and Canada. Therapeutic Advances in Drug Safety. 2019;10:2042098619865413. https://doi.org/10.1177/2042098619865413.

[4] Frawley JE, Anheyer D, Davidson S, Jackson D. Prevalence and characteristics of complementary and alternative medicine use by Australian children. Journal of Paediatric and Child Health. 2017;53(8):782-7. https://doi.org/10.1111/jpc.13555.

[5] Pike A, Etchegary H, Godwin M, McCrate F, Crellin J, Mathews M, et al. Use of natural health products in children: Qualitative analysis of parents' experiences. Canadian Family Physician. 2013;59(8):e372-8. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3743714/.

[6] Awad A, Al-Shaye D. Public awareness, patterns of use and attitudes toward natural health products in Kuwait: A cross-sectional survey. BMC Complementary and Alternative Medicine. 2014;14:105. https://doi.org/10.1186/1472-6882-14-105.

[7] Busse JW, Heaton G, Wu P, Wilson KR, Mills EJ. Disclosure of NHP use to primary care physicians: A cross-sectional survey of naturopathic clinic attendees. Mayo Clinic Proceedings. 2005;80(5):616-23. https://doi.org/10.4065/80.5.616.

[8] Wharry S. Health Canada sounds warning over St. John's wort. CMAJ: Canadian Medical Association Journal. 2000 Jun 13;162(12):1723. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1232522/.

[9] Mills E, Singh R, Ross C, Ernst E, Ray JG. Sale of kava extract in some health food stores. CMAJ: Canadian Medical Association Journal. 2003 Nov 25;169(11):1158-9. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC264954/.

[10] McLellan E, MacQueen KM, Neidig JL. Beyond the qualitative interview: Data preparation and transcription. Field Methods. 2003 Feb;15(1):63-84. https://doi.org/10.1177/1525822X02239573.

[11] DiCicco-Bloom B, Crabtree BF. The qualitative research interview. Medical Education. 2006 Apr;40(4):314-21. https://doi.org/10.1111/j.1365-2929.2006.02418.x.

[12] Turner III DW. Qualitative interview design: a practical guide for novice investigators. The Qualitative Report. 2010 May 1;15(3):754. https://doi.org/10.46743/2160-3715/2010.1178.

[13] Liamputtong P. The sensitive and vulnerable researcher. Researching the vulnerable: A guide to sensitive research methods. London: Sage Publications; 2007. p. 71-94. Available from: https://doi.org/10.4135/9781849209861.

[14] Shaw RM, Howe J, Beazer J, Carr T. Ethics and positionality in qualitative research with vulnerable and marginal groups. Qualitative Research. 2020;20(3). https://doi.org/10.1177/1468794119841839.

[15] Thelwall M. Chapter 20 – Sentiment analysis for small and big data. In: Fielding NG, Lee RM, Blank G, editors. The SAGE handbook of online research methods. 2017. Available from: https://doi.org/10.4135/9781473957992.n20.

[16] Curini L, Fahey RA. Chapter 29 – Sentiment analysis and social media. In: Curini L, Franzese R, editors. The SAGE handbook of research methods in political science and international relations. 2020. Available from: https://doi.org/10.4135/9781526486387.n32.

[17] Gohil S, Vuik S, Darzi A. Sentiment analysis of health care tweets: Review of the methods used. JMIR Public Health and Surveillance. 2018;4(2):e43. https://doi.org/10.2196/publichealth.5789.

[18] Sinnenberg L, Buttenheim AM, Padrez K, Mancheno C, Ungar L, Merchant RM. Twitter as a tool for health research: A systematic review. American Journal of Public Health. 2017 Jan;107(1):e1-8. https://doi.org/10.2105/AJPH.2016.303512.

[19] Suarez-Lledo V, Alvarez-Galvez J. Prevalence of health misinformation on social media: Systematic review. Journal of Medical Internet Research. 2021;23(1):e17187. https://doi.org/10.2196/17187.

[20] Shu K, Wang S, Lee D, Liu H. Mining disinformation and fake news: Concepts, methods, and recent advancements. In: Shu K., Wang S., Lee D., Liu H., editors. Fake News, Disinformation, and Misinformation in Social Media – Emerging Research Challenges and Opportunities. Lecture Notes in Social Networks. [cited 2021 Jan 14]. 2020. Cham: Springer. Available from: https://doi.org/10.1007/978-3-030-42699-6_1.

[21] Greaves F, Ramirez-Cano D, Millett C, Darzi A, Donaldson L. Use of sentiment analysis for capturing patient experience from free-text. Journal of Medical Internet Research. 2013;15(11):e239. https://doi.org/10.2196/jmir.2721.

[22] Bahja M, Lycett M. Identifying patient experience from online resources via sentiment analysis and topic modelling. In: Proceedings of the 3rd IEEE/ACM International Conference on Big Data Computing, Applications and Technologies. 2016. Available from: https://dl.acm.org/doi/abs/10.1145/3006299.3006335.

[23] Greaves F, Ramirez-Cano D, Millett C, Darzi A, Donaldson L. Harnessing the cloud of patient experience: Using social media to detect poor quality healthcare. BMJ Quality & Safety. 2013;22(3). http://doi.org/10.1136/bmjqs-2012-001527.

[24] Zunic A, Corcoran P, Spasic I. Sentiment analysis in health and well-being: systematic review. JMIR Medical Informatics. 2020;8(1):e16023. https://doi.org/10.2196/16023.

[25] Chew C, Eysenbach G. Pandemics in the age of twitter: Content analysis of tweets during the 2009 H1N1 outbreak. PLOS One. 2010;5(11). https://doi.org/10.1371/journal.pone.0014118.

[26] Mavragani A. Infodemiology and infoveillance: Scoping review. Journal of Medical Internet Research. 2020;22(4):e16206. https://doi.org/10.2196/16206.

[27] Eysenbach G. Infodemiology and infoveillance: Tracking online health information and cyberbehavior for public health. American Journal of Preventive Medicine. 2011 May 1;40(5):S154-8. https://doi.org/10.1016/j.amepre.2011.02.006.

[28] Kunneman F, Liebrecht C, Mulken M, van den Bosch A. Signaling sarcasm: From hyperbole to hashtag. Information Processing & Management. 2015 Jul;51(4):500-9. https://doi.org/10.1016/j.ipm.2014.07.006.

[29] Frass M, Strassi R, Friehs H, Mullner M, Kundi M, Kaye A. Use and acceptance of complementary and alternative medicine among the general population and medical personnel: a systematic review. Ochsner Journal. 2012;12:45-56. https://pubmed.ncbi.nlm.nih.gov/22438782/.

[30] World Health Organization. [Internet]. WHO Global Report on Traditional and Complementary Medicine; 2019. [cited 2021 Jan 14]. Available from: https://www.who.int/traditional-complementary-integrative-medicine/WhoGlobalReportOnTraditionalAndComplementaryMedicine2019.pdf.

[31] Ekor M. The growing use of herbal medicines: Issues relating to adverse reactions and challenges in monitoring safety. Frontiers in Pharmacology. 2014 Jan 10;4:177. https://doi.org/10.3389/fphar.2013.00177.

[32] Medical Cannabis Market: Global Industry Trends, Share, Size, Growth, Opportunity and Forecast 2019-2024. Research and Markets Report. April 2019. [cited 2021 Jan 14]. Available from: https://www.researchandmarkets.com/reports/4763121/medical-cannabis-market-global-industry-trends.

[33] Esmail N. Complementary and alternative medicine: Use and public attitudes 1997, 2006, and 2016. Vancouver: Fraser Institute, 2017. [Internet]; 2020. [cited 2021 Jan 14]. Available from: https://www.fraserinstitute.org/sites/default/files/complementary-and-alternative-medicine-2017.pdf.

[34] Government of Canada. Data on cannabis for medical purposes. 2020. [Internet]. Health Canada. [cited 2021 Jan 14]. Available from: https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/research-data/medical-purpose.html.

[35] Veziari Y, Leach MJ, Kumar S. Barriers to the conduct and application of research in complementary and alternative medicine: A systematic review. BMC Complementary and Alternative Medicine. 2017 Dec;17(1):1-4. https://doi.org/10.1186/s12906-017-1660-0.

[36] Gertsch J. Analytical and pharmacological challenges in cannabis research. Planta Medica. 2018;84(04):213. https://doi.org/10.1055/s-0044-101051.

[37] National Academies of Sciences, Engineering, and Medicine. Challenges and barriers in conducting cannabis research. In: The health effects of cannabis and cannabinoids: The current state of evidence and recommendations for research. [Internet]; [cited 2021 Jan 14]. Washington, DC: National Academies Press. Available from: https://www.ncbi.nlm.nih.gov/books/NBK425757/.

[38] Leach MJ, Tucker B. Current understandings of the research – practice gap from the viewpoint of complementary medicine academics: A mixed-method investigation. Explore: The Journal of Science & Healing. 2017;13(1):53-61. https://doi.org/10.1016/j.explore.2016.10.005.

[39] Fischer FH, Lewith G, Witt CM, Linde K, Von AK, Cardini F, et al. High prevalence but limited evidence in complementary and alternative medicine: Guidelines for future research. BMC Complementary and Alternative Medicine. 2014;14:46. https://doi.org/10.1186/1472-6882-14-46.

[40] Broom A, Adams J. Current issues and future directions in complementary and alternative medicine (CAM) research. Complementary Therapies in Medicine. 2007 Sep;15(3):217-20. https://doi.org/10.1016/j.ctim.2006.08.001.

[41] Gray AC, Steel A, Adams J. A critical integrative review of complementary medicine education research: Key issues and empirical gaps. BMC Complementary and Alternative Medicine. 2019 Dec;19(1):1-20. https://doi.org/10.1186/s12906-019-2466-z.

[42] Russo EB. Current therapeutic cannabis controversies and clinical trial design issues. Frontiers in Pharmacology. 2016 Sep 14;7:309. https://doi.org/10.3389/fphar.2016.00309.

[43] Starrels JL, Young SR, Azari SS, Becker WC, Edelman EJ, Liebschutz JM, et al. Disagreement and uncertainty among experts about how to respond to marijuana use in patients on long-term opioids for chronic pain: results of a Delphi study. Pain Medicine. 2020 Feb 1;21(2):247-54. https://doi.org/10.1093/pm/pnz153.

[44] Bottorff JL, Bissell LJL, Balneaves LG, Oliffe JL, Capler NR, Buxton J. Perceptions of cannabis as a stigmatized medicine: A qualitative descriptive study. Harm Reduction Journal. 2013 Feb 16;10:2. https://doi.org/10.1186/1477-7517-10-2.

[45] Bridgeman MB, Abazia DT. Medicinal cannabis: History, pharmacology, and implications for the acute care setting. Pharmacy and Therapeutics. 2017 Mar;42(3):180-8. https://pubmed.ncbi.nlm.nih.gov/28250701/.

[46] Lewis N, Sznitman SR. You brought it on yourself: The joint effects of message type, stigma, and responsibility attribution on attitudes toward medical cannabis. Journal of Communication. 2017 Apr 1;67(2):181-202. https://doi.org/10.1111/jcom.12287.

[47] Pan SY, Litscher G, Gao SH, Zhou SF, Yu ZL, Chen HQ, et al. Historical perspective of traditional indigenous medical practices: The current renaissance and conservation

of herbal resources. Evidence-Based Complementary and Alternative Medicine. 2014;2014:525340. https://doi.org/10.1155/2014/525340.

[48] Wardle J. Respecting science, respecting tradition: Evidence-based care in the integrative medicine professions. Australian Journal of Herbal Medicine. 2015;27:47-55. https://www.researchgate.net/publication/283020199_Respecting_science_respecting_tradition_Evidence-based_care_in_the_integrative_medicine_professions.

[49] Hollenberg D, Muzzin L. Epistemological challenges to integrative medicine: An anti-colonial perspective on the combination of complementary/alternative medicine with biomedicine. Health Sociology Review. 2010;19(1). https://doi.org/10.5172/hesr.2010.19.1.034.

[50] Keshet Y. The untenable boundaries of biomedical knowledge: Epistemologies and rhetoric strategies in the debate over evaluating complementary and alternative medicine. Health (London). 2009 Mar;13(2):131-55. https://doi.org/10.1177/1363459308099681.

[51] Ning AM. How 'alternative' is CAM? Rethinking conventional dichotomies between biomedicine and complementary/alternative medicine. Health (London). 2013 Mar;17(2):135-58. https://doi.org/10.1177/1363459312447252.

[52] Gale N. The sociology of traditional, complementary and alternative medicine. Sociology Compass. 2014 Jun;8(6):805-22. https://doi.org/10.1111/soc4.12182.

[53] Polich G, Dole C, Kaptchuk TJ. The need to act a little more 'scientific': Biomedical researchers investigating complementary and alternative medicine. Sociology of Health and Illness. 2010 Jan;32(1):106-22. https://doi.org/10.1111/j.1467-9566.2009.01185.x.

[54] Derkatch C. Bounding biomedicine: Evidence and rhetoric in the new science of alternative medicine. Chicago, IL: University of Chicago Press; 2016 April 21. Available from: https://press.uchicago.edu/ucp/books/book/chicago/B/bo22776774.html.

[55] Goldberg JM. Lessons learned in 20 years of developing evidence-based medicine. Journal of Paediatric Orthopaedics. 2012;32 Suppl 2:S193-4. https://doi.org/10.1097/BPO.0b013e3182595962.

[56] Wardle J, Adams J, Steel AE, Lui C. Current challenges and future directions for naturopathic medicine in Australia: A qualitative examination of perceptions and experiences from grassroots practice. BMC Complementary and Alternative Medicine. 2013;13:15. https://doi.org/10.1186/1472-6882-13-15.

[57] Singh N, Telles S. Awareness about bibliographic databases among students of Ayurveda and qualified Ayurveda practitioners. Journal of Ayurveda and Integrative Medicine. 2012 Apr-Jun;3(2):59-62. https://doi.org/10.4103/0975-9476.96516.

[58] Power M, Hopayian K. Exposing the evidence gap for complementary and alternative medicine to be integrated into science-based medicine. Journal of the Royal Society of Medicine. 2011 Apr;104(4):155-61. https://doi.org/10.1258/jrsm.2011.100271.

[59] Steel A, McEwen B. The need for higher degrees by research for complementary medicine practitioners. Australian Journal of Herbal Medicine. 2014;26:4. https://www.nhaa.org.au/docs/AJMH/Articles/Need_for_Higher_Degrees_v264_2014.pdf.

[60] Zwickey H, Schiffke H, Fleishman S, Haas M, Cruser DA, LeFebvre R, et al. Teaching evidence-based medicine at complementary and alternative medicine institutions:

Strategies, competencies, and evaluation. Journal of Alternative and Complementary Medicine. 2014 Dec 1;20(12):925-31. https://doi.org/10.1089/acm.2014.0087.

[61] Nissen N, Weidenhammer W, Schunder-Tatzber S, Johannessen H. Public health ethics for complementary and alternative medicine. European Journal of Integrative Medicine. 2013;5(1):62-7. http://doi.org/10.1016/j.eujim.2012.11.003.

[62] Fischer FH, Lewith G, Witt CM, Linde K, Von AK, Cardini F, et al. High prevalence but limited evidence in complementary and alternative medicine: Guidelines for future research. BMC Complementary and Alternative Medicine. 2014 Feb 6;14:46. https://doi.org/10.1186/1472-6882-14-46.

[63] Patel SJ, Kemper KJ, Kitzmiller JP. Physician perspectives on education, training, and implementation of complementary and alternative medicine. Advances in Medical Education and Practice. 2017;8:499. https://doi.org/10.2147/AMEP.S138572.

[64] Tarn DM, Guzmán JR, Good JS, Wenger NS, Coulter ID, Paterniti DA. Provider and patient expectations for dietary supplement discussions. Journal of General Internal Medicine. 2014 Sep;29(9):1242-9. https://doi.org/10.1007/s11606-014-2899-5.

[65] Kemper KJ, Gardiner P, Gobble J, Woods C. Expertise about herbs and dietary supplements among diverse health professionals. BMC Complementary and Alternative Medicine. 2006;6:15. https://doi.org/10.1186/1472-6882-6-15.

[66] Balneaves LG, Alraja A, Ziemianski D, McCuaig F, Ware M. A national needs assessment of Canadian nurse practitioners regarding cannabis for therapeutic purposes. Cannabis and Cannabinoid Research. 2018;3(1):66-73. https://doi.org/10.1089/can.2018.0002.

[67] Takakuwa KM, Mistretta A, Pazdernik VK, Sulak D. Education, knowledge, and practice characteristics of cannabis physicians: A survey of the Society of Cannabis Clinicians. Cannabis and Cannabinoid Research. 2021 Feb 12;6(1):58-65. https://doi.org/10.1089/can.2019.0025.

[68] Philpot LM, Ebbert JO, Hurt RT. A survey of the attitudes, beliefs and knowledge about medical cannabis among primary care providers. BMC Family Practice 2019;20:17. https://doi.org/10.1186/s12875-019-0906-y.

[69] Witt CM. Training oncology physicians to advise their patients on complementary and integrative medicine: An implementation study for a manual-guided consultation. Journal of Alternative and Complementary Medicine. Sep/Oct 2018;24(9-10):1016-17. https://doi.org/10.1002/cncr.32823.

[70] Niemtzow R, Baxter J, Gallagher RM, Pock A, Calabria K, Drake D, et al. Building capacity for complementary and integrative medicine through a large, cross-agency, acupuncture training program: Lessons learned from a military health system and Veterans Health Administration joint initiative project. Military Medicine. 2018 Nov 1;183(11-12):e486-e493. https://doi.org/10.1093/milmed/usy028.

[71] Ring M, Brodsky M, Dog TL, Sierpina V, Bailey M, Locke A, et al. Developing and implementing core competencies for integrative medicine fellowships. Academic Medicine. 2014 Mar;89(3):421-8. https://doi.org/10.1097/ACM.0000000000000148.

[72] Jani AA, Trask J, Ali A. Integrative medicine in preventive medicine education: Competency and curriculum development for preventive medicine and other specialty residency programs. American Journal of Preventive Medicine. 2015 Nov;49(5 Suppl 3):S222-9. https://doi.org/10.1016/j.amepre.2015.08.019.

[73] Allen ES, Connelly EN, Morris CD, Elmer PJ, Zwickey H. A train the trainer model for integrating evidence-based medicine into a complementary and alternative medicine training program. Explore (NY). Mar-Apr 2011;7(2):88-93. https://doi.org/10.1016/j.explore.2010.12.001.

[74] Hwang J, Arneson T, St. Peter W. Minnesota pharmacists and medical cannabis: A survey of knowledge, concerns, and interest prior to program launch. Pharmacy and Therapeutics. 2016 Nov;41(11):716-22. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5083080/.

[75] Verhoef MJ, Brundin-Mather R. A national approach to teaching complementary and alternative medicine in Canadian medical schools: The CAM in UME project. Proceedings of the Western Pharmacology Society Conference; 2007 Jan 1 (Vol. 50, p. 168). Western Pharmacology Society. Available from: https://pubmed.ncbi.nlm.nih.gov/18605258/.

[76] Li C, Xia J, Deng J, Chen W, Wang S, Jiang J, et al. A web-based quantitative signal detection system on adverse drug reaction in China. European Journal of Clinical Pharmacology. 2009;65(7):729-41. https://doi.org/10.1007/s00228-009-0638-3.

[77] Archer M, Proulx J, Shane-McWhorter L, Bray BE, Zeng-Treitler Q. Development of an alert system to detect drug interactions with herbal supplements using medical record data. AMIA Annual Symposium Proceedings. 2014;2014:249-55. https://pubmed.ncbi.nlm.nih.gov/25954326/.

[78] Yap KY, See CS, Kuo EY, Chui WK, Chan A. Utilizing mobile networks for the detection of clinically relevant interactions between chemotherapy regimens and

complementary and alternative medicines. Journal of Alternative and Complementary Medicine. 2012;18(2):165-74. https://doi.org/10.1089/acm.2010.0846.

[79] Clauson KA, Polen HH, Peak AS, Marsh WA, DiScala SL. Clinical decision support tools: Personal digital assistant versus online dietary supplement databases. Annals of Pharmacotherapy. 2008;42(11):1592-9. https://doi.org/10.1345/aph.1L297.

[80] Boehmer S, Karpa K. Evaluating the value of a web-based natural medicine clinical decision tool at an academic medical center. BMC Health Services Research. 2011;11(1):279. https://doi.org/10.1186/1472-6963-11-279.

[81] Fischer JE, Crowell K, Curtis P. Complementary and alternative medical reference software for personal digital assistants: evidence of clinical applicability. Complementary Health Practice Review. 2005;10(1):57-72. https://doi.org/10.1177/1533210104273020.

[82] Spanakis M, Sfakianakis S, Sakkalis V, Spanakis E. PharmActa: Empowering patients to avoid clinical significant drug–herb interactions. Medicines. 2019;6(1):26. https://doi.org/10.3390/medicines6010026.

[83] Institute of Medicine (US) Committee on the Use of Complementary and Alternative Medicine by the American Public. Prevalence, cost, and patterns of cam use. In Complementary and alternative medicine in the United States. Washington, DC: National Academies Press; 2005. Available from: https://www.ncbi.nlm.nih.gov/books/NBK83794/.

[84] Laiyemo MA, Nunlee-Bland G, Lombardo FA, Adams RG, Laiyemo AO. Characteristics and health perceptions of complementary and alternative medicine users

in the United States. American Journal of Medical Science. 2015 Feb;349(2):140-4. https://doi.org/10.1097/MAJ.0000000000000363

[85] Astin JA. Why patients use alternative medicine: results of a national study. JAMA. 1998 May 20;279(19):1548. https://doi.org/10.1001/jama.279.19.1548.

[86] Kristoffersen AE, Stub T, Musial F, Fønnebø V, Lillenes O, Norheim AJ. Prevalence and reasons for intentional use of complementary and alternative medicine as an adjunct to future visits to a medical doctor for chronic disease. BMC Complementary and Alternative Medicine. 2018 Dec;18(1):1-8. https://doi.org/10.1186/s12906-018-2179-8.

[87] McCaffrey AM, Pugh GF, O'Connor BB. Understanding patient preference for integrative medical care: results from patient focus groups. Journal of General Internal Medicine. 2007 Oct 12;22(11):1500-5. https://doi.org/10.1007/s11606-007-0302-5.

[88] Runfola JF, Levine E, Sherman P. Helping patients make decisions about complementary and alternative treatments: the social work role. Journal of Psychosocial Oncology. 2006 Aug 9;24(1):81-106. https://doi.org/10.1300/J077v24n01_07.

[89] Evans M, Shaw A, Thompson EA, Falk S, Turton P, Thompson T, et al. Decisions to use complementary and alternative medicine (CAM) by male cancer patients: Information-seeking roles and types of evidence used. BMC Complementary and Alternative Medicine. 2007 Dec;7(1):1-3. https://doi.org/10.1186/1472-6882-7-25.

[90] Caspi O, Koithan M, Criddle MW. Alternative medicine or “alternative” patients: A qualitative study of patient-oriented decision-making processes with respect to

complementary and alternative medicine. Medical Decision Making. 2004 Jan;24(1):64-79. https://doi.org/10.1177/0272989X03261567.

[91] Cannabis Standard [Internet]. [cited 2021 Jan 14]. Available from: https://cannabisstandard.com/.

[92] Fønnebø V, Grimsgaard S, Walach H, Ritenbaugh C, Norheim AJ, MacPherson H, et al. Researching complementary and alternative treatments – the gatekeepers are not at home. BMC Medical Research Methodology 2007;7:7. https://doi.org/10.1186/1471-2288-7-7.

[93] Verhoef MJ, Lewith G, Ritenbaugh C, Boon H, Fleishman S, Leis A. Complementary and alternative medicine whole systems research: Beyond identification of inadequacies of the RCT. Complementary Therapies in Medicine. 2005 Sep 1;13(3):206-12. https://doi.org/10.1016/j.ctim.2005.05.001.

[94] Wahner-Roedler DL, Lee MC, Chon TY, Cha SS, Loehrer LL, Bauer BA. Physicians' attitudes toward complementary and alternative medicine and their knowledge of specific therapies: 8-year follow-up at an academic medical center. Complementary Therapies in Clinical Practice. 2014 Feb;20(1):54-60. https://doi.org/10.1016/j.ctcp.2013.09.003.

[95] van der Watt ASJ, Nortje G, Kola L, Appiah-Poku J, Othieno C, Harris B, et al. Collaboration between biomedical and complementary and alternative care providers: Barriers and pathways. Quality Health Research. 2017 Dec;27(14):2177-88. https://doi.org/10.1177/1049732317729342.

[96] Nguyen J, Smith L, Hunter J, Harnett JE. Conventional and complementary medicine health care practitioners' perspectives on interprofessional communication: A

qualitative rapid review. Medicina (Kaunas). 2019 Sep 27;55(10):650. https://doi.org/10.3390/medicina55100650.

[97] Skovgaard L, Haahr N, Bjerre L, Launsø L. Types of treatment collaboration between conventional and alternative practitioners – results from a research project at a Danish MS hospital. International Journal of Integrated Care. 2010 Dec 23;10:e119. https://doi.org/10.5334/ijic.540.

[98] Pérard M, Mittring N, Schweiger D, Kummer C, Witt CM. MERGING conventional and complementary medicine in a clinic department – a theoretical model and practical recommendations. BMC Complementary and Alternative Medicine. 2015;15:172. https://doi.org/10.1186/s12906-015-0696-2.

Figures

Figures

Figure 1: Flowchart Depicting the Steps Taken for the Sentiment and Emotion Analysis of CAIM-Related COVID-19 Tweets

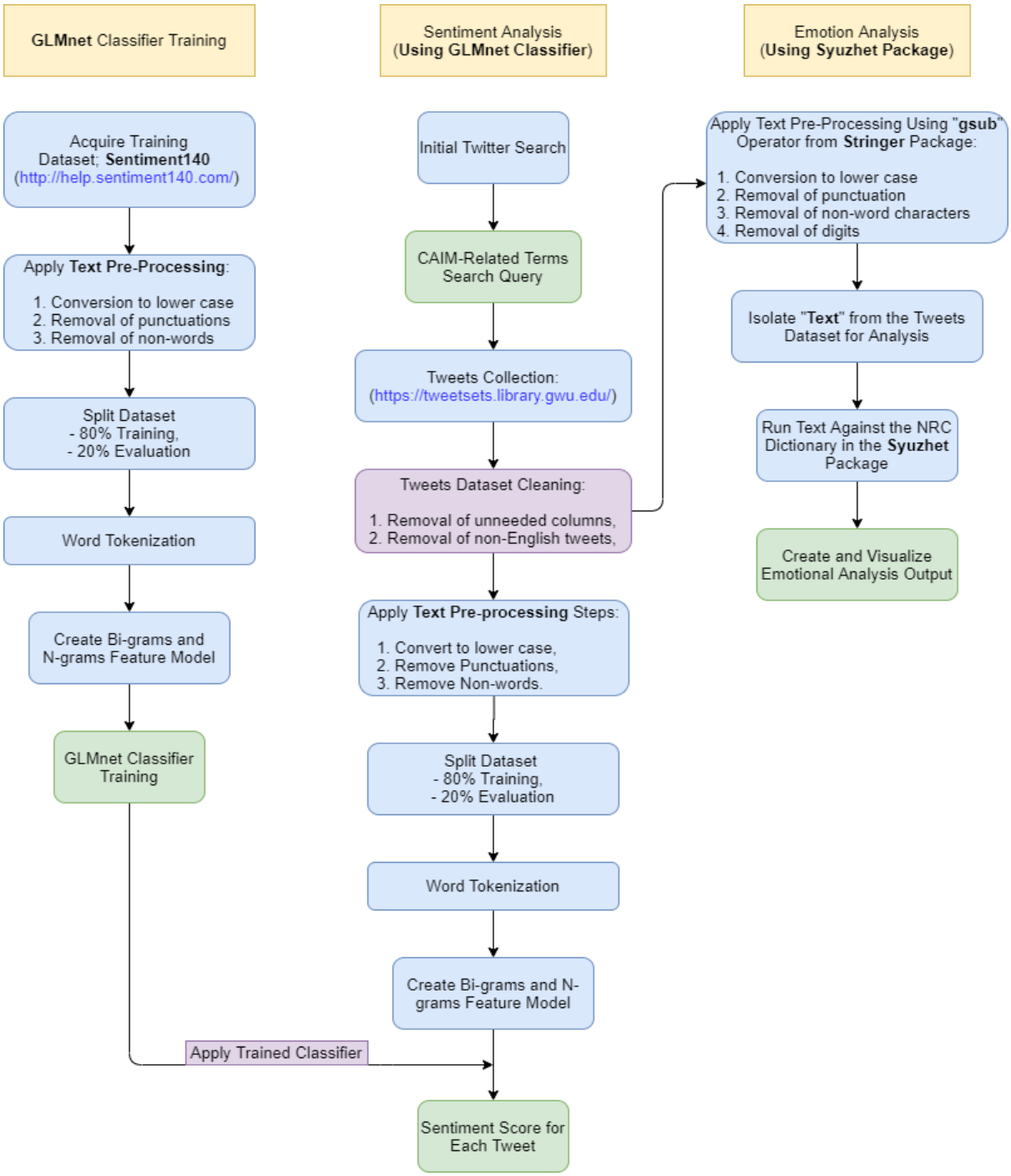


Figure 2: Frequency of CAIM-Related Tweets between March 03, 2020 and June 10, 2020 Shown Across 4-Day Intervals

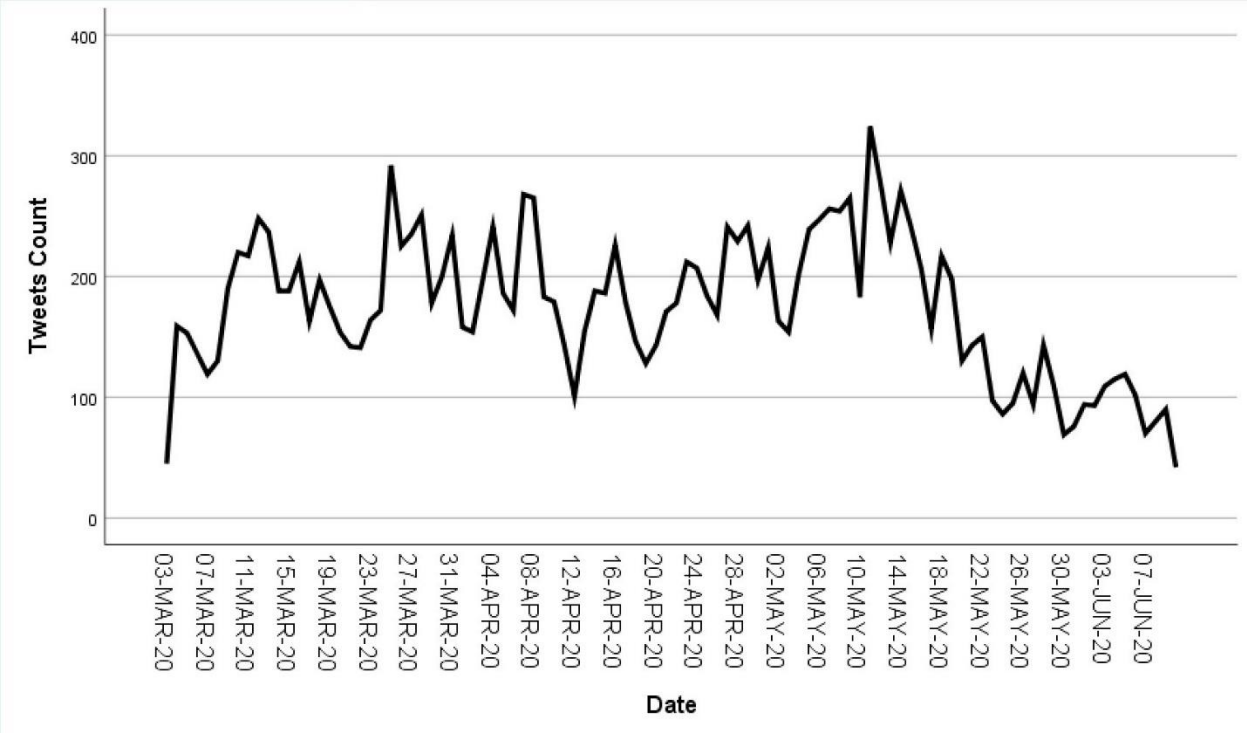


Figure 3A: Receiver Operator Curve Showing Performance of the Sentiment Analysis Classifier

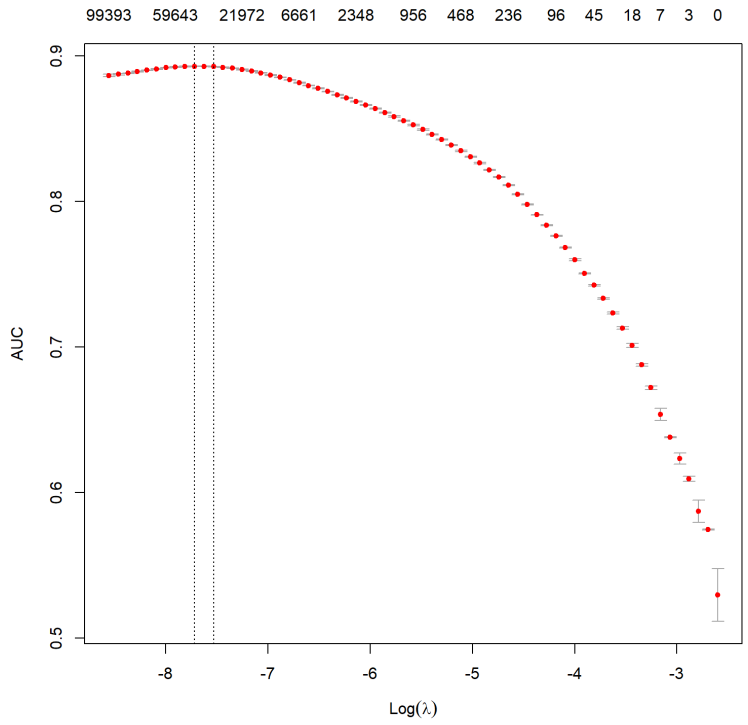


Figure 3B: Distribution of Sentiment Scores, from 0 (Negative) to 1 (Positive); Values between 0.35 and 0.65 are Considered Neutral

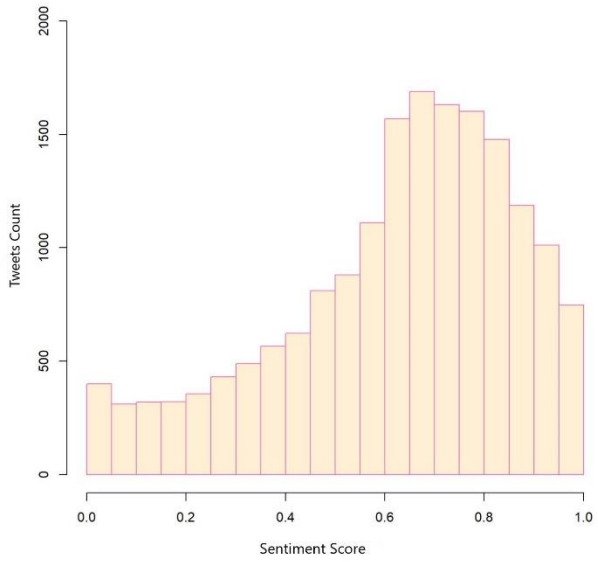
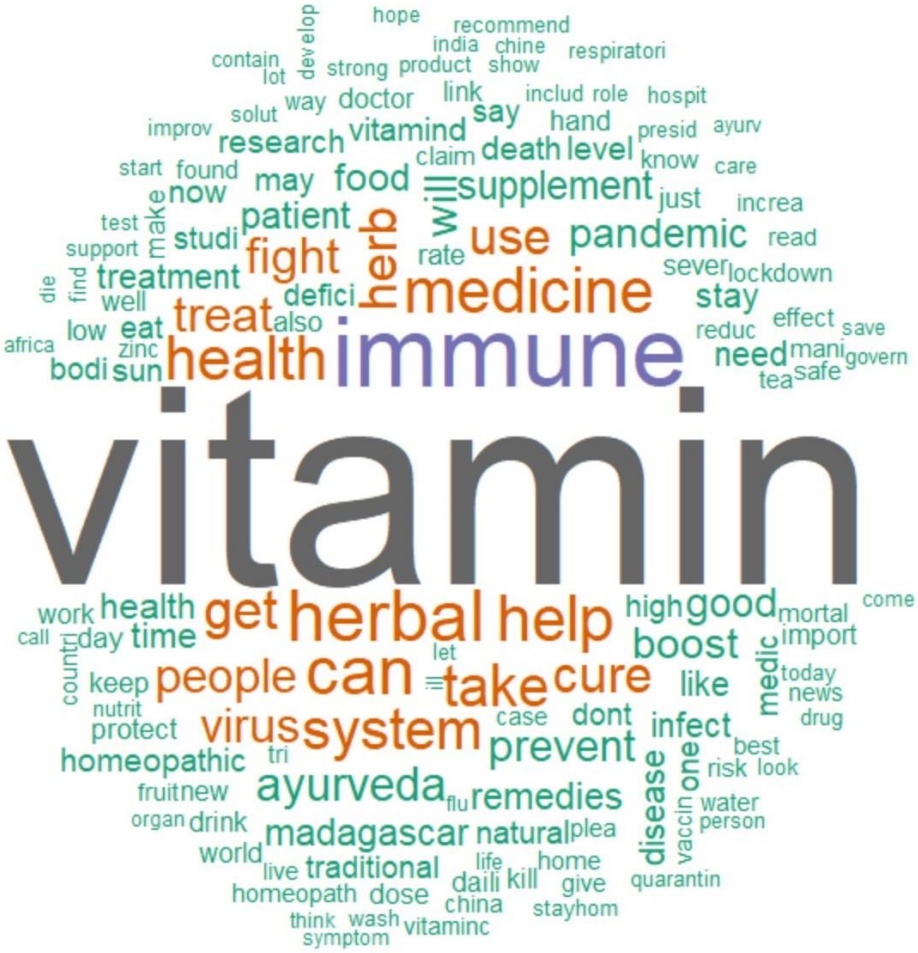


Figure 4: Word Cloud Depicting the Eight Emotions from the NRC Lexicon and Affiliated Terms from CAIM-Related COVID-19 Tweets



Tables

Tables

Chapter 2 Tables

Table 1. Characteristics of Survey Respondents[a]

Mean ± SD Age (range) (y) (n = 267)	40.5 ± 17.2 (range = 16 to 84)
Female Sex (n = 274)	211 (77.0%)
Ethnicity (n = 270)	
White	131 (48.3%)
Asian	29 (10.7%)
Mixed	26 (9.6%)
Jewish	17 (6.3%)
Southeast Asian	15 (5.5%)
Other[b]	52 (19.1%)
Education (n = 273)	
Did Not Graduate High School	12 (4.4%)
Graduated High School	28 (10.3%)
Graduated College	48 (17.6%)
Graduated University	185 (67.8%)
Employed (n = 258)	140 (54.3%)

Referral Source (n = 273)	
Medical Doctor	19 (7.0%)
Self	157 (57.5%)
Other	97 (35.5%)
Time Attending the CCNM Clinic (n = 275)	
First Visit	26 (9.5%)
<1 Month	27 (9.8%)
1–3 Months	35 (12.7%)
3–6 Months	21 (7.6%)
6–12 Months	18 (6.5%)
1–2 Years	48 (17.5%)
2–3 Years	33 (12.0%)
>3 Years	67 (24.4%)
No. of Visits to the CCNM Clinic per Year (n = 271)	
First vVisit	32 (11.8%)
1-3	40 (14.8%)
4-6	38 (14.0%)
7-10	54 (19.9%)

11-15	31 (11.4%)
16-20	27 (10.0%)
>20	49 (18.1%)
No. of Visits to Primary Care MD per Year (n = 272) [c]	
0-3	168 (61.8%)
4-6	48 (17.6%)
7-10	26 (9.6%)
11-15	9 (3.3%)
16-20	3 (1.1%)
>20	4 (1.5%)

[a]Not all respondents answered every question. Data are number (percentage) of respondents unless indicated otherwise. CCNM = Canadian College of Naturopathic Medicine.

[b]Includes African American (n = 12, 4.4%), Middle Eastern (n = 10, 3.7%), Latin American (n = 9, 3.3%), Native North American (n = 2, 0.7%), and "other" (n = 20, 7.4%).

[c]Fourteen respondents (5.1%) reported that they did not have a primary care MD.

Table 2. Specific Natural Health Products Used By Survey Respondents

Natural Product	**Frequency, No. (%)** **(n = 276)**
Vitamins	240 (87.0%)
Vitamin D	187 (67.8%)
Vitamin B(s)	128 (46.4%)
Vitamin C	105 (38.0%)
Multivitamin	77 (27.9%)
Herbs	164 (59.4%)
Tumeric	81 (29.3%)
Green Tea (or extract)	76 (27.5%)
Garlic	66 (23.9%)
Chamomile	62 (22.5%)
Echinacea	56 (20.3%)
Licorice	47 (17.0%)
Astragalus	26 (9.4%)
Milk Thistle	20 (7.2%)
St. John's Wort	8 (2.9%)

Natural Product	**Frequency, No. (%)** **(n = 276)**
Gingko Biloba	14 (5.1%)
Valarian	10 (3.6%)
Kava Kava	8 (2.9%)
Other CAM Products	
Magnesium	151 (54.7%)
Omega-3 fatty acids	138 (50.0%)
Probiotics	122 (44.2%)
Iron Supplement	67 (24.3%)
Topical (applied to skin) Natural Health Products	48 (17.4%)
Melatonin	47 (17.0%)
Calcium	44 (5.9%)
Other[a]	126 (45.7%)
Medical Cannabis	25 (9.1%)

CAM = complementary and alternative medicine.

[a]This category includes alpha lipoic acid, creatine, fibre, flaxseed oil, IPG gold, mushroom extracts, powder supplements, protein powder, royal jelly, sports supplements, tinctures, traditional medicines such as traditional Chinese medicines.

Table 3. Medication Use Reported By Survey Respondents

Type of Medication or Target Condition	**Medications Listed[a]**	**Frequency, No. (%) (n = 121)**
Thyroid Disease	Levothyroxine, Dessicated thyroid hormone	21 (17.4%)
Hypertension	Amlodipine Besylate, Atenolol, Bisoprolol, Candesartan, Furosemide, Hydrochlorothiazide, Irbesartan, losartan, Perindopril, Trandolapril	19 (15.7%)
Birth Control	Desogestrel - Ethinyl Estradiol, Levonorgestrel-Ethinyl Estrad, Levonorgestrel	18 (14.9%)
Depression	Bupropion HCL, Citalopram, Fluoxetine, Paroxetine HCL, Sertraline, Duloxetine, Amitriptyline, Escitalopram, Nortriptyline, Fluvoxamine	16 (13.2%)
Hyper-cholesterol	Atorvastatin, Rosuvastatin, Simvastatin	15 (12.4%)
Epilepsy	Carbamazepine, Clonazepam, Gabapentin, Lacosamide, Lamotrigine, Oxazepam, Pregabalin	11 (9.1%)
Asthma	Fluticasone, Albuterol, Formoterol – Mometasone, Beclomethasone Dipropionate, Albuterol, Glycopyrronium	9 (7.4%)
Diabetes	Insulin, Metformin	7 (5.8%)

Type of Medication or Target Condition	**Medications Listed[a]**	**Frequency, No. (%) (n = 121)**
Nonsteroidal Anti-inflammatory Drugs	Acetylsalicylic Acid, Celecoxib	7 (5.8%)
Ulcer	Dexlansoprazole, Esomeprazole, Omeprazole, Pantoprazole, Rabeprazole	6 (5.0%)
Attention Deficit Hyperactivity Disorder	Dextroamphetamine-Amphetamine, Lisdexamfetamine	5 (4.1%)
Pain	Hydromorphone, Oxycodone-Acetaminophen, Tramadol	4 (3.3%)
Menopause	Estrogen, Natural Progesterone, Progesterone, Bioidentical Progesterone, Estradiol	4 (3.3%)
Psychosis	Aripiprazole, Lurasidone, Risperidone, Quetiapine Fumarate	3 (2.5%)
Other[b]	Other	27 (22.3%)
[a]Some respondents reported their medication by name, and others by the condition targeted by their medication. Some respondents reported use of more than one medication. The		

Type of Medication or Target Condition	Medications Listed[a]	Frequency, No. (%) (n = 121)
reported frequency represents an aggregate of these data. Whenever possible, generic names are provided for reported medications. [b]The following medications taken for their respective disease/conditions were also reported, however, each only by less than 2% of all participants reporting to take medications: alcohol abuse (Naltrexone), allergy (Diphenhydramine, Mometasone) anxiety (Lorazepam), erectile dysfunction (Tadalafil), immunosuppressant (Azathioprine, Leflunomide, Methotrexate), unspecified hormonal therapy (Testosterone, Dehydroepiandrosterone), acne (Tretinoin), breast cancer (Trastuzumab), chest pain (Diltiazem), coagulant (Rivaroxaban), gout (Allopurinol), infection (Antibiotics), infertility (Clomiphene citrate), male pattern baldness (Minoxidil), muscle spasms, (Cyclobenzapine), osteoporosis (Alendronate), ovarian cancer (Lynparza), Parkinson's disease (Pramipexole), probiotic (Lactobacillus helveticus R0052, Bifidobacterium longum R0175), sleep disorder (Zopiclone), and urinary leakage (Fesoterodine).		

Table 4. Predictors of Medical Doctor-Patient Discussion of Natural Product Use

Variable	Univariable Analysis OR (95% CI)	p-value	Multivariable Analysis OR (95% CI)	p-value
Older Age	1.02 (1.01–1.03)	0.01	1.02 (1.00–1.04)	0.08
Female Gender	0.96 (0.55–1.66)	0.87	1.26 (0.64–2.45)	0.51
Level of Education	0.93 (0.70–1.23)	0.60	0.91 (0.65–1.29)	0.60
Duration of Time Attending the CCNM Clinic	1.17 (1.06–1.30)	0.002	1.11 (0.97–1.27)	0.13
Number of Visits per Year to the CCNM Clinic	1.15 (1.06–1.30)	0.03	1.09 (0.92–1.29)	0.32
Number of Visits per Year to One's Primary Care MD	1.13 (0.90–1.42)	0.28	0.96 (0.73–1.27)	0.77
Patient Concern over Interactions between Prescription Medication and Natural Products	2.10 (1.19–3.68)	0.01	1.81 (0.96–3.42)	0.07

Variable	Univariable Analysis OR (95% CI)	p-value	Multivariable Analysis OR (95% CI)	p-value
Primary Care MD Asks about Natural Product Use	5.89 (2.97–11.66)	<0.001	5.27 (2.57–10.78)	<0.001

CCNM = Canadian College of Naturopathic Medicine; OR = odds ratio; 95% CI = 95% confidence interval.

Table 5. Predictors of Whether a Primary Care Medical Doctor Asks About Natural Product Use

VARIABLE	Univariable Analysis OR, 95% CI	p-value	Multivariable Analysis OR, 95% CI	p-value
Older Age	1.01 (0.99–1.03)	0.32	1.01 (0.99–1.03)	0.32
Female Sex	0.95 (0.49–1.81)	0.87	0.96 (0.47–2.00)	0.92
Level of Education	1.15 (0.81–1.62)	0.44	1.21 (0.82–1.79)	0.34
Duration of Time Attending the CCNM Clinic	1.11 (0.99–1.25)	0.08	1.09 (0.94–1.27)	0.23
Number of Visits per Year to the CCNM Clinic	1.12 (0.97–1.30)	0.11	1.07 (0.90–1.28)	0.45
Number of Visits per Year to Primary Care MD	1.16 (0.91–1.48)	0.24	1.10 (0.83–1.46)	0.50
Use of Prescription Medication	1.25 (0.72–2.17)	0.44	1.20 (0.63–2.28)	0.58
Patient Concern of Interactions between Prescription Medication and Natural Products	1.32 (0.71–2.44)	0.38	1.16 (0.60–2.24)	0.66

VARIABLE	Univariable Analysis OR, 95% CI	p-value	Multivariable Analysis OR, 95% CI	p-value
OR = odds ratio; 95% CI = 95% Confidence Interval; N/S = p-values for all ethnic groups were greater than 0.05; CCNM = Canadian College of Naturopathic Medicine; and ND = naturopathic doctor.				

Appendix Table 1. Demographic Characteristics of Respondents from the 2003 and 2019 Surveys

	2003 Survey	**2019 Survey**	
Mean ± SD age (y)	37.7 ± 14.6 (n = 156)	40.5 ± 17.2 (n = 262)	p = 0.09
Female Sex (n, %)	112 (72%) (n = 156)	211 (77%) (n = 274)	p = 0.16
White Ethnicity (n, %)	111 (71%) (n = 156)	131 (47%) (n = 278)	p < 0.001
Education	(n = 156)	(n = 273)	p = 0.01
Did not Graduate High School	9 (6%)	12 (4%)	
Graduated High School	31 (20%)	28 (10%)	
Graduated College	33 (21%)	48 (18%)	
Graduated University	83 (53%)	185 (68%)	
Employed (n, %)	102 (66%) (n = 155)	140 (54%) (n = 260)	p = 0.09

Chapter 3 Tables

Table 1: Participant Demographics

Demographic	Value
Gender, no. (%)	
Male	6 (54.5)
Female	5 (45.5)
Years of age, median (range)	32 (27–74)
Specialization	
Family medicine only	10 (90.1)
Family medicine + public health/preventative medicine	1 (9.9)
Years in practice, median (range)	3.5 (1–33)
Location of medical school training, no. (%)	
Canada	8 (72.7)
Abroad (2 Caribbean; 1 United States)	3 (27.3)
Location of residency training, no. (%)	
Canada	11 (100.0)
Abroad	0 (0.0)
Urban or rural medical practice, no. (%)	
Urban	11 (100.0)
Rural	0 (0.0)
Authorizes or prescribes cannabis, no. (%)	
Yes	4 (36.4)

No	7 (63.6)

Table 2: Participant Quotes Supporting Thematic Analysis

Theme/subtheme	**Representative quote(s)**
Theme 1: Authorization of medical cannabis	
Subtheme 1: lack of evidence	I don't think most of the results of studies are that strong, they're not really well-designed studies for the most part … .(MC001) … some studies show that it's really effective and some studies show that it's not very effective. I suspect we've reached the point where we're probably a little too liberal for the conditions we prescribe it for. (MC009)
Subtheme 2: indications for therapeutic use	It's an okay adjunct, but it wouldn't be my first line for pain control at all. (MC002) "… it's more of a second- or third-line treatment … certain patients will find it helpful. (MC004) "There's very few things, if any, that I would go to medical cannabis as my first medication to treat. (MC008)
Subtheme 3: discomfort with therapeutic use of cannabis	I'm not 100% comfortable prescribing it, I do feel it might be helpful for some conditions, but I'm just not sure of the entire process of how to go about prescribing it and monitoring its use. (MC001) I don't prescribe it at all, I usually refer it out to clinics who are specialized in that. (MC002)

	I would be happy if it went away, in terms of [the] physician's responsibility toward it. I do not want to be prescribing marijuana. (MC006)
Subtheme 4: openness to emerging evidence	I think you have to keep an open mind, and you have to be attuned to what your patients are telling you … if you're not willing to listen to what patients are telling you about what they're using, and you don't present an unbiased front, then people aren't going to tell you what they're doing. (MC009) I think that we need to make sure we are providing our patients with access to evidence-based treatment and addressing any financial barriers and any stigma that may exist around particular treatments. I think we need to be careful of that when we are thinking about prescribing medical marijuana. (MC011)
Theme 2: Harm associated with the use of cannabis	
Subtheme 1: Effect on neurocognitive development	There is so much research saying that the brain is still changing and the reality is we don't know what happens to kids' brains when they take marijuana at the age of 15. And you know, I have so many patients who are young, who are like, "oh well now that is legalized for the age of 18, [and] I'm 14 and I'm so close, I'm sure it is fine". And I think the fact that legalization, especially at such a young age, gives the message to a lot of people that it's safe. (MC010)

Subtheme 2: Harms in the elderly	Maybe sort of looking at long-term effects on older people. All the medications we prescribe, there are certain geriatric populations that take various medications so I just want to know if there's anything in particular or things to watch for. (MC002) "… What is the effect of adding a cannabis product into a geriatric population that tends to be already medically more complex and already on lots of other medications and have multiple comorbidities? So, what impact does that have potentially, on their quality of life, ability to continue to drive a car, ability to continue to take care of themselves, and maybe dependence issues. (MC009)
Subtheme 3: Exacerbation of mental illness	Our patients have mental health issues, ranging from depression to anxiety to schizophrenia, and you know, you worry about harms for people especially for people who have [mental] illnesses. (MC006) So some of the [symptoms] I've noticed so far have been an increase in anxiety, difficulty with sleep, even cases of potential psychosis. (MC007)
Subtheme 4: Concerns regarding cannabis clinics	Cannabis clinics are fairly easy to access for most of these [patients]. (MC004) I would, for the most part, send patients to marijuana [clinics]; there are a couple in Hamilton. Everyone wound up getting it. Most people that did had addiction issues and mental health issues. (MC006) I've had patients who've come in and were prescribed medical cannabis and I would be like "oh you are so young, did the people go

	through the risks with you?" and they were like "no not really" and so I think that concerns me because it seems like even depending on which cannabis clinic certain people are referred to, they are not necessarily being presented with both the pros and the cons. (MC010)
Theme 3: Lack of knowledge surrounding medical cannabis	
Subtheme 1: Inadequate training	I'd say my knowledge of [medical cannabis] is pretty average … average enough to know that I would refer someone else to [authorize] medical cannabis if I thought it would help. And also enough to say that it won't help with your kind of pain or your set of conditions. So, I would know enough about that, but in terms of dosing and things like that I am not as comfortable, but it's not something I sought to really train in. (MC002) I went to medical school 35 years ago, there was zero training about cannabis and anything I learned about cannabis has been through continuing education that consists of online courses and information, position statements and summaries, sessions at conferences... So, the training has been whatever I chose to participate in, there's nothing required of me. (MC005) We did have some lectures from physicians in residency, [and] we also read a few articles during that time as well. I definitely don't know all

	of the up to date research that's ongoing in marijuana, it's just the things that I'm coming across. (MC007)
Subtheme 2: Need for further training and education	I just don't know what the regulations are in terms of how that's monitored, so my [further] education would hopefully help me figure out where I can direct patients to, sort of more, reputable sources of marijuana once it's been prescribed. (MC002) Something that comes out from time to time, that would actually be very helpful to get updates about what's [new] with medical cannabis. (MC007)
Subtheme 3: Physicians' role regarding cannabis	[Regarding medical cannabis], it is still not a prescription. A prescription includes the name of a substance, exactly what is in it, it includes a dosage, frequency, and duration. And it is dispensed by a pharmacist. None of those criteria are being fulfilled by cannabis. I am a little bit lost right now about what my form actually does for anyone. I think anyone and his dog can walk into a drug store and get whatever they want without approval from a physician. (MC004) Pretending that marijuana/cannabis is a prescription has been a joke … There is nothing about dosing or actual content; the traditional approach to making cannabis accessible really has just been to say this person has a medical condition and I believe this person may benefit from medical cannabis … Right now, it's very confusing why I have any role in making cannabis accessible to anyone. Whatever I write or say on a form does not decrease the cost of it. It does not make it

	funded, and it still does not provide any instructions that have to be followed … I would love to see [the] medical profession removed from the transaction completely and to make [cannabis] more like alcohol. (MC005)
Subtheme 4: Recreational vs. medicinal cannabis	I'm not sure how [recreational] products are regulated and if they know how much THC or CBD is in it, so I am not sure if [using recreational cannabis for therapeutic purposes] would be a good idea. (MC003) I think it's still helpful … being prescribed medical cannabis because a lot of people are not sure what's the best time to take it for medical reasons. I still think there's a role for medical cannabis even if recreational cannabis is approved for use now. (MC004)

Chapter 4 Tables

Table 1: Top 10 Most Frequent Terms from the Dataset of 17 528 CAIM-related COVID-19 Tweets

Term	**Tweet Count**
vitamin	10472
herbal	2532
vitamins	2477
Ayurveda	1594
herbs	1588
homeopathy	819
traditional medicine	470
homeopathic	416
herbal medicine	348
naturopathy	113

Table 2: Number of Words Identified in CAIM-Related COVID-19 Tweets Associated with the Eight Emotions from the NRC Lexicon

Emotion	**Word Count**
Trust	13,575
Fear	10,436
Anticipation	9,636
Joy	7,432
Sadness	6,176
Anger	5,515
Disgust	3,961
Surprise	3,771

Table 3: Illustrative Examples of Tweets with a Positive, Neutral, and Negative Sentiments

Tweet Text	**Sentiment Score**
If yall put MORE Trust in Herbal Remedies instead of ALL this #BigPharma Prescription Shit MAYBE you could see that the only ones who will PROFIT from this #COVID19 PLANdemic IS them and the Banks! https://t.co/63G6THEgTH	positive
Even in these troubled times, do not underestimate the benefits of a simply daily #walk. Choose your location carefully but take every opportunity you can to enjoy some fresh air, sunlight and vitamin D. Learn more on Sarahs Style & Dcor #blog #COVID19 https://t.co/KFx28wcasX https://t.co/63v73iMiOH	positive
Everything you need to know about #COVID19 but your government is too afraid to tell you. Get some sunshine on your skin. Eat vitamin D rich foods, and/or supplement. Wear a mask if somewhere crowded. https://t.co/AomlgyAeTChttps://t.co/KimgsPW7K7 https://t.co/xigTQ8SK5E https://t.co/SdKvDBcV1Q	neutral
It still surprises me that there is not more media and doctors on television telling us to strengthen our immune system, take vitamins, eat healthily, get sunlight They only seem to be talking about vaccine and drugs that are in the distant future #COVID19 #coronavirusuk	neutral
A positive test doesn't mean a healthy person is going to be sick. Also it doesn't say for the sick persons if this virus is responsible for the	negative

illness. Fear creates diseases. Be cautious but not fearful. Boost your immune system get vitamin D3 or sunlight once a day #coronavirus	
Disgusting NHS in go-slow on Hydroxychloroquine trials to "justify" the #Lockdown. Delays will probably needlessly kill 100's of patients. Only 2 hospitals No Zinc No Z-Pak or other antibiotic No mention of Vitamins C or D https://t.co/yJunw9PFAE #COVID19 #Covid19	negative

Appendices

Chapter 2 Appendix 1: Participant Information Letter and Informed Consent Form

October 2018

Re: Disclosure of Natural Product Use to Medical Doctors: Cross-sectional Survey of Naturopathic Clinic Attendees: An Update

Dear Madam/Sir,

I am requesting your voluntary participation in a research study that investigates the **Disclosure of Natural Product Use to Medical Doctors: Cross-sectional Survey of Naturopathic Clinic Attendees: An Update.**

My name is Jeremy Ng and I am a PhD student affiliated with the Department of Health Research Methods, Evidence, and Impact at McMaster University. I am conducting this survey as a research project, which will fulfill partial requirement for my doctoral thesis. This research project is supervised by my two co-investigators, Dr. Kieran Cooley (CCNM) and Dr. Jason Busse (McMaster University). We can be reached at any time should you have any questions or concerns about this project. Our contact information is listed at the bottom of this letter.

The purpose of my research project is to learn more about what factors might predict patient-medical doctor disclosure regarding the use of natural products.

What I learn as a result of this research may benefit medical doctors and their patients. By determining the factors that predict nondisclosure of natural product use, this knowledge can assist medical doctors in doing a thorough assessment of patients' use of medicinal products. This is of concern as medical doctors can then be aware of the effects natural products can have on their patients' health. In addition, patients can benefit as medical doctors can then individualize and appropriate the care they will provide and anticipate possible adverse natural product-prescription drug reactions.

If you are a patient who is above the age of 18 visiting the CCNM Robert Schad Naturopathic Clinic (RSNC) and consent to participating in the study, we would appreciate your help in voluntarily completing our questionnaire. This survey asks questions about your demographics, how frequently you visit the RSNC and other medical doctor(s) each year, or if it was your first

time visiting, prescription and natural product use, and the extent to which your medical doctor discussed your use of natural products. The project will begin in October 2018. We aim to recruit responses from 350 individuals from RSNC for this research study.

As indicated in the opening sentence above, participation in this research project is voluntary and not binding. You have not been selected to participate for any reason other than being a patient of RSNC during times that the study is in process. If you choose to participate, you may decline or withdraw from further participation at any time during the research project without negative consequences. No member of your RSNC care team (intern, supervising ND) or your medical doctor will be made aware of your decision regarding participation in this study, and they will absolutely not be made aware of any information that is conveyed.

As a participant in this research project, you will be asked to do the following: complete an 18-item questionnaire that you will submit in a sealed envelope to the receptionist for collection while in the waiting area prior to meeting with your naturopathic intern.

Completing the questionnaire will provide background and demographic information such as age, gender, education level, employment status, and how you found out about the Naturopathic clinic. It will also ask for use of health care patterns such as the length of use of the Naturopathic clinic, frequency of visits to the Naturopathic clinic and family medical doctor, and if you are currently using of prescription medicine or natural products. Lastly, you will be asked if your medical doctor discussed your use of natural products or prescription medicine and why if not, if you are concerned about potential natural product-prescription drug interactions, and if you believe your complementary and alternative medicine therapist should be in contact with your medical doctor. This information will be collected to help us understand what predicts patient nondisclosure of natural product use to their medical doctors.

Your participation in completing the questionnaire will take approximately 10 minutes. Participation is completely voluntary and there will not be any remuneration (payment, reward, prize, honorarium) for participating.

There are no known harms that can arise from participating in this study. As you are only to read and respond to the questions outlined in the survey, this poses no risk of physical harm. The questionnaire also does not ask personal questions that may cause any emotional discomfort, eliminating the risk for psychological harm. Additionally, there are no social risks as you will not be identified after completing the survey. While there may be an understandable self-imposed pressure to participate in the survey or attach judgement-value-based associations regarding non-disclosure, the informed consent will take steps to normalize non-participation and non-disclosure in a manner to reduce any of these potential risks.

Every effort will be made to maintain confidentiality and protect your privacy. We will not use your name or any information that would allow you to be identified in any presentation or publication that results from this study. Your signed informed consent will not be stored near or in association with any of the survey information you provided. In the highly unlikely event that this research information is required by court, you will be notified by a member of this study team.

The information you provide will be kept in a locked cabinet where only members of the study team will have access to it. Information kept on a computer will be protected by a password.

Once the study is complete, an archive of the data, without identifying information, will be deposited in a locked cabinet at CCNM for a period of five years. After this period of time, these records will be shredded.

I have listed my contact information for you below. Should you choose to participate in the research, you can contact me at any time during the research project with any questions that you may not have yet considered. Also listed is the contact information of my co-investigators whom you can contact at any time to verify the accuracy of this information letter. If you have any concerns about your rights as a research participant or in the research process, please contact the Chair of CCNM's Research Ethics Board at REBChair@ccnm.edu.

Thank you for considering participation in my research project.

Sincerely,

Jeremy Y. Ng, MSc, PhD Student, Principal Investigator
Doctoral Student, Department of Health
Research Methods, Evidence, and Impact,
Faculty of Health Sciences, McMaster University
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Dr. Kieran Cooley, ND, Co-Investigator
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Phone: (416) -498-1255 Ext. 324

Jason W. Busse, DC, PhD, Co-Investigator
Assistant Professor, Departments of Anaesthesia and Clinical Epidemiology & Biostatistics
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Hamilton, Ontario L8S 4K1 Canada
Email: bussejw@mcmaster.ca
Phone: (905) 525-9140 Ext. 21731

Free and Informed Consent Form
for
Disclosure of Natural Product Use to Primary Care Medical doctors: Cross-sectional Survey of Naturopathic Clinic Attendees: An Update

I, _____ (your full name), have carefully read and understood the attached Information Letter for the Disclosure of Natural Product Use to Primary Care Medical doctors: A Replication Study. I understand that if I have additional questions, I can contact Jeremy Ng or one of the co-investigators at any time during the research project. I also understand that I may decline or withdraw from participation at any time without negative consequences.

My signature below verifies that I have agreed to participate in the "Disclosure of Natural Product Use to Primary Care Medical doctors: Cross-sectional Survey of Naturopathic Clinic Attendees: An Update" as it has been described in the Information Letter. My signature below also verifies that I am fully competent to sign this Consent Form and that I have received a copy of the Information Letter and the Informed Consent Form for my files.

Agreement to Participate

_____ _____

Participant's Signature Date

_____

Print Name

Chapter 2 Appendix 2: 21-Item Patient Survey

NATURAL PRODUCT USE DISCLOSURE

Supplementary File 1. APPENDIX. The 21-Item Patient Survey

This survey is being conducted as a study for PhD student's project at McMaster University. The goal of this study is to enable all forms of health care to better serve your needs. No identification is required for this survey, and answers will be kept strictly confidential.

UPON COMPLETION PLEASE SUBMIT SEALED IN ENVELOPE TO RECEPTIONIST/RESEARCHER

Note: If you have already completed this survey, please do not submit again.

❑ I choose not to complete this survey
Selecting this option will not affect your treatment in any way.

Please answer the following:

1. Sex: Female❑ Male❑ Other❑

2. Age (yrs): _____

3. Are you currently employed? Yes No

4. What is your ethnic background?
- ❑ African American
- ❑ Asian
- ❑ Jewish
- ❑ Latin American
- ❑ Middle Eastern
- ❑ Native North American
- ❑ Southeast Asian
- ❑ White
- ❑ Mixed
- ❑ Other _____

5. What is your educational level:
- ❑ Not completed high school
- ❑ High school graduate
- ❑ College graduate
- ❑ University degree

6. What brought you to the Naturopathic clinic:
- ❑ Referred by physician
- ❑ Advertising
- ❑ Searched out yourself

Other _____

7. How long have you been accessing the Naturopathic clinic?
- ❑ First visit
- ❑ Less than one month
- ❑ 1-3 months
- ❑ 3-6 months
- ❑ 6-12 months
- ❑ 1-2 years
- ❑ 2-3 years
- ❑ More than 3 years

8. How many visits do you make to the Naturopathic clinic per year?
- ❑ First visit
- ❑ 1-3 visits per year
- ❑ 3-6 visits per year
- ❑ 6-10 visits per year
- ❑ 10-15 visits per year
- ❑ 15-20 visits per year
- ❑ More than 20 visits per year

9. Which of the following do you take on a regular basis (please circle):
- Vitamins and minerals
- Herbal remedies / Herbs
- Homeopathic medicines
- Traditional medicines such as Traditional Chinese Medicines
- Probiotics
- Other_____

10. Do you currently take any of the following (as single ingredients or part of a combination)n and how often?
- Astragalus _____
- Calcium _____
- Chamomile _____
- Echinacea _____
- Garlic _____
- Ginkgo biloba _____

Green tea (or extract)

_____

- Iron _____
- Licorice _____
- Kava kava _____
- Magnesium _____
- Melatonin _____
- Milk thistle _____
- Multivitamin _____
- Omega-3 fatty acids _____
- Probiotics _____
- St. John's wort _____

Turmeric (or curcumin extract)

_____

- Valerian _____
- Vitamin B(s) _____
- Vitamin C _____
- Vitamin D _____
- Topical (applied to skin) natural health products

_____

October 18, 2018 – Version 2

11. Do you take any other natural health products NOT already listed in Question #10? If yes, please list them and how often for each.

Yes No

_____
_____
_____

12. Do you currently take medical cannabis? If yes, what condition(s) do you take it for?

_____
_____
_____

13. How many visits do you make to your family physician per year?

- ❑ I do not have a family physician
- ❑ 0-3 visits per year
- ❑ 3-6 visits per year
- ❑ 6-10 visits per year
- ❑ 10-15 visits per year
- ❑ 15-20 visits per year
- ❑ Greater than 20 visits per year

14. Are you on any medications? Yes No

Please list (if applicable):

_____
_____
_____

15. Has your physician asked you about your use of natural health products?

Yes No

16. Do you discuss your alternative medicine product use with your physicians (i.e. non-naturopathic doctor)?

- ❑ Yes
- ❑ No
- ❑ Sometimes

Other_____

17. If you answered question 16 NO, why not? (check all that apply)

- ❑ They do not approve of alternative medicine use
- ❑ They would not understand
- ❑ I am uncomfortable talking about this with my physician
- ❑ It is none of their business
- ❑ Other_____

18. Do you discuss your prescription medication use with your alternative medicine provider (i.e. naturopathic doctor)?

- ❑ Yes
- ❑ No
- ❑ Sometimes

Other_____

19. If you answered question 18 NO, why not?

- ❑ They do not approve of medication use
- ❑ They would not understand
- ❑ I am uncomfortable talking about this with my complementary and alternative medicine therapist
- ❑ It is none of their business
- ❑ Other_____

20. Are you concerned about potential herb or nutrient interactions with your medications?

- ❑ Yes
- ❑ No
- ❑ Unsure
- ❑ Other_____

21. I believe that my complementary and alternative medicine therapist should be in contact with my physician:

- ❑ Strongly agree
- ❑ Moderately agree
- ❑ Disagree
- ❑ Strongly disagree
- ❑ Uncertain

This is the end of the survey. Thank you for your participation in our research study!

Chapter 3 Appendix 1: Participant Information Letter and Informed Consent Form

March 04, 2019

Title of Study: Attitudes and perceptions towards medical cannabis among family physicians practicing in Ontario

Locally Responsible Investigator and Principal Investigator,
Department/Hospital/Institution: Jason W. Busse, DC, PhD, Co-Investigator
Assistant Professor, Departments of Anaesthesia and Clinical Epidemiology & Biostatistics

---

Dear Ontario Family Physician:

I am requesting your voluntary participation in my research project, which is entitled **Attitudes and perceptions towards medical cannabis among family physicians practicing in Ontario**

My name is Jeremy Ng and I am a doctoral student at the Michael G. DeGroote National Pain Centre at McMaster University. I am a part of a research team that will be conducting a qualitative research project, which will fulfill partial requirement for my doctoral studies. This research will be conducted along with my supervisor and co-investigator Dr. Jason Busse. We both can be reached at any time during this research project to verify everything that I outline in this information letter and to answer any questions about the project that you may have. Our contact information is listed at the bottom of this letter. This study has been reviewed by the Hamilton Integrated Research Ethics Board (HIREB). The HIREB is responsible for ensuring that participants are informed of the risks associated with the research, and that participants are free to decide if participation is right for them. If you have any questions about your rights as a research participant, please call the Office of the Chair, Hamilton Integrated Research Ethics Board at 905.521.2100 x 42013.

The purpose of this research project is to conduct a field study, using qualitative research methods to explore and gather information on the attitudes and perceptions of family doctors based in Ontario towards the use and administration of medical cannabis. What I learn as a result of this research is relevant in the light of public debate of legalizing and decriminalizing cannabis in Canada and may benefit the overall public health in terms of prospective policies and regulations.

The specific study objectives are:

1. To explore the attitudes and perceptions of family doctors toward medical cannabis in Ontario;
2. To explore impressions towards medical cannabis post-legalization of recreational cannabis
3. To explore concerns on the regulations of medical cannabis,
4. To inquire re: perceptions of scientific research on the risks and benefits of cannabis

I intend to accomplish the goal(s) of the research by conducting in-depth one-on-one semi-structured interview with participants. Your participation in an interview will last from thirty minutes to one hour and take place in a mutually convenient location or over the phone. Interviews will be audiotaped for transcription, and hand written notes may be taken as well. As indicated in the opening sentence above, participation in this research project is voluntary and not binding. If you choose to participate, you may decline or withdraw from further participation at any time before the data used in your interview is published.

As a participant in this research project, you will be asked to do the following:

1. Provide a written, informed consent (via email is acceptable) before the interview begins.
2. Answer questions relating to your patients' medical cannabis use

Some sample questions that you will encounter during the interview:

1. Do you have any patients that currently use medical cannabis?
2. What conditions (if any) do you perceive medical cannabis may have role in management?
3. Do you feel they are finding beneficial effects?

Potential Harms, Risks or Discomforts

We do not anticipate that this interview will present any known harms, risks or discomforts. If there are any questions that make you uncomfortable, you can choose to not answer. You may also ask to have any answers removed. If at any point during the interview you wish to stop, you may ask the interviewer to end the interview. If during any stage after the interview you wish to be pulled out of the study, you may ask me (Jeremy Ng) to remove you from any portion of the study. If you choose to withdraw from the study, there will be no consequences to you and all identifying information associated with you will also be removed.

Confidentiality

Throughout the study, the research team will make every effort to maintain confidentiality and you privacy. We will ensure participant names/license numbers, associations to any clinics or hospitals, demographic information or any other identifying information within transcripts of interviews or audio recordings will be removed and replaced with randomized study identification numbers. Anonymity and confidentiality of all study participants will be ensured to prevent privacy breach. All information provided by participants will be locked and only members of the research team will have access to it.

I have listed my contact information for you below. Should you choose to participate in the research, you can contact me at any time during the research project with any questions that you

may not have yet considered. Also listed is the contact information for my co-investigator Dr. Jason Busse, whom you can contact at any time to verify the accuracy of this information letter.

For the purposes of ensuring the proper monitoring of the research study, it is possible that a member of the Hamilton Integrated Research Ethics Board and this institution and affiliated sites may consult your research data for quality assurance purposes. However, no records which identify you by name or initials will be allowed to leave the research office. By signing this consent form, you authorize such access.

Thank you for considering participation in my research project.

Sincerely,

Jeremy Y. Ng, MSc, PhD Student
Doctoral Student, Department of Health
Research Methods, Evidence, and Impact,
Faculty of Health Sciences, McMaster University
Address: Michael G. DeGroote National Pain Centre
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Hamilton, Ontario L8S 4K1 Canada
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and

Jason W. Busse, DC, PhD, Principal Investigator
Assistant Professor, Departments of Anaesthesia
and Clinical Epidemiology & Biostatistics
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Email: bussejw@mcmaster.ca

FREE AND INFORMED CONSENT FORM
for
Attitudes and perceptions towards medical cannabis among family physicians practicing in Ontario

I, _____, have carefully read the attached Information Letter for the **Attitudes and perceptions towards medical cannabis among family physicians practicing in Ontario**. One of the study investigators or one of their research assistants has explained this project to me and has answered all my questions about it. I understand that if I have additional questions, I can contact the Principal Investigator **Jason Busse** at any time during the research project. I also understand that I may decline or withdraw from participation and I am free to ask that my interview and resulting data be removed from the study/destroyed at any time before the data from my interview is published without negative consequences.

1) I agree that the interview can be audio recorded. Yes No

2) I would like to receive a summary of the study's results. Yes No

   If yes, where would you like the results sent?

   Email: _____

   Other: _____

My signature below verifies that I have agreed to participate in the **Attitudes and perceptions towards medical cannabis among family physicians practicing in Ontario** as it has been described in the Information Letter. My signature below also verifies that I am fully competent to sign this Consent Form and I will receive a signed copy of the Information Letter and the Informed Consent Form for my files.

Agreement to Participate

_____	_____
Participant's Signature	Signature of Person Obtaining Consent
_____	_____
Print Name	Print Name
Date: _____	Date: _____

Chapter 3 Appendix 2: Interview Guide

1. Do you have any patients that currently use medical cannabis?
2. What conditions (if any) do you perceive medical cannabis may have role in management?
3. Do you feel that patients who use cannabis experience specific beneficial effects?
4. Are you concerned about harms associated with medical cannabis use?
5. Do you feel that some patients may access medical cannabis for recreational purposes?
6. Should the legalization of recreational cannabis affect use of medicinal cannabis?
7. Do you authorize medical cannabis for patients? Why or why not?
8. What are your impressions about the evidence underlying medical cannabis?
9. What are your thoughts on the Canadian Medical Association's stated position to move away from medical cannabis once recreational use is legal?
10. What is your knowledge regarding medical cannabis?
11. What are your impressions about the current regulation of medical cannabis?
12. What education regarding medical cannabis, if any, would you like to receive?
13. Where do you feel future research regarding medical cannabis should be directed?
14. Are there any final thoughts you would like to add regarding the administration and use of medical cannabis?

Chapter 3 Appendix 3: Summary of McGrath et al. (2019)'s Twelve Tips for Conducting Qualitative Research Interviews

Tip 1	Identify when qualitative research interviews are appropriate
Tip 2	Prepare yourself as an interviewer
Tip 3	Construct an interview guide and test your questions
Tip 4	Consider cultural and power dimensions of the interview situation
Tip 5	Build rapport with your respondents
Tip 6	Remember you are a co-creator of the data
Tip 7	Talk less and listen more
Tip 8	Allow yourself to adjust the interview guide
Tip 9	Be prepared to handle unanticipated emotions
Tip 10	Transcribe the interviews in good time
Tip 11	Check the data
Tip 12	Initiate analysis early

For further reading, please consult the full-text article as follows:

McGrath C, Palmgren PJ, Liljedahl M. Twelve tips for conducting qualitative research interviews. Medical teacher. 2019 Sep 2;41(9):1002-6. https://doi.org/10.1080/0142159X.2018.1497149.