# ACCELERATING INNOVATIONS INTO CARE (AICE) – MARKET ACCESS

## EXAMPLE PROJECT METHODOLOGY

### Background

The following Example Project Methodology is being shared with permission by a previous Applicant to Accelerating Innovations into CarE (AICE). The purpose of this document is to equip prospective Applicants with an awareness regarding the level of detail recommended when writing the Project Implementation portion of applications to AICE-Market Access. It is important to note that this Example Project Methodology is from a previous version of the Program, and as such, the format is substantively different from the current version available through our online portal. Furthermore, in this example, the Applicants were requested to provide additional details prior to making a final decision, which have also been included to support prospective Applicants to AICE-Market Access.

If you have any questions regarding this Example Project Methodology, please contact Graham Anderson, Senior Business Partner, Health Innovation at graham.anderson@albertainnovates.ca

[redacted]

## Section 3: Non-confidential Scientific Abstract

Using scientific terminology, please provide a high-level non-confidential overview of the proposed project and identify the problem you are trying to solve and its potential impact on Alberta's health care system. **Please Note: This section may be provided to a diverse set of stakeholders including the public.** Do not exceed the space below.

Where appropriate, the text may be structured using the following headings:

- Introduction or Objectives, including the health problem that the technology is aimed at
- Methods for implementation, testing and measuring outcomes/success
- Results, including the potential impact on Alberta's health care system in quantitative terms
- Conclusions

High blood pressure is the leading cause of death and disability in the world. High blood pressure is a strong risk factor for stroke. Reducing blood pressure after stroke prevents recurrent stroke and death.

Home blood pressure telemonitoring consists of sending home blood pressure readings securely and instantly to a web portal. These readings can be used by care providers (often called case managers) to determine if a patient's blood pressure is controlled. If it is not, medication adjustments can be made to control the blood pressure. Home blood pressure telemonitoring automates the blood pressure measurement process and quickly summarizes the blood pressure information so that it can be used to make clinical decisions. In addition, home readings are more accorate that clinic readings and contemporary blood pressure guidelines recommend preferential use of home blood pressure measurements instead of clinic blood pressure.

Previous studies have shown that home blood pressure telemonitoring and case management improves blood pressure control. Other data show that achieving blood pressure control in high-risk patients with hypertension is cost-saving to the health care system. However, home blood pressure telemonitoring is not used in Alberta because of a lack of Alberta data and also because of uncertainty about how to implement it and how to reimburse it.

In 50 patients who have had a recent stroke, home blood pressure telemonitoring will be performed. A [redacted] pharmacist case manager will monitor the readings and adjust antihypertensive drug therapy to optimize blood pressure control. This first step in the project will assess if home blood pressure telemonitoring and case management can be implemented in Alberta. Since, it has worked in many other areas of the world, we anticipate that it will be implementable here.

The second part of the project will use data collected from Part 1 to develop an economic model of home blood pressure telemonitoring in Alberta. This will be done to confirm that home blood pressure telemonitoring with case management is cost-effective and even cost-saving in Albertans who have had a recent stroke.

In the third part of the project, assuming that home blood pressure telemonitoring is implementable and cost-effective, we will assemble a group of stakeholders to determine how to implement this intervention all patients who have a stroke in Alberta. This will include holding meetings amongst all relevant stakeholders to achieve consensus on sustainable implementation and funding.

[redacted]

## Section 4: Budget

### A. Estimated Budget Information

Please refer to the AICE Funding Guide for allowable costs and expenditure guidelines.

| | Funds Requested from AIHS (max 50% total project budget) | SME Contributions (min 25% total project budget) | | Other Contributions | |
|---|---|---|---|---|---|
| | | Cash | In kind | Cash | In kind |
| 1. Data Analysts | 31,488 | | | | |
| 2. Management / administration | 80,000 | | | | |
| 3. Other personnel | 11,200 | | | | |
| 4. Equipment | 10,160 | | | | |
| 5. General supplies | | | | | |
| 6. Travel | 14,100 | | | | |
| 7. Other Costs (list)<br>i) System and data transmiss<br>ii) Portal Maintenance<br>iii) Publication costs | 3000 | | [redacted] | | |
| Total (items 1 to 7) | **149,948** | | [redacted] | | |
| **Total Project Budget** | [redacted] | | | | |

[redacted] **AICE Funding Proposal** **Amount requested $149,948**

**Implementation of Blood Pressure Telemonitoring and Case Management After a Cerebrovascular Event**

**Total budget = $299,948 including $149,948 from AIHS and $150,000 in-kind from** [redacted]

**AIHS Justification**

1. **Central coordinator (includes 25% benefits x 18 months) = $80,000**
   Arrange ethics, develop case-report forms, develop manual of operations, schedule meetings, coordinate between investigators and with stakeholders, perform administrative tasks, perform data quality checks, preparation of briefing documents, train data collectors and case managers
2. **Data Analysts = $31,488**
   a. **Economic analysis = $24,488**
      Acquisition, cleaning, and analysis of administrative data for costing (Statistician $47.40/hr x 75 hours = $3555) and economic model construction, calibration, validation, analysis and sensitivity / scenario analysis (Health Economist $55.82/ hour x 375 = $20,933)
   **b. Statistical analysis ($100 per hour x 70 hours = $7000)**
3. **Data collectors (Edmonton and Cochrane = $11,200**
   $40/hour x 6 hours per patient x 40 patients = $9600
   $40/hour x 1 hour per patient x 40 patients = $1600 for screen fails
4. **Case manager (provided in-kind by** [redacted]
   Initiate and titrate antihypertensive drug therapy and to monitor for adverse effects
5. **Linkage to** [redacted] **administrative data (provided in-kind by** [redacted]**)**
   To determine health care utilization prior to baseline and during follow-up
6. **Equipment = $254 x 40 = $10160**
   [redacted] Home BP monitor (Bluetooth Enabled) = $90; Lamprey set-top box = $164
7. **Travel/meetings** = $12,500
   a. **Patient Parking = $1600**
      $10 per visit x 3 visits x 40 patients=$1200
      $10 per visit x 1 visit x 40 patients (screen fails)=$400
   b. PI and central coordinator to travel intraprovincially for meetings with investigators and stakeholders and between study sites. For 1 provincial and 1 national presentation of results. $12,500
8. **Publication fees** = $3000
   to defray the costs of 2 publications in open access format

[redacted] **Justification**

$150,000 in in-kind funding will be committed. These funds will include the following:

| | |
|---|---|
| Project Analysis and Management - Technical & Operations | [redacted] |
| Software Customization | [redacted] |
| Database Development, Data Maintenance | [redacted] |
| Testing - Internal and User Acceptance | [redacted] |
| Deployment, User Training and Post-Deployment Support | [redacted] |
| Network Equipment | [redacted] |
| Hosting | [redacted] |
| Financial Management, Financial Analysis, Funding Model Development | [redacted] |

[redacted] AICE Funding Proposal Amount requested $149,948

**Implementation of Blood Pressure Telemonitoring and Case Management After a Cerebrovascular Event**

## 1.0 Summary

High blood pressure (BP) is a leading risk factor for cerebrovascular disease. Optimizing BP control **prevents recurrent cerebrovascular events and is cost saving**. BP control can be optimized through home BP telemonitoring in conjunction with protocolized case management. Home measurements **are more accurate** than clinic readings and protocolized case management enables timely therapeutic adjustments.

Even though it can be performed easily and relatively cheaply, BP telemonitoring and protocolized case management have yet to be implemented in Alberta. Barriers to implementation include the following: 1. providers and policymakers are unaware of the supportive evidence; 2. a provincial telemonitoring system has not been created; 3. an economic assessment has not been performed in Alberta; and 4. a funding model to reimburse care providers and telemonitoring system industry partners does not exist.

In partnership with [redacted], a Canadian medical diagnostic data service provider, we propose to implement a low-cost home BP telemonitoring system in 40 patients who have had a recent cerebrovascular event and who have elevated BP levels. [redacted] case managers (pharmacists with prescribing privileges) will use this BP telemonitoring system to manage the elevated BP. Over six months, we expect to see clinically important improvements in BP control (i.e., results similar to those reported in multiple previous randomised trials of home BP telemonitoring and case management). An economic assessment will be performed to quantify local costs and assess cost-effectiveness in the Alberta context. Assuming that the expected results are seen and cost-effectiveness is documented, discussions with major stakeholders ([redacted] will be held to sustainable implement and perform home BP telemonitoring and case management in this patient population.

## 2.0 Background

### 2.1 High blood pressure and cerebrovascular disease: common and devastating conditions

High blood pressure, which affects nearly 25% of Canadian adults, is the number one cause of death and disability in the world and a primary risk factor for ischemic and hemorrhagic cerebrovascular disease, heart disease, renal failure and dementia.(1) Cerebrovascular disease (CVD) is the leading cause of chronic disability globally; a major cause of death and dementia; and a significant burden to patients, caregivers, and healthcare systems.(2) In 2011, nearly 50,000 Canadians were hospitalized for stroke; furthermore, an estimated 400,000 Canadians are living with long-term stroke disability.(3) Individuals with CVD are at extremely high risk for recurrence; aggressive risk factor management to prevent recurrent stroke, disability, death, increased health care use, and escalating costs is of paramount importance.(4, 5)

### 2.2 Early control of blood pressure after a cerebrovascular event is critically important

The risk of stroke recurrence in patients with CVD is higher than 10 percent in the first 3 months.(6, 7) Alberta data indicate that 15% of patients suffering a transient ischemic attack or minor stroke had a recurrent and disabling event within 90 days.(8) Uncontrolled blood pressure is the primary cause of preventable stroke - over 75% of stroke survivors have hypertension and less than 50% are controlled to target.(9)

### 2.3 Cost-effectiveness of treating high blood pressure in high-risk individuals

Achieving BP control in high-risk patients, including those who have CVD, **is cost saving** (which is rare, as few medical interventions save money over the long term).(10) Therefore, health care payors can expect initial costs to be offset by substantial downstream savings. In the US, health care payors can spend **an additional $600-1250 USD per patient per year** controlling BP in high-risk patients yet still remain cost-neutral.(10)

### 2.4 Home BP monitoring is the preferred method for monitoring and adjusting therapy

BP measurement is of critical importance and is performed in-office or out-of-office.(11, 12) In-office measurements are used to diagnose and follow the vast majority of Canadians with hypertension even though office BP is often inaccurate.(13) Office measurements require patients to attend appointments, a barrier for patients who have impaired mobility, rural based, or who have financial limitations. Office appointments are sometimes difficult to schedule in a timely manner, limiting the ability to make timely therapeutic adjustments.

The Canadian Hypertension Education Program Recommendations Task Force (CHEP) has strongly endorsed use of out-of-office over in-office measurements. (13) Out-of-office measurements include home BP measurement and 24-hour ambulatory blood pressure measurement (ABPM); both more strongly and consistently predict cardiovascular outcomes and enable identification of white coat (normal out-of-office BP levels and elevated in-office readings) and masked effect (normal manual office measurements yet elevated out-of-office BP levels).(12) White coat effect results in overtreatment, while masked effect in undertreatment. Out-of-office readings are therefore critically important to ensure safe and rational drug use.

ABPM is the gold standard BP measurement method(13) but is not widely available, not widely reimbursed, and is often not well tolerated (because frequent measurements are needed and sleep disturbance may occur). Home BP measurement is thus much more commonly used and Canadian guidelines strongly recommend home BP for follow-up BP measurement because it enables self-monitoring and encourages self-management.(13) (14–16) Nearly 50% of hypertensive Canadians own a home monitor.(17)

### 2.5 Home BP Telemonitoring is the best method for implementing home monitoring

Although the CHEP guidelines strongly endorse home BP measurement, the onus is placed upon the patient to measure, record, and present the readings to their provider. This has many pitfalls. Patients often forget to record measurements or do not follow the recommended protocol (timing, frequency and number of measurements). Patients also may report only selected readings to their provider(18, 19) - less than one-third of patients report ≥80% of measurements.(20) Physicians often do not calculate the mean BP (treatment adjustments are based on the mean), may not scan and upload hand-written BPs into their EMR (thus, no permanent record is available), and may not act to lower elevated readings ('therapeutic inertia').(18, 19)

Home BP telemonitoring, through process automation and protocolization, overcomes these barriers.(20, 21) BP telemonitoring consists of electronically and securely transmitting remotely collected BP measurements in real-time to a central electronic health care portal. Data can be summarized for use by patients and providers – this includes calculating BP means and graphing temporal BP trends. Mean BPs that are too high can be flagged for action whereas those in the normal range provide evidence for optimal control. Telemonitoring may eliminate the need for an in-person clinic visit, thereby increasing health care delivery efficiency, minimizing costs and making more efficient use of provider time. A meta-analysis of 23 RCTs (7037 patients) reported that home BP telemonitoring reduced BP by 5/3 mmHg compared to usual care ($p<0.0001$ for both systolic and diastolic BP).(22) This is a clinically important reduction - a 5-mmHg reduction in BP in high-risk patients reduces cardiovascular events by 15%.(23) A 9 mmHg BP reduction in hypertensive stroke survivors reduces recurrent stroke by 28% (95% CI 17 to 38%).(24)

In most of these trials, telemonitoring was used in conjunction with case management. Case managers, usually nurses or pharmacists, work collaboratively with patients and physicians to optimize health behaviours, monitor risk factors, implement therapeutic adjustments, encourage adherence, and coordinate follow-up.(25–27) Case management works best when the case managers have prescribing authority and use protocols to make guideline-concordant therapeutic adjustments.(25, 28, 29) The PREVENTION Trial, performed in Alberta, demonstrated that pharmacist case management dramatically improves risk factor control post-stroke.(29)

### 2.6 Reasons why home BP telemonitoring is not currently used in Canada

1. **Collaboration between health care providers/decision makers and device makers/technology companies** is required to make telemonitoring feasible. Historically, a lack of dialogue and interaction between these two potential partners has limited collaboration.
2. **Costs**: Historically, this has been a major barrier, primarily because of uncertainty over who will pay for teletransmission, health portal development, and portal maintenance. However, home BP monitors are now inexpensive and widely used ($85 for a Bluetooth-enabled device), cellphone/internet use is very high (enabling convenient, secure electronic data transmission), health portals exist (e.g. NetCare), and established companies exist that specialize in health data transmission [redacted] Thus, overcoming these barriers is feasible.

3. **Need for user training:** This has largely been eliminated through technological advancements. Systems require little additional action (other than BP self-measurement) because BP teletransmission can be automated once the reading is taken.
4. **Requires a shift in reimbursement strategies for physicians:** Currently, physicians are paid primarily for face-to-face visits, although this is changing (Alberta Health and the Alberta Medical Association have recently announced that future fee codes will increasingly be targeted towards reimbursement for electronic or virtual communication between patients and providers [e.g. email and secure messaging]). Importantly, telehealth and telephone fee codes already exist and can be used for reimbursing telemonitoring provision. But, in order to ensure proper uptake, assuming effectiveness and cost-effectiveness is verified, it is important that all stakeholders agree upon the best way to reimburse telemonitoring for blood pressure.
5. **Requires a shift in care provision strategies:** Team based care, where a pharmacist or nurse case manager looks after a roster of patients in collaboration with a physician, is an ideal way to combine telemonitoring and case management. Team based care is used widely in both primary and specialty care in Alberta and pharmacists in this province can hold prescribing privileges. Therefore, this is no longer a major barrier. Nevertheless, determining how post-stroke blood pressure telemonitoring is delivered, by whom, and how transitions in care should occur, is needed.

### 3. Specific aims and primary endpoints

This proposal is a collaboration between academic investigators and experts in hypertension, cerebrovascular disease and technology assisted care; the [redacted] a Canadian company specializing in the secure transmission of health care data. [redacted] has created a BP telemonitoring system that teletransmits BP data securely to a web portal.

**Aim 1:** Implement this telemonitoring system in 40 patients who have had a recent cerebrovascular event recruited from two stroke centres in Alberta – Edmonton and Cochrane. The focus is on demonstrating implementability and feasibility, not on rigorously evaluating effectiveness, which has already been done in over 20 studies. A[redacted] pharmacist case manager already working in these stroke centres will review the readings and initiate/adjust antihypertensive therapy accordingly. We will determine if BP (and other cardiovascular risk factors) improved over a six-month period.
**Aim 2:** Perform an economic analysis to comprehensively assess costs and verify cost-effectiveness.
**Aim 3:** (Assuming Aim 1 and 2 show the expected results), develop and implement a sustainable funding model to support use of home blood pressure telemonitoring in all patients (or a defined subset) with a recent stroke/TIA in Alberta. This will require iterative discussion with major stakeholders and identification of a sustainable care transition model as well as reimbursement strategies for providers [redacted]

### 4. METHODS

#### 4.1 Overall design, setting, and population

In this 6-month **pragmatic, prospective pre-post implementation project**, 40 consenting patients seen in Stroke Prevention Clinics in [redacted] will receive home BP telemonitoring plus protocolized case management upon discharge home.

#### 4.2 Inclusion Criterion

Age ≥18 years with uncontrolled hypertension (BP ≥ 140/90), documented recent cerebrovascular event as diagnosed by a neurologist, English literacy (verbal and written) and a home internet connection

#### 4.3 Exclusion Criteria

1. Systolic BP level >220 mmHg or diastolic BP level >110 mmHg on screening BP measurement (BpTRU device). Immediate consultation with a hypertension specialist will be arranged.
2. Severe cognitive impairment, defined as a score of <5 on the Short Portable Mental Status Questionnaire,(30) or severe depression (Patient Health Questionnaire [PHQ-9] ≥15).(31)

3. Life expectancy less than 1 year

**4.4 Interventions**

All patients will be lent a validated electronic upper arm oscillometric BP device (A&D Ltd. UA-651BLE; San Jose, CA) and a set-top box enabling wireless data transmission (estimated cost $200 for both). This will remain in their home for the study duration. Pushing a single button activates the device and initiates a BP measurement, which is auto-transmitted to the set-top box via Bluetooth. The set-top box will automatically relay each BP reading to a secure health portal without any further action required by the patient.

Our collaborator, [redacted], has just finished a prototype home BP telemonitoring solution that includes a portal that accepts transmissions from the above-described set-top box. This portal, [redacted], provides [redacted]

Patients will be counselled to perform all measurements according to recommended techniques for home BP measurement.(13) Four measurements (duplicate readings in the morning and evening) will be taken daily for 1 week. Readings taken on the first day are discarded and the latter 6 days (24 measurements) are averaged. If BP is uncontrolled, this 1-week of measurements will be done each month until BP is in the therapeutic range (<140/90 mmHg; <130/80 if diabetic). Once controlled, the 1-week protocol will be repeated at the end of the six-month period.(13) Teletransmitted BP readings will be summarized within the health portal [redacted], which will be used to calculate an overall weekly mean (first day measurements discarded; subsequent 24 measurements over the next 6 days averaged).(13) Temporal trends will be plotted.

Patients will be followed by a prescribing pharmacist case manager (working in the local stroke centre) who will teach lifestyle modification, BP self-monitoring, and med adherence; review telemonitored health portal BP summaries; make protocolized therapeutic adjustments; and fax/email via EMR a summary to the patient's physicians (to make them aware of treatment changes). To ensure full guideline concordant standardization of the intervention, the pharmacist case manager will receive Canadian guidelines training prior to study initiation and will follow a guideline-concordant protocol for drug titration. Drugs will be added in guideline-concordant manner(33) in the following order: ACE inhibitor (or angiotensin receptor blocker if ACE intolerant) thiazide diuretic combination, dihydropyridine calcium channel blocker, beta-blocker, spironolactone, doxazosin, clonidine, and hydralazine. Drugs will be reduced/stopped in reverse order. Specific agents and doses will be protocolized. We have previously designed and implemented care similar protocols for case managers to use in high-risk hypertension settings and we will use modified versions of these.(29, 34)

**4.5 Baseline Data**

1. **Demographics and health behaviours:** age, sex, race, marital status, smoking, alcohol intake.
2. **Past medical history:** dyslipidemia, coronary artery disease, stroke, peripheral vascular disease, chronic kidney disease (glomerular filtration rate ≤60 ml/min).
3. **Medication history** including antihypertensive drugs: name, type, dosage, frequency, duration. Based upon self-report but cross-indexed with the patient's pharmacy medication record.
4. **Anthropometric indices:** height, weight, body mass index
5. **Upper mid arm circumference (to determine proper cuff size):** measured half way between the acromion and the olecranon using a tape measure with the arm at heart level.
6. **Screening BP, home BP series, and pulse rate:** Screening BP measurements will be taken with the BpTRU automated device. Home BP and pulse will be measured using the A&D Ltd. UA-651BLE.

7. **Labs** will include serum sodium, potassium and creatinine; glycated haemoglobin (A1c); and fasting lipids (total cholesterol, high-density or HDL cholesterol, low-density or LDL cholesterol, triglycerides)
8. **Health care use in past year:** includes physician visits, emergency department use and hospitalizations ascertained through patient self-report and by linking to [redacted] administrative data sources.
9. **Quality of life and utility measurement**: using EQ-5D to calculate quality-adjusted-life years.(35)

### 4.6 Follow-up Data

Follow-up data collection will be collected at 6 months and will include telemonitored home BP, heart rate, medications, anthropometrics, cardiovascular risk factors (A1c, lipids, smoking), health care use (patient report and [redacted] admin data), quality of life and utilities.

### 4.7 Work Plan

#### 4.7.1 Aim 1: Telemonitoring implementation and blood pressure control

**We will assess 6-month change in home systolic BP as the primary outcome**. Systolic BP is used because it is a stronger predictor of risk.(36) We will also examine the proportion of patients with home systolic and diastolic BP at target (<135/85 mmHg) as well as the change in mean home systolic and diastolic BP; changes in A1c, lipids, anthropometric indices and changes in quality of life/utility scores.

**Data Analysis**: First, variables will be examined descriptively and graphically, including assessments of temporal trends and tests of normality. Second, the 6-month mean change from baseline in each outcome will be calculated. Third, multivariable predictors of the 6-month change in a given outcome will be identified using appropriately constructed and calibrated logistic regression models for dichotomous outcomes (including the primary outcome) or linear regression models for continuous ones.

#### 4.7.2 Aim 2: Economic assessment

Costing will adhere to the three-step micro-costing technique of identification, measurement, and valuation of relevant health care and non-health care resources.(37, 38) Cost by category, including program start-up costs and on-going costs will be tabulated. The cost per patient for telemonitoring will be calculated, and where any uncertainty in resource use or costs exists, plausible ranges of resource use will be determined and tested in sensitivity analysis. Resource use and cost data will be used to determine the overall and per-patient total costs.(37, 38) Economic modeling to verify the cost-effectiveness of telemonitoring over defined time horizons will be performed, similar to past work.(39, 40) Alternate funding models will be assessed (see 4.7.3) in scenario analysis.

#### 4.7.3 Aim 3: Develop and implement a sustainable funding model

This will be informed by the results of Aims 1 and 2. Work that needs to be performed will be guided by a pragmatic nominal group technique process(41) with a focus on collating the opinion of all stakeholders and achieving consensus through vote-based ranking, includes:

1. Identify who will pay for telemonitoring equipment, the equipment vendor, and determine the bulk price. We note that patients currently pay for their home BP monitors; thus, there is a precedent for patients bearing the cost. Equipment rental rather than purchase is another option.
2. Determine [redacted] fees for ongoing telemonitoring.
3. Determine the role of the physician and case manager and finalize associated fees and costs. Develop strategies to avoid duplication of care and costs. This will require discussion with the Alberta Medical Association and Alberta Health. Fee codes for BP telemonitoring need not be specific to this service alone. mHealth fee codes currently being implemented could be used.
4. Outline the workflow, resources and equipment required for provincial implementation, including sending the BP data to a province-wide portal such as NetCare. Related to this is the need to determine a process of linkage to primary care and to identify the optimal care model (likely pharmacist case management in collaboration with a physician). This process will require iterative discussion and collaboration between stakeholders.

5. Implement a final state of telemonitoring and protocolized case management in stroke survivors.

**5. Sample Size**

To detect a 9 mmHg decrease in systolic BP after 6 months, with an alpha=0.05, beta=0.9, SD 18 (calculated from(42) using the 6 month systolic BP decrease in the intervention arm), we will need 36 patients. We will round up to 40 to account for dropouts. A 9 mmHg systolic BP drop in the PROGRESS trial of hypertensive patients with cerebrovascular disease led to a 28% reduction in recurrent stroke (95% CI 17 to 38%).(24) (Note: this is a conservative sample size estimate as we are using a control-subtracted BP reduction for sample size calculation purposes; the actual BP reduction will likely be greater).

**6. Timelines**

Start-up, hiring, case report form development, and telemonitoring and web portal optimization specific to the study will performed in the first 2-3 months. Patient accrual will begin after 2-3 months and follow-up will be completed in all patients by 12 months. Aim 3 will be conducted in the final 6 months.

**7. Data security**

Data security is of utmost importance. HIPPA compliant procedures and encryption methods will be used. Our team will work closely with [redacted] to ensure that data transmission and data storage is secure. [redacted] has extensive experience in providing health care data transmission services to physicians, labs, and hospitals.

**8. Team**

This project represents a collaboration between academic investigators ([redacted], the [redacted], and [redacted] Once the study results are available, further collaboration with Alberta Health and the Alberta Medical Association will be initiated. Please see attached letters of support from all stakeholders. Of note, [redacted] Professor of [redacted], an epidemiologist and outcomes researcher, a hypertension specialist, [redacted]. [redacted] is a physician and experienced Health Economist. [redacted] in Computing Science. [redacted] are academic internists with strong track records in cardiovascular care and outcomes research.

**9. Knowledge Translation (KT)**

**9.1 Integrated KT:** This refers to a collaborative process whereby researchers and end-users work together to develop the research question, design and complete the study, interpret the data, and disseminate and apply the results.(43) All team members will jointly participate throughout the study. Venues include local rounds, medical staff meetings, cardiovascular forums, and targeted [redacted] initiatives on vascular disease.

**9.2 End of Study KT:** This refers to the communication activities undertaken by researchers to make end-users aware of new knowledge and research.(43) Findings will be communicated on a regional, provincial, national, and international levels and have the potential to impact current guidelines. We will use traditional routes of presentation at scientific meetings and publications in peer-reviewed journal; publish design and methods papers in open access journals that have no limits for web-appendices (thus making available all intervention materials, training manuals, and data collection forms). The Canadian Hypertension Congress, Canadian Stroke Congress, and Canadian Cardiovascular Congress will be the primary meetings targeted. Other relevant national and international meetings will also be targeted.

More active dissemination will be undertaken through Hypertension Canada and [redacted] by targeting and tailoring communication beyond academia.(43) This will include dissemination via mainstream media, websites, newsletters and social media (Facebook, Twitter, Linkedin).

[redacted]

## References

1. Lim SS, Vos T, Flaxman AD, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the global burden of disease study 2010. *Lancet* 2012;380:2224-2260.
2. Strong K, Mathers C, Bonita R. Preventing stroke: saving lives around the world. *Lancet Neurology* 2007;6:182-187.
3. Heart and Stroke Foundation of Alberta. Statistics. Accessed on April 24, 2016 at http://www.heartandstroke.ab.ca/site/c.lqIRL1PJJtH/b.3650897/k.35F8/Statistics.htm.
4. Kernan WN, Ovbiagele B, Black HR, et al. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2014;45:2160-2236.
5. Goeree R, Blackhouse G, Petrovic R, Salama S. Cost of stroke in Canada: a 1-year prospective study. *J Med Econ* 2005;8:147-167.
6. Rothwell PM, Giles MF, Chandratheva A, et al. Effect of urgent treatment of transient ischaemic attack and minor stroke on early recurrent stroke (EXPRESS study): a prospective population-based sequential comparison. *Lancet* 2007;370:1432-1442.
7. Giles MF, Rothwell PM. Prognosis and management in the first few days after a transient ischemic attack or minor ischaemic stroke. *Int J Stroke* 2006;1:65-73.
8. Coutts SB, Modi J, Patel SK, et al. CT/CT Angiography and MRI Findings Predict Recurrent Stroke After Transient Ischemic Attack and Minor Stroke: Results of the Prospective CATCH Study. *Stroke* 2012;43:1013-1017.
9. Kesarwani M, Perez A, Lopez VA, Wong ND, Franklin SS. Cardiovascular comorbidities and blood pressure control in stroke survivors. *J Hypertens* 2009;27:1056-1063.
10. Moran AE, Odden MC, Thanataveerat A, et al. Cost-effectiveness of hypertension therapy according to 2014 guidelines. *N Engl J Med* 2015;372:447-455.
11. McKay DW, Campbell NR, Parab LS, Chockalingam A, Fodor G. Clinical assessment of blood pressure. *J Hum Hypertens* 1990;4:639-645.
12. Cloutier L, Daskalopoulou S, Padwal RS, et al. A new algorithm for the diagnosis of hypertension in Canada. *Can J Cardiol* 2015;31:620-630.
13. Daskalopoulou SS, Rabi DM, Zarnke K, for the Canadian Hypertension Education Program. The 2015 Canadian Hypertension Education Program recommendations for blood pressure measurement, diagnosis, assessment of risk, prevention, and treatment of hypertension. *Can J Cardiol* 2015;31:549-568.
14. Staessen JA, Den Hond E, Celis H, et al. Antihypertensive treatment based on blood pressure measurement at home or in the physician's office: a randomized controlled trial. *JAMA* 2004;291:955-964.
15. Cappuccio FP. Blood pressure control by home monitoring: meta-analysis of randomised trials. *BMJ* 2004;329:145-140.
16. Ogedegbe G, Schoenthaler A. A systematic review of the effects of home blood pressure monitoring on medication adherence. *J Clin Hypertens* 2006;8:174-180.
17. Public Health Agency of Canada. What are Canadians with hypertension doing to control their high blood pressure? 2009. Accessed on September 15, 2016 at http://www.phac-aspc.gc.ca/cd-mc/slcdcfs-epamccfi/pdf/SLCDCFactSheet2009-Hypertension-eng.pdf.
18. McKay DW, Godwin M, Chockalingam A. Practical advice for home blood pressure measurement. *Can J Cardiol* 2007;23:577-580.
19. Huff LS, Zittleman L, DeAlleaume L, et al. What keeps patients from adhering to a home blood pressure program? *J Am Board Fam Med* 2011;24:370-379.
20. Milot JP, Birnbaum L, Larochelle P, et al. Unreliability of Home Blood Pressure Measurement and the Effect of a Patient-Oriented Intervention. *Can J Cardiol* 2015;31:658-663.

21. Myers M. Limitations of Home Blood Pressure Monitoring in Clinical Practice. *Can J Cardiol* 2015;31:583-584.
22. Omboni S, Gazzola T, Carabelli G, Parati G. Clinical usefulness and cost effectiveness of home blood pressure telemonitoring. *J Hypertens* 2013;31:455-468.
23. Blood Pressure Lowering Treatment Trialists Collaboration. Blood pressure-lowering treatment based on cardiovascular risk: a meta-analysis of individual patient data. *Lancet* 2014;384:591-598.
24. PROGRESS Collaborative Group. Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6,105 individuals with previous stroke or transient ischaemic attack. *Lancet* 2001;358:1033-1041.
25. Norris SL, Nichols PJ, Caspersen CJ, Glasgow RE, Engelgau MM. The effectiveness of desease and case management for people with diabetes. *Am J Prev Med* 2002;22:15-34.
26. Campbell NC, Murray E, Darbyshire J, et al. Designing and evaluating complex interventions to improve health care. *BMJ* 2007;334:455.
27. Tricco AC, Ivers NM, Grimshaw JM, et al. Effectiveness of quality improvement strategies on the management of diabetes: a systematic review and meta-analysis. *Lancet* 2012;379:2252-2261.
28. McAlister FA, Majumdar SR, Padwal RS, et al. Study protocol: The preventing recurrent vascular events and neurological worsening through intensive organized case-management (PREVENTION) trial protocol. *Implement Sci* 2010;5:27.
29. McAlister FA, Majumdar SR, Padwal RS, et al. Case management for blood pressure and lipid level control after minor stroke: PREVENTION randomized controlled trial. *CMAJ* 2014;186:577-584.
30. Pfeiffer E. A short portable mental status questionnaire for the assessment of organic brain deficit in elderly patients. *Journal of the American Geriatrics Society* 1975;23:433-441.
31. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 2001;16:606-613.
32. [redacted]
33. Leung AA, Nerenberg K, Daskalopoulou SS, et al. Hypertension Canada's 2016 CHEP Guidelines for Blood Pressure Measurement, Diagnosis, Assessment of Risk, Prevention and Treatment of Hypertension. *Can J Cardiol* 2016;32:569-588.
34. Simpson SH, Majumdar SR, Tsuyuki RT, Lewanczuk RZ, Spooner R, Johnson JA. Effect of adding pharmacists to primary care teams on blood pressure control in patients with type 2 diabetes: a randomized controlled trial. *Diabetes Care* 2010;34:20-26.
35. EuroQol Group. EQ-5D: A standardised instrument for use as a measure of health outcome. Accessed at http://www.euroqol.org on June 29, 2014.
36. Franklin SS. Elderly Hypertensives: How Are They Different? *J Clin Hypertens* 2012;14:779-786.
37. Brouwer W, Rutten F, Koopmanschap M. Costing in economic evaluations. In: Drummond M, McGuire A, editors. Economic evaluation in health care: merging theory with practice. Oxford: Oxford University Press; 2001. p. 68.
38. Jacobs P, Roos NP. Standard cost lists for healthcare in Canada. Issues in validity and inter-provincial consolidation. *Pharmacoeconomics* 1999;15:551-560.
39. Simpson SH, Lier DA, Majumdar SR, et al. Cost-effectiveness analysis of adding pharmacists to primary care teams to reduce cardiovascular risk in patients with Type 2 diabetes: results from a randomized controlled trial. *Diabet Med* 2015;32:899-906.
40. Johnson JA, Lier DA, Soprovich A, Qiu W, Al Sayah F, Majumdar SR. Cost-effectiveness evaluation of collaborative care for diabetes and depression in primary care. Am J Prev Med. 2016 (in press – online early).
41. Delbecq AL, VandeVen AH. A group process model for problem identification and program planning. *J App Behav Science* 1971;7:466-491.

42. Margolis KL, Asche SE, Bergdall AR, et al. Effect of home blood pressure telemonitoring and pharmacist management on blood pressure control: a cluster randomized clinical trial. *JAMA* 2013;310:46-56.
43. Graham ID, Logan J, Harrison MB, Straus SE, Tetroe J, et al. Lost in knowledge translation: time for a map? *J Cont Ed Health Prof* 2006;26:13-24.

[redacted]

Alberta Innovates, AICE Grant Review Committee Members

**Dear Committee Members:**
**Re: Blood Pressure Telemonitoring and Case Management after a Cerebrovascular Event**

Thanks for the opportunity to expand on the methodology to be used in this project.

**A. Economic Assessment**
Space limitations precluded a comprehensive overview of the economic assessment; we appreciate the opportunity to provide additional detail. Economic evaluation of usual care vs. telemonitoring and case management will be determined using an economic model adhering to Canadian best practices; our team has extensive experience in this methodology. Model inputs will be based on primary study where possible, including characteristics of the simulated patient population, quality of life (EQ-5D-5L), and incremental differences in blood pressure. Detailed costing information will be captured at both a program and patient level (case report forms), including health care professional time for development and delivery of care, information technology infrastructure, equipment, data, setup and maintenance, physician and other provider visits, and medication use (Appendix Table 1). The primary analysis will use the health care payer however a patient perspective (societal perspective) will be incorporated, and scenarios where costs are borne by either the health payer or patient will be explored (such as data/internet, telemonitoring equipment, etc.). Additional scenarios will examine potential ranges of [redacted] fees, physician and case manager costs (including range of fee codes including mHealth), and varying economies of scale and efficiency of care delivery. Recognizing that there is uncertainty in incremental differences in care delivery (for example, case management may reduce in-office physician visits and associated costs but the true extent is unclear), sensitivity analysis will be performed. In the reference case, a six-month time horizon will be used to determine the cost-effectiveness of usual care vs. telemonitoring with case management using incremental costs and blood pressure as the outcome measure. If telemonitoring with case management is not definitively 'dominant' (lower cost and better outcomes), a second model will be created that uses a lifetime time horizon and includes relevant health states including TIA, minor or major stroke, and cardiac events. The incremental costs of delivery of blood pressure management and achieved blood pressure from the 6-month model will assume to persist, and the probability of adverse health outcomes associated with higher blood pressurewill be estimated from available studies (identified through a focused literature search). The health care costs and utility of each health state will be obtained from a focused review of the literature with preference for Canadian data. Sensitivity analysis will be conducted using one way, scenario, and probabilistic sensitivity analysis including generation of cost-effectiveness acceptability curves.

**B. Data Security and Regulatory Requirements**
HIPPA, which you correctly point out is a US requirement, was incorrectly referenced in the application. For wide scale implementation in Canada, and Alberta, it is important that the proposed telemonitoring system follows the laws for governing health data as described by the PIPEDA. The telemonitoring system to be used in this project was developed according to PIPEDA regulations. PIPEDA is actually stricter than HIPPA. We are using data transmission protocols that include Health Level 7 Fast Healthcare Interoperability Resources (HL-7 FHIR), encryption algorithms, and secure data communication and storage protocols. These processes have also been designed to adhere to the Alberta Health Information Act. We should also note that [redacted] is a company that has specialized in secure health data transmission and has been operating within Canada for over a decade. Therefore, they are very experienced in the requirements for secure data transmission.

The **software application and communication protocols** presented in this application were engineered in [redacted] between Q4 2015 and Q1 2016. During this time, the Health Canada

Investigational Testing Authority provided their assessment towards classification of the system. These functions were ultimately assigned a Class 1 designation, meaning that no further assessment and certification of the application was required by Health Canada, and that we could proceed with final development steps, implementation and use. The blood pressure device (A&D UA-651BLE) itself, however, is a Class 2 device, and, as such, does have Health Canada certification. The license number is 94858. We can provide the certificate, if necessary.

**C. Small Sample Size of Aim 1 in Relation to the Work Outlined in Aim 3**

Aim 1 is purely to demonstrate feasibility of use of telemonitoring and case management within the stroke clinics in Alberta (using the case managers currently working in these clinics) and to demonstrate that a clinically important BP reduction is achieved (hence, the sample size calculation provided in the proposal). Given that telemonitoring and case management has been demonstrated to be effective in over 20 RCTs, we don't feel that duplication of such evidence is required. Besides, such a study would require more funding and more time (our current telemonitoring trial [redacted] is being conducted in very elderly patients and has a budget of nearly 1 million dollars and will require 3 years).

Assuming that feasibility and BP reduction is confirmed in Aim 1 (and assuming that the modeling performed in Aim 2 confirms cost-effectiveness/cost-saving), we will proceed with Aim 3, which focuses on wider implementation in post-stroke patients across the province.

**D. Expertise of the Team to Carry Out Aim 3**

Although we appreciate the comments of the Reviewer 1 with respect to the need for methodological rigour and structure in Aim 3, the intent of this Aim is to implement, not conduct a super-rigorous, internally valid qualitative research study. Aim 3 will by far and away be the most difficult Aim. The proposed 'pragmatic' nominal group technique is simply a way of 'organized brainstorming' to achieve consensus on how to move forward and how to implement. We envision hiring a research coordinator with experience in leading such or similar techniques. However, the nominal group process is expected to be relatively easily performed – what will be difficult will be the work following this process - navigating the vested interests of diverse stakeholders and overcoming reimbursement issues, especially in the context of current fiscal uncertainties, to ultimately achieve sustainable implementation (especially within an 18-month timeline). It will require many follow-up meetings and work.

We acknowledge that we are not experts that spend all of our time focusing on qualitative methodologies. But, our team [redacted] have each done multiple qualitative projects (patient-reported outcomes, surveys, modified Delphi panels, health-related quality of life assessments). Most importantly, we have led large groups focused on Knowledge Translation (e.g. I Chaired the [redacted] for 5 years), have achieved consensus amongst diverse stakeholders, and have led many interdisciplinary collaborations. We have sat/sit on committees within stakeholder organizations or hold cross-appointed chair positions ([redacted] This is a strength of the team and it will be invaluable in achieving sustainable implementation.

**E. Ensuring proper home BP monitoring and adherence to protocols**

This is the responsibility of the case manager. At baseline, the patient will receive brief training on how to perform a proper measurement and will be given a Hypertension Canada pamphlet reviewing proper technique. The patient will be trained in the use of the telemonitoring system (in reality, the patient is only required to measure their BP by pushing a single button, and the rest of the process is automated). The measurements are uploaded in real time. Therefore, the case manager can contact the patient if the required number of measurements is not being performed. Of note, we have now enrolled nearly 40 patients in [redacted] and this aspect of the trial is going very smoothly despite the fact that the patients are very old (80+ years of age) and not technologically savvy. We don't think there will be much issue with obtaining proper protocolized measurements in the younger patients enrolled in this project.

**Table 1. Costing data for economic analysis**

| Identification | Measurement | Valuation | Comments |
|---|---|---|---|
| Program Development | | | |
| Health care professional time (physician, nurse, dietician, administrative assistant) | Estimated hours for each health care professional to create care algorithm (program start up costs)<br>Estimated hours for staff training to administer care algorithm (ongoing costs) | Alberta Health Services (AHS) wage rates, Alberta Health Care Insurance Plan / Alternate Funding Plan | Case management<br>Cost per patient estimated by plausible number of patients in program / managed per staff |
| IT infrastructure | Equipment required to setup BP telemonitoring and hours of IT support will be estimated from local experience and [redacted] input. | Wage rates.<br>Price lists of IT equipment from manufacturer. | Costs apportioned over # of patients monitored in region over 5 years. |
| Program Delivery | | | |
| Equipment | Number of home BP cuffs (standard and telemonitoring) | List price | Includes expected lifetime / repair costs and replacement. |
| Internet / Data | Android smartphone device / data plan. Proportion of patients not requiring additional equipment / data will be determined (tested in sensitivity analysis). | Local cost of lowest priced suitable service | Included in sensitivity analysis, may be paid by health provider or patient (societal perspective) |
| Medication Use | Type, dose, frequency, and duration of use. | Alberta Blue Cross | |
| Health care professional time (physician, nurse, dietician, administrative assistant) | Estimated hours for staff training to administer care algorithm (ongoing costs) | Alberta Health Services (AHS) wage rates, Alberta Health Care Insurance Plan / Alternate Funding Plan | Case management<br>Cost per patient estimated by plausible number of patients in program / managed per staff |

| Identification | Measurement | Valuation | Comments |
|---|---|---|---|
| Staff costs / Infrastructure | IT support / telemedicine portal | [redacted] | Costs apportioned over # of patients monitored in region over 5 years. |
| Physician visits<br><br>Emergency room visits | Number of primary care or hypertension specialist visits over 6 months (patient reported).<br><br>Number of emergency room visits over 6 months attributable to BP or complications of treatment (patient reported) | Alberta Health Ambulatory Care Case Costing (utilizing National Ambulatory Care Reporting System – NACRS).<br>Alberta Schedule of Benefits | Telemonitoring ± case management may reduce need for physician visits for BP management – scenarios tested in SA.<br><br>Study may be underpowered to detect ER visits. Safety endpoints (Section 9.7) will be examined and likely resource use for each safety endpoint will be estimated. |
| Patient costs | Patient and caregiver time costs for physician visits, ER visits, out of pocket medication costs. May also include data / smartphone costs (explored in sensitivity analysis). | Standard Alberta wage rates (human capital approach) | Explored using a societal perspective. |