Project Title: The Second Heart Program: A peer-focused, multidisciplinary harm reduction intervention to improve outcomes for people who inject drugs after admission for infective endocarditis

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Within Canada, there are increasing numbers of persons who inject drugs (PWID) [10]. Infective endocarditis (IE) is a severe complication of injection drug use, and has a lifetime incidence of 1-11% in PWID with an associated mortality of 5-10% [3-5, 8-9]. In February 2018, the Inpatient Addiction Medicine Service was launched to provide medication-assisted treatment to PWID admitted to hospitals in Hamilton. However, substance use treatment is only one factor that impacts health outcomes for PWID. Harm reduction strategies and addressing the social determinants of health are also needed, particularly in the high-risk period 3-6 months post-discharge when PWID experience higher rates of relapse, reinfection, and death following episodes of endocarditis [1]. Currently, no clinical pathway exists that specifically addresses the unique needs of PWID after hospitalization for IE, with a focus on reducing the harms associated with ongoing substance use, obtaining safe housing and secure income, and providing linkages to primary care and community resources. The Second Heart Program is a novel clinical program intended to address this gap. The proposed study will assess the feasibility of a peer-focused, multidisciplinary harm reduction intervention for PWID with IE.

Infective endocarditis in PWID

Infective endocarditis (IE) is a severe and highly prevalent infection among people who inject drugs (PWID) [3-5]. Multiple studies have documented an increasing incidence of IE due to the prevalence of PWID [6, 7].

Local data collected by Alraddadi et al. at the Hamilton General Hospital identified 86 patients with a history of IVDU and surgically managed IE between 2008-2017 [10]. The mortality rate was three-fold higher during outpatient follow-up (24%) than during their hospital stay (8%). In the study sample, the valve re-intervention rate was 5% and the readmission rate was 17% [10]. Notably, 41% of patients were lost to follow-up post-discharge [10]. Alraddadi et al. concluded that while PWID with infective endocarditis have good intra-hospital outcomes, there is a high short-term mortality rate and loss-to-follow-up rate in this population [10].

The local study findings are consistent with a 2015 study of 536 patients with IE who received surgical intervention at Cleveland Clinic between 2007-2012 [1]. This study determined that while patients initially did well following cardiovascular surgery, there was a high-risk period between 3 and 6 months postoperatively where PWID had an increased risk of death and reinfection of IE compared to patients who do not use intravenous drugs. If patients survived this high-risk period, however, they were found to have a risk of death or reinfection comparable to that of patients who did not inject drugs [1].

Addiction and harm reduction intervention in hospital

Despite the well-established link between ongoing substance use and mortality, very little is done in hospital to address the underlying substance use disorders among PWID. A retrospective review of 102 patients hospitalized with injection drug use-associated IE in Boston found that only 23.7% of those patients received an addiction consultation while hospitalized [11]. Furthermore, only 7.8% of those had a plan for medication-assisted treatment, such as opioid substitution therapy, upon discharge [11].

Optimal care for these patients should include efforts to reduce the harm of ongoing substance use [12]. However, harm reduction strategies, such as naloxone distribution, safe injection practices education, and provision of sterile drug use equipment, are rarely applied for hospitalized PWID [11, 13]. Small programs have shown preliminary success at decreasing abscess rates by teaching safe injection practices [14]. The current lack of intervention to reduce the harm of patients' substance use in the context of their IE likely contributes to the high rates of reinfection, re-intervention, and the disproportionate mortality rates experienced by PWID following discharge from hospital.

It is also known that drug use is highly stigmatized in healthcare environments, and that PWID are more likely to have negative interactions with healthcare providers [15]. These experiences can act as a deterrent for PWID to seek healthcare in future, and may contribute to non-adherence to management plans and discharges against medical advice [16]. At the time of discharge planning, socioeconomic barriers are often considered, but there is little infrastructure to ensure stable housing, transportation and income security. These are important factors that influence whether PWID access appropriate follow-up care for IE and increase their risk of post-IE complications. Individuals with lived experience, known as peer support workers, have been shown to improve substance use and recovery outcomes, reduce re-hospitalization and increase post-discharge adherence [17]. Peer workers are underused in hospital settings and could be highly valuable partners in reducing stigma and improving the care of PWID both in hospital and after discharge [16].

Primary care linkage for people who use drugs

Coordination of care by a primary care physician has been shown to improve population health outcomes, health systems efficiency, health quality, and patient satisfaction [19]. Primary care attachment is even more essential for patients with complex chronic health needs, such as those of PWID. Despite these benefits, PWID are less likely to access primary care [20] and more likely to experience adverse health outcomes [21].

Proposed innovation

The proposed innovation (Second Heart Program) is a peer-focused, multidisciplinary harm reduction intervention strategy to address gaps in the current management of PWID with IE. The Second Heart Program is a novel clinical program intended to address the medical, psychosocial, and health system challenges encountered by PWID with IE. The unique multidisciplinary model of addiction medicine physicians, peer

support workers with lived experience, a system navigator, and a primary care physician is intentionally designed to serve the needs of PWID with IE. The Second Heart Program is the first program specifically designed to transition PWID and IE from hospital to community utilizing a multidisciplinary team.

Objective and research questions

The overall objective of this study is to assess the feasibility of the Second Heart Program. For the following research questions, the category of consideration based on recommendations for feasibility studies [23] is noted in parentheses.

(1) What is the enrollment, completion and drop-out rate of participants? (process)
(2) What are the reasons for drop-out among participants? (process)
(3) What is the perceived acceptability of the process of the intervention to eligible participants? (process)
(4) What is the number and nature of unintended (or negative) outcomes? (process)
(5) How often do peer support workers and systems navigator connect with participants? (resources)
(6) What is the nature of the supports/contact points provided by peer support workers and system navigator? (resources)
(7) What are the program costs (i.e., cell phones, human resources, travel)? (resources)
(8) What is the number and nature of challenges in the collection of data throughout study? (management)
(9) What is the reinfection, readmission, and reintervention rates for participants? (scientific)
(10) What is the mortality rate 1-year post-hospitalization for IE? (scientific)
(11) What is the number of touch points with cardiovascular surgery, cardiology, infectious disease, systems navigator, primary care physician, addictions services in hospital and 1-year post-discharge? (scientific)
(12) What are the perceived strengths (impacts), weaknesses (challenges), opportunities, and threats of the program from the perspective of patients, peer support workers, healthcare providers?

Success of the project will be measured by the enrollment rate (N=40) (50%) and retention rate (>75%) in the proposed intervention. Findings from this feasibility study will help inform the design of a larger-scale implementation and evaluation of the program by identifying program challenges and possible solutions.

If found to be feasible, the results of this study will be used to develop a larger cluster RCT in multiple centers in Canada.

Methods

Study design
We will use a convergent mixed-methods study design to test the feasibility of this

intervention [26]. We will concurrently collect quantitative and qualitative data and 'mix' at the interpretation stage of the study to answer our research questions.

Study participants

Our target sample size is 40 intervention participants, which we believe is sufficient to assess the feasibility of our intervention but we acknowledge will not be powered to assess a significant improvement in patient outcomes. We expect that we will successfully enroll 50% of patients approached. This sample size can establish that the rate of success will be between 39% and 61% with 95% confidence. Acknowledging the potential drop-out rates in this population, we will aim to recruit a minimum of 50 intervention participant with an anticipated 25% drop-out rate. The sample size can establish that the rate of dropout is between 14% and 40% with 95% confidence. Between 2008-2017, we identified 86 PWID with surgically-managed IE, with 42 surgically-managed cases in 2016-2017 alone. This data excludes the larger number of IE cases that are managed without surgery. We estimate a total volume of IE cases amongst PWID as 40-50 per year in Hamilton. With a projected enrollment rate of 50%, we believe it is feasible to enroll a minimum of 40 participants over the course of this two-year study.

Inclusion criteria:

1. Age 18 or older
2. Able to provide informed consent in English
3. Admitted to either St. Joseph's Hospital or Hamilton General Hospital located in Hamilton with the diagnosis of infective endocarditis at the time of recruitment
4. History of injection drug use within 3 months of recruitment

Exclusion criteria:

1. Patient does not reside in the City of Hamilton

Recruitment

Recruitment will take place from December 2019-June 2021 (or until the targeted sample size is achieved). The Infectious Disease, Cardiovascular Surgery and Addiction Services are frequently involved with patients admitted with IE. These services will be notified about the study and will notify our research assistant if a patient may be eligible for the study and has agreed to be approached by the researcher to give more information about the study.

Consent

Due to current COVID-19 restrictions, the research assistant will be in contact with patient over the phone or via Ipad made available to them at the hospital. The research assistant will complete an eligibility assessment and obtain verbal consent from the patient while admitted to the hospital. If eligible participants decline to enroll, reason for refusal will be recorded if the individual agrees with us collecting that information. Eligible participants who decline will be asked to participate in a parallel cohort study of patients where baseline demographic and prospective clinical data will be collected, as described below. Patients will have access to a hard copy of the consent form to review

and given the opportunity to ask any questions they have to the research assistant verbally.

Intervention
The Second Heart Program will provide an intervention available to PWID with IE, including both medically and surgically-managed IE. The four components of the study intervention are: (1) peer support worker with lived experience, (2) systems navigator, (3) addiction medicine physician, and (4) primary care physician (if they are currently unattached). Each component is described below.

(1) Peer support worker
An individual with substance use lived experience will provide peer support services. The peer support worker will provide harm reduction education, including safe injection practices and naloxone administration practices, to each patient while in hospital. The peer support worker will also provide support to the patient post-discharge in the community: connecting patients to harm reduction services, providing social support, and assisting patients in attending medical appointments. The peer support worker will make contact with the participant in hospital initially, weekly in the first month post-discharge, and every two weeks thereafter, or upon participant request. For the purposes of this study, peer support workers will be hired through the Canadian Mental Health Association (CMHA) in Hamilton. CMHA provides standardized training for peer support workers working with people with substance use, and will have the organizational structure to support peer workers as employees while contracted to our study.

(2) Systems Navigator
A systems navigator assists clients in coordinating health care and social services. The systems navigator will link participants to community resources, addiction services, income support, transportation resources, follow-up appointments, and other social services. Points of contact will include in hospital, every two weeks for the first 3 months post-discharge, and monthly from 3-12 months, or upon participant request.

(3) Addiction medicine physician
Participants will be offered consultation from the Inpatient Addiction Service. Addiction medicine physician consultation will also be offered as this is currently standard of care in two of our local hospitals – Hamilton General Hospital and St. Joseph's Hospital.

The physician may offer medication-assisted treatment if indicated. If treatment is initiated, a transfer of care will be arranged to appropriate community-based addictions care upon discharge. A consultation from the addiction physician is not a requirement for enrollment. If participants request an addiction consultation as an outpatient, they will be referred to the Rapid Access Addiction Medicine clinic or to a clinic of their preference in the community.

(4) Primary Care Physician
If a patient does not have a primary care physician, they will be connected to one prior to discharge. The family physician will provide primary care to participants following discharge from hospital, and will coordinate their ongoing healthcare needs. If the patient has an existing attachment to a primary care physician, the research team will seek to engage the primary care physician as part of the treatment team. Primary care physicians will be able to access the other members of the intervention team (peer support worker, systems navigator, addiction medicine physician) to assist their patients and maintain open communication throughout the study period.

Usual care

As per the standard of care, an addiction medicine consultation would still be offered to all patients who are admitted with infective endocarditis who have a concurrent substance use disorder. This will continue to be offered regardless of the patient's decision to accept or decline study participation.

While the standard of care regarding the process of connecting patients to primary care prior to discharge varies among hospitals and different medical wards (direct connection prior to discharge vs. directing patients to resources to find a family physician after discharge, etc), we would still encourage that any patient who declines to participate in our study be connected to a primary care physician. However, if the patient was not enrolled in our intervention, this process would be coordinated through the usual care pathway (usually the unit social worker) rather than through the systems navigator working with our study team.

Data collection and outcome measures

Patient information (including descriptive demographic data, social determinants of health, medical history, substance use history, access to harm reduction and community resources, and treatment plan and patient goals) will be collected by a combination of self-report (verbally administered by a research assistant) and electronic medical record chart review at baseline and 12-months post-discharge.

Process feasibility outcomes (enrollment, completion, and drop-out rates, reasons for dropping out/refusal, number and nature of unintended outcomes) will be tracked by the research assistant in a Master file. Perceived suitability and acceptability of the program for the intervention will be explored through an open-ended survey administered by the research assistant verbally with patients in the hospital and 12-months post discharge (post-study).

Resource feasibility outcomes (number and nature of connections with the peer support worker and systems navigator) will be tracked in an appointment tracking file by the peer support worker and system navigator. Program costs will be extracted from financial reports required for reporting purposes for the grant.

Management feasibility outcomes (number and nature of challenges in data collection) will be recorded by a memo note by the research assistant.

Scientific feasibility outcomes (reinfection, readmission, and reintervention rate at 1, 3, 6, and 12-months, 1-year post-discharge mortality rate, number of touch points with cardiovascular surgery, cardiology, infectious disease, systems navigator, primary care physician, addictions services in hospital and 1-year post-discharge) will be extracted from the electronic medical record at Hamilton General Hospital and St. Joseph's Healthcare Hamilton. These outcomes will also be collected via self-report survey at 1, 3, 6, and 12 months.

Perceived strengths, weaknesses, opportunities, and threats of the program (SWOT questions) [18] and *perceived acceptability* will be explored via 1-on-1 semi-structured interviews with patients (at 3- and 12-months post-discharge), peer support workers, addiction medicine physicians, systems navigator, primary care physician, peer support worker coordinator at 12 months. Clinicians who co-manage these patients during their in-patient stay (cardiovascular surgery, internal medicine, cardiology) and other community partners (primary care physicians, addictions care providers) will be asked to complete an open-ended survey to assess their *perceived strengths, weaknesses, opportunities, and threats of the program*, as well as *acceptability* of the program.

Semi-structured interviews (SWOT questions)

A research assistant will conduct 1-on-1 semi-structured interviews that will be audio-recorded and transcribed. As noted above, these interviews will be with patients at 3- and 12-months post-discharge, and with peer support workers, addiction medicine physicians, systems navigator, primary care physician, peer support worker coordinator at 12 months.

Participant-related data collection schedule by participant

Study participant	**In hospital (baseline)**	**Post-discharge**			
		1-month	**3-month**	**6-month**	**12-month**
Patient	Patient information (EMR and self-report) Perceived suitability & acceptability questions Number of touch points with cardiovascular surgery, cardiology, infectious disease, systems navigator, primary care physician, addictions services, peer support worker (EMR and self-report survey)	Reinfection rate, readmission rate, reintervention rate, number of touch points with cardiovascular surgery, cardiology, infectious disease, systems navigator, primary care physician, addictions services, peer support worker (EMR and self-report survey)	Interview (SWOT questions) Reinfection rate, readmission rate, reintervention rate, number of touch points with cardiovascular surgery, cardiology, infectious disease, systems navigator, primary care physician, addictions services, peer support worker (EMR and self-report survey)	Reinfection rate, readmission rate, reintervention rate, number of touch points with cardiovascular surgery, cardiology, infectious disease, systems navigator, primary care physician, addictions services, peer support worker (EMR and self-report survey)	Patient information (EMR and self-report) Interview (SWOT questions) + Perceived acceptability questions Mortality rate Reinfection rate, readmission rate, reintervention rate, number of touch points with cardiovascular surgery, cardiology, infectious disease, systems navigator, primary care physician, addictions services, peer support worker (EMR and self-report survey)
Peer support worker					Interview (SWOT questions) +

					Perceived acceptability questions
Addiction medicine physician					Interview (SWOT questions) + Perceived acceptability questions
System navigator					Interview (SWOT questions) + Perceived acceptability questions
Primary care physician					Interview (SWOT questions) + Perceived acceptability questions
Peer support worker coordinator					Interview (SWOT questions) + Perceived acceptability questions
Clinician who co-manage patients					Open-ended survey (SWOT questions) + Perceived acceptability questions
Other community partners					Open-ended survey (SWOT questions) + Perceived acceptability questions

Patients who refuse or drop-out

We will also collect basic demographic data, follow-up data, and a brief qualitative survey for eligible participants who decline enrollment in our intervention. The data collected from this parallel cohort will not be used to compare outcomes, but rather, the information collected will be used to understand how the program could be adapted to mitigate drop-out or refusal to inform our assessment of feasibility.

Data storage

EMR data will be extracted and entered directly into REDCap, a secure, web-based application for data collection and storage, housed on the Department of Family Medicine secure server. Surveys administered verbally will be entered into REDCap. Program records are used for tracking touch points between the peer workers, systems navigator and patients. This will be an excel file, password protected on the Department of Family Medicine's secure network. The audio recordings will be downloaded immediately from the tape recorded and saved (password protected) on the Department of Family Medicine's secure network, then deleted from the tape recorder. Paper-based study materials (consent forms, open-ended surveys from 'other healthcare providers' and community partners) will be kept in a locked filing cabinet in a locked office in DBHSC (3rd floor).

Data analysis

Means and standard deviations will be used for continuous data and counts and proportions for categorical data. Outcomes between the participants in our intervention cohort and the participants in our nonintervention cohort will also be descriptively compared for the purposes of feasibility and future project design. An inductive and deductive theoretical thematic analysis [24] will be completed by the study team, grounded in SWOT [18]. Rigor will be fostered using recommendations for trustworthiness and authenticity [25]. Mixed analysis will involve examining instances of concordance and discordance.

Below is a table outlining research outcomes, sources, timing and analysis.

Research outcome	Source(s)	Timing	Analysis
Enrollment, completion and drop-out rate of participants	Program records	Post-study	Descriptive statistics
Reasons for drop-out	Program records	Post-study	Content analysis
Perceptions of suitability and acceptability of intervention process	Participant survey	In hospital, Post-study	Descriptive analysis
Number and nature of unintended (or negative) outcomes	Program records	Post-study	Frequency and content analysis

Frequency of peer support worker and systems navigator contact with participants	Program records	Post-study	Frequency
Nature of the supports/contact points provided by peer support worker and systems navigator	Program records	Post-study	Content analysis
Program costs (i.e., cell phones, human resources, travel)	Financial reports	Post-study	Total by expense item
Challenges in the collection of data in study	Memo note	Post-study	Content analysis
Reinfection, readmission, and reintervention rates	Electronic medical records at Hamilton General Hospital and St. Joseph's Healthcare Hamilton, patient survey designed for the study	1, 3, 6, 12 months post-discharge	Descriptive statistics
Mortality rate 1-year post-hospitalization	Electronic medical records at Hamilton General Hospital and St. Joseph's Healthcare Hamilton	12 months	Descriptive statistics
Number of touch points with cardiovascular surgery, cardiology, infectious disease, systems navigator, primary care physician, addictions services in hospital and 1-year post-discharge	Electronic medical records at Hamilton General Hospital and St. Joseph's Healthcare Hamilton, patient survey designed for the study Self-report survey	In hospital, 12-months 1, 3, 6, 12 months post-discharge	Descriptive statistics
Perceived strengths (impacts), weaknesses (challenges), opportunities, and threats of the program	One-on-one interviews with patients, peer support workers, addiction medicine physicians, systems navigator, primary care physician, peer support worker coordinator Open-ended survey for 'other care providers' (cardiovascular surgery,	3 and 12-months for patients; 12-months for other participants	Thematic analysis, grounded in SWOT analysis [18]

	internal medicine, cardiology) and community partners		

Ethical issues and project challenges

People who inject drugs are a stigmatized population. Further, multi-stigma (i.e., intersections of stigma including gender, race, sexual orientation, socioeconomic status among others) may also exist. Further, people who inject drugs may be concerned about the illegality of their substance use. Extra care will be taken during recruitment. Gatekeepers are important in research with stigmatized groups and so the way in which gatekeepers are included will be considered. We anticipate much effort will go into recruitment, and so using the PI's network within addiction treatment programs and harm reduction services will be the starting place. We intend to stay close to stakeholders who work with this group of patients.

Timeline

February 2020: Submit Hamilton Integrated Research Ethics Board application; Initiate recruitment for peer worker and research coordinator
March 2020: Complete hiring and training of peer worker and systems navigator; Active recruitment of participants on a rolling basis with ongoing intervention
September 2021: Closed recruitment of new participants
December 2021: Final data analysis and manuscript development

Participant remuneration

Each participant will receive a total of $250 in remuneration throughout the duration of the study. Participants will receive a $50 stipend in the form of a gift card or e-transfer at each point of contact with the research assistant (initial enrollment and data collection in the hospital, 1-month follow-up survey, 3-month follow-up survey and qualitative interview, 6-month follow-up survey, and 12-month follow-up survey and qualitative interview). Participants will also receive a basic cell phone with talk and text plan throughout the 12-month study period. The cell phone will be used to facilitate contact with the peer support worker, systems navigator, and research assistant. The use of the cell phone is to facilitate connection between participants and study team. If found to be an important component of this intervention, the provision of a cell phone will need to be considered in subsequent studies.

Knowledge translation

The results of this study will be disseminated locally via a written report to all care providers who interacted with the study and who provide care to PWID with IE in hospital and after discharge. Study results will be submitted for presentation at national conferences, including the Canadian Society of Addiction Medicine, the Canadian Cardiovascular Congress, Family Medicine Forum, Canadian Society of Internal Medicine, and the Canadian Association for Clinical Microbiology and Infectious

Diseases Annual Conference. The final manuscript will be submitted for publication in a peer-reviewed medical journal.

Potential impact

A recent paper by Kendall et al. (2017) found that PWID have 7-8x higher rates of emergency department visits and hospitalization. PWID are also more likely to have income assistance or disability, unstable housing, and mental health co-morbidities [2]. It was proposed that improving housing supports and access to primary care and opioid substitution therapy could decrease the need for emergency services [2]. However, there are currently no comprehensive programs available to address this need.

PWID have a high lifetime risk of IE and experience disproportionate rates of post-IE complications and short-term mortality. The unique characteristics of PWID, their risk of ongoing substance use, and the systemic barriers they face upon discharge to the community likely contribute to these adverse outcomes. Therefore, any intervention intended to reduce the adverse outcomes for PWID after hospitalization for IE must be intentionally designed to address these patient factors. The Second Heart will be the first clinical program in any jurisdiction that is specifically designed to link PWID with IE to a multidisciplinary team that will transition with them from hospital to community. The continuity and comprehensiveness of care experienced by participants can potentially significantly improve the patient experience of a traditionally underserved population, and reduce health care costs incurred with readmission and reintervention in the high-risk period after discharge from hospital.

If Second Heart is found to be feasible, the findings will support to design a larger, multi-site cluster RCT sufficiently powered to examine and evaluate specific health outcomes, larger scale implementation and sustainability.

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