

## Supplementary Online Content

Dhalla IA, OBrien, Morra D, et al. Effect of a postdischarge virtual ward on readmission or death for high-risk patients: a randomized clinical trial. *JAMA*. doi:10.1001/jama.2014.11492

### **Study Protocol**

This supplementary material has been provided by the authors to give readers additional information about their work.

## 1 OVERVIEW

We will conduct a pragmatic, randomized controlled trial to evaluate the Virtual Ward as a new model of care for high-risk medical patients after discharge from hospital. Our Virtual Ward combines the best aspects of hospital, primary and home care to deliver integrated care after hospital discharge. Although patients being cared for in the Virtual Ward will reside at home, they will benefit from a hospital-like interdisciplinary team, a shared set of notes, a single point of contact, round-the-clock availability and improved co-ordination of specialist, primary and home-based community care. Our Virtual Ward will also use a clinical prediction rule developed and validated by members of our research team to care for patients who are at high risk of readmission or death. Selecting high-risk patients allows for care to be intensified in a cost-effective manner.

Our project has been developed in partnership with the Ontario Ministry of Health and Long-Term Care, the Toronto Central Local Health Integration Network, the Toronto Central Community Care Access Centre, two acute care hospitals and an ambulatory care hospital. Our approach represents a coordinated, regional approach to reducing hospital readmissions—a problem that individual hospitals, primary care providers and community care agencies have so far been unable to successfully address. Too often, patients have difficulty accessing appropriate primary, community and/or specialist care in the days and weeks after hospital discharge. This mismatch between needed and provided care frequently results in readmission to hospital. Readmission almost always occurs through the emergency department (ED) and therefore contributes to increased ED volumes and wait times. Moreover, patients who are repeatedly admitted to hospital are frequently assigned “alternate level of care” (ALC) status, indicating their needs could be better served outside an acute care hospital. Therefore, reducing readmissions would not only improve health outcomes but also reduce ED wait times and the number of ALC patients, addressing two high-priority issues for Canadian healthcare policymakers.<sup>1,2</sup>

Our proposal is aligned with 3 themes from the 2007 *Listening for Direction III* exercise. First, our proposal is aligned with the **patient flow and system integration** theme because the Virtual Ward will help patients transition between hospital and home and because the Virtual Ward will help integrate primary, hospital and home care for a group of high-risk patients. Also, we propose an integrated, regional solution involving multiple hospitals and the community care provider rather than a sectoral or single-institution approach. Second, our proposal is aligned with the **chronic disease prevention and management** theme because the vast majority of patients admitted to the Virtual Ward will have one or more chronic diseases and because the Virtual Ward team will ensure that evidence-based treatments for these illnesses are provided in a timely fashion. Finally, our proposal is aligned with the **health system financing and sustainability** theme because avoidable readmissions are expensive and the Virtual Ward has the potential to demonstrate that resources can be used more efficiently than is currently the case.

In summary, the Virtual Ward is a new model of care with the potential to improve health outcomes for a large group of patients whose needs are not being effectively met by the health care system as it is currently structured. A randomized controlled trial of the Virtual Ward will provide decision makers with the evidence they need to improve health care for this high-risk population.

## 2 RESEARCH OBJECTIVES

Our main objective is to perform a pragmatic, randomized controlled trial to compare admission to a Virtual Ward following hospital discharge with usual care. We will evaluate whether admission to a Virtual Ward reduces:

- Readmission to hospital within 30 days, 90 days, 6 months and 1 year of discharge
- Death within 30 days, 90 days, 6 months and 1 year of discharge
- Emergency department visits within 30 days, 90 days, 6 months and 1 year of discharge
- Long-term care admission within 30 days, 90 days, 6 months and 1 year of discharge

### 3 RATIONALE

In this section, we describe the Virtual Ward model, the prevalence and importance of readmissions as well as their preventability.

#### 3.1 The Virtual Ward

The Virtual Ward has been defined as “a cadre for providing support in the community to people with the most complex medical and social needs.”<sup>3</sup> In this model, patients who are at high risk for readmission are “admitted” to the Virtual Ward upon hospital discharge. An interdisciplinary team provides care for the patient to improve health outcomes in a cost-effective manner. This care is individualized and may involve medical care (e.g., clinical assessment and medication management), social support (e.g., referrals to appropriate services such as Meals on Wheels), addictions counseling, patient education to improve self-management (e.g., checking feet to avoid diabetic foot infections) or end-of-life counseling and planning. Our Virtual Ward, which will care for patients after hospital discharge, incorporates all five characteristics of successful approaches to reducing readmissions as recommended by the Institute for Healthcare Improvement:<sup>4</sup> (1) comprehensive discharge planning with timely communication; (2) post-discharge support; (3) multidisciplinary team-based management; (4); patient education and self-management support; and (5) remote monitoring.

The Virtual Ward is based on a system of care first developed in Croydon, a suburb of London in the United Kingdom.<sup>5</sup> Although reports suggest that the Croydon model has reduced ED visits and saved money (approximately CDN\$2 million over one year),<sup>6</sup> the model has not yet been rigorously evaluated. Nevertheless, the degree of enthusiasm for the model in the UK and its solid theoretical foundation suggest a high likelihood of success. Therefore, in collaboration with decision makers in Ontario, we have adapted the Croydon model for use in the Canadian context.

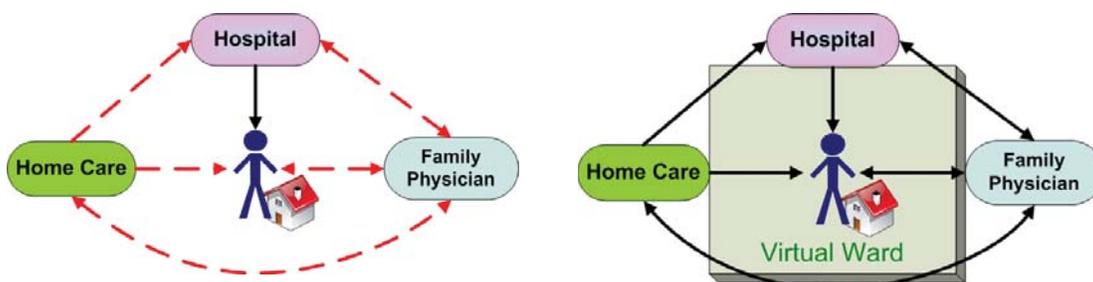


Figure 1. Current model of care compared to Virtual Ward.

#### 3.2 Prevalence and importance of readmissions after medical hospitalization

Readmission after hospital discharge is increasingly recognized as a marker of suboptimal health care.<sup>7</sup> A recent study in the United States demonstrated that 21% of medical patients in the U.S. Medicare population are readmitted within 30 days of hospital discharge.<sup>8</sup> An additional 4% of patients die within 30 days of discharge. Although a comprehensive study of this nature has not yet been performed in Canada, a study of 328 patients admitted to the general internal medicine service at an Ottawa teaching hospital over a 14-week period in 2002 found that 2% died and 17% were readmitted within approximately 30 days of discharge.<sup>9</sup> The work that we have done in preparation for this trial indicates that readmission rates in Toronto are similar (see Section 4 for details).

Readmissions are not only associated with significant morbidity and mortality, they are a highly inefficient use of hospital resources. The dramatic decrease in the intensity of care after discharge leaves many individuals with insufficient medical, nursing and social supports to thrive at home. Individuals with chronic illnesses (e.g., heart failure, diabetes, chronic obstructive pulmonary disease, etc.) often deteriorate to the point where the next health care intervention must occur in an ED during the midst of a

crisis rather than at home or in an outpatient setting. Because the vast majority of readmissions occur via emergency departments, readmissions contribute to increased ED volumes and wait times. Second, patients repeatedly admitted to hospital are often transferred to rehabilitation, complex continuing care or long-term care facilities upon hospital discharge. However, because beds in these facilities are in short supply, patients are often required to wait in hospital for an available bed even though they no longer require hospital-level care. These patient-days are commonly known as “alternative level care” (ALC) days and are considered to be one of the most important contributors to hospital and ED overcrowding.<sup>2</sup> Of note, 86% of ALC bed days in Canada occur in medical patients, and 73% of ALC patients were admitted to hospital via the emergency department.<sup>10</sup>

### 3.3 Preventability of readmissions

Variability in readmission rates,<sup>4,8,11</sup> evidence of inadequate follow up after discharge,<sup>8</sup> patient complaints of inadequate preparation for discharge,<sup>12</sup> and poor doctor-to-doctor communication at the time of discharge<sup>13</sup> suggest that a significant proportion of readmissions may be preventable.

In large part because there is no “gold standard” for post-discharge care, the proportion of readmissions judged to be preventable in peer-reviewed studies varies from as low as 9% to as high as 55%.<sup>14</sup> The Medicare Payment Advisory Commission (MedPAC), an influential governmental agency in the United States, has estimated that up to 76% of readmissions within 30 days of discharge can be prevented.<sup>15</sup> According to MedPAC, preventable readmissions account for approximately US\$12 billion in health care spending in the United States.

Although post-discharge models of care for single diseases (e.g., heart failure) may be highly effective,<sup>16</sup> they have not been implemented widely, primarily because of resource constraints. Just as there are insufficient resources to permit most patients to be admitted to disease-specific hospital wards, it is unlikely that there are sufficient resources available to implement different post-discharge models of care for each disease associated with a high risk of readmission. Therefore, researchers and policymakers are increasingly focusing on interventions designed to address post-discharge health care needs in patient populations with a wide variety of illnesses.

### 3.4 Post-discharge interventions

Although there are several Cochrane reviews on related topics (e.g., telephone follow up after discharge,<sup>17</sup> care at home instead of admission to an acute care hospital,<sup>18</sup> written discharge instructions<sup>19</sup> and discharge planning<sup>20</sup>), there are no Cochrane reviews examining the effectiveness of post-discharge interdisciplinary care. A systematic meta-review of fifteen high quality systematic reviews concluded that “usual care seems to be equally as effective as discharge interventions.”<sup>21</sup> However, a detailed analysis of individual studies suggested that interventions that combined discharge planning and post-discharge support as well as those that provided patient education were beneficial. Moreover, given the importance of post-discharge problems, the authors concluded that “professionals and organizations must consider ways of preventing, easing or solving post-discharge problems.”<sup>21</sup> Similarly, the most comprehensive systematic review in the field concluded that “evidence from RCTs is not available to support ... discharge support schemes as means of improving discharge outcomes” but that “high-quality studies (including, where appropriate, RCTs) are required to explore and develop models of discharge intervention that cross the hospital–community interface.”<sup>22</sup>

At least three post-discharge interventions have been proven effective in heterogeneous populations.<sup>23-25</sup> The first was conducted by Naylor and colleagues in two urban hospitals in Philadelphia between 1992 and 1996.<sup>25</sup> Intervention patients received comprehensive discharge planning in hospital and 4 weeks of post-discharge care coordination provided by an advance practice nurse. Control group patients were almost twice as likely to be readmitted during the 24-week follow-up period (RR 1.8, 95% CI, 1.3-2.6). A key reason why readmissions were reduced was that the advance practice nurse was able to engage in “joint clinical decision making with physicians, [resulting] in timelier

interventions in the home.” An economic evaluation showed that the Naylor intervention saved approximately \$3000 per patient.<sup>25</sup> The second intervention was implemented by Coleman and colleagues at a single Colorado hospital between 2002 and 2003.<sup>23</sup> Intervention patients met with a “transitions coach”, who provided assistance with medication self-management, helped develop a patient-centred health record, helped facilitate timely post-discharge follow up, and provided a list of “red flags” indicative of worsening health status and instructions on how to respond to them. Intervention patients had lower readmission rates at 30 days (8.3% vs. 11.9%,  $P=0.048$ ) and at 90 days (16.7% vs. 22.5%,  $P=0.04$ ). The third study was conducted by Jack and colleagues in Boston during 2006 and 2007.<sup>24</sup> The intervention, which consisted of a nurse discharge advocate who worked with patients during and after their hospitalization, reduced the incidence of post-discharge hospital utilization within 30 days by 30% ( $RR=0.70$ ; 95% CI 0.52 to 0.94). However, this study may not be generalizable to the Canadian context since specific elements of the intervention are already considered to be standard of care in Canada and because a high percentage of patients lacked health insurance.

Despite these examples of successful interventions, most studies in the field have been negative. We believe there are two important reasons why this is the case. First, many post-discharge interventions have been designed or delivered in a suboptimal fashion. For example, few interventions have integrated pre-discharge and post-discharge care. Second, post-discharge interventions have often been indiscriminately applied to patients without risk stratification, which means that many patients at low risk of readmission were included.<sup>22</sup> In contrast, the most successful interventions, including the three described above, have targeted high-risk patients.

#### **4 PRE-TRIAL PREPARATION**

In this section, we describe the work done to prepare for this trial. First, members of our team developed a clinical prediction rule that can be used at the time of discharge to identify high-risk patients. Second, we analyzed administrative data to better understand local readmission rates. Finally, we established a partnership with decision makers to ensure that the Virtual Ward is responsive to system needs and to ensure that our findings are useful to policymakers.

##### **4.1 Identification of high-risk patients at the time of hospital discharge**

An optimal model of transitional care should be cost effective. To maximize cost-effectiveness, interventions should focus on patients who are at highest risk of readmission.<sup>26</sup> We have developed and validated a simple clinical prediction rule, the LACE index, that can be used to predict readmission risk at the time of discharge.<sup>27</sup> The LACE index uses hospital length of stay (L), acuity of admission (A), comorbidities as measured by the Charlson index (C),<sup>28,29</sup> and the number of emergency department visits in the prior six months (E) to estimate the 30-day risk of readmission or death. The LACE index is easy to use and can readily be calculated by physicians and discharge planners using clinical data as well as by researchers using administrative data. The discrimination of the LACE index is similar to that of the widely used Framingham score (used to predict myocardial infarction and death from coronary artery disease)<sup>30-32</sup> indicating that the LACE index has the potential to be useful when applied at the individual patient level.

##### **4.2 Readmissions in the Toronto Central Local Health Integration Network**

Using administrative data housed at the Institute for Clinical Evaluative Sciences (ICES), we have analyzed all 2007 admissions in the Toronto Central Local Health Integration Network (TC LHIN) in preparation for our trial. Of the 26,045 medical admissions in 2007, 34% had a high-risk LACE score (i.e., greater than or equal to 10 points). The most common case-mix groups (CMGs) associated with index admissions in this subgroup were heart failure, pneumonia, gastrointestinal disease, urinary tract infection and cerebrovascular disease. Of the 8,854 patients in the high-risk group, 1,691 (19.1%) were readmitted to hospital within 30 days and 2,811 (31.7%) were readmitted within 90 days. The median

age of the readmitted high-risk patients was 71 years and 90% were living at home prior to their readmission. More than 30% of the readmitted high-risk patients were admitted to a different hospital on their readmission compared to their index admission, clearly illustrating the need for a system-level solution.

#### **4.3 Establishing a partnership with decision makers**

Over the last nine months, we have held approximately 15 meetings with various combinations of researchers and decision makers from the Ontario Ministry of Health and Long-Term Care, the TC LHIN, the Toronto Central Community Care Access Centre, the 3 hospitals involved in this application, and additional hospitals that are not involved in this trial. We have collaboratively developed the Virtual Ward with physicians and administrators from each of these institutions and will be implementing the Virtual Ward model described in this proposal in early 2010.

### **5 METHODS**

In this section, we describe the proposed methods of our randomized controlled trial using the RCT headings recommended by CIHR.

#### **5.1 What is the proposed trial design?**

We propose a randomized, pragmatic trial of the Virtual Ward versus usual care, with the objective of reducing readmissions among high-risk medical patients discharged from hospital. Participants will be recruited from the inpatient general internal medicine clinical teaching units at St. Michael's Hospital and the Toronto General Hospital site of the University Health Network. If patient accrual is slower than expected, additional sites may be added at the discretion of the investigative team. At various intervals following hospital discharge, a research assistant will administer a brief questionnaire over the telephone and review relevant and available hospital records to ascertain outcomes. We consider our trial to be pragmatic<sup>33,34</sup> for the following reasons: (1) the patient population will be broad, with few exclusion criteria; (2) the intervention will be superimposed onto a 'normal' practice setting; (3) the intervention will be applied flexibly and may adapt according to identified needs over the study period; (4) the outcomes are patient-centred; and (5) the trial results will be of interest to decision makers.

#### **5.2 What are the planned trial interventions?**

##### 5.2.1 Control Group

Patients in the control group will receive usual care. At both St. Michael's Hospital and the University Health Network, this includes counseling from the resident physician and/or other members of the health care team, a structured discharge summary provided at the time of discharge, arrangements for home care as needed, and recommendations and/or appointments for follow-up care with the family physician and specialist physicians as deemed appropriate by the hospital team.

##### 5.2.2 Intervention Group

In addition to receiving usual care, patients in the intervention group will be "admitted" to the Virtual Ward on the day of hospital discharge (see Figure 2) where they will receive an individualized care plan as they would in hospital. The Virtual Ward team consists of a rotating physician with inpatient experience, a nurse practitioner, a part-time pharmacist, a case manager and a ward clerk. Daily meetings of the Virtual Ward team will be held at Women's College Hospital. To facilitate interdisciplinary care, the Virtual Ward team will meet daily and use a shared set of notes. The Virtual Ward will also function as a single point of contact for patients, who will be given a phone number that can be used at any time, including nights and weekends, to ask questions or seek care. Patients will be contacted via telephone or seen in person, either at home or in an outpatient clinic at Women's College Hospital, as needed. The Virtual Ward team will collaborate with the patient's regular family physician if the patient has one, and will assist in finding the patient a family physician if the patient does not. The

Virtual Ward team will also help co-ordinate care with specialists, allied health professionals and social care providers. Care will focus on the evidence-based management of chronic disease, the prevention of disease exacerbations (e.g., for heart failure and chronic obstructive pulmonary disease), functional status optimization, patient education, caregiver support and end-of-life planning if appropriate.

Using a collaborative decision-making process incorporating the patient’s family physician, patients will be discharged from the Virtual Ward when medically appropriate. Upon discharge, a structured discharge summary will be provided to the patient, the patient’s family physician, and others involved in the patient’s care. Because the Virtual Ward will provide care for a relatively short period of time (e.g., 2-8 weeks), it is likely to be more cost effective than resource intensive models of longer-term care.

**5.3 What are the proposed practical arrangements for allocating participants to trial groups?**

A research assistant at each of St. Michael’s Hospital and the University Health Network will identify potential participants either on the day of discharge or the day before, screen them for inclusion, and attempt to obtain informed consent. If the patient or surrogate consents, the research assistant will log on to the web-based trials system (administered by the Applied Health Research Centre at St. Michael’s Hospital). The system will prompt the assistant to enter baseline information and then inform the research assistant whether the patient has been assigned to the Virtual Ward group or the usual care group.

**5.4 What are the proposed methods for protecting against sources of bias?**

We have considered many sources of bias in randomized controlled trials.<sup>35</sup> To eliminate *selection bias*, randomization will occur via a web-based system to ensure allocation concealment. *Ascertainment bias* will be minimized by using relatively “hard” clinical outcomes (e.g., readmission, death, etc.) and by blinding the data analyst. The nature of the proposed intervention precludes blinding of the patient or clinical team. We have minimized *population choice bias* by having broad inclusion criteria. Furthermore, patients who decline to enter into the study will have their age, gender, LACE score,<sup>27</sup> discharge location (i.e., home or long-term care) and most responsible diagnosis recorded, so that participants and non-participants can be compared. Although we expect only a very small number of withdrawals, *withdrawal bias* will be minimized by analyzing outcomes in an intention-to-treat fashion. *Selective reporting bias* will be eliminated by publicly registering our trial protocol at

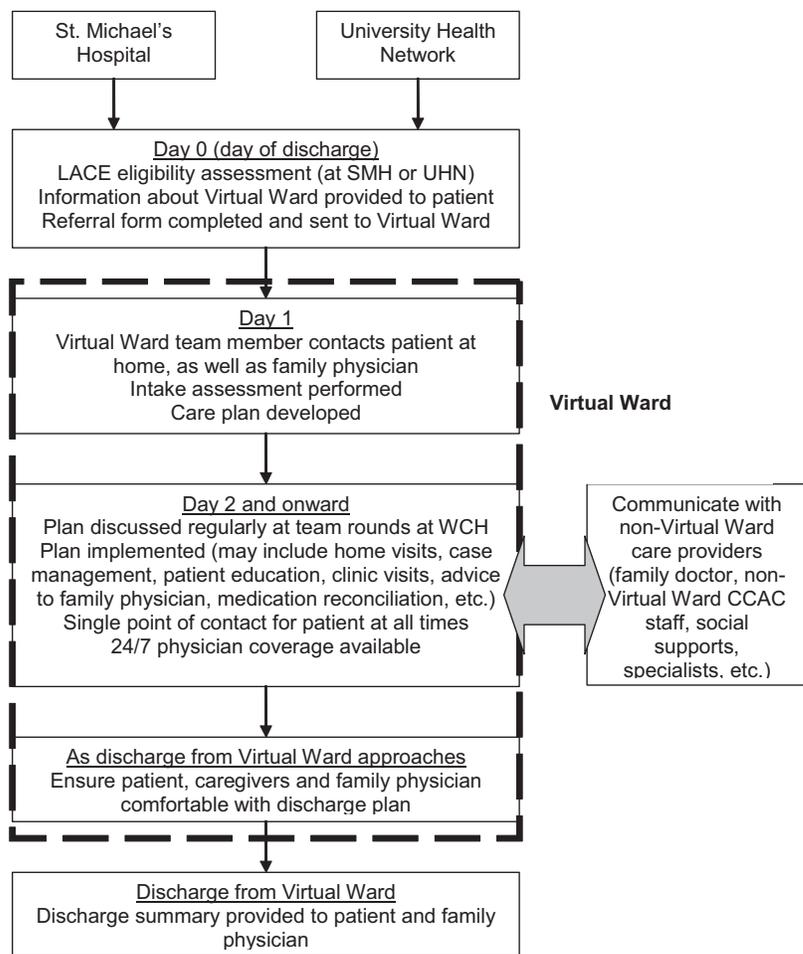


Figure 2. Patient flow through the Virtual Ward

[www.clinicaltrials.gov](http://www.clinicaltrials.gov). Our design also reduces the risk of *contamination*, which can bias a randomized trial toward a negative result. Contamination in controlled trials occurs when patients who were not intended to receive an intervention inadvertently do so. In large part because the Virtual Ward is housed at Women's College Hospital, a different hospital from the two acute care hospitals where patients will be enrolled, the individuals involved in delivering care on the Virtual Ward will be separated from the hospital team. Most importantly, patients in the control group will not have access to the Virtual Ward.

## **5.5 What are the planned inclusion/exclusion criteria?**

### **5.5.1 Inclusion criteria**

- Adults aged 18 years or older
- Discharge from the general internal medicine wards of St. Michael's Hospital or the Toronto General Hospital site of the University Health Network
- Discharge to home or a long-term care facility
- LACE score  $\geq 10$  (i.e., a predicted 30-day readmission risk of 15% or higher)

### **5.5.2 Exclusion criteria**

- Neither patient nor anyone the patient can designate as a surrogate can speak English
- Discharge to a location outside the TC LHIN boundary
- Enrolled in the study during a previous admission

## **5.6 What is the proposed duration of treatment?**

Patients will be recruited from May 1, 2010 until our sample size of 1510 patients is reached. Once enrolled, patients in the intervention group will receive care from the Virtual Ward until the Virtual Ward care team, in concert with the patient and the patient's family physician, believes the patient is ready for "discharge" from the Virtual Ward. Although there are no pre-set limits, we expect this will generally vary from 2-8 weeks depending on individual patient needs.

## **5.7 What is the proposed frequency and duration of follow up?**

A research assistant will contact each patient at 30 days, 90 days, 6 months, and 1 year after enrolment. If the patient cannot be contacted by telephone, records from the 6 hospitals in the TC LHIN will be used to ascertain post discharge utilization. Follow up will cease at 1 year.

## **5.8 What are the proposed primary and secondary outcome measures?**

### **5.8.1 Primary Outcome**

The primary outcome is the composite of readmission to hospital or death within 30 days of discharge. Readmission within 30 days has emerged as the most widely accepted metric for assessing the quality of post-discharge care.<sup>4,7,15</sup> We have included death in the composite outcome because it is an even more important clinical outcome and because it may be influenced by post-discharge care.

### **5.8.2 Secondary Outcomes**

Secondary outcomes include the composite of readmission or death within 90 days, 6 months and 1 year of discharge, as well as readmission, death, emergency department visits, and long-term care admission within 30 days, 90 days, 6 months and 1 year of discharge.

## **5.9 How will the outcome measures be measured at follow up?**

Using a standardized interview guide, a research assistant will telephone enrolled patients (or designated surrogates) at 30 days, 90 days, 6 months and 1 year after enrolment and ascertain emergency department use, hospital readmission, long-term care admission, and vital status. We will also ask patients and surrogates to inform the research assistant if they visit an ED or are admitted to hospital. Previous research by one of the co-applicants has demonstrated the feasibility of this approach.<sup>36</sup> If the patient has been admitted to hospital, the research assistant will review the relevant hospital records, where available, to verify the reason for admission and the length of stay. Where the patient or primary caregiver is unavailable, we will attempt to obtain follow-up information from other family members and health care providers (e.g., the family doctor) if the patient has given permission at enrolment.

### **5.10 Will health service research issues be addressed?**

We will be carefully documenting individual care needs as identified by Virtual Ward patients and care providers as well as the services provided to each Virtual Ward patient. Consistent with pragmatic trial design, this information will be used to optimize the study intervention during the trial. For example, we may make modifications to the staffing complement if services that we expect to be needed uncommonly are in fact frequently required. This information will also be useful in determining what elements of Virtual Ward care are most important to specific patient subgroups, and will feed in to our integrated and end-of-grant KT strategies. Although we do not plan to conduct a formal economic evaluation as part of this study, future studies will examine the cost-effectiveness of the Virtual Ward if it is proven to be an effective method of reducing readmissions.

### **5.11 What is the proposed sample size and what is the justification?**

Based on the results of less comprehensive interventions suggesting a 25-45% reduction in readmissions<sup>23-25</sup> and MedPAC's estimate that 76% of readmissions may be preventable,<sup>15</sup> we conservatively hypothesize that the Virtual Ward will reduce readmissions by 33%. We expect to admit a high-risk population whose risk of readmission within 30 days will be approximately 19%. For the purposes of sample size calculation we have conservatively estimated that the readmission rate of the control group will be 15% and that 10% of the sample will be lost to follow up. In order to detect a relative risk reduction in readmissions of 33% with two-sided  $p=0.05$  and 80% power, 755 individuals will be required in each study arm, or 1510 participants overall.

### **5.12 What is the planned recruitment rate?**

Our preparatory work demonstrates that recruiting 1510 patients in 24 months is feasible. The general internal medicine clinical teaching units at St. Michael's Hospital and Toronto General Hospital discharged a combined total of 5700 patients in 2008. We therefore expect approximately 11400 discharges over 24 months. Our preparatory analyses indicate that 34% of general internal medicine patients in Toronto are at high risk of readmission (i.e., LACE score  $\geq 10$ ). We therefore anticipate that approximately 3850 of the 11400 patients will be eligible for screening. A small proportion of these patients will be ineligible for enrolment because they meet one of the 3 exclusion criteria (see section 5.5.2). Even if we estimate that 33% of patients will be ineligible, over 2500 patients would be eligible for enrolment over 24 months. Because patients usually welcome additional care after hospital discharge, we expect that most eligible patients will agree to participate in the Virtual Ward trial. This expectation is confirmed by high rates of recruitment ( $>75\%$ ) in other studies of post-discharge care.<sup>23-25</sup> Allowing for slow enrolment over the first few months, we therefore expect to recruit 1510 patients in slightly less than two years. To do so, we need to recruit less than 60% of eligible patients.

### **5.13 Are there likely to be any problems with compliance?**

Patients generally welcome additional care after hospital discharge.<sup>23-25</sup> Therefore, we expect that very few patients will refuse Virtual Ward care after agreeing to participate in the trial.

### **5.14 What is the likely rate of loss to follow up?**

We will record patient and caregiver contact information to minimize loss to follow up, which we expect will be far less than the 10% we have assumed in our conservative sample size calculations.

### **5.15 How many centres will be involved?**

Virtual Ward care will be coordinated from Women's College Hospital, an independent ambulatory care hospital. Eligible patients will be recruited at the time of discharge from the two acute care hospitals, St. Michael's Hospital and the University Health Network.

### **5.16 What is the proposed type of analyses?**

#### **5.16.1 Primary Analysis**

- An intention-to-treat, unadjusted comparison of proportions, with readmission to hospital or death within 30 days as the composite outcome of interest.

### 5.16.2 Secondary Analyses

- Unadjusted comparison of proportions, using the following events of interest:
  - Composite of death or readmission within 90 days, 6 months and 1 year of discharge
  - Readmission within 30 days, 90 days, 6 months and 1 year of discharge
  - Emergency department visits within 30 days, 90 days, 6 months and 1 year of discharge
  - Mortality within 30 days, 90 days, 6 months and 1 year of discharge
  - Long-term care admission within 30 days, 90 days, 6 months and 1 year of discharge

Logistic regression models with each of the primary and secondary endpoints as the outcome of interest, with adjustment for pre-specified covariates known to be associated with readmission, will also be constructed. Interaction terms will be included to determine whether Virtual Ward care is more effective for particular subgroups (see Section 5.18). All analyses will be by intention to treat, meaning that all participants will be analyzed in the group to which they were randomized.

### **5.17 What is the proposed frequency of analyses?**

If the Virtual Ward is much more effective than the 33% relative risk reduction assumed in the sample size calculation, its efficacy will be convincingly demonstrated with fewer patients than planned. At that point it would be inappropriate to continue to randomize patients into the control group, and our efforts should be focused on establishing the Virtual Ward as part of routine care. Therefore, we will perform an interim analysis at the half-way point and use the Haybittle-Peto stopping rule (i.e., stop for efficacy if  $p < 0.001$ ).<sup>37</sup>

### **5.18 Are there any planned subgroup analyses?**

By examining the interaction terms described above (see Section 5.16.2), we will look for effect modification by the following potentially important prognostic variables: (1) hospital discharge site (St. Michael's Hospital vs. Toronto General Hospital); (2) discharge location (home vs. long-term care facility); (3) time of enrolment relative to Virtual Ward initiation; (4) LACE score; (5) age; (6) gender; and (7) reason for index admission (heart failure vs. other diagnoses). As recommended, we will not perform separate significance tests comparing the effect of the Virtual Ward within each subgroup.<sup>38</sup>

### **5.19 What are the arrangements for day to day management of the trial?**

#### 5.19.1 Central Coordination

The Applied Health Research Centre (AHRC) at St. Michael's Hospital is a recently established clinical trials support centre. AHRC provides the necessary infrastructure to support multi-centre clinical trials. Services include project management, financial management, randomization services, data management and statistical support. AHRC uses the web-based data capture system Medidata RAVE™ (5.6.3), a secure, encrypted clinical trial data management system. The RAVE software is fully configurable and incorporates sophisticated data validation rules to ensure high quality data capture.

For this study, AHRC will develop the electronic case-report forms (eCRFs) and an associated database in collaboration with the investigative team. The database will incorporate extensive data validation rules to ensure data quality, and AHRC will oversee any data quality and/or database issues as they arise during the course of the study. A study manual will outline methods for eCRF completion and record management. All data will be stored securely on servers housed at St. Michael's Hospital. The trial will be registered online at [www.clinicaltrials.gov](http://www.clinicaltrials.gov) and ethical approval will be obtained from each hospital in the TC LHIN as well as from the Toronto Central Community Care Access Centre.

#### 5.19.2 Patient enrolment

Research assistants at each of the discharging sites will be responsible for identifying patients and obtaining informed consent. Enrolment data will then be entered into the secure, encrypted web-based clinical trial data management system. The web-based system will randomly assign patients to either the intervention group or the control group. The research assistant will inform patients of their

group assignment, and provide an information package to patients who have been assigned to the Virtual Ward.

### 5.19.3 Patient follow up

A research assistant based at the Li Ka Shing Knowledge Institute of St. Michael's Hospital will be responsible for follow-up data collection and will enter information into the electronic case-report forms described above. With 1510 patients enrolled over 2 years, and four telephone interviews per patient, the research assistant will be required to complete 6040 eCRFs over 3 years, or approximately 8-10 per day, a number that is considered to be feasible based on previous work.<sup>36</sup>

## **6 INVESTIGATIVE TEAM**

### **6.1 Research investigators**

The Nominated Principal Applicant is **Dr. Andreas Laupacis**, a general internist and Professor of Medicine and Health Policy, Management and Evaluation at the University of Toronto, Executive Director of the Li Ka Shing Knowledge Institute of St. Michael's Hospital, and an internationally recognized leader in clinical trials, health services research and health policy.<sup>39-44</sup> The Co-Principal Applicant is **Dr. Paula Rochon**, a geriatrician and Professor of Medicine and Health Policy, Management and Evaluation at the University of Toronto, Vice-President of Research at Women's College Hospital, and an internationally renowned researcher in geriatric health services research.<sup>45-49</sup> Drs. Laupacis and Rochon will jointly have overall responsibility for all aspects of the study. **Dr. Irfan Dhalla** is a Co-Applicant who holds a CIHR Fellowship Award supervised by Dr. Laupacis and Dr. Geoffrey Anderson. Dr. Dhalla is a practicing general internist and will oversee the project with Drs. Laupacis and Rochon. Dr. Dhalla will develop the first draft of all publications resulting from this study, oversee day-to-day study co-ordination and lead the integrated KT and end-of-grant KT strategy. Dr. Dhalla has expertise in clinical epidemiology, health services research, health policy and post-discharge care.<sup>27,46,50-52</sup> Other Co-Applicants include **Dr. Geoffrey Anderson**, who has expertise in health services research and health system design and strategy,<sup>46,48,53-56</sup> **Dr. Chaim Bell**, a practicing general internist with expertise in care transitions,<sup>27,36,57-61</sup> **Dr. Wee-Shian Chan**, a practicing general internist and health services researcher<sup>62-64</sup> with practical expertise in the outpatient management of acutely ill patients, **Dr. Andrea Gruneir**, an epidemiologist with a focus on gerontology,<sup>65-68</sup> **Dr. Gillian Hawker**, a renowned health services researcher and Chief of Medicine at Women's College Hospital, where the Virtual Ward will be based,<sup>69-72</sup> **Dr. Geraint Lewis**, the originator of the Virtual Ward in the United Kingdom and an expert in predictive modeling,<sup>5,6,36</sup> **Dr. Dante Morra**, a practicing general internist and expert in health system innovation<sup>73-76</sup> **Dr. Carl van Walraven**, a practicing general internist with research interests in transitions in care and predictive modeling.<sup>9,27,36,77,78</sup> and **Prof. Kevin Thorpe**, a biostatistician with extensive experience in randomized controlled trial methodology and analysis.<sup>33,79-81</sup> The research investigators will serve as the Steering Committee for the trial.

### **6.2 Decision makers and partners**

Decision makers have been involved in our project from its earliest stages. Over the last 9 months, we have been meeting regularly with decision makers and partners from each of the participating hospitals, the Toronto Central Community Care Access Centre, the Toronto Central Local Health Integration Network, the University of Toronto Department Of Medicine and the Health System Strategy Division of the Ontario Ministry of Health and Long-Term Care. In total, we have already had approximately 15 meetings to discuss the implementation and evaluation of the Virtual Ward.

Our decision makers and partners include **Dr. Lorraine Greaves**, Executive Director, Health System Strategy Division, Ontario Ministry of Health and Long-Term Care, **Dr. Robert Howard**, President and Chief Executive Officer, St. Michael's Hospital, **Ms. Heather McPherson**, Vice-President, Women's College Hospital, **Ms. Jeanne Jabanoski**, Vice-President, University Health

Network, **Ms. Stacey Daub**, Director of Client Service, Toronto Central Community Care Access Centre, **Dr. Wendy Levinson**, Chair, Department of Medicine, University of Toronto and **Mr. Matt Anderson**, Chief Executive Officer, Toronto Central Local Health Integration Network. Letters of support from each of these individuals are attached.

## **7 KNOWLEDGE TRANSLATION PLAN**

We will use both integrated and end-of-grant knowledge translation (KT) strategies to improve and promote uptake of our research. In both cases, we will work with our decision maker partners and others, such as the Change Foundation and the Ontario Hospital Association, to disseminate key findings from our trial.

### **7.1 Integrated Knowledge Translation Plan**

The Integrated KT plan includes three primary mechanisms to engage with decision makers at various levels and at various stages of the Virtual Ward implementation and evaluation. Each of these mechanisms, including the relevant decision makers, is described below.

#### 7.1.1 Implementation

*Key decision makers: Hospital administrators, Toronto Central CCAC*

The success of the Virtual Ward is contingent on open and effective communication between the research team, clinical providers and decision makers at the participating hospitals and the Toronto Central Community Care Access Centre (CCAC). During the early stages of the Virtual Ward project, we will collect data on specific aspects of the Virtual Ward implementation and its admitted patients. Examples of the data that will be collected include: assessed needs of patients, number and types of recommended services, and number of spontaneous and planned contacts with the Virtual Ward (by patients, primary caregivers, and family physicians). The purpose of this data collection is to obtain a clear understanding of the types of patients admitted to the Virtual Ward, their needs, and potential service gaps that will need to be addressed. In addition, we will hold bi-weekly meetings (with teleconference capability) where we will focus on obtaining feedback from the clinical team and local decision makers. We will incorporate both formally collected data and informal feedback into Virtual Ward refinement and to identify which services are most heavily used and where there may be unanticipated gaps (e.g., housing or mental health services, particular specialty services, etc.). We will then work with the CCAC and the participating hospitals to identify appropriate providers to close these gaps. The main objective of this phase of the KT plan is to ensure that the Virtual Ward meets patients' needs within provider constraints.

#### 7.1.2 Responsiveness to System Needs

*Key decision makers: Toronto Central LHIN, Ontario Ministry of Health and Long-Term Care*

We will continue to build links with the Toronto Central LHIN and the Health System Strategy Division of the Ontario Ministry of Health and Long-Term Care (MOHLTC). We anticipate that our early-stage findings will provide the LHIN and the MOHLTC with better information on the challenges facing empirically identified high-risk patients following hospital discharge. We will continue to solicit their input on non-clinical factors that are believed to put patients at high-risk for poor outcomes and non-compliance (e.g., gender, ethnicity, housing status, etc.). This input will enable us to better understand the full range of factors that influence the perceived success of the Virtual Ward as well as to be responsive to concerns regarding special populations. With respect to financing, we will keep both the LHIN and MOHLTC informed of Virtual Ward operating costs and will solicit their input on efficiency measures. Because internal analyses conducted by the MOHLTC have identified readmissions as a major source of unnecessary expenditure, key decision makers are likely to be highly engaged. The objective of this phase of the KT plan is to ensure that the interests of system-level decision makers

inform data collection and analysis. Dr. Andrea Gruneir, one of the Co-Applicants, is an MOHLTC Career Scientist and is ideally positioned to help lead this aspect of the KT strategy.

### 7.1.3 Sharing Knowledge

*Key decision makers: Non-study hospitals, LHINs, CCACs, health authorities, etc.*

The final piece of our integrated KT plan will focus on sharing knowledge. We have already met with administrators and physicians at the Toronto East General Hospital who are keen to develop a Virtual Ward to serve their catchment area. Over the course of the study period, we will keep them informed of the processes and the resources needed for the Virtual Ward. We are also building connections with the Ontario Hospital Association (OHA) and will work with them to introduce the Virtual Ward model and our evaluation to other hospitals. We have also met with the Change Foundation, a health care policy think tank with an interest in care integration. The Change Foundation is eager to profile the Virtual Ward on their website and in other communication materials. Within Ontario, we will also reach out to other CCACs and LHINs to provide them with operational details about the Virtual Ward. Lastly, we will foster links with decision makers in other jurisdictions such as Alberta where Dr. Laupacis serves on the Board of Alberta Health Services and chairs its Quality and Safety Committee. Our decision maker applicants, particularly Dr. Lorraine Greaves, Dr. Wendy Levinson and Ms. Stacey Daub, will also use their national and international networks to disseminate information about the Virtual Ward. Our objective in this phase of the KT plan is to share information about the Virtual Ward as widely as possible in order to raise interest at other sites as well as to provide them with the necessary information for planning and implementation. We believe this will increase the likelihood of uptake if the Virtual Ward is proven to be successful.

### **7.2 End-of-Grant Knowledge Translation**

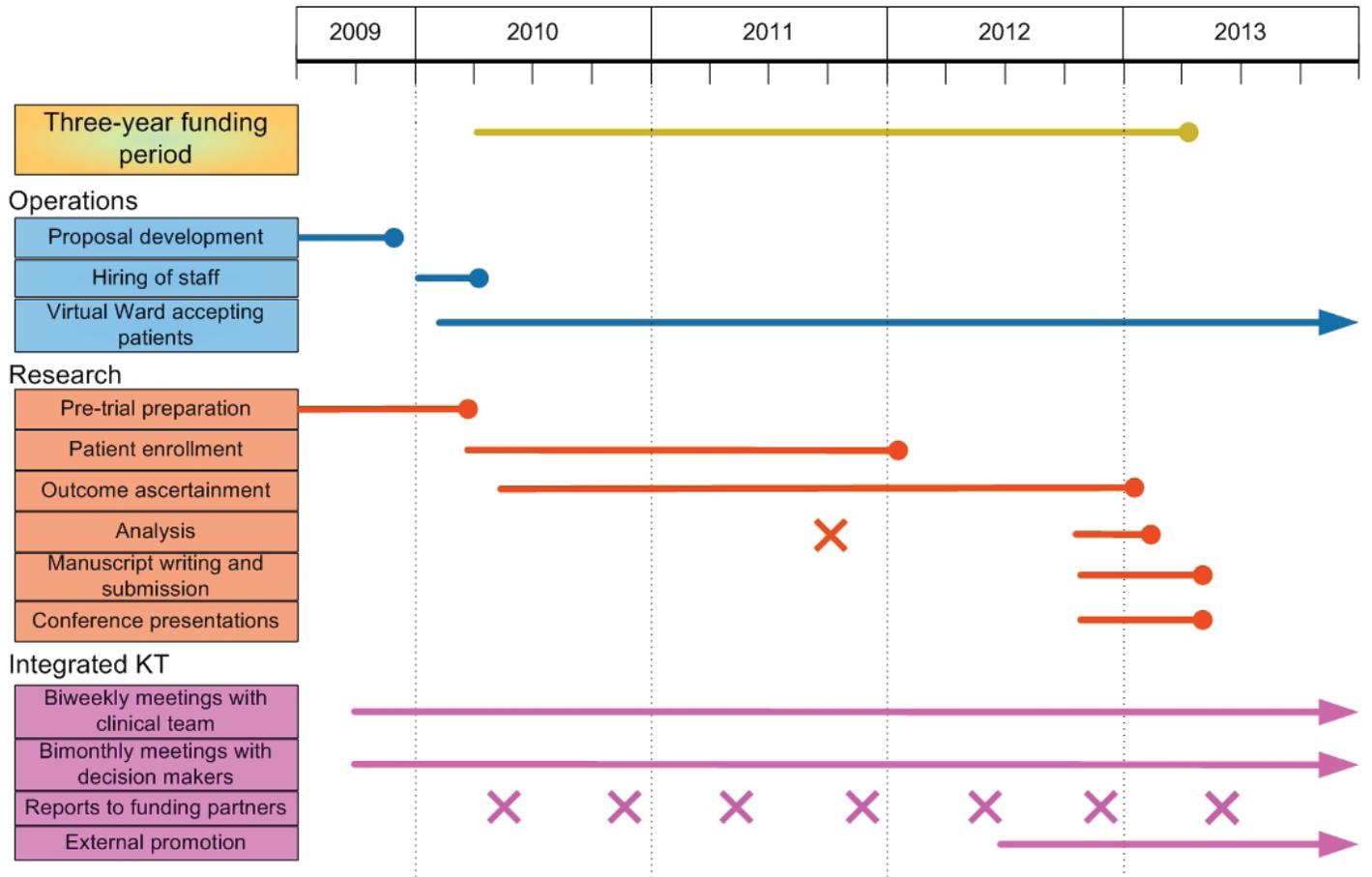
We will use traditional end-of-grant KT strategies (e.g., presentations, publications, press releases, etc.) to share lessons from the Virtual Ward trial as well as to disseminate its results. We will present findings at national and international academic research conferences such as the annual meetings of each the Canadian Association for Health Services and Policy Research and AcademyHealth. We will also seek out opportunities such as the Health Research Showcase hosted by the Ontario Ministry of Health and Long-Term Care and the annual Ontario Hospital Association HealthAchieve conference to share study findings with decision makers. In addition, we will publish research findings in peer-reviewed journals in a format consistent with the CONSORT guidelines<sup>82</sup> extended for pragmatic trials.<sup>83</sup>

## **8 ORIGINALITY AND POTENTIAL IMPACT**

The Virtual Ward is an innovative, systems-level approach to improving health outcomes for a large group of patients whose needs are not being met effectively by the health care system. Although the original Virtual Ward in the United Kingdom is believed to have been successful, the model has never been rigorously evaluated. We have also adapted the model to provide care to patients after discharge from hospital rather than to patients identified in the primary care setting. Our proposed project is therefore highly original, and will provide decision makers and policymakers with the credible information needed to support evidence-informed decision making.<sup>84</sup>

With approximately one million discharges from acute care facilities after medical hospitalization in Canada annually, the potential impact is substantial. If we can demonstrate that the Virtual Ward significantly reduces readmission rates, we believe hospitals and regional health authorities across Canada will move quickly to implement Virtual Wards or similar initiatives to better serve their populations.

**9 TIMELINE**



Protocol amendments to the Virtual Ward trial

The following is a list of all amendments that have been made to the protocol after the grant application was submitted to CIHR.

Enrollment into the Virtual Ward trial commenced on June 29, 2010.

Date of decision	Amendment	Reason
April 14, 2010	Decision to use a different consent form for homeless patients	To permit monthly follow up for the purposes of maintaining accurate contact information.
April 14, 2010	Decision to stratify by homelessness for the purpose of randomization	To avoid an imbalance in homelessness between the two groups
April 14, 2010	Decision to add a subgroup analysis for homelessness	To address the perception that the Virtual Ward may be less effective among homeless patients
June 29, 2010	Decision not to collect LACE score and most responsible diagnosis for patients who are NOT enrolled in the study (except where the reason for exclusion is a LACE score < 10, in which case this is recorded)	Too cumbersome from a practical standpoint
July 3, 2010	Decision to add 2 questions about alcohol and drug use to the baseline data collection form, and to do subgroup analyses on these 2 binary variables	To address the perception that the Virtual Ward may be less effective among patients with drug and alcohol use problems
December 7, 2010	Change p value threshold for interim analysis to 0.0001	At DSMB suggestion, to avoid premature termination
December 7, 2010	Develop standardized review process for unanticipated deaths, send results of review to DSMB chair	At DSMB suggestion, to minimize risk of VW-induced harm going undetected
December 7, 2010	Added secondary outcome of days in hospital (to be analyzed with administrative data, likely in a secondary paper)	At DSMB suggestion, to address the possibility that VW may be shortening the length of readmissions
December 7, 2010	Develop method to address missing data	At DSMB suggestion, noting DSMB opinion that "worst case scenario" approach may be overly conservative. DSMB recommended ignoring missing data if rates of missing data are very low.
March 16, 2011	Add EQ-5D to the follow up questionnaire. Eligibility criteria: family member, patient, caregiver, nurse in nursing home or someone who lives in same house.	To measure quality of life/utility, to facilitate economic evaluation.
July 19, 2011	Procedure for dealing with double enrolment: 1. Discard the second enrollment (i.e., patients only enters the study once) 2. If randomized to the same arm of the study both times, then use data subsequent to the first enrolment as we	To deal with accidental double enrolment

	<p>normally would</p> <p>3. If randomized to VW first and then usual care second, then use data subsequent to the first enrolment as we normally would</p> <p>4. If randomized to usual care first and then VW second, use data from the first enrolment and censor the observation on the day of the re-randomization (which would mean we would still count the readmission that resulted in the second enrolment)</p>	
August 24, 2011	<p>Approach to data handling for missing/unknown data</p> <p>1. Telephone data are the primary source of data.</p> <p>2. If telephone data are missing/unknown then data obtained from hospitals will be used, where such data has been successfully obtained. Such data can only be used to go from unknown/missing to 'yes' and cannot be used to determine that an ED visit or readmission did not occur.</p> <p>3. Where self-report of ED visit or hospital admission have been checked against hospital data, and hospital data do not support the patient self-report, the ED visit/hospitalization will not be counted.</p> <p>4. Data that continue to be missing after the above steps have been taken will not be included in the analysis.</p>	To minimize the amount of missing data
September 2011	<p>Explicit acknowledgment that it is acceptable for patients to be randomized on the day after discharge, when same day randomization is infeasible</p>	Feasibility issue
October 29, 2012	<p>Decision by VW research steering committee to extend enrolment for 6 months</p>	DSMB made this recommendation after reviewing interim data