Daily Delivery and Supervision of Psychotropic Medications for High-Risk Patients with Severe and Persistent Mental Illness

Document Date: January 17, 2018

PROTOCOL CONTENTS

The contents of a study protocol should generally include the following topics:

1 General Information

1.1 Protocol title and date.
Daily Delivery and Supervision of Psychotropic Medication for High-Risk Patients with Severe and Persistent Mental Illness

1.2 Name and address of the sponsor.
Dr. Jeffrey Waldman

1.3 Name and title of the person(s) authorized to sign the protocol and the protocol amendment(s).
Dr. Jeffrey Waldman

1.4 Name and title of the investigator(s) who is (are) responsible for conducting the study, and the address and telephone number(s) of the study site(s): this should include Dr. Ola Norrie's name and address along with others on the study team.

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Olga Norrie, B.Sc. (Pharm), M.Sc., Ph.D., CRE
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1.5 Name(s) and address(es) of any other medical and/or institutions involved in the trial.
Leila Pharmacy 632 Leila Ave., Winnipeg, MB, R2V 3N7

2 Background Information

2.1 Name and description of the study
Name: Daily Delivery and Supervision of Psychotropic Medication for High-Risk Patients with Severe and Persistent Mental Illness

The present study seeks to evaluate the effectiveness of an innovative and collaborative voluntary program for facilitating adherence to medication. This program involves partnering with the patient to develop a treatment plan and then collaborating with a pharmacy who hire staff specifically for the purpose of delivering and observing the patients taking their medication. The program is designed to serve individuals with severe and persistent mental illnesses who have been repeatedly hospitalized, are repeat users of community crisis services, or are frequently in contact with the criminal justice system.

The current study will follow high-risk and high need patients who have severe and persistent mental illness and who are involved with Forensic Services. Forensic Services is a multidisciplinary program based out of the PsycHealth building (Health Sciences Centre campus) and is part of the teaching program at the University of Manitoba's Department of Psychiatry, College of Medicine. The program provides assessment reports for the courts and psychiatric care to accused persons who have been found Not Criminally Responsible for criminal offences because of a mental disorder, or have been found Unfit to stand trial. It also provides care to offenders who have a mental illness and need supervision to manage their risk in the community. The pharmacy partner offering daily dispensing services is Leila Pharmacy 632 Leila Ave, Winnipeg, MB R2V 3N7 (Contact: Carey Lai, pharmacist) who delivers these services as part of the pharmacy's professional practice model.

The objective of this evaluation is to determine the impact of the daily dispensing with supervision program on patient well-being and system costs. Expected program benefits include increasing patients' impression of choice and control in their recovery, reduced visits to ER, crisis clinic and hospital admissions, as well as elimination of contacts with the criminal justice system.

2.2 Summary of the known and potential risks and benefits, if any, to the study's human subjects for participating in the study

The expected program benefits include improved patient satisfaction and autonomy, reduced visits to ER, crisis clinic and hospital admissions, as well as elimination of contacts with the criminal justice system.

No potential risks to project participants were identified.

2.3 Description of and justification for the route of administration, dosage, dosage regimen, and treatment period(s) of the modalities given to the study subjects.

'Daily Delivery and Supervision of Psychotropic Medication for High-Risk Patients with Severe and Persistent Mental Illness' is a MPAN-funded project to evaluate the effectiveness of an innovative and collaborative voluntary program for facilitating adherence to psychotropic medication after involvement with the justice system. The program involves a partnership between patients with severe and persistent mental illness and pharmacies who deliver daily dispensing services as part of their operations in hopes of improving patient outcomes such as patient wellbeing, hospitalizations and incarcerations, and in reducing costs associated with therapeutic non-adherence. Patients are supervised by pharmacy staff in their own home as they orally self-administer their regular daily medications to ensure medication compliance.

2.4 Description of the population to be studied.

Individuals with severe and persistent mental illnesses who have been repeatedly hospitalized, are repeat users of community crisis services, or are frequently in contact with the criminal justice system.

2.5 References to literature and data that are relevant to the study, and that provide background for the trial.

Angermeyer, M. C., & Matschinger, H. (2004). The stereotype of schizophrenia and its impact on discrimination against people with schizophrenia: results from a representative survey in Germany. *Schizophrenia Bulletin*, *30*(4), 1049.

Canadian Institutes of Health Research. (2012). *Guide to Knowledge Translation Planning at CIHR: Integrated and End-of-grant Approaches*. Canadian Institutes of Health Research.

Emsley, R., Oosthuizen, P., Koen, L., Niehaus, D., & Martinez, L. (2013). Comparison of treatment response in second-episode versus first-episode schizophrenia. *Journal of clinical psychopharmacology*, *33*(1), 80-83.

Goeree, R., Farahati, F., Burke, N., Blackhouse, G., O'Reilly, D., Pyne, J., & Tarride, J. E. (2005). The economic burden of schizophrenia in Canada in 2004. *Current Medical Research and Opinion®*, *21*(12), 2017-2028.

Keers, R., Ullrich, S., DeStavola, B. L., & Coid, J. W. (2014). Association of violence with emergence of persecutory delusions in untreated schizophrenia. *American Journal of Psychiatry, 171*(3), 332-339. doi: 10.1176/appi.ajp.2013.13010134

Patel, M. X., De Zoysa, N., Bernadt, M., Bindman, J., & David, A. S. (2009). Are depot antipsychotics more coercive than tablets? *Journal of Psychopharmacology, 24*(10), 1483-1489. doi: 10.1177/0269881109103133

Patel, M. X., de Zoysa, N., Berndt, M., & David, A. S. (2008). A cross-sectional study of patients' perspectives on adherence to antipsychotic medication: depot versus oral. *Journal of Clinical Psychiatry*, *69*(10), 1548.

Rosenberg, M. & Hanna, K. (2012). Caregivers and Schizophrenia: New Survey Reveals Significant Impact on Caregivers' Quality of life. Downloaded on August 3, 2015 from: schizophrenia.ca/docs/CARE Survey News Release Final at.

Rössler, W., Salize, H. J., van Os, J., & Riecher-Rössler, A. (2005). Size of burden of schizophrenia and psychotic disorders. *European Neuropsychopharmacology*, *15*(4), 399-409.

Schooler, N. R. (2005). Relapse prevention and recovery in the treatment of schizophrenia. *The Journal of clinical psychiatry*, *67*, 19-23.

Straus, S., Tetroe, J., & Graham, I. D. (Eds.). (2013). *Knowledge translation in health care: moving from evidence to practice*. John Wiley & Sons.

Thornicroft, G., Brohan, E., Rose, D., Sartorius, N., Leese, M., & INDIGO Study Group. (2009). Global pattern of experienced and anticipated discrimination against people with schizophrenia: a cross-sectional survey. *The Lancet*, *373*(9661), 408-415.

3 Trial Objectives and Purpose

A detailed description of the objectives and the purpose of the study. The objectives should match the study design, methods and data to be used.
The program is designed to serve individuals with severe and persistent mental illnesses who have been repeatedly hospitalized, are repeat users of community crisis services, or are frequently in contact with the criminal justice system. There are several objectives of this new approach. First, we believe that these patients are invested in working with our program to stay well, but individual factors related to their personal background or symptoms of their illness contribute to frequent non-adherence to medications. Non-adherence to medications then leads to behaviour that results in frequent use of very expensive services such as the criminal justice system, acute care hospital beds, and crisis services. Working collaboratively with the patient to improve adherence to medications in partnership with a private pharmacy that absorbs costs of the program is a less coercive model than injectable medications, which is the current standard for working with this population. In addition, oral medications are much less expensive than the newer injectable antipsychotics and the costs of running a "depot clinic" where the injectable medications are provided. At this time, there has been no effective program to ensure compliance with oral medications in the published literature.

The purpose of this research is to evaluate the effectiveness of this intervention on recovery by evaluating patient response to the program through a self-reported measure. In addition, we will be evaluating the effect of this low cost program on decreasing the burden of mental health inpatient and crisis services, as well as the burden on the correctional system.

The primary purpose of this study is to evaluate the effectiveness of this new model for decreasing the harmful effects of relapses to psychosis resulting from non-adherence to medications. Specifically, we plan to examine whether or not this program results in less use of crisis services, acute care hospitalization and less contact with the criminal justice system. We plan to assess client satisfaction by conducting Client Satisfaction Measure survey with participants in the new program. We will also engage key stakeholders during the process (e.g., community mental health workers, probation officers, pharmacists) to gather information and suggestions regarding the daily dispensing program. Based on feedback from clients and stakeholders, we will then aim to implement improvements to the process to optimize its effectiveness.

4 Study Design

The scientific integrity of the study and the credibility of the data from the study depend substantially on the study's design. A description of the study design should include:

4.1 A specific statement of the primary endpoints and the secondary endpoints, if any, to be measured during the study.
The primary endpoints to be measured during the study concern how the daily dispensing program will affect medication compliance and outcomes, hospitalizations, re-incarcerations, and community crisis utilization as

well as participants' perceptions of coercion with regards to taking part in the program and satisfaction with the program.

4.2 A description of the type/design of study to be conducted (e.g., before/after design) and a schematic diagram of study design, procedures and stages of analysis. The ***before-and-after design is a reasonable option for this evaluation.***

This study proposes to employ a crossover design where data is collected for 12 months during the study and compared to baseline data retrieved for 12 months for each patient before enrollment into the project. Each patient acts as their own control. All individuals currently in the Forensics program will be asked for their informed consent to participate in the study. The study proposes to collect some personal health identifiers such as participant's personal health identification number (PHIN) and date of birth to be able to link medical records for crisis services, hospitalizations and pharmacy data. Patient names will also be collected to determine the number of contacts with criminal services. All personal identifiers will be stripped from the data for analysis and only aggregate data will be reported and/or published.

4.3 A description of the study's intervention.

The main study intervention is the daily supervision of participants while they self-administer their medications by trained pharmacy staff to ensure compliance. The staff in question will be provided by Leila pharmacy and will in addition provide support so that individuals can transition back into living independently through reminders to attend regularly scheduled medical appointments and counseling on correct use of prescribed medications.

Leila pharmacy's LEAP program consists of 3 A'S: adherence, accessibility, and autonomy. Regarding adherence, it is common for individuals taking medications to miss doses. The LEAP program dedicates a team to help individuals living in the community to receive their medications daily at their homes. Staff will also spend some time with each individual to ensure the medications are taken appropriately. Missed or refused doses are recorded and reported back to the Leila pharmacy program coordinator.

With respect to accessibility, access to primary care is a growing problem and there are very few solutions available. This is why the Leila pharmacy team includes a nurse practitioner, dietician, pharmacist and other allied professionals. The nurse practitioner is available to provide bridging care until a permanent family physician is available. Further, a common cause of medication discontinuation is due to the side-effects. For anti-psychotic medications, weight gain, dyslipidemia and increase risk of developing diabetes can all deter an individual from taking their medications regularly and ultimately derail them from their path to recovery. The Leila pharmacy dietician is available to any of their clients and they can help address nutritional concerns and develop healthy meal plans. Both these services, like many others, are offered at no additional charge.

Regarding autonomy, staff respect each individual's decision and try to offer support whenever they need assistance. This is why the LEAP program is completely voluntary and their goal is be a transitional program. When an individual has made significant progress, the medical responsibilities are shifted back to the client.

5 Selection and Withdrawal of Subjects

5.1 Subject inclusion criteria.

Individuals currently enrolled in the daily dispensing program that are also part of the Forensics program and suffer from severe and persistent mental illnesses, have been repeatedly hospitalized, are repeat users of community crisis services, and/or are in frequent contact with the criminal justice system.

5.2 Subject exclusion criteria.

Individuals who are not currently in the Forensics program – those who are part of the daily dispensing program, but are not Forensic outpatients.

6 Treatment of Subjects

6.1 Procedures for monitoring subject compliance.
Participants will be visited in home on a daily basis.

7 Statistics

7.1 A description of the statistical methods to be employed, including timing of any planned analysis(ses).
Collected data would be analyzed for significant outcomes comparing before and after (a two year total time frame from pre-index date to post-index date) findings for:

- number of days/visits spent with crisis services (ED & CRC),
- hospital visits/admissions (length of stay) and
- number of incarcerations (as a dependent variable)

These data would be entered into a multivariate analysis of covariance (MANCOVA) model or similar multi-level model with baseline or study time, age and gender as the independent variables. Descriptive statistics would be used to elaborate on patient satisfaction and other variables of interest. Preliminary cost analysis will also be undertaken in anticipation of calculating a net benefit for the daily dispensing services.

7.2 The number of subjects planned to be studied.
N = 32

7.3 The level of significance to be used for any differences
$p < 0.05$

7.4 Criteria for the termination of the study.
Timeframe of study = approximately one year.

7.5 Procedure for accounting for missing, unused, and spurious data.
Cleaning data, missing data analyses and manual review of data collected etc.

7.6 Procedures for reporting any deviation(s) from the original statistical plan (any deviation(s) from the original statistical plan should be described and justified in protocol and/or in the final report, as appropriate).
All deviations from the statistical plan will be based on the quality of data collected during the study and will be filed as amendments to the protocol with the Ethics Board.

7.7 The selection of subjects to be included in the analyses (e.g., evaluable subjects).
Participants who are currently part of the Forensics program and who are enrolled in the daily dispensing program and have participated in the program for at least one month will be included in the analyses.

8 Ethics

Description of ethical considerations relating to the study.
Ethical considerations relating to the study are that participants may be part of a vulnerable population, and participant characteristics need to be considered as well, such as First Nations individuals. Moreover, the participants are also patients of the principal investigator. To address this issue, the principal investigator will not discuss the study with participants, and will neither encourage nor discourage participation. All study contact will be with a research assistant who is not involved in patient care.

9 Data Handling and Record Keeping

All the data will be maintained in a Redcap database with only authorized individuals having access. All data used for analysis will be stripped of personal identifiers and only aggregate data will be reported.

10 Publication Policy

Publication policy, if not addressed in a separate agreement

Appendix 1: Client Self- Reported Measure Instrument Version 1 August 04 2017*

	True	False	Don't Know
1. I feel free to do what I want about taking medication	[ ]	P1 [ ]	[ ]
2. People try to force me to take medication	N2[ ]	[ ]	[ ]
3. I have enough of a chance to say whether I want to take medication	[ ]	V3[ ]	[ ]
4. I choose to take medication	[ ]	P[ ]	[ ]
5. I get to say what I want about taking medication	[ ]	V[ ]	[ ]
6. People threaten me to get me to take the medication	N[ ]	[ ]	[ ]
7. It is my idea to take the medication	[ ]	P[ ]	[ ]
8. Someone physically tries to make me take the medication	N[ ]	[ ]	[ ]
9. No one seems to want to know whether I want to take the medication	[ ]	[ ]	[ ]
10. I am threatened with commitment (being sectioned)	N[ ]	[ ]	[ ]
11. They say they would make me take the medication	N[ ]	[ ]	[ ]
12. No one tries to force me to take the medication (R)	[ ]	N[ ]	[ ]
13. My opinion about taking the medication doesn't matter(R)	V[ ]	[ ]	[ ]
14. I have a lot of control over whether I take the medication	[ ]	P[ ]	[ ]
15. I have more influence than anyone else on whether I take the medication	[ ]	P[ ]	[ ]
16. How does being prescribed the medication make you feel? Does it make you feel:	[ ]	[ ]	[ ]
Angry	[ ]	[ ]	[ ]
Sad	[ ]	[ ]	[ ]
Pleased	[ ]	[ ]	[ ]
Relieved	[ ]	[ ]	[ ]
Confused	[ ]	[ ]	[ ]
Frightened	[ ]	[ ]	[ ]

Perceived coercion	/5
Negative pressures	/6
Voice	/3

(*) adapted from The MacArthur Coercion Study Admission Experience Survey (AES, short form, 16 items)
(1) Perceived coercion subscale: items scored as false=1; true/don't know=0
(2) Negative pressures subscale: items are scored as true=1; false/don't know=0 (except item 12 which is reverse scored)
(3) Voice subscale: items scored as false=1; true/don't know=0 (except item 13 which is reverse scored)
(R) Reverse scored for subscale analysis

Appendix 2: Stakeholder Survey Version 2 September 25 2017

University of Manitoba, Bannatyne Campus Research Ethics Board (May 2013) Online Survey Consent

Study Title: Daily delivery and supervision of psychotropic medications for high-risk patients with severe and persistent mental illness

Organization: University of Manitoba

Thank you for accessing the daily delivery and supervision of psychotropic medications for high-risk patients with SPMI survey on the internet. This study is being conducted by Drs. Jeffrey Waldman and Sabrina Demetrioff who are involved in the Forensics system of mental health.

This survey is being conducted to evaluate the overall satisfaction with, effectiveness of, and ways to improve the proposed medication administration process.

Your feedback will be collected through an online survey which will ask you a series of questions and should take about 5-10 minutes to complete.

Your participation in this online survey is completely voluntary. You are not required to provide any personal information such as your name, address, or telephone number, and you don't have to answer any questions you don't want to. The survey system will not record your email address or IP (Internet protocol) address.

The risks of participating are low. The questions are designed to not be upsetting, but some participants may find some questions personal or of sensitive nature.

If you agree to participate in the survey, please note that you must complete the survey in one setting (in other words, the system won't let you save your survey responses and return to complete them later).

Also, please note that when you submit your responses, you will **not** be able to withdraw them as we cannot link the survey responses back to you.

Your feedback is important to us and will help us evaluate the process of daily delivery and supervision of psychotic medications in the best interest of psychiatrically ill patients. We appreciate your input and will consider any suggestions to further improve the model. If you have any questions about this survey study, please do not hesitate to contact Dr. Jeffrey Waldman at (204) 787-3887.

The study is funded by the Manitoba Patient Access Network (MPAN) and has been approved by the University of Manitoba Health Research Ethics Board.

By continuing on and completing the online survey, you are consenting to participate in the online survey.

Survey Questions

1. My role in the daily dispensing program is:

   _____ _____ _____

   _____ _____ _____

   Other: _____

2. Please describe any major differences that you have noticed in the transition from before the daily dispensing project began to after its onset.

   _____

   _____

   _____

   _____

   _____

Please read the following statements and rate your level of agreement with each item:

3. The new program makes medication adherence more likely to occur.

Not applicable?/ Unable to answer	Strongly disagree	Disagree	Neutral	Agree	Strongly Agree

4. This new program is feasible for all clients.

Not applicable?/ Unable to answer	Strongly disagree	Disagree	Neutral	Agree	Strongly Agree

5. The new program alleviates pressure for mental health inpatient and crisis services.

Not applicable?/ Unable to answer	Strongly disagree	Disagree	Neutral	Agree	Strongly Agree

6. The new program alleviates pressure from the correctional system.

Not applicable?/ Unable to answer	Strongly disagree	Disagree	Neutral	Agree	Strongly Agree

7. The new program is more cost-effective for the mental health system.

Not applicable?/ Unable to answer	Strongly disagree	Disagree	Neutral	Agree	Strongly Agree

8. My workload has increased as a result of the new program.

Not applicable?/ Unable to answer	Strongly disagree	Disagree	Neutral	Agree	Strongly Agree

If yes, please briefly describe: _____

9. The new program provides notable benefits to me.

Not applicable?/ Unable to answer	Strongly disagree	Disagree	Neutral	Agree	Strongly Agree

If so, please describe these benefits.

_____

_____

10. The new program provides disadvantages to me.

Not applicable?/ Unable to answer	Strongly disagree	Disagree	Neutral	Agree	Strongly Agree

If so, please describe these disadvantages.

_____

_____

11. The new program provides notable benefits to clients.

Not applicable?/ Unable to answer	Strongly disagree	Disagree	Neutral	Agree	Strongly Agree

If so, please describe these benefits.

_____

_____

12. The new program provides disadvantages to clients.

Not applicable?/ Unable to answer	Strongly disagree	Disagree	Neutral	Agree	Strongly Agree

If so, please describe these disadvantages.

_____
_____

13. In your opinion, what has worked well in the new program?

_____
_____
_____
_____

14. In your opinion, what has NOT worked well in the new program?

_____
_____
_____
_____

15. Overall, how satisfied are you with the new program?

Not applicable	Very Dissatisfied	Dissatisfied	Neutral	Satisfied	Very Satisfied

16. Please provide suggestions for improving the new daily dispensing program (e.g., ways to improve efficiency, feasibility, cost-effectiveness, benefit the client, etc.)

_____
_____
_____
_____

17. In your opinion, does this program improve public safety?

Yes
(please explain why)

_____
_____
_____

No
(please explain why not)

_____
_____
_____

Appendix 3: Client Satisfaction Measure 1

Patient Satisfaction Survey*:

Hello, my name is Lydia and I wanted to ask you a few questions regarding the Daily Dispensing program that you are involved in. We are doing an evaluation of this program and we'd like to ask for your help with this evaluation by doing a short survey on what you felt while going to the program. The survey takes about 10-15 minutes and is voluntary. All of your answers will be kept separate from the program. Your taking part in the program is not affected by your choice to answer or not to answer this survey. Will you be able to answer a few questions?

If YES: <Proceed with the survey>
If NO: "Thank you for your time." Do you have any further questions?

Instructions for answering the survey

I will give you a number of statements and I would like you to let me know how much you agree with each statement on a scale of 0 to 10 with 0 being 'do not agree at all' and 10 being 'completely agree'. (If ≤ 4 ask to explain rating and enter under comments)

*adapted from Patient Satisfaction Survey CoaguCheck INR, used by Centre for Healthcare Innovation (CHI) to assess patient satisfaction

			Rating 0 to 10 0= not at all 10=fully agree	Comment (if ≤4 enter why here)
Accessibility	1	The hours of the program were convenient.		
	2	I found it easy to get the care that I needed.		
	3	It was convenient to get my medications delivered to me.		
Availability of resources	4	I was able to contact the program easily when I needed to.		
	5	The wait times to get into the program were short.		
Continuity of care	6	It was easy to get a referral when I needed one.		
	7	My doctor knew what was happening with me at the program during my regular visit.		
Outcome of care	8	Participation in the program helped me to improve my overall health.		
	9	I am able to better manage my condition.		
	10	The program made it less likely for me to have to go to the hospital emergency room.		
	11	The program made it less likely that I will get in trouble with the law.		
	12	The program met my needs.		
Humanness	13	The program staff listened to my problems.		
	14	The program staff spent the right amount of time with me.		
	15	The program staff were caring and responsive to my needs.		
Information gathering	16	The program staff kept my information private/confidential.		
	17	I did not need to repeat my information at different departments in the program.		
Information giving	18	The advice I got from the program staff was good for my condition.		
	19	The staff fully answered all of my questions.		
	20	I had all the information I needed to decide to participate in the program.		
	21	I knew what I was signing up for when I agreed to participate in the program.		
Pleasantness of surroundings	22	The program staff were courteous and friendly.		
Quality and/or competence	23	The program staff were competent.		
	24	The quality of my medical care was … (poor to excellent)		
	25	My overall satisfaction with the program is…		
	26	How likely would you be to recommend this program to others?		
Open Ended questions	27	What are some of the things that you liked about participating in the program?		
	28	What are some of the things that made it hard for you to participate in the program?		
	29	In what way could we improve the program?		

Thank you for taking the time to participate in this survey!

Appendix 4: Budget

Daily Delivery and Supervision of Psychotropic Medication for High-Risk Patients with Severe and Persistent Mental Illness Budget:

EXPENSE	**Amount**
PERSONNEL:	
Research Assistant (part-time salary)	14,280
Subtotal	**14.280**
PARTICIPANTS:	
Participant reimbursement	800
Subtotal	**800**
EQUIPMENT AND SUPPLIES:	
Computer supplies and maintenance	800
Computer software	300
Duplication of study materials	200
Miscellaneous costs (e.g., database access)	1,000
Subtotal	**2,300**
COMMUNICATION OF RESULTS	**2,000**
TOTAL DIRECT COSTS	**19,380**