LETTER of INFORMATION and CONSENT to PARTICIPATE in a RESEARCH STUDY

Full Study Title: CLEAN Meds RCT - Measuring the effects of providing carefully selected essential medications at no charge on medication adherence, prescribing appropriateness, health outcomes and health care costs: a randomized controlled trial.

Investigators: (Please call during regular business hours.)

Dr. Nav Persaud  
*Principal Investigator*  
Keenan Research Centre,  
St. Michael’s Hospital  
Tel: 416-864-6060 ext. 77578

Dr. Muhammad Mamdani  
*Co-investigator*  
Applied Health Research Centre,  
St. Michael’s Hospital  
Tel: 416-864-3037

Dr. Andreas Laupacis  
*Co-investigator*  
Li Ka Shing Knowledge Institute,  
St. Michael’s Hospital  
Tel: 416-864-5780

Dr. Andrew Pinto  
*Co-investigator*  
Family & Community Medicine,  
St. Michael’s Hospital  
416-867-3728

Dr. Richard Glazier  
*Co-investigator*  
Centre for Research on Inner City Health,  
St. Michael’s Hospital  
Tel: 416-864-6060 ext. 77444

Dr. Stephen Hwang  
*Co-investigator*  
Centre for Research on Inner City Health,  
St. Michael’s Hospital  
Tel: 416-864-5991

Introduction:

You are being invited to consider participating in a clinical trial (human research study). Before agreeing to participate, it is important that you read and understand the following
explanation of the proposed study procedures and your right to refuse to participate or withdraw from the study at any time. The following information describes the purpose, procedures, benefits and risks associated with participating in this study. It also describes your rights as a voluntary participant in a clinical trial if you choose to be part of this research.

To decide whether you wish to participate in this research study, you should understand enough about the study, its risks and benefits to be able to make an informed decision. This is known as the informed consent process. Please take your time to review this information and discuss any questions that you may have with the study staff. You may take your time to make your decision about participating in this clinical trial and you may discuss it with your regular doctor, friends and family before you make your decision.

The information and consent may contain words that you do not understand. Please ask the study doctor or study staff to explain any words or information that you do not clearly understand. Please make sure all your questions have been answered to your satisfaction before agreeing or signing this document.

24 hour /Emergency contact: If you have a medical emergency please call 911 (emergency services) or go to your nearest hospital. Please use this contact only if your health care provider requires immediate information about this trial or you are reporting an emergency regarding a trial participant. The emergency contact person for this trial is: ______________ at ________________.

Research Assistant contact: If you have any questions regarding this research study, you may call: ______________ at ______________, or via email at ______________ during regular business hours.

Conflicts of Interest: None

Sponsors/Funders:

1. Canadian Institutes for Health Research (CIHR)
   Address: 160 Elgin Street, 9th Floor, Ottawa ON K1A 0W9
   Tel: 613-941-2672 or 1-888-603-4178 (toll free)

2. St. Michael’s Hospital (SMH)
   Address: 30 Bond Street, Toronto ON M5B 1W8
   Tel: 416-360-4000
3. Toronto Central Local Health Integration Network (TCLHIN)
   Address: 425 Bloor Street East, Suite 201, Toronto ON M4X 1LZ
   Tel: 416-921-1701 or 1-866-383-5446 (toll free)

4. Ministry of Health and Long-Term Care (MOHLTC)
   Address: 8TH Floor Hepburn Block, 80 Grosvenor Street, Toronto, ON M7A 1R3
   Tel: 416-327-7759

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Purpose of Research:

Purpose
The purpose of this study is to measure the effects of giving patients free and convenient access to medications (the intervention). This is considered research as we are investigating how effective (or not) this method can be.

Background
The ability to get (access) medications and take medications as directed (adherence) are important for good health. There are many barriers to Canadians accessing medications. Some of these barriers are drug costs, medication errors made by clinicians (such as doctors) and lack of healthcare integration (links between your healthcare providers).

About one half of medications for chronic diseases (such as diabetes and hypertension) are not taken as directed. High prices for medications is one of the reasons for persons not being able to take their medications as directed. Canada is the only developed country where health care is publicly funded for people but medications are not covered for everyone. In Canada, at least 2.4 million adults do not take their medications as directed because of the cost of their medications. The large number of drugs in Canadian medication lists (formularies) may cause the high prices of medications here in Canada.

Justification
We believe that our study intervention of giving patients free and convenient access to essential medications (by mail) may improve the health of patients by increasing their access to the best available medications while reducing health care costs.

Similar interventions from Sweden, the United Kingdom and managed care settings in the United States have improved care and appropriate prescribing by clinicians and reduced healthcare costs. No such interventions have been tested in Canada.

In our research study intervention, you will be mailed your prescribed medications. Some research studies have shown that patients tend to take their medications as prescribed when they are mailed their medications. In Canada, patients can have most of their prescription medications mailed to them for easier access.
Description of the Research:

You will be randomly assigned to one of two groups. You have a 50% chance of being assigned to each of the two groups (like flipping a coin).

If you are assigned to the control group you will receive usual care and will have the usual access to medications for 12 months.

If you are assigned to the intervention group you will have free access to a carefully selected set of medications for 12 months. You may decide to take other medications. Most medications will be mailed to an address of your choosing (e.g. your home) and a pharmacist will provide you with information about taking the medications over the telephone. Some medications will be available at your clinic.

We expect that after participation for 12 months, individuals in the intervention arm will no longer receive free medications. It is possible that our research study will receive more funding to continue paying for the medications. If we receive more funding, we will inform you. At this point, we would like to request your permission to participate for 24 months, in case we are able to extend the study. We would like to add that you can choose to withdraw your participation at any point, with no impact on your care.

Regardless of which group you are assigned to, we will ask you questions about your use of medications, review your medical records to determine how often medications are prescribed, and you may receive medications in a bottle that tracks the number of times the bottles are opened. Research staff may review your medical records to determine how well any chronic diseases are controlled. Your care providers will continue to order tests for you as they usually do but they may adjust the timing of those tests for purposes of this research study.

We will also ask you to complete a short questionnaire that asks for personal information. This information allows us to perform different analyses with the final results. You may choose to not answer any questions.

Your responsibilities

As a participant in this study you will be expected to go to regular follow up visits and do tests as requested by your primary healthcare provider. You will also be expected to report any medication side effect(s), injury or harms related to this study to your primary healthcare provider (such as your family doctor) or pharmacist and the research coordinator (contact details listed below). In the case of emergencies you are expected to follow the instructions of the 24 hour/emergency contact listed below and when possible your primary healthcare provider.

Eligibility
You may be able to participate in this study if:

- You have reported cost-related medication non-adherence in last 12 months (you have not taken your medications as prescribed because of their cost)
- You are an adult (age 18 years and over)

You may not be able to participate in this study if:

- You have a family member living at same address who is already enrolled in this trial.
- You joined or registered with your current family doctor within the last 3 months.

Potential Harms: (Injury, discomforts or inconvenience)

You may be inconvenienced by telephone calls from the pharmacist. You will have to collect medications from the address of delivery that you choose.

In addition to the usual risks associated with all medications that you will experience regardless of your assignment to the control (usual care) group or the intervention group, if you are in the intervention group you are also at risk of being exposed to or experiencing:

i. Errors in switching to medications on the list of essential medications
ii. Dissatisfaction with the new medications
iii. Discontinuation effects of medications at the conclusion of the study (e.g. harms from abruptly stopping medications)

Your risk of medication errors will be reduced by having the pharmacist receiving the prescribed medication order review your electronic medical record which includes the history of medications previously prescribed. In order to switch you to listed medications, the pharmacist will use a widely accepted standard for determining equivalent doses between medications. This standard is called defined daily doses (DDD) and has been defined by the World Health Organization. These type of substitutions are currently routine for hospitalized patients. You will also be contacted about the change in medications. Errors will thus only effect the medications taken by you if they are prescribed by clinicians and missed by both the pharmacist and you. Medication errors will be monitored by the Data and Safety Monitoring Board (DSMB). The DSMB is an independent group of experts tasked with reviewing data in the study as it is collected and monitoring adverse drug reactions such as side effects. The DSMB will then make decisions regarding the continuation, modification or termination of the trial.

In some cases, you will be switched from brand name to generic products. There is clear evidence that generics and brand name medications have similar clinical effects, however, there is a perception that generics are inferior. To protect you, medication adverse effects will be monitored by the DSMB.

At the end of the study, if you are in the intervention group you will revert to your usual access to medications. This may mean you will continue to access medications or you may experience cost-related nonadherence after the conclusion of the trial. There are potential
harms of stopping certain medications that have withdrawal symptoms (e.g. antidepressants). We are warning you of this possibility before you enroll in the study and also before you start the medications. We will provide clinicians with instructions about how to manage any discontinuation effects that you may experience, which usually resolve spontaneously. Discontinuation effects will be reported as medication adverse effects.

You will have to do usual, regular follow up and tests (blood works). As with usual health care, you will need to have re-visits (follow up) with health care providers to have your health assessed, prescriptions refilled and to do tests to assess response to treatment. There are minimal risks associated with these such as loss in personal time or loss of earnings from missing work and minimal discomfort and expected outcomes from needle sticks for blood works (tests) and tightening of arm cuffs for the measurement of blood pressure. These risks are expected and occur in usual or everyday health care situations.

The study may involve risks which are currently unforeseeable.

**Reproductive risks**

There are no specific risks related to reproduction. Care providers will continue to prescribe medications based on their benefits and risks to you including to women of childbearing potential.

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**Potential Benefits:**

**Your benefits**

You may not directly benefit from participating in this trial. You will still have your usual access to all medications (that is, you can choose to pay for medications that are not on the list).

**Benefits to society**

The results of this study will help policy makers who are discussing what access Canadians should have to medications. Right now medications are provided to outpatients in other developed countries where healthcare services are publicly funded. In Canada, this does not happen. There have been strong arguments for providing medications without charge (pharmacare plan), but this has not yet happened. This study will give evidence related to prescribing patterns, medication adherence, health outcomes and costs, and will provide evidence in support of a national pharmacare plan if the results are positive.

**Alternatives to Participation:**

If you decide not to participate in the study you will have your usual access to medications. There may be programs available to help you access medications.

**Protecting your Health Information:**
All study information (including your personal health information) and your participant’s questionnaires will be entered and maintained on a secure, password protected database developed using Medidata RAVE (www.mdsol.com) and will only be accessible by authorized persons via the internet for data entry purposes.

In this study we will need access to your Personal Health Information (PHI). This information may include your name, date of birth, physical and mental health, family and medical history, treatment and medications among other information. PHI is private and is protected under the Personal Health Information Protection Act (PHIPA), 2004 in Ontario. PHIPA covers information collected, used or disclosed by custodians (e.g. health care providers) of your information for your care, treatment, health research and managing Canada’s publically funded health system. The researchers for this trial will abide by the PHIPA to protect your rights while they use your medical records and your contributions to this trial for research purposes. For more information on PHIPA you can visit the Department of Justice Canada online (www.justice.gc.ca).

All records that can potentially identify you will be kept confidential and, to the extent permitted by PHIPA, will not be made publically available. The study monitor(s), auditor(s), Data Safety and Monitoring Board members will be granted access to your original medical records for verification of the study procedures and/or data collected, without violating your confidentiality, to the extent permitted by PHIPA.

By signing the informed consent (signature page) you or your legally acceptable representative (substitute decision maker) is authorizing access and use of your information for the purposes of research. If at any time you choose to stop participating in this study you can withdraw your consent to use of your information. The information which is linked to you will be removed from the study database.

Federal and Provincial Data Protection regulations, including the Personal Information Protection and Electronic Documents Act (PIPEDA 2000), protect your personal information. They also give you the right to control the use of your personal information (including personal health information) and require your written permission for this personal information to be collected, used, or disclosed for the purposes of this study, as described in this consent form. You have the right to review and copy your personal information collected in this study. However, if you decide to be in this study or choose to withdraw from it, your right to look at or copy your personal information related to this study will be delayed until after the research is completed.

The study investigators will keep your study records securely stored for a period of 5 years.

We will keep your contact information on file on our secure database for at least 12 months. If we are able to extend our research to 24 months, we will continue to store your information for the extended period of time.
Study Registration and Study Results:

A description of this clinical trial should be available on http://www.ClinicalTrials.gov. This website will not include information that can identify you. At most, the website will include a summary of the trial and its results. You can search this website at any time.

The researchers plan to publish the study findings in peer-reviewed medical journals which may also be accessed via the internet. A clinical study report will also be filed with the Canadian Institutes of Health Research (CIHR) and persons wishing to review the study results can access the report as per CIHR regulations. These findings and reports will not include information that can identify you.

Communication with your Family Doctor:

Your primary healthcare provider (such as your family doctor) will be informed about your participation in this study. It is important that your healthcare provider is aware of this so that they can provide the best care and follow up for you. We will need your personal health information from your primary care provider for the purposes of this study. Please take time to read all of the information provided carefully and to discuss this information and any concerns that you may have with your primary care provider before you decide to participate.

Potential Costs to Participation and Reimbursement to Participants:

If you choose to participate you should not expect any additional costs for your existing health care services including doctor’s visits, blood works and other tests, imaging, referrals and medication. As a voluntary participant in this study, you should not expect any reimbursements (that is, you will not be paid).

Compensation for Injury:

In the event that you suffer any health related injury as a result of this research study, regular public health insurance coverage (like the Ontario Health Insurance Plan - OHIP) can be used to get immediate medical care for you. By consenting and participating in this study, you have not waived any rights to legal recourse in the event of research-related harms.

Participation, Withdrawal & Termination:
Your participation in this study is voluntary. You have the right to refuse to participate in this study. If you decide to participate, you may still choose to withdraw from the study at any time without any negative consequences to the medical care, education, or other services to which you are entitled or are presently receiving.

The study will come to an end (terminate) 12 months after you have started (or enrolled into the study), regardless if you are in the control or intervention group. At the end of the study you will go back to receiving your regular, usual care from your healthcare providers.

Please review the consent document (signature page) below carefully when deciding whether or not you wish to be part of the research. If you wish to participate in this study, you will be asked to sign the consent form. Only sign the consent if you accept the terms and conditions stated on the signature page.

**New Findings or Information:**

You or your legally acceptable representative (substitute decision maker) will be informed in a timely manner if any new information becomes available that may be relevant to your willingness to participate in this research study.

**Research Ethics Board contact:**

If you have any questions regarding your rights as a research participant, you may call the Chair, St. Michael’s Hospital Research Ethics Board at 416-864-6060 ext. 2557, during regular business hours.

**Study Contacts:**

**Research Assistant contact:** If you have any questions regarding this research study, you may call: ______________ at ______________, or via email at ______________ during regular business hours.

**24 hour /Emergency contact:** If you have a medical emergency please call 911 (emergency services) or go to your nearest hospital. Please use this contact only if your health care provider requires immediate information about this trial or you are reporting an emergency regarding a trial participant. The emergency contact person for this trial is: ________________.

**Long Term Follow Up - Optional**
We would like to request your permission to use your OHIP (health card) number to link the information collected in this study with your doctor's medical records and provincial health records. The provincial health records are stored at the Institute for Clinical Evaluative Sciences (ICES), a non-profit organization that manages research on health care delivery in Ontario. Giving us permission to work with ICES will allow us to follow your future health care needs and conditions over the long-term. This additional information will be de-identified once received (OHIP number will be replaced with your study number) and will be very useful in identifying gaps and needs for the ongoing care of people who have difficulty paying for their medications. We will use this link through ICES for a period of 5 years. This portion of the study is optional, and you may opt out of this by checking "I DO NOT AGREE" on the signature page of the Informed Consent Form.

If you choose to participate only in the main part of the study, you can do so without having to participate in the Long Term Follow Up.
SIGNATURE PAGE
Documentation of Informed Consent

Full Study Title: CLEAN Meds RCT - Measuring the effects of providing carefully selected essential medications at no charge on medication adherence, prescribing appropriateness, health outcomes and health care costs: a randomized controlled trial.

Please read the following carefully. If you agree, please sign this form.

The research study has been explained to me, and my questions have been answered to my satisfaction. I have been informed of the alternatives to participation in this study. I have the right not to participate and the right to withdraw without affecting the quality of medical care at St. Michael’s Hospital for me and for other members of my family. As well, the potential harms and benefits (if any) of participating in this research study have been explained to me.

I have been told that I have not waived my legal rights nor released the investigators, sponsors, or involved institutions from their legal and professional responsibilities. I know that I may ask now, or in the future, any questions I have about the study. I have been told that records relating to me and my care will be kept confidential and that no information will be disclosed without my permission unless required by law. I have been given sufficient time to read the above information.

I consent to participate. I have been told I will be given a signed copy of this consent form.

Please NOTE: By agreeing to the above and signing this form you are giving your informed consent to be a voluntary participant in this research study.

Optional Long Term Follow Up

☐ I agree to allow my health card number to be linked for the optional long-term follow-up as described in this consent form (previous page)

☐ I do not agree to allow my health card number to be linked for the optional long-term follow-up as described in this consent form (previous page)

Participant’s Name                  Participant’s Signature                  Date
___________________________________________________                          _____________________________________  __________

Substitute’s Name  Relationship                      Substitute’s Signature  Date
(if applicable)                      _______________________________  _______________________________  __________
___________________________________________________  _____________________________________  __________
Consenter Name | Position | Consenter Signature | Date
---|---|---|---
_______________________ | __________________________ | _____________________________________ | ____________

Witness Name (if applicable) | Relationship to participant | Witness Signature | Date
---|---|---|---
_______________________ | __________________________ | _____________________________________ | ____________

Interpreter (if applicable) | __________________________ | _____________________________________ | ____________

“I have been requested to interpret the consent discussion for the potential research participant named below.

**Participant’s Name**

___________________________________________________

I am competent in the English language and in the language of choice of the potential participant.

**Language of choice of the potential participant**

___________________________________________________

I am not involved in the research study.

I agree to keep confidential all personal information of the potential participant.

I have interpreted the consent discussion. The potential participant has advised me in his/her own language that he/she has been informed about the research study, the nature and extent of his/her participation, including the risks involved. The potential participant freely gives his/her consent to participate in this study.

Signature of Interpreter

___________________________________________________

Printed Name of Interpreter

___________________________________________________
Relationship or Position of Interpreter

______________________________

Contact Information of Interpreter

______________________________

Date

______________________________