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Effectiveness of a structured behavioural communication intervention programme in enhancing adherence amongst outpatients with mental illness at Tara Outpatient Clinic: a randomised prospective descriptive study

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EFFECTIVENESS OF A STRUCTURED BEHAVIOURAL COMMUNICATION INTERVENTION PROGRAMME IN ENHANCING ADHERENCE AMONGST OUTPATIENTS WITH MENTAL ILLNESS AT TARA OUTPATIENT CLINIC: A RANDOMISED PROSPECTIVE DESCRIPTIVE STUDY

By

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Declaration

I, **Diana Sheila Lutaaya** hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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List of abbreviations

SMS:	Short message service
SADAG:	South African Depression and Anxiety Group
RSAP:	Reminder and Support Adherence Program
WHO:	World Health Organisation
STEP-BD:	Systematic Treatment Enhancement Program for Bipolar Disorder
AUD:	Alcohol use disorder
MEMS:	Medication event monitoring system
RIA:	Research ICT Africa
MAQ:	Morisky Green Adherence Questionnaire
CI:	Confidence Interval
P:	Probability
BDI:	Becks Depression Inventory
CAD:	Cumulative Abstinence Duration
SUD:	Substance use disorder
CBT:	Cognitive Behaviour Therapy
MMAS-8:	Morisky 8-Item Medication Adherence Scale
AppTot:	number of visits out of a maximum of 6

ScripTot: number of pickups out of a maximum of 6

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Abstract

Background

Poor adherence amongst patients with mental disorders continues to pose a major treatment challenge in psychiatry. Despite the presence of innovative agents with fewer disabling side effects, patients' failure to comply with their prescribed medication causes failure of the expected benefits.

Objectives

An adherence study was undertaken at the Tara outpatient clinic in collaboration with the South African Depression and Anxiety Group (SADAG). The study explored the socio demographic factors associated with non-adherence and helped to determine whether a short message service (SMS) based intervention program would be useful in improving clinic attendance and medication adherence.

Methods

The research project was a prospective descriptive double–blind study, with participants being randomly assigned to the 'treatment as usual' group or the intervention group. The participants in the 'treatment as usual' group continued to receive their regular follow up consultations with the treatment team at the Tara Outpatient Clinic. The trial took place over a period of six months.

The study group consisted predominantly of middle-aged white women who were unemployed and fell into the lowest income group bracket. The predominant diagnosis was a mood disorder which had no significant effect on adherence.

Results

The study showed that daily treatment reminders via SMS may not have enhanced overall adherence to treatment however it did manage to arrest the decline in adherence. It also showed a decline in adherence in the 'treatment as usual' group whereas there

was no change in adherence in the treatment group. It found a significant relationship between substance use disorder and adherence. There was a decline in adherence in those with a substance use disorder in the 'treatment as usual' group, whereas the treatment group showed no change in adherence.

Conclusion

The SMS adherence program did not improve adherence rates but did stabilize attrition rates. An effective adherence program may decrease the rates of relapse and readmission and will in the long term decrease the burden of disease on our health care services.

Chapter 1

1.1 Introduction

Poor adherence amongst patients with mental illnesses continues to pose a major treatment challenge. Despite the presence of newer innovative agents with fewer and less disabling side effects, failure of patients to comply with their prescribed medication is one of the causes of the failure of materialisation of the expected benefits of these new medications. Non-adherence to medication is associated with an increased risk of relapse, hospitalisation and a poorer prognosis [1, 2, 3].

An adherence study was undertaken at the Tara Outpatient Clinic, a tertiary psychiatric hospital situated in Johannesburg that provides both inpatient and outpatient psychiatric services. A study on adherence in this setting set out to explore the socio demographic factors associated with non-adherence and helped to determine whether a Short Message Service (SMS) based intervention program would be useful in improving clinic attendance and medication adherence.

This study was done in collaboration with the South African Depression and Anxiety Group (SADAG). SADAG is Africa's largest mental health support and advocacy group. It is a non-profit organisation that was established 18 years ago and provides counselling services, mental health awareness programs, media campaigns and rural outreach initiatives to patients, families and communities across South Africa. SADAG has developed a Reminder and Support Adherence Program (RSAP) that serves to remind patients to take their medication and in addition offers free ongoing telephonic support. The program includes weekly phone calls, free telephonic counselling, reminder SMS messages, brochures and information to improve mental health literacy. This program was specifically created for the study and is not currently available at the Tara outpatient clinic. In partnership with SADAG, the Tara Outpatient Department carried out a study to determine the effectiveness of such a structured behavioural and communication intervention program on adherence.

1.2 Adherence

Adherence can be challenging to define as it has different meanings across various studies. The World Health Organisation (WHO) defines adherence as the extent to which a person's

behaviour, such as taking medication, corresponds with the agreed recommendations from a health care provider[4]. Adherence is the preferred term used to describe a person's behaviour as opposed to compliance, as it is viewed as a more positive and proactive role that patients adopt regarding their health. Medication adherence falls in a spectrum as it ranges from individuals who choose not take their medication to those who take it as prescribed[5]. In order to better define adherence, it has been categorically outlined to better encompass its wide range of meanings. Full adherence is present when there is complete adherence to all the providers' instructions. Selective adherence occurs when the patient adheres with some but not all the instructions. When a patient chooses to take their treatment only during certain periods (e.g. treatment is not taken when abusing substances), this is referred to as intermittent adherence. Late adherence is when patients are initially non-adherent and then later become adherent. This increased adherence over time may be as a result of improved insight into illness or a specific intervention effort utilized. Abuse occurs when a patient takes more than is required of a certain medication. This however does not happen often and thus more of the concern lies in patients who take less than is prescribed. Behavioural non-adherence occurs when patients are adherent to non-medication aspects of treatment such as presenting for appointments or following a recommended lifestyle[6].

Non-adherence to medication is prevalent in psychiatric populations and is closely related to high rates of relapse and re-admission[1, 2]. Multiple factors are thought to play a role in non-adherence ranging from simply forgetting to take medication to the related side effects[5]. The most stated reasons for intentional non-adherence to antipsychotic medication are side effects (50%), being symptom free (50%) and believing that a smaller dose would be fine (42%)[2].

1.3 Rates of Non-adherence

A high prevalence of non-adherence was found amongst patients treated for a range of chronic illnesses including hypertension and gastro-oesophageal reflux disease with rates of up to 45% being reported across all conditions[5]. Patients with mental illness were however found to have higher rates of non-adherence in comparison to those with organic illness[5, 7]. A review of

medication adherence in psychiatric and organic disorders done from 1975-1996 reported that the mean amount of prescribed medication taken to be 58% for patients prescribed antipsychotics, 65% for those prescribed antidepressants and 76% for those prescribed medication for physical disorders[5]. There are several factors that make adherence more so challenging in mental illness as some factors are more unique to this group. They include a lack of illness awareness, social isolation, the direct impact of symptoms and stigma[5]. Patients with schizophrenia have rates of medication non-adherence approaching up to 50% during the first year following discharge and non-adherent patients have an average risk of relapse that is 3.7 times greater than adherent patients[1]. Antipsychotic medication has been found to be effective in preventing relapse, especially after a first episode. It has however been found that between 35-75% of patients stop their antipsychotic medication within 1-2 years of follow-up[2].

Rates of medication non-adherence among bipolar patients were also found to be high with up to 60 % of patients discontinuing their medication[5]. High rates of non-adherence have also been found amongst psychiatric patients who abuse illicit substances with an increased use predominating in patients who have been diagnosed with bipolar disorder. Co-morbid substance use and bipolar disorder have displayed rates of non-adherence approaching 14-65%[5]. The Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) study showed that substance abuse predicted poorer adherence with subsequent lower social functioning. [5.] Little research has been done on interventions that can be used to improve adherence amongst bipolar patients.

Depression and co-morbid alcohol use disorder (AUD) have also been found to co-occur at higher rates than expected with associated non-adherence. It was found that 80% of patients with AUD complained of depressive symptoms at some point in their lives[8]. According to the WHO, depression and co-morbid AUD are the leading causes of disability in the world. These individuals tend to pose a greater challenge with regards to treatment as they would have more severe symptoms than an individual with a single disorder[8]. This group has also been found to have numerous factors associated with treatment challenges and these include a higher likelihood of suicide attempts and completed suicides, poorer quality of life and a greater economic burden to society due their higher use of treatment services[8]. The cost of nonadherence has placed a great

strain on not only the health care system but also on the family members resulting in caregiver burn out. Relapses disrupt psychosocial and vocational adjustment, increase the risk of hospitalisations, arrest, violence, substance abuse and suicide[2, 5].

1.4 Factors Associated with Non-adherence

Forgetting to take one's medication has been highlighted as one of the most common reasons for non-adherence[2, 4]. This emphasizes that there are both intentional and unintentional factors associated with non-adherence. Intentional non-adherence occurs when a patient deliberately decides not to take their medication as they may have decided that the disadvantages of medication outweigh the advantages. Unintentional non-adherence encompasses various reasons such as not understanding instructions given by the health care provider on medication-taking and difficulty collecting medication due to travel or financial barriers. Both types of non-adherence may occur in the same patient thus illustrating the need for a use of a range of interventions to improve non adherence[5]. The use of SMS reminders solely would most likely benefit the individual who simply forgets to take their medication as opposed to the individual who has a negative attitude towards their medication[2]. The combination of reminders and motivational content may maximise the benefits of SMS based interventions[2].

Poor adherence to medication amongst patients with schizophrenia can be as a result of several factors including, poor insight, lack of routine, lack of symptoms, poor therapeutic alliance, poor family support, concern about stigma and persistent symptoms or side effects. Although side effects have often been cited as a significant factor for non-adherence, many patients have stated that a lack of knowledge about their medication is often a significant contributing factor. It has been found that if a patient perceives a drug as beneficial and important to their health, they are more likely to comply with their set regimen despite it causing side effects. A patient however with little insight and who sees no benefit of the drug to their health is more likely going to discontinue their medication at the first sign of side effects. This highlights that a patient's attitude to their medication may play a greater influence in promoting medication adherence.

Bipolar disorder has also been associated with high rates of non-adherence. Factors that predict non- adherence include a history of non-adherence, high complexity of treatment regimen, poor

insight into illness, negative beliefs about medication, the presence of psychotic features and a personality disorder[5]. The greatest predictor of nonadherence amongst bipolar patients is however the co-morbid presence of substance use disorder as mentioned earlier[5]. Both bipolar disorder and substance use disorder, separately, are associated with high rates of non-adherence with the combination of both further increasing the risk. Various reasons have been documented for non-adherence amongst patients with comorbid substance use and bipolar disorder. It was found that this group of patients was more vulnerable to non-adherence because they were more inclined to 'self-medicate' with substances in order to improve their mood symptoms than take their medication. Even though many of these individuals may recognize the benefits of their medication, many are reluctant to combine their medication with illicit substances for fear of negative consequences and thus chose to discontinue their treatment[5]. The use of illicit substances has been shown to exacerbate the symptoms of bipolar disorder often leading to a relapse and possible re-hospitalisation. Interactions between illicit substances and medication may also increase the side effects resulting in a reluctance to continue with medication. Other negative factors that are related to the co-morbid use of substances in bipolar disorder include an earlier age of onset, higher frequency of mood episodes, greater symptom severity and impairment, shorter time to relapse and higher rates of suicide attempts[5]. The combination of a dual diagnosis and non-adherence shortens the time between hospital discharge and re-admission [9].

Lack of support from family members and a poor therapeutic alliance with health care providers has also been shown to contribute to non-adherence amongst patients. Having an established support system in place encourages adherence however what has been found amongst mental health care users with co-morbid substance use, is a fractured family resulting from ongoing drug use. Re-current relapses and hospitalisations results in care giver burn out and ultimately disinterest in the welfare of the patient. This furthermore worsens the pattern of non-adherence as there is a poor motivation for change. Ongoing substance use furthermore interferes in the social support structure. An established therapeutic alliance between the patient and the health care provider also needs to be present as this encourages the patient to maintain follow-up visits

at their clinic. The patient's attitude to their medication has been found to be closely linked to their relationship with their health care provider[5]. A positive relationship with a good communication medium is more likely going to encourage medication adherence. Other factors such as having a single, consistent health care provider and ensuring sufficient time during appointments to discuss the overall treatment plan are important in ensuring adherence. Our settings however do not allow for this as often the clinics are over booked and patients present on incorrect appointment days as they have failed to reschedule missed appointments. The staff are often overworked and there is a high turnover of health care providers in clinics thus preventing continuity of care. All these factors hinder the development of a positive therapeutic alliance[5].

Missed appointments can compromise the quality of psychiatric care and contribute to increased health care costs[10]. They also discourage patients from taking their medication. Non-attendance has been associated with transport difficulties, conflict with other appointments, family responsibility and simply forgetting one's appointment. In a study done on the use of SMS reminders to improve non- adherence at an internal medicine outpatient clinic, they found that the non-attendance rate was much higher amongst patients who had their first visit compared with those who had prior contact with the hospital. This finding is in line with other studies done and suggests that patients may have formed a therapeutic alliance with their provider thus making them more motivated to attend their appointments[11]. Demographic factors such as age, sex and nationality were found not to influence attendance rates in one study however another study found that the male gender was associated with an increase in risk of intentional nonadherence. This study however also found that the male gender was associated with increased substance use and lower socio economic settings. [1, 2].

1.5 Measures of Adherence

Much research has been done on strategies to improve and measure adherence amongst patients. Methods of measurement are often divided into objective and subjective strategies. Subjective measures include validated questionaries' that can either be administered by the

clinician or patient themselves. They are often the easiest to use and cost efficient however they have poor validity and may underestimate non-adherence. Objective measures provide a more accurate method of measuring adherence. The medication event monitoring system (MEMS) is the reference standard in adherence studies[5]. The MEMS medication bottle cap is equipped with a microprocessor that records each time the bottle is opened. The disadvantage is that one is unable to monitor whether the tablet was ingested following removal from the container. This form of monitoring is also costly and time consuming despite the development of real-time wireless monitoring of medication. The pill count may be more cost effective than MEMS however it would require more regular follow-up and it would be difficult to account for the pills that may have been discarded by the patient.

Biological markers can also be used to objectively measure adherence. In psychiatry, mood stabilisers can be monitored as they are available clinical biological markers however there are not available for antipsychotics. There is little data available on the therapeutic plasma levels of most second-generation antipsychotics. With regards to mood stabilisers the time at which the plasma levels are monitored is important because if measured at incorrect times this may give misleading results. Furthermore, plasma levels only provide information about medication adherence in the days immediately prior to the sampling time. If patients were to attempt to conceal non-adherence, they could do this by taking a loading dose prior to the plasma sampling time. Pharmacokinetic drug interaction, medication metabolism and smoking may also interfere with the accuracy of the results. Several studies have compared the use of plasma levels as a tool of measuring adherence against other objective methods and have found this method to be unreliable due to mixed results. In one study, a non-adherence rate of 23% and 40% was found with plasma levels and the pill account, respectively. However another study showed a nonadherence rate of 51% and 37% with plasma levels and MEMS respectively[5].

Another method of measuring adherence would be to observe the intake of oral medication however this can only be done in an inpatient setting. This method also has its set of challenges as patients have found methods of concealing medication intake. These include hiding medication under the tongue and spitting it out later[5].

The electronic 'ingestible event marker' that forms part of a digital health feedback system is a most recent introduction to the objective measurement of adherence. A non-toxic digital ingestion sensor, approximately 1mm square, is embedded into a tablet[5]. Once it has been activated by gastric fluids, the ingested sensor wirelessly sends data to a small external monitor that is a skin patch device worn by the patient. It can record the date and time of ingestion[5]. The sensor becomes inactive after several minutes of transmission and is then eliminated in the faeces. A small study (n=28) done to determine its feasibility and safety amongst patients with schizophrenia and bipolar found the system to be safe and accurate. It offers superior advantage over the MEMS as it can record the ingestion of the tablet. It is however a costly measure and further larger studies need to be done to assess its feasibility[5].

1.6 Interventions to Improve Adherence

Psychoeducation is an intervention that has been found to increase a patient's understanding of their illness. This is usually carried out during clinic appointments or in structured sessions. Individual patients have their own beliefs, perceptions and concerns around their illness and medication-taking. A better understanding of a patient's outlook would assist in helping to educate them around misconceptions regarding medication. Patients who are involved in their treatment plan are more likely to be motivated to adhere to treatment despite the accompanying side effects as they are aware of the benefits of adherence. It is important to enquire about side effects as some patients may be reluctant to volunteer this information and opt to rather discontinue with treatment. A good therapeutic alliance encourages patients to speak about their concerns around treatment. Managing side effects with patients as they arise has also been found to be very crucial. This may include reducing the dose, adding a drug to treat the side effects, changing the schedule or negotiating a medication change. Many of the side effects however arise during medication initiation and dose titration, so making a patient aware of this and reassuring them during this period helps to discourage discontinuation of medication.

Polypharmacy is likely to worsen side effects due to drug to drug interaction so adhering to a simple schedule may encourage compliance. Studies have shown that although psychoeducation does result in increased knowledge of the patients' illness, it does not however result in a change

in adherence. This highlights that a combination of interventions needs to be utilized in order to encourage adherence.

Behavioural interventions have been reported to improve adherence to medication. These may include building of life skills and re-enforcement strategies. Other methods include motivational interviewing, patient and family psychoeducation and cognitive and behavioural approaches. Behavioural approaches that have been used include reminders, self-monitoring tools and cues. They have been found to be easy to implement however have not shown overwhelming success in improving adherence[1].

1.7 Mobile Phones

One of the behavioural methods that have been explored includes the use of mobile phones in reminding individuals to adhere to medication and clinic appointments. This method also allows for a method of communicating relevant educational information to patients.

Mobile phones are widely used across different age and social groups and are the most widely used method for communication. SMS texting has been found to be most popular among the younger age groups[3]. Patients aged between 15 and 25 were found to be the least likely to attend clinic appointments however they also have been identified as the group that makes the greatest use of mobile phones[12, 13]. A study showed that missed appointment rates averaged between 40-60% amongst adolescents with mental problems thus placing a significant barrier to adequate treatment of this particular age group. The use of text message reminders to improve outpatient therapy attendance would thus prove useful as this age group shows an increased propensity for the use of cell phones and texting and furthermore this popularity spans across racial/ethnic groups and social class[14]. Text messaging amongst adolescents appears to have surpassed phone calls as the preferred mode of communication.

Household surveys conducted by Statistics South Africa and Research ICT Africa (RIA) showed an increase in ownership of mobile phones in South Africa from 32.3% in 2001 to 72.9% in 2007 [8].

In an era where the majority of the South African population has access to mobile phones, the use of mobile phones may be an inexpensive way of encouraging adherence to medication and appointment dates[7].

Studies have been done on the perceptions of individuals to text-based messages regarding adherence. They have shown a positive response to text-based messages. One study looked at the perceptions of patients with AUD and co-morbid depression on the usefulness of supportive text-based messages. Many patients stated that these text-based messages played a useful role in helping them remain abstinent from alcohol and preventing relapse[15].

Mobile messages have many advantages over other methods as they are convenient, inexpensive and can reach the intended individual immediately [1, 4,2,11,13,10]. They are personal and so enhance privacy for the intended individual[11]. Various methods including posted letters, automated and personalized telephone calls have been shown to improve non-attendance rates however they have been found to be labour intensive[3]. Not only can mobile messaging be used to improve medication adherence, but it can also improve appointment adherence and assist with health promotion[4, 11]. It has been shown to be effective in various settings including primary care clinics and emergency departments[11]. It also has the advantage of being location independent, meaning that the health care provider is not limited to a single location8.

SMS reminders can easily be integrated into a hospital's existing information technology (IT) system to allow for the sending of automated SMS reminders[11]. As it is an automated service, very little staff involvement is required[3]. There are other potential uses for SMS technology. It can be used for more interaction with patients by allowing patients to reply to reminders by texting their reply, cancellation or rebooking of an appointment[3, 10]. However in the South African setting many public hospitals do not have an established electronic database and thus this may pose a challenge for this particular kind of intervention.

Other methods that have been studied to remind patients about their appointments include personal phone calls, automated phone calls and mailed letters. Some of these methods have proven to be effective however the limitations with telephone reminders are that they are costly and repeated calls may be needed to reach the patients[11]. Mobile phones may provide greater access to the intended population.

1.8 Results from Studies

Failure to attend scheduled appointments falls along the continuum of non-adherent behaviour and few studies have explored the use of SMS based prompts in encouraging clinic attendance and medication adherence.

Other medical specialities have shown interest in the use of mobile text messaging to improve adherence to medication. A cluster randomised trial was done in China looking at the effectiveness of text messaging and medication monitoring to improve medication adherence to tuberculosis treatment amongst patients with tuberculosis. The study found that reminders from medication monitors reduced poor adherence by between 40 and 50% whereas text message reminders had no effect [16].

A study was done at the Helen Joseph hospital outpatient department looking at the communication and adherence of psychiatric patients. One of the objectives of the study was to investigate medication adherence and attendance at baseline and after the 'Reminder and Support Adherence Program' (RSAP) was implemented. The RSAP consists of focused communication interventions, including weekly phone calls; free telephonic counselling; reminder SMS-messages; brochures and information; SMS reminders for workshops, support groups and press notifications; an online website with information; monthly newsletters; and free support groups in different regions[17]. The study found that the study group attended 74% of booked visits compared to 66% of the control group. The booking ratio for the study group pre and post intervention was observed, showing that there was no significant change between the two periods. This implies that the RSAP may not have resulted in an improvement in attendance rate of the participants in the program[17].

A study done to evaluate the efficacy of SMS reminders in patients with schizophrenia with cognitive impairment showed that there was no change in adherence. It was suggested that combining prompting with interventions that enhance motivation may have been helpful[6]. Another similar study done amongst patients with schizophrenia showed that SMS based interventions were more likely to benefit patients who had simply forgotten to take their

treatment and would be unhelpful to those who refuse to take it because they lack acquired routines, are unaware of the benefits or have cognitive deficits[1].

A similar study was done on a short message service (SMS) - based strategy for enhancing adherence to antipsychotic medication in schizophrenia. This study was conducted in Spain and was an open- label, controlled, 6-month study with clinically stabilized outpatients with schizophrenia. Patients assigned to the intervention group received daily SMS reminders to take their medication for 3 months. Self-reported medication adherence was determined using the Morisky Green Adherence Questionnaire (MAQ). An improvement in adherence was observed amongst patients receiving SMS text messages compared with the control group. The mean change in MAQ total score from baseline to month 3 was -1.0 (95% confidence interval (CI) -1.02, -0.98) and -0.7 (95% CI -0.72, -0.68), respectively (P=0.02).

A study was done on the use of supportive text messaging for depression and comorbid alcohol use disorder. The study included 54 participants with a DSM IV diagnosis of unipolar depression and AUD who had completed an in-patient dual diagnosis treatment program. 26 of these patients were randomized to receive twice daily supportive messages and 28 were scheduled to receive' thank you text messages' fortnightly for three months. The study showed that there was a statistically significant difference in the three-month Becks Depression Inventory (BDI-II) scores between the intervention and treatment group. The study also showed a trend for a greater Cumulative Abstinence Duration (CAD) in the text message group than the control group[8]. The trial has shown the supportive text messaging added to standard care has the potential to improve outcomes in patients with co-morbid depression and alcohol dependency[8].

Adolescents with mental illness have been shown to have high rates of missed appointments thus contributing to the barriers to treatment. Adolescent characteristics that were shown to be associated with non-attendance included ethnic minority status, greater symptom severity, conduct problems and Attention Deficit/Hyperactivity Disorder (ADHD). A pilot study was done on the usefulness of text message reminders to improve outpatient therapy attendance amongst adolescents. A sample of 24 adolescents (aged between 13 and17) receiving reminder text messages was compared to a control group (n=24) who received treatment as usual. Adolescents

who received treatment reminders attended significantly more of their sessions (65%) compared to the control group (49%). A limitation that was encountered in the study was that the participants in the treatment group who failed to receive reminders reported a damaged or lost phone[14].

As mentioned earlier, there are many challenges encountered when addressing non-adherence in individuals with co-morbid bipolar disorder and SUD. Research has found that the use of psychotherapy may be useful. Unfortunately, there are few studies that have been done to investigate the useful approaches to improving non-adherence in bipolar disorder. Studies done on adherence in patients with co-morbid bipolar and substance use disorder show that treatment strategies such as cognitive behaviour therapy (CBT), psychoeducation and family based interventions may play an important role in adherence.

A study done on CBT in bipolar disorder patients with substance use disorder, whereby 45 patients were recruited to receive group CBT (12-20 sessions) or outpatient pharmacotherapy and other community treatments showed that after a period of 6 months those receiving CBT showed a greater improvement in addiction severity, manic symptoms and percentage of months abstinent. There was however no group difference in self-reported medication adherence although overall adherence in the group was good[5]. There is much research that still needs to be done to explore strategies needed to improve adherence in this group.

1.9 Conclusion

Few studies have been done on the long-term effectiveness of SMS based reminders. Many studies have shown that the use of text messaging improves adherence, however there is a scarcity of studies investigating the sustained effects following cessation of text based interventions. [18]. One study showed that the effects of sending SMS reminders seemed to attenuate 3 months after stopping them[1]. A study was done on the six-month outcome of a randomized trial of supportive text messaging for depression and co-morbid alcohol use disorder. The primary study compared the use of support text messaging between a treatment and control group over a three-month period. The study showed that there was a statistically significant difference in the three-month Becks Depression Inventory (BDI-II) scores between the

intervention and treatment group. The study also showed a trend for a greater Cumulative Abstinence Duration (CAD) in the text message group than the control group[8].

This follow-up study however showed that there was no statistically significant difference in the six months BD-II and CAD between the intervention and control group. The patients in the intervention group however had significantly higher days to the first drink compared to those in the control group. This suggests that the effects of the intervention were not sustained beyond the period that the patients were receiving the intervention[18]. This raises the question of whether text messages would only be useful if carried out over a longer period.

Chapter 2

2.1 Aims and Objectives

The purpose of this study was to determine whether a reminder and support adherence program (RSAP) at Tara Outpatient Clinic can improve clinic attendance and medication adherence. The objectives of the study were to determine whether socio-demographic factors are associated with non-adherence, to examine whether the relationship between the diagnosis, duration of illness and dosing schedule have an effect on adherence.

2.2 Methods

The research project was a prospective descriptive double–blind study that was conducted at the Tara Outpatient Clinic. The sampling method used in this study for recruiting participants was convenience sampling as participants were invited to participate in the study as they awaited appointments in the waiting area. The inclusion criteria included all patients' aged between18 and 65 years who had access to a mobile phone. Smartphones were not a requirement as mobile phones are able to receive and send SMSs. Patients who were involved in any SADAG adherence programs were excluded. There was no set recruiting period and participants were recruited until the required numbers were achieved. The participants were randomly assigned to the 'treatment as usual group' or the intervention group. The participants in the 'treatment as usual' group continued to receive their regular follow up consultations with the treatment team at the Tara Outpatient Clinic. The visits followed regular intervals as determined by the psychiatrist or registrar and medication was collected monthly. The trial took place over a period of six months.

All participants had to complete a pre-questionnaire at the beginning of the study. The prequestionnaire included information on demographics, diagnosis, medication, clinic attendance and medication adherence. The Morisky 8-Item Medication Adherence Scale (MMAS-8) was used to measure adherence at baseline, 3 and 6 months. The MMAS-8 is a self- rated questionnaire that contains 8 questions with closed dichotomous (yes/no) answers. Each item measured specific adherence behaviour. A score resulting from the sum of all correct answers determined the degree of adherence: high adherence (0 points), medium adherence (< 2 points) and low adherence (>2 points). It addressed how patients may fail to take medication as

prescribed due to reasons ranging from forgetfulness to adverse side effects. Adherence to clinic attendance was reviewed in patients' files. On those days where participants were scheduled to attend the pharmacy, their scripts were reviewed. In order to avoid marking those participants who had rescheduled their appointments as 'absent', the nurses booking diary was consulted to provide further information on rescheduled appointments.

During the study period, the intervention group was exposed to the SADAG reminder and support adherence program (RSAP) over 6 months or until a patient withdrew from the study. The Reminder and Support Adherence Program (RSAP) reminded patients to take their medication (according to their dosing schedule) and offered free on-going telephonic support. The program also included weekly phone calls, free telephonic counselling, reminder SMS messages, brochures and information. The control group continued to receive standard treatment and care at the outpatient clinic. This included continued monthly follow-up appointments with their doctor and/or collection of medication. Patients who were assessed by their doctors as requiring closer follow up were scheduled for earlier appointments. Patients also continued to have necessary investigations done, such as blood tests. They continued to receive care from relevant members of the multi-disciplinary team.

The study group was compared at baseline with the control group with regards to demographic, clinical and attendance profile. The groups were compared with regards to medication adherence at 3 and 6 months. A change in adherence from baseline to 3 months and 6 months was assessed. The number of appointments and scripts kept over 6 months was compared between the groups. An association between adherence and demographic factors was tested. An association between adherence and clinical factors was also investigated.

2.3 Statistical Analysis

Data analysis was carried out using SAS. The X2 test was used to assess the relationships between categorical variables. Fisher's exact test was used for 2 x 2 tables or where the requirements for the X2 test could not be met. The strength of the associations was measured by Cramer's V and the phi coefficient respectively. The following scale of interpretation was used:

0.50 and above high/strong association

0.30 to 0.49	moderate association
0.10 to 0.29	weak association
Below 0.10	little if any association

The relationship between continuous and categorical variables (group) was assessed by the test. Where the data did not meet the assumptions of these tests, a non-parametric alternative, the Wilcoxon rank sum test was used. The strength of the associations was measured by the Cohen's d for parametric tests and the R-value for the non-parametric tests. The following scale of interpretation was used:

0.80 and above	large effect
0.50 to 0.79	moderate effect
0.20 to 0.39	small effect

The 5% significance level was used throughout, unless specified otherwise. In other words, p values <0.05 indicate significant results.

Using a significance level of 5%, a power of 80% and a small (d=0.2), medium (d=0.5) and large (d=0.8) effect size, a sample size of 824, 134 and 54 is required. The actual sample size of 62 (29 and 33) is thus adequate for the determination of only large effect sizes (up to d=0.74)

2.4 Ethics Approval

The study protocol was submitted, and approval granted by the Human Research Ethics. Funding was acquired for the study to enable SADAG to provide the RSAP and test whether it is a cost-effective intervention.

Committee (HREC) – certificate number M130244 (Appendix 7).

2.5 Funding

The implementation and assessment of the SADAG RSAP at the Tara psychiatric out-patient department was sponsored by SADAG and Janssen Pharmaceuticals.

Chapter 3

3.1 Results

Of the 69 outpatients who were recruited for the study, only 62 met the criteria for the study. 8 of the participants were excluded as they were receiving SADAG support at the start of the study and/or had not indicated their willingness to receive reminders.

Of the 62 patients in the study group, 29 (46.8%) were a part of the treatment group, with the remainder (n=33; 53.2%) in the control group (Figure 1).

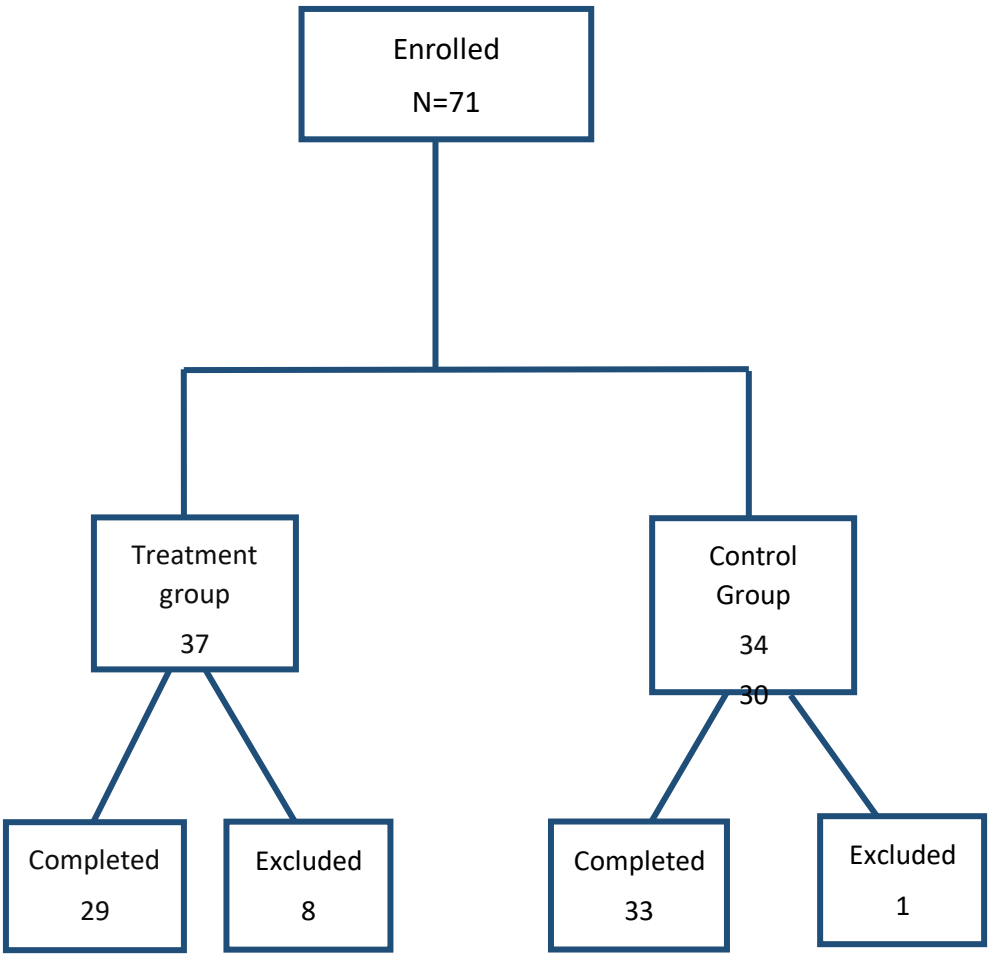


Figure 1:Participants enrolled into study

3.1.1 Demographics

The study group consisted predominantly of middle aged (41-65y) white females who were not in a relationship (Figure 2 and 3). Within the group aged 51-65years; 36.4% and 37.9% of the participants were in the control and treatment group respectively. With regards to race 72.7%, in the control group were white and 27.3% were black (Figure 4). The treatment group consisted of 86.2% white participants, 10.3% black and 3.4% coloured participants. Many of the participants were not in a relationship, with the control group consisting of 69.7% and the treatment group consisting of 65.5%. In the 'not in a relationship' category, the individuals included those who were single, divorced and widowed (Figure 5 and 6). There was no significant difference, between the groups, in age (p=0.64), gender (p=1.00) and race distribution (p=0.12).

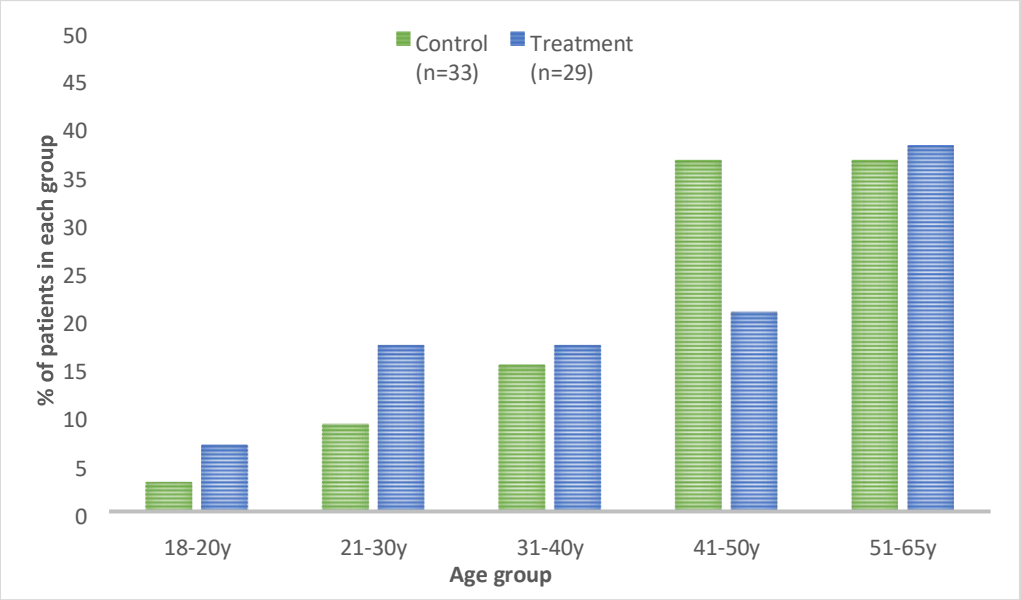


Figure 2: Age group

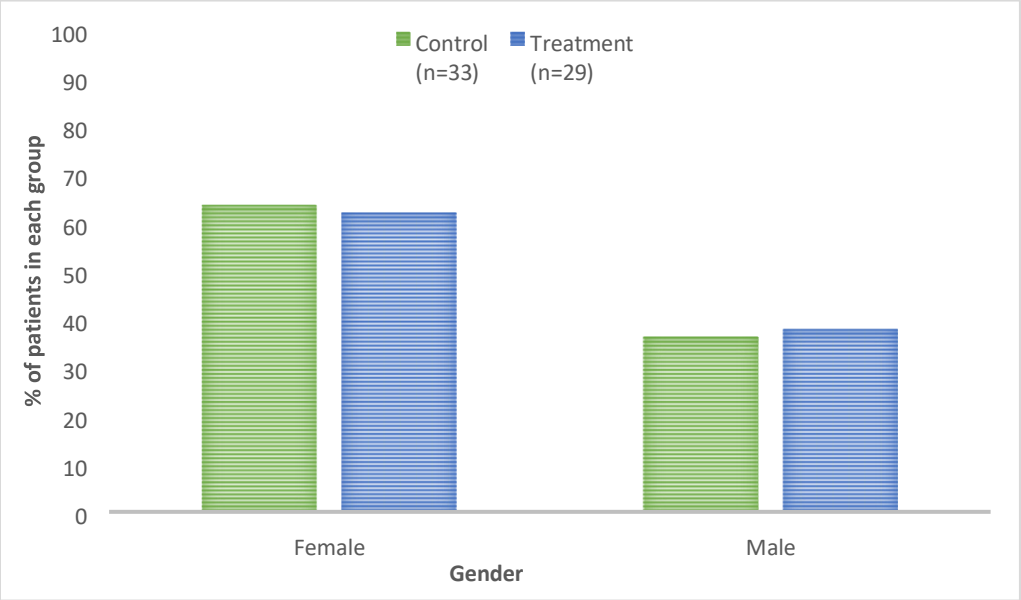


Figure 3: Gender

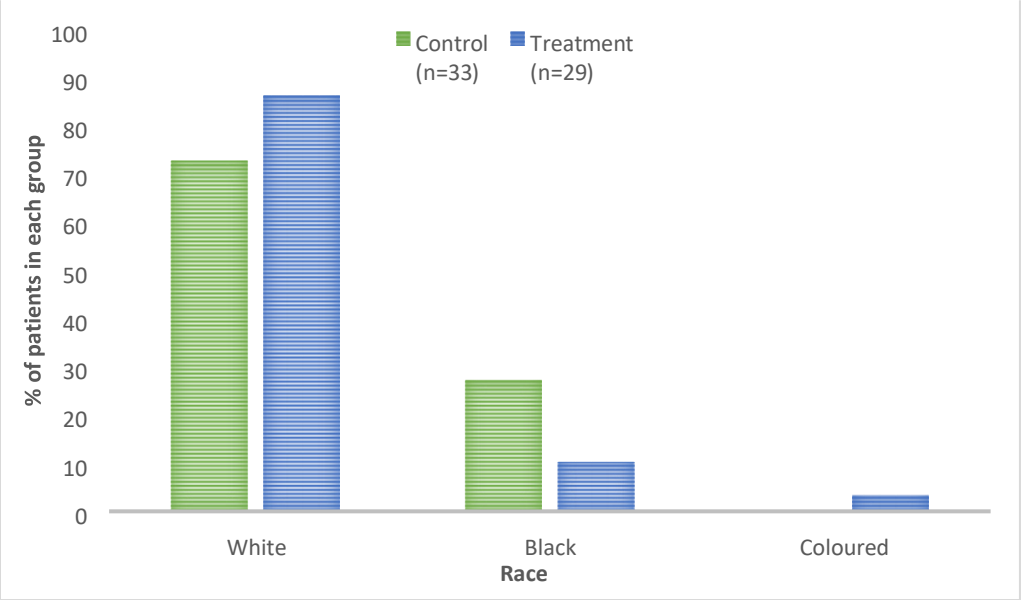


Figure 4: Race distribution

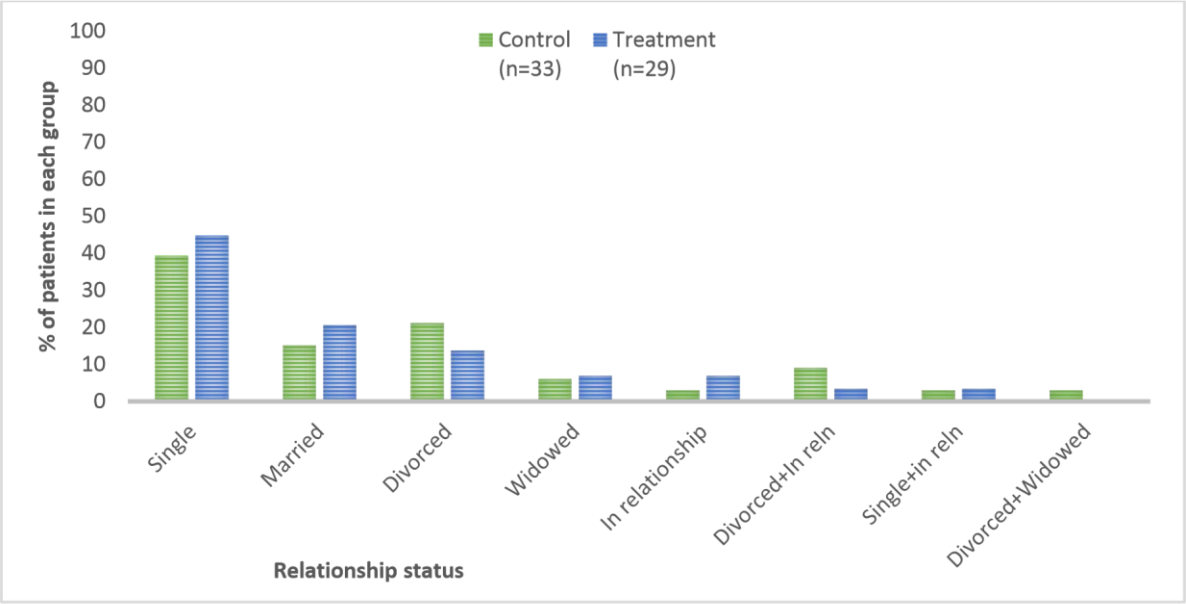


Figure 5: Relationship status

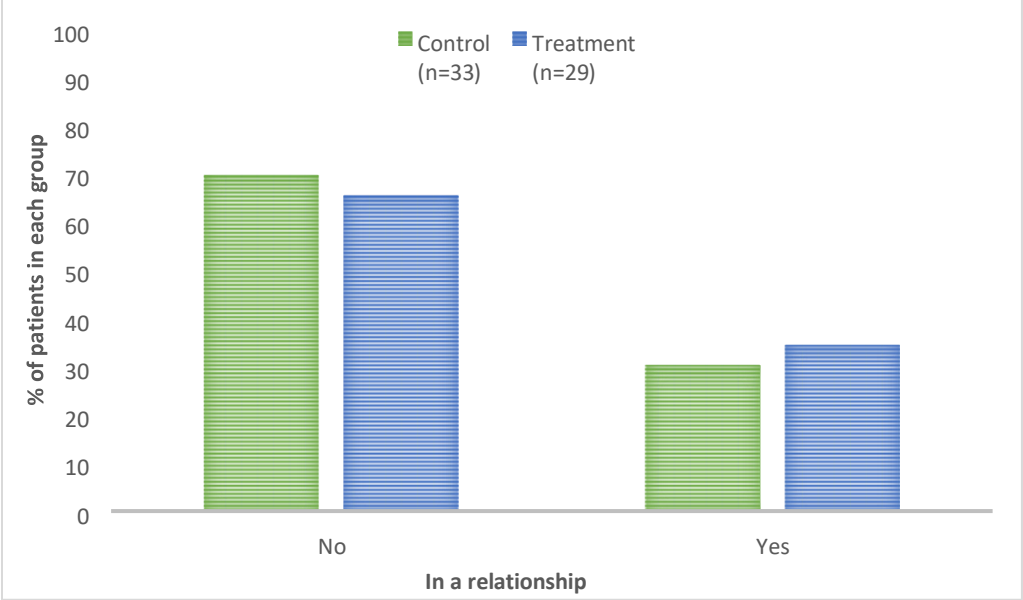


Figure 6: Percentage in a relationship

The participants were predominantly unemployed and fell into the lowest income group bracket (< 36000 per annum). The control group consisted of 57.6% unemployed individuals with the control group consisting of 65.5% (Figure 8). There was missing data on one individual from each group. Within the control group 60.6% earned less then R36000 pa, 3% less than R72000pa,

12.4% more than R72000pa with 8 individuals with missing data (Figure 9). Within the treatment group, 55.2% earned less than R36000 pa, 13.8% less than R72000pa, 3.4% more than R72000pa with 8 individuals with missing data (Figure 9). The group was predominantly high-school and tertiary educated with 39.9% within the control group and 44.8% within the treatment group falling into this category (Figure 10). There was no demographic difference between the treatment and control groups.

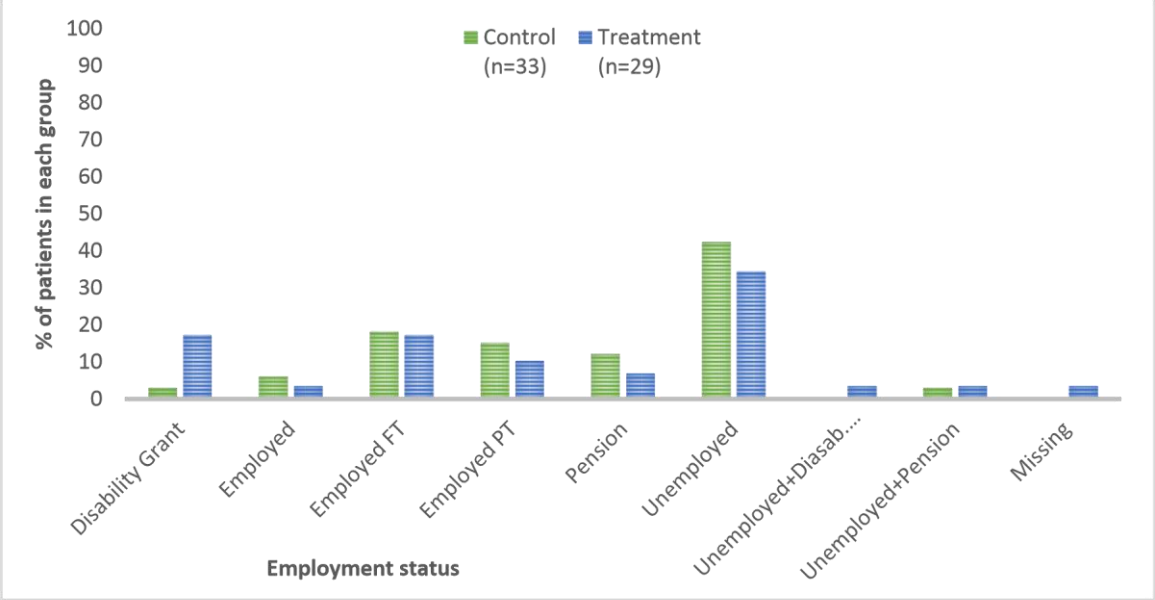


Figure 7: Employment status

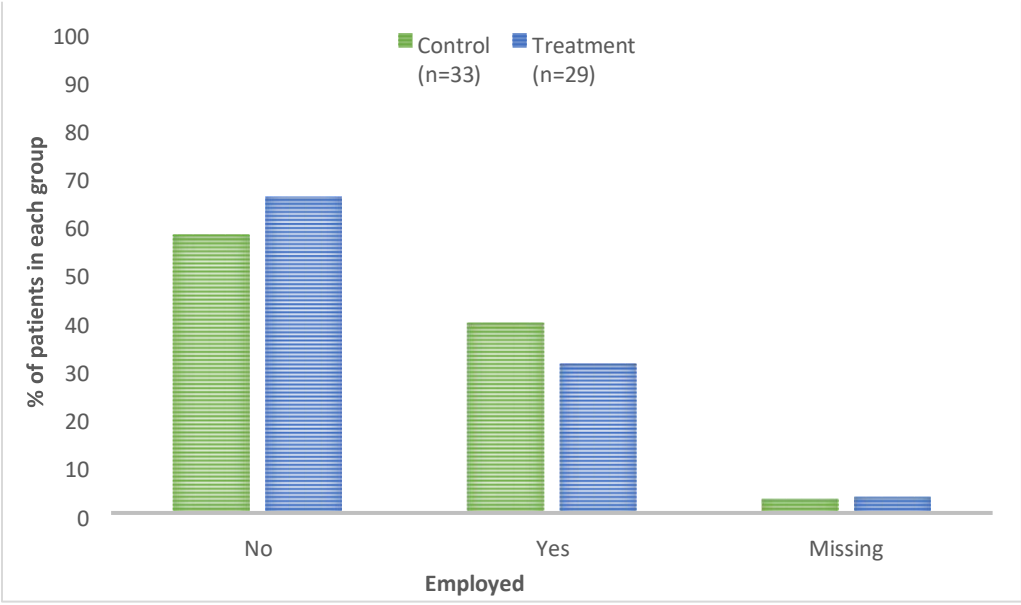


Figure 8: Percentage employed

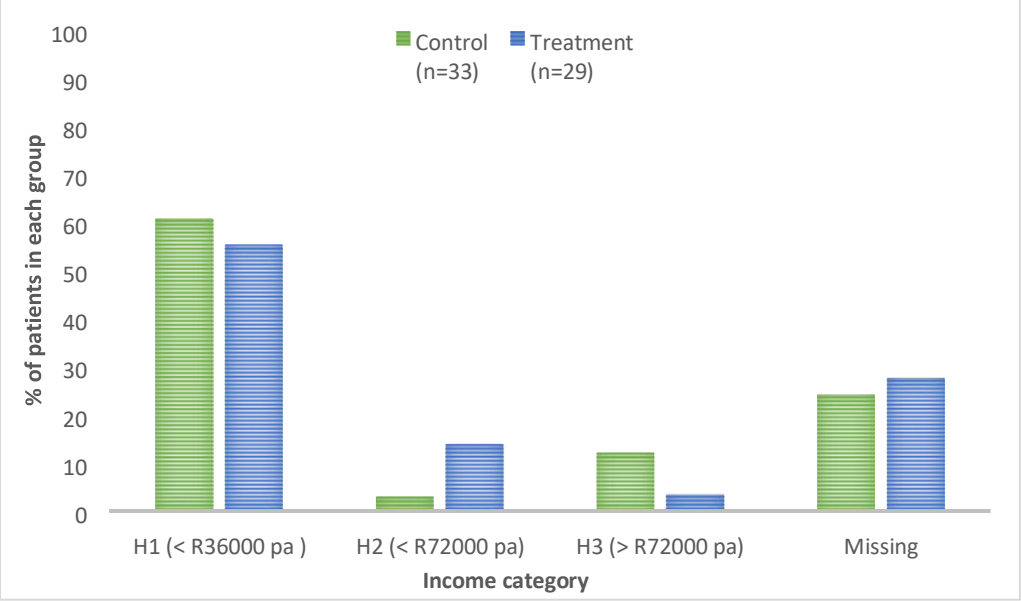


Figure 9: Income category

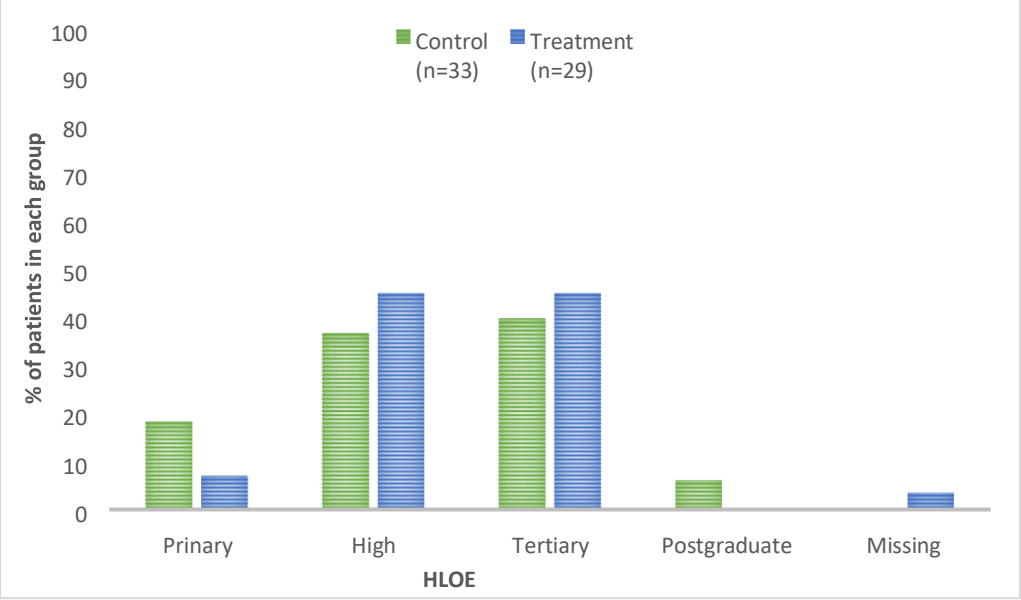
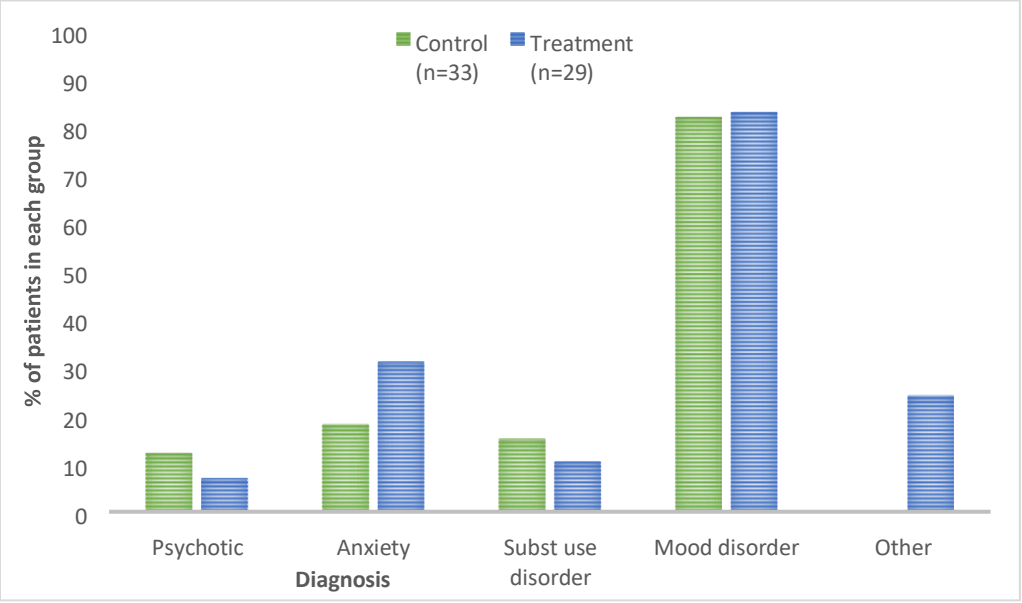


Figure 10: Level of education

3.1.2 Clinical Factors

The predominant diagnosis was mood disorder with a predominant duration of diagnosis of more than 5 years. Mood disorders included bipolar and depressive disorders. The percentages do not sum up to 100% as some patients had more than one diagnosis. 81.8% and 82.8% in the control

and treatment group respectively had a mood diagnosis (Figure 11). 15.2% and 10.3% in the control and treatment group respectively had co-morbid substance use disorder (Figure 11). 12.1% and 6.9% in the control and treatment group respectively had a psychotic disorder (Figure 11). 18.2% and 31% in the control and treatment group respectively had an anxiety disorder (Figure 11). 69.7% and 58.6% in the control and treatment group respectively had been diagnosed with a mental illness for over 5 years (Figure 12). 12.1% and 31% in the control and treatment group respectively fell into the group of having a mental illness between 1-5years (Figure 12). 15.2% in the control had a diagnosis for less than a year with none in the treatment group (Figure 12). 1 and 3 individuals in the control and treatment group respectively had missing data (Figure 12). There was a significant difference in time since diagnosis between the two groups (p=0.026; phi coefficient=0.35): The treatment group had more patients in the 1-5y group and fewer in the <1y group, compared to the control group (Figure 12).



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Figure 11: Psychiatric diagnosis

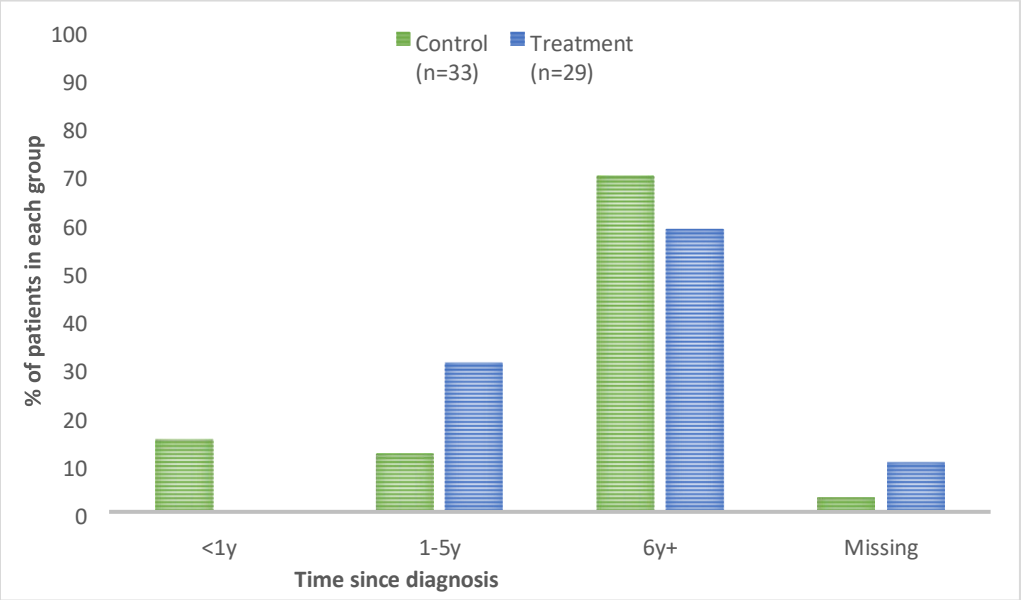


Figure 12: Duration of illness

90.9% and 100% of participants in the control and treatment group respectively were on one or more medications (Figure 13). The percentages do not sum up to 100% since some patients were on more than one medication type. 66.7% and 62.1% in the control and treatment group were on antipsychotics, respectively (Figure 13). 60% and 65.5% in the control and treatment group were on antidepressants, respectively. 43,3% and 62.1% in the control and treatment group were on a mood stabilizer, respectively (Figure 13). There was no significant difference between the two groups for any of the medication types.

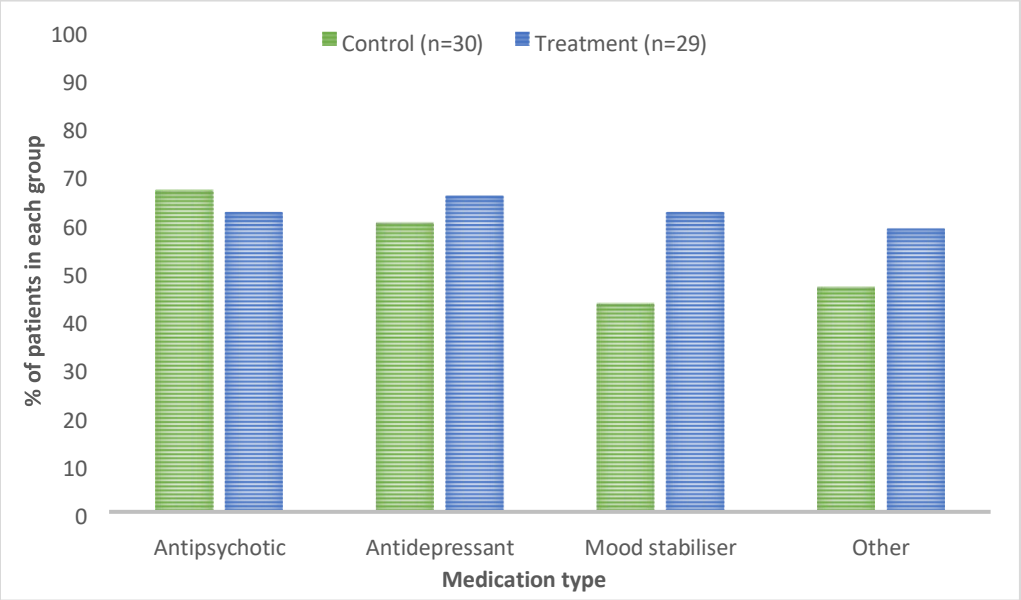


Figure 13: Medication type

3.1.3 Dosing Schedule

The study group was predominantly on a twice-a- day schedule. 45.5% and 62.1% in the control and treatment group, respectively, were on a twice-a-day dosing schedule. 9.1% and 20.7% in the control and treatment group, respectively, were on a three-times-a-day schedule (Figure 14). There was no significant difference in dosing schedule between the two groups.

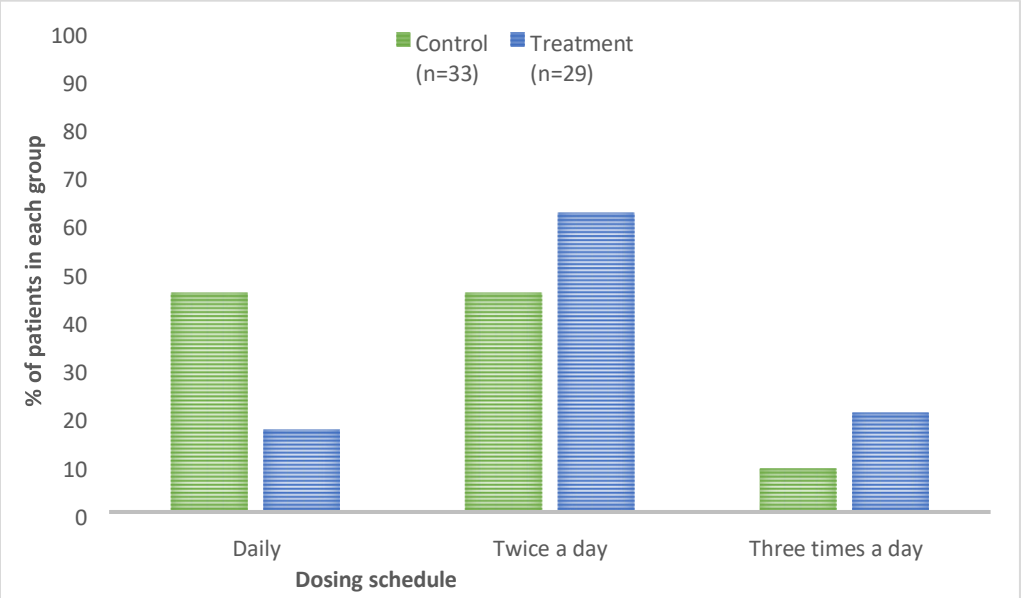


Figure 14: Dosing schedule

3.1.4 Baseline Medication Adherence

The study group reported a high level of medication defaulting in the baseline questionnaire (54.5% and 65.5% for the control and treatment groups, respectively) (Figure 16). There was no significant difference in reported medication defaulting between the two groups (p=0.44). Of the 37 patients who reported defaulting on their medication, the reasons for this are illustrated in Figure 16. The reasons were varied and ranged from simply forgetting to take medication (19 participants) to related side effects (15 participants) predominating. The groups also cited that the unavailability of medication (8 participants), feeling like the medication doesn't work (2 participants) and an improvement in their condition (12 participants) as reasons for nonadherence. There were no significant differences between the two groups with respect to any of the reasons given.

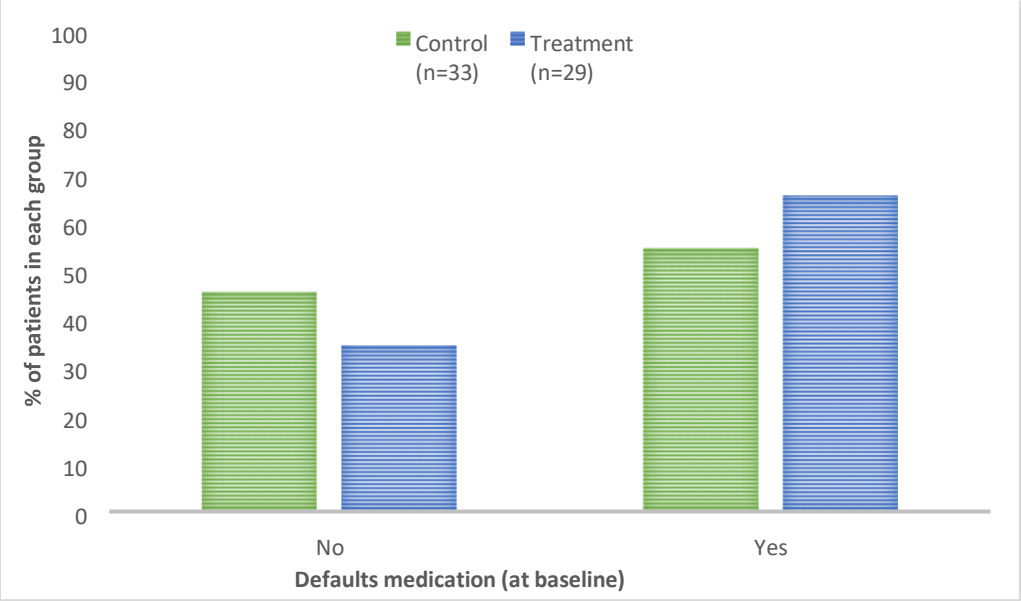


Figure 15: Non-adherence to medication at baseline

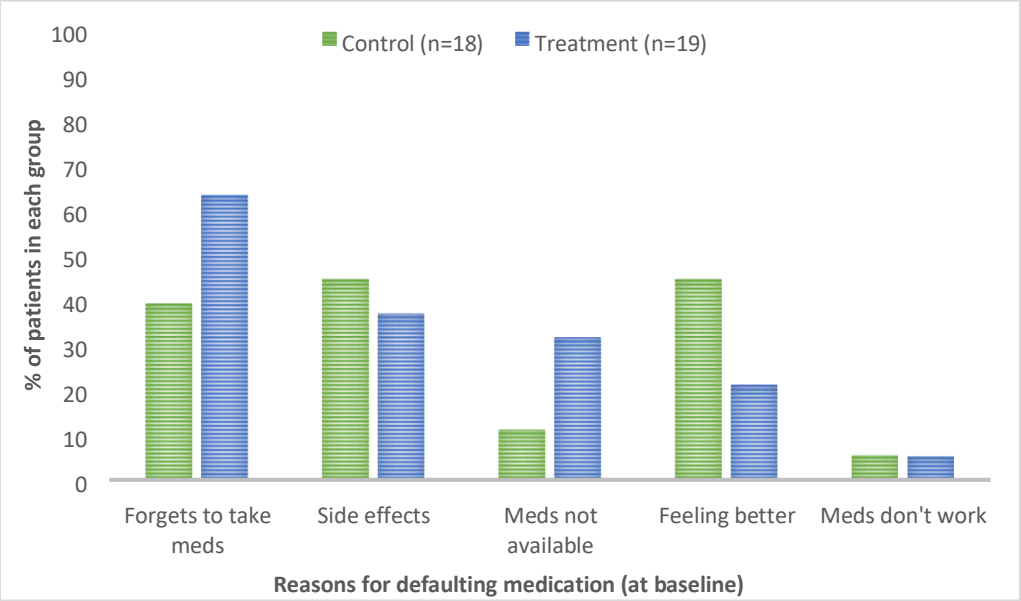


Figure 16: Reasons given for medication non-adherence

3.1.5 Baseline Appointment Adherence

The study group reported a high level of appointment defaulting in the baseline questionnaire (57.6% and 58.6% for the control and treatment groups, respectively) (Figure 17). There was no significant difference in reported medication defaulting between the two groups (p=1.00). Of the 36 patients who reported defaulting on their appointments, the reasons for this are illustrated in Figure 18. The reasons were varied with no significant difference between the two groups with respect to any of the reasons. The reasons for defaulting included transport difficulties (12 participants), financial (11 participants) and time constraints (8 participants), not having time (8 participants) and the stigma of not wanting others to know about their illness. 10 participants stated other reasons for defaulting their appointment dates. These reasons included, forgetting about the appointment (4 participants), having other activities scheduled for that day (3 participants), hospitalisation (2 participants), not well enough to leave the house (1 participant).

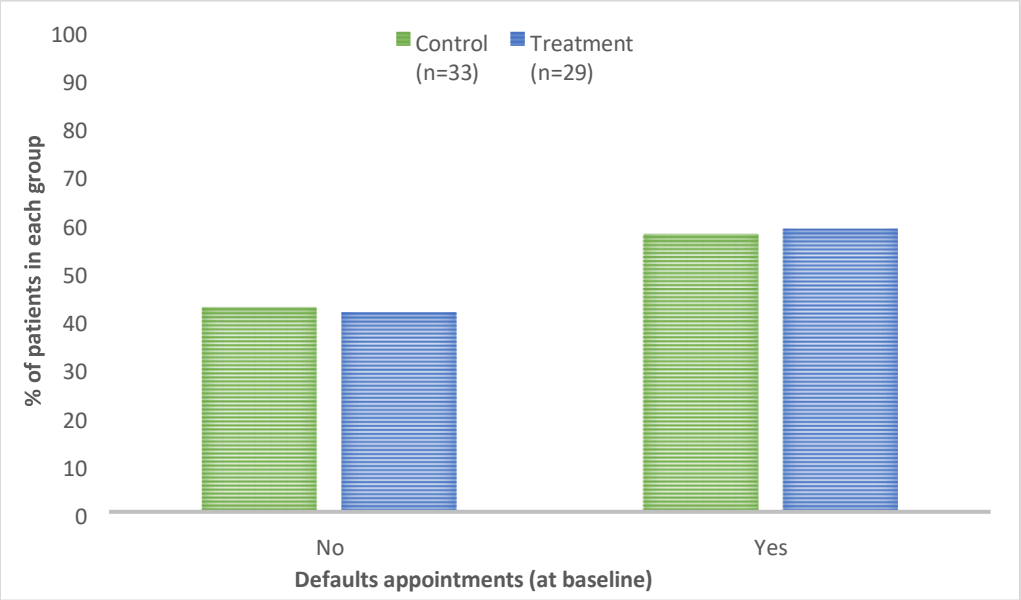


Figure 17: Non-adherence to appointments at baseline

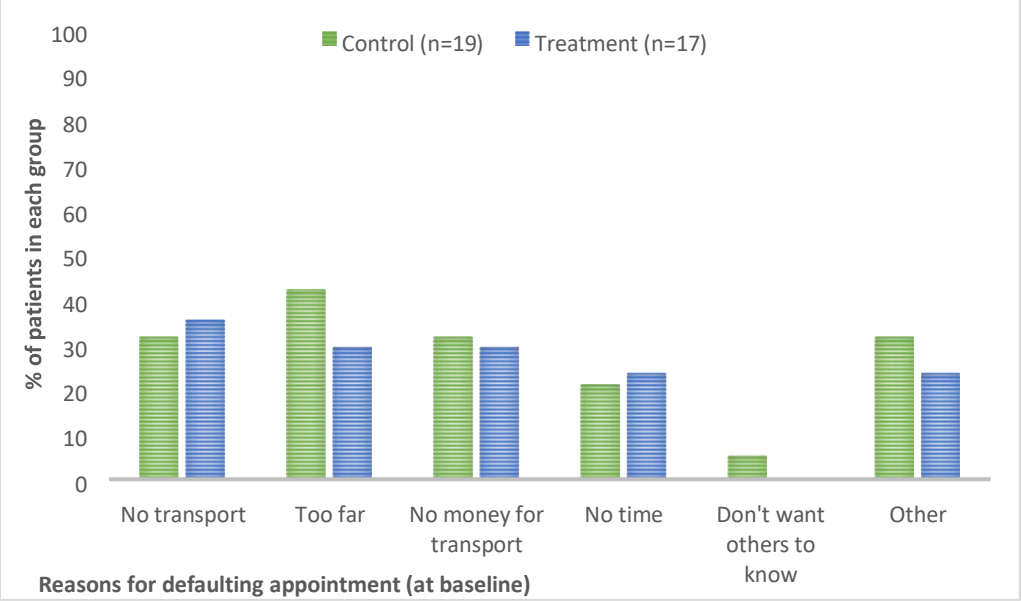


Figure 18: Reasons given for appointment non-adherence

3.1.6 Visit Schedule

The study group was predominantly on a monthly visit schedule (Figure 19). There was no significant difference in visit schedule between the two groups (p=0.12). 72.7% and 89.7% in the control and treatment group respectively fell into the monthly visit schedule.

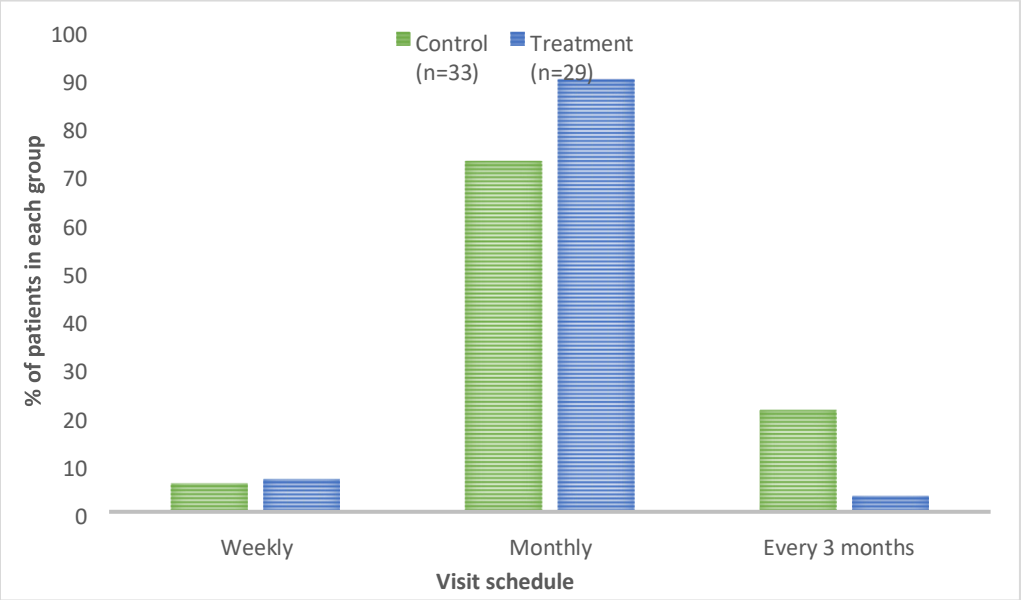


Figure 19: Medication schedule

3.1.7 Other Support Services

There was no significant difference between the two groups with respect to any of the support services received (Figure 20). One individual was a part of the SABDA support group.

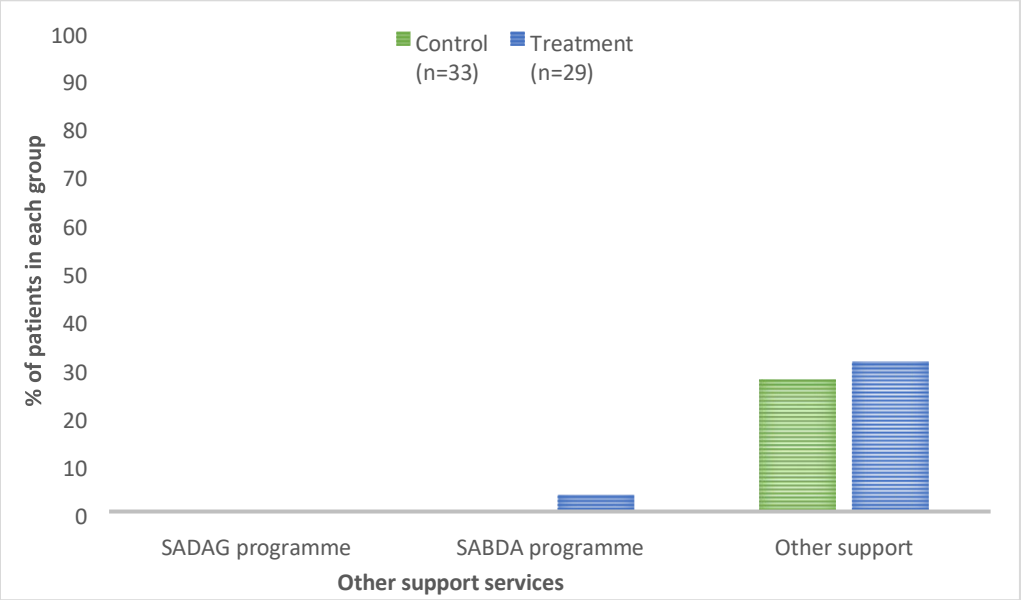


Figure 20: Support services accessed by participants

3.1.8 Adherence at Baseline

There was a significant difference in categorised adherence at baseline between the two groups

(p=0.0064; phi coefficient=0.39). The treatment group had more patients with low (vs medium) adherence, while the reverse was true for to the control group. These results are also reflected in the median MMAS-8 score at baseline: the median score for the treatment group of 3 was higher than that for control group of 1.5 (p=0.028; r=0.29 (small effect size). There thus may have been some clinical biases between the groups at baseline however with regards to adherence, the treatment group was not biased towards greater adherence (Figure 21).

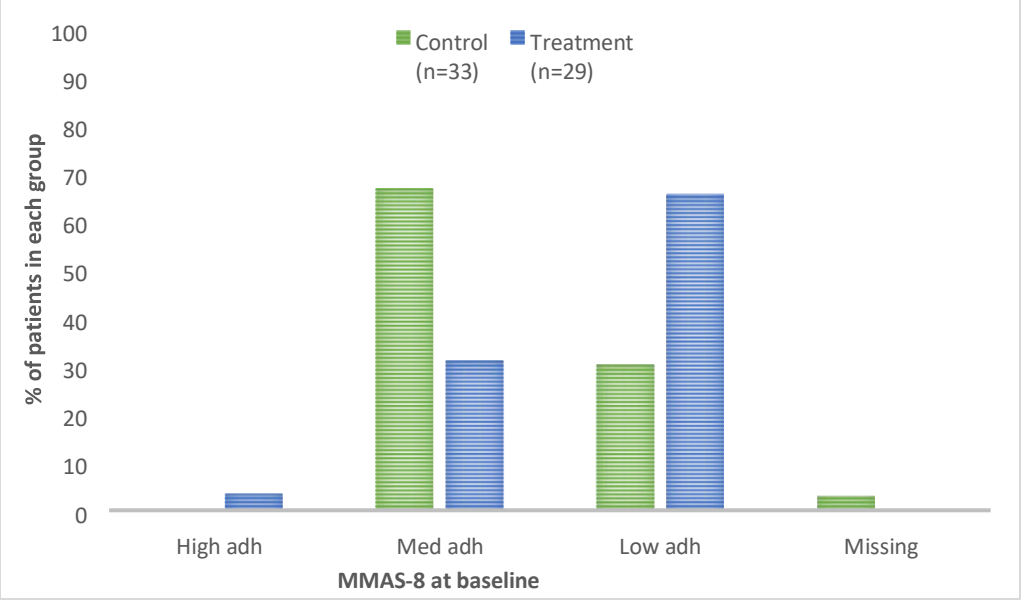


Figure 21: MMAS-8 scores at baseline

3.1.9 Adherence at 3 Months

There was no significant difference in categorised adherence at 3monthsbetween the two groups (p=0.052). There were however high levels of missing data with 21.2% and 20.7% for the control and treatment group respectively. The difference however was not significant (p=0.96). The median scores for MMAS-8 at 3 months were also not significantly different (p=0.051) (Figure 22).

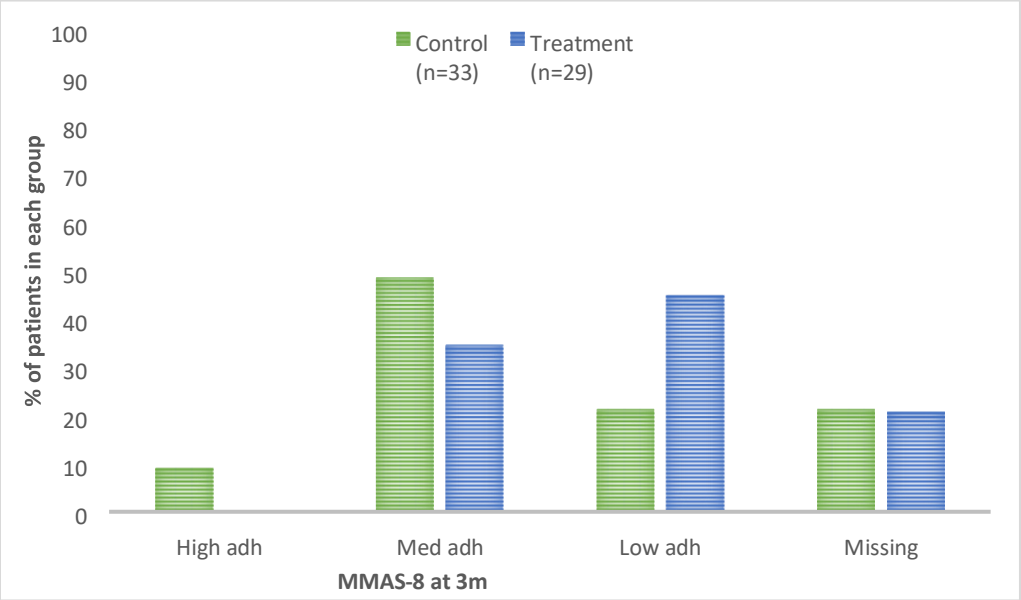


Figure 22: MMAS-8 scores at 3 months

3.1.10 Change in Adherence from Baseline to 3 Months

With regards to the change in adherence from baseline to 3 months, there was no significant difference in this outcome between the two groups (p=0.83) (Figure 23).

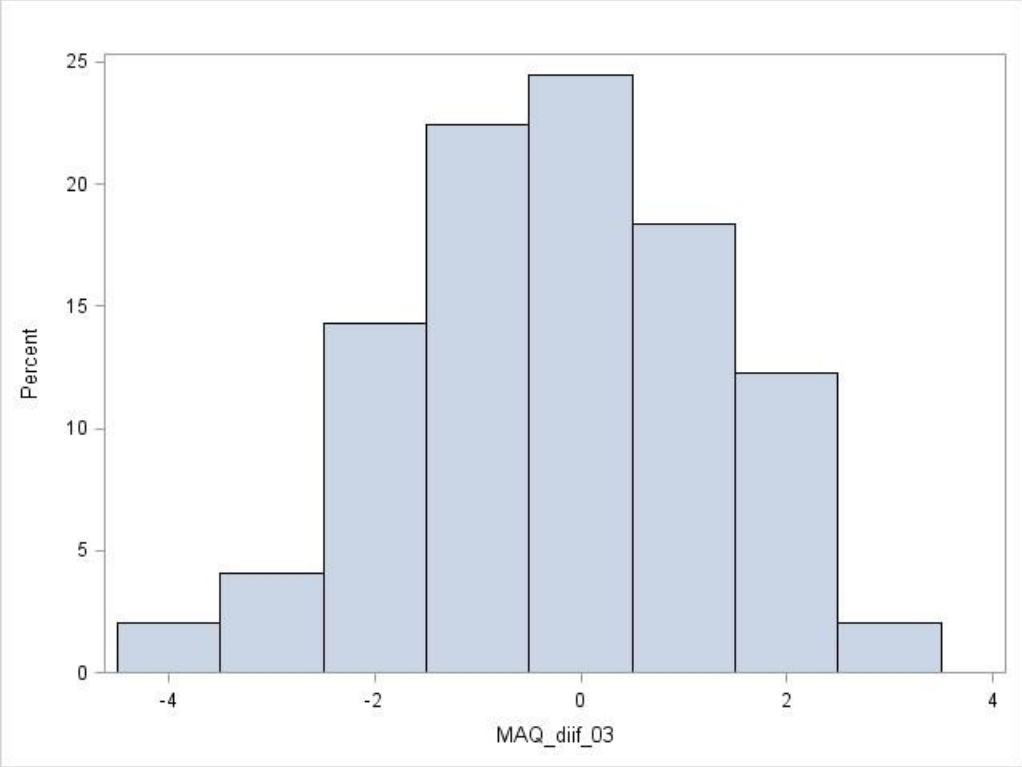


Figure 23: Change in adherence from baseline to 3 months

3.1.11 Adherence at 6 Months

There was no significant difference in categorised adherence or raw MMAS-8 scores at 6months between the two groups (p=0.33 and 0.43 respectively). There were however high levels of missing data with 30.3% and 55.2% for the control and treatment group respectively. The difference was however not significant (p=0.11) (Figure 24).

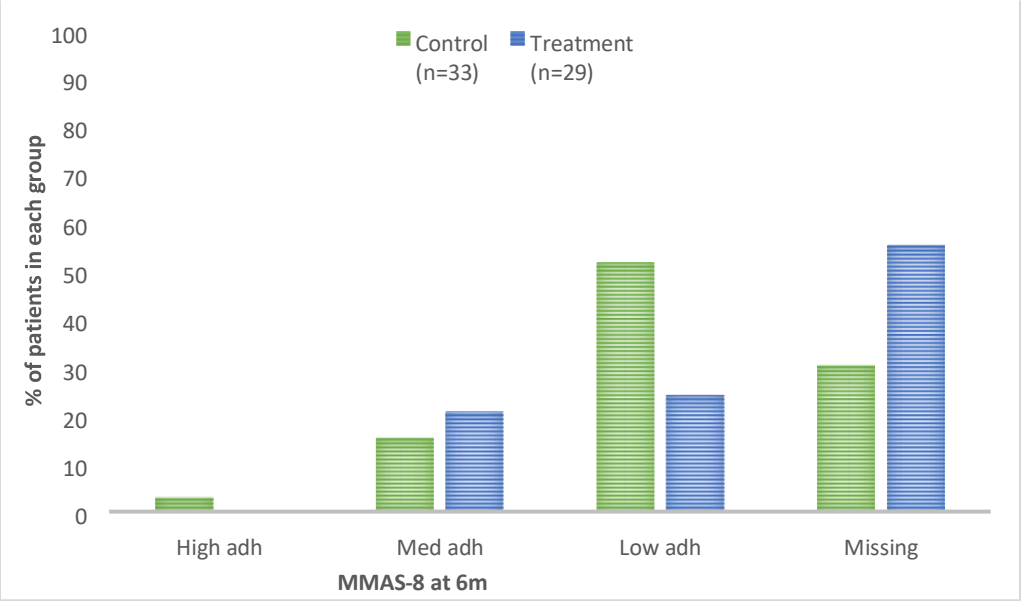


Figure 24: MMAS-8 scores at 6 months

3.1.12 Change in Adherence from Baseline to 6 Months

With regards to the distribution of the change in MMAS-8 score from baseline to 6months, there was a significant difference in this outcome between the two groups (p=0.017; Cohen's d=0.90; large effect). The mean change for the control group was 1.0 (95%CI: 0.2-1.9), i.e. a decline in adherence) while the mean change for the treatment group was -0.7 (95%CI: -2.0 – 0.6), i.e. no change in adherence (Figure 25).

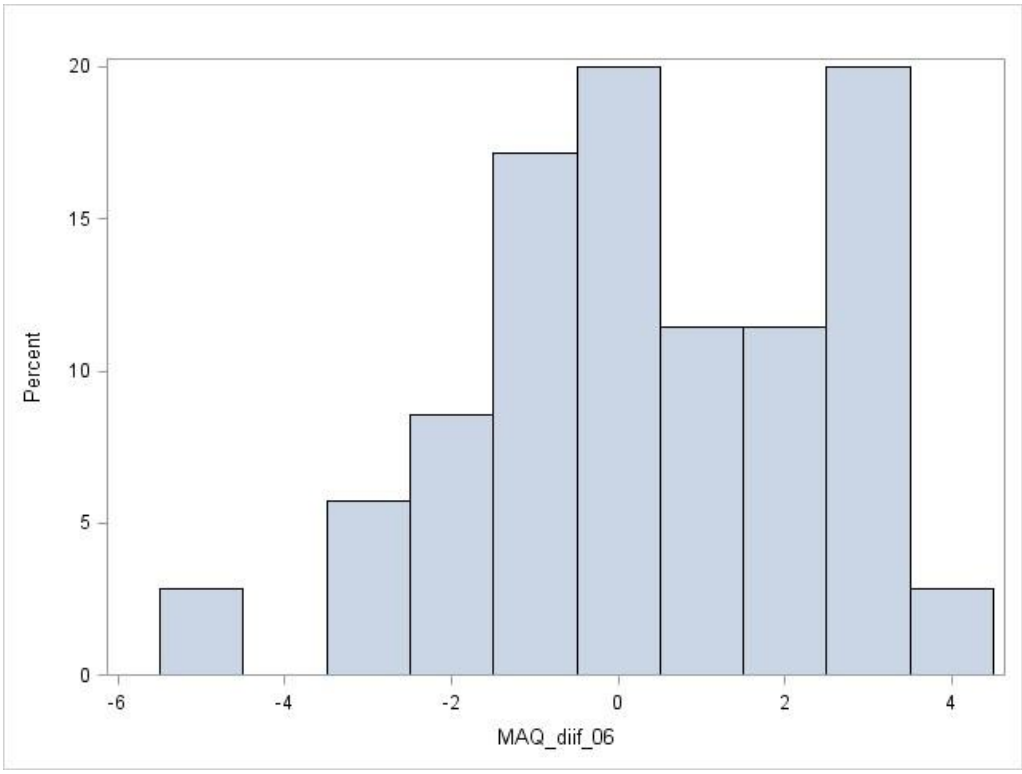


Figure 25: Change in adherence from baseline to 6 months

3.1.13 Number of Appointments Kept and Scripts Collected Over 6 Months

The median number of appointments kept for both groups was 3 (out of 6) (Figure 26). There was no significant difference between groups (p=0.76).

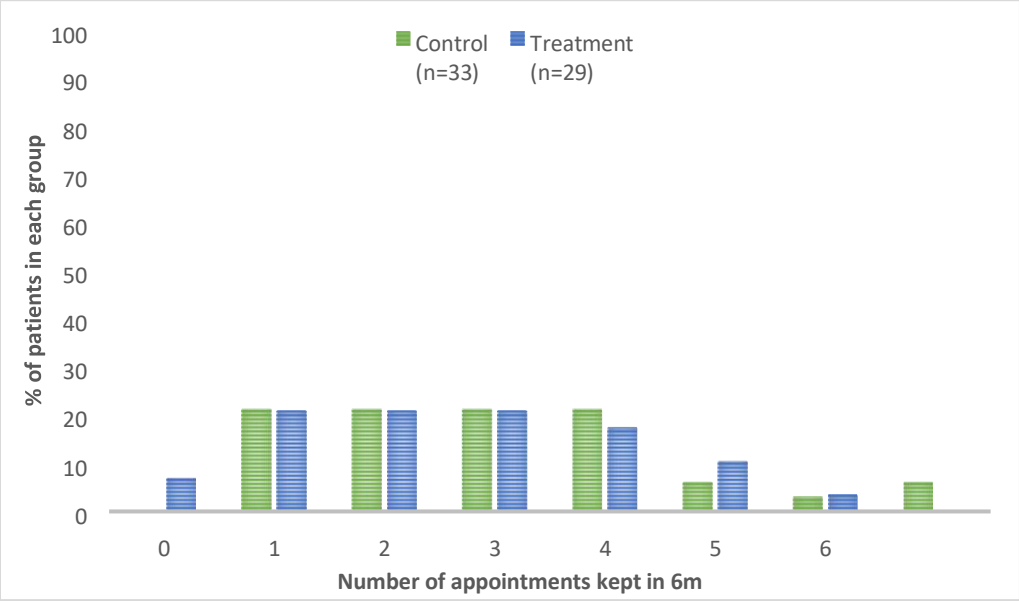


Figure 26: Number of appointments adhered to at 6 months

The median number of appointments for scripts kept for both groups was 5 (out of 6) (Figure 27). There was no significant difference between groups (p=0.42).

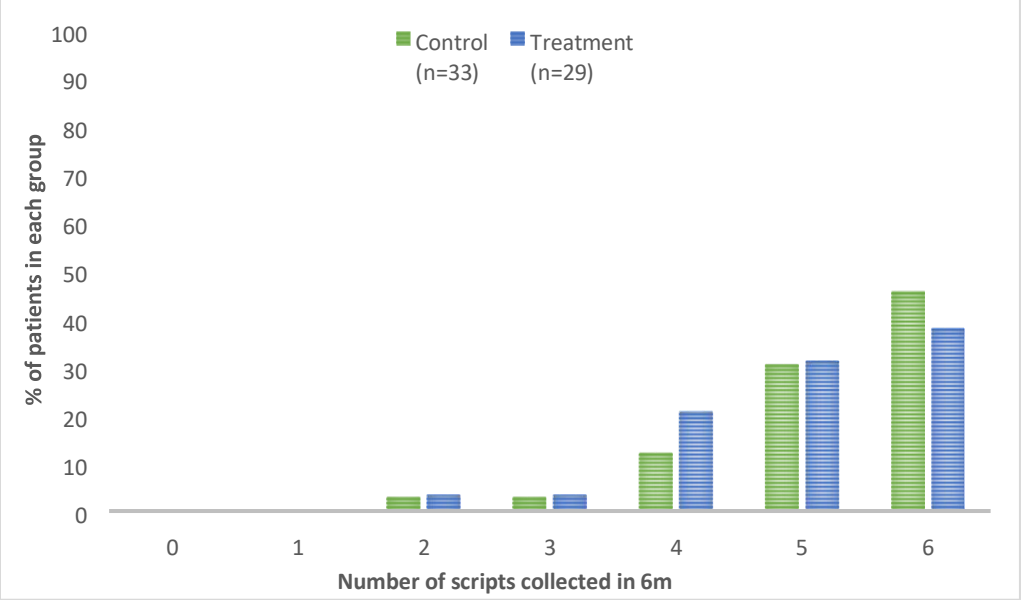


Figure 27: Number of scripts collected at 6 months

3.1.14 Comparison of MMAS-8 scores between 0, 3 and 6 Months

The categorised MMAS-8 scores were compared between 0 and 3 months, 0 and 6 months and 3 and 6 months using the Stuart-Maxwell test for paired categorical data. The cross-tabulations are given in the spreadsheet, and the results are summarised below.

Comparison in months (m)	Number of patients	p-value for Stuart-Maxwell test
0m vs 3m	49	0.54
0m vs 6m	35	0.14
3m vs 6m	29	0.041

Table 1: Comparison of MMAS-8 scores between 0,3 and 6 months

There was a significant difference between the 3month- and 6month-categorised scores. Inspection of the cross-tabulation shows shift mainly from medium to low adherence (Table 1).

3.1.15 Association between Adherence Measures

At the end of 6 months clinic adherence was measured as the actual number of visits made against a maximum of 6. The total number of visits a maximum of 6 is referred to as total appointments (AppTot) in Table 2. Medication collections as a measure of adherence at the end of 6 months was measured as the actual number of collections against a maximum of 6 The maximum of 6 collections is referred to as total scripts (ScripTot) in Table 2. The pairwise associations between the four outcomes, as well as between the actual MMAS-8 scores at 3months and 6months and AppTot and ScripTot were tested by means of the gamma test (similar to the X^2 test, but accounting for the fact that the categories are ordinal). The results are given in the spreadsheet and summarised below (Table 2).

Pair of variables	N	gamma	p-value for H0: gamma=0
MMAS-8_diff (0 vs 3m) / MMAS-8_diff (0 vs 6m)	29	0.57	0.0001
MMAS-8_diff (0 vs 3m) / AppTot	49	-0.11	0.28
MMAS-8_diff (0 vs 3m) / ScripTot	48	0.008	0.96
MMAS-8_diff (0 vs 6m) / AppTot	34	-0.065	0.19
MMAS-8_diff (0 vs 6m) / ScripTot	34	-0.003	0.99
AppTot / ScripTot	59	0.40	0.0011
MMAS-8_3m / AppTot	49	-0.24	0.13
MMAS-8_3m / ScripTot	48	-0.40	0.0059
MMAS-8_6m / AppTot	35	-0.11	0.51
MMAS-8_6m / ScripTot	35	-0.25	0.22

Table 2: Association between adherence measures

There was a significant, positive, relationship between the two MMAS-8 outcomes (at 3months and 6months) (p=0.0001), as might be expected.

There was a significant, positive, relationship between AppTot and ScripTot (p=0.0011); as one increased, so did the other.

There was a significant, negative relationship between the MMAS-8 score at 3months and ScripTot (p=0.0059); as adherence decreased (MMAS-8 score increased), ScripTot decreased.

3.1.16 Adherence versus Demographic Factors

None of the demographic variables were found to have a significant effect on adherence.

3.1.17 Adherence versus Clinical Factors

In the analysis of data investigating a correlation between clinical factors and outcome, it was found that there was a significant relationship between substance use disorder (SUD) and the difference in MMAS-8 score between baseline and at 6months (p=0.029). Controlling for group, the mean change in the MMAS-8 score for those with a SUD was 2.7 (95%CI: 0.4-4.9), i.e. a decline in adherence) while the mean change for those without a SUD was 0.0 (95%CI: -0.7–0.7), i.e. no

change in adherence. None of the other clinical variables were found to have a significant effect on any of the four outcomes.

Chapter 4

4.1 Discussion

4.1.1 Adherence

This study showed that daily treatment reminders via SMS may not have enhanced overall adherence to treatment however it did manage to arrest the decline in adherence rates. The study showed a decline in adherence rates in the control group whereas there was no change in adherence in the treatment group. This is not in keeping with a similar study done in Spain amongst patients with schizophrenia. This study showed that daily treatment reminders via SMS were efficacious in the enhancement of adherence to antipsychotic treatment. This sample population however comprised of clinically stable patients taking a single oral antipsychotic drug thus making it difficult to compare it our study where the patients were less stable and receiving multiple oral agents[1].

However, in a similar study done at Helen Joseph outpatient department using the RSAP, the study found that the study group attended 74% of booked visits compared to 66% of the control group. The booking ratio for the study group pre and post intervention was observed, showing that there was no significant change between the two periods. This implies that the RSAP may not have resulted in an improvement in attendance rate of the participants in the program[17].

There have however been various studies done that showed varying results with regards to overall adherence with the use of SMS reminders. A study done in Saudi Arabia showed that SMS reminders were not effective in reducing non-attendance rates in all clinic types to the same degree[11]. Similarly, a study was done to evaluate the efficacy of SMS text messages to compensate for the effects of cognitive impairment in schizophrenia. Prompting was shown not to have a positive effect on medication adherence[6]. 'According to a behavioural learning theory, sending daily SMS reminders is an intervention aimed at increasing medication adherence by modifying patient behaviour through the reception of external stimuli. Once the behaviour of taking medication is maintained, the habit will be acquired'[1]. Patients who forget to take their medication as a result of lack of acquired routines should benefit from this intervention. Patients who however intentionally choose to discontinue their medication or who are cognitively

impaired are least likely to benefit from this intervention. Other possible reasons for variations in these studies include a difference in settings or socio-cultural differences between patients[3].

4.1.2 Demographics

The study group consisted predominantly of middle aged (41-65y), white females who were not in a relationship. The participants were predominantly unemployed and fell into the lowest income group bracket (< 36000 per annum). None of the demographic variables were found to have a significant effect on adherence. Similarly, in a RCT that examined the use of short message reminders (SMSs) to improve attendance at an outpatient clinic, sex and nationality did not affect attendance rates[11]. A study on patient adherence to treatment also noted that demographic variables were poor indicators of adherence[13]. However, a study done at the University of Kwa-Zulu Natal on medication adherence of psychiatric patients found that age and race were significant predictors of medication adherence[21]. In this study, younger patients and black African patients were found to have the lowest levels of adherence.

This study group was predominantly female which is not in keeping with similar studies that have shown a predominance of males. The male gender has been associated with an increased risk of intentional non-adherence[2]. Factors not usually related to non-adherence such as female gender and having a higher level of education were noted in this study. It has been hypothesized that patients with better preserved functionality, as is described for women with respect to men with schizophrenia, and being able to support their own routines, such as working, would obtain lesser benefits from an intervention based on receiving a reminder of the medication at a fixed time of day to acquire a routine[1]. The predominant diagnosis in this study was found to be bipolar disorder.

4.1.3 Duration of Illness

There was no significant effect on the duration of illness on adherence. The study group was predominantly diagnosed more than 5 years before the study took place. This is not in keeping with similar studies done where non-adherence rates were much higher among patients who had their first visit compared with those who had prior contact with the hospital. Follow-up patients were more likely to be adherent as they were comfortable with the system and a therapeutic alliance had been established with their provider[11].

4.1.4 Diagnosis

The predominant diagnosis in this study was a mood disorder which had no significant effect on adherence. This is in keeping with a similar study done at Helen Joseph Hospital on communication and adherence in outpatients whereby they documented that major depressive disorder and bipolar disorder to be the most common diagnosis. However, a study done in Pakistan found that individuals with psychotic illnesses were more likely going to be nonadherent to medication compared to those with mood disorders. Various factors from the unpleasant side effects of psychotropics to a lack of insight may account for this finding[19]. The study found a significant relationship between substance use disorder and adherence. There was found to be a decline in adherence in those with a substance use disorder in the control group, whereas the treatment group showed no change in adherence. This is in keeping with studies that have been done on adherence looking at bipolar disorder and co-morbid substance use. Comorbid substance use disorder and bipolar disorder have displayed rates of non-adherence approaching 14-65%. The Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) study showed that substance abuse predicted poorer adherence with subsequent lower function[5]. Depression and co-morbid alcohol use disorder (AUD) have also been found to co-occur at higher rates than expected. It was found that 80% of patients with AUD complained of depressive symptoms at some point in their lives. As a result of this, the risk of poor outcome is higher amongst those with substance use and mood disorders compared with those who have a single disorder[5].

4.1.5 Medication Adherence

The study group reported a high level of medication non-adherence at the start of the trial. The reasons were varied, with simply forgetting to take medication (19 participants) and the related side effects (15 participants) predominating. The groups also cited that the unavailability of medication, feeling like the medication doesn't work and an improvement in their condition as reasons for non-adherence. This is in keeping with similar studies done on reasons for nonadherence[2, 4, 11]. Other studies cited a lack of insight as a significant contributing factor to nonadherence. This could be inferred based on the individuals who did not take their medication as they felt an improvement in their condition. Another study showed that the clinician-patient

relationship played an important role when it came to medication non-adherence. A patient's understanding of their illness and medication related side effects reduced rates of nonadherence thus emphasising the important role of psychoeducation in this setting [19].

4.1.6 Appointment Adherence

The reasons for appointment non-adherence included transport difficulties, financial and time constraints, not having time and the stigma of not wanting others to know about their illness. Other reasons stated for missed appointments included, forgetting about the appointment, having other activities scheduled for that day, hospitalisation, not well enough to leave the house[11]. Another reason not explored in this study were patients' cultural beliefs around their illness and their need to consult traditional healers. A study found that patients' held myths and beliefs about mental illness and their use of alternative medicines contributed to a lack of adherence[19].

4.1.7 Association between Adherence Measures

There was a significant, positive relationship between total appointments and total scripts collected because as one increased, so did the other. There was a significant, negative relationship between the MMAS-8 score at 3months and total scripts collected because as adherence decreased (MMAS-8 score increased), the total scripts collected decreased.

Chapter 5

5.1 Limitations

There were some limitations that were noted in the study. Firstly, the sample population was small consisting of 62 participants. This means that the study would have only been able to detect significant effects. The length of the study was however was in keeping with similar studies done but it did not incorporate the confounding effect of seasonality and monthly variation in attendance. Although patients recruited into the study were randomized into the treatment and control group in order to avoid bias, it is possible that the non-adherent patients would have been reluctant to participate in the study.

More complete and accurate data may have been obtained if the MMAS-8 scoring sheet had been completed by the researcher in consultation with the patients rather than requiring the patient to independently complete the questionnaire on return visits. The study population consisted generally of white, females who had a high level of education. This is in keeping with some but not most studies done. This is not representative of the general population and thus the results may not be able to be generalized.

Ownership of mobile phones among patients with severe mental illness is lower than in the general population[2, 20, 21].

A study showed that only 62% of psychiatric inpatients owned a mobile phone[2]. The most frequently reported barrier to mobile device ownership was cost reflecting the relationship between poverty and severe mental illness[2].

All patients who were included in the study had access to a mobile phone. However certain restrictions would have made it difficult to confirm if all patients had received an SMS reminder in the intervention group. These include loss of the device, technical problems with the device, frequent change of mobile numbers which would require regular updates, mobile phones being turned off or having being sold by the patient[3, 12]. All SMS reminders were in English meaning that non- English speaking and illiterate individuals may have not been able to read the messages. Some participants may have also not been familiar with reading and sending text messages.

Adherence was measured using a self-rated scale. Self-reports have been criticized for underestimating the true extent of poor adherence[2, 22]. Perhaps a combined method using both objective and subjective methods for assessing adherence may have been more accurate.

The South African and Anxiety Group (SADAG) used their already existing IT infrastructure to send SMS reminders. For this intervention to be replicated, an established electronic database with IT infrastructure needs to be present. A report done by the World Health Organisation (WHO) found that one of the biggest challenges to the use of mobile devices in health care was the lack of infrastructure. One indicator of infrastructure is the level of cellular network coverage. Although network coverage is expanding dramatically across the globe, this is seen to be happening in urban areas more than rural areas that stand to benefit more from mobile health services.[23]

The SMS based service has many benefits that make it appropriate for the use in a healthcare context. These include features like being able to send messages to many recipients simultaneously and potentially in several different languages. These messages can also be prewritten, minimising time and effort in data entry and communication for providers but it also allows manual or custom messaging.[24] A limitation however in the study was the inability of patients to interact with the health care providers by example responding to a message. Future considerations for SMS technology would allow for perhaps more interactive communication whereby patients can reply to reminders. This would allow patients to cancel or reschedule appointments or even receive test results or instructions before the scheduled tests[3]. This would however add to labour and staff costs.

SMS reminders have shown to be effective in patients who simply forget to take their medication. There are however other reasons for patients refusing to take their medication including poor insight, stigma, cognitive deficits and poor therapeutic alliance. An additional intervention may need to be combined with SMS reminders to increase adherence[2]. This study could only have been useful to patients who simply forgot to take their medication and not those who intentionally refused to take it[1].

A survey on patient's perceptions of the SMS reminder may have been useful to include in the study. Text messages may at times be interpreted as intrusive and there is the potential that

some patients may experience message fatigue if they were to receive daily reminders for a long period of time

There are few studies that have looked at the long-term effects of SMS reminders on adherence. It would have been interesting to follow-up patients who previously received SMS reminders to see if this would have had an impact on future adherence[1]. A study that followed up patients who had received SMS reminders for 3 months found that the effect of sending SMS reminders attenuated 3 months after stopping them[1].

Despite these limitations, the study had some strengths. It was a prospective study done over a period of 6 months. The use of randomization allowed us to obtain two groups of patients with similar baseline characteristics.

5.2 Conclusion

Poor adherence to long-term therapies is an important topic in public health. Mental disorders together with HIV, TB and non-communicable diseases together represent 54% of the burden of chronic diseases worldwide. As the burden of chronic diseases increases, so does the challenge of non-adherence[4]. It has been shown that even partial non-adherence to psychotropic medication is associated with an increased likelihood of morbidity and mortality. Mental illness is further burdened by the challenge of dual diagnosis which is independently associated with poorer outcome overall [9]. Few local studies have explored the use of text-based prompts in increasing medication and appointment adherence. This study showed that daily treatment reminders via SMS may not have enhanced overall adherence to treatment however it did manage to arrest the decline in adherence. An effective adherence program may decrease the rates of relapse and readmission and will in the long term decrease the burden of disease on our health care services.

5.3 Recommendations

The study revealed that there is a paucity in available literature regarding effective communication intervention programs to enhance adherence amongst mentally ill patients. We

recommend further research, in a similar setting, be done to better understand the effects of a communication intervention program in enhancing patient adherence. We believe that such research will be beneficial in not only enhancing adherence but also in reducing the burden of disease on our health care systems.

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Appendices

Appendix 1: Tara Hospital Adherence Program: Data Collection Sheet

Allocation no			Race	B	W	C	I	O	Gender	M	F			
Age		Marital Status	S	M	D	W	Phone	(C)		(H)				
Address														
Level of education	Primary		High School		Tertiary		Post graduate							
Income classification	H1		H2		H3		Diagnosis category	Mood disorder						
Psychotic Disorder	Substance Use Disorder		Anxiety Disorder		Other (specify)									
Date of diagnosis			Duration of illness (months)											
Dosing schedule	od	bd	tds	qid	Other (specify)									
No of drugs														
Clinical attendance (weekly)	2	4	8	12	16	20	24							
MMAS-8 Score	Baseline		3 months		6 months									

Tara Hospital Adherence Program: Data Collection Sheet

Allocation no			Race	B	W	C	I	O	Gender	M	F			
Age		Marital Status	S	M	D	W	Phone							
Address														
Level of education	Primary		High School		Tertiary		Post graduate							
Income classification	H1		H2		H3		Diagnosis category	Mood disorder						
Psychotic Disorder	Substance Use Disorder		Anxiety Disorder		Other (specify)									
Date of diagnosis			Duration of illness (months)											
Dosing schedule	od	bd	tds	qid	Other (specify)									

No of drugs							
Clinical attendance (weekly)	2	4	8	12	16	20	24
MMAS-8 Score	Baseline		3 months		6 months		

Appendix 2: Income Classification

H1: Individuals with Income less than R36 000 pa and Household with income less than R50 000 pa

H2: Individuals with Income less than R72 000 pa and Household with income less than R100 000 pa

H3: Individuals with Income greater or equal to R72 000 pa and Household with income equal to or greater than R100 000 pa

Appendix 3: Informed Consent

Good day my name is Dr Lutaaya/ Lian Taljaard

I would like to invite you to consider participation in a research study entitled:

' Effectiveness of a Structured Behavioural Communication Intervention Programme amongst Outpatients Patients with Mental Illness: a Randomised Prospective Descriptive Study'

My name is Sheila Lutaaya and I am the principle investigator on this research project. This project is being conducted in partnership with the South African Depression and Anxiety Group (SADAG).

This informed consent form has two parts

- Information sheet (to share information about the research with you)
- Certificate of Consent (for signatures if you agree to take part)

You will be given a copy of the Informed Consent Form

I am Dr Sheila Lutaaya, a registrar in Psychiatry at the University of Witwatersrand. I would also like to introduce you to my research assistant Lian Taljaard. Lian Taljaard is a research assistant employed by SADAG. SADAG is South Africa's largest consumer advocacy group and will be providing the Structured Behavioural Communication Intervention Programme. The cost of providing the program has been kindly sponsored by Janssen Pharmaceuticals.

We are doing research to find out whether a reminder and support programme will help patients take their medication and attend their appointments at the Tara Outpatient clinic. I am going to give you information about the study and invite you to be a part of it. You do not have to decide today whether or not you will participate in the study. There may be some words that you do not understand. Please ask me to stop as we go through the information and I will take time to explain. If you have questions later, you can ask them of me or Lian Taljaard.

There are many reasons why patients do not take their medication and this may be because of the side effects or simply forgetting to take it. We are doing research to find out whether receiving a short message service (SMS's), a weekly telephone call and educational information will help you to take your medication and present for monthly clinic appointments. The study will take place over 6 months.

There will be two groups in the study. They will be selected by chance. The one group will continue to receive their usual treatment at the Tara clinic. The other group will receive daily SMS's, weekly telephone calls and educational information. All the information that we collect from this study will be kept confidential.

It is your choice whether to participate or not. Whether you choose to participate or not, all the services that you receive at this clinic will continue and nothing will change. You may also change your mind later and stop participating even if you agreed earlier.

Please do not hesitate to contact me at 011 535 3000 and ask to speak to Dr Lutaaya with further questions. This proposal has been reviewed and approved by the University of Witwatersrand Ethics Committee.

Certificate of Consent

I have read and understood the information above on the study and what will happen during the study. I understand that:

(1) I am a voluntary participant in this study

(2) I can decline to participate in this study on invitation or at any other time during the study without prejudice and that it can or will in no way be used to my disadvantage

(3) I may refuse to answer any questions with which I am not comfortable

(4) I am assured that no information that could cause my identity to be revealed will be included in the research report and all responses and assessment scores will remain confidential

(5) I am also assured that in the event of the study results being published, that my identity and responses to questions will remain confidential

(6) I understand that there are no direct risks or benefits involved in participation in this study

(7) I accept that there is no remuneration or reimbursement for participating in the study and there are no direct costs to me

Print Name of Participant _____

Signature of Participant_____

Date_____

Day/month/year

Alternatively,

Print name of witness_____ Or Thumb print

Signature of witness_____

Date_____

Day/month/year

Appendix 4: Tara Adherence Programme Pre-questionnaire

Allocation no: _____

Demographic Data

Age: 18-20 ☐ 20-30 ☐ 30-40 ☐ 40-50 ☐ 50-65 ☐

Gender: Male ☐ Female ☐

Race/Ethnic Group:

Black ☐ Indian ☐

White ☐ Coloured ☐

Asian ☐ Other (specify) _____

Marital Status:

Single ☐ Married ☐

Divorced ☐ Widowed ☐

In a ☐ Relationship

Highest level of education:

Primary ☐

High School ☐

Tertiary ☐

Post Graduate ☐

Employment:

Employed ☐ Pension ☐

Unemployed ☐ On a Disability Grant ☐

Income Classification: H1 (< R36000 pa) ☐

H2 (< R72000 pa) ☐

H3 (> R72000 pa) ☐

Clinical Information

Diagnosis:

Psychotic Disorder ☐

Anxiety Disorder ☐

Substance Use Disorder ☐

If yes, specify_____

Mood Disorder ☐

Depression ☐

Other (specify) _____

Date Of first diagnosis:

Medication

What medication are you currently being prescribed at Tara hospital?

_____
_____
_____
_____

How often do you take your medication?

☐

Daily ☐

Twice a day

Three times a day ☐

Other (specify) _____

If you do not take your medication regularly; what are the reasons for this?

I get side effects on my medication Y ☐ N ☐

I am feeling much better Y ☐ ☐ N

I forget to take my medication Y ☐ N ☐

The medication wasn't available at the pharmacy Y ☐ ☐ N

I don't think the medication is working Y ☐ N ☐

If you are unable to present for you clinic appointment; what are the reasons for this?

I have no transport to come to the clinic Y N ☐☐

I am unable to take time off work Y ☐ N ☐ Other

I stay far away Y ☐ N ☐

I didn't have money for transport Y ☐ N ☐

I don't want people to know I'm taking medication Y ☐ N ☐
(specify)_____

How often do you have to return to outpatients for your medication?

Weekly (specify) _____

Monthly ☐

Every 3 months ☐

May we remind you of your visit 2 days before your visit to the clinic? Yes No

When would you like us to SMS you?

8 AM ☐

6 PM ☐

Both ☐

When would you prefer us to call you?

Morning ☐

Afternoon ☐

Evening ☐

Are you currently involved in any SADAG programmes? Yes No

Are you currently involved in the SABDA support group? Yes No

Are you receiving any other support services? Yes No If yes,

indicate which of the following:

Psychologist ☐

Support group ☐

Occupational therapy ☐

Counsellor ☐

Other (specify)_____

Thank you for taking the time to complete this form

Appendix 5: SADAG Reminder and Support Adherence Program (RSAP)

With regard to SADAG counsellors, all counsellors are trained by SADAG Board Members, consisting of HPCSA registered psychiatrists and psychologists. Counsellors undergo extensive external and on-site training in the SADAG call centre, as well as additional capacity skills building on a monthly basis at SADAG's monthly counsellor meetings. All materials and educational information provided by SADAG were standardized and approved by the SADAG Board including members such as Dr. Frans Korb (private practice), Prof. Dan Stein (UCT), Dr Dora Wynchank (private practice), Dr. Collinda Linde (private practice). The **SADAG Reminder and Support Adherence Program (RSAP)** was developed to regularly remind patients to take their medication, as well as offering them free on-going telephonic support and information to help them cope. The Program consists of the following components: weekly phone calls to participants; free telephonic counseling, seven day a week; reminder SMS-messages; brochures and information; SMS reminders for workshops, support groups, press notifications; online website with information; monthly newsletters; and free regional support groups.

1. **Weekly phone calls to participants**

The **RSAP** offers participants on-going support and information to help them cope. By remaining in touch with patients during the initial stages of treatment, SADAG's telephonic support service is able to debunk common medication myths as well as ensure that participants are taking their medication correctly and feel more empowered. Users enrolled in the **RSAP** will receive an initial start-up call from trained SADAG personnel, who logs all the participants' important details and information, such as history of illness, medication history, previous experience of side effects, who referred the patient to the programme, providing them with support and guidance etc.

2. **Free telephonic counseling seven day a week**

As an added support structure for users, each participant will have full access to the free telephonic support available to them seven days a week, including public holidays, from 8am to 8pm with an emergency after hours number in case they need crisis intervention after 8pm. Users will be able to speak to SADAG at no cost to them at all on your toll-free helpline number. They will receive free telephonic support as well as referral information and assistance to psychologists, free counselling centres and support groups. In cases of severe crisis intervention or an emergency, SADAG will refer users to the appropriate specialist or clinic.

3. **Reminder SMS-messages**

As a way to ensure that users stay on their medications, especially in the first 8 to 12 weeks of starting a new medication, SADAG have developed an SMS-reminder initiative as a way to regularly remind participants to take their medication, to motivate and reassure them and to encourage them during the treatment journey. Initially, from week 1 to 6, participants will receive a weekly phone call as well as daily SMS's to remind them to take their medication or of followup visits, information or motivational messages. During week 7 to13, participants will receive phone-calls every other week and we continue to SMS the participants four times during that week, or every second day. With each SMS goes a simple message, based on common myths surrounding adherence to medication. It is very important that the participants know the toll-free number in case they need support or information, so each SMS includes the helpline number which participants can have easy access to on their phone when they need it, or they can save it directly into the phonebook. If a participant doesn't have enough airtime and doesn't have access to a landline to call on the toll-free number, they will also be sent the SMS number which is monitored constantly by SADAG personnel. If they SMS directly to SADAG, we call them back and help them immediately.

4. **Brochures and information**

Knowledge is power, and it is one of SADAG's main objectives to educate and empower participants about their illness. There is so much stigma and misinformation surrounding mental illness, and for a new health care user especially, a mental health diagnosis can be overwhelming and scary. Psychiatrist do not always have the time to answer a myriad of questions, so what SADAG would offer to each participant on the **RSAP** is full access to all our practical information, brochures and hand-outs on various mental health issues such as **major depression, bipolar mood disorder, anxiety, schizophrenia and substance use disorders**. It is important that participants become experts in their own illness, so during the first week of being on the **RSAP**, we will send all the relevant information, brochures and hand-outs via post or email. The participants will also have full access throughout the entire programme to all of our information which is very practical and offers self-help tips too, such as "no cost ways to treat depression yourself", "self-help for bipolar disorder and how to fill in a mood diary", "importance of sticking to your medication", "controlled breathing", "how to help a loved one", "what to say someone who is depressed or who has bipolar", etc. We can also help participants with medical aid queries and are able to send them relevant information on medical aid Prescribed Minimum Benefits (PMBs) or how to get their treatment covered by their medical aid. If they have any problems, we can direct them to the appropriate organisations with step by step instructions on how to work with their medical aid.

5. **SMS reminders for workshops, support groups, press notifications**

As a way to keep participants aware of different events or workshops happening in their area, we send them SMS-reminders of workshops on a variety of topics, support group meetings in their area as well as any relevant press and media such as interesting newspaper articles as well as TV or radio shows on mental illness. This is an added benefit to allow participants to become more aware and educated about their mental health issue.

6. **Online website with information**

Participants who are part of the adherence programme have full access to our online website (www.sadag.org) which has over 600 000 hits per month and is updated on a daily basis. The website is very comprehensive and has information on all mental health issues in the form of hand-outs, brochures, online videos, book lists, local and international articles, online forum discussions, etc. The complete list of contact details is available online and participants are able to utilise this free service as an additional part of their treatment plan for themselves or their family. The website is approved by registered psychiatrists or psychologists from SADAG Board Members.

7. **Monthly newsletters**

SADAG compiles a comprehensive monthly newsletter which is sent out to a database of over 22 000 members country wide. The newsletter is up-to-date with up-coming patient workshops or online discussions, interesting articles both in local or international press, new support groups, etc. Participants are able to keep up to date with new happenings in the field of mental health in the country. The newsletter is approved by registered psychiatrists and psychologists from SADAG Board Members.

8. **Free support groups**

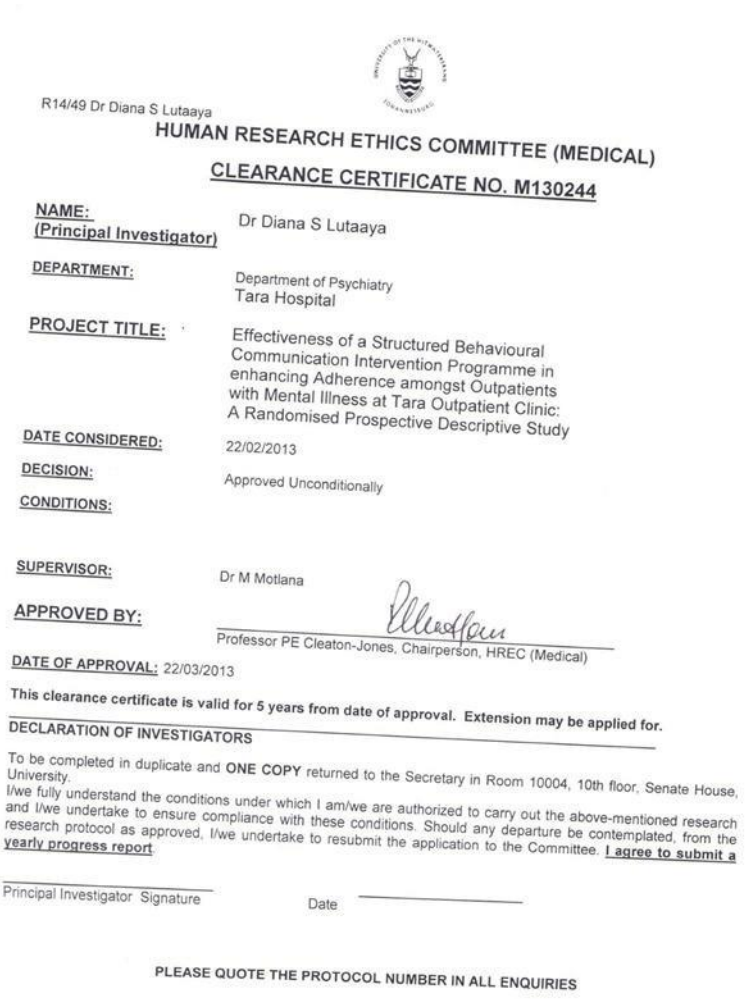
Support Groups are incredibly useful and helpful during treatment, as the participants are able to connect and network with other people who may have a better understanding and insight into mental illness. First-hand experience in a confidential and caring environment offers further support. SADAG has over 160 support groups throughout the country, and participants are able to attend the monthly or bi-weekly meetings for free. We encourage all participants to attend their nearest support group and SADAG will provide them with information such as dates, time and venue to the patient. Support groups are also open to family members and loved ones as a way to educate and inform them on how to further help and support their loved one who has a mental illness. This encourages and promotes adherence. Mental Illness does not only affect the individual, it also affects the entire family. It is important to equip the family with information, brochures, access to free telephonic support and information, as well as the support groups so they can fully understand and support their loved one. SADAG can provide contacts to specific support groups in the Helen Joseph Hospital 'catchment area' such as Alberton, Benoni, Daveyton, Diepsloot, Edenvale, Lenasia, Kwateme, Soweto, Sandton, Randburg, Germiston, Parktown, Kagiso, Blairgowrie, Roodepoort, Tshepisong or Muldersdrift.

Appendix 6: Morisky 8-Item Medication Adherence Questionnaire

Allocation no: _____

1) Do you sometimes forget to take your medicine? (Y/N)
2) People sometimes miss taking their medicines for reasons other than forgetting. Thinking over the past 2 weeks, were there any days when you did not take your medicine? (Y/N)
3) Have you ever cut back or stopped taking your medicine without telling your doctor because you felt worse when you took it? (Y/N)
4) When you travel or leave home, do you sometimes forget to bring along your medicine? (Y/N)
5) Did you take all your medicines yesterday? (Y/N)
6) When you feel like your symptoms are under control, do you sometimes stop taking your medicine? (Y/N)
7) Taking medicine every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan? (Y/N)
8) How often do you have difficulty remembering to take all your medicine?
   A. Never/rarely
   B. Once in a while
   C. Sometimes
   D. Usually
   E. All the time

Appendix 7: Ethics Clearance Certificate



R14/49 Dr Diana S Lutaaya

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M130244

NAME: (Principal Investigator) Dr Diana S Lutaaya

DEPARTMENT: Department of Psychiatry
Tara Hospital

PROJECT TITLE: Effectiveness of a Structured Behavioural Communication Intervention Programme in enhancing Adherence amongst Outpatients with Mental Illness at Tara Outpatient Clinic: A Randomised Prospective Descriptive Study

DATE CONSIDERED: 22/02/2013

DECISION: Approved Unconditionally

CONDITIONS:

SUPERVISOR: Dr M Motlana

APPROVED BY: Professor PE Cleaton-Jones, Chairperson, HREC (Medical)

DATE OF APPROVAL: 22/03/2013

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Secretary in Room 10004, 10th floor, Senate House, University.
I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**.

Principal Investigator Signature _____ Date _____

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES



Appendix 8: Turnitin Originality Report

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