<u>**Abstract/Summary/Specific Aim**</u>

In Canada, over 80% of lower extremity amputations are related to diabetes and vascular disease. Due to the devastating and preventable nature of lower extremity amputation, health agencies at multiple levels have used diabetes-related amputations as a metric for evaluating population health. Amputations also serve as a marker for health disparities, and it has been well documented that these disparities exist as it relates to access to care, and post-operative outcomes in patients undergoing amputations.

Epidemiologic data for lower extremity amputations is lacking in the province of Quebec. Furthermore, there is little evidence on the impact of patient-level, clinician-level, and system-level factors on lower extremity amputations institutions across Quebec. This proposal seeks to address these critical gaps in knowledge by integrating database registry and lived experiences of patients who underwent limb salvaging procedures and lower-extremity amputations, caregivers of those impacted, and clinician involved in amputation prevention locally and provincially across Quebec.

Inequities exist in our health care environment, including amputation prevention. This study seeks to highlight these geospatial disparities, the reasons for these disparities, and develop and tailor an amputation prevention program. The overarching goal is to facilitate ***equitable access*** to amputation prevention in Quebec. As such, this program uses community engaged research (CEnR) and patient-centred outcomes research (PCOR) to address the following aims:

Aim 1 (Quantitative Aim): Evaluate the geospatial and temporo-spatial distribution of minor and major lower extremity amputations related to diabetes and vascular disease in Quebec. Using the Régie de l'Assurance de Maladie du Quebec (RAMQ) administrative database, we will identify the "hot spots" for lower extremity amputations using geospatial analytics and temporo-spatial analysis will identify regions of amputation improvement (high performance) or worsening (low performance).

Aim 2 (Qualitative Aim): Determine the patient-reported, caregiver-reported, and clinician-reported enablers and barriers to care related to lower extremity amputation prevention in 2 high performing and 2 low performing regions identified from Aim 1. Techniques used will be purposeful sampling with maximum variations. Interviews will be done 1:1 using a semi-structured format. Patients with who have undergone limb salvaging interventions or amputations, caregivers, and clinicians will be invited to participate.
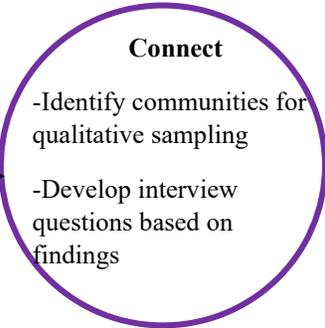
Aim 3*: *Develop and perform initial field testing and peer review of an Amputation Prevention Program implementation toolkit that empowers patients and caregivers to engage in amputation prevention shared decision-making process and offers methods to clinicians to overcome challenges of the multidisciplinary team approach. Using the Consolidated Framework for Implementation Research (CFIR) we will co-develop an amputation program that takes into account the barriers and enablers we have identified in Aims 1 and 2.

Quantitative Aim #1

Data source: RAMQ and MSSS registry

Data: Minor and major lower extremity amputations in Quebec

Outcome: Geospatial analysis and temporospatial analysis of lower extremity amputations identifying areas of worsening and improvement
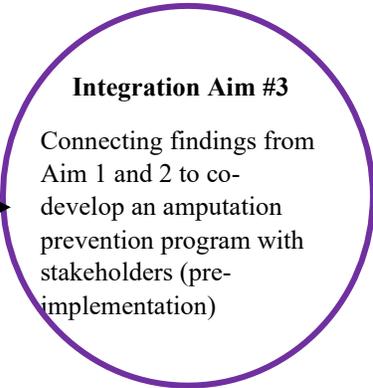
Connect

-Identify communities for qualitative sampling

-Develop interview questions based on findings

Qualitative Aim #2

Data source: Patients, caregivers, clinicians identified from vulnerable communities in Quantitative Aim

Data: 1:1 semi-structured interviews

Outcome: Themes and quotes organized within the CFIR framework

Integration Aim #3

Connecting findings from Aim 1 and 2 to co-develop an amputation prevention program with stakeholders (pre-implementation)

Public Health Relevance Statement

Amputations are a public health concern. Lower extremity amputation is a devastating complication of diabetes and vascular disease, resulting in emotional distress, diminished quality of life, and lack of autonomy with ensuing costs to the healthcare system. Amputations may also be largely preventable with timely and appropriate care from foot care specialists and vascular specialists.   With the exponential growth of our aging population, the rates of diabetes and vascular disease are on the rise globally, and this has significant implications for the incidence of complications from these disease processes, including amputation[1, 2]. In Quebec, over 675,000 people live with diabetes and the prevalence of diabetes has grown 42% between 2001 and 2019[3]. Furthermore, the financial and emotional costs of amputation are high. Hospital charges for amputation, readmission, rehabilitation, and institutionalization in the US totalling $8 billion dollars annually, and when it is compared to amputation prevention, it is clear that amputation prevention is cost effective to the healthcare system[4].

This program will have a ***positive impact*** with the goal to reduce amputations across Quebec and facilitate equitable access to care for amputation prevention. The **expected outcomes** of this study are 3-fold:1) To establish epidemiological evidence of lower extremity amputations secondary to diabetes and vascular disease in Quebec 2) To advance understanding of previously little studied factors associated with access to care for amputation prevention from the patient, caregiver and clinician lived experiences, and 3) To engage patients and communities to participate in amputation prevention research that is meaningful to them.

Environment – Facilities and Other Resources

Early research career: Upon completion of my research and clinical training, I joined the Centre Hospitalier de l'Université de Montréal (CHUM) as a vascular surgeon and Innovation Hub unit at the Centre de Recherche du CHUM (CRCHUM), in Dr Lise Gauvin's team. I obtained an independent researcher status at the CRCHUM in July 2021, along with start up operating funds of $135 000 from the CRCHUM and $30 000 from the Department of Surgery with 50% protected research time, and $50 000 salary support for three years from the Division of Vascular Surgery. I am also the PI on 3 separate funded projects from the *Association de chirurgie vasuclaire et endovasculaire au Québec (ACVEQ)*, *Société de sciences vasculaires du Québec (SSVQ)*, and the CSVS totalling $8,000. I am also involved in three major research networks, including the Qualitative and Mixed Methods Learning Lab, Association of Academy Surgery, Surgical Outcomes Club, and Cardiometabolic Health, Diabetic, Obesity Research Network (CMDO). As member of these groups, I have access to cutting-edge expertise in mixed methods research and community engaged studies, which I propose in my research program. I was also the co-chair of the Society for Vascular Surgery Postgraduate Committee on Peripheral Arterial Disease at the 2022 Vascular Annual Meeting seeking to improve comprehensive vascular care for PAD globally.

Network and Consolidated Expertise : I have established collaborations with a multidisciplinary network of established researchers from various specialties relevant to comprehensive vascular care for limb salvage, medical sociology, and public health. *At the CRCHUM*, Drs Lise Gauvin (epidemiology and population health), Januz Krakowsky (medical sociology), and Marie-France Raynault (population health) are Fonds de Recherche Quebec sante (FRQS)-supported scientists who will be local investigators and a part of my mentorship committee. Dr Gilles Soulez is an FRQS-funded scientist care and collaborator on these projects. He has a clinical interest in limb salvage and performs hundreds of complex peripheral endovascular procedures for limb preservation. He will play a facilitating role in implementing the program at the CHUM. Dr Stephane Elkouri is the Chief of Vascular Surgery at University of Montreal and the CHUM and has played a key role in helping me build the research infrastructure for vascular surgery at the CHUM and CRCHUM, and he continues to support my early career and promote research in our clinical division. Finally, Dr Andrée Boucher is the Chief of Endocrinology at the CHUM and Director for the Center of Expertise in Diabetes and is a partner to develop a dedicated Foot Care Clinic for Amputation Prevention at the CHUM. **At McGill University,** Dr Jonathan Afilalo is cardiologist and FRQS-funded scientists, and seasoned clinical epidemiologist and has been providing me with mentorship for the past 7 years. His expertise in clinical epidemiology and vulnerable populations with frailty have been a great contribution to the study design of Aims 1 and 2 and he will also help the development of a subsequent substudy on the budget impact of the study findings. At **UCLA, West Virginia University, Stanford, and Johns Hopkins**, Dr Karen Woo, Dr. Samantha Minc, Dr Shipra Arya, and Dr. Caitlin Hicks respectively are vascular surgeons and all are nationally funded scientists. They have expertise in epidemiology, mixed methodology, qualitative analytics, and implementation science. They have provided consistent mentorship over the past 3 years. They have been

instrumental in the development of this research platform and design particularly for Aims 2 and 3.

Our team will also include two ***patient and community collaborators***, recruited with the help and support from the Centre of Excellence on Partnership with Patient and the Public located at the CHUM. Our patient's collaborators will be actively involved throughout the projects, including informing the design, questionnaires, recruitment strategies, helping face potential challenges and find mitigation strategies along the way; they will also be actively involved in knowledge translation strategies.

Environment and Feasibility: The environment for the proposed research is strong. The University of Montreal and CRCHUM is a land-grant institution, with various community outreach sites across our catchment area, and a strong academic mission that supports interdepartmental collaboration. I am a vascular surgeon with expertise in PAD research, limb salvage, and training in health disparities research and implementation science. My **research team** consists of 1 full-time research coordinator, 1 Master's student, 3 medical students, 2 bachelor students, and 1 biostatistician with experience in managing large datasets. A qualitative researcher with significant expertise in qualitative research for clinical problems in rural populations will be contributing time as a consultant and will be leading one-on-one interviews, and a collaborator at West Virginia University with significant geographic information systems expertise will have supported time. Members of my research team are experienced, enthusiastic, motivated, and have been trained in coordination, management, and recruitment in prospective and qualitative studies in vascular medicine.

In summary, my research is focused on improving care for vascular surgery patients with PAD. My overarching goals are to engage with patients and communities using team science to understand the determinants and risk factors for lower extremity amputation. My goal is to design and co-develop an amputation prevention program and implement a tailored amputation prevention program across diverse communities in Quebec. My clinical and administrative activities allow me privileged access to my population of interest, also facilitating translation of research findings into clinical practice. I receive strong mentorship, financial and administrative support from the CRCHUM, *Université de Montréal*, and CHUM Department of Surgery to support my transition as an independent clinical researcher.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES**.

NAME: Drudi, Laura Marie

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: Assistant Professor of Surgery

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Dawson College, Montreal, Quebec, Canada	D.E.C.	06/2007	Health Sciences
Technical University of Graz, Graz, Austria	Diploma	08/2011	Space Medicine
McGill University, Montreal, Quebec, Canada	MD, CM	06/2013	Medicine
McGill University, Montreal, Quebec, Canada	MSc	06/2017	Epidemiology, Biostatistics, and Occupational Health
McGill University, Montreal, Quebec, Canada	FRCSC	06/2020	Vascular Surgery
Az Sint Blasius, Dendermonde, Belgium	Fellow	06/2021	Limb Salvage Fellowship
Univesity of California San Francisco, San Francisco, California	Diploma	Ongoing	Implementation Science

A. Personal Statement

I am a vascular surgeon, clinician-scientist, and Assistant Professor of Surgery with a clinical practice and research platform focused on limb salvage. Given the advancing age and complexity of our vascular patients, there is a growing need to personalize care to the individual at hand. Risk prediction models are central to this process; however, existing models are far from perfect, and particularly underperform in the elderly. My primary research interest is to improve risk prediction in elderly vascular patients with the most severe form of peripheral arterial disease (PAD). My research focus is centred on the impact of frailty and health care disparities in this patient population. I conducted a prospective study of elderly patients undergoing peripheral vascular interventions (FRAILED Study) and performed a head-to-head analysis demonstrating the ideal frailty tool to be used in patients with PAD. Simultaneously, I have recognized the importance of integrating patient partners in qualitative research to improve quality of care delivered. As such, I have undertaken formal didactic training in qualitative and mixed methods design. I am continuing to build a multi-disciplinary collaboration dedicated to improving care for patients with PAD and improve patient and clinical centred outcomes for patients with PAD. I have authored a number of publications pertaining to frailty and healthcare disparities, and obtained my Master's degree in Epidemiology on this subject. I am pursuing postgraduate training in implementation science to begin implementing and disseminating an amputation prevention program in Quebec. For each project, I work with investigators and collaborators from my own institution and other institutions nationally and internationally to develop study protocols, collect and analyse the data and present and publish the findings to improve care for patients with PAD globally.

B. Positions and Honors

Positions and Employment

2021-present	Assistant Professor, Surgery, Université de Montréal, Montreal, Quebec, Canada
2021-present	Attending, Vascular Surgery, Centre Hospitalier de l'Université de Montréal (CHUM), Montreal, Quebec, Canada
2021-present	Researcher, Innovatiokn Hub, Centre de Recherche du CHUM, Montreal, Quebec, Canada

Honors

2021	Canadian Society for Vascular Surgery Young Investigator Award
2020	Université de Montréal Yvon Chartier Scholarship
2020	Royal College of Physicians and Surgeons of Canada Detweiler Traveling Fellowship
2019	McGill University MedStar Award
2017	Association of Quebec Vascular Surgeons Henri Paul Scholarship
2017	Fonds de recherche du Québec – Santé (FRQS) Master's Grant
2017	Canadian Institutes of Health Research Canada Graduate Scholarship

Professional Societies

Professional Societies - National

2022-present	Member, Young Surgeons Steering Committee, Society for Vascular Surgery
2021-present	Member, SVS Foundation VISTA Pilot Projects, Society for Vascular Surgery
2020-present	Member, Diversity, Equity, and Inclusions Committee, Society for Vascular Surgery
2018-present	Member, Wellness Task Force, Society for Vascular Surgery
2018-present	Chair, Newsletter Sub-Committee,Vascular and Endovascular Surgical Society
2018-present	Peer Reviewer, Journal of Vascular Surgery
2018-2021	Trainee Editor, Vascular Specialist Newsletter

Professional Societies – Regional

2022-Present	Member, Website Committee, Association of Quebec Vascular Surgeons (ACVEQ)
2022-Present	Member, Eastern Vascular Society (EVS)
2013-Present	Member, Canadian Society for Vascular Surgery (CSVS)

Université de Montréal

2022-Present	Lead, Diversity, Equity, and Inclusion, Program Committee

C. Contribution to Science

1. My early research thus far has focused on frailty assessment in our patients with vascular disease. I have focused my attention on risk prediction in patients with peripheral arterial disease (PAD) and critical limb threatening ischemia (CLTI). Through this research we have been able to identify predictors that lead to adverse outcomes following peripheral vascular interventions.

   a. **Drudi LM**, Ades M, Mancini R, Boudrias C, Obrand DI, Steinmetz OK, Afilalo J. Frailty assessment in older adults undergoing interventions for peripheral arterial disease. J Vasc Surg. 2019 Nov;70(5):1594-1602.e1. doi: 10.1016/j.jvs.2018.12.052. Epub 2019 May 18. PMID: 31113723.

   b. **Drudi LM**, Ades M, Landry T, Gill HL, Grenon SM, Steinmetz OK, Afilalo J. Scoping review of frailty in vascular surgery. J Vasc Surg. 2019 Jun;69(6):1989-1998.e2. doi: 10.1016/j.jvs.2018.10.053. Epub 2018 Dec 24. PMID: 30591292.

c. **Drudi LM**, Phung K, Ades M, Zuckerman J, Mullie L, Steinmetz OK, Obrand DI, Afilalo J. Psoas Muscle Area Predicts All-Cause Mortality After Endovascular and Open Aortic Aneurysm Repair. Eur J Vasc Endovasc Surg. 2016 Dec;52(6):764-769. doi: 10.1016/j.ejvs.2016.09.011. Epub 2016 Oct 21. PMID: 27776940.

d. **Drudi LM,** Tat J, Ades M, Mata J, Landry T, MacKenzie KS, Steinmetz OK, Gill HL. Preoperative Exercise Rehabilitation in Cardiac and Vascular Interventions. J Surg Res. 2019 May;237:3-11. doi: 10.1016/j.jss.2018.11.042. Epub 2019 Jan 9. PMID: 30694788.

2. **Professional Wellness and Burnout**: As a member of the Wellness Task Force, we are focused on improving wellness and avoiding burnout in our vascular surgery workforce. We have surveyed our task force in 2018 and have identified gender specific associations to burnout and suicidal ideations. We have further implemented a Peer Support Group and Coaching services for our SVS membership to address personal and professional conflicts. I am further invested in addressing factors that may impact wellness including professionalism, pay equity, and ergonomic issues.

a. **Drudi LM**, Mitchell EL, Chandra V, Coleman DM, Hallbeck MS, Mannoia K, Money SR, Brown KR; SVS Wellness Task Force. A Gender-Based Analysis of Predictors and Sequelae of Burnout Amongst Practicing American Vascular Surgeons. J Vasc Surg. 2021 Oct 8:S0741-5214(21)02195-9. doi: 10.1016/j.jvs.2021.09.035. Epub ahead of print. PMID: 34634416.

b. **Drudi LM,** Woo K, Ziegler KR, O'Banion LA. Professionalism in (vascular) surgery: What does it mean? J Vasc Surg. 2021 Aug;74(2S):93S-100S. doi: 10.1016/j.jvs.2021.04.020. PMID: 34303465.

c. Lin JC, Bowser KE, **Drudi LM**, DiLosa KL, Yi J. Equal pay for equal work: Disparities in compensation in vascular surgery. J Vasc Surg. 2021 Aug;74(2S):21S-28S. doi: 10.1016/j.jvs.2021.03.052. PMID: 34303455.

d. **Drudi LM**, Nishath T, Ma X, Mouawad NJ, O'Banion LA, Shalhub S. The impact of the COVID-19 pandemic on wellness among vascular surgeons. Semin Vasc Surg. 2021 Jun;34(2):43-50. doi: 10.1053/j.semvascsurg.2021.04.003. Epub 2021 May 21. PMID: 34144747.

e. Coleman DM, Money SR, Meltzer AJ, Wohlauer M, **Drudi LM**, Freischlag JA, Hallbeck S, Halloran B, Huber TS, Shanafelt T, Sheahan MG; SVS Wellness Task Force. Vascular surgeon wellness and burnout: A report from the Society for Vascular Surgery Wellness Task Force. J Vasc Surg. 2021 Jun;73(6):1841-1850.e3. doi: 10.1016/j.jvs.2020.10.065. Epub 2020 Nov 25. PMID: 33248123.

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/1-38ezyskLs5x/bibliography/public/

Budget

Budget for entire proposed project period: direct costs only				
Budget Category Totals	Aim 1	Aim 2	Aim 3	
Personnel: Salary and fringe benefits				
PI Laura Marie Drudi	0	0	0	
Geospatial statistician	4,800	0	0	
Qualitative analyst	0	3,000	3,000	
Patient advisors	300	300	300	
Consultant Costs: graphic design	0	0	1,500	
Database costs (RAMQ)	5,000	0	0	
Supplies: toolkit/office supplies (DeDoose)	0	400	0	
Travel	0	10,000	0	
Inpatient Care	0	0	0	
Outpatient Care	0	0	0	
Other Expenses: interview transcription, patient participant compensation		2,000	400	
Academic Development Courses (ie advanced geospatial analysis, implementation science)	2,000	1,000	1,000	
Total Direct Costs	12,100	16,700	6,200	
Total Direct Costs For Entire Proposed Project Period				35,000
Other funding from CHUM Department of surgery				10,000
Funding requested from Eastern Vascular Society				25,000

Budget Justification

Laura Marie Drudi, MD, Principal Investigator will provide expertise in treating patients with PAD as a Vascular Surgeon, as well as expertise in qualitative analysis and implementation science. She will provide overall oversight for implementation, managing recruitment progress, preparing summary results for review, finalizing implementation toolkits, and publications. Furthermore, she will conduct data collection (interviews), and perform analysis on the DeDoose software.

Kristina Shanahan and Julia Rodighiero (6000$) will provide expertise in qualitative research and in conjunction with Dr Drudi will conduct data collection (interviews), and perform analysis.

RAMQ database Geospatial Analysis Costs ($9,800): Administrative costs to RAMQ for access to data along with consultant costs for geospatial analysis are estimated at 9,800$

Consultant Costs ($1,500): Patient education and implementation toolkit design will be contracted to a professional graphic designer for a one-time fee.

Academic Development Courses Costs ($4,000): I will be taking advanced geospatial analysis courses as well as completing my Diploma of Implementation Science at UCSF. The knowledge acquired in these courses will be directly translated to the conduct of this study.

Other Costs ($2,400): We expect to interviewing patients, caregivers, and health care professionals in 4 regions. Interviews will be recorded and professionally transcribed. We are estimating 45 minutes per interview at a transcription cost of $1.15 per minute. We will be compensating each participant $30 per interview.

Research Plan: Significance

Geography and Social Vulnerability Matters: In Canada, over 80% of lower extremity amputations are related to diabetes and vascular disease. Lower extremities amputations secondary to diabetes and vascular disease are a marker of health care disparities. Several studies across North America identified geographic variation in amputation rates[5-7]. While the risk for amputation is highest in communities with a higher prevalence of diabetes, cardiovascular disease and tobacco use, it is also disproportionately higher in communities affected by high economic hardship, chronic external stressors, and social vulnerability[6]. Vulnerability is defined as a diminished capacity of an individual or a group to anticipate, cope, resist and recover from the impact of a stressor, such as a surgery[8]. It has been demonstrated that social vulnerability is associated with disparities in access to care, clinical and surgical care, and post-operative outcomes[9-11], including amputation. Amputations serve as a marker for health disparities, and it has been well documented that these disparities exist as it relates to access to care, and post-operative outcomes in patients undergoing lower extremity amputations. Rural and remote populations are highly vulnerable groups that tend to be older and poorer, with higher levels of chronic disease, riskier health behaviours and greater barriers to accessing health care[12, 13]. It therefore follows patients with diabetes and vascular disease who are socially and geographically vulnerable are at higher risk for amputation, and studies suggest that they undergo amputation at rates 50% higher than do non-rural patients[14]. The issues of geospatial disparities and social vulnerability have not been explored in our local environment in Montreal, nor in the province of Quebec.

Multidisciplinary care improves improve patient-centered and clinical outcomes: Optimizing _multidisciplinary care coordination_ is a top priority for national action to transform health care quality, as defined by the Institute of Medicine (IOM)[15]. Multidisciplinary teams have been shown to improve clinical outcomes and increase the power to address challenging medical problems by incorporating input from multiple specialties[16]. Many institutions and most practice settings have little or no experience with multidisciplinary teams, or lack existing infrastructure to support such teams. These barriers may impede implementation of an Amputation Prevention Program structure needed. In such practice settings, the sooner clinicians are able to identify barriers and develop potential solutions, the sooner they will be able to institute the recommended team structure. Therefore, our proposed research aims to achieve the _essential_ first steps in paving the way for appropriate adoption and implementation of a multidisciplinary team coordination for amputation prevention. We will do so by exploring literature-derived and stakeholder derived potential barriers and facilitators of multidisciplinary care teams among the affected patients, caregivers, and clinicians within diverse practice settings, and determining whether proven approaches can be applied to amputation prevention care. We will use our findings to create a prototype of an Amputation Prevention Program Implementation toolkit in which we will conduct initial field testing and peer review, to inform implementation testing.

Innovation

This study will use a mixed-methods sequential explanatory design in which the study team collects quantitative data in the first phase, analyses the results, then uses the results to inform the second, qualitative phase. Quantitative results typically inform the types of participants or communities to be selected for the qualitative phase and the types of questions that will be asked[17]. This integrated approach is critical to allow us to get **a clear picture** of the challenges and experiences of Quebecers at risk for diabetes and vascular-related

amputation and to help us with our long-term goal of creating a community-based intervention to prevent these amputations. Applying mixed-methods research methodology to vascular research is **innovative** as the majority of research performed on this issue uses uniquely quantitative methodology alone and there is extremely limited qualitative data available[18]. A mixed-methods, sequential explanatory model combines the strengths of both methodologies and is a unique approach to this problem and this population. Achieving the specific aims of this project will provide unique data that will be used to create an evidence-based, community-based intervention to prevent amputation. The data will be used to educate community members in high-risk areas, mobilize stakeholders, and provide a baseline to test intervention efficacy.

Research Strategy

AIM #1 (QUANTITATIVE AIM): ESTABLISH EPIDEMIOLOGICAL DATA REGARDING AMPUTATIONS IN QUEBEC

Hypothesis: Quebec will have higher rates of amputation in rural and remote communities. We also hypothesize that rural and remote communities, will have higher amputation rates due to a disproportionate burden of diabetes and PAD-related risk factors, as well as geographic barriers to care and a cultural distrust of the healthcare system.

Objectives:

1. To identify the prevalence of minor and major lower extremity amputation among patients with diabetes and/or peripheral vascular disease in the province of Quebec
2. To identify geographic area with higher than expected minor and major amputations using advanced spatial analysis while controlling for comorbidities
3. To perform a temporo-spatial analysis evaluating regions of improvement and worsening rates of minor and major lower extremity amputations using advanced spatial analysis while controlling for comorbidities

Study design: This is a retrospective data using administrative data from RAMQ

Data Collection and Management: This study will use data from 2000 to 2022 Régie de l'Assurance de Maladie du Quebec (RAMQ) administrative databases.

Inclusion criteria: The target population will be limited to adult patients ($\geq$18 years old) with the diagnosis of diabetes or PAD. Our population of interest are admissions for residents of Quebec with minor and major amputations (please see appendix of codes). Minor amputations were defined as any toe, phalanx, or trans-metatarsal amputation (or partial foot amputation). Major amputation was defined as any below-the-knee or above-the-knee amputation. All diagnoses and procedures are defined using the International Classification of Diseases (ICD)-9 codes from January 1, 2010 to September 30, 2015 and ICD-10 codes from October 1, 2015 to May 30, 2022. **Exclusion criteria:** Patients with trauma related amputations, patients who did not have a postal code of residence available, and patients who were not residents of the province of Quebec were excluded from the analysis. This has been approved by the CHUM Institutional Review Board.

Data Analysis: Descriptive characteristics will be summarized using χ^2 tests and independent samples *t*-test for categorical and continuous variables respectively. Descriptive statistics will be generated for the following outcomes: minor amputation, major amputation, any

amputation. For geographic analysis, data will be aggregated to postal code levels of patient residence (not the facility where the amputation occurred) as well as region. The relative risk of minor and major amputations will be assessed separately as outcome variables in the model. Relative risk will be estimated by dividing the rate of amputation at an individual location by the province rate. Relevant comorbid conditions included rate (per 1000 persons) coronary artery disease, renal failure, obesity, hypercholesterolemia, diabetes, PAD, and diabetes with PAD. In addition, spatial patterns of these conditions will be controlled in the model because of their association with minor and major amputation and known geographic variations in their prevalence. We will calculate rates for the outcome and comorbid conditions using the total number of diabetes and/or PAD admissions in Quebec as the denominator to better represent the population at risk. Hierarchical Bayesian spatial models will be fit using the integrated nested lattice approximation package. The relative risk of amputation given the relevant comorbid conditions and risk factors listed above will be modelled using a Poisson gamma distribution, and as a function of (1) a random spatial effect accounting for spatial dependence, and (2) a nonspatial random effect accounting for residual variation that is not spatially dependent[19]. The value of this method for quantitative health studies has been cited extensively elsewhere[20, 21]. Posterior predicted mean for relative risk of major and minor amputation as well as deviance information criteria (DIC) will be exported and visualized in ArcMap 10.5 using thematic maps. The use of DIC has been one of the most extensively cited measures used in both spatial and nonspatial Bayesian modeling.[22-24]. Generally, differences in DIC from 5 to 10 indicate potentially substantial change in model performance; lower DIC indicates a better model fit[23]. Temporal trends will be divided into 2 time periods: 2000-2010 and 2010-2020.

AIM 2: (QUALITATIVE AIM) STUDYING BARRIERS AND ENABLERS TO AMPUTATIO PREVENTION

Objectives:

1. To explore barriers and enablers to amputation prevention in high and lower performing communities identified in Aim 1
2. To inform about the construction of an amputation prevention implementation toolkit by in-depth interviewing.

Study design: Qualitative study design

Recruitment and Eligibility: We will recruit participants in geospatial hot spots for amputation worsening and amputation improvement. Please see the inclusion and exclusion criteria for our listed participant categories:

Patients and Caregivers: Patients and caregivers will be recruited from the communities who have been identified in Aim 1 as either those having improvement and worsening rate of amputation. All patients and caregivers of patients who have undergone treatment for limb salvage and/or lower extremity aged >18 will be eligible to participate. Exclusion criteria for patients and caregivers include: 1) not English- or French-speaking, or able to communicate through a translator; 2) inability to understand the consent process and/or give consent; 3) significant cognitive impairment, 4) undergoing emergent surgery, and 5) unable to access video or telephone calls for the interview.

Clinicians: Inclusion criteria: Currently seeing patients with diabetes or PAD and/or lower extremity amputation in the vulnerable communities identified in Aim 1.

For all participants, we will use purposeful sampling to address sex as a biological variable and mitigate any biases based on sex, race and/or ethnicity allowing for heterogeneity of clinician and patient characteristics that may be associated with decision-making preferences.

Interviews: The semi-structured interview guides consist of open-ended, qualitative questions that allow and encourage participants to elaborate as they like, which we expect to yield rich personal narratives. The patient interview guide questions will focus on barriers and enablers to care for amputation prevention, access to care, engagement in limb salvage teams, and partnering with clinicians and individuals involved in the decision-making process. Questions from the clinician interview guide will focus on preferences and attitudes about the needed multidisciplinary execution of limb salvage teams, patient involvement, and clinical management of amputation prevention, and barriers and enablers to equitable care for limb salvage. We based the clinician interview guide on published barriers/facilitators of multidisciplinary teams[25]. Interviews will be conducted by trained interviewers with experience in implementation science, qualitative research, and speaking with vulnerable populations. Interviews will be done remotely using teleconferencing (Zoom) or via telephone and recorded using the application Tape-A-Call Pro. We will use the machine transcripts generated by Zoom and used a professional transcription company to check the accuracy of the transcripts.

Sample Size: Sample sizes for qualitative methods studies cannot be determined *a priori*[26]. Data collection will continue until data saturation, the point at which no new data is emerging and the analysis reveals nuanced themes[26]. Accordingly, we will interview the patient, caregiver, and health care professionals until reaching data saturation. Most qualitative studies reach saturation at 12 patients. We estimate the sample size needed to reach data saturation in the proposed project will be ~12 patient participants per group. After saturation has been reached, we will perform 3 additional interviews to confirm saturation.

Data Analysis: The analytic method uses thematic analysis. Following the principle of constant comparison, transcripts will be analyzed as interviews are conducted. First-cycle codes will be derived directly from the data.[27] Codes consist of a short phrase generated by the researcher that captures the essence or attributes of a data segment. Open coding will be used and the codes will be applied to data sections that the team deemed appropriate. We will use constant comparison to examine the data and make comparisons both within a given interview and across interviews. We will analyze interviews from the clinician group and patients and caregivers as a separate group. We will use the software DeDoose (version 9.0.46), which is a qualitative data analysis software analyze the data and record codes. When 12 interviews will be completed for the patient, caregiver, and clinician participant groups, we will search for themes by analyzing the initial codes to determine how the codes could be grouped into themes. Themes are constructs that succinctly capture an important pattern in the data in relation to the research question.[27] We will review the candidate themes and read the data extracts for each theme to determine if the data fit the candidate themes. If not, we will then decide if certain data extracts fail to fit the theme, or if the theme needs to be re-worked. If the data do fit the candidate theme, then we will assess if the set of themes accurately reflects the meanings and relationships of the whole data. Identification and

revision of themes will take place simultaneously, as interviews continue until data saturation will be reached. As the themes matured, we will determine how the themes fit together to tell the overall narrative. We will ensure there was minimal overlap between themes, and identified any sub-themes that may be contained within a given theme.

Ensuring Rigor: To enhance scientific rigor, we will conduct the study and report our findings in accordance with the Consolidated Criteria for Reporting Qualitative Research (COREQ).[28] We will ensure credibility by attaining prolonged engagement in each interview, and continuing interviews until reaching data saturation, which is at the point where the data reveals no new themes. Repeat interviews will be used as necessary to clarify or expand upon any issues not completely explored in the initial interviews. Interviews will be analysed as they are completed, and constant comparison used to test for saturation. Patient, caregiver, and clinician group results will be analysed separately. For each group, 3 additional interviews will be conducted after saturation has been determined, to confirm that saturation has been reached.

AIM 3: CO-DEVELOPMENT OF AN AMPUTATION PREVENTION TOOLKIT
Objectives:

1) To co-create an amputation prevention implementation toolkit with stakeholders

2) To field test this toolkit in a vulnerable community and determine the impact of the program on implementation outcomes and clinical outcomes: 1 year on amputation free survival, time to wound healing, quality of life, disability, institutionalization, and cost;

3) To evaluate patient, caregiver, and clinician experience with the new toolkit

Study design: This study proposes **a pre-implementation** framework for the development and pre-implementation of amputation prevention toolkit.

Implementation Toolkit as a Shared Decision-Making Tool: The decision-support aid will use the Ottawa decision-support framework, which is based on expectancy value, decisional conflict and social support theories.[29] We will construct this tool according to the *International Patient Decision Aid Standards*[30], ensuring that the tool provides *a)* sufficiently detailed information about options for decision-making, *b)* probabilities of outcomes in an unbiased and understandable way, *c)* methods for clarifying and expressing patients' values, and *d)* structured guidance in deliberation and communication. We will use plain language written at a grade 8 equivalent or less, assessed by the readability score. This tool will be intended for provision to patients before initiating implementation. We anticipate it will have 4 major components: education materials, personal goals and expectations, care-related preference assessment, and questions to ask the multidisciplinary team. ***Clinician Tools*** will focus on facilitating patient engagement, optimizing the patient experience and simplifying the multidisciplinary approach:1. Discussing patient preference, 2) clinical management, and 3) logistics of multidisciplinary team.

Using the Consolidated Framework for Implementation Research (CFIR) we will structure themes taking into account the barriers and enablers we have identified in Aims 1 and 2. After developing the prototype implementation toolkit, we will invite patients, caregivers, and clinicians to contribute in co-developing the toolkit by field testing the prototype with those who wish to participate and collecting their feedback via individual interviews. We will subject the toolkit to peer review by interviewing participants. We plan to interview 10 patients and 10 clinicians.

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JOHNS HOPKINS
M E D I C I N E

July 28, 2022

RE: 2022 Eastern Vascular Society (EVS) Research Seed Grant

To Whom It May Concern,

Please accept this letter as my highest recommendation for Dr. Laura Marie Drudi's application for the 2022 EVS Research Seed Grant. Dr. Drudi completed her residency training in vascular surgery at McGill University, fellowship training in advanced peripheral endovascular techniques, and now has been recruited as faculty at the Centre Hospitalier de l'Université de Montréal (CHUM) in Montreal, Quebec, Canada.

Throughout her training. Dr. Drudi has been committed to pursuing a career in academic vascular surgery. She obtained a MSc in Epidemiology, Biostatistics, and Occupational Health at McGill University, and is currently completing a Diploma of Implementation Science at UCSF. Dr. Drudi has already demonstrated excellence in her academic pursuits, including numerous grants and prizes in relation to her research studies, and has 48 peer-reviewed publications to date. She began her practice in August 2021, and is an early-career surgeon-scientist with her program of research centred around limb salvage.

I have grown to know Dr. Drudi over the past couple of years through her clinical training and involvement at the Vascular and Endovascular Surgery Society (VESS) and Society for Vascular Surgery (SVS). I have also worked closely with her on the upcoming October 2022 Issue of *Seminars in Vascular Surgery,* for which she is serving as Guest Editor for an issue focused on Research Methods. Dr. Drudi is hard working, innovative, and committed to excellence. She has been a beacon of light in every setting in which I have worked with her, and I know others in our field feel similarly when I say she is the person you want working on your team.

Dr. Drudi's research seeks to improve limb salvage care in Quebec and Canada through a mixed methods design study with the goal to implement an Amputation Prevention Program locally and nationally. She will be driving the research efforts in Division of Vascular Surgery at the CHUM in Montreal, and support of her work via the EVS Research Seed Grant will allow her to grow and flourish as an academic vascular surgeon whose research endeavours are centred around health services research and implementation science. I believe the mentorship Dr. Drudi will receive and the support acquired from this award will enable her to be successful as a junior faculty and early career researcher. She is growing as an expert in complex peripheral endovascular interventions, and I will continue to support her as she develops into a leading academic vascular surgeon.

In summary, I fully support Dr. Drudi's application for the 2022 EVS Research Seed Grant. I am an active member of the EVS, and I commit to providing the time and the means to support Dr Drudi as an early career academic vascular surgeon, and to provide the necessary mentorship so that she executes her project successfully.

Sincerely,

Caitlin W. Hicks MD, MS, FACS
Associate Professor of Surgery
Director, Johns Hopkins Center for Surgery Outcomes Research (JSCOR)
Director of Research, Multidisciplinary Diabetic Foot & Wound Service
Associate Fellowship Program Director

July 25, 2022

Dr. Laura Drudi
Principal Scientist
CHUM Research Centre

Re: Letter of support for Eastern Vascular Society grant application titled: "A mixed methods exploration of enablers and barriers to lower extremity amputation prevention in patients with diabetes and vascular disease in Quebec"

Dear Dr. Drudi,

On behalf of Diabetes Canada, it is a great pleasure for me to provide a letter of support for your grant submission titled "A mixed methods exploration of enablers and barriers to lower extremity amputation prevention in patients with diabetes and vascular disease in Quebec", to facilitate equitable access to amputation preventions for patients with vascular disease and diabetes.

Diabetes Canada's mission is to lead the fight against diabetes, help those affected by diabetes to live healthy lives, prevent the onset and consequences of diabetes, and work to find a cure. Our value driven culture is committed to excellence, partnership, innovation, integrity, and respect, and we deliver on our mission by providing education and services, advocating on behalf of people with diabetes, supporting research, and translating research into practical applications.

As an organization committed to leading the fight against diabetes, Diabetes Canada enthusiastically supports this grant. By evaluating data on diabetes and vascular disease in Quebec, and performing interviews with patients, caregivers, and healthcare providers to understand enablers and barriers to care, this project will support the development of an amputation prevention program that considers health barriers and enablers and empowers patients and caregivers to engage in shared decision-making in their healthcare. This grant supports our commitment to help people living with diabetes to prevent or delay complications of the disease and promotes the importance of research in new areas of diabetes.

Diabetes Canada has developed an outstanding research knowledge translation strategy and is supported by a dynamic community-based network of professional volunteers (physicians, nurses, dietitians, researchers, educators, etc.). Because of this dynamic relationship with diabetes health-care professionals, we are well positioned to seek opportunities to communicate any new findings to the broader community through our annual professional conference and meetings, as well as related communications materials and through our clinical practice guidelines.

Diabetes Canada is proud to support such research and we wish you the best of luck with your application.

Sincerely,

Russell Williams
Senior Vice President, Mission
Diabetes Canada