Clozapine, concomitant medications and consumers: Assessing the accuracy of medication records and the lived experience of people prescribed clozapine under shared care arrangements

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STATEMENT OF ORIGINALITY

This work has not previously been submitted for a degree or diploma in any university. To the best of my knowledge and belief, the thesis contains no material previously published or written by another person except where due reference is made in the thesis itself.

(Signed) (Date)

Kate Murphy

ACKNOWLEDGEMENT OF PAPERS INCLUDED IN THIS THESIS

Section 9.1 of the Griffith University Code for the Responsible Conduct of Research ("Criteria for Authorship"), in accordance with Section 5 of the Australian Code for the Responsible Conduct of Research, states:

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- acknowledge all those who have contributed to the research, facilities or materials but who do not qualify as authors, such as research assistants, technical staff, and advisors on cultural or community knowledge. Obtain written consent to name individuals.

Included in this thesis are papers in Chapters 5 and 6 that are co-authored with other researchers. My contribution to each co-authored paper is outlined at the front of the relevant chapter.

The bibliographic details for the published paper included in Chapter 5 are:

Murphy K, Coombes I, Moudgil V, Patterson S, Wheeler A. (2017) Clozapine and concomitant medications: Assessing the completeness and accuracy of medication records for people prescribed clozapine under shared care arrangements. *Journal of Evaluation in Clinical Practice* 23, 1164-1172. https://doi.org/10.1111/jep.12743

The manuscript included in Chapter 6 has been submitted to the Australian Journal of Primary Care. The details of this paper, including all authors, are:

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Permission has been granted to reproduce the works in the thesis (Appendix 1).

(Signed) (Date)

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Supervisor: Amanda Wheeler

Supervisor: Ian Coombes

PUBLICATIONS AND PRESENTATIONS

In addition to the peer-reviewed publication as detailed above, the work in this M.Phil. was presented in the following manner:

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LIST OF TERMS

ADE	Adverse Drug Event
CMHS	Community Mental Health Service
CPMS	Clozaril® Patient Monitoring System
DAA	Dose Administration Aid
EPSE	Extrapyramidal Side Effects
FBC	Full Blood Count
GP	General Practitioner
HREC	Human Research and Ethics Committee
MO	Medical Officer
MH	Mental Health
MNMHS	Metro North Mental Health Service
MAP	Medication Action Plan
NC	Neutrophil Count
RBWH	Royal Brisbane and Women's Hospital
TRS	Treatment-Resistant (or -Refractory) Schizophrenia
T2DM	Type 2 Diabetes Mellitus
WCC	White (Blood) Cell Count

ABSTRACT

Schizophrenia is a serious long-term mental illness associated with significant morbidity and mortality. Clozapine is the most effective antipsychotic medication for the treatment of schizophrenia, however, due to potentially life-threatening haematological adverse effects, its use is restricted to people who have not responded to an adequate trial of at least two other antipsychotic medications. The high risk of adverse effects, associated mandatory monitoring and prescribing restrictions all mean that clozapine consumers often continue to be managed in a secondary care public mental health (MH) service.

In people stabilised on maintenance treatment living in the community, a shared care model, involving collaboration between a psychiatrist in secondary care, a general practitioner (GP) and community pharmacy in primary care is a management option. The aim of shared care is to lessen the burden on the consumer and on the secondary care service by allowing the GP to undertake the majority of monitoring and reduce the frequency of secondary care appointments.

While this may appear to be an ideal arrangement, discrepancies in medication information at transitions of care from one health service to another are common and contribute to prescribing errors. Where clinicians do not have full medication information there is potential for inappropriate clinical decision-making and the consumer can be exposed to adverse drug events (ADEs), which are defined as any harm occurring during drug therapy.

The overall aim of the study was to generate information and form recommendations to optimise communication pathways and access to accurate medication information between and for stakeholders (secondary care, general practice and community pharmacy) and consumers of a clozapine shared care service. The study was designed to assess the completeness and accuracy of consumer medication records held by shared care stakeholders and to describe the experiences of the consumers.

This was an exploratory mixed methods study undertaken in two parts. Firstly, a quantitative approach was used to examine secondary and primary care medication records in a public MH service setting. Fifty-five consumers (aged 18–65 years) prescribed clozapine under shared care were eligible to participate. Information from medication and dispensing records was used by a pharmacist to compile a best possible medication history for each consumer. Discrepancies were identified through reconciliation of stakeholder records with the medication history. Discrepancies were defined as an omission, addition, or administration discrepancy (difference in dose, frequency, or clozapine brand).

Thirty-five consumers who had previously consented to review of their medication records were then eligible to participate in Part Two of the study. Participants completed a semi-structured interview that included a number of questionnaires. The questionnaires focused on beliefs about illness and medicines, adverse effects, medication adherence and treatment burden, while the interview focused on advantages and disadvantages of clozapine, shared care, and communication pathways. Analysis was descriptive and thematic.

In Part One, 35 (63.5%) consumers consented to review of their records. Overall, 32 of the 35 consumers had at least one discrepancy in their records, with a mean of 4.9 discrepancies per consumer. Of 172 discrepancies, 127 (73.8%) were omissions. Primarily, concomitant medicines were omitted in 19/35 (54%) of secondary care records, while clozapine was omitted in 13/32 (40.6%) of community pharmacy records. In Part Two, 10/35 (28.6%) consumers agreed to participate in an interview. Findings included a low

level of treatment burden with minimal adverse effects and medium-to-good adherence. Four inter-related themes surrounding treatment in the clozapine shared care program were identified: (i) understanding of illness and recovery; (ii) positive outcomes of treatment; (iii) treatment burden and acceptance and (iv) communication pathways. All participants described a positive experience with treatment in the clozapine shared care program, citing the efficacy of clozapine and the GP relationship as major benefits. Other findings included the fact that consumers were mostly unaware of any communication that took place between their shared care clinicians and assumed that clinicians had access to accurate medication information.

In summary, discrepancies were highly prevalent in the shared care medication records of clozapine consumers in this service, however participants reported positive treatment outcomes. Improved documentation and timely access to accurate and complete medication records for shared care stakeholders is needed to reduce the risk for suboptimal clinical decision-making and ADEs. Expanding the pharmacist's role in this setting could improve timeliness and accuracy in medication-related documentation and communication and make shared care an option for a wider group of clozapine consumers.

1. INTRODUCTION

Clozapine is the most effective antipsychotic medication used in treatment-resistant schizophrenia (TRS) (1-3). It has proven superior efficacy but its use in many countries, including Australia, is restricted due to its high-risk adverse effect profile and stringent haematological monitoring (4). These high-risk adverse effects, prescribing restrictions and complex monitoring may increase the treatment burden for the consumer and the public health service and contribute to the underuse of clozapine in people with TRS (1, 5).

In Australia, prescribing of clozapine is restricted to psychiatrists, and together with the dispensing pharmacist, they must be registered with the relevant manufacturer's monitoring service to check blood test results (6, 7). In some states of Australia, general practitioners (GPs) can prescribe clozapine after initiation by a psychiatrist but cannot alter the dose (6). Such restrictions and monitoring requirements mean that consumers often continue to be managed in a public mental health service (6).

At Royal Brisbane and Women's Hospital (RBWH), a consumer prescribed clozapine as an outpatient is required to have a blood test in the community, attend the outpatient appointment with the psychiatrist at the hospital then have the prescription dispensed at the hospital pharmacy every four weeks. For the consumer, such a treatment regimen may include issues such as significant time spent on travel to and attendance at the hospital, cost for travel and parking and taking time off work due to hospital appointments. Sav et al. have described factors such as these as contributing to the burden of treatment for people managing chronic illness (8).

For people living in the community whose illness is stable, a shared care model for the prescribing, dispensing and monitoring of clozapine involving collaboration between the psychiatrist, GP and community pharmacy may be an appropriate management option. The concept of shared care is to lessen the treatment burden on the consumer and on the public mental health (MH) service. Working with the GP to undertake the majority of monitoring and management reduces the frequency of hospital outpatient appointments (9).

However, discrepancies in medication information at transitions of care from one health care service to another are common (10, 11) and the absence of a single medication record allows for potential information gaps and ineffective clinical handover, including medication liaison, between the various stakeholders involved in shared care. Where stakeholders do not have complete records of concomitant medication there is a potential risk of adverse drug events (ADEs) (10, 12). Few publications are available that inform us about medication discrepancies for consumers who are prescribed clozapine under shared care arrangements.

There is evidence that the health care system itself can contribute to treatment burden for the consumer due to poor co-ordination between clinicians and poor relationships between the clinicians and the consumer (8). In people with a serious mental illness, it is recognised there is a need for greater consumer involvement in decisions about treatment options, although this may also contribute to treatment burden (13). The views and experiences of clozapine consumers who are involved in shared care models have been lacking (13). By exploring consumers' opinions about their experience with clozapine in a shared care program, we can explore areas of good practice and areas for improvement.

2. REVIEW OF THE LITERATURE

2.1 Schizophrenia

Schizophrenia is a serious long-term mental illness with an estimated global prevalence rate of 1% (14). The disorder is associated with significant morbidity and increased mortality, due to various physical health issues and completed suicide, as well as contributing to substantial economic costs (14, 15). Alarmingly, the difference in mortality for people with schizophrenia compared with the general population has increased in the past 30 years, indicating that people with schizophrenia have not benefitted from improvements in health care seen in the general population (16-18). Schizophrenia is characterised by psychotic symptoms that are generally categorised as positive and negative. Positive symptoms include hallucinations, delusions, disorganised speech and behaviour, while negative symptoms comprise emotional withdrawal, blunted affect, psychomotor retardation and disorientation (1, 15). People with schizophrenia also have worse physical health and higher rates of drug and alcohol abuse than the general population (14). In order to effectively treat schizophrenia and physical health issues, a multidisciplinary team approach is recommended, encompassing specialist MH services, general practice and community pharmacy (14, 15).

Antipsychotic medications are the mainstay of treatment for schizophrenia in the acute and long-term phases of the illness (14, 15). Various antipsychotic medications are used and choice of treatment is influenced by adverse effects, treatment of specific symptoms, co-morbidities, and concomitant medications, potential for non-adherence and consumer preference (14, 19). It is estimated that approximately one-third (20, 21) of people diagnosed with schizophrenia experience incomplete remission of positive symptoms, have pervasive negative symptoms and are at significant or persistent suicide risk, despite treatment with at least two different antipsychotics; such individuals are defined as having treatment-resistant (or -refractory) schizophrenia (TRS) (14, 20, 21).

2.2 Clozapine in treatment-resistant schizophrenia

It is widely accepted in the literature that clozapine is the most effective medication for TRS, with 30%–60% of people showing improvement when switching to clozapine (2, 22).

Clozapine has also been shown to reduce overall mortality, mainly by reducing the number of completed suicides (19, 23, 24). Kane et al. established that the superiority of clozapine was not confined to particular aspects of psychopathological characteristics but involved all the major psychotic signs and symptoms associated with TRS, including negative symptoms, which are often the most difficult to treat (2). When compared with other antipsychotic medicines, clozapine not only demonstrates superior efficacy, but is relatively free from extrapyramidal side effects, such as tremor and muscle rigidity, tardive dyskinesia and hyperprolactinaemia. As such, clozapine is the preferred option in treatment-intolerant consumers who have experienced these adverse effects with other antipsychotic medications (2).

Despite its proven efficacy and lack of extrapyramidal side effects, the use of clozapine in many countries, including Australia, remains limited to people diagnosed with TRS and treatment intolerance, due to major safety concerns that mainly involve life-threatening agranulocytosis (4, 19). Clozapine has been shown to induce neutropenia and

agranulocytosis; the risk is highest within the first three months of treatment and the development of these safety concerns requires clozapine to be ceased immediately (7, 25). Clozapine is also associated with other serious adverse effects including myocarditis and cardiomyopathy, metabolic effects such as type 2 diabetes mellitus (T2DM), weight gain and elevated cholesterol levels, as well as seizures and gastric hypomotility, which can result in severe constipation (25, 26) . Pharmacotherapy may be needed to manage adverse effects (25), adding to the number of medications and increasing the risk of ADEs and treatment burden for the consumer (4, 27). Table 1 provides a summary of the serious adverse effects associated with clozapine.

Table 1: Serious adverse effects of clozapine^

ADVERSE EFFECT	INCIDENCE AND ONSET	OUTCOME	MANAGEMENT
Agranulocytosis	In Australia: 0.9% - agranulocytosis alone 2.6% - agranulocytosis, neutropenia and leukopenia combined (28) Highest risk is in the initial 6–18 weeks (29)	3–4% mortality rate (25) No deaths have been recorded in Australia (28)	Stop clozapine, monitor for signs of infection, consult haematologist. Supportive therapy as needed
Myocarditis & cardiomyopathy	0.015–0.188% (9) Myocarditis occurs in the initial 6–8 weeks Cardiomyopathy can occur at any time	Potentially fatal	Stop clozapine, pharmacological treatment as needed
Type 2 diabetes mellitus	Up to 36.6% (4)	Increases risk of cardiovascular disease and related death	Conventional treatment for T2DM including pharmacological treatment
Weight gain	>20% of consumers gain >10% of baseline weight within a year, peaking in the initial 4–12 weeks (25, 29)	Associated risk with hypertension, type 2 diabetes mellitus and coronary heart disease	Diet and exercise, pharmacological treatments have limited evidence (30)
Seizures	3% - associated with high clozapine plasma levels (25)	Potentially fatal	Electroencephalo-gram, monitor clozapine plasma level, dose reduction, pharmacological treatment (anticonvulsant)
Constipation	Up to 60% (31) - usually persists throughout treatment	Mild symptoms to intestinal obstruction and potentially death	Prevention with high-fibre diet, bulk-forming laxatives, pharmacological treatment

^Modified from: Queensland Government Adult Clozapine Titration Chart, Version 1.00 - 10/2011

Clozapine is primarily metabolised by the cytochrome P450 enzyme 1A2 and has potential for significant pharmacokinetic interactions with concomitant medications, tobacco smoke and caffeine (32). These interactions may alter clozapine plasma levels and potentially result in its toxicity or inefficacy (19, 32). Toxicity can cause loss of consciousness, delirium, coma, seizures, arrhythmias, aspiration and respiratory depression (32). Table 2 lists some of the more common medications that can affect clozapine plasma levels.

Table 2: Medications that affect clozapine levels (32)

Medications that **increase** plasma clozapine levels	Fluoxetine, fluvoxamine, paroxetine, sertraline, citalopram, venlafaxine, haloperidol, olanzapine (theoretical), risperidone, erythromycin
Medications that **decrease** plasma clozapine levels	Phenytoin, carbamazepine, omeprazole, St John's Wort, tobacco smoke

Pharmacodynamic interactions are caused by additive effects of both clozapine and concomitant medications (19). Effects such as hypotension, myocarditis, sedation, effect on cardiac QTc interval and agranulocytosis can be exacerbated when taking clozapine and concomitant medications (19). In particular, combining clozapine with adjunctive treatments that may cause neutropenia and agranulocytosis must be done cautiously. If neutropenia occurs, concomitant medicines must be considered as a possible causative factor (25, 33). A Finnish study involving 163 cases of clozapine-induced agranulocytosis found that 40% of all agranulocytosis and 80% of fatal agranulocytosis involved concomitant medications (34).

The significant adverse effects and drug interactions associated with clozapine require that all clinicians involved, including the psychiatrist, GP, pharmacist and case manager, as well as the consumers themselves need to be aware of the total pharmacotherapy load to minimise potential ADEs.

In many countries, including Australia, specific monitoring requirements must be followed when prescribing clozapine to minimise the impact of haematological adverse events (4). The pharmaceutical manufacturer must support strict full blood count monitoring and medical review involving the registration of people prescribed clozapine on a centrally administered data network (35). The introduction of strict haematological monitoring and tighter restrictions in use (i.e. restricted for use in TRS) has resulted in the overall decline of the incidence of agranulocytosis as well as its risk of fatality (2, 25). No deaths have been reported in Australia related to agranulocytosis since the introduction of the Clozaril patient monitoring system (CPMS®) in 1993 (7). (7). The CPMS® protocols include the following requirements (7):

- The registered Medical Officer (MO) reviews all white cell counts (WCC) and neutrophil counts (NC) and clinically assesses the consumer;
- The WCC and NC are monitored weekly for the first 18 weeks then every four weeks (or 28 days) thereafter, providing WCC >3.5 x 109/L and NC >2.0 x 109/L;
- Within a 48-hour period commencing the morning of when the blood sample is due the following must be completed:
- A blood sample taken (WCC & NC);
- Haematology examination performed by the laboratory;

- Clinical assessment of the consumer by the MO for signs of infection;
- Review of blood results by the MO (and a prescription written if necessary);
- Results recorded onto a blood count form or entered into the database;
- Medication dispensed after pharmacist reviews blood results and prescription;
- If applicable fax the completed blood count form to the CPMS®.

In addition, protocols cover the dispensing of additional clozapine, therapy interruption or treatment cessation due to a non-haematological reason.

Table 3: Assessment of blood test results (7)

WCC* & NC** RESULTS	RANGE	ACTION
WCC >3.5 x 109/L and NC >2.0 x 109/L	GREEN	Continue with treatment
WCC 3.0–3.5 x 109/L and/or NC 1.5–2.0 x 109/L	AMBER	Increase blood count monitoring to twice weekly
WCC <3.0 x 109/L and/or NC <1.5 x 109/L	RED	STOP clozapine immediately, repeat test in 24 hours. Monitor for signs of infection
*WCC = white cell count; **NC = neutrophil count.		

While haematological monitoring during clozapine treatment is well established, more recently there has been research about appropriate monitoring and treatment for cardiovascular, metabolic and gastrointestinal adverse effects (4). Although not mandatory, monitoring for such serious adverse effects is strongly advised (4, 14, 35). and health services including in Queensland have developed monitoring protocols for these adverse effects (36). Table 4 summarises the recommended monitoring in Australia by the Australian Commission on Safety and Quality in Health Care (37).

Clozapine is known to be an effective treatment for TRS and, with appropriate monitoring, the risks associated with clozapine can be minimised (1, 2, 4). However, such rigorous monitoring can place a significant burden on the consumer and public health service, resulting in reduced accessibility and global underuse (5, 24, 29, 35, 38). One Australian study has suggested that the national rates of clozapine use seem to be appropriate (20). By examining statistical databases of the two drug companies that supply clozapine to the Australian market, Malalagama et al. estimated that 58% of people diagnosed with TRS are treated with clozapine (20). Given that 30–60% of people with TRS are likely to respond favourably to clozapine therapy, they surmise that the national rate of 58% appears appropriate. Conversely dispensing data from Queensland estimates that in 2013 only 8.3% of people with schizophrenia were dispensed clozapine (39). In addition there is evidence that clozapine is underused internationally; therefore, efforts are warranted to implement models of service delivery to improve access to clozapine and its superior outcomes (40). Shared care is one such model of service delivery in Australia that could reduce treatment costs and burden for the public MH service, while allowing the service to accept new consumers, in addition to reducing treatment burden for consumers, yet there has been little research into systemic models for supporting people taking clozapine (6).

Table 4: Non-haematological monitoring recommendations for clozapine

ADVERSE EFFECTS	MONITORING	TIMEFRAMES
Cardiac effects: cardiomyopathy, myocarditis, tachycardia, postural hypotension	Blood pressure (lying down and standing), pulse, respiration, temperature; Troponin, C-reactive protein, ECG*; Transthoracic echocardiogram.	Baseline, then TWICE DAILY (pre-dose and 4–6 hours post- dose) while titrating dose; Baseline, weekly for 4 weeks, then at 3 months, then annually; Baseline then annually or as per local procedure.
Metabolic effects: glucose intolerance, type 2 diabetes mellitus, hypercholesterolaemia, weight gain	Plasma glucose (fasting); Fasting total cholesterol, LDL*, HDL*, triglycerides; Weight, body mass index, waist circumference.	Baseline, then every 6 months; Baseline, at 3 months, then 6 monthly; Baseline, weekly for 4 weeks then 6 monthly.
Toxicity (seizures, excess sedation)	Clozapine plasma level	Weekly for the first 4 weeks then as required per clinical response, side effects/sign of toxicity, change in consumer's smoking status.
Gastrointestinal (gastric hypomotility, constipation, nausea)	Consumer feedback, bowel chart (for inpatients)	As clinically indicated, preventative treatments are recommended.
*Abbreviations: ECG = electrocardiogram, LDL = Low-density lipoprotein, HDL = High-density lipoprotein.		

2.3 Shared care for treatment-resistant schizophrenia

Shared care has been described as the "joint participation of GPs and hospital consultants in the planned delivery of care for patients with a chronic condition, informed by enhanced information exchange over and above routine discharge and referral letters" (41).The term shared care has also been described by Lester as a team approach to care, "with both primary and secondary care practitioners contributing to elements of a patient's overall care package, communicating effectively and working together to make that patient's pathway through the system as smooth as possible" (42).

The intention of a primary and specialist shared care model in the MH setting is to improve access, lessen the burden on the consumer and the health service as well as to facilitate treatment of physical health issues (9, 42). This aligns with the key recommendations of the clinical practice guidelines for treatment of schizophrenia issued by the Royal Australian and New Zealand College of Psychiatrists (RANZCP) which promote primary care management (14). Filia et al. described shared care as offering the person who is taking clozapine a less intensive and restrictive management option, as well as "more normality,

flexibility, improved quality of life, greater satisfaction and reduced stigma" (9). A shared care approach can also facilitate self-management with greater consumer involvement in decision-making by addressing time constraints and providing extra opportunities for consumer engagement in discussion with their various clinicians on treatment-related concerns (43).Self-management has been identified as major contributor to recovery from mental illness (44) which has been defined as "the development of new meaning and purpose in one's life as one grows beyond the…effects of mental illness" (45). The recovery model focuses on relapse prevention and the potential for wellbeing in people living with a long-term mental illness rather than a cure (44).

As consumers on clozapine require regular MH assessments as well as physical assessments to identify signs and symptoms of infection and to review adverse effects and blood test results, it is important that shared care models ensure safety and no loss of quality of care for the consumer. By reviewing medical records and developing a questionnaire for clinicians, Filia et al. found that successful transition and long-term success of public hospital MH consumers shifting to GP shared care arrangements required the selection of appropriate consumers and careful planning and preparation (6). Additionally, the consumer and their family/carers should be active participants in the shared care arrangement (6, 35). Factors that may influence a consumer's successful transition to shared care include (36):

- The consumer being at a point in therapy where their mental state, functional level, clozapine dosage and any adverse effects of the medication are considered to be at a stable or optimum level;
- The consumer having a history of medication adherence;
- The consumer having the ability to attend appointments, blood tests and other investigations independently;
- The consumer having the ability to access a GP and community pharmacy;
- The consumer's satisfaction with the transition.

Shared care at Royal Brisbane and Women's Hospital

In the shared care model in the setting of this study at RBWH, a psychiatrist or trainee undertakes a clinical assessment with the consumer and prescribes clozapine every 12 weeks rather than the routine four weeks. The mandatory four-weekly monitoring and clinical assessment is undertaken by the GP who communicates with the hospital pharmacy to dispense clozapine based on satisfactory blood test results. At the time of the study, communication of blood test results involved the GP completing and signing the CPMS® blood test result form which was then faxed to the hospital pharmacy. The hospital pharmacy dispenses the prescription, written by the psychiatrist (or trainee), and arranges delivery to the community pharmacy or GP for consumer to collect. Thus, the frequency of hospital outpatient appointments is reduced, as is the associated cost and time burden for the consumer and secondary care service (9). Medicines other than clozapine may be prescribed by the psychiatrist, the GP or others and are dispensed at their community pharmacy, ideally with the clozapine.

Despite the potential benefits, there are well-documented risks associated with the shared care model, primarily with the issue of a lack of effective and timely communication between the different health care services (13, 42, 46, 47). An Australian study proposed that, for successful collaboration in the MH shared care setting, emphasis should be on improving MH expertise among GPs and community pharmacists and information sharing between clinicians and health care settings (43). Suboptimal communication and information sharing can result in inappropriate prescribing and ADEs. This was demonstrated in an analysis of physician error reports in the United States, which found

that poor communication and lack of access to a medical record caused more than two-thirds of treatment errors in medical practice (48). Communication gaps between clozapine shared care stakeholders is an area that requires further research to identify areas of improvement that may enhance the efficacy of current shared care models and reduce the risk of ADEs with this high-risk medication.

It is also important to take into account the role of community pharmacies in the clozapine shared care arrangement. Community pharmacies often dispense other medications required by a consumer and prepare a dose administration aid (DAA) that contains all or most prescribed medicines in a tablet or capsule form. This is another interface where information discrepancies can occur (49, 50).

A shared care arrangement is an effective and less restrictive approach for consumers prescribed clozapine in the community. However, the absence of timely and accurate communication from one health provider to another increases the risk that discrepancies between medication records may occur, resulting in ADEs caused by suboptimal prescribing and interactions (10, 11, 51).

2.4 Information discrepancies and medication errors

Medication errors, principally discrepancies in medication information, are common at transitions of care from one health care service to another and well documented in the literature (10, 11, 51-57). The Australian Commission on Safety and Quality in Health Care found that, at a minimum, the following medication information should be recorded at transitions of care (58):

- medication name, dose, frequency, route and purpose (indication);
- whether medications are current, changed or ceased;
- medication allergies and adverse drug reactions;
- medication error risk;
- name and contact details of the community pharmacist.

Discrepancies in medication records between primary care and specialist clinicians, particularly in the management of long-term illness in the outpatient setting, is an important issue and a priority for further research (10, 11, 27, 50, 53).

The most common type of medication error at transitions of care consists of discrepancies in the medication record, which are known to contribute to prescribing errors (51, 53). Discrepancies are typically defined as an addition, omission or change in dose or frequency of medication from what the consumer is actually taking to what is logged in the medication record (11, 59). Omissions have been found to be the most common discrepancy (11, 12, 51, 59).

Australian research has identified a high rate of discrepancies in the medication records of people with chronic illness in the outpatient setting who are managed by primary care and public hospital services. One study describing medication-related problems in 46 people referred to aged care and memory clinics at a tertiary care hospital found that “85% of people had omission of therapy in the GP medical record to that documented by the pharmacist in medication reconciliation, and 45% had dose discrepancies” (60). Similarly, another study found high rates (>80%) of medication discrepancies consisting mostly of omissions in GP referral letters when compared with interview information from people with T2DM referred from primary care to a tertiary ambulatory clinic (11). A third Australian study

compared the GP referral letter with a consumer interview in a cohort of patients referred to a public hospital general nephrology/hypertension outpatient clinic and reported that 42% of letters contained inaccuracies for drug or dose in the medication list documented in the consumer interview (10). Comparable results from a study in an outpatient practice in the United States identified medication discrepancies in 76% of the cohort; again, the majority of discrepancies were omissions, when medical records were compared with consumers' own medicines and interview material (59). These studies did not compare the GP medication lists with the record of medication from either the hospital or community pharmacy.

In the MH outpatient setting in the United Kingdom (UK), a study compared medication lists between GPs and hospital records but did not interview consumers. Clark found that in records of 19 MH consumers with diverse diagnoses, 41 out of 58 medicines (that people were taking) were omitted in either the primary care (GP) or secondary (hospital) care records (12).

A literature review examining medication errors in psychiatry found that studies on this topic were almost exclusively in the hospital setting and thus little is known about the prevalence and implication in outpatient and community settings (53). The risks of medication discrepancies in the community MH setting includes the fact that consumers cross between primary and secondary and community interfaces. Psychiatric medicines are often dispensed by community pharmacists who may be unfamiliar with them, GP records often omit drugs including clozapine prescribed by community mental health teams (CMHT), while MH services tend to omit non-psychotropic medicines and often fail to monitor for adverse effects and physical comorbidities (12, 49, 50).

A further complication is that MH consumers are often taking multiple medications for their mental illness and physical conditions. A study in New South Wales of pharmacist-led medication reviews for 48 community MH consumers found that the average number of medicines taken per consumer was seven and comorbid mental and physical illness was described as being common (49). A study from the Netherlands found that 78% of people with schizophrenia taking an antipsychotic medication used at least one concomitant medication (61). Another UK study audited 193 case notes of people dispensed clozapine at a hospital pharmacy and found that that up to 31% of people taking clozapine were also concurrently prescribed additional antipsychotics (62).

The risks surrounding communication gaps with regards to medication records are particularly relevant in consumers who are prescribed clozapine in a GP shared care arrangement, with contributing factors such as the high-risk adverse effects of clozapine, multiple prescribers and pharmacies and the likelihood of comorbidities and concomitant medications. There is little research about medication discrepancies in the medication records of consumers prescribed clozapine under a shared care arrangement between the specialist MH services, the GP and the community pharmacy.

2.5 The consumer experience

A key principle of recovery from mental illness is self-management, which encourages the consumer to be as involved as possible in their treatment (44). Furthermore, consumers with long-term health conditions, such as schizophrenia, can be seen as "experts" of their illness and treatment and provide valuable insight and information into management of their health (63, 64). In an Australian review on effective collaborative care for people with severe mental illness, Lee et al. recognised "the need for MH consumers and carers to

have a stronger involvement in decisions about treatment options or referrals to collaborating services" (13). However, there is limited data on mental health consumers' perspectives on their treatment, particularly regarding clozapine and shared care.

Self-management is accompanied by treatment burden, which refers to the workload imposed by health care on consumers in proactively treating and managing chronic illness and the effect this has on quality of life (8, 65). Components of treatment burden include: financial burden, time and travel burden, medication burden and health care access burden (8). In people with multiple and chronic illnesses, treatment burden is a crucial outcome for disease management (65). Health care professionals are often not aware of the significant time, money and effort spent by people on health-related activities (65). If unaddressed, treatment burden can result in relapse of illness, decline in health, decreased survival and ineffective use of health resources (8).

In a study involving group interviews with outpatient MH consumers, Happell et al. reported that consumers self-adjusted their doses of antipsychotic medication, due to the burden of adverse effects (66). These consumers were reluctant to speak with MH clinicians about this, due to perceived negative repercussions (66). The literature suggests that when consumers are actively engaged in their treatment they are more likely to adhere to a medication regimen (67).

It could be expected that consumers prescribed clozapine may have significant treatment burden due to the long-term nature of schizophrenia, the potential for severe side effects, the strict monitoring requirements, as well as the high incidence of co-morbidities and concomitant medications (14). Consumer interviews may be able to identify areas of treatment burden relating to clozapine treatment and potential interventions to reduce them.

Despite its potential for significant adverse effects and treatment burden, research that has focused on consumer perspectives of clozapine treatment has found that views are generally favourable (68-72). A Canadian study administered a 37-item survey to 130 clozapine consumers in the inpatient and outpatient settings and found that the majority reported improvement in their level of satisfaction, quality of life, adherence, thinking, mood and alertness, as well as an overall positive regard for clozapine (70). A study in Germany interviewed clozapine consumers at discharge from a psychiatric hospital and found that consumers noted the calming and relaxing effect of clozapine as well as improved sleep as positive effects, with fatigue and sedation being the most common negative effects (69). In the UK, the largest survey of consumer perceptions of clozapine was given to outpatients to complete, with 570/1284 survey forms returned (71). Results found that 88.6% of respondents believed the advantages, particularly efficacy, of clozapine treatment outweighed the disadvantages such as blood tests and adverse effects (71). The majority of respondents (64%; viewed blood tests as "okay", as they were a necessary part of treatment (71). In contrast, a UK survey of 144 hospital practitioners who were predominantly trainee psychiatrists found that practitioners identified barriers to prescribing clozapine as being predominantly consumer-focused such as consumer refusal of blood test monitoring or concerns about tolerability (73). A more recent Australian study that compared clozapine consumers' views with those of their MH clinicians found that consumers taking clozapine were happier and more satisfied with their treatment than their clinicians believed them to be (72). Clinicians' views were likely influenced by the potential for high-risk side effects and the burden of mandatory monitoring, whereas consumers were less concerned with these factors when they noted the benefits in their daily life (72).

To date, relatively little has been published about MH consumers' experiences in a shared care outpatient setting (6, 42, 66). A UK study that interviewed consumers with schizophrenia who were receiving care in a shared care program focused on their

satisfaction with primary care. Findings suggested that satisfaction was “rarely expected or achieved” and that a GP’s support for a consumer’s hope for recovery was important (74). Another study explored views of MH consumers in a shared care program and found generally high scores for satisfaction with primary care services in treating physical health issues, however, they had mixed views about GP involvement in their MH care (47). A further study from the UK interviewed consumers with various chronic illnesses about their experience of the transition between primary and secondary care. It reported that many consumers felt they were “left in limbo” due to a lack of continuity and communication (75). This study also highlighted the difference of the consumer’s relationship with the GP and the secondary care clinician. The GP relationship was seen as more familiar and allowed for more discussion of issues. In comparison, the relationship with the secondary care specialist was viewed as more impersonal, with less time and fewer opportunities for consumer involvement (75). An Australian study interviewed clinicians, MH community staff and GPs about the barriers and benefits of a clozapine shared care approach and did not involve the consumers, although consumer interviews were identified as a future research project (6).

2.6 Summary

Schizophrenia is a serious mental illness with significant morbidity and mortality. Clozapine is the most effective antipsychotic in the treatment of schizophrenia but has high-risk adverse effects and mandatory monitoring, restricting its use. Treatment with clozapine in a shared care arrangement is an option used in MH services to improve access, reduce the consumer and public MH service burden, as well as support GP relationships, which can improve treatment of physical illnesses. Effective treatment in a shared care program requires involvement of consumers and carers in treatment decisions, including those about medication (13). To date there has been no literature reporting the perspective of clozapine consumers about their experience of taking clozapine in a shared program and their potential treatment burden within this setting. Exploring these issues is an important means of informing interventions, to optimise consumer experience and adherence, and minimise the risk of ADEs.

3. AIM AND OBJECTIVES

The overall aim of this thesis was to generate information and form recommendations to optimise communication pathways and access to accurate medication information, between and for stakeholders (secondary care, general practice and community pharmacy) and consumers of a clozapine shared care service.

The study was informed by a literature review and designed to achieve two specific objectives:

1. Assess the completeness and accuracy of medication records held by stakeholders (secondary care, general practice and community pharmacy) for consumers prescribed clozapine managed in a shared care program; and
2. To describe the experiences of consumers prescribed clozapine within a shared care program.

4. METHODS

4.1 Study design and setting

This was an exploratory, mixed-methods descriptive study, which was undertaken in two parts between February 2015 and July 2016.

In Part One, the study assessed the completeness and accuracy of medication records for consumers prescribed clozapine under shared care arrangements, to identify medication discrepancies between the stakeholders records. Part Two of the study addressed the research objective to describe the lived experience of clozapine treatment in a shared care setting through a semi-structured interviews and questionnaires with consumers. Figure 1 gives an overview of the study design.

The study was set in the clozapine shared care service of the RBWH. The hospital forms part of the Metro North Mental Health Service (MNMHS), which is a large, urban, public MH service in Queensland, Australia, with a catchment population of 135,000 (76).

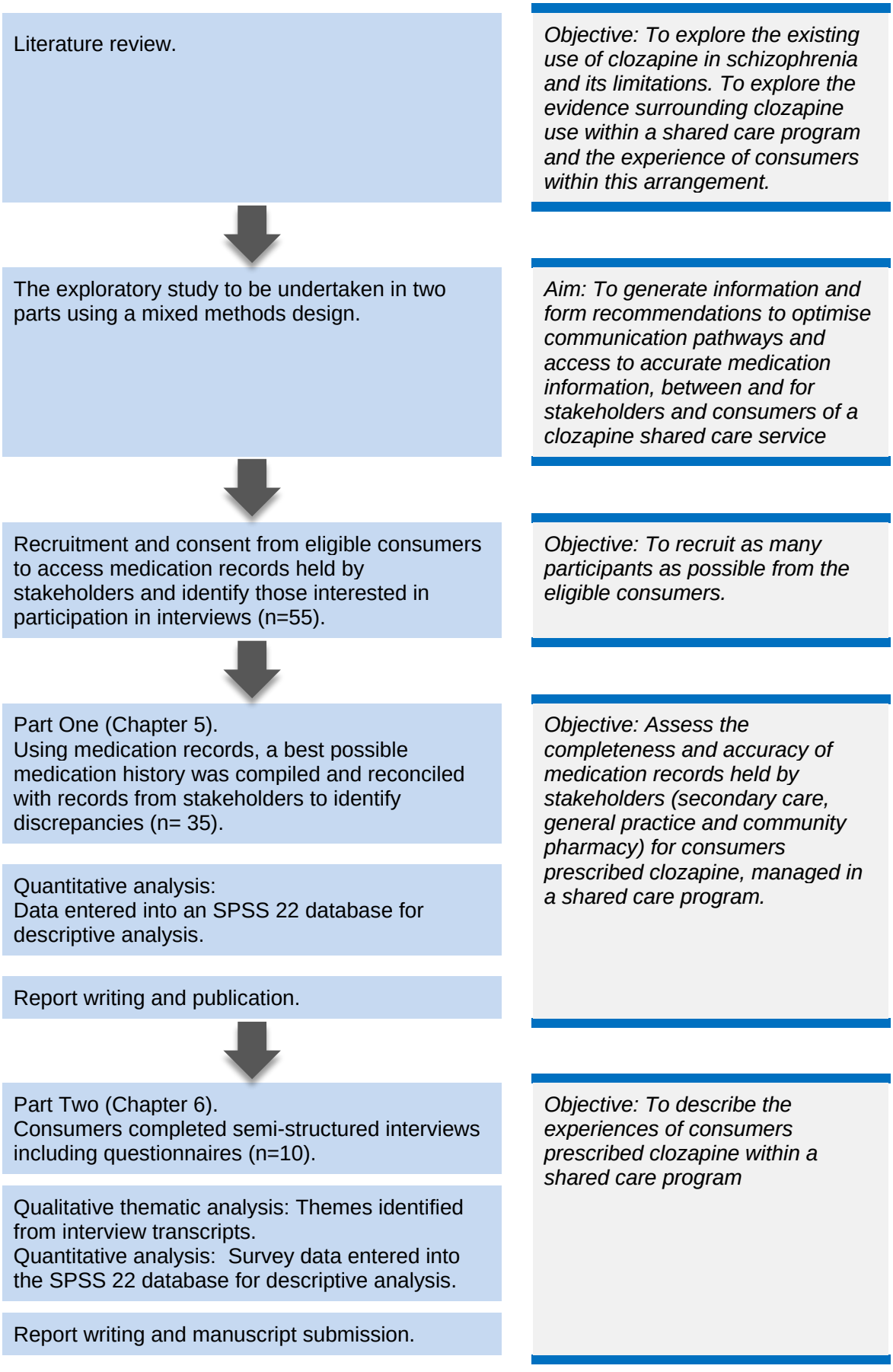

Figure 1: Study design

4.2 Study participants

Study participants were drawn from consumers of MNMHS. To be eligible to participate, consumers were aged 18–65 years, prescribed clozapine at MNMHS-RBWH, had their care managed under formal shared care arrangements with a nominated GP and had capacity to consent (n=55). All consumers who met these criteria were invited to participate in both parts of the study. Consumers could opt to participate in Part One only but could only participate in Part Two if consent was given to participate in Part One.

Potential participants were identified from hospital records and were provided with study information sheets (Appendices 2 and 3) about the two parts of the study either with their clozapine delivery or posted to their home address along with a letter explaining the research (Appendix 4). The researcher or clozapine coordinator then met with the consumer at their next regular hospital clozapine clinic appointment to discuss participation and consent. Consumers who consented to Part One of the study were invited to express their interest in participation in Part Two. They were asked to provide contact details for the researcher to contact them about an interview at a later time.

Sampling decisions were made opportunistically, with the aim of recruiting as many participants as possible from the 55 eligible consumers.

4.3 Data collection

At the time of providing initial consent for Part One of the study, consumers were asked to nominate GPs and community pharmacies. Nominated GPs and community pharmacies were sent a letter explaining the research (Appendices 5 and 6), then contacted by phone and fax to provide a current medication or dispensing record for the consumer. Data from MNMHS- RBWH was obtained from available hospital records including the Consumer Integrated Mental Health Application (CIMHA), Integrated Electronic Medication Record (IEMR) and iPharmacy program.

Data was recorded on a devised template, modified from the Medication Action Plan (MAP) developed by the Queensland Government Medicines Regulation and Quality Unit (Appendix 7). The MAP is a standardised form for recording the best possible medication history and reconciling discrepancies. It is currently used throughout Queensland Health facilities including MNMHS-RBWH and incorporates the minimum data set for a medication history outlined in guiding principle 4 – accurate medication history, which is part of the Australian Pharmaceutical Advisory Council‘s guiding principles to achieve continuity in medication management (77).

For the purpose of this study, the researcher used all information from available medication records to compile a best possible medication history, which was recorded on a modified version of the MAP. Medication data from MNMHS-RBWH, general practice and community pharmacy records was reconciled with the medication history. Medication reconciliation is described as the “formal process of obtaining, verifying and documenting an accurate list of a patient’s current medicines and comparing this list to other orders (including on admission or discharge to hospital or on transfer between different health care services), to identify and resolve discrepancies” (54). Reconciliation allowed for identification of discrepancies, which were classified as an omission, addition, dose increase or decrease, or change in administration method (i.e. difference or omission of dose or frequency of administration and a difference in the clozapine brand) from what was in the medication history.

Other data included participant demographics, duration of schizophrenia, duration of treatment with clozapine and participation in the shared care program, as well as contact details for the GP, community pharmacy and clinicians at MNMHS.

Participation in Part Two involved the consumer meeting with the researcher, completing an interview and questionnaires related to illness and medication beliefs, adherence, shared care, communication and perceived treatment burden. Consumers who agreed were contacted via their preferred means by the researcher to confirm their continued interest and to arrange a mutually convenient time and place that was comfortable for both the researcher and participant. A telephone interview was offered as an alternative option. The participant was invited to bring a support person to the meeting if they wished. Participants signed a consent form that included their permission to audio-record the interview. The interviews were audio-recorded, transcribed and after quality-checking, the recording was deleted. The participant was offered a $25 Coles/Myer shopping voucher in appreciation for their time. Interviews ranged in time from 24 to 57 minutes. The participants were supported to complete the questionnaires where appropriate and the researcher used opportunities to explore responses to achieve the study aims.

In Part Two of the study, data was obtained from a medication history including demographics, semi-structured interview questions and questionnaires. Using the modified version of the MAP from Part One (Appendix 7), participants were asked about their medication history, including what medication they were currently taking, doses, frequencies and indications. This information was compared to the best possible medication history that was compiled by the researcher in Part One of the study.

An interview guide, including questionnaires, was developed by the researcher in collaboration with experienced researchers and clinicians working in the psychiatry field; a psychiatrist, psychologist and pharmacists (Appendix 8). Validated questionnaires were identified and selected to meet the aims of the study. Where applicable, approval was obtained to use the questionnaires for this research. The semi-structured interview included open-ended questions related to topics of illness, medication (clozapine), adherence, shared care, communication and perceived treatment burden. The use of these questions was guided by information collected during the questionnaire completion and aimed to explore the participants' experiences and views of taking clozapine and shared care, in their own words. The interviews were conducted in a conversational style and were designed to be flexible to follow leads in a way that optimised engagement and expression of views and encouraged the participants to explore their thinking around 'issues'. For example, when discussing illness, the term schizophrenia was not used unless the participants themselves used that term. The aim was to focus on the narratives of lived experience by setting the agenda but allowing the participant's responses to determine the kinds of information produced and their importance (78). This allowed for flexibility as well as a rich and detailed account of the consumer's experiences.

The questionnaires used were:

- The Brief Illness Perception Questionnaire (Brief IPQ)[1] explored consumers' perceptions and experiences of their illness. The scale measures consumers cognitive and emotional representations of their illness including consequences, timeline, personal control, treatment control, identity, coherence, concern, emotional response and causes (Appendix 9) (79).

[1] Use of the Brief IPQ was approved by the author at lizbroadbent@clear.net.nz

- The Beliefs about Medicines Questionnaire (BMQ) allowed consumers to discuss their beliefs about and concerns about their medications and whether these influenced adherence (Appendix 10) (80) .
- The Glasgow Antipsychotic Side-effects Scale for Clozapine (GASS-C) explored potential adverse effects experienced due to clozapine. Adverse effects may influence adherence and beliefs and experiences about illness and medications (Appendix 11) (81, 82).
- The 8-item Morisky Medication Adherence Scale (MMAS-8)[2]. This questionnaire explored medication management and issues with adherence (Appendix 12) (83-85).
- The Treatment Burden Questionnaire (TBQ) (modified) assessed the burden associated with taking medicine, self-monitoring, laboratory tests, doctor visits, the need for organization, and administrative tasks in different treatment areas and contexts (Appendix 13) (65).

4.4 Data analysis

Data was analysed using Microsoft applications Word, Excel and Statistical Program for the Social Sciences (SPSS). To address the research objectives, analysis was both quantitative and qualitative.

In Part One, the objective was to describe the completeness and accuracy of medication records held by stakeholders relating to consumers prescribed clozapine under shared care arrangements. To achieve this, analysis was descriptive with data entered into an SPSS database, including:

- consumer demographics; duration of clozapine treatment and duration of shared care;
- number of medicines taken;
- number of discrepancies found in each stakeholder medication record;
- types of discrepancies i.e. an omission, addition, change in dose or frequency, or clozapine brand.

Analysis involved computation of frequencies, with the mean and range where applicable of the above data in a collective fashion, by stakeholder, by discrepancy type and by participant.

In Part Two, the objective was to describe the experiences of consumers prescribed clozapine within a shared care program. To achieve this, questionnaire responses were analysed descriptively while data from semi-structured interviews was analysed using a qualitative approach.

Data from medication histories and surveys was entered into an SPSS database and included discrepancies in the consumer medication history compared with the medication history compiled in Part One, as well as scores from the questionnaire responses. Data was analysed to describe frequencies, with the mean and range as applicable.

[2] Use of the ©MMAS is protected by US copyright laws. Permission for use is required. A License Contract is available from: Donald E. Morisky, ScD, ScM, MSPH, Professor, Department of Community Health Sciences, UCLA School of Public Health, 650 Charles E. Young Drive South, Los Angeles, CA 90095-1772, dmorisky@ucla.edu.

Using an interpretative approach, data from semi-structured interviews was analysed with the objective of gathering in-depth information about a consumer's experiences of mental illness, clozapine treatment, perceived treatment burden, shared care and communication. The researcher was aware of the ways in which data results from the specific interaction in the interview between the researcher and the participant.

The use of thematic content analysis is common in qualitative research, particularly in the interpretative paradigm. It aims to produce a rich, detailed understanding by presenting the key elements of participants' accounts by summarising the variation and regularities within the data (78). A theme can be explained as a "pattern found in the information that at minimum describes and organizes the possible observations and at maximum interprets aspects of the phenomenon" (Boyzatis 1998, p4) (86); the identification and interpretation of these themes is thematic analysis (87). Identification of themes can be 'deductive' or 'theoretical' where the themes are derived primarily from a pre-existing theory, or literature, or 'inductive' where the identification of themes are primarily from the data collected without trying to fit the data to pre-existing concepts or ideas (78, 87). The research objective was explored by identifying themes around clozapine treatment in a shared care model and opportunities to improve practice while still remaining responsive to other themes in participants' accounts.

Predicting adequate sample sizes in qualitative research is difficult, as themes may be identified in a single interview and sampling to saturation is not always possible (78). It is suggested that in studies with a relatively homogenous group of individuals where the aim is to understand common perceptions and experiences, 6 to 12 interviews should be considered adequate (88).

The basis of thematic analysis is to reduce the complexity in participants' accounts by looking for patterns or themes; the techniques for doing this are outlined by Green and Thorogood (78):

- familiarisation with the data by repeatedly listening to interviews and reading notes and transcripts;
- identifying codes and themes by comparing participants' accounts to look for regularities and differences;
- coding the data by applying a list of code names to the data, for example understanding, benefits of treatment, burden, communication pathways;
- organisation of the codes and themes where data relating to the same codes are collated.

Interview recordings were transcribed verbatim by the candidate (four transcriptions) and an external transcriber (six transcriptions). Each recording was then repeatedly listened to by the candidate while the transcription was read. This allowed each transcription to be checked for accuracy and also led to data familiarisation. The first interview was listened to by the research supervisor to give feedback on interview technique and content. As there were no significant changes to the interview process, the first interview was included in the data. Transcripts were then sent to the research supervisors for identification of initial themes. The candidate and supervisors then decided on themes by group discussion. The candidate organised the data by cutting and pasting information (codes) from transcriptions to fit under these themes. Themes that overlapped were combined into an overarching theme that was divided into subthemes. An external researcher with experience in the topic area and methodology reviewed coding and analysis for trustworthiness. To ensure reliability, transcripts were re-read by the candidate to confirm the overarching themes and subcategories, which were agreed upon by the research team (Appendix 14).

4.5 Ethical considerations

When undertaking research that relies on human subjects to talk honestly about their experiences, researchers have an obligation to protect the life, health, privacy and dignity of the human subject and to seek ethical review (78). RBWH, where the research was undertaken, has a formal ethical review process that required approval from an ethics committee, which ensured the research was in line with the principles of voluntary participation, informed consent, confidentiality and the importance of accuracy (89). The research protocol and National Ethics Application Form (NEAF) was approved by the RBWH Human Research Ethics Committee (HREC/14/QRBW/48, Appendix 15).

An issue regarding participants' capacity to give informed consent was raised by the ethics committee: "Informed consent meaning that individuals should not be coerced, or persuaded, or induced, into research 'against their will' but that their participation is based on voluntarism, and on a full understanding of the implications of participation" (78). Schizophrenia is a serious mental illness that is "manifested by distortions in perception, disorganization of thought, and weakening of motivation and emotional responsivity" (Carpenter et al. 2000, p533) (90). In theory, any of these symptoms have the potential to reduce an individual's capacity to make decisions, although research suggests that consumers with schizophrenia participating in research are able to understand and retain consent information (90).

When taking consent, the researcher checked capacity for autonomous decision-making and the voluntary nature of consent by asking the potential participants to describe in their own words what they were being asked to do, why they were being asked to do 'it', and what participation would involve. Participants were also invited to discuss participation with anyone of their choosing. Situational ethical issues, such as the researcher having concerns about a participant's mental state, did not arise during this research.

Confidentiality is a key criterion for ethical research. To ensure this, once participants gave consent they were identified by a unique study identification code (ID code) in the data collection and analysis stages of the research. Every effort has been made to store all data in a secure and appropriate manner. Original field notes from data collection have been kept in a secure, locked cupboard while at Griffith University or RBWH. No photocopies of the original field notes have been made. Data entered into SPSS uses the participant's ID code only. All identifying data has been removed from interview transcriptions.

The research protocol was also approved by Griffith University (HSV/10/14/HREC, Appendix 16) and meets the principles and practices set out in the Australian Code for the Responsible Conduct of Research (2007 Universities Australia) and the ICH Harmonised Tripartite Good Clinical Practice (GCP) Guidelines. Throughout the research project, progress reports and amendments made to the protocol or forms were forwarded to the RBWH HREC and Griffith University as applicable.

The research received funding from the Royal Brisbane and Women's Hospital Foundation and all resource requirements for the completion of the research were supplied through existing Griffith University and RBWH systems and supports.

5. CLOZAPINE AND CONCOMITANT MEDICATIONS: ASSESSING THE COMPLETENESS AND ACCURACY OF MEDICATION RECORDS FOR PEOPLE PRESCRIBED CLOZAPINE UNDER SHARED CARE ARRANGEMENTS

5.1 Introduction

This chapter addresses the first objective of this thesis, which was to describe the completeness and accuracy of medication records for people prescribed clozapine under shared care arrangements. Although it is known that medication discrepancies are common at transitions of care, this research makes a worthy contribution to the literature, as this topic has not been widely studied in the mental health outpatient setting and not with clozapine specifically. This is of significance, as clozapine is a high-risk medication with mandatory monitoring requirements that may inhibit its use in the community. Furthermore, the potential for serious adverse effects and drug interactions with clozapine may put the consumer at risk of ADEs, where concomitant medications are not documented. Assessing the accuracy of medication information in this shared care program allowed for identification of issues and recommendations regarding the documentation and sharing of medication information, to minimise the risk of ADEs.

5.2 Statement of contribution to co-authored published paper

This chapter is presented as a co-authored paper. This peer-reviewed original research article titled “Clozapine and concomitant medications: assessing the completeness and accuracy of medication records for people prescribed clozapine under shared care arrangements” was accepted for publication in the Journal of Evaluation in Clinical Practice (JECP) and published 22nd December 2017. DOI:10.1111/jep.12743. The authors are Kate Murphy, Ian Coombes, Vikas Moudgil, Susan Patterson and Amanda Wheeler. The paper is presented in the thesis as a PDF of the published paper.

The contribution to the paper by the thesis author involved: conducting a literature review, development of participant information sheets and consent forms with Sue Patterson, Ian Coombes and Amanda Wheeler, development of a data collection tool, undertaking data collection and data analysis with Ian Coombes and Amanda Wheeler, preparing discussion with supervisors and recommendations with Vikas Moudgil, writing the first draft, responding to feedback from co-authors and peer reviewers, overseeing the submission process and overall responsibility for the manuscript integrity.

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ORIGINAL ARTICLE

Clozapine and concomitant medications: Assessing the completeness and accuracy of medication records for people prescribed clozapine under shared care arrangements

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Funding information
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Abstract

Rationale, aim, and objective: The objective of the study is to assess the completeness and accuracy of medication records held by stakeholders (secondary care, general practice, and community pharmacy) for clozapine consumers managed in a shared care programme.

Methods: This was an exploratory, descriptive study examining secondary and primary care medication records in a large, urban, public mental health service setting in Queensland, Australia. Consumers (18-65 years old) prescribed clozapine under shared care management with capacity to consent were eligible (n = 55) to participate. Information from medication and dispensing records was used by a pharmacist to compile a best possible medication history for each consumer. Discrepancies were identified through reconciliation of stakeholder records with the history. Discrepancies were defined as an omission, addition, or administration discrepancy (difference in dose, frequency, or clozapine brand).

Results: Thirty-five (63.6%) consumers consented for records to be reviewed. Overall, 32 (91.4%) consumers had at least 1 discrepancy in their records with a mean of 4.9 discrepancies per consumer. Of 172 discrepancies, 127 (73.8%) were omissions. Primarily, concomitant medicines were omitted in 19/35 (54%) of secondary care records while clozapine was omitted in 13/32 (40.6%) of community pharmacies records.

Conclusions: Discrepancies were highly prevalent in the shared care medication records of clozapine consumers of this service. Where there is incomplete and inaccurate medication information, there is a risk of suboptimal clinical decision making, increasing the likelihood of adverse drug events. This study demonstrates a need for improved documentation and timely access to accurate and complete medication records for shared care stakeholders. Expanding the pharmacist's role in this setting could improve medication accuracy in documentation and related communication.

KEYWORDS

clinical safety, evaluation, health services research, health care, patient-centered care, public health

1 | INTRODUCTION

Clozapine is the most effective antipsychotic medication used in treatment resistant schizophrenia.[1,2] Its use is restricted, however, in many countries, including Australia, because of potentially fatal side effects of neutropenia and agranulocytosis and the consequent haematological monitoring requirements.[3] Clozapine is also associated with other serious side effects including myocarditis, cardiomyopathy, type 2 diabetes mellitus, weight gain, elevated cholesterol levels, seizures, gastric hypo motility, and severe constipation.[3,4] Furthermore, clozapine has potential for significant pharmacokinetic interactions primarily via the cytochrome P450 enzyme 1A2 pathway.[5] These interactions may alter clozapine plasma levels and potentially result in its toxicity or inefficacy.[5] Other interactions are caused by additive effects. Effects such

as agranulocytosis, hypotension, myocarditis, constipation, sedation, and effect on cardiac QTc interval can be exacerbated when taking clozapine and concomitant medications that cause them.[6] The potential side effects, interactions, prescribing restrictions, and monitoring contribute to high treatment burden for consumers and workload for the public health service.[7]

Restrictions related to clozapine have extended to prescription and dispensing. In Australia, prescribing of clozapine is commonly restricted to psychiatrists and supervised trainees, but in some states, including Queensland, general practitioners (GPs) may prescribe clozapine as maintenance therapy after initiation by a psychiatrist and with certain restrictions.[7,8] Historically, dispensing of clozapine has been primarily through hospital pharmacies due to prescription-claiming requirements with the Australian Pharmaceutical Benefits Scheme (PBS).[9] Recent changes to the PBS, however, allow community pharmacies to dispense clozapine. All clozapine prescribers and dispensing pharmacists must be registered with a clozapine manufacturer for each clozapine brand (Novartis or Hospira) to review blood results for a safe supply.[7,10] The prescribing protocol requires that people prescribed clozapine (consumers) have their full blood count monitored weekly for the first 18 weeks of treatment and 4 weekly thereafter. A maximum of 4 weeks supply of clozapine can be dispensed on the basis of a normal full blood count although an increased quantity may be obtained in certain circumstances.[10] As monitoring is managed by the manufacturer, clozapine brands are not interchangeable.

Prescribing restrictions, monitoring requirements, and the absence of a standard national protocol mean that clozapine remains most commonly accessed through public and private hospital mental health services rather than primary care.[7,8] An unintended impact of this is limited development of relationships between consumers and GPs. Such relationships are of particular importance for clozapine consumers as people with schizophrenia have high rates of physical health co-morbidities and poorer outcomes than the general population.[11] Physical illnesses are often inadequately managed and contribute to the lower life expectancy of people with schizophrenia.[12]

In Australia, shared care is an option for consumers prescribed clozapine. Shared care aims to improve access, reduce the burden for the consumer and the public mental health service, and promote primary care management.[13,14] While various models exist, shared care is characterized by formal arrangements among nominated psychiatrists (or supervised trainees), GPs, and community pharmacists regarding the prescribing, dispensing, and monitoring of the effects of clozapine. Shared care may be arranged once clozapine therapy has been initiated and stabilized in a specialist setting.[8]

In the shared care model studied, a psychiatrist or trainee reviews the consumer's well-being and blood test results and prescribes clozapine every 12 weeks rather than the routine 4 weeks. The mandatory 4 weekly monitoring is undertaken by the GP who informs the hospital pharmacy to dispense clozapine on the basis of blood test results. The hospital pharmacy dispenses the prescription, written by the psychiatrist (or trainee), and arranges delivery to the community pharmacy or GP for collection by the consumer. Thus, the frequency of hospital outpatient appointments is reduced, as is the associated cost and time burden for the consumer and the secondary care service.[13]

Despite potential benefits, the shared care arrangement is not without challenges. Discrepancies in the medication record, the most common type of problem when consumers move between health care providers,[15] are a known causative factor in prescribing errors.[16] Discrepancies are typically defined as an addition, omission, change in dose, or frequency of medication, from what the consumer is actually taking, to what is recorded in the medication record.[17] When the various stakeholders do not have complete and accurate medication records, there is a risk of inappropriate clinical decision making, potentially exposing the consumer to adverse drug events (ADEs).[18,19]

Research into medication-related discrepancies has to date focused on transitions within the hospital inpatient setting with only limited research into concordance of the medication records of GPs and secondary care specialists treating people with chronic illness.[17] Pharmacist interventions in the inpatient setting have demonstrated improvements in clinical outcomes such as a reduction in adverse drug reactions and medication errors, through interaction with other health care teams, patient interviews, medication reconciliation, and discharge medication counselling.[20] A systematic review evaluating the impact of pharmacists in mental health (both in inpatient and outpatient settings) concluded that although the evidence is limited, it supports the role of clinical pharmacists in collaborative care models noting a favourable effect on clinical and economic outcomes.[21]

A recent abstract published in the United Kingdom reported an evaluation of the transfer of information about clozapine prescribing from specialist secondary care to primary care. This study found that clozapine was omitted on the primary care medication record for 40% of consumers.[22] This indicates that for some clozapine consumers, medication records were inaccurate and incomplete. Still, little is known about the rate and type of medication discrepancies and communication between multiple health care providers for shared care programmes involving clozapine. This is important to explore for clozapine consumers who commonly have physical health co-morbidities that require treatment with multiple medications.[11,12] To ensure the quality and safety of both mental and physical health care for consumers in the shared care programme, stakeholders must have complete and accurate information including the medication record.

The aim of this study was to assess the completeness and accuracy of medication records held by stakeholders (secondary care, general practice, and community pharmacy) for consumers prescribed clozapine, managed in a shared care programme.

2 | METHODS

2.1 | Study design and setting

This was an exploratory, descriptive study involving examination of secondary and primary care medication records for people prescribed clozapine under shared care arrangements (n = 55). The study was undertaken at a large, urban, public mental health service in Queensland, Australia[23] (catchment population of 135 000), between February 2015 and April 2016.

Medication records held by each of the shared care stakeholders were compared to a best possible medication history, described as a

"comprehensive drug history obtained by a clinician that includes a thorough history of all regular medicines used, including non-prescription and complementary medicines and is verified by more than one source."[24] The researcher (an experienced clinical pharmacist) used all information available from the medication and dispensing records to compile a history for each consumer. Records were then reconciled and discrepancies with the history recorded, as documented in Table 1. Discrepancies were not mutually exclusive, meaning there could be more than 1 discrepancy per medication listed. Clozapine discrepancies were counted overall and separately and included brand differences. The brand was identified in the records where the name or tablet strengths differed, as some strengths are unique to the specific brand. Medicines that were prescribed and dispensed at regular intervals or in a dose administration aid (DAA) were included in the study. Medicines prescribed "when required" were excluded from data extraction because of a lack of reliability about how and if these medicines were being taken. Short courses of medicines such as antibiotics were also excluded. Figure 1 gives an overview of the study design.

2.2 | Study participants

Consumers of the service aged between 18 and 65 years, prescribed clozapine under shared care management and with capacity to consent, were eligible to participate (n = 55). Potential participants identified from hospital records were provided with a study letter and information sheet either with their clozapine delivery or posted to their home address. The researcher or clozapine coordinator then met with the consumer at their regular hospital clinic appointment to discuss participation and consent.

The research protocol was approved by both the hospital and university Human Research and Ethics Committees (HREC/14/QRBW/48; HSV/10/14/HREC).

2.3 | Data collection

Data were recorded on a modified form of the Medication Action Plan. The Medication Action Plan is a standardized form for recording a medication history and reconciling discrepancies, currently used throughout Queensland Health.[25] At the time of providing consent, consumers nominated their GP and community pharmacy. They were sent study information, then contacted by phone and fax to provide a current medication or dispensing record for the consumer. Secondary care data were extracted from the electronic health record and the pharmacy dispensing system.

Medications from stakeholder records were individually reconciled with the history taken by the researcher, and discrepancies were

TABLE 1 Discrepancies in the medication record: type and definition[17]

Discrepancy type	Definition	Example
Omission	Medication listed in the medication history but not listed in the record of the stakeholder	The total number of medications in the medication history is 13, while the secondary care record lists 1 medication (clozapine).
Addition	Medication listed in the record of the stakeholder but not in the medication history	The secondary care record lists citalopram as a current medication; however, it is not a current medicine in the medication history.
Administration (1) Increase, decrease, or omission of dose or frequency of administration	A dose listed in the record of the stakeholder is higher or lower than the dose listed in the medication history or is not specified. The frequency of medication administration is different or omitted (total daily dose remains the same)	The clozapine dose per the medication history is 175 mg at night, whereas the GP record lists the dose as 25 mg in the morning and 175 mg.
(2) Difference in brand of clozapine	The clozapine brand is different in the record of the stakeholder from the medication history	The correct medication history for one consumer is Clozaril® (Novartis) while the GP record lists Clopine® (Hospira).

Abbreviation: GP, general practice.

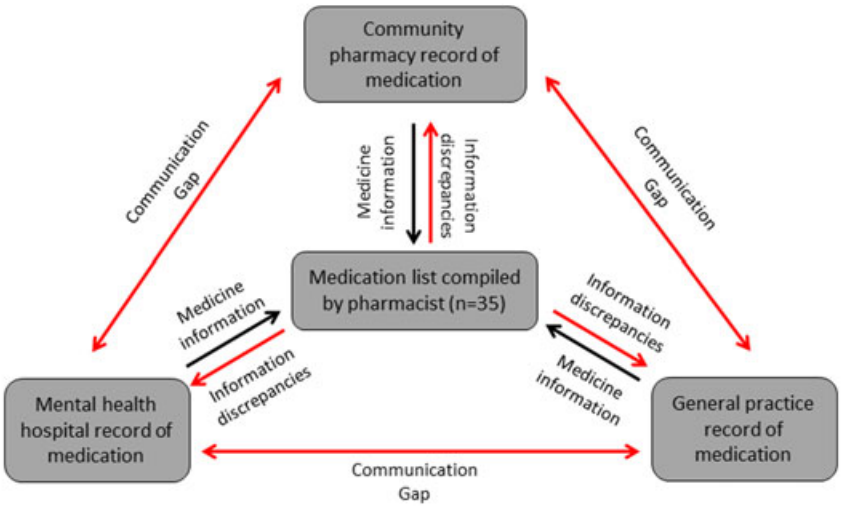

FIGURE 1 Overview of study design

annotated. Other data collected included (1) consumer demographics, (2) duration of treatment with clozapine, (3) duration of time in the shared care programme, and (4) whether a DAA was used.

2.4 | Data analysis

Data were entered into an IBM SPSS Statistics version 22 database for descriptive analysis. The total number of medications taken and the number and type of discrepancies found were entered for each consumer and stakeholder.

3 | RESULTS

A total of 35/55 (63.6%) consumers gave consent to collection and review of records. The majority were male (n = 25), and the mean age was 51.7 years (Table 2). There was a mean of 5.2 medications (range = 1-13) recorded per consumer with more than half of consumers prescribed 4 or more medications (57.0%) and receiving medications via a DAA supplied by their community pharmacy (51.4%). No medication record was available from the GP for 15 consumers (42.9%), and 3 consumers did not nominate a regular community pharmacy.

Overall, 32/35 (91.4%) consumers had at least 1 discrepancy in their medication records, with a total of 172 medication discrepancies identified. Because either pharmacy or GP records were not available for 2 of the 3 consumers for whom 0 discrepancies were identified, we can only be sure that the records of a single consumer contained 0 discrepancies. We identified a mean of 4.9 discrepancies (range = 0-16) per consumer (Table 3). Most discrepancies were omissions (n = 127/172; 73.8%), followed by administration (dose/frequency/brand) discrepancies (n = 32/172; 18.6%) and additions (n = 13/172; 7.6%).

Secondary care records contained the highest number of discrepancies (n = 26/35; 74.3%), followed by GP records (n = 14/20; 70.0%) and community pharmacy records (n = 20/32; 62.5%) (Table 4). Over half of the secondary care records (n = 19/35; 54.3%) recorded clozapine as the only medication, omitting all other concomitant medications. In one example (Table 5), the secondary care record listed only clozapine out of 13 medications taken by the consumer, resulting in 12 omissions. Table 5 details examples of discrepancies identified and their clinical significance.

Of the 172 discrepancies identified, 36 (20.0%) involved clozapine (Table 6). Most of these were in the records of community pharmacies (n = 18/36; 50.0%) and the GP (n = 16/36; 44.4%). Clozapine was omitted in 13/32 (40.6%) community pharmacy records, with one exception it was only recorded at the community pharmacies where DAAs were provided.

TABLE 2 Consumer demographics (n = 35)

Gender, n (%)	
Male	25 (71.4)
Female	10 (28.6)
Age, y	
Mean (range)	51.7 (28-70)
Dose administration aid, n (%)	
Yes	18 (51.4)
No	17 (48.6)
Duration of clozapine treatment, y	
Mean (range)	12.3 (2-21)
Duration of shared care (y), n (%)	
<2	7 (20.0)
2-5	10 (28.6)
6-10	11 (31.4)
11-20	5 (14.3)
Unknown	2 (5.7)

4 | DISCUSSION

Reconciliation of records held by stakeholders in formal clozapine shared care arrangements with a best possible record demonstrated a high prevalence of discrepancies. The inaccuracy and incompleteness of records is cause for grave concern and demonstrates a need for improvement. This finding indicates a significant communication gap between the stakeholders. Suboptimal communication and inconsistency of medication information held by the shared care stakeholders could lead to inappropriate clinical decision making, compromising safe and quality use of medications.

The high rate of discrepancies in medication records found in our study is consistent with previous research, with omissions the most common discrepancy.[15,17,19,28] For example, an Australian study of consumers with type 2 diabetes found high rates (>80%) of medication discrepancies, which were mostly omissions, in their GP referral letters.[17] Similarly, high rates were found in another study involving reconciliation of medication histories compiled by a pharmacist with hospital medical records and referral correspondence for consumers referred to aged care and memory clinics; omissions were identified in 85% of cases and dose discrepancies in nearly half (43%) the hospital records.[28]

In our study, the high prevalence of omissions in the secondary care records commonly related to inaccuracies and incomplete information about concomitant medications (medications other than clozapine) between primary and secondary care. Similarly, a study in the United Kingdom compared medication information held by psychiatrists and GPs and found the most common discrepancy was omission of nonpsychotropic medication in the psychiatrists record.[19] More recent research in Australia studied the pharmacist's role in community mental-health teams and found that secondary care records were often incomplete, particularly with respect to medications prescribed by GPs for physical health conditions.[29] As people with a serious mental illness collectively have worse physical health than the general population, it is imperative that mental health clinicians are proactive in their prevention, monitoring, and treatment.[12] The omission of medication to treat metabolic effects associated with clozapine such as dyslipidaemia is seen in consumer CCM111 (Table 5). In this example, the medications prescribed indicated that the consumer was being treated for significant dyslipidaemia, which if omitted, could not only have adversely impacted the consumer's physical health but also could have potentially hindered successful clozapine treatment.[3]

TABLE 3 Total number of medications and discrepancies by stakeholder and type

Consumer ID N = 35	Medication history	Secondary care record	General practitioner record	Community pharmacy record	Number of discrepancies per consumer
1	13	1 (−12)	17 (+4)	13 (s)	16
2	8	1 (−7)	Data missing	8 (s)	7
3	3	1 (−2)	Data missing	3 (s)	2
4	1	1 (s)	Data missing	1 (s)	Nil
5	5	4 (−1)	Data missing	5 (s)	1
6	1	1 (s)	Data missing	1 (Δ1)	1
7	1	1 (s)	1 (Δ3)	0 (−1)	4
8	2	1 (−1)	2 (s)	2 (s)	1
9	12	1 (−11)	13 (+1, Δ2)	10 (−2)	16
10	4	1 (−3, Δ1)	4 (s)	4 (s)	4
11	3	3 (−1, +1, Δ1)	Data missing	3 (Δ1)	4
12	10	5 (−5, Δ1)	9 (−1, Δ3)	Data missing	10
13	4	2 (−2)	3 (−1)	3 (−1)	4
14	13	2 (−11)	Data missing	13 (s)	11
15	6	1 (−5)	Data missing	6 (Δ1)	6
16	9	1 (−8)	Data missing	9 (Δ1)	9
17	8	7 (−1, +1, Δ1)	Data missing	8 (Δ1)	4
18	8	7 (−2, +1, Δ1)	9 (+1)	7 (−2, +1)	8
19	7	7 (s)	7 (s)	7 (s)	Nil
20	1	1(s)	1 (Δ2)	0 (−1)	3
21	4	2 (−2)	Data missing	4 (s)	2
22	1	1 (s)	1 (Δ1)	0 (−1)	2
23	7	4 (−4, +1, Δ2)	5 (−2)	7 (s)	9
24	2	1 (−1)	n.a.	2 (s)	1
25	2	1 (−1)	2 (Δ1)	1 (−1)	3
26	1	1 (s)	1 (s)	Data missing	Nil
27	7	3 (−4, Δ1)	7 (Δ2)	5 (−2)	9
28	3	3 (−1, +1)	3 (s)	2 (−1)	3
29	12	1 (−11)	Data missing	12 (Δ1)	12
30	3	1 (−2)	3 (Δ1)	1 (−2, Δ1)	6
31	1	1 (s)	2 (+1)	Data missing	1
32	6	5 (−1)	6 (s)	5 (−1)	2
33	2	2 (s)	2 (Δ1)	1 (−1)	2
34	4	4 (Δ1)	Data missing	3 (−1)	2
35	8	2 (−6)	Data missing	7 (−1)	7

Abbreviations and symbols: − = omission; + = additions; Δ = administration discrepancy including difference or omission of dosage and frequency or a difference in clozapine brands; s = same (nil discrepancy).

TABLE 4 Total discrepancies in the medication record by discrepancy type

	Total records reviewed			
	Secondary care (n = 35/35)	GP (n = 20/35)	Community Pharmacy (n = 32/35)	Total
Omissions (−)	105	4	18	127
Additions (+)	5	7	1	13
Administration discrepancies[a] (Δ)	9	16	7	32
Total	119	27	26	172

Abbreviation: GP, general practice.

[a]Includes differences or omission of dose or frequency of administration and a difference in the clozapine brand.

Other examples of medications omitted in the secondary care record (Table 5).included venlafaxine, citalopram, and omeprazole. All of these have the potential to affect clozapine plasma levels resulting in toxicity or reduced efficacy.[26] Clozapine plasma levels above 1000 mcg/litre have been associated with confusion, delirium, and generalized seizures, and plasma levels below 350 mcg/litre may be

TABLE 5 Examples of medication discrepancies with clinical significance

Consumer ID	Discrepancies	Issues
CCF100	Omission: 12 concomitant medicines omitted in the secondary care record including levetiracetam, citalopram, diazepam, omeprazole, paracetamol/codeine, and propranolol. Nil aperients recorded.	Citalopram: an increased risk of QT-interval prolongation and increase in clozapine plasma levels.[26] Propranolol: an increased risk of orthostatic hypotension and increase in clozapine plasma levels.[26] Omeprazole: can reduce clozapine plasma levels by up to 45%.[5] Diazepam: increased risk of sedation and respiratory depression.[27] Codeine: increased risk of side effects such as sedation and constipation (may result in obstruction, paralytic ileus, and death).[27] In addition, although there is not a direct interaction between clozapine and the anticonvulsant levetiracetam, seizures are a common side effect associated with high clozapine plasma levels.[5]
CCM121	Omission: Ivabradine and atorvastatin omitted in the secondary care record.	Ivabradine is a medication indicated for treatment of serious cardiac conditions such as angina or chronic heart failure. Atorvastatin is indicated in dyslipidaemia and to reduce risk of cardiovascular events.[27] There are precautions of using clozapine in people with a history of cardiac illness due to side effects such as cardiomyopathy and myocarditis.[27] In addition, there is an increased risk of QT-interval prolongation with concomitant use.[26]
CCM117	Omission: Clozapine omitted in the GP and community pharmacy record. The GP concomitantly prescribed fluoxetine.	Fluoxetine can increase clozapine plasma levels by up to 76% increasing the risk of its toxicity.[26]
CCM109	Omission: Benzhexol (trihexyphenidyl) omitted in the secondary care record. In addition to clozapine, the consumer was concomitantly prescribed olanzapine, flupenthixol, citalopram, and benzhexol.	Benzhexol is indicated to treat antipsychotic-induced extrapyramidal side effects and has been used to treat clozapine-induced hypersalivation.[4] Concomitant use of clozapine and benzhexol increases the risk of anticholinergic side effects such as constipation (may result in obstruction, paralytic ileus, and death).[26,27]
CCM111	Omission: Ezetimibe, fenofibrate, and atorvastatin omitted in the secondary care record.	The concomitant medications omitted are indicated for treatment of dyslipidaemia; clozapine is associated with metabolic effects including dyslipidaemia, which increases risk of cardiovascular disease.[4]
CCM106	Omission: Secondary care record omits all 6 concomitant (psychotropic and non-psychotropic) medicines including amisulpride, venlafaxine, omeprazole, allopurinol, docusate & senna, iron, and folic acid.	Amisulpride when used concomitantly with clozapine can cause QT-interval prolongation.[26] Venlafaxine may also contribute to potential for QT-interval prolongation and in addition, alter clozapine plasma levels.[26] Omeprazole can reduce clozapine plasma levels by up to 45%.[5]
CCF114	Omission: Aripiprazole omitted in GP record. Dose discrepancy: GP recorded an incorrect dose of clozapine lower than what is prescribed.	Concurrent use of aripiprazole and clozapine may result in an increased risk of QT-interval prolongation and increased plasma levels of aripiprazole, clozapine, or both potentially leading to toxicity or reduced efficacy.[26]

Abbreviation: GP, general practice.

TABLE 6 Clozapine discrepancies

	Secondary care record (n = 35)	GP Record (n = 20)	Community pharmacy record (n = 32)
Nil discrepancy	33 (94.3%)	**11** (55.0%)	**14** (43.8%)
Clozapine omission	Nil	**1** (5.0%)	**13** (40.6%)
Dose discrepancy	**1** (2.9%)	**1** (5.0%)	Nil
Brand discrepancy	Nil	2 (10.0%)	5 (15.6%)
Frequency discrepancy	**1** (2.9%)	Nil	Nil
Dose and brand discrepancy	Nil	3 (15.0%)	Nil
Dose, brand, and frequency discrepancy	Nil	2 (10.0%)	Nil

Abbreviation: GP, general practice.

associated with reduced efficacy.[5] Other medicines omitted in the secondary care record included amisulpride, ivabradine, diazepam, benzhexol (trihexyphenidyl), and propranolol. These medicines have common adverse effects with clozapine and when used concomitantly, may have potentiated effects such as QT-interval prolongation, respiratory depression, constipation, anticholinergic effects, and orthostatic hypotension.[26] Without complete knowledge about such medication interactions, perceived treatment failure with clozapine could have caused it to be ceased unnecessarily or other medications to be added for symptoms of emergent side effects.

In the example of consumers CCF100 and CCM109 (Table 5). medications that cause constipation were prescribed (codeine and benzhexol) by the GP. Concomitant use of clozapine with these medications can result in an additive effect of a common side effect such as constipation. Up to 60% of people treated with clozapine report constipation,[30] which can result in mild symptoms through to the

development of ileus impaction, intestinal obstruction, faecal impaction, and death.[31] A recent systematic review reported that "for every 1000 patients treated with clozapine, between 300 and 600 will develop constipation and four will develop serious gastrointestinal complications from which one will die."[32] Therefore, constipation needs to be monitored vigilantly in clozapine consumers, and wherever possible, concomitant use of constipating agents should be avoided.[31]

Similarly, GPs could be unaware of secondary care prescribed psychotropic medication doses or changes.[19,22,29] The clozapine-related discrepancies in the GP record could result in inappropriate clinical decision making regarding concomitant medications or inaccurate interpretation of therapeutic drug monitoring leading to inaccurate information about clozapine dose and administration being given to the consumer. In the example of consumer CCM117 (Table 5). if the GP altered the dose of fluoxetine, they could have unknowingly caused clozapine toxicity or reduced efficacy.

Community pharmacy records contained the most clozapine discrepancies, primarily omissions. With one exception records did not include information that a consumer was taking clozapine unless a DAA was provided. In such instances, community pharmacists were dispensing prescriptions for concomitant medications without the knowledge that clozapine was also prescribed for the consumer. In the example of the potential interaction between fluoxetine and clozapine (Table 5). when dispensing the fluoxetine (without knowledge of the consumer taking clozapine), the pharmacist is unable to monitor and manage the potential adverse effect or provide appropriate counselling.

Recent changes to the PBS mean that community pharmacists can dispense clozapine to consumers who are established on continuing therapy.[9] Consequently, clozapine would be included in the dispensing record giving the community pharmacist a more complete and accurate medication record and potentially reducing the risk of errors. Furthermore, having community pharmacies supply clozapine has been identified to increase flexibility and level of independence for the consumer.[33]

The major side effects and drug interactions associated with clozapine require that all clinicians involved in the care of a clozapine consumer need to be aware of the total pharmacotherapy package to ensure safe and quality use of medications and minimize possible ADEs.[5] The high rate of medication discrepancies identified in our study shows that there is an urgent need for improved accuracy and completeness in medication information for all clozapine shared care stakeholders.

4.1 | Strengths and limitations

To our knowledge, no other studies have examined medication discrepancies among secondary care, GPs, and community pharmacies involved in a clozapine shared care programme. While our sample size is modest, our robust approach and the high rates of discrepancies identified that this is a problem needing attention.

The records were compared with a best possible medication history rather than simply comparing the records of the stakeholders with each other, which is consistent with current medication reconciliation practice in Australia[34]; however, there were some limitations with data collection. First, although medication information was verified with at least 2 sources, the medication history was not confirmed with consumers themselves. While a subsequent study involved an interview with consumers, this was undertaken at a later stage, and unfortunately, only a small number of the consumers agreed to participate. Another limitation with data collection was the possibility that stakeholders had knowledge about medications without this being documented in the record that was evaluated. Additionally, a GP medication record was not received for nearly half of the consumers, meaning that data were not able to be reconciled. This in itself could be considered evidence of suboptimal communication. An added issue was that consumers may have accessed psychiatric or nonpsychiatric medications from multiple pharmacies and prescribers without clinicians being aware of this. Finally, the issue surrounding broader communication and access to electronic records by all health care clinicians was not addressed in the study.

4.2 | Implications for practice, policy, and research

Lack of effective and timely communication between different health care providers is known to constrain effectiveness of shared care arrangements,[14,35] but there is little evidence to inform practical strategies to improve this.

Electronic prescribing with a shared platform for secondary and primary care would allow timely access to medication information for prescribers and could potentially include dispensing information. However, this would involve major infrastructure changes to the current system be expensive and take considerable time. In Australia, My Health Record, an opt-in consumer managed electronic health record system, was introduced with the aim of improved access and communication of information across different health care services.[36,37] My Health Record could improve access to information for stakeholders and empower consumers to manage their health care; however, clozapine consumers may, at times of acute illness, lack capacity to participate fully in their treatment management. Use of My Health Record would still require regular medication reconciliation to ensure the currency and accuracy of the electronic record.[36] A consumer held medication card is an option that would be relatively inexpensive, but similarly, this would be reliant on regular reconciliation and the consumer to be engaged in the process.

Another possibility is to change current prescribing practices to limit prescribing in the community, including clozapine, to the GP. Secondary care services would continue to provide specialist care, including the overseeing of a medication management plan for consumer's mental health, at regular intervals. This could reduce the potential for prescribing errors caused by omissions in the GP medication record. However, in Queensland, there are restrictions on GP's prescribing clozapine.[38] The level of GP prescribing is unknown, but it is not believed to be extensive, and this strategy would require a greater uptake of GPs becoming authorized prescribers. This would also require GPs to be upskilled in the prescribing and monitoring of clozapine to ensure quality and safe use.

The use of community pharmacies to supply clozapine has been considered to be beneficial as they record information about concomitant medicines, are generally more accessible, and may, through working with patients, improve adherence.[33,39] Similarly, as with GPs, pharmacists would need to be upskilled about the risks and monitoring requirements of clozapine to ensure its safe use. A lack of

remuneration for community pharmacies is a potential barrier for a wide expansion of these clinical roles that add value to their dispensing and advisory roles.[33]

Using a clinical pharmacist as part of the secondary care mental health team is an achievable option that could bridge the communication gap about medications between shared care stakeholders.[29] In the setting of the shared care clozapine programme, the pharmacist could have a role in preparing a medication history before the consumer's psychiatrist appointment providing the psychiatrist with an accurate medication record, which could then be updated after the appointment if there were any changes made. Copies of the medication record would then be distributed to the stakeholders and the consumer (and carer). Furthermore, clinical pharmacists are pharmacotherapy experts; they can provide education and advice for health professionals and consumers.[21,29]

We have identified that the current method of recording medications in the shared care programme studied needs to be improved. A relatively inexpensive and achievable option would be the use of consumer held medication records. Their accuracy and uptake by consumers would need evaluation. Another option is the implementation and evaluation of using a clinical pharmacist as part of a community health team. In addition to improving medication record documentation, the pharmacist would contribute to other relevant clinical activities including education. This option would require funding, and a cost benefit analysis would need to be part of the evaluation.

This exploratory study shows there is a high rate of discrepancies in the medication records held by shared care stakeholders potentially subjecting clozapine consumers to ADEs. Building on these results, future research investigating the wider prevalence of the risks associated with and the strategies to prevent medication discrepancies is indicated. The implications of this study are transferable to people with other chronic illnesses who are often prescribed multiple medications from a range of prescribers across different health care services.

5 | CONCLUSION

Discrepancies were highly prevalent in medication records of clozapine consumers under shared care arrangements signifying substantial gaps in medication information between stakeholders. Where records are incomplete and inaccurate, suboptimal clinical decision making could occur and expose consumers to ADEs. Our study demonstrates the need for improvement of medication documentation and access to accurate and complete records for all shared care stakeholders. Involving a pharmacist to undertake medication reviews, document, and communicate accurate medication information between stakeholders is a recommendation. Evaluation of medication records and feedback from shared care stakeholders would inform the efficacy of this strategy in improving completeness and accuracy of records.

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5.3 Summary

This chapter presents an important paper describing the extremely high discrepancy rate found in medication records of consumers prescribed clozapine under shared care arrangements of this service. This is an issue of concern, as medication discrepancies are a significant factor in prescribing errors, putting the consumer at risk of ADEs. Safe and quality use of medications is a priority and therefore improved communication and documentation of medication information is required. The group of consumers who consented to this part of the study were invited to participate in semi-structured interviews to discuss their own experiences of clozapine shared care. This forms Part Two of the study, which is detailed in the next chapter.

6. CLOZAPINE AND SHARED CARE: THE CONSUMER EXPERIENCE

6.1 Introduction

Following Chapter 5, which described the findings detailing the high rate of discrepancies in the medication of this shared care program, this chapter describes Part Two of the study, in which qualitative analysis is used to understand the viewpoint of this group of clozapine consumers about their treatment in the shared care program. In long-term health conditions, consumers may often have a better understanding of their condition and management than their clinicians; the experience and knowledge of consumers is a valuable resource (63). In health care, qualitative research, particularly studies involving the lived experience of the health consumer, informs part of quality improvement and is essential for optimal treatment (78). Data collected from consumer interviews and surveys was analysed descriptively and thematically to meet the second objective of the thesis, which was to describe the experiences of consumers prescribed clozapine within a shared care program.

6.2 Statement of contribution to co-authored submitted manuscript

This chapter is presented as a co-authored paper. This original research article was submitted to the journal Australian Journal of Primary Health in March 2018. It has been included as the draft submitted. The authors are Kate Murphy, Ian Coombes, Sara McMillan and Amanda Wheeler.

The contribution to the paper by the thesis author involved: responsibility for the literature review, responsibility for questionnaire choice with Ian Coombes and Amanda Wheeler, development of the interview guide with Amanda Wheeler and Ian Coombes, leading the thematic analysis with Amanda Wheeler, Ian Coombes and Sara McMillan, leading discussion and recommendations, authorship of the first draft, response to feedback from co-authors, and overseeing the submission process for the paper.

Australian Journal of Primary Health

Clozapine and shared care: The consumer experience

Journal:	*Australian Journal of Primary Health*
Manuscript ID	Draft
Manuscript Type:	Research paper
Keyword:	Community mental health: services, Continuity of patient care, Medication therapy management, Mental health, Primary health care

Abstract

Background: Clozapine is a high risk medication with restrictions that may increase treatment burden for consumers. Shared care aims to improve access, reduce burden and promote primary care management. However there is limited knowledge about the consumer experience of clozapine treatment within a shared care setting. The aim of this study was to explore the consumer experience within this setting.

Method: This mixed-methods study examined consumer's experiences with a clozapine shared care program in an urban setting in Queensland, Australia. Consumers who consented to access of their medication records (n=35) were eligible to participate in a semi-structured interview including a survey. Analysis was descriptive and thematic.

Results: Ten (28.6%) consumers participated. Survey results found a strong belief in the necessity for clozapine, with a low level of reported treatment burden and minimal adverse effects. Four themes were identified from the interviews: (i) understanding of illness and recovery; (ii) positive outcomes of treatment; (iii) acceptance of treatment burden; (iv) communication pathways. Overall, participants had a positive experience in the clozapine shared care program, citing clozapine's efficacy and the general practitioner relationship as key benefits.

Conclusions: Consumers reported positive outcomes and minimal treatment burden with the shared care program, however communication between clinicians and consumers must be enhanced to reduce risk of suboptimal treatment and adverse drug events.

Keywords

Community mental health: services, continuity of patient care, medication therapy management, mental health, primary health care

Summary statement

What is known about this topic?

- Clozapine is a highly effective but high risk antipsychotic medication with supply often restricted to secondary care.
- Consumers have reported positive views about clozapine treatment.
- Poor communication, including discrepancies in the medication records of the shared care health professionals, may increase the risk of adverse drug events.

What does this paper add?

- Reinforces positive consumer views of clozapine treatment and describes views about clozapine shared care which has not been reported previously, to our knowledge.
- Reveals the importance that the consumer places on the relationship with their GP in the management of their mental health and wellbeing.
- Highlights the lack of formal communication processes between the shared care health professionals and clozapine consumers, which increases consumer risk of adverse drug events.
- Explores the potential for capacity building of the clozapine shared care program.

1. Introduction

Schizophrenia, with an estimated global prevalence rate of 1%, is a serious mental illness associated with significant morbidity and increased mortality (Edward and Alderman 2013). Clozapine is the most effective medication for the treatment of schizophrenia (Siskind *et al.* 2016). However, clozapine use is restricted to consumers who have not responded to an adequate trial of at least two other antipsychotics because of potentially life-threatening haematological adverse effects and mandatory monitoring requirements (Siskind *et al.* 2016). These factors contribute to clozapine access commonly restricted to public hospitals (Filia *et al.* 2013).

Shared care is the "joint participation of general practitioners (GPs) and hospital consultants in the planned delivery of care for patients with a chronic condition, informed by enhanced information exchange over and above routine discharge and referral letters" (Hickman *et al.* 1994). Once clozapine has been initiated in a hospital setting, shared care may be an appropriate option for stabilised consumers to improve their healthcare access, reduce treatment burden and promote primary care and self-management (Filia *et al.* 2013).Within the context of this study, a psychiatrist or psychiatric trainee reviewed a clozapine consumer's mental and physical wellbeing and haematology results and provided a three-month clozapine prescription every 12 weeks (instead of every four weeks). The four-weekly mandatory monitoring was undertaken by the GP who contacted the hospital pharmacy to dispense and deliver clozapine to the preferred community pharmacy or GP for consumer collection.

Inadequate communication between shared care stakeholders (psychiatrist, GP, community pharmacist and consumer or carer) may result in medication discrepancies, which is common when consumers visit multiple clinicians or healthcare settings. This can result in prescribing errors and adverse drug events (ADEs) (Procyshyn *et al.* 2010). The first stage of our study assessed the completeness and accuracy of medication records held by stakeholders of this clozapine shared care program (Murphy *et al.* 2017). Results

showed that 32/35 (91.4%) consumers had at least one discrepancy in the stakeholder records, with a mean of 4.9 discrepancies/consumer (Murphy *et al.* 2017). This second stage aimed to explore the clozapine consumer's experiences in this shared care program.

2. Methods

2.1 Study design and setting

This was a mixed-methods study in a large, urban, public mental health service in Queensland, Australia with a catchment population of 135,000 (Queensland Government: Department of Health 2016); data were collected between February 2015 and July 2016. An interpretative qualitative approach was employed, which is used increasingly in health research to enhance understanding of health, health behaviour and health services often for quality improvement purposes (Green and Thorogood 2014). Ethics approval was obtained from the hospital and university Human Research Ethics Committee (HREC/14/QRBW/48; HSV/10/14/HREC). All participants gave informed consent.

2.2 Study participants

Clozapine consumers (18-65 years) in the shared care program who consented to a review of their medical records (first stage) were eligible to participate in stage two (n=35). The lead researcher re-contacted these consumers; interviews were arranged at a convenient time, either face-to-face or by telephone. A $25 gift voucher was provided in appreciation of participants' time.

2.3 Data collection

Participants completed a survey together with the researcher prior to an interview. Interviews, including discussions during survey completion, were audio-recorded for transcription purposes. Consumer demographics and medication information was obtained from stage one data (Murphy *et al.* 2017). The medication history incorporated a modified version of the Medication Action Plan which is used Queensland-wide in the

public health service for recording and reconciling medication histories (Department of Health: Medicines Regulation and Quality 2014). Participants were asked about the medication they were currently taking, the dose, frequency and reason/s for use. This information was compared to the medication history from stage one.

Validated questionnaires were chosen to explore participant beliefs about illness, medications, adherence, adverse effects and treatment burden (Table 1).

Semi-structured interview questions were related to the topics of illness, clozapine, shared care, communication and treatment burden. The interview guide was developed by a team of health professionals, including experienced mental health researchers from multi-disciplinary backgrounds. Interviews were guided by the survey responses and conducted in a flexible, conversational style to follow leads in a way that optimised engagement and expression. Interviews ranged in time from 24 to 57 minutes (mean 44 minutes).

2.4 Data analysis

Participant demographics and survey responses were analysed descriptively using SPSS Version 22. Interview recordings were transcribed verbatim by the lead researcher (four transcriptions) and an external transcription company; transcriptions were de-identified by applying a unique study alias per participant (ie Sally, Simon etc.). All transcriptions were quality checked for accuracy by the lead researcher and thematically analysed independently by three research team members (KM, IC, AW). Thematic categories were developed and defined into themes through group consensus with overlapping themes combined into an overarching theme. An external researcher with subject experience (SM) reviewed coding and analysis for trustworthiness. Transcripts were re-read by the lead researcher for theme confirmation and agreed upon by all researchers. Given the sample size, five interviews was considered a minimum, and ten or more adequate for thematic analysis (Green and Thorogood 2014).

3. Results

Ten of the 35 eligible consumers participated in an interview (28.6%); nine interviews were conducted face-to-face. Participants were predominantly male and the mean age was 55 years (Table 2). Each participant was taking a mean of 6.5 medicines (range 2-13), including clozapine.

3.1 Medication history

Less than half (n=4/10) of participants gave a complete and accurate medication history when compared to stage one data (Table 3). These four participants were taking between two and eight medicines and did not use a dose administration aid (DAA). Five out of the six other participants were using a DAA and taking between six and 13 medications.

3.2 Questionnaires

The majority (n=7/10) of participants reported none or only mild adverse effects with clozapine, and medium to high levels of adherence (Table 3). Treatment burden was reported as low. All participants agreed/strongly agreed with the necessity of their medication; only 3/10 participants agreed that they were concerned about adverse effects from medication, and all agreed that the necessity of medication outweighed these concerns. Participants believed that they had a significant amount of control and understanding of their illness and treatment.

3.3 Semi-structured interviews

Four themes were identified from thematic analysis: (i) understanding of illness and recovery; (ii) positive outcomes of treatment; (iii) treatment burden and acceptance; and (iv) communication pathways. Quotes are provided as evidence of themes in Table 4.

(i) Understanding of illness and recovery

Each participant had a unique understanding of their mental illness and demonstrated an insight into the need for treatment. The high level of understanding aligned with questionnaire results, although some participants did not agree with a diagnosis of

schizophrenia or perceive their illness as long-term. Some participants explained that when they felt well and were functioning "normally" they did not consider themselves be mentally ill. For example one participant, Brian, believed that his illness would only last a short time but later stated he was diagnosed with schizophrenia 40 years ago. On further discussion, Brian explained that he had not been ill during this entire time. Similarly, several other participants believed that they did not have to worry about their illness as long as they kept taking clozapine. This underscored their belief that they had a degree of control over their illness, which was identified in the questionnaire results (Table 3). There was generally a high level of understanding of illness and recovery from schizophrenia, and for all participants, clozapine was a significant part of this journey.

(ii) Positive outcomes of treatment

Clozapine as a long term medication

The benefit of clozapine compared to other antipsychotics was mentioned, with reference to its calming, stabilising and relaxing effects. Although daytime sedation was a potential problem, clozapine's sedative effects improved rest and reduced fast thinking for one participant (Simon). Optimistic life changes noted by participants since taking clozapine included taking public transport, studying at university and socialising, and there was a strong belief about the influence of clozapine on recovery. Only one participant (Sally) discussed that she had benefited from taking clozapine in the past, but since recovering did not accept the need for continuing treatment.

Regular GP contact

The GP relationship was highly valued by participants; some did not have this prior to involvement in the shared care program. Routine GP visits were seen as beneficial for their physical health management, and were preferred to psychiatrist visits as they were more convenient in terms of time and travel and posed less of a psychological burden. Participants viewed their relationship with the GP as more familiar and trusting than that with their psychiatrist. Overall, all participants had favourable experiences as part of the

clozapine shared care program, reporting positive outcomes on their mental and physical health.

(iii) Acceptance of treatment burden

Participants acknowledged that treatment-related activities could, at times, be an inconvenience, but were accepted as part of treatment. Having a routine was viewed as an essential part of self-management and recovery, and lessened the inconvenience associated with treatment-related activities particularly with regards to medication adherence. Participants reported a low level of treatment burden despite taking on additional responsibilities. For example, lack of timely communication between clinicians, delayed blood test results or service closure on public holidays meant that, in some instances, clozapine supply was not received on time. Participants managed this by contacting their GP to ensure timely communication of blood test results, getting early blood tests when needed or having extra clozapine supply.

Clozapine adverse effects

No major concerns regarding adverse effects were articulated by participants, which were assumed as a normal part of clozapine treatment. Sedation and hypersalivation were commonly mentioned, yet participants believed that there was little that could be done about them. The potential for more serious adverse effects such as cardiac and haematological effects was a concern, however, it was recognised that monitoring was in place to manage these risks.

(iv) Communication pathways

GP and psychiatrist communication

Participants mostly assumed that clinicians did communicate with each other, however, there was a lack of awareness of what communication pathways were in place. Some participants saw themselves as an integral part of the communication process between their clinicians. Another participant, Sally, was hopeful that her GP could discuss the

cessation of clozapine with her psychiatrist, however she was dissatisfied with the level of communication between them. Although all participants recognised the importance of communication between their health professionals, most had little knowledge about what communication took place and all recognised its importance for everyone involved to have access to full medication information.

Consumer and clinician communication

All participants, except one, reported satisfaction with the extent of communication between themselves and their clinicians regarding their medication. Most were content to follow clinicians' instructions. One participant (Simon) shared his insight from previous experiences and was more confident with communicating with his psychiatrist. Sally expressed frustration that multiple psychiatrists (or trainees) did not communicate with her. Although there was variable consumer involvement in medication decisions most reported satisfaction with their level of communication with clinicians.

4. Discussion

Overall, clozapine treatment was associated with positive outcomes and the shared care model was preferred by participants, with regular GP contact highly valued. Establishment of routines were important to optimise adherence and minimise treatment burden. However, clozapine consumers perceived that their clinicians were in communication with each other and had access to full medication information. .

Understanding of illness affected beliefs about medicines and the need for treatment. All participants strongly believed that the necessity of clozapine outweighed medication—related concerns. These results align with a United Kingdom study; 87% of those surveyed perceived the advantages of taking clozapine outweighed the disadvantages (Taylor *et al.* 2000). Our study participants described clozapine as a major factor in their recovery, with improvements in their mental health and quality of life. Favourable consumer views about clozapine treatment have been shown in other studies (Wolfson

1996; Taylor *et al.* 2000; Waserman 2000; Angermeyer 2001; Hodge and Jespersen 2008).

Additionally, our study explored consumer perspectives about shared care. A major benefit was regular GP contact, meaning less frequent psychiatrist visits. Participants recognised that increased access to primary care could improve their physical health. This is important, as people with schizophrenia have high rates of physical health comorbidities, particularly cardiovascular disease, diabetes and dyslipidaemia, which are often inadequately managed and contribute to a lower life expectancy than the general population (Crawford *et al.* 2014).

It could be assumed that clozapine's mandatory monitoring, restrictions on access and possible severe adverse effects could be a significant burden for participants. However this was not found in our study, with these factors accepted by participants as part of recovery from their illness. Similarly, an Australian study which compared consumer and clinicians views about clozapine found that consumers accepted adverse effects and mandatory monitoring, and thought of them as less of a burden than their clinicians did (Hodge and Jespersen 2008).

Communication about medication between shared care stakeholders was identified as a significant area of concern in the first stage of our study, where discrepancies in medication records of shared care stakeholders were highly prevalent (Murphy *et al.* 2017). However, with one exception, this was not a concern shared by participants as it was assumed, by our participants that clinicians were in communication with each other and had access to full medication information. This assumption and the high prevalence of discrepancies found, highlight an urgent need for improved communication and particularly timely accurate medication liaison to prevent inappropriate clinical decision-making and ADEs.

Optimal care for consumers with chronic conditions requires an interactive partnership between consumer and clinician (Bodenheimer 2002). However in this study, eight of ten

participants were comfortable in the traditional "patient" role, trusting in their clinician's expertise with little input into treatment decisions. This was also reported in a Scottish study, which interviewed inpatients with schizophrenia about their perspectives of medication management (Stewart *et al.* 2010); most participants were happy to leave decisions to clinicians and were reluctant to assume responsibility for medication management (Stewart *et al.* 2010). Considering the high rate of identified discrepancies in medication records (Murphy *et al.* 2017), participants should be encouraged to take a more active role in their medication management.

4.1 Strengths and limitations

This study involved a specific group of participants stabilised on clozapine treatment and is not representative of all clozapine consumers. This was a convenience sample which was limited by the small number of eligible participants and those who agreed to participate. However interview data was sufficient to carry out thematic analysis. The researcher was known to participants as the hospital mental health pharmacist. This appeared to be a positive as good rapport was developed, however, a potential limitation was that participants may not have felt comfortable to disclose negative experiences or admit to medication-related concerns.

4.2 Practice implications

Given that shared care was preferable to standard clozapine management it is worth exploring ideas for capacity building. In Australia 2015, changes in the Pharmaceutical Benefits Scheme (PBS) allow for clozapine dispensing by community pharmacists who are not necessarily attached to a mental health service (Winckel 2015). This change may increase uptake of GP prescribing, dependent on current state and territory regulations (Winckel 2015). Less restrictive clozapine prescribing and dispensing protocols would allow for an increase in the existing capability of shared care programs. For example, in some cases, extending the time between psychiatrist visits may be an option; the GP and community pharmacy could take responsibility for clozapine prescribing and dispensing.

Reducing the frequency of psychiatrist appointments would allow for increased enrolment of consumers into the shared care program, lessen the emotional burden and promote consumer self-management. In Australia, training and knowledge of clozapine is needed for GPs and community pharmacists, as this has not been formally addressed at a national level even with the PBS changes (Winckel 2015). The issue of governance and clinical support for a relapse of illness or serious adverse effect would also require clarification (Winckel 2015). However successful continuum of care for consumers in a shared care model requires as a priority the introduction of formalised, transparent and routine communication pathways to ensure all stakeholders, including consumers, have timely access to appropriate medication information.

4.3 Conclusion

Participants described a positive experience with the shared care program and clozapine treatment despite potential for significant treatment burden. Importantly, participants noted benefits of regular GP contact, such as treating physical comorbidities, as well as being more convenient and less stressful than psychiatric appointments. This study shows that clozapine, a high risk medication, can be managed effectively in the community with positive outcomes, however, improved communication between clinicians is essential.

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Conflicts of interest

307 The authors declare no conflicts of interest

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309 **Table 1: Description of questionnaires**

Name	Description	Interpretation	Objective
8-item Morisky Medication Adherence Scale (MMAS-8)* (Morisky *et al.* 2008; Krousel-Wood 2009; Morisky and DiMatteo 2011)	8-item questionnaire to assess adherence to prescribed medication	Scores are coded resulting in a scale from low adherence to high adherence	Adherence is important to explore as part of the experience of taking a medication for a chronic illness and treatment burden
The Glasgow Antipsychotic Side-effect Scale for Clozapine (GASS-C) (Hynes 2015)	18-item questionnaire about potential side effects of clozapine	Total scores indicate whether the consumer experiences nil /mild side effects, moderate side effects or severe side effects	Used to determine if consumers are experiencing from excessive side effects. Side effects may influence adherence and beliefs and experiences about illness and medications
The Brief Illness Perception Questionnaire (Brief IPQ) (Broadbent 2006)	8- item questionnaire to measure cognitive and emotional representations of illness including consequences, timeline, personal control, treatment control, identity, coherence, concern, emotional response and causes	Allows a simple interpretation of scores using a Likert scale from 0 to 10. Increases in item scores represent linear increases in the dimension measured	Aims to provide a rapid assessment of illness perceptions. Has been chosen to explore the consumer's perceptions and experience of their illness and is useful for populations who would find completion of a long questionnaire difficult
Beliefs about Medicines Questionnaire (BMQ) (Horne *et al.* 1999)	10-item questionnaire to assess the consumer's beliefs about the necessity of and concerns about medications prescribed	Scores from individual items (1-strongly disagree to 5-strongly agree) are summed to get a total score between 5 and 25. Higher scores indicate stronger beliefs. i.e. either stronger beliefs in the necessity of medicines or stronger concerns about medication	Allows consumers to discuss their beliefs about and concerns about their medications and whether these beliefs influence adherence. The difference between the necessity and concerns scores indicates if consumers believe that necessity outweighs concerns
The Treatment Burden Questionnaire (TBQ) (modified) (Tran *et al.* 2014)	15- item questionnaire to assess the burden associated with taking medicine, self-monitoring, laboratory tests, doctor visits, need for organisation, administrative tasks in different treatment and contexts	Using a Likert scale, each answer scores from 0 (no problem) to 10 (big problem) and scores are added to reach a total score out of 100. The higher the score, the more associated treatment burden	Used to explore perceptions of treatment burden and may aid to identify areas for improvement. Higher TBQ scores are associated with lower adherence to medications and lower quality of life

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313 **Table 2. Participant demographics (n=10)**

Gender - n (%)	
Male	7 (70)
Female	3 (30)
Age (years)	
Mean (range)	55 (39-70)
Dose Administration Aid - n (%)	
Yes	5 (50)
No	5 (50)
Duration of clozapine treatment - (years)	
Mean (range)	12.7 (2-19)
Duration of shared care (years) – n (%)	
<1	1 (10)
1-2	2 (20)
3-5	1 (10)
>5	6 (60)

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315

316 **Table 3. Questionnaire results (n=10)***

Questionnaire	Results	
Medication history - **n (%)**	Accurate & complete Inaccurate/incomplete Unable to complete	4 (40) 5 (50) 1 (10)
Glasgow Antipsychotic Side Effect Scale for Clozapine (GASS-C) – **n (%)**	Absent/mild side effects Moderate side effects Severe side effects	7 (70) 3 (30) 0
8 item Morisky Medication Adherence Scale (MMAS – 8) – **n (%)**	Low adherence Medium adherence High adherence	1 (10) 4 (40) 5 (50)
Treatment Burden Questionnaire, modified (TBQ) - **Mean (range)**	0 (no burden) - 100 (greatest burden)	22.8 (0-63)
Beliefs About Medicine Questionnaire - Specific (BMQ -specific) - **Mean (range)**	Necessity scale: Belief in the necessity of medication for maintaining health 5 (little belief) – 25 (strong belief) Concerns scale: Concerns about medication 5 (little concern) - 25 (strong concern)	20.9 (16-25) 11.8 (8-16)
Brief Illness Perception Questionnaire (Brief IPQ) – **Mean (range)**	1. How much does your illness affect your life? (0 not at all – 10 extremely) 2. How long do you think your illness will continue? (0 – a very short time – 10 forever) 3. How much control do you feel you have over your illness? (0-none at all – 10 extreme amount of control) 4. How much do you think your treatment can help your illness? (0 not at all – 10 extremely helpful) 5. How much do you experience symptoms from your illness? (0 None at all – 10 many severe symptoms) 6. How concerned are you about your illness? (0 not all – 10 extremely) 7. How well do you feel you understand your illness? (0 – not at all – 10 understand very clearly) 8. How much does your illness affect you emotionally? (0 Not all – 10 extremely affected)	4.1 (0-10) 5.1 (0-10) 6.9 (2-10) 7.8 (3-10) 3.6 (0-10) 5.4 (0-10) 7.4 (2-10) 5.1 (0-10)

317 *except for TBQ where n=9

318 Table 4. Themes and quotes

Themes and sub themes	Quotes
(i) Understanding of illness and recovery	*"… (I) put my hand up and said yes I had some sort of mental breakdown and mental illness, I accept it now."* [Sally]
	"(I've experienced) voices and manic attacks, also I've been a bit suicidal…but I get over those times and get right again…I've had a normal life and I've worked…so I have become very well, even now, and not sort of sick again" [Brian]
(ii) Positive outcomes of treatment	*"It* (clozapine) *stops the symptoms because it makes you go to sleep at night and your thinking slows down considerably and you fall asleep which means you have a good night sleep every night. It rests your brain so you can just function like normal…my illness is caused by fast thinking, so I take my clozapine and lithium and I know that I am going to fall asleep in 15 minutes, I jump into bed, I think as much as I want, and then it just slows down and I'm so sedated that I can't think at all, my thinking completely stops."* [Simon]
Clozapine as a long term medication	*"Prior* (to clozapine) *I would go from one thing to the next and I wasn't making any sense. It's completely different, I'm a lot calmer and…I am facing reality now, prior to that I was more hiding away like a hermit…I can go to the hospital today by myself, I didn't need anyone to come with me. Prior I always had someone with me so there has been big changes there."* [Sally]
	"It's helped me… it's a happy drug for me, it's taken away all those sorts of things I used to have on other medications – voices and manic attacks, I don't get them anymore hardly now. I've got nothing to worry about. It's been a really good drug…I have become very well" [Brian]
	"I think I would be a lot worse if I wasn't taking medication (clozapine)*"* [Robert]
	"It helped me at the time but I no longer need it" [Sally].
Regular GP contact	*"My GP gets all the medication for me every month and I get to talk to them about physical ailments, food intake or junk food intake and any other medical things like blood pressure, standing on weighing machine, new authority scripts for medication and stuff like that"* [Robert]
	"When I see my psychiatrist, it is quite a big commitment emotionally…I don't like thinking about my illness. When I go there I have to think about my illness and what I'm going to say to my psychiatrist. It is a big event…it is emotionally draining…I prefer not to see my psychiatrist so often, I don't mind seeing them once every three months or so…" [Simon]
	"He [GP] *knows what's going on in all the different areas* (of my health and life) *and he's also known me a long, long time"* [Sally]
	"Two heads (psychiatrist and GP) are better than one I think…it's all an advantage if they are keeping me healthy…" [Michael]
Table continued on next page…	

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320 **Table 4: continued.**

Themes and sub themes	Quotes
(iii) Acceptance of treatment burden	*"I am just so used to it now and I accept it…with the doctor, the blood tests, ring you guys* (hospital pharmacy) *up. Just in a routine, it is just something you have to do."* [Sally]
	"…there's a lot of responsibility for the person who is taking that medication to organise it…I have to organise a lot more" [Simon]
Clozapine adverse effects	*"Waking up with the wet pillow from the saliva it's a bit of a drag… guess there is nothing they can really do about it."* [Jeff]
	"I was told when they started me on it, it (clozapine) *could have a detrimental side effect of killing off my white blood cell count and I have a blood test taken every one month to check for exactly that…so far nothing has happened"* [Robert]
(iv) Communication pathways	*"They should know…they probably should communicate…I hope he* (psychiatrist) *does* (know about concomitant medications)" [Brian]
GP and psychiatrist communication	*"I am not sure but I assume they don't* (communicate) *because the GP never talks about the psychiatrist…I'm the link"* [Simon]
	"About four or five times he (GP) *has requested something and no-one's returning his calls or email…at least someone* (should) *ring Dr L* (GP) *because he knows what's going on…"* [Sally]
Consumer and clinician communication	*"I rely on my doctors opinions…Basically I do what you doctors tell me to do because you guys have been to university for years, you know your job, so I thought what the doctor orders goes"* [Robert]
	"I don't try and encourage my psychiatrist to reduce my meds (medication) *and that's very important because before I told you that I went through all those medications right. Well I was always telling the psychiatrist that I want less medication…and what happened was…several psychiatrists they reduced the meds and then I got sick…for about the last 3 years I never encouraged my psychiatrist to reduce my medication and that is probably the biggest reason why I haven't got sick…"* [Simon]
	"*The lady doctor* (psychiatrist), *I don't know how many I have seen here, they write things down like she's schizophrenia* (sic), *she is hearing voices, I have never had that, never."* [Sally]

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6.3 Summary

This chapter has described the experiences of consumers prescribed clozapine within a shared care program of this MH service. Reported experiences were favourable for both treatment with clozapine and the shared care program, and with a low level of perceived treatment burden. A concerning theme was the lack of awareness about possible gaps or inadequacies in the quality and completeness of communication between the shared care stakeholders and the general lack of self-involvement in treatment decisions by participants. Optimal treatment of long-term health conditions involves a proactive partnership between informed clinicians and consumers (64). Timely quality medication liaison between all members of the medication management and greater health care team that focuses on the individual consumer is essential for safe and effective care. Improved communication pathways are therefore needed to improve medication-related communication and documentation.

7. DISCUSSION AND CONCLUSION

This thesis describes the high rate of discrepancies in medication records held by stakeholders of a clozapine shared care program as well as the lived experiences of participating consumers. The results show that discrepancies were extremely common in the medication records of shared care stakeholders, although most consumers had an expectation that their clinicians had access to accurate medication information. Furthermore, the majority of participants were reliant on their clinicians to make informed decisions about their medications, while taking a more passive approach themselves. It was unclear to all participants how or if their clinicians communicated with each other about their treatment, although all participants thought that it was important.

Findings from this research show that shared care was a preferred option for participants, but also that there was a need for formal, routine, accurate and timely communication between shared care stakeholders and consumers, as well as access to accurate medication records to optimise clinical decision-making and minimise ADEs. This may be achieved by a formal collaboration between clinical pharmacists and stakeholders and greater consumer involvement in medication management. This chapter reflects on the implications and key findings of this research, as well as the strengths, limitations and recommendations for future research.

7.1 Summary of key findings

The overall aim of this research was to generate information and form recommendations to optimise access to accurate medication information and communication pathways between stakeholders and consumers of a clozapine shared care service. To meet this aim, the study was designed to achieve two objectives: firstly, to assess the completeness and accuracy of medication records held by stakeholders for consumers prescribed clozapine within a shared care program; and secondly, to describe the experiences of consumers prescribed clozapine within a shared care program. The study was undertaken in two parts. Part One used descriptive analysis to define discrepancies in the medication records of shared care stakeholders. Part Two used both descriptive and thematic analysis to give an in-depth understanding of the consumer's experience.

Discrepancies were highly prevalent in medication records held by shared care stakeholders in this service. Over 90% of consumers had at least one discrepancy in a medication record held by the shared care stakeholders when reconciled with a best possible medication history. This finding indicates a significant communication gap regarding medication information between shared care stakeholders, which is a serious safety issue.

It is estimated that 30% of medication discrepancies cause ADEs that are potentially harmful (54). Omission of medications in the stakeholder's record as compared with the medication history were the most common type of discrepancies found in this study. This aligns with comparable research in the outpatient setting (11). Specifically, this research found that omissions of concomitant medications (i.e. other than clozapine) in the secondary care record were the most common type of discrepancy overall. Similar findings have been described in research reviewing psychiatrists' medication records, where non-psychotropic medications were often omitted (12, 91). Although the secondary care prescriber is not responsible for prescribing concomitant medications, the examples

presented in Chapter 5 show that lack of full medication information in the secondary care record can result in unintended drug interactions or adverse effects. This could have been harmful for the consumer and limit the potential for positive outcomes with clozapine treatment.

Similarly, GPs or community pharmacists may be unaware of secondary care prescribing of psychotropic medication doses or changes and will therefore not be prompted to advise consumers of changes, monitor for ADEs and ensure appropriate continuity of care.

The significantly high rate of discrepancies is important because this is the first known study to describe the type and frequency of discrepancies in the medication records of people prescribed clozapine, a high-risk medication, in a shared care program. Furthermore this demonstrates that for quality and safe use of medicines, significant improvement in the documentation and communication of medication information in this shared care service is required. Consumers or carers may be able to provide relevant information to improve medication-related documentation and communication.

The positive lived experience of consumers in the clozapine shared care program

Consumer views are a valuable resource, particularly in the management of long-term health conditions like schizophrenia, as lived experiences and an insight into consumers understanding and expectations have the potential to improve the quality of this service as well as being a beneficial source of information to others who are beginning their recovery journey (63). There have been no other studies found that have explored clozapine consumers' experiences in a shared care setting. All participants described having a positive experience, despite the potential for significant treatment burden.

The findings from this study are supported by the literature, where consumer perspectives on clozapine as a treatment option have been reported to be positive and the benefits outweigh the risks (71). Positive views in this study extended to the shared care program, with the GP relationship being an important factor. Significantly, all participants preferred to visit their GP rather than their psychiatrist, because of a greater level of trust, strong GP participant relationship and reduced emotional burden. This aligns with results from a UK study where consumers appreciated the familiar relationship they had with their GP as they did not have to repeat their story, unlike in secondary care, where they often saw different clinicians (74).

Shared care, with less frequent psychiatrist visits should therefore reduce treatment burden for consumers; as reported in this study with a low level of treatment burden being reported. Interestingly, other potential contributors to treatment burden such as adherence, adverse effects, doctors' appointments and mandatory monitoring were accepted by participants as part of a routine that maintained their recovery. In contrast, it was concerning that, most participants trusted that their clinicians were in communication with each other and had access to full medication information, as was the consumers' lack of self-involvement in clinical decision-making regarding prescribed medications. The deficiency of participants' knowledge about the gaps in communication and information sharing within the shared care program highlights the need for formalised, routine communication pathways. Furthermore, consumers should be encouraged to be involved in communication and information sharing about medication-related decisions.

Improved accuracy of medication information and communication is needed in the clozapine shared care program to enhance continuity of care and reduce adverse drug events

In order to reduce the risk of ADEs from medication discrepancies, there is a need for improved accuracy of medication documentation and formalised pathways of communication between all stakeholders and the consumer/carer. Participant's assumptions about stakeholders access to medication records likely influenced them to take on a more "traditional" patient role with little self-involvement in medication-related decisions. Care of long-term health conditions such as schizophrenia is optimal when a "prepared, proactive practice team interacts with an informed, activated patient" (Bodenheimer 2002, p 2469)(64). In shared decision-making, both clinicians and consumers are assumed to be experts, with clinicians contributing through provision of current clinical information on illness and treatment options, while consumers contribute their own values, preferences and treatment goals (92).

The three key findings from this study have led to recommendations for practice and future research that involve a number of factors to improve documentation of medication information as well as communication pathways in this shared care service. In addition, there is a recommendation for increasing the number of consumers that are able to access the shared care program once the identified risks are minimised.

7.2 Recommendations for practice and future research

There are two main recommendations arising from this research. The first is to improve the timeliness, quality and accuracy of medication documentation and communication in the clozapine shared care program. Formalised, routine and accurate documentation and communication pathways between stakeholders within the clozapine shared care program needs to be introduced. The second is to seize the opportunity and the potential to expand the shared care program. Evaluation of practical strategies to put these recommendations into place are important areas for future research and could be transferable to shared care programs involving treatment of other long-term health conditions.

Improving medication liaison in the clozapine shared care program

Reliable and timely communication between primary and secondary care clinicians and consumers/carers is essential for effective shared care. Practical strategies to formalise communication pathways between shared care stakeholders in this service may include a consumer-held medication card or involve the use of electronic systems. Consumer-held medication cards would be a relatively inexpensive and achievable option (93). This would involve a document that the consumer brings to each appointment, which records medical information including regular medication details as well as important physical health parameters and clinician contact details. In an Australian study, where the consumer-held medication card was trialled with consumers at an outpatient clozapine clinic, consumers found it beneficial, particularly as a communication tool (93). Another option would be to use an electronic tool such as My Health Record, which is an Australian opt-in consumer-managed electronic health record system.

However, it is the content rather than the form of the documentation that is most important. As previously described, the Australian Commission on Safety and Quality in Health Care recommend a minimum requirement for documentation of medication information at

transitions of care. Regular medication review and reconciliation would be required to ensure the appropriateness, currency and accuracy of the record.

Medication reconciliation is a means to reduce medication errors and prevent ADEs (94). It is routinely undertaken by a clinical pharmacist at hospital admission and discharge at the site of this study setting, however, there is a gap in the MH outpatient setting. A clinical pharmacist can undertake regular medication reviews and reconciliation, identify medication-related problems and develop a plan to address the problems. Medication reconciliation would include the documentation of the consumer's current medication list including adverse drug reactions, doses, frequencies and indications, any recent changes, medication-related problems or interventions made. This is an opportunity for clinical pharmacists to expand their role as part of the clozapine shared care team with the aim of improving accuracy of medication documentation and bridging the communication gap between shared care stakeholders.

At the service involved in this study, the pharmacist-generated medication record could be automatically uploaded onto The Viewer®, an electronic program used by the public hospital that can be viewed by GPs as well as be manually uploaded to the specific electronic system used by the public mental health service (CIMHA®). In addition, pharmacists can provide expert advice and education for shared care stakeholders, including consumers and carers. Studies have shown that having a pharmacist as part of the mental health team improves medication-related outcomes such as reducing adverse effects, increasing adherence, reducing physician workload, reducing costs and increasing consumer satisfaction (16). The capability of pharmacists to play an extended role has been described in the primary care setting and is an area worthy of exploration for the management of clozapine services (95). This recommendation would require the creation of guidelines and funding for remuneration of pharmacist services. Additional research would be needed to evaluate outcomes and potential cost benefits. It still remains necessary that all shared care stakeholders take responsibility for medication reconciliation, documentation and communication, especially where there are no or limited clinical pharmacy resources. Improving medication liaison between different mental health care providers and with consumers/carers is an important and vast topic that requires further research.

Expansion of the shared care program

The increasing demand of MH services and a shortage of MH workers (16) is a global issue (96). Consequently, expanding the capability of effective and safe clozapine shared care in the community setting is an important area for future research. Participants in this study all had a favourable view of the clozapine shared care program and described positive outcomes, making shared care a potential option for a wider group of consumers. In Australia, the change in PBS restrictions with clozapine allows for greater GP and community pharmacy management of clozapine, recognising that many people living with schizophrenia are being treated in the community setting. However, the uptake of this in practice has not been reported. In Queensland, regulations require that in order to prescribe, a GP must be in a shared care arrangement with the local MH service. The expansion of the role for GPs and community pharmacists to manage clozapine in the community is accompanied by extra responsibility. Education and training is essential for primary care clinicians to ensure safe and positive treatment outcomes. Currently, training of GPs and community pharmacists regarding the provision of clozapine is left to the management of the local MH service. A national accreditation program, similar to that for GP prescribing of antiretroviral medication for HIV, is a recommendation. As well as confirming consistency and quality of training, it would increase the accountability of GPs

and community pharmacists to provide safe and quality clozapine management. Potentially this could be incorporated into the education and training tools currently provided by the brand-specific clozapine patient monitoring systems. Barriers to effective shared care, such as poor documentation and communication as outlined previously, would need to be addressed.

7.3 Strengths and limitations

This research has added to the body of literature with new information on the rate and type of discrepancies in a clozapine shared care program which has not been reported before. Additionally, it has provided a deeper understanding of the lived experience of people taking clozapine in a shared care program in the community setting.

As with all studies, there are a number of limitations that should be considered. The small sample size is the primary limitation of this research. However, it was an exploratory study, influenced firstly by the small number of consumers in the clozapine shared care service and secondly by the number of consumers who were willing to participate. The small sample size meant that some results, including medication discrepancies and survey responses, could not be analysed to a level of statistical significance.

The sample population was a specific group of clozapine consumers who had been stable on clozapine maintenance treatment for a number of years. They were not necessarily representative of the larger group of consumers prescribed clozapine, who may not have experienced such positive outcomes. Results may therefore not be transferable to the wider group of consumers who take clozapine.

Secondly, in Part One, the best possible medication history was not confirmed with consumers, subsequently consumers may have been taking medications differently to what was recorded in the history. Additionally, they may have accessed medication from other prescribers and pharmacies that were unknown to the researcher.

Another limitation was that stakeholders may have had knowledge about medications without documenting this in the record that was assessed by the researcher. Furthermore, data was not available for a number of GP records.

The objective of this exploratory study was to assess the completeness and accuracy of medication by describing the rate and type of discrepancies. Analysis of the clinical significance and risk rating of the potential ADEs due to medication discrepancies was not undertaken. However, potential drug interactions were presented in examples in Chapter 5.

Furthermore, it must be recognised that the participant's account is something that is shaped by prior cultural understandings, including how they respond to the interviewer (97). The researcher was known to consumers as the hospital MH pharmacist. This could be considered a strength, as a good rapport was easily developed with the participants. However, participants may have been wanting to please the researcher with their answers. For example, they may have felt uncomfortable about admitting to non-adherence with clozapine or may have given what they believed was a desired response.

7.4 Conclusion

Medication discrepancies were highly prevalent in the records of clozapine shared care stakeholders, increasing the risk for suboptimal clinical decision-making and the potential for ADEs. Consumers reported positive experiences in the shared care program and most assumed their clinicians had knowledge of their full medication information. There is a need for formal, routine, accurate and timely medication liaison between shared care stakeholders, and consumers/carers, and access to accurate medication information. Regular medication review and reconciliation is recommended. With improved medication documentation and communication, clozapine shared care may be an option for a greater number of consumers living in the community, relieving the burden for the consumer and the public mental health system.

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9. APPENDICES

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9.2 Appendix 2: Part One participant information sheet

Royal Brisbane and Women's Hospital
Metro North Hospital and Health Service

Clozapine communication: setting the record straight.
Participant Information and Consent Form:
Part One **Protocol *V1.1 20.01.2014***

You are invited to take part in a research project exploring communication about medication and your views about how medication is managed under shared care arrangements. The aim of the research is to provide information which can be used to improve the ways mental health services, GPs and pharmacists communicate and work with each other and with you. The purpose of this is to promote safe use of medicines. The study is in two parts. This information sheet is about Part One. Part Two is described in a separate information sheet.

So that you can make an informed decision about whether to participate it is important that you understand why the research is being done, who is doing it and what taking part will involve. This Participant Information Sheet (PIS) tells you about the research project. It explains what will happen and what you will be asked to do if you decide to take part. Please take time to read the following information carefully and discuss it with others if you wish. Ask the researcher about anything that is not clear or for any more information you would like.

This study has been approved by the Royal Brisbane and Women's Hospital Human Research Ethics Committee: HREC/14/QRBW/48

Why have I been invited to take part?
You are being invited to take part because you are prescribed clozapine by a mental health doctor at the RBWH under shared care arrangements.
Who is conducting the study?
This study is being carried out within Metro North Mental Health-RBWH by a team of researchers and clinicians. The research is led by Ms Kate Murphy who will be supervised by Professors Ian Coombes from the RBWH and Amanda Wheeler from Griffith University. Other members of the team are Dr Vikas Moudgil, Dr Sue Patterson and Ms Elsie Peusschers. The study has been funded by the RBWH Foundation.

Do I have to take part?
No. Participation in the research is entirely voluntary. It is up to you to decide whether you do so. Deciding not to take part will involve have no effect on the care you are provided now or in the future. Your rights to health and social care are unchanged whether you take part or not. The researchers will not tell anyone who did or did not take part but you are free to tell anyone you wish about your decision.

The research is being conducted in two parts. You may choose to participate only in Part One or could choose also to participate in Part Two. You can only participate in Part Two if you participate in Part One. This information tells you about Part One. If you agree to Part One we will give you more information about Part Two and if you are interested arrange to contact you again in the next couple of months.

If you agree to take part you will be asked to complete a consent form as a record that you have agreed. You will be given a copy of the consent form to keep.

If you decide to take part you are free to withdraw at any time without giving a reason. However, if you do decide to withdraw we may not be able to remove any information about you or provided by you from the analysis. Whether we can remove information would depend on when you told us you withdraw.

Withdrawing, or not participating in the study, will not affect your routine care or your relationship with the Royal Brisbane and Women's Hospital or Metro North Hospital and Health Service or your treating team. None of your legal rights will be affected in any way.

What will participation involve?
Participation in Part One involves giving the research team permission to access records of your medication held by Metro North Mental Health-RBWH, GPs involved in prescribing medication for you and community pharmacies who dispense any medication you are prescribed. If you agree to this you will be asked to tell us the names of any GPs you visit and the names of pharmacies where you collect medication. We will ask you to sign a letter which we can give to the pharmacy and GP to tell them that it is alright for us to look at your records.

If you consent we will first get your medical record from the mental health service. We will write down information about the medication you are prescribed by the mental health doctor and make a note of any other medications listed in the record. We will then get in touch with the GP who provides shared care and any others you tell us about and the pharmacies where you get your medications. We will ask the GPs and pharmacies to tell us what their records say you are prescribed or dispensed. We are only interested in medication prescribed or dispensed in the previous three months.

If you agree to participate we will also ask you whether it is alright to contact you about Part Two and make arrangements if you agree to that.

How will my identity and information be kept confidential and what will happen to the information I provide?
Everything you tell us will be confidential, except as required by law or Queensland Health Code of Conduct. All information collected for the research will be looked after as required by law and Queensland Health Policies. All documents will be stored securely on Queensland Health or Griffith University facilities in locked cabinets and password protected computer files on Queensland Health or Griffith University computers. Most information will be identified only by code allocated to you when you agree to take part. So that we can check records if we have to, we will keep a list of the code with your name but this will be kept away from the records. Only members of the research team who need the information will have access to any information linked to your name and the record of your name will be stored only at Queensland Health facilities.

No identifying information will be included in any reports of the study which will draw on analysis of information provided by all those who take part. No person will be identified in any reports made within the organisation and your colleagues will not be told what you have said.

We will analyse the information from your records in two stages. First we will compare the records from the mental health service at RBWH, GPs and pharmacies to see how accurate and complete each record is. We will make a note of when medications are missing or not recorded accurately in GP or mental health records using the dispensing record. Where we find differences in information about medications in the records we will write down the type of difference – noting for example, whether it is missing, a different

dose or an extra one. Next we will count up the number and types of differences in medication information in your records, if we find any. This will let the research team describe how accurate and complete the information held by the mental health service, GPs and pharmacies is. These findings will be used in reports of the study for dissemination in various forums.
We will use the information we collect to compile a complete medication record which we will share with the doctors and pharmacists and you may have a copy if you wish.

Who will know I have taken part?
Only the researchers conducting the study will know you take part. You may tell anyone you wish.

What are the benefits of taking part?
There are no immediate tangible benefits to you for taking part. However research has shown that some people find taking part in research beneficial because they value contributing to ongoing development of services for people like them.

What if I am harmed by taking part?
We do not anticipate any harm resulting from participation in this study. You will be asked only to identify GPs and pharmacists involved in prescribing or dispensing medication and to sign letters consenting to release of information.

Who has reviewed the research project?
All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the HREC of the Royal Brisbane and Women's Hospital: HREC/14/QRBW/48

If you wish complain, or have any concerns about any aspect of the way you have been treated while taking part in the study, then you can contact the, Chairperson of the Royal Brisbane and Women's Hospital Human Research Ethics Committee on (07) 3646 6132.

This project will be carried out according to the National Statement on Ethical Conduct in Human Research (2007). This statement has been developed to protect the interests of people who agree to participate in human research studies.

Thank you for taking time to read this information sheet. Please ask if you would like anything explained or have any questions.

9.3 Appendix 3: Part Two participant information sheet

Royal Brisbane and Women's Hospital
Metro North Hospital and Health Service

Clozapine communication: setting the record straight.
Participant Information and Consent Form:
Part Two **Protocol *V1.1 16.02.2015***

You are invited to take part in a research project exploring communication about medication and your views about how medication is managed under shared care arrangements. The aim of the research is to provide information which can be used to improve the ways mental health services, GPs and pharmacists communicate and work with each other and with you. The purpose of this is to promote safe use of medicines. The study is in two parts. This information sheet is about Part Two.

So that you can make an informed decision about whether to participate it is important that you understand why the research is being done, who is doing it and what taking part will involve. This Participant Information Sheet (PIS) tells you about the research project. It explains what will happen and what you will be asked to do if you decide to take part. Please take time to read the following information carefully and discuss it with others if you wish. Ask the researcher about anything that is not clear or for any more information you would like.

This study has been approved by the Royal Brisbane and Women's Hospital Human Research Ethics Committee: HREC/14/QRBW/48

Why have I been invited to take part?
You are being invited to take part because you are prescribed clozapine by a mental health doctor at the RBWH under shared care arrangements **and** you gave consent in Part One of the study for us to look at records held by the mental health service, GPs and pharmacists about your medication.

Who is conducting the study?
This study is being carried out within Metro North Mental Health-RBWH by a team of researchers and clinicians. The research is led by Ms Kate Murphy and supervised by Professors Ian Coombes from the RBWH and Amanda Wheeler from Griffith University. Other members of the team are Dr Vikas Moudgil, Dr Sue Patterson, and the study has been funded by the RBWH Foundation.

Do I have to take part?
No. Participation in the research is entirely voluntary. It is up to you to decide whether you do so. Deciding not to take part will involve have no effect on the care you are provided now or in the future. Your rights to health and social care are unchanged whether you take part or not. The researchers will not tell anyone who did or did not take part but you are free to tell anyone you wish about your decision. '

If you agree to take part you will be asked to complete a consent form as a record that you have agreed. You will be given a copy of the consent form to keep.

If you decide to take part you are free to withdraw at any time without giving a reason. However, if you do decide to withdraw we may not be able to remove any information about you or provided by you from the analysis. Whether we can remove information would depend on when you told us you withdraw.

Withdrawing, or not participating in the study, will not affect your routine care or your relationship with the Royal Brisbane and Women's Hospital or Metro North Hospital and Health Service or your treating team. None of your legal rights will be affected in any way.

What will participation involve?
Participation in Part Two involves meeting with a researcher and completing a questionnaire and answering some questions related to medication. The meeting will take a maximum of 45 minutes and be arranged for a time and place convenient to you. You may bring someone of your choosing to the meeting if you wish.

The questionnaire asks for some information about you and your medications. The researcher can help you complete this if you wish. The researcher will ask questions about your beliefs about medication, how involved you are in decisions about your medication, how regularly you take your medications and what influences whether you take them or not. The researcher will also ask about your experiences of shared care and communication about medication. You will have the opportunity to tell the researcher anything that is important to you about how your medication is managed and how this could be improved.

We would like to record the meeting using a digital audio recorder and write out the recording for reading and analysis. You will be asked for permission to start the recorder at the meeting and recording will only go ahead with permission. If you do not give permission for recording, the researcher will make notes during and/or after the meeting.

The researcher will NOT be able to provide advice about medication but can help you access information you might want. If you have any questions the researcher could refer you to a person who can answer them or provide you with some printed information.

What are the benefits of taking part?
You will be offered a $25 Coles/Myer shopping voucher to say thank you for your time. You will also be given back money you spend on transport (as agreed with the researcher) to attend the meeting. There are no other tangible benefits to you for taking part. However some people find it helpful to be able to share their views with an impartial researcher and/or find taking part in research beneficial because they value contributing to on-going development of services for people like them.

What if I am harmed by taking part?
We do not anticipate any harm resulting from participation in this study. You may experience some inconvenience attending the meeting and perhaps some emotional discomfort talking about your experiences with medication. If you become distressed during the interview the researcher will ask you what you would like to do and if you wish, will talk to your treating team so that they can help you. You can take a break at any time and you always have the right to end the interview without giving a reason. You can also refuse to answer any questions if you wish.

If you are harmed by taking part in this research project, there are no special compensation arrangements. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been treated during the course of this study then you should immediately inform one of the principal researchers
A/Professor Ian Coombes|Director of Pharmacy|Royal Brisbane and Women's Hospital|Ph. 3646 7040|
Email. ian.coombes@health.qld.gov.au OR

Professor Amanda Wheeler|Griffith University|Ph.3382 1068 |Email. a.wheeler@griffith.edu.au

How will my identity and information be kept confidential and what will happen to the information I provide?
Everything you tell us will be confidential, except as required by law or Queensland Health Code of Conduct. All information collected for the research will be looked after as required by law and Queensland Health Policies. All documents will be stored securely on Queensland Health or Griffith University facilities in locked cabinets and password protected computer files on Queensland Health or Griffith University computers. Most information will be identified only by code allocated to you when you agree to take part. So that we can check records if we have to, we will keep a list of the code with your name but this will be kept away from the records. Only members of the research team who need the information will have access to any information lined to your name and only coded information will be stored on Griffith University facilities.

No identifying information will be included in any reports of the study which will draw on analysis of information provided by all those who take part. No person will be identified in any reports made within the organisation and your colleagues will not be told what you have said.

The information you will be analysed with information provided by other consumers who take part in the study. We will count the answers people provide to the items on the questionnaire so that we can describe the proportions of people who have similar views or experiences. For your answers to questions put to you by the researcher we will use a process called thematic analysis so we can describe the different views and experiences people have.

We will write about our research and our findings to share with consumers, doctors and pharmacists and other researchers. We will provide you with a summary of the research if you wish.

Who will know I have taken part?
Only the researchers conducting the study will know you take part and will not tell anyone without your permission, or if required by law or for your safety to do so. You may tell anyone you wish.

Who has reviewed the research project?
All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the HREC of the Royal Brisbane and Women's Hospital : HREC/14/QRBW/48

If you wish complain, or have any concerns about any aspect of the way you have been treated while taking part in the study, then you can contact the, Chairperson of the Royal Brisbane and Women's Hospital Human Research Ethics Committee on (07) 3646 6132.

This project will be carried out according to the National Statement on Ethical Conduct in Human Research (2007). This statement has been developed to protect the interests of people who agree to participate in human research studies.

Thank you for taking time to read this information sheet. Please ask if you would like anything explained or have any questions.

9.4 Appendix 4: Consumer information letter

Metro North Hospital and Health Service
Metro North Mental Health

Royal Brisbane and Women's Hospital
E Floor, Mental Health Centre
Herston QLD 4029

24th February 2015

Clozapine and concomitant medicines: setting the record straight.

Dear

I am writing to tell you about a research study being run at Metro North Mental Health-RBWH. The study is being run by a team of researchers including doctors and pharmacists who work for Royal Brisbane and Women's Hospital and Griffith University.

The study is looking into how accurate and complete the medication records held by RBWH, GPs and community pharmacies are. The researchers are also interested in your experiences of how your medication is managed. The included information sheet tells you more about who is doing the study, why it is important and what taking part would involve. You may read this when it suits you and talk to anyone about it, if you wish. Please contact me if you have questions. You do not need to do anything now.

When you come to your next clinic appointment I will ask you if you are willing to meet and talk to you more about the study and ask if you want to take part.

With kind regards

Kate Murphy
Senior Pharmacist
Phone: 3646 1112; email: kate.murphy@health.qld.gov.au

9.5 Appendix 5: General practitioner information letter

Metro North Hospital and Health Service
Metro North Mental Health

Royal Brisbane and Women's Hospital
Butterfield Street
Herston Qld 4029

25th February 2015

Clozapine and concomitant medicines: setting the record straight.

Dear Dr.

We write to let you know about a research study looking into the management of medications for people prescribed clozapine through Metro North Mental Health – RBWH under shared care arrangements. The project has been initiated by the RBWH Mental Health- Pharmacy Research Collaborative and endorsed by Dr Vikas Moudgil, Clinical Director of Metro North Mental Health. The research will be undertaken by Ms Kate Murphy, a clinical pharmacist, as part of her Higher Degree Research project at Griffith University and will be supervised by A/Professor Ian Coombes Director of Pharmacy at RBWH and Prof Amanda Wheeler from Griffith University. The study has two parts, the first is designed to assess the accuracy and completeness of medication records held by the mental health service, GPs and community pharmacists. The second part will examine patients' medication beliefs and perceived burden of medication management under current arrangements. The study has been approved by the RBWH Human Research Ethics Committee HREC/14/QRBW/48 and the RBWH research governance office.

We will be approaching patients managed under shared care arrangements and inviting them to participate in the study over the coming months. Consenting to Part One of the study involves giving permission for researchers to gather information about medication prescribed and dispensed from nominated GPs and community pharmacies. We will collect the necessary information and reconcile the records held by each service provider.

If a patient for whom you manage care consents to participation we will ask them to sign a release of information form for you. A researcher working on the study will contact you and make arrangements to collect the necessary data. We will minimise any inconvenience to you and your practice. You do not need to do anything at this stage.

If in the meantime you have any questions, please contact Kate Murphy on 3646 1112 or kate.murphy@health.qld.gov.au

Yours sincerely,

Dr Vikas Moudgil

A/Professor Ian Coombes

Kate Murphy

9.6 Appendix 6: Community pharmacist information letter

Metro North Hospital and Health Service
Metro North Mental Health

Royal Brisbane and Women's Hospital
Butterfield Street
Herston Qld 4029

24th February 2015

Clozapine and concomitant medicines: setting the record straight.

Dear Colleague

I write to let you know about a research study looking into the management of medications for people prescribed clozapine through Metro North Mental Health- RBWH under shared care arrangements. The study, is being undertaken by Kate Murphy, a clinical pharmacist, as part of her Higher Degree Research project through Griffith University and will be supervised by A/Professor Ian Coombes, Director of Pharmacy at RBWH and Prof Amanda Wheeler from Griffith University. The study has two parts. The first is designed to assess the accuracy and completeness of medication records held by the mental health service, GPs and community pharmacies. To do this we are planning to compare the records held by the Mental Health Service and GPs with the dispensing records held by pharmacies providing medication to participants. The second will examine patients' medication beliefs and perceived burden of medication management under current arrangements. The study has been approved by the RBWH Human Research Ethics Committee HREC/14/QRBW/48 and the RBWH research governance office.

We will be approaching patients managed under shared care arrangements and inviting them to participate in the study over the coming month. Consenting to Part One of the study involves giving permission for researchers to gather information about medication prescribed and dispensed from nominated GPs and community pharmacies. We will collect the necessary information and reconcile the records held by each service provider.

If a person prescribed clozapine under shared care arrangements for which you dispense medication consents to participation we will ask them to sign a release of information form for you. A researcher working on the study will contact you and make arrangements to collect the necessary data. We will minimise any inconvenience to you and your practice. You do not need to do anything at this stage.

If in the meantime you have any questions, please contact Kate Murphy on 3646 1112.

Yours sincerely,

A/Professor Ian Coombes

Kate Murphy

9.7 Appendix 7: Medication action plan (modified)

Clozapine & Concomitant Medicines: data collection tool – medication reconciliation

Modified from the Medication Action Plan with permission from Medicines Regulation and Quality, Queensland Government

ITO/CTO: YES☐ No ☐	PATIENT DETAILS
Date of Diagnosis:	Date: URN: Sex: M ☐ F ☐
Clozapine initiation date:	DOB: Study ID:
Shared care start date:	ATTACH PATIENT STICKER

Medicines taken prior to presentation

Key: ✓ *Same* **x** *Omission* + *Addition* Δ *Change (administration instructions)* ↑ *Dose increase* ↓ *Dose decrease*

MEDICATION Drug / dose / frequency / indication	Reconciliation (Include details of discrepancies)					
	Med Hx	CP	GP	RBWH CIMHA	RBWH i-pharm	Consumer
Documented by *(name & signature)* **& dates information accessed:**						

For Consumer interview only: did consumer bring own medicines? ☐All ☐Some ☐ None

Created on 23/01/2018 8:11:00 AM:\Documents\MPhil - cloz research project\Thesis2017\Appendices\Appendix7_MAP_modified.doc

General Information

Medicines usually administered by: ☐ Self ☐ Other (specify):
Preferred administration method:

GP Details

Contact details:

Date contacted:

Medication summary provided: YES☐ NO ☐

Last Appointment Date:

Comments:

Community Pharmacy Details

Contact details:

Date contacted:

DAA: YES☐ NO ☐ **Staged Supply:** YES☐ NO ☐ **Delivery / Collection Details:**

Dispensing summary provided: YES☐ NO ☐ **DAA packing list provided:** YES☐ NO ☐

Comments:

RBWH Details

Treating Psychiatrist:
Appointment frequency:
Last medical review date in CIMHA / IEMR:
Case Manager:
Comments:

Additional Comments (eg recent changes to shared care, medications, practitioners etc)

Assessment of medication self-management needs

Lives alone	☐Yes ☐No ☐N/A	Has difficulty measuring liquids	☐Yes ☐No ☐N/A
Lives in residential care facility	☐Yes ☐No ☐N/A	Uses medication list	☐Yes ☐No ☐N/A
Uses dose administration device	☐Yes ☐No ☐N/A	Has had a recent Home Medicines Review	☐Yes ☐No ☐N/A
Uses administration aid	☐Yes ☐No ☐N/A	Has suspected non adherence	☐Yes ☐No ☐N/A
If *yes*, specify:		*Assess adherence by asking:*	
Has impaired hearing	☐Yes ☐No ☐N/A	• *"People often have difficulty taking their pills for one reason or another…have you had any difficulty taking your pills?"*	
Has impaired vision	☐Yes ☐No ☐N/A		
Has impaired cognition	☐Yes ☐No ☐N/A		
Has swallowing issues	☐Yes ☐No ☐N/A	• *"About how often would you say you miss taking your medicines?"*	
Has difficulty reading / comprehending labels	☐Yes ☐No ☐N/A		
Has difficulty understanding English	☐Yes ☐No ☐N/A		
If *yes*, language spoken:		.....	.....
Has difficulty opening bottles	☐Yes ☐No ☐N/A		

Medication history checklist

☐ Prescription medicines	☐ Complementary medicines (e.g. vitamins, herbal or natural therapies)
☐ Sleeping tablets	☐ Inserted medicines (e.g. nose / ear / eye drops, pessaries, suppositories)
☐ Inhalers, puffers, sprays, sublingual tablets	☐ Injected medicines
☐ Oral contraceptives, hormone replacement therapy	☐ Recently completed courses of medicine
☐ Over-the-counter medicines	☐ Other people's medicine
☐ Analgesics	☐ Social and recreational drugs
☐ Gastrointestinal drugs (for reflux, constipation, diarrhoea)	☐ Intermittent medicines (e.g. weekly or twice weekly)
☐ Topical medicines (e.g. creams, ointments, lotions, patches)	

9.8 Appendix 8: Interview guide

Clozapine and concomitant medication: Setting the record straight

Part Two (questionnaires and interview)

Interview Process and Topic Guide v1.6 2.07.2015

1. Introduction

- Introduce yourself and thank participant for meeting;
- Review purpose of the meeting:
  - to complete questionnaires and explore views about management of medication, beliefs about clozapine and shared care and perceived treatment burden;
- Confirm consent to participate, right to withdraw and permission for audio; recording and/or note taking – turn recorder on if permission given;
- Confirm if the participant has any questions.

Conduct the meeting in a conversational style; be curious and follow leads in the conversation where appropriate to explore views and experiences. Manage process in a way that optimizes engagement and expression of views and encourage participant to explore thinking around 'issues'.
Support participant to complete questionnaires as appropriate and use opportunities to explore responses to achieve study aims.

2. Medication history

Using the original data collection tool (modified version of the MAP) from part one, confirm with participant the medications they are currently taking including dose, frequency and indication.

3. Survey (Questionnaires)

Participant to complete supported by the researcher

(a) Brief Illness Perception Questionnaire (Brief IPQ) (1);

(b) Beliefs about Medicines Questionnaire (BMQ) (2);

(c) Glasgow Antipsychotic Side-effect Scale for Clozapine (GASS-C) (3);

(d) Morisky Medication Adherence Scale (MMAS-8) (4-6);

(e) Treatment burden questionnaire (TBQ) (7).

1

Date.....Consumer ID.....Researcher.....

4. Guided Questions (use judiciously dependent on information collected during survey completion)

Thinking particularly about clozapine,

(a) What role does medication play in your life?

Prompt re perceived need, usefulness, advantages / disadvantages including side effects.

(b) How does this help you?

Explore:
- *beliefs about perceived indication / need;*
- *beliefs about benefits – how do you think clozapine helps with symptoms of schizophrenia?;*
- *any perceptions of risk … what are the potential risks, how might that affect you?*

(c) Are there any downsides/disadvantages to being treated with clozapine?

- *Explore beliefs about perceived treatment burden of taking clozapine (ie regular blood tests, psychiatrist appointments at hospital, not being able to be dispense at local CP etc);*

Prompts, costs, time taken, travel etc – refer back to TBQ if relevant.

(d) How involved are you in decisions about medication (clozapine)?

- *Prompt for satisfaction with current situation.*

(e) If you have problems with your clozapine who would you approach?

Prompt for GP, mental health doctor, carer, friend, mental health clinician, other health professional.

(f) Who else is involved in managing your medications?

Prompt for carer, friend, mental health clinician, other health professional;

- *What roles do these people play and how helpful is that?*

(g) How well do you think the GP and the psychiatrist (mental health doctor) communicate about your medication?

Prompt for what makes them think this.

Date……Consumer ID……Researcher……

(h) What are the advantages/disadvantages of shared care program compared with coming each month to the hospital to collect?

- *Prompt communication between shared care stakeholders (Mental health service, GP, community pharmacy);*
- *Prompt time, travel, convenience.*

(i) Anything else you'd like to tell us about shared care arrangements or the way your medication is managed?

Thank participant for time, offer voucher as a thank you and ask whether they'd like to receive a copy of findings of study – make arrangements as appropriate.

1. Broadbent E, Petrie KJ, Main J, Weinman J. The brief illness perception questionnaire. J Psychosom Res. 2006;60(6):631-7.
2. Horne R, Weinman J, Hankins M. The beliefs about medicines questionnaire: the development and evaluation of a new method for assessing the cognitive representation of medication. Psychol Health. 1999;14(1):1-24.
3. Hynes C, Keating D, McWilliams S, Madigan K, Kinsella A, Maidment I, et al. Glasgow antipsychotic side-effects scale for clozapine — development and validation of a clozapine-specific side-effects scale. Schizophr Res. 2015;168(1-2):505-13.
4. Morisky DE, Ang A, Krousel-Wood MM. Predictive validity of a medication adherence measure for hypertension control. J Clin Hypertens. 2008;10(5):348-54.
5. Krousel-Wood MM, Islam T, Webber LS, Re R, Morisky DE, Muntner P. New medication adherence scale versus pharmacy fill rates in seniors with hypertension. Am J Manag Care. 2009;15(1):59.
6. Morisky DE, DiMatteo MR. Improving the measurement of self-reported medication nonadherence: response to authors. J Clin Epidemiol. 2011;64(3):255.
7. Tran V-T, Harrington M, Montori VM, Barnes C, Wicks P, Ravaud P. Adaptation and validation of the treatment burden questionnaire (TBQ) in english using an internet platform. BMC Med. 2014;12(1):109.

Date.....Consumer ID.....Researcher.....

9.9 Appendix 9: Brief illness perception questionnaire (79)

The Brief Illness Perception Questionnaire

For the following questions, please circle the number that best corresponds to your views:

How much does your illness affect your life?										
0 no affect at all	1	2	3	4	5	6	7	8	9	10 severely affects my life
How long do you think your illness will continue?										
0 a very short time	1	2	3	4	5	6	7	8	9	10 forever
How much control do you feel you have over your illness?										
0 absolutely no control	1	2	3	4	5	6	7	8	9	10 extreme amount of control
How much do you think your treatment can help your illness?										
0 not at all	1	2	3	4	5	6	7	8	9	10 extremely helpful
How much do you experience symptoms from your illness?										
0 no symptoms at all	1	2	3	4	5	6	7	8	9	10 many severe symptoms
How concerned are you about your illness?										
0 not at all concerned	1	2	3	4	5	6	7	8	9	10 extremely concerned
How well do you feel you understand your illness?										
0 don't understand at all	1	2	3	4	5	6	7	8	9	10 understand very clearly
How much does your illness affect you emotionally? (e.g. does it make you angry, scared, upset or depressed?										
0 not at all affected emotionally	1	2	3	4	5	6	7	8	9	10 extremely affected emotionally
Please list in rank-order the three most important factors that you believe caused <u>your illness</u>. *The most important causes for me:-*										
1. _____										
2. _____										
3. _____										

9.10 Appendix 10: Beliefs about medicine questionnaire (80)

- These are statements other people have made about their medication.
- Please indicate the extent to which you agree or disagree with them by placing a cross in the appropriate box.
- There are no right or wrong answers. I am interested in your personal views.
- Please only cross one box per question.

1. My health at present depends on my medicines

1. Strongly agree ☐ 2.Agree ☐ 3.Uncertain ☐ 4.Disagree ☐ 5. Strongly disagree ☐

2. Having to take medication worries me

1. Strongly agree ☐ 2.Agree ☐ 3.Uncertain ☐ 4.Disagree ☐ 5. Strongly disagree ☐

3. My life would be impossible without my medication

1. Strongly agree ☐ 2.Agree ☐ 3.Uncertain ☐ 4.Disagree ☐ 5. Strongly disagree ☐

4. Without my medication I would be very ill

1. Strongly agree ☐ 2.Agree ☐ 3.Uncertain ☐ 4.Disagree ☐ 5. Strongly disagree ☐

5. I sometimes worry about the long term effects of my medication

1. Strongly agree ☐ 2.Agree ☐ 3.Uncertain ☐ 4.Disagree ☐ 5. Strongly disagree ☐

6. My medication is mystery to me

1. Strongly agree ☐ 2.Agree ☐ 3.Uncertain ☐ 4.Disagree ☐ 5. Strongly disagree ☐

7. My health in the future will depend on my medication

1. Strongly agree ☐ 2.Agree ☐ 3.Uncertain ☐ 4.Disagree ☐ 5. Strongly disagree ☐

8. My medication disrupts my life

1. Strongly agree ☐ 2.Agree ☐ 3.Uncertain ☐ 4.Disagree ☐ 5. Strongly disagree ☐

9. I sometimes worry about becoming too dependent on my medication

1. Strongly agree ☐ 2.Agree ☐ 3.Uncertain ☐ 4.Disagree ☐ 5. Strongly disagree ☐

10. My medication protects me from becoming worse.

1. Strongly agree ☐ 2.Agree ☐ 3.Uncertain ☐ 4.Disagree ☐ 5. Strongly disagree ☐

9.11 Appendix 11: Glasgow antipsychotic side-effect scale for clozapine (82)

This questionnaire is being used to determine if you are suffering from excessive side effects from your medication. Please put a tick in the column which best indicates how often or how severely you have experienced the following side effects.

Over the **past week**		Never	Once	A few times	Everyday	Tick if severe or distressing
1	I felt sleepy during the day					
2	I felt drugged or like a zombie					
3	I felt dizzy when I stood up or have fainted					
4	I have felt my heart beating irregularly or unusually fast					
5	I have experienced jerking limbs or muscles					
6	I have been drooling					
7	My vision has been blurry					
8	My mouth has been dry					
9	I have felt sick (nauseous) or have vomited					
10	I have felt gastric reflux or heartburn					
11	I have had problems opening my bowels (constipation)					
12	I have wet the bed					
13	I have been passing urine more often					
14	I have been thirsty					
15	I have felt more hungry than usual					
16	I have been gaining weight					
17	I have felt breathless					
18	I have had chest pain					

I have also experienced: (please write down any other side effects that you may have experienced over the past week)

Caffeine intake: Y/N .....cups/day; Smoker: Y / N .....cigarettes/day;

Has there been a recent change in your smoking habit?

Increase/Decrease by . . . . . .cigarettes/day

9.12 Appendix 12: Morisky medication adherence scale (83-85)[3]

This is a generic adherence scale and the name of the health concern can be substituted in each question item.

You indicated that you are taking medication(s) for your (identify health concern, such as "high blood pressure"). Individuals have identified several issues regarding their medication- taking behavior and we are interested in your experiences. There is no right or wrong answer. Please answer each question based on your personal experience with your [Mental Health]
medication.

(Please mark your response below)

	No=1	Yes=0
1. Do you sometimes forget to take your [health concern] medication(s)?		
2. People sometimes miss taking their medications for reasons other than forgetting. Thinking over the past two weeks, were there any days when you did not take your [health concern] medication(s)?		
3. Have you ever cut back or stopped taking your medication(s) without telling your doctor, because you felt worse when you took it?		
4. When you travel or leave home, do you sometimes forget to bring along your [health concern] medication(s)?		
5. Did you take your [health concern] medication(s) yesterday?		
6. When you feel like your [health concern] is under control, do you sometimes stop taking your medication(s)?		
7. Taking medication(s) every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your [health concern] treatment plan		
8. How often do you have difficulty remembering to take all your medication(s)? Never/Rarely 4 Once in a while 3 Sometimes 2 Usually 1 All the time 0	Please circle answer	

[3] Use of the ©MMAS is protected by US copyright laws. Permission for use is required. A License Contract is available from: Donald E. Morisky, ScD, ScM, MSPH, Professor, Department of Community Health Sciences, UCLA School of Public Health, 650 Charles E. Young Drive South, Los Angeles, CA 90095-1772, dmorisky@ucla.edu.

9.13 Appendix 13: Treatment burden questionnaire (65)

The following questions are about the potential burden that your treatment(s) have on your life. For each question, **please select the ONE answer** that comes closest to the way you feel about your treatment. **When thinking about your treatment(s), how would you rate the following?**

a) The impact and inconvenience caused by your treatment or medication (e.g. taste, shape or size of your tablets or use of puffers, ointments, chemotherapy etc.)										
0	1	2	3	4	5	6	7	8	9	10
No burden					Some burden					Considerable burden
b) The number of times you have to take your medication every day										
0	1	2	3	4	5	6	7	8	9	10
No burden					Some burden					Considerable burden
c) The things you do to remind yourself to take your daily medication and/or to manage your treatment when you are not at home										
0	1	2	3	4	5	6	7	8	9	10
No burden					Some burden					Considerable burden
d) The specific requirements of taking your medication (e.g. taking it at a specific time of the day or meal, not being able to do certain things after taking it – like driving or lying down)										
0	1	2	3	4	5	6	7	8	9	10
No burden					Some burden					Considerable burden
e) The side-effects of your medication, treatment and medical tests										
0	1	2	3	4	5	6	7	8	9	10
No burden					Some burden					Considerable burden
f) Medical tests and other exams (such as frequency, time needed and inconvenience)										
0	1	2	3	4	5	6	7	8	9	10
No burden					Some burden					Considerable burden
g) Self-monitoring (e.g. taking your blood pressure or measuring your blood sugar yourself; think about the frequency, time needed and inconvenience of this monitoring)										
0	1	2	3	4	5	6	7	8	9	10
No burden					Some burden					Considerable burden
h) The frequency and time needed for treatment visits										
0	1	2	3	4	5	6	7	8	9	10
No burden					Some burden					Considerable burden
i) Arranging appointments, scheduling visits to doctors and healthcare professionals										

and arranging medical tests										
0	1	2	3	4	5	6	7	8	9	10
No burden					Some burden					Considerable burden
j) The burden associated with taking care of paperwork from health insurance agencies, welfare organisations, hospitals and/or social care services										
0	1	2	3	4	5	6	7	8	9	10
No burden					Some burden					Considerable burden
k) The constraints associated with changing your diet (e.g. not being allowed to eat certain foods, quitting alcohol or quitting smoking)										
0	1	2	3	4	5	6	7	8	9	10
No burden					Some burden					Considerable burden
l) The burden associated with the lifestyle (e.g. recommendations from your healthcare professionals for regular physical exercise, relaxation or different sleep habits)										
0	1	2	3	4	5	6	7	8	9	10
No burden					Some burden					Considerable burden
m) The impact of your healthcare on your social relationships (e.g. needing assistance or being concerned about taking your medication in front of people)										
0	1	2	3	4	5	6	7	8	9	10
No burden					Some burden					Considerable burden
n) The financial impact of your medication and treatment (e.g. paying for medication & healthcare professional fees, paying private health insurance premiums, losing your income, etc.)										
0	1	2	3	4	5	6	7	8	9	10
No burden					Some burden					Considerable burden
o) The impact of needing healthcare: 'Needing frequent healthcare reminds me of my health problems'										
0	1	2	3	4	5	6	7	8	9	10
No burden					Some burden					Considerable burden

9.14 Appendix 14: Organisation of themes

Thematic Level	Theme One	Theme Two	Theme Three	Theme Four
Overarching theme	Understanding of illness and recovery	Positive outcomes of treatment	Acceptance of treatment burden	Communication pathways
Sub categories	Beliefs about illness, Need for treatment	Clozapine as a long term medication, Regular GP contact	Self-management, Clozapine's adverse effects	GP & psychiatrist, Consumer & clinicians
Codes	Wellness, Recovery, Control, Insight	Effects of clozapine, GP relationship, Recovery	Routine, Adherence, Responsibility, Concerns	Level of self-involvement, Trust, Level of satisfaction

9.15 Appendix 15: Royal Brisbane and Women's Hospital ethics

Queensland Government

Royal Brisbane & Women's Hospital
Human Research Ethics Committee

Metro North
Hospital and Health Service

Enquiries to: Ann-Maree Gordon
A/Coordinator
Telephone: 07 3646 5490
Facsimile: 07 3646 5849
File Ref: HREC/14/QRBW/48
Email: RBWH-Ethics@health.qld.gov.au

A/Prof Ian Coombes
Department of Pharmacy
Level 1, Ned Hanlon Building
Royal Brisbane & Women's Hospital
Herston Q 4029

Dear Dr Coombes,

Re: Ref Nº: HREC/14/QRBW/48: Clozapine and concomitant medications: Assessing the completeness and accuracy of medication records for people prescribed clozapine under shared care arrangements

Thank you for submitting the above research project for single ethical review. This project was considered by the Royal Brisbane & Women's Hospital Human Research Ethics Committee (RBWH HREC) **(EC00172)** at its meeting held on 10 February, 2014.

I am pleased to advise that the RBWH Human Research Ethics Committee has granted ethical approval of this research project.

The nominated participating site for this project is:

- Royal Brisbane & Women's Hospital, Qld

This letter constitutes ethical approval only. This project cannot proceed until separate research governance authorisation has been obtained from the CEO or Delegate of the Royal Brisbane & Women's Hospital under whose auspices the research will be conducted.

The approved documents include:

Document	*Version*	*Date*
Covering Letter		25 January 2014
Application: NEAF *(Submission Code: AU/1/3A76113)*	2.1 (2013)	24 January 2014

Royal Brisbane & Women's Hospital
Level 7 Block 7
Butterfield Street, Herston Qld 4029
Australia

Telephone +61 7 3646 5490
Facsimile +61 7 3646 5849
www.health.qld.gov.au/rbwh/research/hrec.asp

Approval

Document	*Version*	*Date*
Protocol	1.1	20 January 2014
Participant Consent Form - Part One	1.1	20 January 2014
Participant Information Sheet - Part Two	1.1	20 January 2014
Participant Consent Form - Part Two	1.1	20 January 2014
Interview Process and Topic Guide	1.1	20 January 2014
Initial Health Review		
First Contact Letter to consumers on shared-care	1.1	20 January 2014
Letter to shared-care GP	1.1	20 January 2014
Letter to shared-care Pharmacies	1.1	20 January 2014
Curriculum Vitae of Ian Coombes		
Curriculum Vitae of Prof Amanda Wheeler		
Curriculum Vitae of Dr Vikas Moudgil		
Curriculum Vitae of Susan Patterson		
Letter and articles from Dr Susan Patterson regarding Question 8 of the HREC Review		
Article: *"Decisional Capacity for Informed Consent in Schizophrenia Research"*		
Article: *"Decisional Capacity of Patients with Schizophrenia to Consent to Research: Taking Stock"*		
Response to Request for Further Information		05 March 2014
Participant Information Sheet - Part One	1.1	20 January 2014
Data Collection Sheet	1.1	20 January 2014

Approval of this project from the RBWH HREC is valid from **21.03.2014** to **21.03.2017** subject to the following conditions being met:

- The Coordinating Principal Investigator will immediately report anything that might warrant review of ethical approval of the project.
- The Coordinating Principal Investigator will notify the RBWH HREC of any event that requires a modification to the protocol or other project documents and submit any required amendments in accordance with the instructions provided by the HREC. These instructions can be found at http://www.health.qld.gov.au/rbwh/research/hrec.asp.
- The Coordinating Principal Investigator will submit any necessary reports related to the safety of research participants in accordance with the RBWH HREC policy and procedures. These instructions can be found at http://www.health.qld.gov.au/rbwh/research/hrec.asp.

- In accordance with Section 3.3.22 (b) of the National Statement the Coordinating Principal Investigator will report to the RBWH HREC annually in the specified format, the first report being due on **21.03.2015** and a final report is to be submitted on completion of the study. These instructions can be found at http://www.health.qld.gov.au/ohmr/html/regu/reporting_templates.asp.

- The Coordinating Principal Investigator will notify the RBWH HREC if the project is discontinued before the expected completion date, with reasons provided.

- The Coordinating Principal Investigator will notify the RBWH HREC of any plan to extend the duration of the project past the approval period listed above and will submit any associated required documentation. Instructions for obtaining an extension of approval can be found at http://www.health.qld.gov.au/rbwh/research/hrec.asp.

- The Coordinating Principal Investigator will notify the RBWH HREC of his or her inability to continue as Coordinating Principal Investigator including the name of and contact information for a replacement.

- A copy of this ethical approval letter together with completed Site Specific Assessment (SSA) and any other requirements must be submitted by the Coordinating Principal Investigator to the Research Governance Office at the Royal Brisbane & Women's Hospital in a timely manner to enable the institution to authorise the commencement of the project at its site.

- Should you have any queries about the RBWH HREC's consideration of your project please contact the HREC Coordinator on 07 3646 5490. The RBWH HREC's Terms of Reference, Standard Operating Procedures, membership and standard forms are available from http://www.health.qld.gov.au/rbwh/research/hrec.asp.

The RBWH HREC wishes you every success in your research.

Yours sincerely,

Dr Conor Brophy
Chairperson RBWH Human Research Ethics Committee
Metro North Hospital and Health Service
21.03.2014

This HREC is constituted and operates in accordance with the National Health and Medical Research Council's (NHMRC) *National Statement on Ethical Conduct in Human Research (2007)*. The processes used by this HREC to review research proposals have been certified by the National Health and Medical Research Council.

Royal Brisbane and Women's Hospital
Metro North Hospital and Health Service

Queensland Government

Enquiries to: Prof Keshwar Baboolal Executive Director MNHHS-RBWH & or delegate
Professor Lawrie Powell Director of Research MNHHS-RBWH CACR
Phone: 07 3646 2352

A/Prof Ian Coombes
Department of Pharmacy
Level 1 Ned Hanlon Building
RBWH, Herston QLD 4029

Dear A/Prof Ian Coombes

Re: HREC/14/QRBW/48: Clozapine and concomitant medications: Assessing the completeness and accuracy of medication records for people prescribed clozapine under shared care arrangements

Thank you for submitting your research protocol approved by the Royal Brisbane and Women's Hospital HREC on the 21 Mar 2014. I am pleased to inform you that authorisation has been granted for this study to be conducted at the MNHHS-Royal Brisbane and Women's Hospital. Your trial meets the principles and practices set out in the Australian Code for the Responsible Conduct of Research (2007 Universities Australia) and the ICH Harmonised Tripartite Good Clinical Practice (GCP) Guidelines.

All of the documents approved by above mentioned HREC are accepted for the MNHHS-RBWH site.

When submitting electronically an HREC approved amendment to the RGO please provide the description and the rationale for it and attach the related documents that have been approved. This will assist in the governance review to see if any further documentation is required for our MNHHS-RBWH site.

If you have any questions relating to this authorisation please contact the Research Governance Officer on 3646 8579.

I wish you continued success with your research.

Yours sincerely

Professor Keshwar Baboolal
Executive Director &/or Delegate
Professor Lawrie Powell AC MD PhD
Director of Research, MNHHS-RBWH, Centre for the Advancement of Clinical Research
3/6/14

cc.

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Fax
(07) 3646 4240

9.16 Appendix 16: Griffith University ethics approval

GRIFFITH UNIVERSITY HUMAN RESEARCH ETHICS COMMITTEE

03-Apr-2014

Dear Prof Wheeler

I write further to the additional information provided in relation to the conditional approval granted to your application for ethical clearance for your project "PR: Clozapine and concomitant medications: Assessing the completeness and accuracy of medication records for people prescribed clozapine under shared care arrangements." (GU Ref No: HSV/10/14/HREC).

This is to confirm receipt of the remaining required information, assurances or amendments to this protocol.

Consequently, I reconfirm my earlier advice that you are authorised to immediately commence this research on this basis.

The standard conditions of approval attached to our previous correspondence about this protocol continue to apply.

Regards

Policy Officer

Office for Research

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