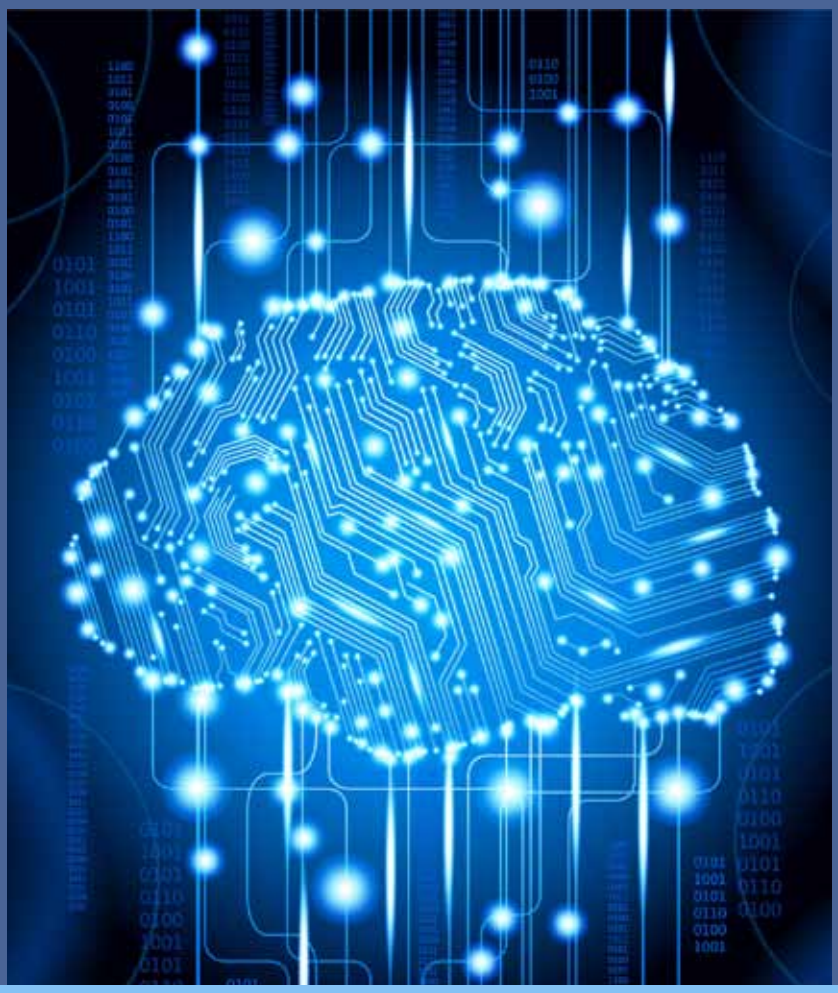


Medication self-management during hospitalisation in severe mental illness

Elke LOOTS

University of Antwerp
Faculty of Medicine and Health Sciences

Medication self-management during hospitalisation in severe mental illness

Zelfmanagement van medicatie tijdens een ziekenhuisopname bij patiënten met ernstige psychiatrische aandoeningen

Thesis submitted for the degree of Doctor of Medical Sciences
at the University of Antwerp to be defended by

Proefschrift voorgelegd tot het behalen van de graad van doctor in de Medische Wetenschappen aan de Universiteit Antwerpen te verdedigen door

Elke LOOTS

Supervisors:
Prof. dr. Tinne Dilles
Prof. dr. Manuel Morrens
Prof. dr. Bart Van Rompaey

Antwerp, 2024

Members of the jury

Prof. dr. Hilde Bastiaens (chair)
Department of Family Medicine and Population Health, Faculty of Medicine and Health Sciences, University of Antwerp, Antwerp, Belgium

Prof. dr. Didier Schrijvers
Department of Psychiatry, Collaborative Antwerp Psychiatric Research Institute (CAPRI), Faculty of Medicine and Health Sciences, University of Antwerp, Antwerp, Belgium
Department of Psychiatry, University Psychiatric Center Duffel, Belgium

Dr. Jasper Vanhoof
KU Leuven, Department of Public Health and Primary Care, Academic Centre for Nursing and Midwifery, Leuven
University Psychiatric Centre (UPC) KU Leuven, Competence Centre of Nursing, Kortenberg

Dr. Silvio van den Heuvel
Saxion University of Applied Sciences, School of Health
Deventer, the Netherlands

Funding
This doctoral study was completed independently and did not receive any external funding or financial support.

Medication self-management during hospitalisation in severe mental illness
Faculteit Geneeskunde en Gezondheidswetenschappen,
Universiteit Antwerpen, Antwerpen 2024
Thesis Universiteit Antwerpen – with summary in Dutch

Lay-out and cover: Dirk De Weerdt (www.ddwdesign.be)

Digital version available at www.nuphac.eu or scan QR-code:

Table of contents

A detailed table of contents is given at the start of each chapter

List of Abbreviations

BD	Bipolar Disorder
CI	Confidence Interval
COREQ	Consolidated Criteria for Reporting Qualitative Research
COVID-19	Coronavirus Disease 19
CRS	Compliance Rating Scale
DSM	Diagnostic and Statistical Manual of Mental Disorders
FDR	False Discovery Rate
ICD	International Statistical Classification of Diseases and Related Health Problems
JCI	Joint Commission International
LAI	Long-Acting Injectable
MAQ	Medication Adherence Questionnaire
MARS	Medication Adherence Rating Scale
MCAR	Missing Completely At Random
MEMS®	Medication Event Monitoring Systems
MeSH	Medical Subject Headings
MMU	Medication Management and Use
MPR	Medication Possession Ratio
MSM	Medication Self-Management
N/A	Not Applicable
OR	Odds Ratio
PAR	Participatory Action Research
PLA	Participatory, Learning and Action method
Q&A	Questions and Answers
RCT	Randomized Controlled Trial
RR	Relative Risk
SAM	Self-Administration of Medication
SDM	Shared Decision-Making
SMS	Short Message Service
SSD	Schizophrenia Spectrum Disorder
STROBE	Strengthening The Reporting Of Observational Studies in Epidemiology
TAU	Treatment As Usual
TRQ	Tablets Routine Questionnaire
WHO	World Health Organization

Chapter 1

General introduction

Chapter 1: Contents

1.1. Background

Schizophrenia spectrum and bipolar disorders are severe psychiatric disorders, with schizophrenia spectrum disorders (SSD) affecting around 1% and bipolar disorders (BD) affecting about 3% worldwide [1-3]. The majority of the psychiatric pathologies at the admission is in Schizophrenia and other psychotic disorders category in Belgium (Namely, 41% in Flanders, 88% in Brussels and 49% in Wallonia) [4].

Patients with SSD and BD suffer from perturbing psychotic episodes, characterised by recurrent episodes of hallucinations and delusions (positive symptoms), chronic shallowing of feelings and apathy (negative symptoms) and cognitive impairment [5, 6].

During the acute psychotic episode, hospitalisation with the need for immediate psychiatric care. Once psychotic symptoms have been abolished or improved as far as possible, one enters the maintenance phase. Here the concern shifts to prophylaxis (which often includes maintenance medication) and in- and outpatient rehabilitation [7]. In Flanders (Belgium), acute mental health care for patients with SSD or BD is organised in 31 psychiatric hospitals, supplemented with specialized beds in psychiatric units of general hospitals [8].

After an acute psychotic episode, patients transfer to a resocialisation unit. These units provide education of both the patient and patients' family and the adaptation of pharmacological and psychoeducation treatments with the aim to prepare the patient for discharge [7].

1.1.1. Overall treatment of SSD and BD

Together with psychoeducation, pharmacotherapy is often the first line of treatment of these severe psychiatric disorders [9-12]. Antipsychotics have been available since the mid-1950s and are the best treatment now available for SSD and BD. These agents mainly affect the positive symptoms of the disease and thus reduce hallucinatory experiences and delusional thinking. In addition, antipsychotics have also been shown to modestly improve negative and cognitive symptoms [13]. Little evidence exists however to support the choice of one medicine over the other [7]. Most patients receive oral antipsychotics, and second-generation antipsychotics are most frequently prescribed [14]. In recent years, long-acting injectable (LAI) antipsychotic medication gained more attention and accounted for 9% of total use in schizophrenia patients in the US [15]. LAI antipsychotic

medication is known to be at least as effective as oral antipsychotics for treating patients with SSD or BD [15-18].

LAI antipsychotics were developed to enable maintenance of stable plasma drug levels and consequently reduce the risk of psychotic relapse. Moreover, they have a few advantages over oral antipsychotics, including ensuring clinician awareness of non-adherence due to absence or tardiness at injection appointments, reduction in oral medicines burden, and reduced consequences of planned or unplanned treatment gaps [19].

In Belgium antipsychotic sales increased considerably over the past 15 years and this growth was mainly explained by a 3-fold increase in prescription by psychiatrists and neurologists [14]. Next to pharmacotherapy, psychoeducation is a well-known and commonly used intervention in SSD and BD treatment [9, 12, 20-35].

Psychoeducation may be defined as the education, with the focus on knowledge, of a person with psychiatric disorder in subject areas that serve the goals of treatment and rehabilitation. The aim of psychoeducation is to increase patients' knowledge and understanding of their disease and treatment to cope more effectively with their disease to enable the patient to engage in behaviour change to prevent hospitalisation [26, 30, 34].

1.1.2. Non-adherence and relapse

Medication non-adherence represents a paramount challenge encountered by healthcare providers in the management of psychotic disorders. Patients with treatment failure have a high risk of relapse resulting in acute psychosis, leading to psychiatric (re)hospitalizations and considerable economic costs [4, 36].

Non-adherence is highly prevalent, ranging between 63–74% in patients with SSD and about 50% in patients with BD [1, 37-39]. About 25% of patients discontinue their medication within the first week after discharge from inpatient treatment [16]. Medication non-adherence is one of the most consistent predictors of relapse [40].

Non-adherence puts patients at risk for exacerbations of psychosis and relapse resulting in hospital visits and admission [4, 12, 17, 41]. Relapse rates appear to be high at 78–82% for SSD and 60% for BD [42, 43]. Non-adherent patients have an average relapse risk that is 3.7 times greater than adherent patients [44].

Reasons for non-adherence include, amongst others, lack of knowledge of the disease and/or the disease severity, the (anxiety of) side-effects of medication, difficulty recognising symptoms, not acknowledging the need for antipsychotic therapy, distrust in the effectiveness (the effect of non-

adherence to antipsychotic treatment on rehospitalisation in patients with psychotic disorders), negative attitudes towards medication, past history of non-adherence, substance abuse, cognitive impairments (predictors) and deficient communication between inpatient units and primary health-care providers [45, 46]. The model of four dimensions of medication non-adherence in patients with psychotic and mood disorders shows that non-adherence is a multidimensional problem (Figure 1.1). Understanding the dimensions and understanding that many of these factors represent health equality opportunities allows us to assess and predict adherence problems and target interventions to improve adherence.

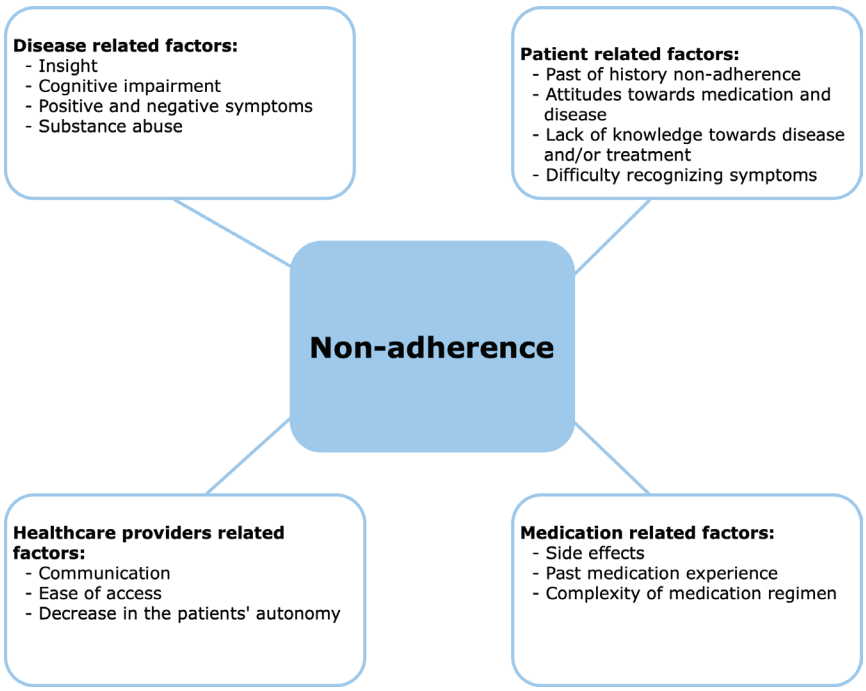


Figure 1.1: Model of dimensions of medication non-adherence in patients with psychotic and mood disorders.

1.1.3. Definition of medication adherence

Medication adherence is, however, a complex behaviour comprising a series of interrelated steps involving patients, their providers, and the healthcare system [9]. Adherence to medication is defined as "the process by which patients take their medication as prescribed, including not only the correct dose, frequency, and spreading, but also its continued safe use over time [47].

A well-known problem in the literature is the lack of uniformity in the terminology used to describe deviation from prescribed medication regimens. Most of the studies defined adherence as taking more than 70% of prescribed doses [20]. This cut-off has validity in predicting subsequent hospitalisation [48].

Medication non-adherence can occur in the following situations or combinations thereof: late or non-initiation of the prescribed treatment, suboptimal implementation of the dosing regimen or early discontinuation of the treatment. For many patients, it is important to be able to self-manage their medications successfully, as they are often expected to do after discharge. Patients who are not able to self-manage their medication, but are expected to do MSM after discharge, should be given the opportunity to learn to self-manage their medication whilst in hospital. Providing the innovative possibility to self-manage medication in a controlled environment enables healthcare providers to immediately intervene when medication related problems occur.

1.2. Medication self-management

Medication self-management (MSM) programmes, in which patients manage their own medication, have been reported in the literature since 1959 [49]. MSM is defined as a person's ability to cope with medication treatment for a chronic condition, along with the associated physical and psychosocial effects that the medication causes in their daily lives [49-51].

As shown in Figure 1.2, the process of MSM has been translated into a model [52]. First, there is the decision point for which medication and how to take them. Questions concerning treatment options, effectiveness, and risk must be answered. The second step starts with a prescription, which has to be filled and picked up. Once the patient obtains the medication, the next step is to learn how to take their medication safely and appropriately. The ability to name, identify, and understand how to take medicines in one's medication regimen is a fundamental yet often overlooked part of MSM. Patients should be able to track what they are taking, why they are taking it, and how it should be taken to ensure safe and effective use. In addition, to understanding how to take their medication correctly, it is essential for patients to organise their medication use around their daily schedule. Actually, taking the prescribed medication was described in the fifth step of the model. Subsequently, patients monitor their medication intake and evaluate possible side effects or symptoms related to their medicines in order to undertake any action if needed. The last step con-

cerns the act of sustaining a correct medication intake routine in a safe and appropriate way.

MSM is believed to increase patients' understanding about their treatment and to promote their independence and autonomy during hospitalisation [53].

It is facilitated by social support and information, but hindered by difficulties associated with medication regimens, as well as by physical and psychological symptoms [54, 55].

Research conducted in five psychiatric units; the results revealed 32% of the patients hospitalized on these units did self-manage (a part of) their medication. Nevertheless, this study identified a serious lack of guidelines to support the implementation of MSM in daily practice. Due to the fact medication management is both the responsibility of nurses, physicians and hospital pharmacists, a multidisciplinary approach was proposed [56].

Hospital MSM guidelines often incorporate several stages of increasing patient independence and decreasing healthcare providers involvement as patients become more competent [53]. Nurses may initially administer medicines to patients. Following this, patients may request medicines from the nurse and self-administer their medicines under supervision.

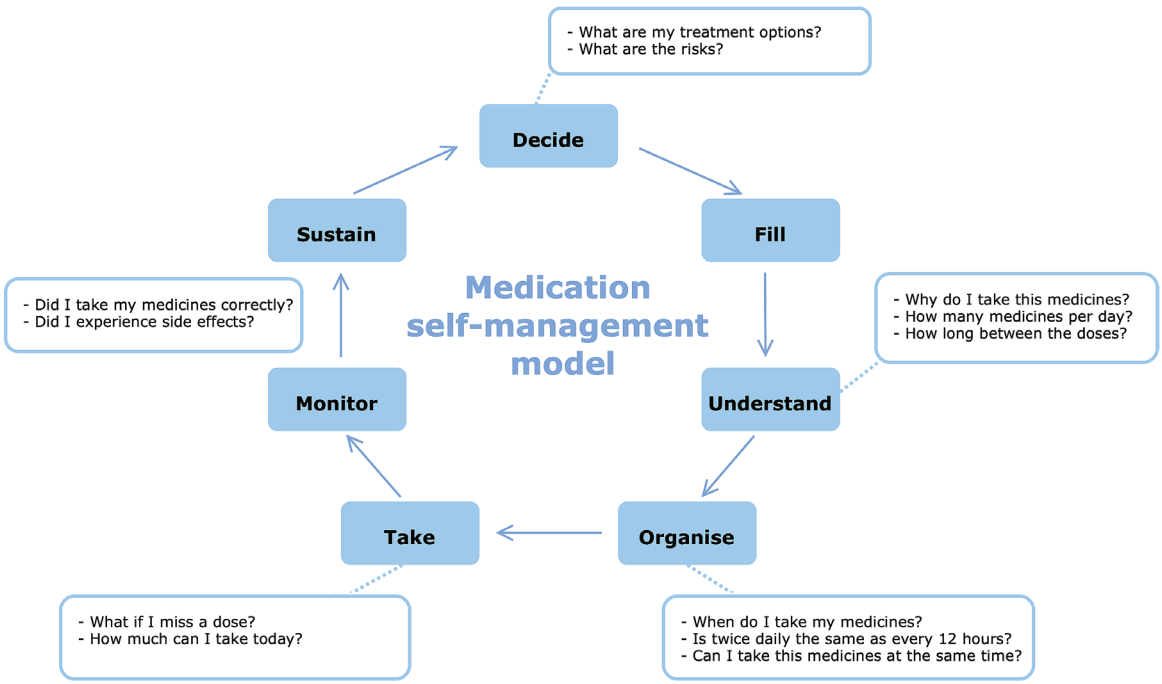


Figure 1.2: Medication self-management model [52].

1.2.1. Medication self-management during hospitalisation

Western healthcare systems have been constructed upon an acute, episodic model of care, wherein healthcare providers are regarded as primary agents, and patients are perceived as passive recipients of care [57].During hospitalisation, nurses often take over the patient's medication management [56-58]. This results in a disruption in the continuity of the patient's medication home routines [59]. Providing the innovative possibility to self-manage medication in a controlled environment enables healthcare providers to immediately intervene when medication related problems occur. As patients are not capable of self-managing their medication, aid is often required.

In addition, MSM is becoming an increasingly important element in rehabilitation programs. The attitudes of patients and healthcare providers play a crucial role in the effectiveness of MSM and the related support. On the one hand, patients' beliefs and perceptions influence their willingness to actively engage in managing their medication. On the other hand, healthcare providers have a significant impact on the extent to which they support patients in developing the necessary MSM skills. Mapping these attitudes is essential to identifying potential barriers or facilitators that may affect the development and implementation of successful MSM strategies. Without a clear understanding of these attitudes, interventions aimed at improving MSM may be suboptimal, as they may fail to address underlying perceptions or resistance from both stakeholders.

Healthcare providers can support and coach patients towards self-management of their medication. Therefore, MSM during hospitalisation could provide continuity in the medication home routines of the patient, detect problems related to MSM and intervene by for example providing education, and result in an improvement of MSM competences and adherence to treatment [50, 53, 60, 61]. During MSM in hospital, patients are monitored and supported by their healthcare providers.

1.3. The rationale of the doctoral study

Relapses due to non-adherence to treatment remain a major problem for patients with SSD or BD [39, 40]. In addition, non-adherence to treatment leads to poorer patient outcomes, reduced quality of life as well as higher economic costs for inpatient care were discussed in literature. Therefore, focusing on medication adherence in this population is foremost important. From the current body of evidence, we can conclude a multidimensional and multidisciplinary approach including psychoeducation, to be more specific education concerning disease insight and medication management [20]. A structured program for MSM, assisting patients to self-manage their medicines during hospitalisation supervised, coached and supported by healthcare providers, is hypothesised to improve adherence and relapse rates after discharge.

Previous research proved pharmacotherapy and psychoeducation are often the first line of treatment in patients with SSD or BD, this indicates the medication management process of antipsychotics can still be improved [9-11, 20, 39]. There is a huge contrast between inpatient and outpatient treatment. During the inpatient treatment, all medication is administrated and prepared, while at home the patient is often on his own. Patients suddenly must be able to read their medication schedule, pick up the prescribed drugs at the pharmacy, and prepare and take them at the right time [53, 62, 63].

MSM needs to be stimulated and can provide continuity in the patients' medication management routines, detect problems related to medication and intervene by for example providing education, and result in a better medication management, patient autonomy and satisfaction, self-reliance, disease insight and adherence to treatment.

Research on MSM guidelines in patients with SSD or BD is currently lacking. Therefore, the need for further researching into the topic of MSM in Belgian psychiatric hospitals.

1.4. Aim of the doctoral study

The general aim of this study was to identify interventions to improve medication adherence in patients with SSD or BD. Because of the expected positive impact of Medication Self-Management (MSM) during hospitalization, we studied patients' and healthcare providers' attitude regarding MSM during hospitalisation, to facilitate the development and implementation of a MSM program. Specific research aims for this dissertation derived from the general aim:

- Explore the impact of interventions on medication adherence in patients with SSD or BD.
- To describe the prevalence of MSM in Flemish psychiatric hospitals.
- Explore the perspectives of all stakeholders involved in the MSM procedure in patients with severe mental illness.
- To describe psychiatric healthcare providers' willingness to MSM and their attitude, prerequisites, benefits, and ability towards it during hospitalisation.
- To describe the attitudes of patients with SSD or BD regarding MSM during hospitalisation. A secondary aim is to identify various factors associated with patient willingness to participate in MSM and to describe their assumptions concerning needs and necessary prerequisites, as well as their attitudes towards their medication.

1.5. Outline of the doctoral study

The outline of this doctoral study is aligned with the research aim and consist of 7 chapters. Following the general introduction, the results of our research are presented in the next chapters (2-6) based on articles published in, or submitted to, international peer reviewed journals. The results are followed by the general discussion, practical implications, recommendations, and a conclusion.

Chapter 1 – General introduction

Chapter 2 – Interventions to improve medication adherence in patients with Schizophrenia or Bipolar Disorders: A systematic review and meta-analysis

This chapter opens with an overview of the already existing evidence concerning the impact of interventions on medication adherence in pa-

tients with SSD or BD.

Loots E, Goossens E, Vanwesemael T, Morrens M, Van Rompaey B, Dilles T. Interventions to Improve Medication Adherence in Patients with Schizophrenia or Bipolar Disorders: A Systematic Review and Meta-Analysis. Int J Environ Res Public Health. 2021 Sep 28;18(19):10213. doi: 10.3390/ijerph181910213. PMID: 34639510; PMCID: PMC8508496.

Chapter 3 – Medication self-management in Flemish psychiatric hospitals: A prevalence study in hospitalised patients with Schizophrenia Spectrum or Bipolar Disorders

In this chapter, we aimed to describe daily practices related to MSM in hospital. This chapter comprised an evaluation of the prevalence rates of MSM in hospital, and how MSM is managed in daily practice in patients with SSD or BD.

Loots E, Van Rompaey B, Morrens M, Dilles T. Medicatie zelfmanagement in Vlaamse psychiatrische ziekenhuizen: Een prevalentiestudie bij gehospitaliseerde patiënten met een schizofrenie spectrum of bipolaire stoornis. Nursing. 2023;38(2):14-21.

Chapter 4 – Medication Self-Management in Hospitalised Patients with Schizophrenia Spectrum or Bipolar Disorders: The Perceptions of Patients and Healthcare Providers

We explore the perspectives of hospitalised patients with SSD or BD and their healthcare providers on MSM during hospitalisation through a qualitative descriptive design with an exploratory approach within a pragmatic paradigm. Forty-nine interviews were completed to unravel their opinions.

Loots E, Leys J, Proost S, Morrens M, Glazemakers I, Dilles T, Van Rompaey B. Medication Self-Management in Hospitalised Patients with Schizophrenia or Bipolar Disorders: The Perceptions of Patients and Healthcare Providers. Int J Environ Res Public Health. 2022 Apr 15;19(8):4835. doi: 10.3390/ijerph19084835. PMID: 35457700; PMCID: PMC9027742.

Chapter 5 – The attitude of healthcare providers towards medication self-management in hospitalised patients with Schizophrenia Spectrum or Bipolar Disorders

In this chapter, we describe healthcare providers' willingness and attitude towards MSM during hospitalisation. A multicentre, quantitative cross-sectional observational design was used. Psychiatric healthcare providers were surveyed by use of a structured questionnaire assessing their willingness, attitudes towards MSM as well as their assumption on needed prerequisites, ideas about benefits, and patients' ability of MSM.

Loots E, Dilles T, Hadouchi S, Van Rompaey B, Morrens M. The attitude of healthcare providers towards medication self-management in hospitalized patients diagnosed with schizophrenia or bipolar disorders. J Psychiatr Ment Health Nurs. 2023

Aug;30(4):761-772. doi: 10.1111/jpm.12903. Epub 2023 Feb 4. PMID: 36691725.

Chapter 6 – The attitude of patients with Schizophrenia Spectrum or Bipolar Disorders towards medication self-management during hospitalisation

The primary objective of this study was to describe the attitudes of patients with SSD or BD regarding MSM during hospital admission. A secondary aim was to identify various factors associated with patient willingness to participate in MSM and to describe their assumptions concerning needs and necessary prerequisites, as well as their attitudes towards their medication.

Loots E, Dilles T, Van Rompaey B, Morrens M. Attitudes of patients with schizophrenia spectrum or bipolar disorders towards medication self-management during hospitalisation. J Clin Nurs. 2024 Apr;33(4):1459-1469. doi: 10.1111/jocn.16936. Epub 2023 Dec 1. PMID: 38041238.

Chapter 7 - General discussion, practical implications, recommendations, and conclusion

In this final chapter we discuss the results of the individual studies included in this doctoral study. Furthermore, several topics are discussed such as the context for the implementation of MSM, potential hurdles for MSM during hospitalisation and the methodological strengths and limitations of this doctoral study.

We formulate practical implications and recommendations for a future MSM intervention and implications for daily practice and future research.

To conclude this doctoral thesis, a summary is provided, with a list of tables and figures, acknowledgements, and the curriculum vitae of the candidate.

1.6. References

1. World Health Organization. The Global Economic Burden of Non-Communicable Diseases; World Economic Forum: Geneva, Switzerland. 2013.
2. McGrath J, Saha S, Welham J, El Saadi O, MacCauley C, Chant D. A systematic review of the incidence of schizophrenia: the distribution of rates and the influence of sex, urbanicity, migrant status and methodology. BMC Med. 2004;2:13.
3. Perälä J, Suvisaari J, Saarni SI, Kuoppasalmi K, Isometsä E, Pirkola S, et al. Lifetime prevalence of psychotic and bipolar I disorders in a general population. Arch Gen Psychiatry. 2007;64(1):19-28.
4. Mistiaen P, Cornelis J, Detollenaere J, Devriese S, Farfan-Portet M, Ricour C. Organisation of mental health care for adults in Belgium. Health Services Research (HSR) Brussels: Belgian Health Care Knowledge Centre (KCE). KCE Reports. 2019;318.
5. Van Os J, Kapur S. Schizophrenia. Lancet. 2009;374(9690):635-45.
6. Van Os J, Linscott R, Myin-Germeys I, Delespaul P, Krabbendam L. A systematic review and meta-analysis of the psychosis continuum: evidence for a psychosis proneness-persistence-impairment model of psychotic disorder. Psychol Med. 2009;39(2):179-95.
7. Semple D, Smyth R. Oxford handbook of psychiatry. Oxford Handbooks. 2013.
8. FOD Volksgezondheid. Technische commissie voor verpleegkunde Gezondheidszorgberoepen en beroepsuitoefening: vragen en antwoorden. 2019.
9. Hartung D, Low A, Jindai K, Mansoor D, Judge M, Mendelson A, et al. Interventions to Improve Pharmacological Adherence Among Adults With Psychotic Spectrum Disorders and Bipolar Disorder: A Systematic Review. Psychosomatics. 2017;58(2):101-12.
10. Mibel F, Heikki E. Non-compliance to medication in Psychiatric patients. Tuku University of Applied Sciences. 2013.
11. Cramer JA, Rosenheck R. Compliance with medication regimens for mental and physical disorders. Psychiatr Serv. 1998;49(2):196-201.
12. Colom F, Lam D. Psychoeducation: improving outcomes in bipolar disorder. Eur Psychiatry. 2005;20(5-6):359-64.
13. Arciniegas DB. Psychosis. Continuum (Minneap Minn). 2015;21(3 Behavioral Neurology and Neuropsychiatry):715-36.
14. Morrens M, Cleymans S, Van der Spek S, Dom G. Evolution of First-generation and Second-generation Antipsychotic Prescribing Patterns in Belgium Between 1997 and 2012: A Population-based Study. Journal of Psychiatric Practice. 2015;Vol. 21, No. 4:248-58.
15. Marcus SC, Zummo J, Pettit AR, Stoddard J, Doshi JA. Antipsychotic Adherence and Rehospitalization in Schizophrenia Patients Receiving Oral Versus Long-Acting Injectable Antipsychotics Following Hospital Discharge. J Manag Care Spec Pharm. 2015;21(9):754-68.
16. Keith SJ, Kane JM. Partial compliance and patient consequences in schizophrenia: our patients can do better. J Clin Psychiatry. 2003;64(11):1308-15.
17. Terkelsen KG, Menikoff A. Measuring the costs of schizophrenia. Implications for the post-institutional era in the US. Pharmacoeconomics. 1995;8(3):199-222.
18. Velligan D, Mintz J, Maples N, Xueying L, Gajewski S, Carr H, et al. A randomized trial comparing in person and electronic interventions for improving adherence to oral medications in schizophrenia. Schizophr Bull. 2013;39(5):9.
19. McEvoy JP. Risks versus benefits of different types of long-acting injectable antipsychotics. J Clin Psychiatry. 2006;67 Suppl 5:15-8.

20. Loots E, Goossens E, Vanwesemael T, Morrens M, Van Rompaey B, Dilles T. Interventions to Improve Medication Adherence in Patients with Schizophrenia or Bipolar Disorders: A Systematic Review and Meta-Analysis. Int J Environ Res Public Health 2021, 18, 10213 https://doiorg/103390/ ijerph181910213. 2021.
21. Aho-Mustonen K, Tiihonen J, Repo-Tiihonen E, Ryynänen OP, Miettinen R, Räty H. Group psychoeducation for long-term offender patients with schizophrenia: an exploratory randomised controlled trial. Crim Behav Ment Health. 2011;21(3):163-76.
22. Atkinson JM, Coia DA, Gilmour WH, Harper JP. The impact of education groups for people with schizophrenia on social functioning and quality of life. Br J Psychiatry. 1996;168(2):199-204.
23. Awan NR, Jehangir SF, Irfan M, Naeem F, Farooq S. Explanatory model of illness of the patients with schizophrenia and the role of educational intervention. Schizophr Res. 2017;190:68-73.
24. Barkhof E, Meijer CJ, de Sonneville LM, Linszen DH, de Haan L. The effect of motivational interviewing on medication adherence and hospitalization rates in nonadherent patients with multi-episode schizophrenia. Schizophr Bull. 2013;39(6):1242-51.
25. Battle EH, Halliburton A, Wallston KA. Self medication among psychiatric patients and adherence after discharge. J Psychosoc Nurs Ment Health Serv. 1982;20(5):21-8.
26. Bäuml J, Pitschel-Walz G, Volz A, Lüscher S, Rentrop M, Kissling W, et al. Psychoeducation Improves Compliance and Outcome in Schizophrenia Without an Increase of Adverse Side Effects: A 7-Year Follow-up of the Munich PIP-Study. Schizophr Bull. 2016;42 Suppl 1(Suppl 1):S62-70.
27. Dolder CR, Lacro JP, Leckband S, Jeste DV. Interventions to improve antipsychotic medication adherence: review of recent literature. J Clin Psychopharmacol. 2003;23(4):389-99.
28. Eker F, Harkın S. Effectiveness of six-week psychoeducation program on adherence of patients with bipolar affective disorder. J Affect Disord. 2012;138(3):409-16.
29. Guo X, Zhai J, Liu Z, Fang M, Wang B, Wang C, et al. Effect of antipsychotic medication alone vs combined with psychosocial intervention on outcomes of early-stage schizophrenia: A randomized, 1-year study. Arch Gen Psychiatry. 2010;67(9):895-904.
30. Javadpour A, Hedayati A, Dehbozorgi GR, Azizi A. The impact of a simple individual psycho-education program on quality of life, rate of relapse and medication adherence in bipolar disorder patients. Asian J Psychiatr. 2013;6(3):208-13.
31. Mueser KT, Deavers F, Penn DL, Cassisi JE. Psychosocial treatments for schizophrenia. Annu Rev Clin Psychol. 2013;9:465-97.
32. Pakpour AH, Modabbernia A, Lin CY, Saffari M, Ahmadzad Asl M, Webb TL. Promoting medication adherence among patients with bipolar disorder: a multicenter randomized controlled trial of a multifaceted intervention. Psychol Med. 2017;47(14):2528-39.
33. Sajatovic M, Tatsuoka C, Cassidy KA, Klein PJ, Fuentes-Casiano E, Cage J, et al. A 6-Month, Prospective, Randomized Controlled Trial of Customized Adherence Enhancement Versus Bipolar-Specific Educational Control in Poorly Adherent Individuals With Bipolar Disorder. J Clin Psychiatry. 2018;79(6).
34. Xia J, Merinder LB, Belgamwar MR. Psychoeducation for schizophrenia. Cochrane Database of Systematic Reviews 2011, Issue 6. Art. No.: CD002831. DOI: 10.1002/14651858.
35. Zygmunt A, Olfson M, Boyer CA, Mechanic D. Interventions to improve medication adherence in schizophrenia. Am J Psychiatry. 2002;159(10):1653-64.
36. El Abdellati K, De Picker L, Morrens M. Antipsychotic Treatment Failure: A Systematic Review on Risk Factors and Interventions for Treatment Adherence in Psychosis. Front Neurosci. 2020;14:531763.
37. Miasso AI, Cassiani SH, Pedrão LJ. [Affective bipolar disorder and ambivalence in relation to the drug treatment: analyzing the causal conditions]. Rev Esc Enferm USP. 2011;45(2):433-41.

38. Young JL, Zonana HV, Shepler L. Medication noncompliance in schizophrenia: codification and update. Bull Am Acad Psychiatry Law. 1986;14(2):105-22.

39. Semahegn A, Torpey K, Manu A, Assefa N, Tesfaye G, Ankomah A. Psychotropic medication non-adherence and its associated factors among patients with major psychiatric disorders: a systematic review and meta-analysis. Syst Rev. 2020;9(1):17.

40. Chan KY, Zhao FF, Meng S, Demaio AR, Reed C, Theodoratou E, et al. Prevalence of schizophrenia in China between 1990 and 2010. J Glob Health. 2015;5(1):010410.

41. Sajatovic M, Tatsuoka C, Cassidy K, Klein P, Fuentes-Casiano E, Cage J, et al. A 6-Month, Prospective, Randomized Controlled Trial of Customized Adherence Enhancement Versus Bipolar-Specific Educational Control in Poorly Adherent Individuals With Bipolar Disorder. The Journal of Clinical Psychiatry. 2018;79.

42. Robinson D, Woerner MG, Alvir JM, Bilder R, Goldman R, Geisler S, et al. Predictors of relapse following response from a first episode of schizophrenia or schizoaffective disorder. Arch Gen Psychiatry. 1999;56(3):241-7.

43. Kebede D, Alem A, Shibire T, Deyassa N, Negash A, Beyero T, et al. Symptomatic and functional outcome of bipolar disorder in Butajira, Ethiopia. J Affect Disord. 2006;90(2-3):239-49.

44. Fenton WS, Blyler CR, Heinssen RK. Determinants of medication compliance in schizophrenia: empirical and clinical findings. Schizophr Bull. 1997;23(4):637-51.

45. Lacro DL, Dolder CR, Leckband SG, Jeste DV. Prevalence of and risk factors for medication nonadherence in patients with schizophrenia: a comprehensive review of recent literature. J Clin Psychiatry. 2002;Oct; 63(10):892-909.

46. Haynes YX, Degani A, Kripalani S, Garg A, McDonald HP. Interventions to enhance medication adherence. Cochrane Database Syst Rev. 2005.

47. Vrijens B, De Geest S, Hughes DA, Przemyslaw K, Demonceau J, Ruppar T, et al. A new taxonomy for describing and defining adherence to medications. Br J Clin Pharmacol. 2012;73(5):691-705.

48. Simpson SH, Eurich DT, Majumdar SR, Padwal RS, Tsuyuki RT, Varney J, et al. A meta-analysis of the association between adherence to drug therapy and mortality. Bmj. 2006;333(7557):15.

49. Parnell MA. Medicines at the bedside. Am J Nurse. 1959;59:1417-8.

50. Wright J, Emerson, A, Stephens, M, & Lennan, E. Hospital inpatient self-administration of medicine programmes: a critical literature review. Pharm World Sci. 2006;28(3):140-51.

51. Beentjes TAA, van Gaal B, van Achterberg T, Goossens P.J.J. Self-Management Support Needs From the Perspectives of Persons With Severe Mental Illness: A Systematic Review and Thematic Synthesis of Qualitative Research. J Am Psychiatr Nurses Assoc. 2020;26 (5):464-82.

52. Bailey Stacy C, Christine U, Oramasionwu, Wolf MS. Rethinking Adherence: A Health Literacy–Informed Model of Medication Self-Management. Journal of Health Communication. 2013;18:20-30.

53. Richardson SJ, Brooks H, Bramley G, & Coleman J. Evaluating the effectiveness of self-administration of medication (SAM) schemes in the hospital setting: a systematic review of the literature. PLoS One. 2014;9(12).

54. Audulv Å GS, Kephart G, Warner G, Packer TL. The Taxonomy of Everyday Self-management Strategies (TEDSS): a framework derived from the literature and refined using empirical data. Patient Educ Couns. 2019;102(2):367–375. .

55. Morrison CF, Martsolf D. Facilitators and Barriers to Self-Management for Adolescents and Young Adults Following a Hematopoietic Stem Cell Transplant . Journal Oncol Nurs Jan/Feb;35(1):36-42. 2018.

56. Vanwesemael T, Petrovic M, Boussery K, Dilles T. SelfMED: Self-Administration of Medication in Hospital: A Prevalence Study in Flanders, Belgium. Nurs Scholarsh. 2017;49:277-85.

57. Barlow J, Wright C, Sheasby J, Turner A, Hainsworth J. Self-management approaches for people with chronic conditions: a review. Patient Educ Couns. 2002;48(2):177-87.

58. Loots E, Van Rompaey B, Morrens M, Dilles T. Medicatie zelfmanagement in Vlaamse psychiatrische ziekenhuizen: Een prevalentiestudie bij gehospitaliseerde patiënten met een schizofrenie spectrum of bipolaire stoornis. Nursing. 2023;38(2):14-21

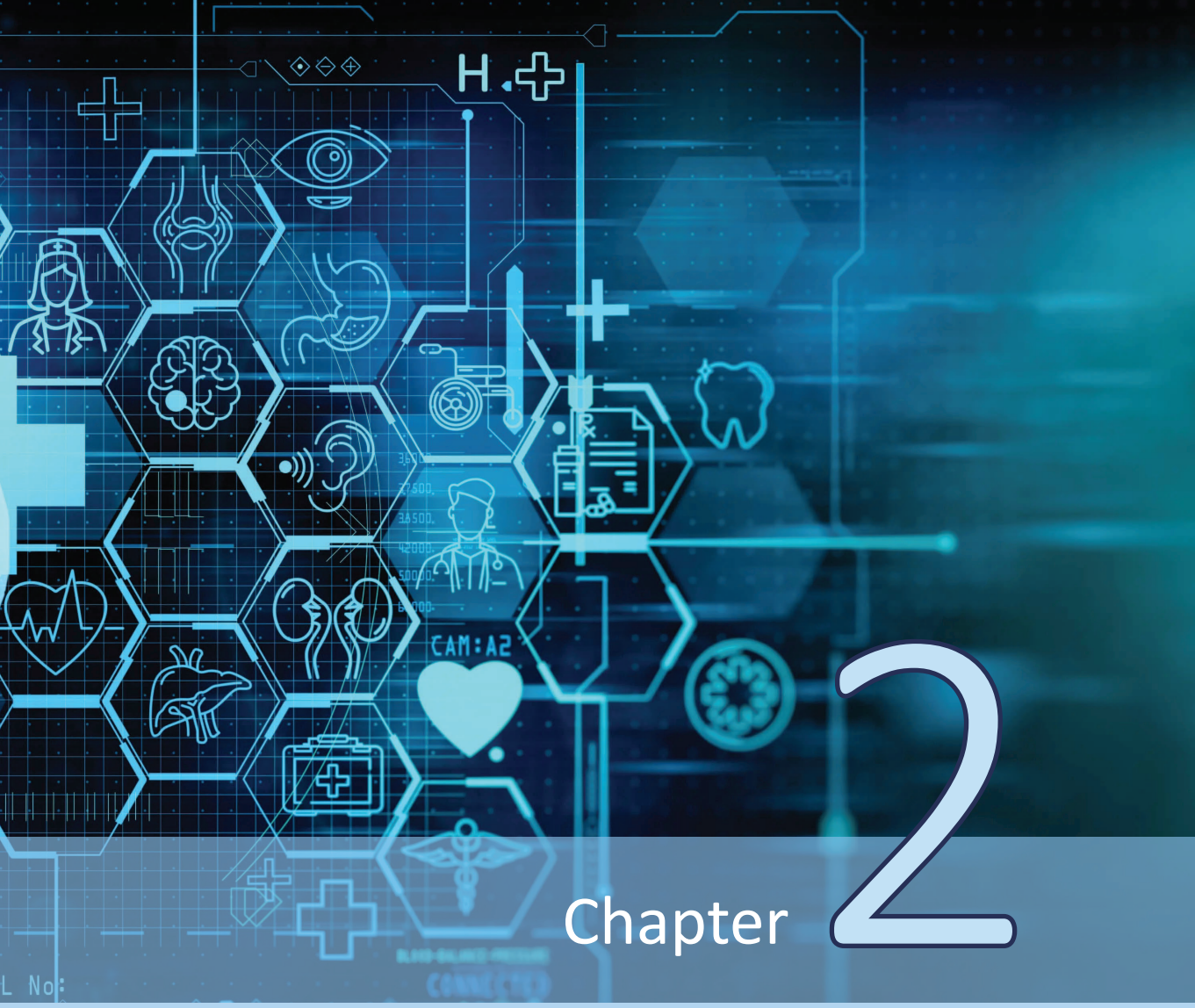
59. Murray A. The implementation of a self-administration of medication programmes within Older Persons Mental Health. Journal of Psychiatriac Mental Health Nursing. 2011;18(2).

60. Zhou B, Gu Y. Effect of self-management training on adherence to medications among community residents with chronic schizophrenia: a singleblind randomized controlled trial in Shanghai, China. Shanghai Arch Psychiatry. 2014;26(6):332-8.

61. Valenstein M, Kavanagh J, Lee T, Reilly P, Dalack GW, Grabowski J, et al. Using a pharmacy-based intervention to improve antipsychotic adherence among patients with serious mental illness. Schizophr Bull. 2011;37(4):36.

62. Davis A, Muir P, Allardice J, Clark K, Groves J, Molenaar M, Robson G. SHPA Guidelines for Self-Administration of Medication in Hospitals and Residential Care Facilities. Journal of Pharmacy Practice and Research, 32(4), 324-325. 2002.

63. Richard A, Shea K. Delineation of self-care and associated concepts. J Nurs Scholarsh. 2011;43(3):255-64.



Chapter 2

Interventions to improve medication adherence in patients with schizophrenia or bipolar disorders: *A systematic review and meta-analysis*

This chapter has been published as:
Loots E, Goossens E, Vanwesemael T, Morrens M, Van Rompaey B, Dilles T.
Interventions to Improve Medication Adherence in Patients with Schizophrenia or Bipolar Disorders: A Systematic Review and Meta-Analysis.
Int J Environ Res Public Health. 2021 Sep 28;18(19):10213.
doi: 10.3390/ijerph181910213. PMID: 34639510; PMCID: PMC8508496

Chapter 2: Contents

Abstract

Background: Adherence to prescribed medication regimes improves outcomes for patients with severe mental illness such as schizophrenia or bipolar disorders. The aim of this systematic review and meta-analysis was to compare the effectiveness among interventions to improve medication adherence in patients with schizophrenia or bipolar disorders.

Methods: Literature published in the last decade was searched for interventions studies to improve adherence in patients with schizophrenia or a bipolar disorder. Interventions were categorised on the basis of type, and the context and effectiveness of the interventions were described. Two review authors independently extracted and assessed data, following criteria outlined by the Cochrane Handbook for Systematic Reviews of Interventions. The GRADEPro (McMaster University, 2020, Ontario, Canada) was used for assessing the quality of the evidence.

Results: Twenty-three publications met the selection criteria. Different types of interventions aiming to improve adherence were tested: educational, behavioural, family-based, technological, or a combination of previous types. Meta-analysis could be performed for 10 interventions. When considered separately by subgroups on the basis of intervention type, significant differences ($p= 0.02$) were found in adherence among subgroup interventions ($p= 0.03$; $I^2= 53\%$).

Conclusion: This review concluded that successful interventions used a combination of behavioural and educational approaches that seem easy to implement in daily practice.

2.1. Introduction

Psychiatric disorders are a public health challenge and comprise 13% of the total global disease burden [1]. Schizophrenia and bipolar disorders are severe major psychiatric disorders, with schizophrenia affecting about 23 million people and bipolar disorders affecting about 60 million people worldwide [2]. Together with psychoeducation, pharmacotherapy is often the first line of treatment of these major psychiatric disorders. Hence, maintaining medication adherence is crucial [3-6]. Varieties of risk factors for disease relapse have been reported, including medication non-adherence, substance abuse and stressful life events. A recent systematic review analysed risk factors for relapse in the early course of psychosis in patients with schizophrenia [7]. Among all associated factors, non-adherence appeared to be the strongest predictor for relapse. Discontinuing antipsychotic pharmacotherapy increased the risk of relapse by almost five times [8]

Non-adherence is highly prevalent, ranging between 63–74% in patients with schizophrenia and about 50% in patients with bipolar disorders [9-11]. About 25% of patients discontinue their medication within the first week after discharge from inpatient treatment [12]. Non-adherence puts patients at risk for exacerbations of psychosis and relapse resulting in hospital visits and admission [6, 13-22]. Relapse rates appear to be high at 78–82% for schizophrenia and 60% for bipolar disorders [23, 24]. Non-adherent patients have an average relapse risk that is 3.7 times greater than adherent patients [16].

Medication adherence is, however, a complex behaviour comprising a series of interrelated steps involving patients, their providers, and the healthcare system [3]. Adherence to medications can be defined as "*the process by which patients take their medication as prescribed, described by three quantifiable phases: initiation, implementation, and discontinuation*" [25]. Non- adherence is defined as taking less than 80% of prescribed doses. This cut-off has validity in predicting subsequent hospitalisation [26].

Patient-related factors impeding medication adherence in schizophrenia or bipolar dis- orders include medication side effects, lack of insight into the illness, cognitive dysfunction, regimen complexity and substance use [7, 27-29].

A variety of interventions have been used to improve medication adherence, such as cognitive behavioural therapy, psychoeducation, family interventions, motivational interviewing techniques, and mixed interventions [30-35]. To date, however, a detailed overview of the effectiveness of these

interventions at improving medication adherence in patients affected by schizophrenia or bipolar disorders is lacking.

Hence, the aim of this systematic review and meta-analysis was to explore the impact of interventions on medication adherence in patients with schizophrenia or bipolar disorders in patients with schizophrenia or bipolar disorders.

2.2. Methods

2.2.1. Overview

A systematic review, comprising a meta-analysis, was performed including a detailed assessment of the quality of evidence. Furthermore, the certainty of evidence related to interventions, designed to improve medication adherence in patients with schizophrenia or bipolar disorders, was systematically rated using the GRADE approach [36]. The review protocol was registered at PROSPERO (PROSPERO 2020 CRD42020153237).

2.2.2. Electronic searches

The review focused on studies examining the effectiveness of interventions aimed at improving adherence in patients with schizophrenia or bipolar disorders. PubMed and Web of Science were systematically reviewed for relevant intervention studies published between 2009 and 2019. Studies had to be published in Dutch, English or French. Details on the applied search string can be found in Table 2.1. Using the snowball method, reference lists of all retrieved articles were screened to identify additional publications.

2.2.3. Selection criteria

Types of studies and study population

full-text (quasi-)randomised controlled trials and prospective trials, comparing adherence- enhancing interventions versus no or other interventions, were selected. Control groups or treatment as usual (TAU) should have received no intervention, other interventions, or usual care. The study population consisted of (i) adults (≥18 years); (ii) diagnosed with schizophrenia, schizoaffective disorder, or Bipolar I/II disorder, according to an official classification system such as the Diagnostic and Statistical Manual of Mental Disorders (DSM-criteria) or International Classification of Diseases

Table 2.1: Search string.

Concept	Keywords[a]	Keywords[b]
Outcome: Medication adherence	"Medication Adherence" [Mesh]) OR medication adherence[Title/Abstract]) OR medication compliance[Title/Abstract]) OR medication persistence[Title/Abstract]) OR medication training[Title/Abstract]) OR medication management[Title/Abstract]) AND	TITLE:(medication adherence) OR TITLE:(medication compliance) OR TITLE:(medication persistence) OR TITLE:(medication training) OR TITLE:(medication management) AND
Participants: Patients with schizophrenia or bipolar disorders	"(schizophreni*) OR bipolar disorder*) OR bipolar mood disorder*) OR schizoaffective disorder*) OR "Schizophrenia"[Mesh]) OR "Bipolar Disorder"[Mesh]) AND	TITLE: (schizophren*) OR TITLE: (bipolar disorder*) AND
Exposure	intervention*[Title/Abstract]) NOT protocol[Title]	TOPIC: (intervention*) NOT TITLE: (protocol*)
Filters*	Clinical Study, Clinical Trial, Comparative Study, Controlled Clinical Trial, Pragmatic Clinical Trial, Randomized Controlled Trial	psychiatry, medicine general internal or nursing

[a]Used in PubMed
[b]Used in Web of Knowledge
*The filters were activated after entering the search terms

(ICD) and had to be made by a physician; and (iii) cared for within in- or outpatient setting(s) [37, 38]. Studies that examined patients with a first episode of psychosis, or patients with neurological comorbidities, such as mental retardation, were excluded. All retrieved hits were initially screened for eligibility based on title and abstract by two independent researchers (EL, TVW). Subsequently, a full text appraisal was performed. Two authors (EL, EG) independently decided on inclusion or exclusion of selected studies. All discrepancies were discussed until consensus was achieved. Detailed information about the search strategies can be found in Figure 2.1.

2.2.4. Outcome measures

The outcome was medication adherence, irrespective of the definition of adherence used in the manuscripts. All studies investigating adherence as an outcome were included. No distinction was made among studies investigating adherence as either a primary or secondary outcome. Studies could employ both objective metrics of adherence, such as pharmacy claims, pill counts or blood plasma concentration levels, as well as subjective measures such as clinician-rated or self-reported measures of medication adherence using standardised and validated assessments. The effects

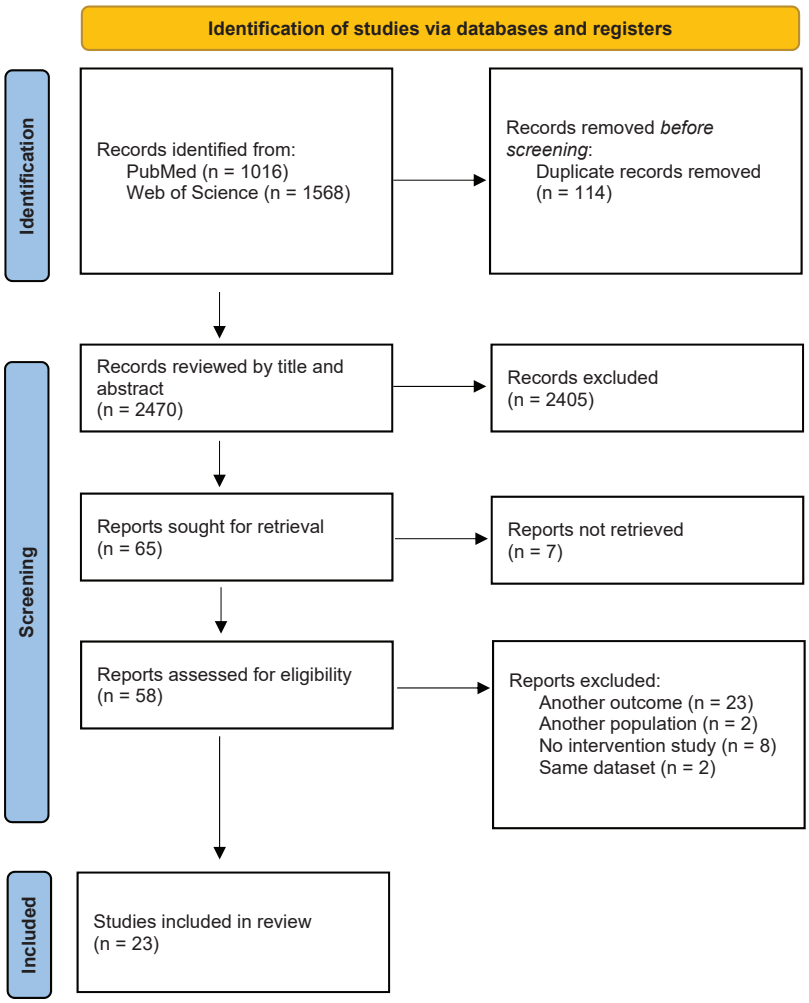


Figure 2.1: Selection flowchart.

of the different interventions were assessed using effect sizes (Cohen's d). In line with Cohen's classification, effect sizes were divided into five levels: trivial (Cohen's $d \leq 0.2$), small (Cohen's $d > 0.2$), moderate (Cohen's $d > 0.5$), large (Cohen's $d > 0.8$) and very large (Cohen's $d > 1.3$) [39, 40].

2.2.5. Data extraction and management

Two authors (EL, EG) extracted data until the end of November 2019, including details of study methodology, outcome measurement(s), demo-

graphics and clinical sample characteristics, eligibility criteria, details of the intervention, baseline and post-intervention results, methods of analysis and follow-up time. Information was recorded in the 'Cochrane Airways' and authors were contacted in case of missing information or when clarification was needed [41].

2.2.6. Risk of bias assessment

Two authors (EL, EG) independently assessed the methodological quality of selected studies using the Cochrane Risk of bias tool version 1.0, described in the Cochrane Hand- book for Systematic Reviews of Interventions. For each respective domain, the risk of bias was assessed as either high, low or unclear. Furthermore, the studies' overall risk of bias was determined on the basis of the following criteria as either low [i.e., low risk of bias for all domains), unclear (i.e., unclear risk of bias for one or more domains) or high (i.e., high risk of bias for one or more domains) [42].

In addition, the overall strength of evidence on outcomes was evaluated using the GRADE approach [36]. The outcomes included effects on adherence on the basis of behavioural, educational and mixed interventions. The GRADE approach considers evidence from randomised controlled trials as high quality, although this level may be downgraded on the basis of five areas of consideration: design, consistency across studies, directness of the evidence, precision of estimates and presence of publication bias [42].

2.2.7. Data synthesis

Firstly, the clinical heterogeneousness of studies was determined on the basis of their clinical characteristics including the intervention, control group, outcome assessment and follow-up window. When similarity among studies allowed data pooling, the Review Manager 5.3 data analysis tool was used for the assessment of statistical heterogeneity, as indicated in the forest plots measuring the treatment effect. I^2 and Chi^2 statistics were applied to determine statistical heterogeneity. Data were considered heterogeneous when p-value was ≤0.10. I^2 thresholds, as described in the Cochrane Handbook, were used as a guide for interpretation. Furthermore, we use the I^2 statistic to quantify the amount of heterogeneity. We considered an I^2 < 40% as low heterogeneity; 0% to 40%: might not be important, 30% to 60%: may represent moderate heterogeneity, 50% to 90%: may represent substantial heterogeneity, 75% to 100%: considerable heterogeneity [42].

Results in terms of adherence concerning intervention compared to

treatment as usual (TAU) were used. Forest plots were used to present results obtained from the meta-analysis. Narrative syntheses were used when studies were not eligible for meta-analysis. These data are presented in Supplementary Table S1.

2.3. Results

2.3.1. Study characteristics

Results of the search

The systematic search yielded 2584 results. Of those, 1568 studies were retrieved from Web of Science and 1016 from PubMed. After removal of 114 duplicates, 2470 references were screened on the basis of title and abstract. Sixty-five studies were assessed on the basis of full text, of which 42 were excluded. Reasons for exclusion were: full text was unavailable (n= 7), studies did not contain any data on adherence (n= 23), including other study populations (n= 2), no interventional study design (n= 8) and segmented publications (n= 2). Twenty-three studies were included in this systematic review and meta-analysis. A selection flow chart is provided at Figure 2.1.

All included studies were randomised controlled trials and compared intervention versus no intervention or another intervention, except for one study that compared an educational intervention, a behavioural intervention and a control group, respectively [43]. The follow-up time ranged from one month to 30 months (see Supplementary Table S1).

Participants and setting

A total of 4238 participants, ranging from 30 to 1268 per study, were included. Of the total sample, 2967 patients (70%) were patients diagnosed with schizophrenia or schizoaffective disorders and 1271 patients (30%) were diagnosed with a bipolar disorder. Studies were performed across three continents: eight studies in Asia [44-51], ten studies in Europe [21, 52-60] and six in North America [19, 27, 43, 61-63]. Study settings were categorised on the basis of the setting where interventions were initiated as part of the patient's healthcare journey. Most of the interventions were conducted at outpatient community mental health centres (65%) or in psychiatric hospitals (35%).

A range of complex interventions was used across selected studies including the provision of patient education and information, family involve-

ment, intensified patient care (e.g., sending out reminders, telephone calls), complex behavioural approaches (e.g., increasing motivation by interviews, group sessions) and mixed therapies (Table 2.2). Due to the heterogeneous nature of the interventions, three categories were used including behavioural, educational or mixed (i.e., behavioural and educational approach) interventions. Nine studies examined 11 behavioural interventions, 11 studies involved educational interventions focussing on medication and treatment, and six studies combined educational and behavioural elements.

Table 2.2: Overview of the types of interventions included in selected literature.

	Behavioural interventions	**Educational interventions**	**Mixed interventions**
Examples	Motivational interviewing SMS[1] reminders Alarms Checklists MEMS®[2] Meetings	Education sessions Website tool	Combination behavioural and educational intervention(s)
Number of interventions	11	11	6

[1]Short Message Service; [2]Medication Event Monitoring System

A range of behavioural interventions were used: six interventions focused on pharmacotherapy combined with text messages or telephone calls [19, 49, 59, 61], three interventions practised motivational interviewing [21, 45, 53], one study used cognitive behavioural therapy [57] and one study provided participants with electronic reminders [63]. Education sessions were organised in groups or one-on-one with a nurse or another healthcare provider [43, 44, 48, 52-56, 58, 62, 64]. Participants received information concerning medication strategies such as the use of a pill container, medication, symptoms and had the opportunity to have a 'Question and Answer' (Q&A) session with their healthcare provider. Five interventions combined education and motivational interviewing related to medication use [43, 46, 47, 50, 60]. One intervention combined medication skills training, family involvement and cognitive behavioural therapy [64].

2.3.2. Medication adherence assessment

Three categories of adherence assessment were identified, including (i) direct measures, such as blood serum levels, (ii) indirect measures such as pill counts, electronic monitoring, prescription refill rate, and (iii) subjective measures such as patients' and nurses' self-report adherence rating scales or interviews. Three studies used direct measures such as blood se-

rum levels [50, 54, 60]. Indirect measures included use of pill counts [60, 61, 63] and an electronic monitoring cap recording the number and timing of bottle openings [63, 64]. Subjective measures such as the Compliance Rating Scale [44, 52], the Medication Adherence Questionnaire [53, 59], the Medication Adherence Rating Scale [19, 48, 50, 56], the Morisky scale [21, 49, 51, 55, 58], the Visual Analog Scale for Assessing Treatment Compliance [46], the Stephenson Medical Adherence Questionnaire [57], the composite adherence measure and the medication possession ratios were used [62]. Two studies used an unknown Likert scale assessment tool [43, 45] and two studies were unclear about the assessment tool used [47, 65].

Adherence rates were reported as mean or median scores or percentages or percentages of complete doses taken or assessment tool scores. Follow-up time ranged from one to 84 months. Most of the studies defined adherence as taking more than 70% of prescribed doses. Six studies did not provide any definition for adherence [19, 50, 56, 60, 61, 64].

2.3.3. Effectiveness of interventions

Behavioural interventions

Six of nine included studies compared a behavioural intervention to usual care [19, 21, 45, 49, 51, 59] and three studies compared a behavioural intervention versus other interventions [53, 61, 63]. In all studies, the outcome was adherence. All interventions aimed at improving medication adherence; however, the intervention was unclear [21], one study focused on general health [53], and one on diagnosis and identification of recovery-informed therapy goals [57]. Details on the main findings, related to the effect of behavioural interventions on adherence, can be found in Table 2.3.

SMS interventions were associated with significant improvements in medication adherence after three-month follow-up with a moderate effect size of 0.64 ($p<0.001$) and after six-month follow-up ($p= 0.04$) [49, 59].

Motivational interviewing was performed in two studies. One study recruited 114 patients with schizophrenia with poor adherence to medication. The intervention was based on motivational interviewing in eight sessions during a four-month program. Medication adherence in the intervention group showed a significantly greater improvement at 6-month follow-up, with a moderate effect size of 0.72, as compared to TAU ($p= 0.007$) [45].

The PharmCAT individualised intervention used signs, alarms, pill containers and checklists to improve medication adherence. Participants were

Table 2.3: Summary of results on the effectiveness of behavioural interventions.

Reference	Assessment methods	Follow-up	Number of participants	Cohen's d	Study results
Barkhof (2013)	Medication Adherence Questionnaire	Baseline, 6 and 12 months	Motivational interviewing (n= 55)Health education (n= 59)	0.29	At both follow-up assessments, there were no significant differences between motivational interviewing and health education on 6 and 12 months follow-up (p= 0.34).
Beebe (2014)	Pill counts	Baseline and 3 months	Telephone call (n= 10) SMS (n= 10) Telephone + SMS (n= 10)	-0.19 0.36 -0.70	No significant difference in adherence was noted between the groups based on pill counts (p= 0.31).
Beebe (2016)	Medication Adherence Rating Scale	Baseline and 3 months	n= 140	0.29	Self-reported medication adherence was higher in the intervention group after 3 months but the differences were not statistically significant.
Chien Tong (2015)	Unclear	Baseline, immediately post intervention and 6 months post intervention	Motivational interviewing (n= 57)TAU (n= 57)	0.72	The medication adherence of the motivational interviewing group showed a significantly greater improvement over time with a moderate effect size of 0.72, when compared with the control group (p= 0.007).
Ertem (2018)	Morisky scale	Baseline, immediately post intervention, 3 and 6 months	Motivational interviewing (n= 20)TAU (n= 20)	N/A	Participants in the motivational interviewing group showed a significant improvement after 3 months follow-up post intervention (p<0.001) and 6 months follow-up (p<0.001).
Jones (2015)	Stephenson Medical Adherence Questionnaire	Baseline, 6, 12 and 15 months post intervention	Cognitive behavioural therapy (n= 34)TAU (n= 33)	N/A	No significant difference in adherence was noted between the two groups based on self-reports at baseline, 6 and 12 months follow-up.
Menon (2018)	Morisky scale	3 months	SMS intervention (n= 62) TAU (n= 70)	0.64	The SMS intervention was associated with significant improvement in medication adherence at the end of the 3-month intervention (p<0.001).
Montes (2012)	Morisky scale	Baseline, 3 and 6 months post intervention	SMS intervention (n= 100) TAU (n= 154)	N/A	A significantly greater improvement in adherence was observed among participants receiving SMS text messages compared with the control group based on self-reports after 3 months (p= 0.02) and after 6-months follow-up (p= 0.04).
Velligan (2013)	MEMS Pill counts	9 months	Med-eMonitor (n= 48) PharmCAT (n= 47) TAU (n= 47)	0.98 1.03	The two different behavioural interventions showed a statistically significant enhancement in medication adherence at all time points through treatment and after 9 months follow-up when compared with the control group (p<0.001). Differences between the two behavioural interventions were not significant (p>0.50).

seen once weekly at home. The Med-eMonitor intervention consisted of a therapist who programmed prescription information into the device and set the device up at home to fit into the patient's routine (e.g., set alarm to take medication). These two behavioural interventions showed a statistically significant enhancement in medication adherence at all time points during treatment and after nine-month follow-up as compared to TAU ($p<0.001$). The PharmCAT reached a very large effect size of 1.03 and the Med-eMonitor a large effect size of 0.98. Differences between the two behavioural interventions were not significant ($p>0.50$) [63].

In summary, 6 out of 12 behavioural interventions showed a statistically significant improvement on adherence. These interventions used an individualised approach to enhancing medication adherence. Motivational interviewing, daily SMS reminders, medication reminders at patients' homes and medication self-management training were beneficial for patients' adherence [21, 45, 49, 59, 63]. SMS and phone calls focused on problem solving strategies and cognitive behavioural therapy did not prove beneficial for patients' adherence.

Education interventions

Nine of the 11 included studies compared an educational intervention to usual care [43, 44, 48, 52, 54-56, 58, 62] and three compared it to other interventions [27, 43, 53]. Eight studies investigated the effect of an intervention focusing on knowledge about medication and symptoms. Two studies were unclear about the content of the intervention [52, 56] and one study focused on education covering the topic of general health [53].

Eight of eleven educational interventions had a statistically significant improvement of adherence [43, 44, 48, 55, 56, 62, 64]. Education sessions focused on diagnosis, symptoms, medication, relapse, Q&A, medication skills and medication adherence. These educational interventions were individualised and were provided on a one-on-one basis with a healthcare provider or in small group sessions. Education focused on stress reduction and problem-solving strategies did not show beneficial effects on patients' adherence. Details on the main findings related to the effect of educational interventions on adherence can be found in Table 2.4.

Mixed interventions

Four of six included studies compared mixed interventions to usual care [46, 47, 50, 60] and two studies compared it to other interventions [30, 43, 64]. Four studies focused their mixed intervention on medication [43,46,60,64] and two studies did not provide sufficient detail about the

Table 2.4: Summary of results on the effectiveness of educational interventions.

Reference	Assessment	Follow-up	Number of participants	Cohen's d	Study results
Aho-Mustonen (2010)	Compliance Rating Scale	Baseline and 3 months post treatment	Psychoeducation (n= 19) TAU (n= 20)	0.53	No significant difference in adherence was noted between the two groups based on self-reports at the baseline (p= 0.81) and after 3 months follow-up (p= 0.86).
Awan Riaz (2017)	Compliance Rating Scale	Baseline and 3 months	Intervention group (n= 53) TAU (n= 50)	/	At baseline, there were 24% participants in intervention while 46% in control group who had complete adherence rate (p= 0.022). On 3 months follow-up, there were 96% cases in the intervention group and 47% in the control group with complete adherence (p<0.001).
Bäuml (2016)	A four-step ordinal scale Plasma drug levels	24 months and 84 months	Intervention group (n= 21) TAU (n= 20)	/	At both follow-up assessments post intervention, there were no significant differences in adherence between the groups (p= 0.09).
Barkhof (2013)	Medication Adherence Questionnaire	Baseline, 6 and 12 months	Health education (n= 59) Motivational interviewing (n= 55)	0.0	At both follow-up assessments, there were no significant differences between motivational interviewing and health education on the two adherence measures (p= 0.34).
Çetin (2018)	Medication Adherence Rating Scale Morisky scale	Not reported	Intervention group (n= 55) TAU (n= 80)	0.56	The mindfulness-based intervention was associated with significant improvement in medication adherence (p<0.05).
Eker (2012)	Medication Adherence Rating Scale	2,5 months	Psychoeducation group (n= 35) TAU (n= 36)	/	The participants' adherence in the psychoeducation group significantly increased (86.7%) after psychoeducation (p<0.01).
Javadpour (2013)	Medication Adherence Rating Scale	Baseline, 6, 8, 12 months	Psychoeducation group (n= 54) TAU (n= 54)	/	Participants in the psychoeducation group showed a statistically significant enhancement in medication adherence compared to the control group at all assessments (p= 0.008).
Kopelowicz (2012)	Unclear assessment tool	Baseline, 4, 8, 12, 18 and 24 months	Education (n= 64) Mixed (n= 53 TAU (n= 57)	/	The education intervention showed a statistically significant higher medication adherence than the mixed group after 18-months follow-up (p= 0.01) but not at 24 months (p= 0.20). More participants in education group were fully adherent than those in TAU at all assessments (p<0.01).

Table 2.5: Summary of results on the effectiveness of mixed interventions.

Reference	Assessment	Follow-up	Number of participants	Cohen's d	Study results
Dahan (2016)	Visual Analog Scale for Assessing Treatment Compliance	Unclear	Intervention group (n= 31) TAU (n= 32)	0.75	No significant differences between intervention group and TAU in medication adherence (p>0.05). The intervention group presents a positive correlation between attitudes and adherence before intervention (r= 0.51, p<0.05) and a positive correlation between attitudes and adherence after the intervention (r= 0.59, p<0.001). The TAU also presents a correlation between attitude and adherence before the intervention (r= 0.52, p<0.001).
Guo (2010)	Unclear	12 months	Intervention group (n= 633) TAU (n= 635)	/	Non-adherence was noted in 2.8% of participants in the mixed intervention group and 5.7% in the control group (p= 0.006).
Kopelowicz (2012)	Unclear assessment tool	Baseline, 4, 8, 12, 18 and 24 months	Mixed group (n= 53) Education group (n= 64) TAU (n= 57)	/	The mixed intervention showed a statistically significant lower medication adherence than the education group after 18-months follow-up (p= 0.01) but not at 24 months (p= 0.20). There was no significant difference at any point between the mixed intervention group and the TAU.
Pakpour (2017)	Medication Adherence Rating Scale Plasma levels	Baseline and 6 months post intervention	Intervention group (n= 134) TAU (n= 136)	0.84	Measured by the Medication Adherence Rating Scale, the intervention group showed a significantly higher medication adherence compared to TAU both 1 month (p<0.001) and 6 months (p<0.001) after the intervention. Analysis of the objective measures of medication adherence such as plasma level of mood stabilisers indicated that participants in the control group had slightly decreased levels at 6 months post intervention, suggesting that they may not have been adhering to their medication regimen. In contrast to participants in the intervention group had increased levels at 6-months follow-up supporting the beneficial effects of the intervention suggested by self-report measure of adherence. After controlling for study centre and repeated measurement, participants in the intervention group had significantly higher plasma levels of mood stabilisers than did participants in the control group at 1 month (p<0.001) and 6 months (p<0.001) follow-up post intervention.
Sajatovic (2018)	-TRQ -MEMS	Baseline, 10 weeks, 14 weeks and 6 months	Mixed group (n= 92) Education group (n= 92)	0.91	The mixed intervention showed a statistically significant higher medication adherence than the education intervention group after 6 months follow-up (p= 0.048).

content of the intervention [47,50]. Details on the main findings can be found in Table 2.5.

One mixed intervention combined education of patients and family members with motivational interviewing. Using the Medication Adherence Rating Scale, the intervention group showed a significantly higher medication adherence compared to TAU, both at one ($p<0.001$) and six months ($p<0.001$) post-intervention (large effect size of 0.84). Analysis of the objective measures of medication adherence, such as plasma level of mood stabilisers indicated that participants in TAU had slightly decreased levels at six months post-intervention, suggesting they may not have been adhering to their medication regimen. In contrast, the intervention group had increased levels at six-month follow-up supporting the beneficial effects of the intervention suggested by self-report measure of adherence. After controlling for study centre and repeated measurements, the intervention group had significantly higher plasma levels of mood stabilisers as TAU at one ($p<0.001$) and six months ($p<0.001$) post- intervention [50].

In total, five of six mixed interventions had a positive impact on adherence. These mixed interventions were focused on an individualised approach of medication adherence. Interventions involving patients' family members, medication preparing in a controlled environment and individualised interventions with medication techniques and an adequate follow-up with telephone calls were beneficial for patients' adherence. There was not a beneficial effect on adherence from the combination of motivational interviewing and cognitive behavioural therapy [43,46].

2.3.4. Effects on adherence

Four interventions of eleven studies reported effect sizes. Additionally, 11 interventions reported sufficient information to calculate effect sizes. For these 15 interventions, effect sizes could be appreciated as very large for one intervention [50], large for three interventions [50,63,64], moderate for six [45,46,49,52,55,62], small for three [19,53,61] and only a trivial effect for two interventions [53,61]. Fourteen interventions did not report sufficient information to calculate effect sizes.

Meta-analysis could be performed for 10 interventions in eight studies that involved dichotomous measures (Figure 2.2). The analysis was divided into three categories on the basis of the type of intervention provided: behavioural interventions (n= 1 study with two different behavioural interventions), educational interventions (n= 5 studies) or mixed interventions (n= 3 studies). The respective forest plots (presented on a logarithmic scale) showed pooled treatment effects of interventions in all categories as

compared with usual care (TAU) for adherence at short-term and long-term follow-up (i.e., one month until 84 months). When considered separately by subgroups on the basis of intervention type, significant differences (p= 0.02) were found in adherence among subgroup interventions (p= 0.03; I^2= 53%).

A significant difference in adherence rates was found between behavioural interventions and TAU; 92% versus 72% adherence in the PharmCAT intervention and 89% versus 72% in the Med-eMonitor intervention. Meta-analysis using a random-effects model estimated an odds ratio of 3.65 (95%CI: 1.60-8.31).

Five studies were included in meta-analysis for educational interventions. There was considerable heterogeneity (I^2= 72%). Pooling of data used dichotomous measures of adherence at 2.5 to 84-month follow-up range involving 408 participants. Using a random- effects model, pooled results showed that adherence was greater in the intervention group (estimated odds ratio= 4.86; 95%CI: 2.96-7.97). The educational intervention of Bäuml (2016) [54] had no significant improvement on adherence when comparing the intervention group with TAU at 84-month follow-up (95%CI: 0.19-5.99).

Regarding the effect of mixed interventions, data of 1451 participants

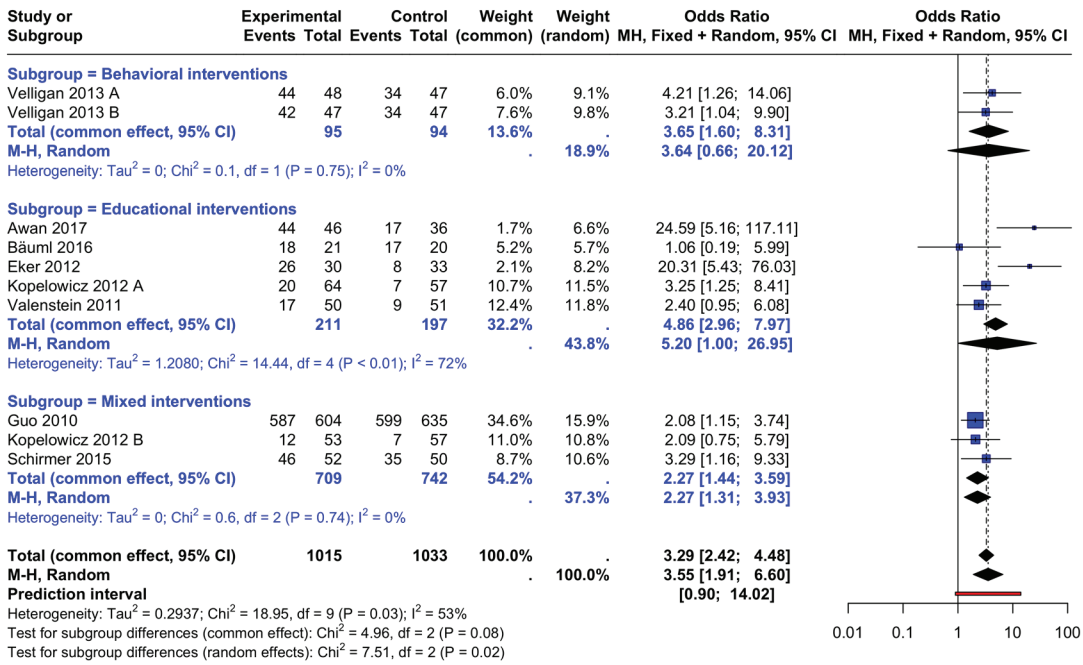


Figure 2.2: Interventions versus usual care grouped by type of intervention (dichotomous).

were pooled using dichotomous measures of adherence at 1- to 24-month follow-up. Using a random effects model, meta-analysis showed mixed interventions increased the proportion of adherent patients (estimated odds ratio= 2.27; 95%CI: 1.44-3.59). There was no evidence of significant heterogeneity (I^2= 0%).

2.3.5. Risk of bias

The risk of bias of each included study is summarised in Figures 2.3 and 2.4. Descriptions for each respective domain are provided below.

Allocation

Risk of bias for random sequence generation was low in 16 studies (70%), unclear in five studies (22%) and high in two studies (8%). Eight trials used computer-generated randomisation, which we considered to be an adequate randomisation procedure [43–45,49,50,53,60,63].

Blinding

Six studies (26%) were considered to have low risk of performance bias, 12 studies (52%) were unclear about blinding of participants and personnel, and five studies (22%) were considered to have high risk of performance bias. Blinding of healthcare providers was reported in six studies [45,47,48,52,53,57]. None of the studies reported blinding of participants to the intervention they were receiving, as this was not deemed feasible given the nature of the interventions. Eight studies reported blinding of outcome assessors and hence were considered to have a low risk of detection bias [43,45,47–49,51,53,57,60].

Incomplete outcome data

Twelve studies (52%) were assessed as having low risk of bias mainly due to low attrition rates and the use of intention-to-treat analysis (ITT). Attrition >20% was considered to indicate a high risk of bias. Nine studies (39%) were considered to have incomplete outcome data because of high attrition rates, and therefore identified as having a high risk of attrition bias. Two studies (9%) did not report information on missing data [19,64].

Selective reporting

Selective outcome reporting bias occurred if adherence frequency was measured and analysed but was not reported in the study results. One study (4%) was considered to have a high risk of reporting bias due to risk

of multiple testing [21]. Six studies (25%) reported their results insufficiently [19,43,44,47,52,56,61].

Seventeen studies (71%) were assessed as having a low risk of selective reporting bias due to transparency in results and publishing of all expected outcomes.

Other potential sources of bias

Other potential sources of bias contained limited follow-up, self-reported assessment tools, small sample sizes and an unclear assessment tool for adherence. Risk of bias for other potential sources of bias was low in 13 studies (54%) and high in 10 studies (42%). Two studies (4%) were found to be free of other sources of bias [50, 64]. Six studies reported the combination of a limited follow-up time and a self-reported assessment tool [19,44,46,52,56,58]. Two studies performed appropriate sample size calculations in combination with limited follow-up [57,61,65]. Seven studies only reported a self-reported assessment tool [21,48,49,51,53,57,59] and two studies contained a limited follow-up [60,63,65). Four studies reported insufficient information about their assessment tool [43,45,47,62].

Overall strength of evidence (GRADE)

The studies were, overall, low in quality (see Table 2.6); some studies appeared to have a considerable risk of bias. Additionally, the length of follow-up applied in the respective studies ranged from one to 84 months. Short-term follow-up makes it difficult to ascertain whether interventions with promising adherence-improving effects can safeguard and maintain

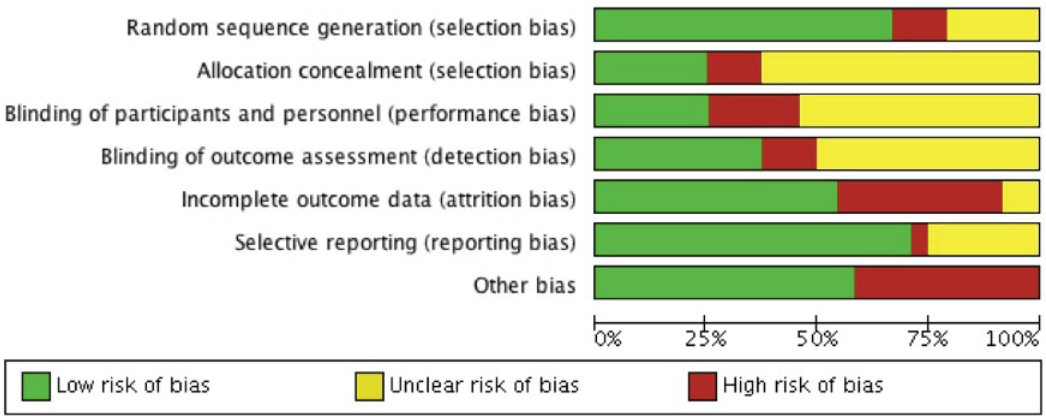


Figure 2.3: Risk of bias graph.

their effects over time. The nature of the studied interventions implied that blinding of participants and personnel was not possible. Hence, we did not downgrade the evidence for lack of blinding.

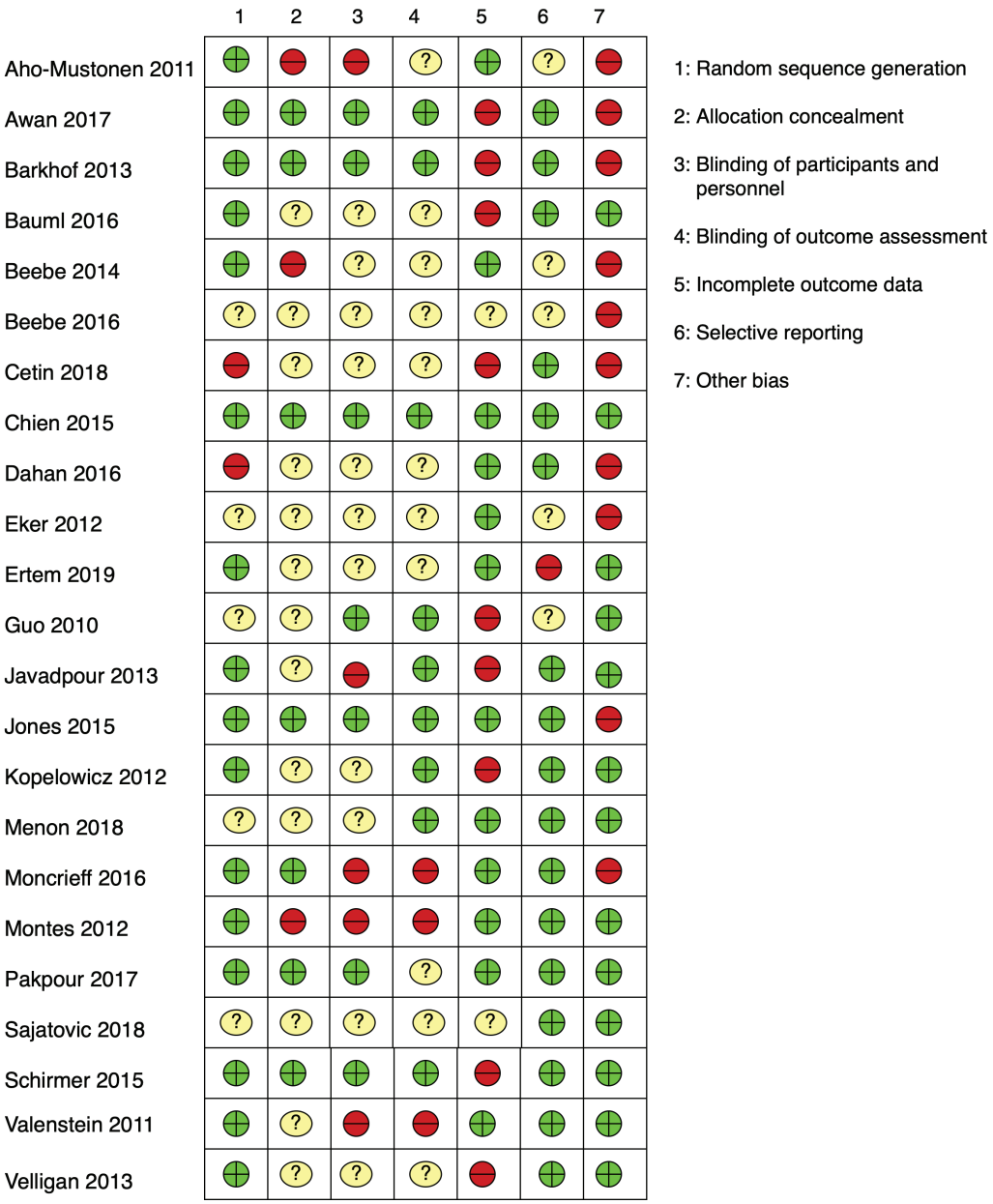


Figure 2.4. Risk of bias assessment of included studies using the Cochrane Risk of bias tool.

Table 2.6: Summary of findings for the main comparison.

Outcomes	Anticipated absolute effects* (95%CI)		Relative effect (95% CI)	No of participants (studies)	Quality of evidence (GRADE)
Effects on adherence (behavioural interventions) assessed with: MAQ, MARS, MEDAD, MEMS, Morisky and pill counts. Follow-up: range 1,5 month to 15 months.	Risk with no intervention or other intervention	Risk with adherence-enhancing intervention	N/A	1059 (9 RCTs)	Very Low[1,2,3]
Effects on adherence (educational interventions) assessed with: CRS, MARS, MAQ, Morisky, MPR, MEMS and TRQ. Follow-up: range 1 month to 7 years.	No estimable see comments	No estimable see comments	N/A	1134 (11 RCTs)	Very Low[1,2,3]
Effects on adherence (Mixed interventions) assessed with: MARS, MEMS, plasma concentrations, pill counts, TRQ and VASTEC. Follow-up: range 1 month to 24 months.	No estimable see comments	No estimable see comments	N/A	2045 (6 RCTs)	Low[1,2]

* The risk in the intervention group (and its 95%confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95%CI). CI: Confidence interval; RR: Risk ratio; OR: Odds ratio.

GRADE Working Group grades of evidence:
High quality: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

[1]Downgraded due to unclear risk of bias for allocation concealment, blinding of participants and outcome assessors or both.

[2]The quality of the evidence of the studies measuring this outcome was downgraded due to the lack of precision or lack of consistency, or both.

[3]Downgraded due to high risk of bias for allocation concealment, blinding of participants and outcome assessors or both.

2.4. Discussion

This is the first systematic review providing a synthesis of the effectiveness of interventions improving medication adherence in patients with schizophrenia or bipolar disorders, including a meta-analysis.

2.4.1. Summary of main results

On the basis of a synthesis of 23 studies, a total of 28 different, complex and heterogeneous interventions were identified. These interventions comprised behavioural, educational and mixed interventions, and were compared versus usual care or other types of interventions. Various interventions produced favourable results regardless of type, duration or setting. On the basis of this detailed assessment, motivational interviewing, daily SMS medication reminders, medication reminders at patients'

home, education sessions focused on diagnosis, symptoms, medication, and relapse were found to be beneficial for patients' adherence [49,59,63]. Educational interventions were individualised and were provided on a one-on-one basis with a healthcare provider or in small group sessions [43,44,48,62,64]. The interventions with the strongest of body of evidence were two interventions combining motivational interviewing techniques with patient-tailored education [50,60). These two studies had a very low risk of bias and used a combination of two or more adherence measurement tools, including serum levels. One of the mixed interventions found to be effective had a large effect size at six-month follow-up and combined education of patients and family members with motivational interviewing (50]. Family members and patients were given information about symptoms, prognosis of the condition, as well as the prescribed medication and their possible side effects.

Each family member was provided information about the importance of medication adherence and the risks of discontinuing these medications. At the end of the sessions, family members were given a booklet with information about the diagnosis and possible treatments. Unfortunately, interventions aiming to include and target interventional components to family members are challenging to implement in everyday practice and generally create a high workload. One intervention used an intensive training program comprising one-to-one lessons provided by skilled nurses. Participants should learn to prepare their medication themselves during the hospital stay in the same way they are expected to do it autonomously after discharge [60]. Unfortunately, this intervention was only tested at short-term follow-up of one month. Our review concluded the difficulty of evaluating of the effectiveness of all interventions against each other due to the heterogeneous and complex nature of the interventions and variations in adherence measures (i.e., different follow-up range, and various pathologies). Our results showed the use of short duration interventions produces equally favourable results as long-term interventions. Problems with adherence are recurrent, and therefore booster sessions are needed to maintain adherence.

2.4.2. Long-term follow-up

Studies including adequate and extensive follow-up periods are important, as re- searchers need to measure the immediate effects of their intervention(s) on adherence, but also intermediate and long-term effects. Education focusing on medication, symptoms, treatment and diagnosis resulted in achieving favourable results on adherence at six-month follow-up

with a large effect size [64] and 12-month follow-up with moderate effect sizes [48,62]. A 12-month intervention focused on medication adherence, including education and motivational interviewing, resulting in favourable results on adherence at 12-month follow-up with a large effect size, but not at 24-month follow-up. Repeating the intervention may improve this result [43]. One behavioural intervention study provided a long-term follow-up of nine months with a large effect size. This intervention used signs, alarms, pill containers and checklists to improve medication adherence. Participants were seen once weekly at home [63]. Two other studies, where motivational interviewing focused on medication and medication changes were used, achieved favourable results on adherence at six-month follow-up with a moderate effect size [21, 45].

2.4.3. Assessment of adherence

No single measurement method can be regarded as the best available approach given the various patient-related factors (i.e., lack of disease insight, and forgetfulness). Hence, the use of multiple measurement methods of adherence is highly recommended. The wide variety of settings, intervention types, medications prescribed, adherence measures and follow-up time precluded summarising findings to reach reliable general conclusions.

2.4.4. Critical appraisal of the methodology

The strength of our review is the performance of a thorough literature search, which was performed using a strict and systematic approach when selecting studies for inclusion, as well as extracting and analysing data. Furthermore, the body of evidence was evaluated using the GRADE approach for the outcome of medication adherence (see Table 2.6). Twelve authors were contacted to clarify missing information concerning the interventions and data results. Unfortunately, we received the missing information from only two authors [19, 63]. The studies were overall low in quality (see Table 2.6); some studies appeared to have a considerable risk of bias. Additionally, the length of follow-up applied in the respective studies ranged from one to 84 months.

A well-known problem in the literature is the lack of uniformity in the terminology used to describe deviation from prescribed medication regimens. The conceptual definitions vary resulting in conceptual confusion, which adds to the methodological weakness in this field [25]. This heterogeneity of operational definitions for medication (non-)adherence was the main obstacle experienced when comparing study findings in this system-

atic review and meta-analysis. The included interventions differed not only in terms of interventional components, but also in terms of their comparison group (no intervention or other intervention), duration of interventions and follow-up time. The performance of a meta-analysis was only possible for 10 interventions described in eight studies.

Concerns could be raised related to inconsistencies due to the heterogeneous and complex nature of the interventions and variations in outcome measures (i.e., follow-up range and methods of measuring adherence). Sixteen out of 24 studies followed patients up for six months or more. Most studies used patient self-reported measures, which are known to overestimate adherence rates [66,67]. Regarding the problem of non-adherence, the different rates reported in the publications may partly reflect methodological obstacles concerning the difficulty to relabelling measurements reported in the respective papers. A reliable measurement is a prerequisite for addressing non-adherence. Definitely, no such method exists at this moment. Direct measurements such as blood or urine drug levels are less subjective to bias as compared to indirect measurements such as self-reports, pill counts or refill rates. Practically every method aiming to determine adherence rates has specific limitations [63,68].

Although interventions were categorised as either having a behavioural, educational or mixed interventional focus, low to high heterogeneity was evident contributing to the limited certainty of results derived from literature. Concerns related to imprecision were present for behavioural and educational interventions, for which participant numbers were low and confidence intervals were wide. In line with previously published literature, our systematic review revealed that currently high-quality evidence is lacking addressing the effectiveness of interventions improving medication adherence in patients with schizophrenia or bipolar disorders. Furthermore, variabilities in the study methodology applied, interventions used, and outcome measures selected made it difficult to draw any firm conclusions in terms of the most effective intervention improving medication adherence in patients with schizophrenia or bipolar disorders. However, it is difficult to establish the relationship between the different interventions and adherence, as different measurement points and definitions of adherence were used.

2.4.5. Future prospects

Our findings emphasise the need for future studies using mixed interventions. These interventions comprising elements of education, motivational interviewing and medication self-management, evaluating adherence

rates by using a combination of measurement tools during longer-term follow-up times. The use of checklists, pill containers, one-to- one medication education and medication self-management techniques are hypothesised to result in favourable outcomes. Researchers should minimise the risk of bias by using suitable randomisation techniques, allocation concealment and double blinding techniques.

Researchers should strongly consider prospective trial registration and publication of study protocols using standard reporting checklists such as the Standard Protocol Items: Recommendations for Interventional Trials [66]. This will help to ensure clearer and more consistent reporting of outcome variables impacting medication adherence. In terms of study design, studies of duration are important, as researchers need to be able to made valid assessments of the short-term, mid-term and long-term effects of their intervention on adherence.

2.5. Conclusions

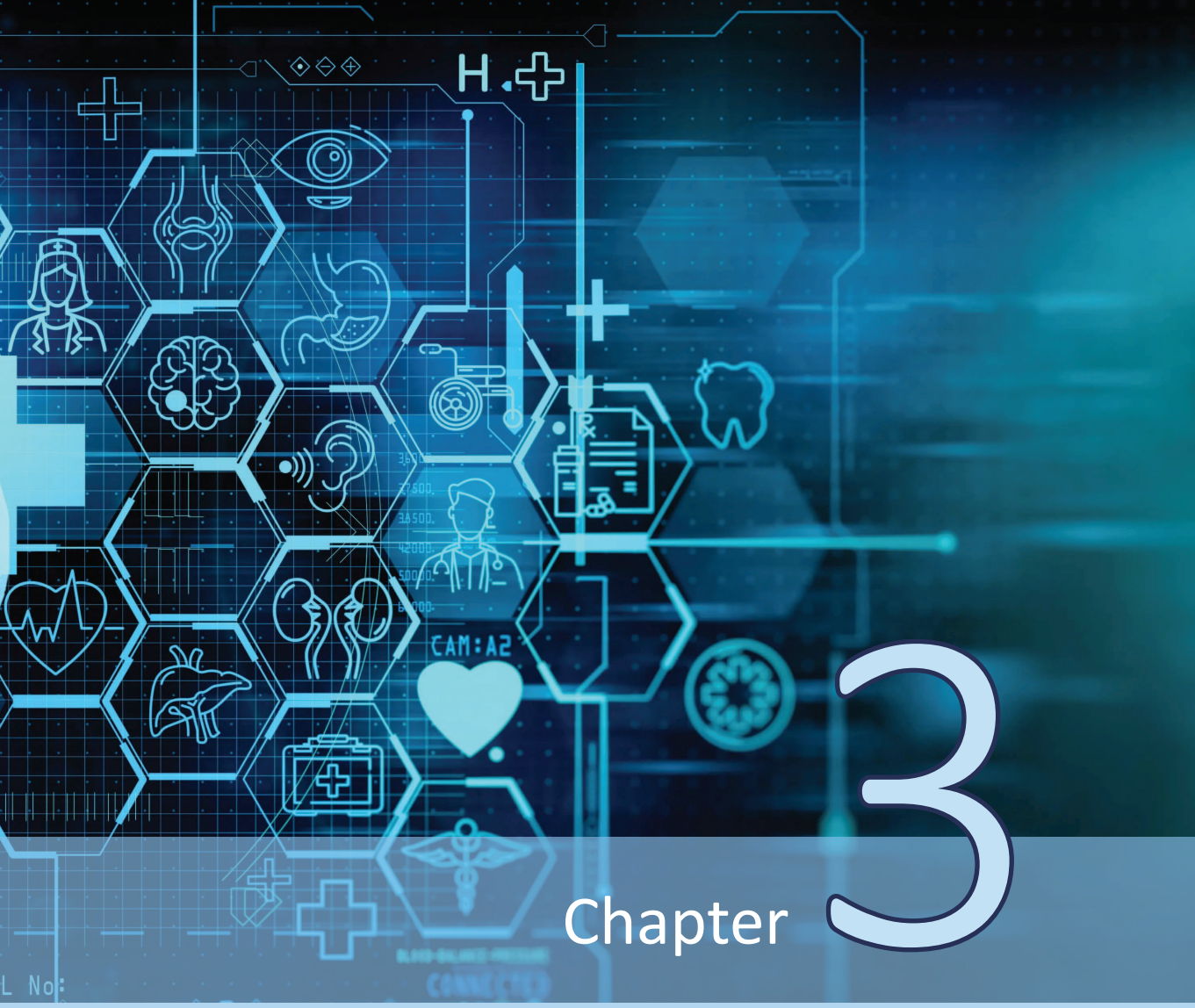
Our review is the first to provide a synthesis on the effectiveness of interventions aiming to improve medication adherence in patients with schizophrenia or bipolar disorders. Successful interventions used a combination of educational and behavioural strategies. The combined use of education sessions focusing on diagnosis, symptoms, medication and relapse, with medication reminders at patients' home and an intensive training program provided on a one-to-one basis by skilled nurses can improve medication adherence. Furthermore, such mixed interventions are deemed feasible to implement in daily practice. Our findings emphasise the need for future studies evaluating the effectiveness of such mixed interventions. These interventions comprising elements of education, motivational interviewing and medication self-management, evaluating adherence rates using a combination of measurement tools during longer-term follow-up periods.

2.6. References

1. World Health Organization. The Global Economic Burden of Non-Communicable Diseases. World Economic Forum, Geneva, Switzerland. Mental health atlas. 2011.
2. World Health Organization. The Global Economic Burden of Non-Communicable Diseases; World Economic Forum: Geneva, Switzerland, 2018.
3. Hartung D, Low A, Jindai K, Mansoor D, Judge M, Mendelson A, et al. Interventions to Improve Pharmacological Adherence Among Adults With Psychotic Spectrum Disorders and Bipolar Disorder: A Systematic Review. Psychosomatics. 2017;58(2):101-12.
4. Mibel F, Heikki E. Non-compliance to medication in Psychiatric patients. Tuku University of Applied Sciences. 2013.
5. Cramer JA, Rosenheck R. Compliance with medication regimens for mental and physical disorders. Psychiatr Serv. 1998;49(2):196-201.
6. Colom F, Lam D. Psychoeducation: improving outcomes in bipolar disorder. Eur Psychiatry. 2005;20(5-6):359-64.
7. Sendt KV, Tracy DK, Bhattacharyya S. A systematic review of factors influencing adherence to antipsychotic medication in schizophrenia-spectrum disorders. Psychiatry Res. 2015;225(1-2):14-30.
8. Xiao J, Mi W, Li L, Shi Y, Zhang H. High relapse rate and poor medication adherence in the Chinese population with schizophrenia: results from an observational survey in the People's Republic of China. Neuropsychiatr Dis Treat. 2015;11:1161-7.
9. World Health Organization. The Global Economic Burden of Non-Communicable Diseases; World Economic Forum: Geneva, Switzerland. 2013.
10. Miasso AI, Cassiani SH, Pedrão LJ. [Affective bipolar disorder and ambivalence in relation to the drug treatment: analyzing the causal conditions]. Rev Esc Enferm USP. 2011;45(2):433-41.
11. Young JL, Zonana HV, Shepler L. Medication noncompliance in schizophrenia: codification and update. Bull Am Acad Psychiatry Law. 1986;14(2):105-22.
12. Keith SJ, Kane JM. Partial compliance and patient consequences in schizophrenia: our patients can do better. J Clin Psychiatry. 2003;64(11):1308-15.
13. Terkelsen KG, Menikoff A. Measuring the costs of schizophrenia. Implications for the post-institutional era in the US. Pharmacoeconomics. 1995;8(3):199-222.
14. Gilbert PL, Harris MJ, McAdams LA, Jeste DV. Neuroleptic withdrawal in schizophrenic patients. A review of the literature. Arch Gen Psychiatry. 1995;52(3):173-88.
15. Weiden PJ, Olfson M. Cost of relapse in schizophrenia. Schizophr Bull. 1995;21(3):419-29.
16. Fenton WS, Blyler CR, Heinssen RK. Determinants of medication compliance in schizophrenia: empirical and clinical findings. Schizophr Bull. 1997;23(4):637-51.
17. Atkinson JM, Coia DA, Gilmour WH, Harper JP. The impact of education groups for people with schizophrenia on social functioning and quality of life. Br J Psychiatry. 1996;168(2):199-204.
18. Battle EH, Halliburton A, Wallston KA. Self medication among psychiatric patients and adherence after discharge. J Psychosoc Nurs Ment Health Serv. 1982;20(5):21-8.
19. Beebe LH, Smith K, Phillips C. Effect of a Telephone Intervention Upon Self-Reported Medication Adherence and Self-Efficacy in Outpatients With Schizophrenia Spectrum Disorders (SSDs). Issues Ment Health Nurs. 2016;37(10):708-14.
20. Svarstad BL, Shireman TI, Sweeney JK. Using drug claims data to assess the relationship of medication adherence with hospitalization and costs. Psychiatr Serv. 2001;52(6):805-11.

21. Ertem MY, Duman ZC. The effect of motivational interviews on treatment adherence and insight levels of patients with schizophrenia: A randomized controlled study. Perspect Psychiatr Care. 2019;55(1):12.
22. Sajatovic M, Tatsuoka C, Cassidy KA, Klein PJ, Fuentes-Casiano E, Cage J, et al. A 6-Month, Prospective, Randomized Controlled Trial of Customized Adherence Enhancement Versus Bipolar-Specific Educational Control in Poorly Adherent Individuals With Bipolar Disorder. J Clin Psychiatry. 2018;79(6).
23. Robinson D, Woerner MG, Alvir JM, Bilder R, Goldman R, Geisler S, et al. Predictors of relapse following response from a first episode of schizophrenia or schizoaffective disorder. Arch Gen Psychiatry. 1999;56(3):241-7.
24. Kebede D, Alem A, Shibire T, Deyassa N, Negash A, Beyero T, et al. Symptomatic and functional outcome of bipolar disorder in Butajira, Ethiopia. J Affect Disord. 2006;90(2-3):239-49.
25. Vrijens B, De Geest S, Hughes DA, Przemyslaw K, Demonceau J, Ruppar T, et al. A new taxonomy for describing and defining adherence to medications. Br J Clin Pharmacol. 2012;73(5):691-705.
26. Simpson SH, Eurich DT, Majumdar SR, Padwal RS, Tsuyuki RT, Varney J, et al. A meta-analysis of the association between adherence to drug therapy and mortality. Bmj. 2006;333(7557):15.
27. Sajatovic M, Valenstein M, Blow FC, Ganoczy D, Ignacio RV. Treatment adherence with antipsychotic medications in bipolar disorder. Bipolar Disord. 2006;8(3):232-41.
28. Hui CL, Chen EY, Kan C, Yip K, Law C, Chiu CP. Anti-psychotics adherence among out-patients with schizophrenia in Hong Kong. Keio J Med. 2006;55(1):9-14.
29. World Health Organization. Adherence to Long-Term Therapies: Evidence for Action Section I—Setting the Scene; World Health Organization: Geneva, Switzerland. 2003.
30. Mueser KT, Deavers F, Penn DL, Cassisi JE. Psychosocial treatments for schizophrenia. Annu Rev Clin Psychol. 2013;9:465-97.
31. Kemp R, Kirov G, Everitt B, Hayward P, David A. Randomised controlled trial of compliance therapy. 18-month follow-up. Br J Psychiatry. 1998;172:413-9.
32. Dolder CR, Lacro JP, Leckband S, Jeste DV. Interventions to improve antipsychotic medication adherence: review of recent literature. J Clin Psychopharmacol. 2003;23(4):389-99.
33. Zygmunt A, Olfson M, Boyer CA, Mechanic D. Interventions to improve medication adherence in schizophrenia. Am J Psychiatry. 2002;159(10):1653-64.
34. Kelly GR, Scott JE, Mamon J. Medication compliance and health education among outpatients with chronic mental disorders. Med Care. 1990;28(12):1181-97.
35. Lincoln TM, Wilhelm K, Nestoriuc Y. Effectiveness of psychoeducation for relapse, symptoms, knowledge, adherence and functioning in psychotic disorders: a meta-analysis. Schizophr Res. 2007;96(1-3):232-45.
36. Brozek JL, Akl EA, Alonso-Coello P, Lang D, Jaeschke R, Williams JW, et al. Grading quality of evidence and strength of recommendations in clinical practice guidelines. Part 1 of 3. An overview of the GRADE approach and grading quality of evidence about interventions. Allergy. 2009;64(5):669-77.
37. Fusar-Poli P, Solmi M, Brondino N, Davies C, Chae C, Politi P, et al. Transdiagnostic psychiatry: a systematic review. World Psychiatry. 2019;18(2):192-207.
38. World Health Organization. The ICD-10 classification of mental and behavioural disorders: Clinical descriptions and diagnostic guidelines. . Geneva: World Health Organization. 1992.
39. Cohen J. Statistical Power Analysis for the Behavioral Sciences; Lawrence Erlbaum Associates: Hillsdale, NJ, USA. 1998.
40. Cohen J. A power primer. Psychol Bull. 1992;112(1):155-9.
41. Cochrane. Cochrane Airways data-collection.

42. Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. Bmj. 2011;343:d5928.
43. Kopelowicz A, Zarate R, Wallace CJ, Liberman RP, Lopez SR, Mintz J. The ability of multifamily groups to improve treatment adherence in Mexican Americans with schizophrenia. Arch Gen Psychiatry. 2012;69(3):73.
44. Awan NR, Jehangir SF, Irfan M, Naeem F, Farooq S. Explanatory model of illness of the patients with schizophrenia and the role of educational intervention. Schizophr Res. 2017;190:68-73.
45. Chien WT, Mui JH, Cheung EF, Gray R. Effects of motivational interviewing-based adherence therapy for schizophrenia spectrum disorders: a randomized controlled trial. Trials. 2015;16:270.
46. Dahan S, Behrbalk P, Stolovy T, Greenberger C. Improving Adherence in Hospitalized Patients Diagnosed With Schizophrenia: An Integrative One-on-One Intervention. Arch Psychiatr Nurs. 2016;30(6):660-5.
47. Guo X, Zhai J, Liu Z, Fang M, Wang B, Wang C, et al. Effect of antipsychotic medication alone vs combined with psychosocial intervention on outcomes of early-stage schizophrenia: A randomized, 1-year study. Arch Gen Psychiatry. 2010;67(9):895-904.
48. Javadpour A, Hedayati A, Dehbozorgi GR, Azizi A. The impact of a simple individual psycho-education program on quality of life, rate of relapse and medication adherence in bipolar disorder patients. Asian J Psychiatr. 2013;6(3):208-13.
49. Menon V, Selvakumar N, Kattimani S, Andrade C. Therapeutic effects of mobile-based text message reminders for medication adherence in bipolar I disorder: Are they maintained after intervention cessation? J Psychiatr Res. 2018;104:163-8.
50. Pakpour AH, Modabbernia A, Lin CY, Saffari M, Ahmadzad Asl M, Webb TL. Promoting medication adherence among patients with bipolar disorder: a multicenter randomized controlled trial of a multifaceted intervention. Psychol Med. 2017;47(14):2528-39.
51. Zhou B, Gu Y. Effect of self-management training on adherence to medications among community residents with chronic schizophrenia: a singleblind randomized controlled trial in Shanghai, China. Shanghai Arch Psychiatry. 2014;26(6):332-8.
52. Aho-Mustonen K, Tiihonen J, Repo-Tiihonen E, Ryynänen OP, Miettinen R, Räty H. Group psychoeducation for long-term offender patients with schizophrenia: an exploratory randomised controlled trial. Crim Behav Ment Health. 2011;21(3):163-76.
53. Barkhof E, Meijer CJ, de Sonneville LM, Linszen DH, de Haan L. The effect of motivational interviewing on medication adherence and hospitalization rates in nonadherent patients with multi-episode schizophrenia. Schizophr Bull. 2013;39(6):1242-51.
54. Bäuml J, Pitschel-Walz G, Volz A, Lüscher S, Rentrop M, Kissling W, et al. Psychoeducation Improves Compliance and Outcome in Schizophrenia Without an Increase of Adverse Side Effects: A 7-Year Follow-up of the Munich PIP-Study. Schizophr Bull. 2016;42 Suppl 1(Suppl 1):S62-70.
55. Çetin N, Aylaz R. The effect of mindfulness-based psychoeducation on insight and medication adherence of schizophrenia patients. Arch Psychiatr Nurs. 2018;32(5):737-44.
56. Eker F, Harkın S. Effectiveness of six-week psychoeducation program on adherence of patients with bipolar affective disorder. J Affect Disord. 2012;138(3):409-16.
57. Jones SH, Smith G, Mulligan LD, Lobban F, Law H, Dunn G, et al. Recovery-focused cognitive-behavioural therapy for recent-onset bipolar disorder: randomised controlled pilot trial. Br J Psychiatry. 2015;206(1):58-66.
58. Moncrieff J, Azam K, Johnson S, Marston L, Morant N, Darton K, et al. Results of a pilot cluster randomised trial of the use of a Medication Review Tool for people taking antipsychotic medication. BMC Psychiatry. 2016;16:205.



Chapter 3

Medication self-management in Flemish psychiatric hospitals: *A prevalence study in hospitalised patients with schizophrenia spectrum or bipolar disorders*

This chapter has been published as:
Loots E, Van Rompaey B, Morrens M, Dilles T.
Medicatie zelfmanagement in Vlaamse psychiatrische ziekenhuizen:
Een prevalentiestudie bij gehospitaliseerde patiënten met een schizofrenie spectrum of bipolaire stoornis.
Nursing. 2023;38(2):14-21

Chapter 3: Contents

Abstract

Background: Medication self-management (MSM) represents a pivotal component in the process of recovery and preserving health. Nonetheless, its significance tends to diminish notably during hospitalisation. The proposition of patient self-administration of their medication amidst hospitalisation emerges as potentially advantageous in terms of enhancing patient satisfaction, promoting adherence to pharmacotherapy, and augmenting self-care proficiency. This study aimed to characterize the prevalence and potential organizational factors of MSM during hospitalisation in patients with SSD od BD.

Method: A multicentre cross-sectional observational study was conducted in 31 psychiatric hospitals in Flanders where patients with schizophrenia spectrum or bipolar disorder were hospitalised.

Results: MSM was implemented in 11 of the 48 participating units (23%), of which nine units (82%) applied to all oral prescribed medications except for depot medication.

Analysis of patients' medical files revealed that only 4% of the included patients were on MSM during the inclusion period with 84% of the total medication amount being self-administered.

Conclusion: MSM is only allowed in a minority of Flemish psychiatric hospitals. On nine of the eleven units where MSM was allowed, no distinction was made between medication types, except long-acting injectable (LAI) antipsychotics.

3.1. Introduction

Schizophrenia and bipolar disorders are severe psychiatric disorders, with schizophrenia affecting around 1% and bipolar disorders affecting about 3% people worldwide [1]. They are often complicated by recurring relapses [2, 3]. Non-adherence, substance abuse, and stressful life events are risk factors for this relapse, in which non-adherence is the most common cause [2]. Discontinuation of antipsychotic pharmacotherapy is associated to a fivefold risk of relapse [3]. Together with psychoeducation, pharmacotherapy is often the first line of treatment of these major psychiatric disorders. Patients can learn how to manage their medication during their hospital admission. This approach allows for the detection and correction of problems, such as non-adherence to treatment, before the patient is left to manage their medication on their own at home [4]. In addition, patients who are not able to self-manage their medication, but are expected to do it after discharge, should be given the opportunity to learn to self-manage their medication whilst in hospital.

Medication self-management (MSM) in hospital was already mentioned in the literature in 1959, and it has since been studied internationally for many years [5].

Literature revealed several interventions to improve medication adherence in patients with schizophrenia spectrum disorder (SSD) or bipolar disorder (BD), such as cognitive behavioural therapy, psychoeducation, family interventions, and motivational interviewing [6]. Most interventions focus on changing in attitudes and cognitions to improve adherence by increasing in disease and medication knowledge. However, disease insight and adherence are only moderately correlated [7]. To increased insight, patients should be enabled to recognize their medication and to organize its' intake autonomously in full self-responsibility [8].

Medication self-management (MSM) is defined as a person's capability to cope with medication treatment for a chronic condition and the physical and psychosocial effects and changes it causes in their daily life. MSM is facilitated by social support and information, but hindered by difficulties with medication regimens, and physical and psychological symptoms [8, 9]. Considering this definition, the MSM process can determine a sequence a patient must follow to safely and effectively take their medications after hospital discharge [10]. In our research, MSM was defined as patients who store, prepare, and administer their medication themselves [10, 11] {Bailey Stacy C., 2013 #106;Bailey Stacy C., 2013 #106}{Richardson, 2014 #70;Davis, 2002 #112;Bailey Stacy C., 2013 #106}. MSM is legally allowed

in Belgian hospitals under specific prerequisites such as a clear registration in the patient's personal medical file and it has to be clearly described which medication is self-administered and which is administered by nurses. Healthcare providers always have a duty of care and a duty of surveillance during hospitalisation. If any problems occur during MSM, these have to be noted in the patient's personal medical files [12]. Literature describes that patients with psychotic and mood disorders and mental healthcare providers are positive towards to inpatient MSM [13, 14]. They stated MSM during hospitalisation increased patients' autonomy, confidence, self-reliance, appreciation, and satisfaction. [14, 15]. To date, research into the prevalence of MSM in patients diagnosed with SSD or BD during hospitalisation is lacking.

A prevalence study on MSM in general hospitals in Flanders did not distinguish between non-psychiatrics and psychiatric units within the hospital setting [16]. A cross-sectional multicentre observational study of Belgian general hospitals revealed that 22% of the 1269 patients did self-manage at least one medicine during their hospitalisation. Nurses stated that 41% of the hospitalised patients would have been able to self-manage their medication during their hospital admission (independently prepare and take their medication correctly during hospitalisation). These results revealed that many more patients would have been able to self-manage their medication during hospitalisation. Although MSM was possible, only 18% of the 57 units had a MSM procedure and 7% of the units only had an assessment tool to assess patients' competence to MSM [16]. According to the literature, a complete MSM procedure consists of an readiness assessment tool, [17], an observation tool to assess the patient's needs on MSM [6, 14], a tool to monitor medication adherence during hospitalisation and the possibility to provide support patients on MSM during their hospital admission (e.g.. Education sessions or workshops)[6, 18]. This study aimed to characterize the prevalence and potential organizational factors of MSM during hospitalisation in patients with SSD od BD.

3.2. Methods

3.2.1. Design

A multicenter, quantitative cross-sectional observational study was conducted in 31 psychiatric hospitals in Flanders, Belgium, from November 2020 to April 2021. Data were registered on the prevalence of MSM and demographic characteristics of each patient, and organizational characteristics of the included units.

3.2.2. Participants and setting

Hospital units accommodating hospitalised patients diagnosed with SSD or BD were selected. Specifically, the research included patients from both resocialization units and chronic psychosis units.

All 52 units in Flanders (the Dutch-speaking region of Belgium) were contacted, of which 48 units (92%) participated. In order to obtain sufficient data variation, convenience sampling was used to select patients with SSD or BD. All patients of the participating units who self-administered at least one medicine were included.

3.2.3. Data collection

The data collection was conducted on unit and patient level according to a self-developed structured questionnaire and based on results from a previous study on MSM in a non-psychiatric setting [18, 19]. The definition of MSM was explained in detail at the beginning of the survey. The questionnaires were presented to a panel of psychiatric nurses, physicians, and two independent researchers. This resulted in minor alterations in some answer categories.

At the level of the unit, data were collected on the type of unit, procedures for self-management of medication, intake of home medication, the storage of medication in the patient's room and possible tools such as the use of medicine boxes.

In addition, data on the decision-making process concerning participation in MSM was collected after consultation with the head nurse.

To describe the population, the following data were retrospectively collected: age, gender, educational level, work and hospital characteristics, disease, reason for hospitalisation and medication characteristics.

Medical files of patients who did not do MSM during hospitalisation were excluded.

Data collected on medication characteristics concerned the number of medications taken at home, the number of medications taken during hospitalisation, and the number and type of changes in the medication schedule used at home compared to the medication used during hospitalisation.

In addition, a clear distinction was made between the medication taken by the patient during hospitalisation and which was not. If the patient did self-administer medication, the name and route of administration of self-administered medication were registered. Afterwards, they were coded using the Anatomical-Therapeutic-Chemical classification.

3.2.4. Data analysis

Data were analysed using IBM SPSS Statistics V.24.0 (SPSS Inc, Chicago, IL, USA). The normality of the data was tested using the absolute z-value [20]. Discontinuous and categorical data were described using frequency distributions, while mean and standard deviations were used for continuous data. A two-sided level of significance of 0.05 was applied. Nonparametric statistics were used to analyse the data. To evaluate the statistical significance of the differences between the two patient groups, the Fisher's Exact and $\chi 2$ test for dichotomous data and the Mann-Whitney U test for continuous data was used.

3.2.5. Ethical considerations

The local ethics committees and the Ethics Committee of the University Hospital of Antwerp formally granted ethical approval (reference B3002020000188). In each involved hospital unit, informed consent was obtained from the head nurse. Data pertaining to patients were acquired through interviews conducted with nurses. No direct interaction with patients occurred, and all collected data were anonymized through coding, thereby excluding any patient identification information.

3.3. Results

3.3.1. Population

All 52 units in Flanders were contacted, of which 48 units (92%) participated.

MSM was applied in 11 of the 48 units (23%). During the inclusion period, the personal medical files of 37 patients self-administered their medication during hospitalisation were analysed.

Only 37 patients self-administered at least one medicine during hospitalisation (Table 3.1). The average age of participants was 43 years [SD 12], 68% had a diagnosis of BD and the majority were female (60%). The majority of the participants received support from significant others both during and after hospitalisation (84%).

Table 3.1: Demographic characteristics.

Demographic data	**SSD** (n= 12)	**BD** (n= 25)	**Total** (n= 37)	**p-value**
Gender, n (%)				0.036[1]
Male	8 (53)	7 (47)	15 (40)	
Female	4 (18)	18 (82)	22 (60)	
Age (years)				0.314[2]
Mean [SD]	49 [11]	44 [13]	43 [12]	
Education, n (%)				0.094[2]
Primary education	0	10 (40)	10 (27)	
Secondary education	4 (34)	11 (44)	15 (41)	
Higher education	1 (8)	4 (16)	5 (14)	
Unknown	7 (58)	0 (0)	7 (18)	
Supported by significant others, n (%)	10 (83)	21 (84)	31 (84)	0.959[3]

[1] Fisher's Exact Test
[2] Mann-Whitney U test
[3] χ^2 test

3.3.2. Prevalence of MSM in Flemish psychiatric hospitals

MSM was implemented in 11 of the 48 participating units (23%), of which nine hospital units (82%) applied to all oral prescribed medications except for long-acting injectable (LAI) antipsychotics.

Two hospital units indicated multiple reasons for prohibiting MSM for Lithium and Benzodiazepines during hospitalisation. Reasons for prohibiting MSM were: the health status of the patient, history of suicide and/or medication abuse and the psychiatrists' opinion on MSM.

Only a few hospital units (15%) had an available procedure and screen-

ing tool to assess the competence of the patients to self- manage their medication.

The decision-making process concerning participation in MSM was largely shared between only the treating physicians (45%) and the paramedic team (55%). In only one hospital unit, the general practitioner, the hospital pharmacist and the patient's significant others were involved in the MSM decision. Patients were systematically involved in the MSM decision and the storage of medication (Table 3.2), taking into account the patient's preferences, needs, beliefs and concerns about treatment in general.

Table 3.2: Medication management characteristics at level of the unit.

Storage of medicines		**Hospital units** (n= 11)
Nurses' station		3
Patient room	Medicine package	3
	Medicine box	2
	Safe of the patient	2
	Other	1
Tools	Medication schedule	9
	Medicine box	11
	Alarm	1
	App	2

3.3.3. Organisational and medication characteristics associated with MSM

The MSM characteristics were presented in Table 3.3. Patients are encouraged to self-manage all their prescripted medicines, including newly started medicines during hospitalisation.

Hospitalised patients took on average six different self-administered medicines [Range 16] during hospitalisation, with a minimum of one medicine and a maximum of 17 different medicines. Moreover, 84% of the total number of medicines were self-managed except for LAI antipsychotics (16%).

The majority of self-managed medicines were antidepressants (20%), antipsychotics (19%), benzodiazepines (8%) and vitamins (9%) and others (13%). The category others consisted mainly of contraception, antiepileptics, inhaled corticosteroids, diuretics, melatonin and antithrombotic medicines (Table 3.3).

In 89% of the hospitalised patients, the transition from home to the

hospital resulted in one or more changes in the medication schedule. The most frequent change was a new prescription in 73% of the patients, with a minimum of one new medicine and a maximum of seven new medicines. In 40% of patients, the decision was made to stop at least one medicine, with a maximum of five medicines. Additional analysis revealed a positive correlation between age and the number of medications taken during hospitalisation (r= 0.332, p= 0.045).

Table 3.3: Medication management characteristics.

Medication management characteristics	**Patients** (n= 37)
Number of medications (n= 230), median [range]	6 [15]
Classification, n (%)	
Antidepressants	46 (20)
Antipsychotics	41 (19)
Others	29 (13)
Benzodiazepines	19 (8)
Vitamins	21 (9)
Gastrointestinal medications	14 (7)
Beta blockers	10 (4)
Statins	10 (4)
Diabetic medications	9 (4)
Analgetics	8 (3)
Corticosteroids	8 (3)
Antihypertensives	5 (2)
Antihistamines	5 (2)
Withdrawal medications	3 (1)
Lithium	2 (1)
Number of self-managed medications during hospitalisation, median [range]	6 [16]
Number of changes in medication schedule during hospitalisation (n= 96), %	89

3.4. Discussion

3.4.1. Main results

MSM in patients with SSD or BD is only possible in a minority of Flemish psychiatric hospitals. Most units applied to all oral prescribed medications except for LAI antipsychotics. Only a few units had an available procedure and screening tool to assess the competence of the patients to self- manage their medication. These findings are in line with previous research [16] indicating that 21% of hospitalised patients self-managed their medication. Most of these units involved in that study were medical and surgical units, with a minority being psychiatric units [16].

3.4.2. Policy

Previous research in a non-psychiatric setting clearly describes that an assessment is always needed to objectively evaluate the actual competencies of the patient. This assessment should consider various aspects, such as patients' specific prerequisites, mental and physical condition, and possible side-effects of their current medication [17, 18].

In previous similar research in general hospitals, physicians stated that it was difficult to assess patients' MSM competences and their follow-up due to their short hospital admission [17]. The literature clearly describes that the most prevalent reasons for patients not to participate in MSM during hospitalisation: not capable of handling changes in their medication regimen (49%), mentally not capable to self-manage medication (48%), or not preparing their own medication at home (47%). Physicians reported the reasons for prohibiting MSM during hospitalisation: a history of medication non-adherence, lack of confidence and various changes in the medication schedule [17, 18].

Several existing programs for MSM incorporate an evaluation tool for the competences of patients. Only one study described the validation of a tool, the Self-Administration of Medication (SAM) [19]. This tool intends to objectively determine the extent to which patients can self-manage their medication [19, 21]. The findings overall confirm the need for further research on the validation of tools for use in psychiatry, as this topic currently represents a gap in the literature.

Additional research outlining the prevalence and profile of patients' ineligible for MSM during hospitalisation could be an added value. This would make it possible to establish a risk profile for patients who, for one reason or another, are not eligible for MSM resulting in an increased risk

of relapse [2, 3].

3.4.3. Legal context

There are no Royal Decrees in Belgium that describe MSM during hospitalisation. The formulation of policies in this regard falls within the purview of the individual hospitals. If MSM occurs, this has to be noted in the patient's personal medical file and it has to be clearly described which medication is self-managed and which is administered by nurses. Healthcare providers have a duty of care and a duty of surveillance during hospitalisation. If any problems occur during MSM, these problems have to be noted in the patient's medical file [22].

The decision-making process concerning participation in MSM is largely shared between the treating physician, the nursing team and the patient. This is in contrast with the recommended practice in healthcare communication, shared decision-making, in which the emphasis is on the patient as a person, considering the patient's preferences, needs, beliefs and concerns about treatment in general. At the same time, however, they often report a lack of sufficient involvement in decision-making concerning antipsychotics [23, 24]. Mental healthcare providers often have difficulty using SDM in decisions about psychiatric medication, as it is often perceived as posing risks for clinicians (e.g. liability or making medication errors) and concerned over patients' medication under- and misuse [24]. MSM requires an integrated multidisciplinary approach to ensure that patients get maximum benefit from their therapy.

3.4.4. MSM in clinical practice

MSM is becoming an increasingly important element in rehabilitation programs. As patients are not capable of MSM, aid is often required. Healthcare providers can support and coach patients towards self-management of their medication. Patients who are not able to self-manage their medication, but are expected to do MSM after discharge, should be given the opportunity to learn to self-manage their medication whilst in hospital [14, 25, 26].

Research revealed that patients' medication knowledge increases with participation in MSM [27, 28] and MSM appears to be an effective intervention for improving adherence in patients with SSD after discharge from hospital [29]. Literature describes that patients and healthcare providers are positive towards MSM when asked to rate their satisfaction with inpatient MSM. Yet not all healthcare providers are willing to participate in

MSM. This may reflect the current culture in hospitals, where there is an expectation from patients that they will assume a more passive role and an expectation from the healthcare providers that they will assume responsibility for patients' medical care, regardless of patients' level of involvement in their care prior to admission. Alternatively, it may be a response to the initial increases in some aspects of staff workload, such as patient education and preparation of MSM [30]. External support from family or relatives is desirable due to the positive impact that a familiar carer may have on patients' willingness to MSM [15], as well as the potential for reducing staff workload if relatives are willing to be involved in patients' care [30].

In addition, they could assist nurses in screening patients and following up on them after hospitalisation. Future research should therefore focus on what significant others need to assist and support patients in their treatment.

3.4.5. Strengths and limitations

The willingness to participate in our study was high. In total, all 52 units of 31 psychiatric hospitals in Flanders were contacted of which 48 units participated in this study. It is important to consider the low sample size when interpreting the results. MSM was implemented in 11 of the 48 participating units (23%), of which 15% had an available procedure and screening tool to assess the competence of the patients to self- manage their medication. Content details regarding these tools were not questioned. Analysis of patient's personal medical files revealed that MSM was often not explicitly mentioned, medication details were unclear or incomplete or even missing. These limitations give an incomplete view of the current situation in clinical practice.

3.5. Conclusion

MSM was implemented in 11 of the 48 participating units (23%), of which nine units (82%) applied to all oral prescribed medications except for long-acting injectable (LAI) antipsychotics. Only 15% of the units had an available procedure and screening tool to assess the MSM competences of the patients. Analysis of patients' personal medical files revealed that only 4% of the included patients were on MSM during the inclusion period with 84% of the total medication amount being self-administered. The results of our study confirm that MSM has not yet been widely implemented in Flemish psychiatric hospitals.

3.6. References

1. World Health Organization. The Global Economic Burden of Non-Communicable Diseases; World Economic Forum: Geneva, Switzerland, 2018.
2. Sendt BS. A systematic review of factors influencing adherence to antipsychotic medication in schizophrenia-spectrum disorders. Psychiatry Res. 2015;225(1-2):14-30.
3. Jingbo X, Ying S, Hongyan Z. High relapse rate and poor medication adherence in the Chinese population with schizophrenia: results from an observational survey in the People's Republic of China. Neuropsychiatr Dis Treat. 2015;11:1161–7.
4. Morant N, Kaminskiy E, Ramon S. Shared decision making for psychiatric medication management: beyond the micro-social. Health Expect. 2016;19 (5):1002-14.
5. Parnell MA. Medicines at the bedside. Am J Nurse. 1959;59:1417-8.
6. Loots E, Goossens E, Vanwesemael T, Morrens M, Van Rompaey B, Dilles T. Interventions to Improve Medication Adherence in Patients with Schizophrenia or Bipolar Disorders: A Systematic Review and Meta-Analysis. Int J Environ Res Public Health 2021, 18, 10213 https://doiorg/103390/ ijerph181910213. 2021.
7. Beck CM, Kvrgic S, Kleim B, Vauth R. Are we addressing the 'right stuff' to enhance adherence in schizophrenia? Understanding the role of insight and attitudes towards medication. Schizophr Res-Oct; 132(1). 2011:42-9.
8. Audulv Å GS, Kephart G, Warner G, Packer TL. The Taxonomy of Everyday Self-management Strategies (TEDSS): a framework derived from the literature and refined using empirical data. Patient Educ Couns. 2019;102(2):367–375. .
9. Morrison C, Martsolf D. Facilitators and Barriers to Self-Management for Adolescents and Young Adults Following a Hematopoietic Stem Cell Transplant . Journal Oncol Nurs Jan/Feb;35(1):36-42. 2018.
10. Bailey S, Christine U, Wolf M. Rethinking Adherence: A Health Literacy–Informed Model of Medication Self-Management. Journal of Health Communication. 2013;18:20-30.
11. Richard A, Shea K. Delineation of self-care and associated concepts. J Nurs Scholarsh. 2011;43(3):255-64.
12. FOD Volksgezondheid. Technische commissie voor verpleegkunde Gezondheidszorgberoepen en beroepsuitoefening: vragen en antwoorden 2015-2019. 2015.
13. Vanwesemael T, Boussery K, Manias E, Petrovic M, Fraeyman J, Dilles T. Self-management of medication during hospitalisation: Healthcare providers' and patients' perspectives. J Clin Nurse. 2018;27 (3-4): 753-68.
14. Loots E, Leys J, Proost S, Morrens M, Glazemakers I, Dilles T, Van Rompaey B. Medication Self-Management in Hospitalised Patients with Schizophrenia or Bipolar Disorder: The Perceptions of Patients and Healthcare Providers. Int J Environ Res Public Health 2022, 19, 4835 https://doiorg/103390/ ijerph19084835. 2022.
15. Richardson S, Brooks H, Bramley G, Coleman J. Evaluating the effectiveness of self-administration of medication (SAM) schemes in the hospital setting: a systematic review of the literature. PLoS One. 2014;9(12).
16. Vanwesemael T, Van Rompaey B, Petrovic M, Boussery K, Dilles T. SelfMED: Self-Administration of Medication in Hospital: A Prevalence Study in Flanders, Belgium. Nurs Scholarsh. 2017;49:277-85.
17. Vanwesemael T, Dilles T, Van Rompaey B, Boussery K. An Evidence-Based Procedure for Self-Management of Medication in Hospital: Development and Validation of the SelfMED Procedure. Pharmacy (Basel). 2018;77.

18. Vanwesemael T. Proefschrift voorgelegd tot het behalen van de graad van Doctor in de Medische Wetenschappen aan de Universiteit Antwerpen. In: Faculteit geneeskunde en gezondheidswetenschappen. Universiteit Antwerpen. 2018:95-109.
19. Anderson J, Manias E, Kusljic S, Finch S. Testing the validity, reliability and utility of the Self-Administration of Medication (SAM) tool in patients undergoing rehabilitation. Res Social Adm Pharm 10 (1), 204-216. 2014.
20. Kim HY. Statistical notes for clinical researchers: Assessing normal distribution, using skewness and kurtosis. Restor Dent Endod. 2013;38:52–4.
21. Manias E, Beanland C, Riley R, Hutchinson A. Development and validation of the self-administration of medication tool. Ann Pharmacother 40 (6), 1064-1073. 2006.
22. Zorginspectie van de Vlaamse Afdeling Welzijn VeG, persoonlijke communicatie, oktober 2015.
23. Moncrieff J, Azam K, Johnson S, Marston L, Morant N, Darton K, et al. Results of a pilot cluster randomised trial of the use of a Medication Review Tool for people taking antipsychotic medication. BMC Psychiatry. 2016;16:205.
24. Zisman-Ilani Y, Lysaker P. Shared risk taking: shared decision making in serious mental illness. Psychiatr Serv. 2021;72:10.
25. Beentjes T, van Gaal B, Van Achterberg T, Goossens P. Self-Management Support Needs From the Perspectives of Persons With Severe Mental Illness: A Systematic Review and Thematic Synthesis of Qualitative Research. J Am Psychiatr Nurses Assoc. 2020;26 (5):464-82.
26. Wright J, Emerson A, Stephens M, Lennan E. Hospital inpatient self-administration of medicine programmes: a critical literature review. Pharm World Sci. 2006;28(3):140-51.
27. Furlong S. Do programmes of medicine self-administration enhance patient knowledge, compliance and satisfaction? Journal of advanced nursing. 1996;23:9.
28. Lowe C, Courtney E, Purvis J, Teale C. Effects of self-medication programme on knowledge of drugs and compliance with treatment in elderly patients. British Medical Journal. 1995;310:1229–31.
29. Schirmer UB, Steinert T, Flammer E, Borbe R. Skills-based medication training program for patients with schizophrenic disorders: a rater-blind randomized controlled trial. Patient Prefer Adherence. 2015;9:9.
30. Pearce M. Pilot study of self-medication: pharmacy workload appraisal. New Zealand Pharmacy. 1991;11:18-9.

Chapter 4

Medication self-management in hospitalised patients with schizophrenia spectrum or bipolar disorder: *The perceptions of patients and healthcare providers*

This chapter has been published as:
Loots E, Leys J, Proost S, Morrens M, Glazemakers I, Dilles T, Van Rompaey B. Medication Self- Management in Hospitalised Patients with Schizophrenia or Bipolar Disorder: The Perceptions of Patients' and Healthcare Providers'. Int. J. Environ. Res. Public Health 2022, 19, 4835. https://doi.org/10.3390/ ijerph19084835

Chapter 4: Contents

Abstract

Background: The concept of MSM pertains to the practice wherein hospitalised patients, rather than healthcare professionals, undertake the preparation and consumption of their medications autonomously. Existing literature posits potential benefits associated with MSM during hospitalisation, including heightened patient satisfaction, improved adherence to pharmacotherapy, and enhanced self-care proficiency. The aim of the study was to explore perspectives of hospitalised patients with Schizophrenia Spectrum or a Bipolar Disorder and their healthcare providers on medication self-management.

Methods: In a qualitative descriptive design, semi-structured interviews were used. Forty-nine interviews were completed (nurses n= 18; psychiatrists n= 3; hospital pharmacists n= 2; patients n= 26). Data analysis was iterative using an inductive and thematic approach.

Results: From the thematic analysis of the interviews, three main themes emerged: monitoring and shared decision- making, relationship based on trust, and patient satisfaction and rehabilitation; as well as three sub- themes: available tools, patient readiness, and safety. Regular monitoring and follow-ups were considered prerequisites for medication self-management. All stakeholders considered that the patient, the nursing staff, and the psychiatrist should all be involved in the process of medication self-management. All healthcare providers emphasized the importance of regular re-evaluations of the patient and were worried about medication errors and misuse. Most patients considered medication self-management during hospitalisation to increase their confidence, self-reliance, and satisfaction. Many participants thought it would make a positive contribution to the recovery process.

Conclusion: All stakeholders were positive towards medication self-management under specific prerequisites. According to the participants, medication self-management offered many benefits, including the implementation of more structure for the patient, an ameliorated preparatory phase towards discharge, and an actual improvement of future adherence. All participants considered medication self-management to contribute to more profound medication knowledge and an overall improvement of their health literacy.

4.1. Introduction

Schizophrenia Spectrum Disorders (SSD) or a Bipolar Disorders (BD) are severe major psychiatric disorders. They are often complicated by recurring relapses [1]. Non-adherence, substance abuse, and stressful life events are risk factors for this relapse, in which non-adherence is the most common cause [2]. Patients interrupting or discontinuing their medication are five times more likely to relapse [3]. Interventions targeting the improvement of adherence in patients with SSD or BD are heterogeneous. Current techniques to improve patients' adherence nearly exclusively use cognitive-behavioural or psycho- education approaches [4-8]. However, about 25% of patients discontinue their medication within the first week after discharge from inpatient treatment [9]. A multidisciplinary approach during hospitalisation, focusing on the guidance and coaching of patients in their medication management, seems necessary to prevent relapse. In recent years, the management of chronic illnesses, such as SSD or BD, has taken a key place in the patients' own care process [10, 11]. Patients learn to cope more effectively with symptoms, disease, and management of their medication regimens [12, 13]. The development and implementation of a medication self-management (MSM) procedure can facilitate these implementations [14]. MSM has been defined as the extent to which a patient takes medication as prescribed, including not only the correct dose, frequency, and spreading, but also its continued safe use over time [15]. Considering this definition, medication self-management can be deconstructed to identify the patients' pathway to take medications safely and effectively after hospital discharge (15).

MSM was first mentioned in the literature in 1959, and hence has been internationally studied for many years [16-18]. MSM in hospital includes a wide range of activities, such as patient education about medication and monitoring patients while self-managing their medication [19]. In Belgian hospitals, MSM is legally allowed under condition of clear registration in the patient's record and availability of a list of the medications managed by the patient and those managed by the health care provider. The attending physician is responsible for authorizing and evaluating the self-management of the medication process [20]. MSM offers some advantages over administration of medication by nurses, such as increased patient satisfaction and improved adherence to pharmacotherapy and self-care competences [17]. Research conducted in the general hospitals of Flanders' (the Dutch-speaking region of Belgium) general hospitals showed that 41% of patients (general and surgical units) are capable of MSM during hospitalisa-

tion. Most of these units were medical, surgical, rehabilitation, or geriatric units, not including psychiatric units. A total of 89% of the nurses, 75% of the physicians, and 100% of the hospital pharmacists were willing to allow MSM [21]. Little is known about the perception of MSM in patients with SSD or BD. The aim of this study is to gain insights into the perspectives of all stakeholders involved in the MSM procedure in patients with SSD or BD. Insights into the benefits, disadvantages, and prerequisites of MSM during hospitalisation are necessary for the development and implementation of a MSM intervention. These insights are essential to describe which factors may influence the implementation of a MSM procedure.

4.2. Materials and methods

4.2.1. Research team and author reflexivity

EL, TD, and BVR developed the study protocol and topic guide, and EL, JL, and SP conducted the interviews. EL is a doctoral student, researching MSM in patients with SSD or BD. JL and SP are Master's students with no affinity with this research. EL, TD, BVR, IG, and MM did the conceptualisation, methodology, investigation, and validation. TD, BVR, and MM are the supervisors and have an affinity with this research. IG is a qualitative expert with no affinity with this research project.

4.2.2. Design

In this study, we used a qualitative descriptive design with an exploratory approach within a pragmatic paradigm. The goal was to describe the perceptions around MSM during hospitalisation from the different stakeholders. Benefits, disadvantages, and prerequisites for the development and implementation of a MSM intervention must be explored. This research involved patients and healthcare providers from both resocialization and chronic psychosis hospital units. Semi-structured interviews were conducted with hospitalized patients with Schizophrenia Spectrum Disorder or a Bipolar Disorder, Type I or Type II and healthcare providers who were directly involved in patients' medication process. Findings were synthesised in one comprehensive report on different perspectives. The methods section is described following the consolidated criteria for reporting qualitative studies (COREQ) checklist.

4.2.3. Recruitment

In order to obtain sufficient data variation, convenience sampling was used. We recruited interviewees in four psychiatric inpatient hospitals in Belgium. Units accommodating hospitalised patients with SSD or BD were selected. Eligible participants were hospitalised patients with SSD or BD and healthcare providers who were directly involved in management of patients' medication, being a nurse, a psychiatrist, or a hospital pharmacist. Patients were included after consultation with the head nurse and the attending psychiatrist of the unit. Patients had to meet all the following inclusion criteria: adult hospitalised patients diagnosed with SSD or BD type I or II, mentally and physically able to formulate an opinion. Exclusion criteria for patients were patients staying in either an acute or an outpatient unit. In two hospitals, in consultation with the psychiatrist and the head nurse, the researcher informed patients about the study. In the two other hospitals, the psychiatrist and head nurse or team coordinator identified the patients in advance. Subsequently, the first author (EL) personally informed those interested about the study. Healthcare providers were selected after consultation with the director of nursing or head nurse. The healthcare providers were personally invited and informed about the study by the head nurse or researcher considering the structure of each department and the COVID-19 measures. All potential participants were informed personally through an information letter. All eligible participants were informed about the study. Inclusion of new participants was ceased when new information, new ideas, or insights from the interviews no longer emerged and data sufficiency was reached.

4.2.4. Data collection

The interviews were conducted in Dutch between January 2019 and March 2021. The semi-structured interviews used a topic list based on previous research on MSM in hospitalised patients. This process resulted in a topic guide with eight questions. The interview guide was pilot tested with four nurses, three patients, and a psychiatrist, resulting in minor revisions to the content and structure of the guide. The pilot tested interviews were not deleted because nothing was changed in the questions of the topic guide. Only more detailed information on MSM during hospitalisation at the beginning of the interviews was provided. The pilot interviews showed that participants did not always know well what MSM entails. All interviews took place in a quiet room at the unit. Demographical data was noted at the beginning of each interview. All interviews were audio-record-

ed, and notes were taken during each interview. At the completion of the interview, the interviewer reflected the key-points to the interviewee. No personal or professional relationships existed between the participants and the interviewer prior to the interview. In advance of the interview, participants were informed of the aim and goals of the study.

4.2.5. Data analysis process

The data analysis started immediately after the first interview and has been continuously iterative using an inductive and thematic analysing approach. The data collection and analysis proceeded in parallel. All interviews were transcribed verbatim line by line and cleaned of all identifying information. Microsoft Excel® was used to manage the data. A systematic multistage approach guided this analysis: familiarization, identifying and indexing, mapping, and interpretation [22, 23]. After all interviews had been transcribed, data were re-read multiple times to obtain familiarization. Important fragments were assigned to an open, descriptive code which was then converted into an interpretative code. To improve the confirmability of the study, three team members (EL, JL, SP) independently coded four transcripts and compared coding line by line. Any discrepancies were discussed until consensus was achieved. The remaining transcripts were coded independently by the same three team members to identify common high-level concepts. The coding included memos for each transcript and reflections on analysis. The data were discussed at regular intervals to provide consistency in coding. After coding, themes were identified in the mapping stage. We grouped similar codes into those themes and compared themes between patients and healthcare providers. During the interpretation, major themes and associated quotes were identified to summarize the results [22-24].

4.2.6. Ethical considerations

The appropriate local ethics committee and the Ethics Committee of the University Hospital in Antwerp formally granted ethical approval (reference B300202042928). All participants received information on the purpose, design, and execution of the study. Participation was voluntary and signed informed consent was obtained from all participants prior to the interview. Participants had the right to withdraw consent at any time. Participants also agreed with them being audio recorded.

4.2.7. Participants

A total of three psychiatrists, 18 nurses, two hospital pharmacists, and 26 patients were interviewed. In two hospitals, psychiatrists indicated not being able to participate due to lack of time. Interviewing hospital pharmacists was possible in one hospital only. The interviews ranged from 21 to 60 min. On average, an interview with a physician took 28 min (range 23–32

Table 4.1: Demographic characteristics of the interviewed participants per hospital.

	University psychiatric hospital	**Regional psychiatric hospital**	**Public psychiatric hospital**	**Private psychiatric hospital**	**Total sample**
Number of hospital beds	601	747	263	313	1924
Codes interviewed groups*					
Patients					
SSD	7	1	3	6	17
BD	3	1	3	2	9
Psychiatrists	2	1	0	0	3
Nurses	6	2	4	6	18
Hospital pharmacists	0	2	0	0	2
Gender (n)					
Patients					
Male	6	1	6	4	17
Female	4	1	2	2	9
Psychiatrists					
Male	2	1	0	0	3
Nurses					
Male	2	1	1	2	6
Female	4	1	3	4	12
Hospital pharmacists					
Female	0	2	0	0	2
Total sample		Mean [SD]		Median (min-max)	
Age patients (years)					
		44 [12]		43 (26-62)	
Years working					
Psychiatrists		14 [12]		13 (2-27)	
Nurses		13 [9]		10 (1-27)	
Hospital pharmacists		3 [1]		3.5 (3-4)	
Duration of the interviews in minutes					
Patients		40 [12]		37 (21-60)	
Psychiatrists		27 [5]		27 (23-32)	
Nurses		45 [10]		42.9 (27-60)	
Hospital pharmacists		53 [5]		53 (50-56)	

min), with a nurse 45 min (range 27–60 min), with a hospital pharmacist 53 min (range 50–56 min), and with a patient 40 min (range 21–60 min). Table 4.1 shows the demographic characteristics of the interviewed participants per hospital.

4.3. Results

4.3.1. Themes

From the thematic analysis of the interviews, three main themes and three sub- themes emerged (Table 4.2).

Table 4.2: Main and sub-themes.

Theme	Sub-theme
1. Monitoring and shared-decision making	- Available tools
2. Relationship based on trust	- Patient readiness - Safety
3. Patient satisfaction and rehabilitation	

Theme 1: monitoring and shared decision-making

Monitoring and shared decision-making was a frequently discussed item between patients, nurses, and psychiatrists. Regular monitoring and follow-up were considered crucial prerequisites for MSM during hospitalisation. Many healthcare providers were concerned about losing an overview or control over the actual medication intake or perhaps not noticing mistakes, overdoses, and/or misuse. Healthcare providers emphasised the daily monitoring to check whether the patient had effectively taken their medication. However, it was noted that there is never absolute certainty about the medication intake, even when administered under supervision. Patients and nurses indicated that patients should always be guided and monitored by healthcare providers during MSM. Additionally, the follow-up during and after hospitalisation was considered to be important in order to reduce potential medication errors (wrong time or product or improper dose).

Many participants considered the patient, the nurse, and the psychiatrist should all be involved in the process of MSM. Specific prerequisites were described that the organisation had to meet in order to organise MSM during hospitalisation. Participants were convinced that this approach would also enhance medication adherence.

"Especially in the beginning, I think eh... eh... especially with people who have never done that. Do regular sampling to see if the medication has been taken. Regular monitoring is very important." (Patient 8, bipolar disorder)

"You have to do some checking every day. You still have to go in the room or everyone's medication tray in the evening... and look in the bin... are they not in the bin? Have they not been flushed down the toilet?..." (Nurse, 16)

"That supervision and guidance from the nurse is important but you should not last longer than necessary." (Patient 4, schizophrenia)

"I think that's also an important part of 'How do you as a patient see this? Would you like to take it?... 'Are there any problems? How did it go in the past? How do you feel about taking the medication?' That this is important, otherwise we will interpret it in the place of the patient." (Nurse 6)

Available tools

Many participants considered the organisation should provide some tools such as the use of pillboxes, medication schedules, electronic reminders, and applications. In addition, psychiatrists and nurses considered that the hospital should provide a MSM protocol. Another important condition was how and where to safely store self-management medication. Many participants were concerned about medication abuse or theft of medication. Healthcare providers indicated that providing workshops on MSM is an important condition for the implementation of MSM. During these workshops, patients could practice MSM, ask for tips and tricks, and formulate possible questions. During these exercise sessions, healthcare providers obtained an immediate insight into the patient's condition.

"I would perhaps like there to be a kind of community group, where the patients who are almost discharged can go and practice to do their own medication self-management. Uh... a group with stable people with whom we work towards home that we... who have their own living space or something, so that we really are a separate target group actually... in which you can work very intensively with their medication." (Nurse 2)

"I tell you, with me one of the tools is also setting my alarm clock...there are also those boxes or those things, shall I say, that remind you of that or something..., those little machines... " (Patient 9, bipolar disorder)

Theme 2: Relationship based on trust

All healthcare providers considered it as important to re-evaluate the

patients on a regular basis and were worried about medication errors and misuse.

Patient readiness

Many healthcare providers were concerned about the difficulty of correctly assessing patients' eligibility for medication self-management. Psychiatrists believed patients are often overestimated, while sometimes being underestimated.

"I think one of the risks is that people will think 'He can't do that' and so, we don't do it. That is a risk, that from themselves, there is... It's very difficult to assess the extent to which people can do things. Sometimes people are chronically overestimated, sometimes they are underestimated." (Psychiatrist)

Safety

The experience of medication side-effects can lead to many discomforts and to stopping the medication with the higher risks as a result, according to patients and nurses. Possible dangers included medication errors, medication intoxication, suicide (attempt), and medication abuse with eventual medical damage to the patient's health, to others, and to the environment. Despite their willingness to practice MSM, patients with SSD were especially anxious and stressed about making medication errors during medication self-management. Patients and nurses were particularly concerned about hoarding the medication.

"And... yes, maybe from the social aspect, peer pressure, swapping medication, theft... that kind of thing." (Psychiatrist)

"The threat for the patient is also thinking about it yourself, taking it yourself, yes... and forgetting to take it out of unwillingness, that you forget. It may be that you really forget, it may be that you don't want to..." (Patient 17, bipolar disorder)

Theme 3: Patient satisfaction and rehabilitation

Patient satisfaction and rehabilitation were the frequently discussed items. Nurses, hospital pharmacists, and patients suggested that MSM could be beneficial to the hospital and the hospital image due to the potential positive experiences and higher patient satisfaction. Most patients believed MSM during hospitalisation increased their autonomy, confidence, self- reliance, appreciation, and satisfaction.

Many participants perceived that MSM makes a positive contribution

to the recovery process. According to the participants, medication self-management during hospitalization offers many advantages, such as more structure for the patients, preparation for discharge and an improvement of adherence.

All stakeholders reported that MSM would contribute to better medication knowledge, an improvement of disease insight, and reflection on their own vulnerabilities through the psycho-education and guided training sessions. In addition, nurses suggested that an individual psycho-education program and MSM training should be included in the current therapy program for a group of stable patients who are about to be discharged.

Patients considered that they should continue the medication management routines that they used to do at home during hospitalisation. This process allowed patients to take their medication at the same time as they were used to at home. Participants were convinced that this approach would also enhance medication adherence.

"I think that also gives the patient a feeling of, yes... perhaps also of 'I can do this myself'... 'I can...'. They also say to me that I can take responsibility for this', so I think that's something the patient can be proud of." (Hospital pharmacist 1)

"By the time, when you come home, you will know how to do it. Yes, then you learn it by the time you get back home." (Patient schizophrenia, 13)

"The opportunities are that he is more aware of what he is taking, that he has more of a routine, of 'ah, I have to take my medication' in the morning and that that would certainly be a good idea in function of going back home after discharge." (Nurse 4)

"I also think if... he prepares it himself that, he might become more aware of the need for his medication." (Psychiatrist)

"You would like to do medication self-management. You also see the opportunity of... to be able to do that yourself in preparation to go home, you also say... one week is not enough, it would be better to be able to practice here for three or four weeks in order to be able to go home... to make it your own and build a routine into it... And you believe that this will also benefit the medication adherence." (Patient 17, bipolar disorder)

4.4. Discussion

4.4.1. Main findings

Most patients already took responsibility for medication prior to admission or shared this responsibility with significant others. In addition, several participants had previous experiences of partial or complete MSM during hospitalisation. Overall, it may be stated that MSM during hospitalisation was found to be very beneficial, especially for patients and for nurses. Results showed differences in patients' MSM views. At the beginning of the interviews, patients with SSD were not eager to MSM during hospitalisation. When the concept of MSM was explained again, with the emphasis on continued support by healthcare providers, they were willing to try MSM.

Three main themes were revealed to consider the implementation of a MSM tool during hospitalisation. Participants reported the importance of monitoring and shared decision-making, a relationship based on trust, and patient satisfaction and rehabilitation. Many of these results aligned with earlier qualitative studies and a systematic review from research in general hospitals [17, 25, 26]. In studies, the benefits for patients practicing MSM during hospitalisation resulted in an increased patient confidence before discharge, an improved disease insight, improved medication knowledge, and an improved therapeutic adherence after discharge [17, 25-27]. MSM during hospitalisation would rely on a collaborative and trusting relationship. Moreover, patients might become more confident in MSM if they feel supported by nurses. These results aligned with our results. Literature suggested patients were recognised as experts in their own disease management and were able to make decisions about their own care, goals, and values [28]. In our study, psychiatrists noted that MSM empowers patients. MSM created possible dangers, such as the possible misuse of medication or increased incidence of medication errors. Currently, a small body of evidence suggests that MSM would result in reduced medication errors in a non-psychiatric population [17].

In addition, separately packaged medications in unidoses in the hospitals were seen as an obstacle before and after discharge as they are not user-friendly and not the same as patients' medication at home. Healthcare providers were particularly concerned about the responsibility of each stakeholder. It was unclear to nurses and patients who has the final responsibility for the health status of patients on admission MSM during hospitalisation. Therefore, all stakeholders stated that the hospital should

have guidelines so that each stakeholder knows their role and responsibility. Many participants reported the importance of the presence of regular monitoring. This monitoring is used not only to prevent abuse, but also to prevent behavioural changes and side effects of medication [28, 29].

Previous research reported similar results. Information and communication about pharmacological therapy are important points of attention during the treatment process of patients [30-32].

4.4.2. Strengths and limitations

One of the strengths of this study was the inclusion of the perception of patients, nurses, physicians, and hospital pharmacists situated in four different psychiatric hospitals. The interviews provided valuable in-depth insights into the specific concerns of patients with SSD or BD who have complex psychiatric problems requiring medication. The study offers the possibility to develop a MSM procedure according to the needs of the stakeholders.

There are a few limitations to this study. First, despite our best efforts, we encountered challenges recruiting hospital pharmacists and physicians to participate in this study. We had limited perspectives from hospital pharmacists and psychiatrists, and other professionals may have a different opinion. Second, the participants were selected and addressed by the head nurse or department manager. This method of recruitment could have caused selection bias, as the participating stakeholders were interested in the topic. This way of recruitment is due to the COVID-19 pandemic as access to the units was limited. Finally, according to many patients, significant others and general practitioners are also important stakeholders in the medication process. They should be included in future research.

4.4.3. Implications for practice

The findings of this study created new opportunities for practice. First, operational strategies can be developed in tools and feasible activities for MSM: a patient assessment tool for deciding whether the patient is capable of MSM, a monitoring tool for medication intake, and different education sessions and supporting during hospitalisation. Second, these strategies may include individual adaptation and simplification of learning and practice opportunities, identification, and management of individual barriers, ensuring patient support structures and improving self-efficacy. Finally, these strategies can form fundamental pillars for the development and testing of a MSM toolbox in an intervention study.

4.5. Conclusions

Patients with SSD or BD, nurses, psychiatrists, and hospital pharmacists were generally positive about MSM during hospitalisation, but only under certain prerequisites. Monitoring and shared decision- making is a much-discussed issue. Patients should be willing to prove themselves during hospitalization and must possess certain competences which are regularly reassessed by healthcare providers. In addition, the organisation should offer a procedure and workshops for MSM. Many healthcare providers are concerned about the difficulty of correctly assessing patients' eligibility for MSM. Healthcare providers consider it as important to re-evaluate the patients on a regular basis. All participants consider that MSM would contribute to better medication knowledge and improvement of their health literacy.

4.6. References

1. World Health Organization. The global economic burden of non-communicable diseases. World Economic Forum, Geneva, Switzerland. Mental health atlas. 2011.
2. Pitanupong J, Ratanaapiromyakij P, Teetharatkul T. Factors Associated with Low Relapse Rates of Schizophrenia in Southern Thailand: A University Hospital-Based Study; Research Square: Durham, NC, UAS. 2021.
3. Rzewuska M. Drug maintenance treatment compliance and its correlation with the clinical picture and course of schizophrenia. Prog Neuro-Psychopharmacol Biol Psychiatry. 2002;26:811–4.
4. Xiao J, Mi W, Li L, Shi Y, Zhang H. High relapse rate and poor medication adherence in the Chinese population with schizophrenia: results from an observational survey in the People's Republic of China. Neuropsychiatr Dis Treat. 2015;11:1161-7.
5. Fenton WS, Blyler CR, Heinssen RK. Determinants of medication compliance in schizophrenia: empirical and clinical findings. Schizophr Bull. 1997;23(4):637-51.
6. Valenstein M, Kavanagh J, Lee T, Reilly P, Dalack GW, Grabowski J, et al. Using a pharmacy-based intervention to improve antipsychotic adherence among patients with serious mental illness. Schizophr Bull. 2011;37(4):36.
7. Velligan D, Mintz J, Maples N, Xueying L, Gajewski S, Carr H, et al. A randomized trial comparing in person and electronic interventions for improving adherence to oral medications in schizophrenia. Schizophr Bull. 2013;39(5):9.
8. Guo X, Zhai J, Liu Z, Fang M, Wang B, Wang C, et al. Effect of antipsychotic medication alone vs combined with psychosocial intervention on outcomes of early-stage schizophrenia: A randomized, 1-year study. Arch Gen Psychiatry. 2010;67(9):895-904.
9. Pakpour AH, Modabbernia A, Lin CY, Saffari M, Ahmadzad Asl M, Webb TL. Promoting medication adherence among patients with bipolar disorder: a multicenter randomized controlled trial of a multifaceted intervention. Psychol Med. 2017;47(14):2528-39.

10. Sajatovic M, Tatsuoka C, Cassidy K, Klein P, Fuentes-Casiano E, Cage J, et al. A 6-Month, Prospective, Randomized Controlled Trial of Customized Adherence Enhancement Versus Bipolar-Specific Educational Control in Poorly Adherent Individuals With Bipolar Disorder. The Journal of Clinical Psychiatry. 2018;79.
11. Bodenheimer T, Holman H, Grumbach K. Patient self-management of chronic disease in primary care. JAMA. 2002;288(19):2469–75.
12. Holman H, Lorig K. Patients as partners in managing chronic disease. Partnership is a prerequisite for effective and efficient health care. BMJ. 2000;320(7234):526–7.
13. Clark N, Janz N, Lorig K, Rakowski W, Anderson L. Self-management of chronic disease by older adults: a review and questions for research. J Aging Health. 1991;3(1):3-27.
14. Wagner E, Davis C, Hindmarsh M, Schaefer J, Bonomi A. Improving chronic illness care: translating evidence into action. Health Aff (Millwood). 2001;20(6):64–78.
15. Barlow J, Sturt J, Hearnshaw H. Self-management interventions for people with chronic conditions in primary care: examples from arthritis, asthma and diabetes. Health Educ J. 2002;61(4):365–78.
16. Stacy C, Oramasionwu C, Wolf M. Rethinking Adherence: A Health Literacy–Informed Model of Medication Self-Management. Journal of Health Communication. 2013;18:20-30.
17. Parnell MA. Medicines at the bedside. Am J Nurse. 1959;59:1417-8.
18. Richardson S, Brooks H, Bramley G, Coleman J. Evaluating the effectiveness of self-administration of medication (SAM) schemes in the hospital setting: a systematic review of the literature. PLoS One. 2014;9(12).
19. Lobban F, Glentworth D, Pinfold V, Wainwright L, Dunn G. A Systematic Review of Randomised Controlled Trials of Interventions Reporting Outcomes for Relatives of People With Psychosis. Clinical psychol rev. 2013;2013 Apr;33(3):372-82.
20. Vanwesemael T, Petrovic M, Boussery K, Dilles T. SelfMED: Self-Administration of Medication in Hospital: A Prevalence Study in Flanders, Belgium. Nurs Scholarsh. 2017;49:277-85.
21. Vanwesemael T. Proefschrift voorgelegd tot het behalen van de graad van Doctor in de Medische Wetenschappen aan de Universiteit Antwerpen. In: Faculteit geneeskunde en gezondheidswetenschappen. Universiteit Antwerpen. 2018:95-109.
22. Vanwesemael T, Boussery K, Van den Bemt P, Dilles T. The willingness and attitude of patients towards self-administration of medication in hospital. her Adv Drug Saf. 2018;9 (6):309-21.
23. Gough G. Self-Management: A Comprehensive Approach to Management of Chronic Conditions. American Journal of Public Health. 2014;Vol 104, No. 8.
24. Rasheeda Hall JR, Cathleen C, Laura J. Fish. Unmet Needs of Older Adults Receiving In-Center Hemodialysis: A Qualitative Needs Assessment. Kidney Med. 2020;5:543-51.
25. Vaismoradi M, Bondas T. Content analysis and thematic analysis: Implications for conducting a qualitative descriptive study. Nurs Health Sci. 2013;15(3):398–405.
26. Tracy S. Qualitative Quality: Eight “Big-Tent” Criteria for Excellent Qualitative Research. Qualitative Inquiry. 2010;16:837–51.
27. Manias E, Beanland C, Riley R, Baker L. Self-administration of medication in hospital: patients’ perspectives. J Adv Nurs. 2004;46 (2):194-203.
28. Williams A, Low J, Manias E, Crawford K. The transplant team’s support of kidney transplant recipients to take their prescribed medications: A collective responsibility. Journal of Clinical Nursing. 2016;25(15–16):2251–61.
29. Brady T, Sacks J, Terrillion A, Colligan E. Operationalizing Surveillance of Chronic Disease Self-Management and Self-Management Support. Prev Chronic Dis. 2018;15.

30. Beentjes T, van Gaal B, van Achterberg T, Goossens P. Self-Management Support Needs From the Perspectives of Persons With Severe Mental Illness: A Systematic Review and Thematic Synthesis of Qualitative Research. J Am Psychiatr Nurses Assoc. 2020;26 (5):464-82.

31. Zou H, Li Z, Nolan M, Wang H, Hu L. Self-management among Chinese people with schizophrenia and their caregivers: a qualitative study. Arch Psychiatr Nurse. 2013;27(1):42-53.

32. Costa E, Giardini A, Savin M, Menditto E, Lehane E, Laosa O, Pecorelli S, Monaco A, Marengoni A. Interventional tools to improve medication adherence: review of literature. Patient Prefer Adherence. 2015;9:1303-14.

Chapter 5

The attitude of healthcare providers towards medication self-management in hospitalized patients diagnosed with schizophrenia spectrum or bipolar disorder

This chapter has been published as:
Loots, E., Dilles, T., Hadouchi, S., Van Rompaey, B., & Morrens, M. (2023). The attitude of healthcare providers towards medication self-management in hospitalised patients diagnosed with schizophrenia or bipolar disorders. Journal of Psychiatric and Mental Health Nursing, 00, 1–12. https://doi.org/10.1111/jpm.12903

Chapter 5: Contents

Abstract

Background: Medication self-management (MSM) is considered an important aspect of pharmacotherapy and plays an essential role in the treatment of various illnesses. To date, research into the willingness and attitude of psychiatric healthcare providers towards MSM in patients diagnosed with Schizophrenia Spectrum Disorder (SSD) or Bipolar Disorder (BD) during hospitalisation is lacking.

Aim: The aim of this study was to identify healthcare providers' willingness to MSM and assess their attitude, conditions, benefits, and ability towards it during hospitalisation.

Methods: A multicentre, quantitative cross-sectional observational design was used to study psychiatric healthcare providers' attitude to MSM during hospitalisation in patients diagnosed with SSD or BD.

Results: In this study, 173 healthcare providers, of which 147 were nurses and 26 psychiatrists, participated. During hospitalisation, 86% of the healthcare providers were willing to MSM. Regularly evaluating patients' ability, regarding MSM during hospitalisation was seen as an important condition (94%). Psychiatrists were significantly less convinced that MSM during hospitalisation has a positive impact on adherence when compared to nurses (respectively 54% vs 77%, p= 0.009).

Conclusion: Most healthcare providers indicated that they were willing to MSM in patients diagnosed with SSD or BD during hospitalisation under specific conditions.

5.1. Introduction

Schizophrenia Spectrum and Bipolar Disorders are severe psychiatric disorders, with Schizophrenia Spectrum Disorders (SSD) affecting around 1% and Bipolar Disorders (BD) affecting about 3% people worldwide (1). Together with psychoeducation, pharmacotherapy is often the first line of treatment of these major psychiatric disorders. A systematic review analysed risk factors for relapse in the early course of psychosis in patients diagnosed with SSD (2). Among all associated factors, non-adherence appeared to be the strongest predictor for relapse. Discontinuation of antipsychotic pharmacotherapy is associated to a fivefold risk of relapse (3).

Non-adherence is highly prevalent, ranging between 63-74% in patients diagnosed with SSD and about 50% in patients with BD (4-6). About 50% of patients discontinue their medication within the first month and 80% within six months after discharge from inpatient treatment (7). Insufficient knowledge of the disorder and treatment, lack of insight into the illness, and deficient communication between inpatient units and primary healthcare providers are various non-adherence factors (8, 9).

Interventions targeting the improvement of adherence in patients diagnosed with SSD or BD are heterogeneous. A variety of them have been used to improve medication adherence, such as cognitive behavioural therapy, psychoeducation, family interventions, and motivational interviewing (10). Nearly all programs focus on a modification of attitudes and cognitive aspects to enhance adherence by the improvement of knowledge and insight. Yet insight into the illness and adherence are only moderately intercorrelated (11). In addition to increased insight, patients should be enabled to recognize their medication and to organize its' intake autonomously in full self-responsibility (12). Medication self-management (MSM) is defined as a person's capability to cope with medication treatment for a chronic condition and the physical and psychosocial effects and changes it causes in their daily life. MSM is facilitated by social support and information, but hindered by difficulties with medication regimens, and physical and psychological symptoms (12, 13). Considering this definition, the MSM process can determine a sequence a patient must follow to safely and effectively take their medications after hospital discharge (14). There is a huge contrast between inpatient and outpatient treatment. During the inpatient treatment, all medication is administrated and prepared, while at home the patient is often on his own. Patients suddenly must be able to read their medication schedule, pick up the prescribed drugs at the phar-

macy, and prepare and take them at the right time (15, 16).

Therefore, MSM is becoming an increasingly important element in rehabilitation programs. As patients are not capable of self-managing their medication, aid is often required. Healthcare providers can support and coach patients towards self-management of their medication. Firstly, nurses can assess and evaluate the precise self-care deficits related to MSM in hospital (14, 16, 17). Subsequently, a care plan is provided defining the extent to which a patient should be supported. In addition, patients who are not able to self-manage their medication, but are expected to do MSM after discharge, should be given the opportunity to learn to self-manage their medication whilst in hospital (17).

MSM in hospital was already mentioned in the literature in 1959, and it has since been studied internationally for many years (18-23). In a non-psychiatric population, nurses, hospital pharmacists, and physicians were all willing (to varying degrees) to let patients self-manage their medication during hospitalisation (17). They stated MSM could result in several positive patient related and staff related outcomes. To date, research into the willingness and attitude of psychiatric healthcare providers towards MSM in patients diagnosed with SSD or BD during hospitalisation is lacking.

Hence, the aim of this study was to describe their willingness to MSM and their attitude, conditions, benefits, and ability towards it during hospitalisation.

5.2. Methods

5.2.1. Design

A multicentre, quantitative cross-sectional observational design was used to study psychiatric healthcare providers' attitude to MSM during hospitalisation. Between November 2020 and March 2021 healthcare providers were surveyed by use of a structured questionnaire assessing their willingness, attitudes towards MSM as well as their assumption on needed conditions, ideas about benefits, and patients' ability of MSM.

5.2.2. Participants and setting

In order to obtain sufficient data variation, convenience sampling was used to select nurses and psychiatrists. We recruited participants in psychiatric inpatient hospitals in Belgium. Units accommodating hospitalised patients diagnosed with SSD of BD were selected. All 52 units in Flanders

(the Dutch-speaking region of Belgium) were contacted, of which 48 units (92%) participated. Eligible participants were nurses and psychiatrists within these units and being directly involved in managing of patients' medication. Healthcare providers who were employed solely at crisis admission as well as students were excluded.

5.2.3. Data collection

The data collection was performed in several steps. One nursing association published the hyperlink on their website and invited their readers to complete the online survey. By means of an electronic newsletter, the association of psychiatrists provided the invitation with the hyperlink to participate in the study to its members.

The survey was developed using results from a previous study on MSM in a non-psychiatric setting (17, 24), and on recent results of a qualitative descriptive study of MSM in patients diagnosed with SSD or BD (25). The definition of MSM was explained in detail at the beginning of the survey.

The willingness of healthcare providers to MSM during hospitalisation was questioned in one question (5-point Likert scale; absolutely not willing, rather not willing, neutral, rather willing, absolutely willing). Secondly, the attitude towards MSM was evaluated with the use of six statements (5-point Likert scale: strongly disagree, disagree, neutral, rather agree, strongly agree). The third section of the questionnaire concerned 12 statements regarding conditions for MSM. Conditions related to the patient and organisation were evaluated. Additionally, nine statements concerning benefits of MSM related to the patient, organisation, and healthcare providers were evaluated. In conclusion, a set of nine statements concerning patients' ability of MSM were assessed. The statements were rated on the use of a five-point Likert scale (Strongly disagree, disagree, neutral, agree, strongly agree).

To describe the population, healthcare providers were questioned on demographic characteristics and information concerning their work environment. The following demographic data was collected: age; gender; profession; and years of work experience.

5.2.4. Data analysis

Data were analysed using IBM SPSS Statistics V.24.0 (SPSS Inc, Chicago, IL, USA). The normality of the data was tested using the absolute z-value (26). Discontinuous and categorical data were described using frequency distributions, while mean and standard deviations were used for continu-

ous data. A two-sided level of significance of .05 was used. Nonparametric statistics were used to analyse the data. Differences in opinion between nurses and psychiatrists were explored. To evaluate the statistical significance of the differences between the two healthcare provider groups, $\chi 2$ test for dichotomous data and Kruskal-Wallis test for ordinal data was used. Little's missing completely at random (MCAR) test was performed for variables with missing values and did not show any systematic patterns in missing data X^2 (29, *N= 173)*= 28.303, *p*= 0.502. The Benjamini-Hochberg procedure was used to adjust for the False Discovery Rate (FDR) in order to control for multiple testing (27).

5.2.5. Ethical considerations

The local ethics committees and the Ethics Committee of the University Hospital of Antwerp formally granted ethical approval. All participants received information on the purpose, design, and execution of the study. Participation was voluntary and participants had the right to withdraw consent at any time. All collected data were pseudonymized to ensure privacy.

5.3. Results

5.3.1. The research population

A total of 173 healthcare providers participated in this study, including 147 nurses and 26 psychiatrists **(Table 5.1)**. The participants had an average of 16 years [s= 11.9] of work experience, and the majority was female (66.5%). All 173 healthcare providers were employed in a psychiatric unit where hospitalized patients diagnosed with SSD or BD resided.

5.3.2. Healthcare providers' willingness towards medication self-management

Healthcare providers' willingness towards MSM during hospitalisation were presented in **Table 5.2.** A total of 86.1% of the healthcare providers were willing to MSM (p= 0.208). The willingness of healthcare providers positively correlated with their years of work experience (Spearman's rho, *r*= 0.214, p= 0.005).

Table 5.1: Demographic and work characteristics.

Demographic data	**Psychiatrists** (n= 26)	**Nurses** (n= 147)	**Total** (n= 173)	***p*-value**
Gender, N (%)				
Male	16 (61.5)	42 (28.6)	58 (33.5)	
Female	10 (38.5)	105 (71.4)	115 (66.5)	0.001[1]
Age (year)				
Mean [σ]	42.3 [12.5]	40.37 [11.3]	40.7 [11.5]	0.438[2]
Work experience (year)				
Mean [σ]	15.9 [12.6]	16.1 [11.8]	16 [11.9]	0.937[2]

[1] χ2 test

[2] Independent t-test

Table 5.2: Willingness of healthcare providers to medication self-management in hospital.

Willingness to MSM, N (%)	**Psychiatrists** (n= 26)	**Nurses** (n= 147)	**Total** (n= 173)	***p*-value**[1]
Absolutely willing	5 (19.2)	49 (33.6)	53 (31.4)	
Rather willing	17 (65.4)	77 (52.7)	94 (54.7)	
Neutral	2 (7.7)	14 (9.6)	16 (9.3)	
Rather not willing	2 (7.7)	6 (4.1)	8 (4.7)	0.208

[1] Difference between the willingness of the two disciplines Mann-Whitney U.

5.3.3. Medication management during hospitalisation

A home medication schedule was generally prepared (96%) and 70% of the healthcare providers discussed the medication schedule with the patient or caregivers at patients' discharge. A medication list was discussed by psychiatrists (77%) compared to 55% of the nurses (*p*= 0.037).

The decision-making process concerning participation in MSM was largely shared between the treating physician (44%), the nursing team (54%) and the general practitioner (2%). Patients were systematically involved in the MSM decision, taking into account the patient's preferences, needs, beliefs and concerns about treatment in general.

5.3.4. Attitude towards medication self-management

The attitude of healthcare providers (N= 172) towards MSM in patients diagnosed with SSD or BD was surveyed with a 5-point Likert scale based on six statements **(Table 5.3).** When patients are able according to healthcare

Table 5.3: Attitude towards medication self-management.

Attitude towards medication self-management (n= 172)		**Agree*** n (%)	**Neutral** n (%)	**Disagree*** n (%)	***p*-value**[1]
If patients wish to self-manage and can, healthcare providers should be creating an environment of MSM during hospitalisation	Total	132 (77)	24 (14)	16 (9)	
	Nurses	113 (77)	19 (13)	14 (10)	
	Psychiatrists	19 (73)	5 (19)	2 (8)	0.687
It is always the duty of nurses to prepare and manage medication, even for patients who are able to do this themselves	Total	35 (20)	24 (14)	113 (66)	
	Nurses	29 (20)	22 (15)	95 (65)	
	Psychiatrists	6 (23)	2 (8)	18 (69)	0.597
MSM during hospitalisation should not be allowed if the patient has a history of suicide and/or abuse related to medication	Total	49 (29)	38 (22)	85 (49)	
	Nurses	42 (29)	32 (22)	72 (49)	
	Psychiatrists	7 (28)	6 (23)	13 (50)	0.979
Patients can only self-manage their medication during hospitalisation if a healthcare provider monitors the medication intake	Total	84 (49)	34 (20)	54 (31)	
	Nurses	71 (49)	31 (21)	44 (30)	
	Psychiatrists	13 (50)	3 (12)	10 (39)	0.462
Nurses spend too much time on medication management (preparation, monitoring, and administration)	Total	65 (38)	33 (19)	74 (43)	
	Nurses	54 (37)	29 (20)	63 (43)	
	Psychiatrists	11 (42)	4 (15)	11 (42)	0.819
It is necessary to involve the hospital pharmacist in the process of MSM during hospitalisation	Total	77 (45)	40 (23)	55 (32)	
	Nurses	70 (48)	32 (22)	44 (30)	
	Psychiatrists	7 (27)	8 (31)	11 (42)	0.139

*Agree: sum of % healthcare providers who indicated agree and strongly agree.

*Disagree: sum of % healthcare providers who indicated disagree and strongly disagree.

[1] Differences between healthcare providers was calculated with the use of the $\chi 2$ test.

providers and seek MSM during hospitalisation, most healthcare providers (77%) agreed on participating in MSM. About half of healthcare providers (49%) deemed patients can only self-manage their medication during hospitalisation when healthcare providers can monitor the medication intake. Healthcare providers were convinced that MSM could still be allowed if the patient had a history of suicide and/or medication abuse (49%).

5.3.5. Conditions for medication self-management

Patient conditions participating in MSM during hospitalisation were presented in **Figure 5.1.**

Patients' willingness was a prerequisite for MSM (97%) and a regular evaluation of patients' MSM competences during hospitalisation was considered necessary (94%). Psychiatrists were significantly less convinced that patients' willingness was an important condition for MSM (respectively 88% vs nurses 99%, $p= 0.003$, FDR $p= 0.036$). In addition, the healthcare providers agreed that medication should always be stored in a safe place

in the patient's room (92%), patients should have a medication schedule on paper (81%), and that MSM can only be implemented after education about medication (77%). The following statements were not prominent prerequisites: only MSM when the patient returns home (36%), the patient was already self-managing medication at home (30%), and only MSM with the medication that the patient was already taking at home (5%).

A mere 30% of the healthcare providers stated MSM was only allowed if the reason for admission was not related to non-adherence. However, psychiatrists were less convinced of this premise than nurses (respectively 49% vs 77%, p= 0.011, FDR p= 0.066).

5.3.6. Benefits of medication self-management

Nurses and psychiatrists (N= 169) reflected on nine potential benefits of MSM **(Figure 5.2)**. Most healthcare providers agreed that the patient would feel more autonomous and independent (94%), and that the patients' MSM abilities could be better assessed during hospitalisation (90%). Nevertheless, psychiatrists agreed a little less with the statement that patients would experience a positive sense of confidence by applying MSM (respectively 77% vs nurses 90%, p= 0.145). In addition, psychiatrists were significantly less convinced that MSM during hospitalisation had a positive impact on adherence (respectively 54% vs nurses 77%, p= 0.009, FDR p= 0.081).

5.3.7. Patients' ability for medication self-management

A set of nine potential competences to assess patients' ability for MSM, was provided (**Table 5.4**). Most of the healthcare providers considered all competences to be important. In addition, all nurses compared to psychiatrists (94%), stated that patients should have sufficient knowledge concerning their medication schedule, such as how to read it correctly (p= 0.023, FDR p= 0.207). Psychiatrists attached less importance on adequate knowledge about medication (e.g. side effects) than did nurses (respectively 54% vs 76%, p= 0.453).

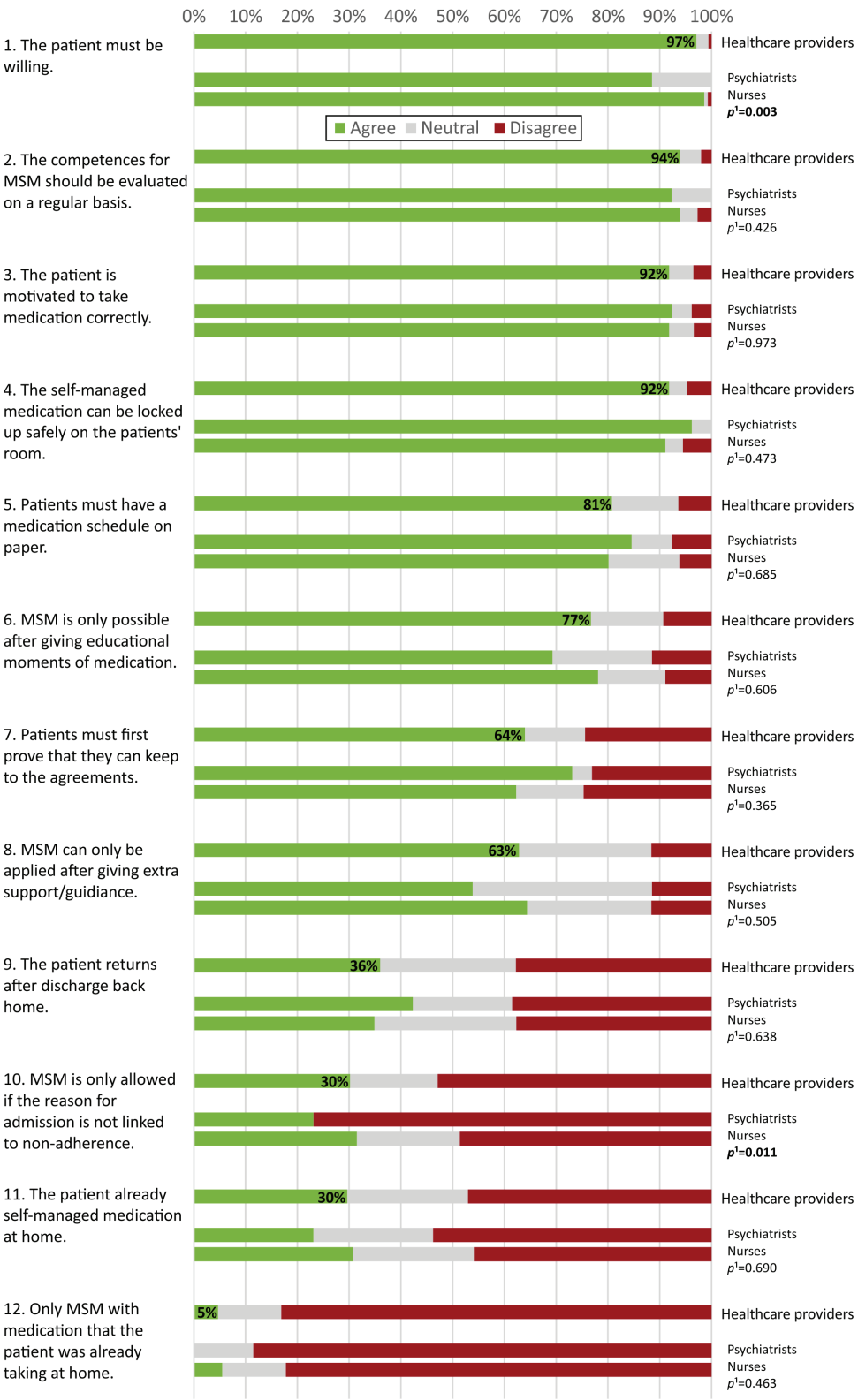


Figure 5.1: Patient conditions participating in MSM during hospitalisation.

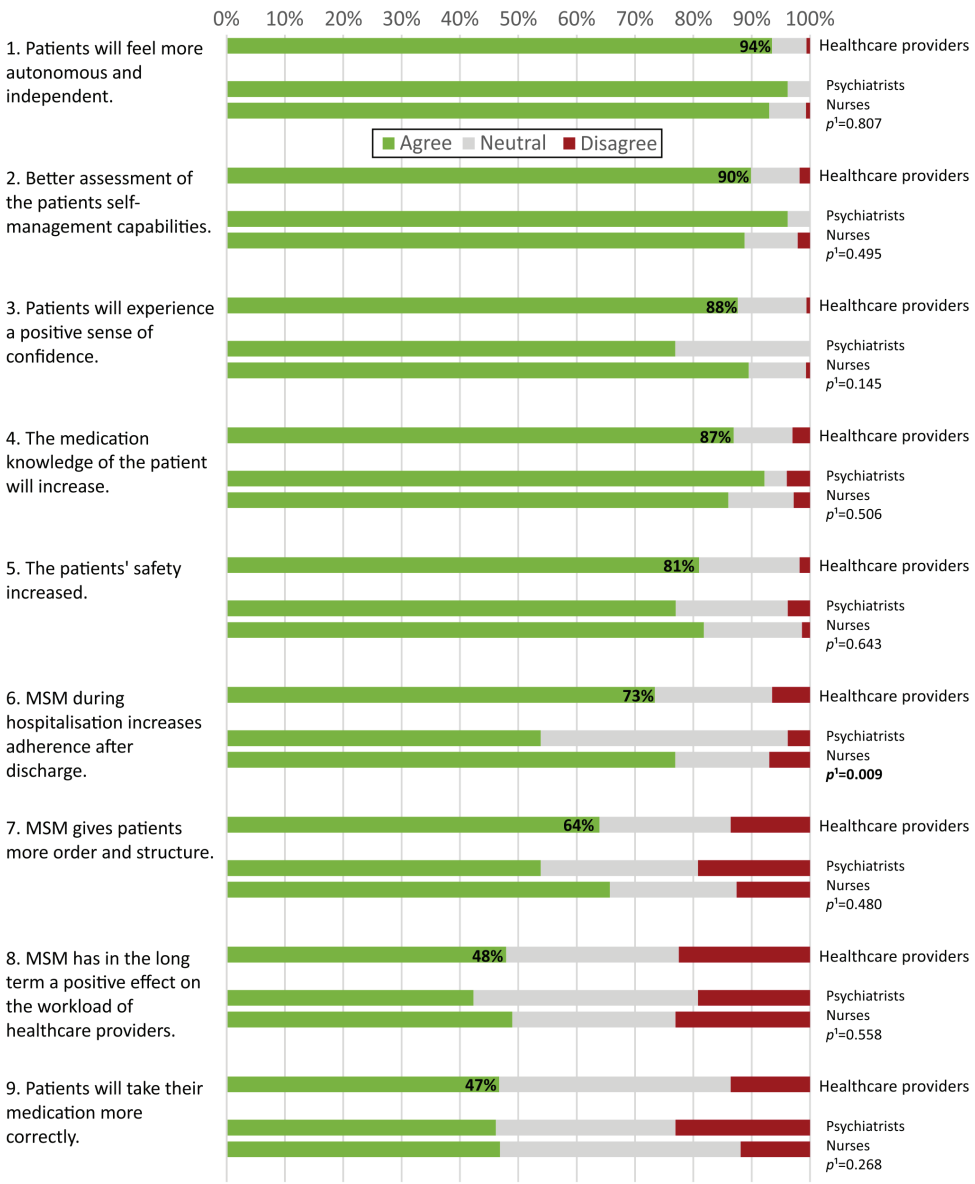


Figure 5.2: Benefits of MSM during hospitalisation

Table 5.4: Patients' ability to MSM.

Patients' competences	Psychiatrists* (n= 26)	Nurses* (n= 143)	Total* (n= 169)	*p*-value[1]
1. Understand the benefits of the medication	89.5%	88.5%	89.3%	0.241
2. Have sufficient knowledge about the medication schedule	93.8%	100.0%	94.6%	0.023
3. Have sufficient knowledge about their medication (e.g., side effects)	76.2%	53.8%	72.7%	0.453
4. Ability to take medication out of a blister	83.2%	96.1%	85.2%	0.499
5. Can work with tools	78.3%	76.9%	78.1%	0.386
6. Adherence to treatment	83.3%	76.9%	82.3%	0.101
7. Ability to make needs/problems clear	81.1%	73.1%	79.8%	0.288
8. Being able to communicate with caregivers concerning medication	96.5%	100.0%	97.0%	0.417
9. Ability to oriented in time and place	94.5%	96.1%	94.7%	.235

*Sum of % healthcare providers who indicated strongly agree and agree

[1]Differences between healthcare providers was calculated using $\chi 2$

5.4. Discussion

This study clearly describes insights into the attitude of healthcare providers towards MSM in patients diagnosed with SSD or BD during hospitalisation. The attitude to MSM, their willingness, assumptions on conditions, and benefits for patients towards it and patients' ability according to nurses and psychiatrists were investigated.

5.4.1. Healthcare providers' willingness and attitude

Most healthcare providers indicated that they were willing to MSM in patients diagnosed with SSD or BD during hospitalisation. Nurses were more willing than psychiatrists. These findings were in line with previous qualitative research (25). Psychiatrists were more worried about the risks associated with MSM in the hospital, such as the difficulty in assessing the patients, the social aspect (e.g. peer pressure and medication mix-ups,...) and medication errors (25). Besides the insight gained into the willingness of healthcare providers towards MSM, the results indicated that some implementation aspects are lacking. Literature on the prevalence of MSM in

psychiatric hospitals is limited. Our research was conducted in 48 psychiatric units where hospitalised patients diagnosed with SSD or BD resided. Literature describes that patients and healthcare providers are positive towards MSM when asked to rate their satisfaction with inpatient MSM. Yet not all healthcare providers are willing to participate in MSM. This may reflect the current culture in hospitals, where there is an expectation from patients that they will assume a more passive role and an expectation from the healthcare providers that they will assume responsibility for patients' medical care, regardless of patients' level of involvement in their care prior to admission. Alternatively, it may be a response to the initial increases in some aspects of staff workload, such as patient education and preparation of MSM (28). External support from family or relatives is desirable due to the positive impact that a familiar carer may have on patients' willingness to MSM (22), as well as the potential for reducing staff workload if relatives are willing to be involved in patients' care (28).

5.4.2. Conditions for medication self-management

This study showed a willingness of healthcare providers towards MSM under specific conditions. A significant difference between psychiatrists and nurses concerned the condition 'MSM is only allowed if the reason for admission is not related to non-adherence'. Psychiatrists were less convinced of this than nurses (respectively 49% vs 77%). Research shows that an evaluation is necessary to objectively assess the patient's actual competences. This assessment should consider several aspects, such as specific conditions of the patients, mental and physical condition, and possible side-effects of the current medication (17). Also, patients should be hospitalised for a sufficient period to be able to assess their willingness and competences. Several existing programs for MSM incorporate an evaluation tool for the competences of patients. Only one study described the validation of a tool, the Self-Administration of Medication (SAM) (22). This tool intends to objectively determine the extent to which patients can self-manage their medication (29, 30). The findings overall confirm the need for further research on the validation of tools for use in psychiatry, as this topic currently represents a gap in the literature.

5.4.3. Benefits of medication self-management

Nurses and psychiatrists agreed that the patient would feel more autonomous and independent. Our study confirms previous research indicating that the patients' abilities to MSM could be better assessed during

hospitalisation (25, 31). Nurses, hospital pharmacists, and patients suggested that MSM could be beneficial to the hospital and the hospital image due to the potential positive experiences and higher patient satisfaction. They believed MSM during hospitalisation increased patients' autonomy, confidence, self-reliance, appreciation, and satisfaction. Nevertheless, psychiatrists agreed less with the statement that patients would experience a positive sense of confidence by applying MSM (17, 25).

Psychiatrists were less convinced that MSM during hospitalisation has a positive impact on adherence when compared to nurses. Previous research including patients, nurses, psychiatrists, and hospital pharmacists suggested MSM makes a positive contribution to the recovery process. According to the participants, MSM during hospitalisation offers many advantages, such as more structure for the patients, preparation for discharge, and an improvement of adherence (25). There was some evidence to suggest that patients' medication knowledge increases through MSM, but in contradiction to other research not whether MSM improves adherence(32, 33). Previous research in a non-psychiatric setting, demonstrated that most patients were successful in self-managing medication, and patient characteristics, setting, or medication factors might be related to this success. There was some weak evidence that patients with greater cognitive function were more likely to be successful (34, 35). However, these patients may have been targeted because they were more likely to successfully self-manage their medications (36, 37). Due to the heterogenous nature of the studies it is not possible to determine the extent to which this relationship may exist. Certain patients failed to MSM or had to withdraw, which may suggest that MSM schemes are not universally appropriate for all patients in all medical specialties. However, the identification of these patients suggests that MSM protocols may be an effective way to identify patients who would fail at self-manage their medications at home after discharge, hence, preventing potential adverse outcomes (22).

5.4.4. Patient's ability for medication self-management

It is shown that all psychiatrists – when compared to nurses – stated that patients should have sufficient knowledge concerning their medication schedule, such as how to read it correctly. The literature clearly describes that an assessment is always needed to objectively evaluate the actual competencies of the patient. This assessment should consider various aspects, such as patients' specific conditions, mental and physical condition, and possible side-effects of their current medication (17, 25, 31). When comparing our results with the literature, it is possible to draw some

conclusions. The literature indicates patients' medication knowledge and disease insight increase with MSM, nevertheless it is not clear which aspects significantly improve (e.g. medication knowledge on name, dosage, side effects...). Also, previous literature used different types of education, so results should be interpreted with caution (22).

5.4.5. Strengths and limitations

Several hospitals were involved in this study, resulting in healthcare providers with varying work environments and a broad range of work experience. The absence of selection and participation bias can not be guaranteed. Nevertheless, it is possible that respondents with a more outspoken opinion on MSM would be more likely to complete the questionnaire. Unfortunately, a calculation of the response rate was not possible due to the digital distribution of the survey. Moreover, the absence of non-response bias can not be guaranteed due to the small sample size and number of psychiatrists who participated.

It is necessary to further investigate the willingness of other stakeholders, such as pharmacists. Previous research demonstrated that active involvement of hospital pharmacists in the patient's meditation process resulted in the reduction of medication errors on medical and surgical units (38). Specifically for MSM in psychiatric hospitals, pharmacists can provide counselling sessions for patients, clarify discharge prescriptions, and they can support nurses in educating patients on medication (39).

From a policy point of view, our study provided useful insights into how healthcare providers look at MSM to enable the development of future strategies. Since psychiatrists and nurses are willing to implement MSM in their daily practice, this may facilitate its implementation.

5.4.6. Implications for practice and those with lived experience

Future research should focus on the development of a feasible MSM tool for patients with SSD or BD: a patient assessment tool for deciding whether the patient is capable of MSM, a monitoring tool for medication intake, and different education sessions and support during hospitalisation. In order to evaluate the actual impact of a MSM tool on healthcare providers and the organisation related outcomes in daily practice, an intervention study should be installed. This intervention must ensure all involved stakeholders are willing to facilitate and assist MSM.

Interventions using a combination of educational and behavioural strategies have a positive impact on medication adherence. The combined use

of education sessions focusing on diagnosis, symptoms, medication, and relapse, alongside medication reminders at patients' homes, and an MSM training program provided on a one-to-one basis by skilled nurses, could all improve medication adherence (40). In addition, ongoing medication counselling and regular consultations help build confidence and understanding for patients to adhere to their treatment plan.

However, no standardized guideline exists for assisting individuals with preparing for therapy. An instrument for measuring self-reliance and a MSM program hold potential for helping patients with preparing to their treatment plan. Furthermore, questionnaires assessing self-reliance may be useful in clinical settings and pharmacies to guide medication counselling.

5.5. Conclusion

Nurses and psychiatrists are willing to MSM under specific conditions. Patients should be willing, MSM abilities should be evaluated on a regular basis during hospitalisation and patients should be motivated to take their medication correctly. Psychiatrists and nurses argued that MSM can result in several positive patient-related outcomes as the patient would feel more autonomous and independent. The patients' abilities to MSM could be better assessed during hospitalisation.

5.6. References

1. World Health Organization. The Global Economic Burden of Non-Communicable Diseases; World Economic Forum: Geneva, Switzerland. 2013.
2. Sendt KV, Tracy DK, Bhattacharyya S. A systematic review of factors influencing adherence to antipsychotic medication in schizophrenia-spectrum disorders. Psychiatry Res. 2015;225(1-2):14-30.
3. Jingbo Xiao WM LL, Ying Shi, and Hongyan Zhang. High relapse rate and poor medication adherence in the Chinese population with schizophrenia: results from an observational survey in the People's Republic of China. Neuropsychiatr Dis Treat. 2015;11:1161–7.
4. World Health Organization. The global economic burden of non-communicable diseases. World Economic Forum, Geneva, Switzerland. 2018.
5. Young JL, Zonana HV, Shepler L. Medication noncompliance in schizophrenia: codification and update. Bull Am Acad Psychiatry Law. 1986;14(2):105-22.
6. Miasso AI, Cassiani SH, Pedrão LJ. Transtorno afetivo bipolar e a ambivalência em relação à terapia medicamentosa: analisando as condições causais [Affective bipolar disorder and ambivalence in relation to the drug treatment: analyzing the causal conditions].Rev Esc Enferm USP. 2011;Apr;45(2).
7. Morrens M, Destoop M, Cleymans S, Van Der Spek S, Dom G. Evolution of First-generation and Second-generation Antipsychotic Prescribing Patterns in Belgium Between 1997 and 2012: A Population-based Study. J Psychiatr Pract. 2015 Jul;21(4):248-58.
8. Lacro DL, Dolder CR, Leckband SG, Jeste DV. Prevalence of and risk factors for medication nonadherence in patients with schizophrenia: a comprehensive review of recent literature. J Clin Psychiatry. 2002;Oct; 63(10):892-909.
9. Haynes RB, Yao X, Degani A, Kripalani S, Garg A, McDonald HP. Interventions to enhance medication adherence. Cochrane Database Syst Rev. 2005 Oct 19;(4):CD000011. doi: 10.1002/14651858.CD000011.pub2. Update in: Cochrane Database Syst Rev. 2008;(2):CD000011.
10. World Health Organization. Adherence to Long-Term Therapies: Evidence for Action Section I—Setting the Scene; World Health Organization: Geneva, Switzerland. 2003.
11. Beck CM, Kvrgic S, Kleim B, Vauth R. Are we addressing the 'right stuff' to enhance adherence in schizophrenia? Understanding the role of insight and attitudes towards medication. Schizophr Res-Oct; 132(1). 2011:42-9.
12. Audulv Å GS, Kephart G, Warner G, Packer TL. The Taxonomy of Everyday Self-management Strategies (TEDSS): a framework derived from the literature and refined using empirical data. Patient Educ Couns. 2019;102(2):367–375.
13. Morrison CF, Pai ALH, Martsolf D. Facilitators and Barriers to Self-Management for Adolescents and Young Adults Following a Hematopoietic Stem Cell Transplant. J Pediatr Oncol Nurs. 2018 Jan/Feb;35(1):36-42.
14. Bailey Stacy C., Christine U., Oramasionwu, Wolf MS. Rethinking Adherence: A Health Literacy–Informed Model of Medication Self-Management. Journal of Health Communication. 2013;18:20-30.
15. Richard AA, & Shea, K. Delineation of self-care and associated concepts. J Nurs Scholarsh. 2011;43(3):255-64.
16. Davis A, Muir P, Allardice J, Clark K, Groves J, Molenaar M, Robson G. 2002, SHPA Guidelines for Self-Administration of Medication in Hospitals and Residential Care Facilities, Journal of Pharmacy Practice and Research, 32, doi: 10.1002/jppr2002324324.
17. Vanwesemael T. Proefschrift voorgelegd tot het behalen van de graad van Doctor in de Medische Wetenschappen aan de Universiteit Antwerpen. In: Faculteit geneeskunde en gezondheidswetenschappen. Universiteit Antwerpen. 2018:95-109.

18. Parnell MA. Medicines at the bedside. Am J Nurse. 1959;59:1417-8.

19. Wright J, Emerson A, Stephens M & Lennan E. Hospital inpatient self-administration of medicine programmes: a critical literature review. Pharm World Sci. 2006;28(3):140-51.

20. Beentjes T, Van Gaal B, Van Achterberg T, Goossens P. Self-Management Support Needs From the Perspectives of Persons With Severe Mental Illness: A Systematic Review and Thematic Synthesis of Qualitative Research. J Am Psychiatr Nurses Assoc. 2020;26 (5):464-82.

21. Clark NM, Janz NK, Lorig K, Rakowski W, Anderson L. Self-management of chronic disease by older adults: a review and questions for research. J Aging Health. 1991;3(1):3-27.

22. Richardson SJ, Brooks HL, Bramley G, Coleman JJ. Evaluating the effectiveness of self-administration of medication (SAM) schemes in the hospital setting: a systematic review of the literature. PLoS One. 2014 Dec 2;9(12):e113912.

23. Vanwesemael T, Van Rompaey B, Petrovic M, Boussery K, Dilles T. SelfMED: Self-Administration of Medication in Hospital: A Prevalence Study in Flanders, Belgium. J Nurs Scholarsh. 2017 May;49(3):277-285.

24. Manias E, Beanland C, Riley R, Baker L. Self-administration of medication in hospital: patients' perspectives. J Adv Nurs. 2004;46 (2):194-203.

25. Loots E, Leys J, Proost S, Morrens M, Glazemakers I, Dilles T, Van Rompaey B. Medication Self-Management in Hospitalised Patients with Schizophrenia or Bipolar Disorder: The Perceptions of Patients and Healthcare Providers. Int J Environ Res Public Health. 2022 Apr 15;19(8):4835.

26. Kim HY. Statistical notes for clinical researchers: Assessing normal distribution, using skewness and kurtosis. Restor Dent Endod. 2013;38:52–4.

27. Thissen D, Steinberg L, Kuang D. Quick and Easy Implementation of the Benjamini-Hochberg Procedure for Controlling the False Positive Rate in Multiple Comparisons. Journal of Educational and Behavioral Statistics. 2002;27(1):7.

28. Pearce M. Pilot study of self-medication: pharmacy workload appraisal. New Zealand Pharmacy. 1991;11:18-9.

29. Anderson J, Manias E, Kusljic S, Finch S. Testing the validity, reliability and utility of the Self-Administration of Medication (SAM) tool in patients undergoing rehabilitation. Res Social Adm Pharm. 2014 Jan-Feb;10(1):204-16.

30. Manias E, Beanland CJ, Riley RG, Hutchinson AM. Development and validation of the self-administration of medication tool. Ann Pharmacother. 2006 Jun;40(6):1064-73.

31. Vanwesemael T, Boussery K, Manias E, Petrovic M, Fraeyman J, Dilles T. Self-management of medication during hospitalisation: Healthcare providers' and patients' perspectives. J Clin Nurse. 2018;27 (3-4): 753-68.

32. Klein RH, Lynn EJ, Axelrod H, Dluhy J. Self-administration of medication by psychiatric inpatients. J Nerv Ment Dis. 1974 Jun;158(6):450-5.

33. Furlong S. Do programmes of medicine self-administration enhance patient knowledge, compliance and satisfaction? Journal of advanced nursing. 1996;23:9.

34. Taylor M. Self-medication on a rehabilitation unit. Archives of Physical Medicine and Rehabilitation 6. 1984: 612–3.

35. Tran T, Taylor SE, Woodward MC. A self-administration of medications program to identify and address potential barriers to adherence in elderly patients. Annals of Pharmacotherapy. 2011;45:201–6.

36. Lam P, George J. Impact of a self-administration of medications programme on elderly inpatients' competence to manage medications: a pilot study. Journal of Clinical Pharmacy Therapy. 2011;36:80–6.

37. Newcomer DR, Anderson RW. Effectiveness of a Combined Drug Self-Administration and Patient Teaching Program. Drug Intelligence & Clinical Pharmacy. 1974;8(6):374-381

38. Keers RN, Williams SD, Cooke J, Walsh T, Ashcroft DM. Impact of interventions designed to reduce medication administration errors in hospitals: a systematic review. Drug Saf. 2014 May;37(5):317-32.

39. Onatade R, Miller G, Sanghera I. A quantitative comparison of ward-based clinical pharmacy activities in 7 acute UK hospitals. Int J Clin Pharm. 2016 Dec;38(6):1407-1415.

40. Loots E, Goossens E, Vanwesemael T, Morrens M, Van Rompaey B, Dilles T. Interventions to Improve Medication Adherence in Patients with Schizophrenia or Bipolar Disorders: A Systematic Review and Meta-Analysis. Int J Environ Res Public Health. 2021 Sep 28;18(19):10213.

Chapter 6

The attitude of patients with schizophrenia spectrum or bipolar disorders towards medication self-management during hospitalisation

This chapter has been published as:
Loots E, Dilles T, Van Rompaey B, Morrens M.
Attitudes of patients with schizophrenia spectrum or bipolar disorders towards medication self-management during hospitalisation.
J Clin Nurs. 2024 Apr;33(4):1459-1469.
doi: 10.1111/jocn.16936. Epub 2023 Dec 1. PMID: 38041238.

Chapter 6: Contents

Abstract

Background: Medication self-management (MSM) is defined as a person's ability to cope with medication treatment for a chronic condition, along with the associated physical and psychosocial effects that the medication causes in their daily lives. For many patients, it is important to be able to self-manage their medication successfully, as they will often be expected to do after discharge.

The aim of this study was to describe the willingness and attitudes of patients with schizophrenia spectrum or bipolar disorders regarding MSM during hospital admission. A secondary aim was to identify various factors associated with patient willingness to participate in MSM and to describe their assumptions concerning needs and necessary conditions, as well as their attitudes towards their medication.

Methods: A multicentre, quantitative cross-sectional observational design was used to study the willingness and attitudes of psychiatric patients regarding MSM during hospitalisation. The study adhered to guidelines for Strengthening the Reporting of Observational Studies in Epidemiology (STROBE).

Results: In this study, 84 patients, of which 43 were patients with schizophrenia spectrum disorders and 41 were patients with bipolar disorders, participated. A majority of the patients (81%) were willing to participate in MSM during their hospitalisation. Analysis revealed patients are more willing to MSM if they are younger ($r= -0.417$, $p<0.001$) and a decreasing number of medicines ($r= -0.373$, $p= 0.003$). Patients' willingness was positively associated with the extent of support by significant others during and after hospitalisation (Pearson's $r= 0.298$, $p= 0.011$). Patients were convinced that they would take their medication more correctly if MSM were to be allowed during hospitalisation (65%).

Conclusion: Most of the patients were willing to self-manage their medication during hospitalisation, however, under specific conditions such as being motivated to take their medication correctly and to understand the benefits of their medication.

6.1. Introduction

Patients play a limited role in the administration of their medications while hospitalised, as traditionally, it is primarily the responsibility of nurses. Nevertheless, medication self-management programmes, in which patients manage their own medication, have been reported in the literature since 1959 [1]. Medication self-management (MSM) is defined as a person's ability to cope with medication treatment for a chronic condition, along with the associated physical and psychosocial effects that the medication causes in their daily lives. It is facilitated by social support and information, but hindered by difficulties associated with medication regimens, as well as by physical and psychological symptoms [2, 3].

For many patients, it is important to be able to self-manage their medications successfully, as they are often expected to do after discharge. Nonetheless, the degree of implementation of MSM during admission of psychiatric patients has not been the subject of extensive study. Research conducted in the general hospitals of Flanders (the Dutch-speaking region of Belgium) indicated that 22% of hospitalised patients self-managed at least one medication during their hospitalisation. According to the opinion of the head nurses in that study, almost twice this number would have been able to self-manage their medication during admission (41%) [4]. Most of these units were medical and surgical, with the minority being psychiatric units [4].

The decision-making process concerning participation in MSM is largely shared between the treating physician, the nurse and the patient. This is in contrast with the recommended practice in healthcare communication, shared decision-making (SDM), in which the emphasis is on the patient as a person, taking into account the patient's preferences, needs, beliefs and concerns about treatment in general. SDM has potential to improve treatment decisions and health outcomes [5, 6]. At the same time, however, they often report a lack of sufficient involvement in decision-making concerning antipsychotics [7, 8].

Psychiatric healthcare providers often have difficulty using SDM in decisions about psychiatric medication, as it is often perceived as posing risks for clinicians (e.g. liability or making medication errors) and concerned over patients' medication under- and misuse [9]. However, according to Formby [10], Furlong [11] and Garfield [12], in comparison with nurse-managed medication, MSM reduces medication errors and increases the knowledge, adherence to treatment and satisfaction of patients with regard to medica-

tion. This form of decision-making has therefore been encouraged in many hospitals worldwide [10-12].

In a recent study [13] conducted in psychiatric hospitals in Flanders, patients and psychiatric healthcare providers tend to be of the opinion that the patient, the nurse and the psychiatrist should all be involved in the process of MSM. They further state that MSM would be likely to enhance their medication knowledge and improve their health literacy [13]. To date, there appears to be a lack of studies on the attitudes of patients with SSD or BD to participate in MSM during hospitalisation.

To address this gap in the literature, the primary objective of this study was to describe the attitudes of patients with Schizophrenia Spectrum Disorder or a Bipolar Disorder, Type I or Type II regarding MSM during hospital admission. A secondary aim is to identify various factors associated with patient willingness to participate in MSM and to describe their assumptions concerning needs and necessary conditions, as well as their attitudes towards their medication. Such insights are necessary to develop and implement MSM interventions.

6.2. Methods

6.2.1. Design

A multicentre, quantitative cross-sectional observational design was used to study the willingness and attitudes of psychiatric patients regarding MSM during hospitalisation. Between December 2020 and April 2022, patients were surveyed using a structured questionnaire to assess their attitudes towards MSM, their assumptions regarding needs and necessary conditions, and their attitudes towards their medication.

6.2.2. Participants and setting

In order to obtain sufficient data variation, convenience sampling was used to select patients. We recruited patients in three inpatient psychiatric hospitals in Flanders, Belgium. Units accommodating hospitalised patients with schizophrenia spectrum or bipolar disorders were invited. Specifically, the research included patients from both resocialization units and chronic psychosis units. Eleven units were contacted, and five units ultimately participated. Patients were included after consultation with the head nurse and had to meet all the following inclusion criteria: 18 years of age or older, hospitalisation and a diagnosis of Schizophrenia Spectrum Disorder or a

Bipolar Disorder, Type I or Type II. Exclusion criteria for patients were as follows: staying in either an acute or an outpatient unit or inability to speak Dutch.

6.2.3. Data collection

The survey was conducted according to a self-developed structured questionnaire and

based on results from a previous study on MSM in a non-psychiatric setting [14], as well as on the results of a recent qualitative descriptive study of MSM in patients with SSD or BD [13]. The definition of MSM was explained in detail at the beginning of the survey.

To describe the population, the following data were collected: age, gender, educational level, work and hospital characteristics, disease, reason for hospitalisation and medication characteristics.

Firstly, the willingness of patients to participate in MSM during hospitalisation was assessed with to one question (6-point Likert scale; absolutely unwilling, somewhat unwilling, unwilling, willing, somewhat willing, absolutely willing).

Subsequently, the attitudes of patients towards MSM during hospitalisation were assessed according to a set of 10 questions of which were combined into a scale to describe the overall attitude towards MSM (Table 4). This scale was constructed by summing the scores for these 10 questions, resulting in a score between 0 and 50.

The second section of the questionnaire included 11 different statements (5-point Likert scale: strongly disagree, disagree, neutral, somewhat agree, strongly agree) regarding attitudes towards medication of which were combined into a scale to describe the overall medication attitude (Figure 1). Higher scores indicate more positive patient attitudes. Cronbach's alpha scores were calculated to evaluate the internal consistency of the scales [15]. The overall attitude was calculated by summing the scores for the 10 statements, which were integrated into a scale defining the overall attitude of patients towards MSM in hospital (α= 0.734).

The overall attitude towards medication was calculated by summing the scores for 10 statements (Questions 1–10), which were integrated into a scale defining the overall medication attitude of patients towards their medication (α= 0.713).

Logistic regression analysis was used to identify factors influencing the willingness of patients to participate in MSM.

Finally, possible prerequisites for MSM, relating to the patient, organisation and medication knowledge were questioned. Perceived impact was

evaluated by six statements concerning possible benefits and five statements on possible disadvantages of MSM relating to the patient and organisation. The statements were rated along a 6-point Likert scale (strongly disagree, somewhat disagree, disagree, agree, somewhat agree, strongly agree) (Appendix 1).

6.2.4. Data analysis

Data were analysed using IBM SPSS Statistics V.24.0 (SPSS Inc, Chicago, IL, USA). The normality of the data was tested using the absolute z-value [16]. Discontinuous and categorical data were described using frequency distributions, while mean and standard deviations were used for continuous data. A two-sided level of significance of 0.05 was applied. Nonparametric statistics were used to analyse the data. To evaluate the statistical significance of the differences between the two patient groups, the $\chi 2$ test for dichotomous data and the Mann-Whitney U test for ordinal data was used.

A post-hoc power analysis using G*power 3.1 was used to calculate the overall statistical power of the data [17]. With a statistical power of 0.64, as calculated with an a error probability of 0.05, the sample size was moderate in our study. To control for multiple testing, the Benjamini-Hochberg procedure was used to adjust for the false discovery rate (FDR) [18].

6.2.5. Ethical considerations

The local ethics committees and the Ethics Committee of the University Hospital of Antwerp formally granted ethical approval (reference B3002020000245). All participants received information on the purpose, design and execution of the study. Participation was voluntary, and signed informed consent was obtained from all participants prior to the questionnaire. Participants had the right to withdraw consent at any time. All data collected were coded.

6.3. Results

6.3.1. The research population

A total of 84 patients participated in this study, including 43 patients with schizophrenia spectrum and 41 patients with bipolar disorders (Table 6.1). The average age of participants was 41 years [SD 13], and the majority were male (57%). More than half of the participants were unemployed

(66%), and 7% were working in healthcare. Each participant had an average of four hospitalisations [SD 4], the average duration of illness for the entire sample was nine years [SD 11] and most participants were hospitalised for relapse (86%). Duration of illness was related to relapse. Patients who were hospitalised for relapse had a significantly longer duration of illness than did other patients (10 years and 4 years, respectively; Mann-Whitney U, p= 0.034). The majority of the participants received support from significant others both during (91%) and after hospitalisation (92%).

Table 6.1: Demographic and work characteristics .

Demographic data	**SSD** (n= 43)	**BD** (n= 41)	**Total** (n= 84)	**p-value**
Gender, n (%)				0.850[1]
Male	25 (58)	23 (56)	48 (57)	
Female	18 (42)	18 (44)	36 (43)	
Age (years)				0.278[2]
mean [SD]	39 [14]	42 [12]	41 [13]	
Level of education, n (%)				0.053[2]
None	2 (5)	0 (0)	2 (2)	
Primary education	6 (14)	2 (5)	8 (10)	
Secondary education	21 (50)	21 (51)	42 (51)	
Higher education	6 (14)	4 (10)	10 (12)	
Bachelor	3 (7)	8 (20)	11 (13)	
Master	4 (10)	6 (15)	10 (12)	
Occupation, n (%)				0.323[1]
Unemployed	31 (72)	24 (59)	55 (66)	
Employed	8 (19)	14 (34)	22 (26)	
Working in healthcare	3 (7)	3 (7)	6 (7)	
Retired	1 (2)	0 (0)	1 (1)	
Duration of illness (years)				0.695[2]
mean [SD]	10 (11)	9 (10)	9 (11)	
Number of psychiatric hospitalisations				0.146[2]
mean [SD]	3 (3)	4 (4)	4 (4)	

SSD: Schizophrenia spectrum disorders, BD: Bipolar disorders

[1] χ^2 test

[2] Mann-Whitney U test

6.3.2. Medication management

Most of the participants (86%) took medications at home, with an average of 4 [range 0-13] medications before hospitalisation (Table 6.2). The majority of patients (70%) had completely self-managed these medications at home. Analysis revealed a positive correlation between age and the number of medicines taken at home (Spearman's rho, r= 0.423, p<0.001).

Moreover, they reported having sufficient support to take their medication correctly during their hospitalisation (89%) and to follow up on their treatment plans after hospitalisation (71%).

Table 6.2: Medication management.

	SSD (n= 43)	**BD** (n= 41)	**Total** (n= 84)	**Test value**	**p-value**
Number of medicines taken before hospitalisation, mean [range]	2 [0-13]	3 [1-11]	4 [0-13]	507.5	0.005[1]
Medication management at home, n (%),					
MSM	32 (74)	37 (90)	69 (83)	4.8	0.039[2]
Fully MSM	22 (54)	32 (89)	54 (70)	11.4	<0.001[2]
MSM during hospitalisation, n (%)	10 (23)	7 (17)	17 (20)	0.5	0.590[2]

SSD: Schizophrenia spectrum disorders, BD: Bipolar disorders

[1] Mann-Whitney U test

[2] χ^2 test

6.3.3. Willingness to participate in medication self-management during hospitalisation

A majority of the patients (81%) were willing to participate in MSM during their hospitalisation (Table 6.3). Patients with a BD were more willing compared to patients with SSD (83% vs 79%; W= 834, p= 0.627). A smaller share (52.6%) were only willing to self-manage their home medication during hospitalisation (p= 0.484). Analysis revealed patients are more willing to MSM if they are younger (Pearson's r, r= -0.417, p<0.001) and a decreasing number of medicines (Pearson's r, r= -0.373, p= 0.003). In addition, willingness was positively associated with the extent of support by significant others during and after hospitalisation (Pearson's r, r= 0.298, p= 0.011).

Table 6.3. Willingness to participate in MSM during hospitalisation.

Willingness to participate in MSM, n (%)	**SSD** (n= 43)	**BD** (n= 41)	**Total** (n= 84)	**Test value**	**p-value[1]**
Absolutely willing	28 (65)	23 (56)	51 (61)		
Somewhat willing	5 (12)	10 (24)	15 (18)		
Willing	1 (2)	1 (2)	2 (2)	834	0.627
Somewhat unwilling	1 (2)	1 (2)	2 (2)		
Absolutely unwilling	8 (19)	6 (15)	14 (17)		

SSD: Schizophrenia spectrum disorders, BD: Bipolar disorders

[1] Difference between the willingness of the two disciplines, Mann-Whitney U test

6.3.4. Attitudes towards medication self-management during hospitalisation

The attitudes of patients (n= 64) towards MSM during hospitalisation was assessed along a 6-point Likert scale based on 10 statements (Table 6.4). Most patients (88%) were of the opinion that MSM during hospitalisation had a positive impact on their sense of confidence. However, patients with SSD were less convinced of this premise than were patients with BD (80% vs 97%; W= 527, p= 0.023).

Patients were convinced that they would take their medication more correctly if MSM was allowed (65%). The willingness of patients was positively correlated with their overall attitudes towards MSM (Pearson's r, r= 0.297, p= 0.019).

6.3.5. Attitudes towards medication

The attitudes of patients (n= 82) towards their medication was assessed along a 6-point Likert scale based on 11 statements (Figure 6.1). Most patients agreed that their future health status would depend on their medicines (71%), and they reported being concerned about the long-term effects of their medicines (70%). Patients with bipolar disorders were slightly less in agreement with the statement that medicines have unpleasant side-effects, as compared to other patients (28% vs 42%; X^2= 5, p= 0.270). In addition, patients with bipolar disorders stated that they were not sufficiently informed about the effects of their medicines, as compared to patients with schizophrenia spectrum disorders (62% vs 37%; X^2= 7, p= 0.168).

6.3.6. Factors influencing the willingness of patients to participate in medication self-management during hospitalisation

We applied univariate logistic regression analysis to examine the association between willingness and age, overall attitude towards MSM during hospitalisation and extent of support by significant others (Table 6.5). Patients who were willing to self-manage their medication during hospitalisation were younger than those who were unwilling to do so (mean 38 [SD 12] vs mean 50 [SD 11]; W= 10.81; p= 0.001). The overall attitude towards MSM was less positive amongst patients who were unwilling to self-manage their medication during hospitalisation than amongst those who were willing to do so (mean 36 [SD 6] vs mean 31 [SD 10]; W= 3.88; p= 0.049). Furthermore, patients who reported receiving more support from significant others during and after hospitalisation were more likely to be

willing to participate in MSM during hospitalisation (OR= 1.24; 95% CI [1.04-1.08]).

Table 6.4: Attitudes towards medication self-management.

Attitudes towards medication self-management (n= 64)	**Agree*** n (%)		**p-value**[1]
I currently feel that I have enough support to take my medication correctly during hospitalisation	**Total**	**73 (89)**	0.844
	SSD	38 (90)	
	BD	35 (73)	
I currently feel that I have sufficient follow-up for my medication after discharge	**Total**	**57 (71)**	0.304
	SSD	26 (67)	
	BD	31 (76)	
I will take my medication more correctly	**Total**	**49 (65)**	0.533
	SSD	23 (64)	
	BD	26 (67)	
MSM will increase my own safety	**Total**	**42 (55)**	0.829
	SSD	21 (60)	
	BD	21 (55)	
MSM will result in fewer problems with my medication after discharge	**Total**	**69 (87)**	0.979
	SSD	35 (88)	
	BD	34 (87)	
My medication knowledge will increase	**Total**	**56 (73)**	0.591
	SSD	28 (72)	
	BD	28 (74)	
MSM during hospitalisation will allow me to experience a positive sense of confidence	**Total**	**69 (88)**	**0.023**
	SSD	32 (80)	
	BD	37 (97)	
MSM during hospitalisation gives me more order and structure	**Total**	**59 (75)**	0.958
	SSD	30 (75)	
	BD	29 (74)	
MSM may be unsafe in case of forgetfulness	**Total**	**36 (44)**	0.711
	SSD	21 (49)	
	BD	15 (38)	
MSM may be unsafe if I do not have enough knowledge about my medication	**Total**	**45 (54)**	0.483
	SSD	25 (58)	
	BD	20 (50)	

[1] Mann-Whitney U test.
Agree: sum of patients indicating absolutely agree, somewhat agree and agree
Disagree: sum of patients indicating disagree, somewhat disagree and strongly disagree.
MCAR: X^2 (75, N= 64)= 89.959, p= 0.115

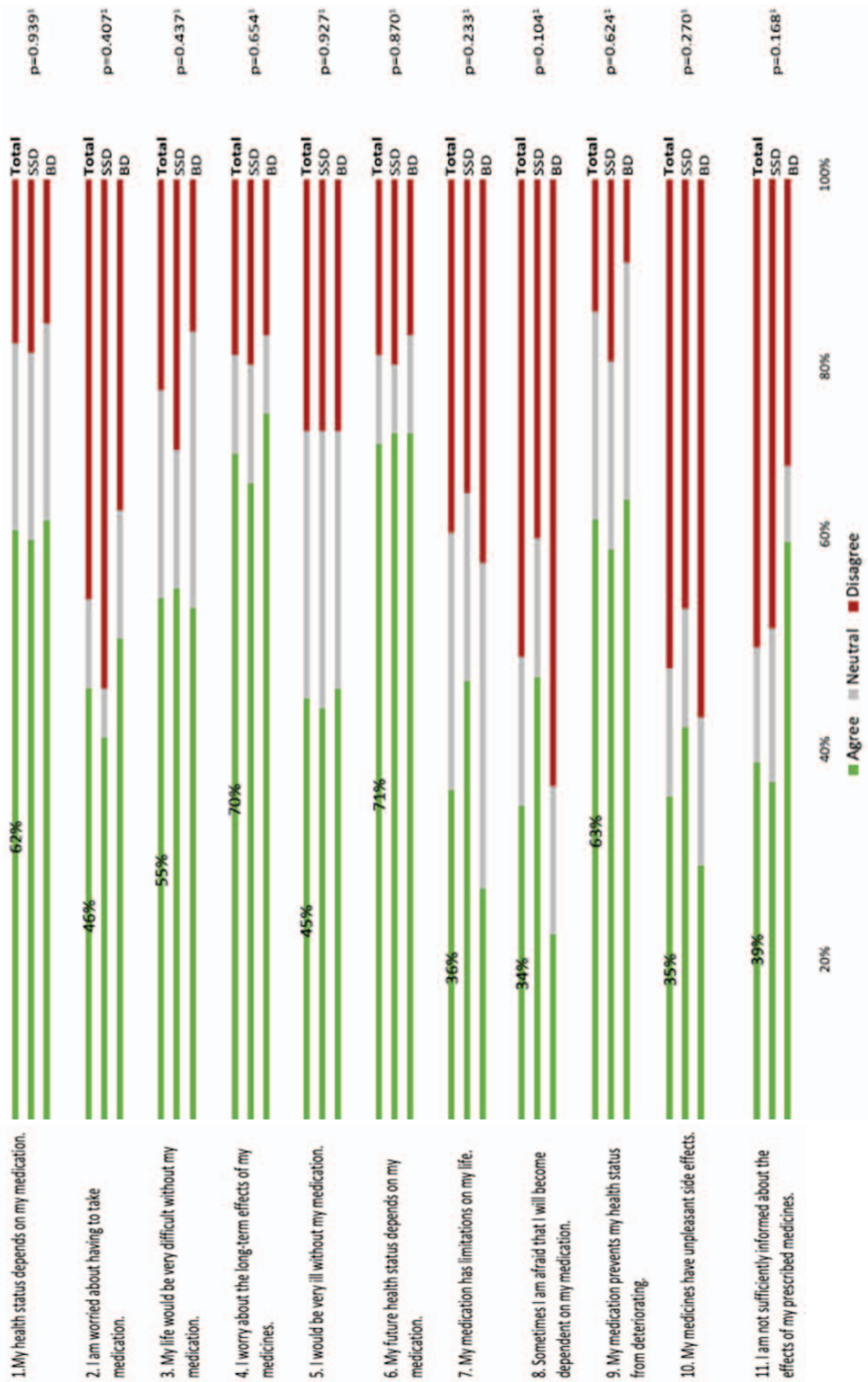


Figure 6.1: Attitudes towards medication.

SSD: Schizophrenia spectrum disorders, BD: Bipolar disorders.[1] χ2 test; Total patients (n= 82): SSD (n= 40), BD (n= 42);
Agree: sum of % patients indicating agree and strongly agree;
Disagree: sum of % patients indicating disagree, somewhat disagree and strongly disagree.

Table 6.5: Univariate logistic regression analysis.

Variable	Yes[1]	No[2]	Wald	OR [95% CI]	p-value
Age	n= 61	n= 19			
mean [SD]	38 [12]	50[11]	10.81	0.92 [0.88–0.97]	**0.001**
MSM Attitude (score 0–50)	n= 48	n= 14			
mean [SD]	36 [6]	31 [10]	3.88	1.09 [1.01–1.19]	**0.049**
Extent of support from significant others (score 0–70)	n= 56	n= 17			
mean [SD]	28 [15]	19 [13]	0.18	1.24 [1.04–1.08]	**0.036**

OR: Odds ratio;
CI: Confidence interval;
[1] Patients who were willing to participate in MSM during hospitalisation (sum of patients indicating agree, somewhat agree and strongly agree)

6.3.7. Prerequisites for medication self-management

The majority of participants (96%) indicated that they needed to be motivated to take their medication correctly and understand the benefits of their medication. They further acknowledged the importance of regular evaluations of their ability to continue MSM during hospitalisation (96%). Opinions were divided concerning locking up self-managed medication during hospitalisation. Some patients considered this precaution necessary, while others did not. The analysis did not reveal any statistically significant differences.

6.4. Discussion

Most of the patients in our study indicated that they were willing to self-manage their medication during hospitalisation. Furthermore, willingness to participate in MSM was positively associated with the extent of support provided by significant others during and after hospitalisation. Patients who were willing to self-manage their medication during hospitalisation were younger than those who were unwilling to do so. The overall attitude towards MSM was less positive amongst patients who were unwilling to self-manage their medication during hospitalisation than amongst those who were willing to do so.

6.4.1. Attitudes towards medication self-management during hospitalisation

The majority of patients in our study perceived that MSM during hospitalisation had positively affected their sense of confidence, although patients with SSD were less convinced of this premise than were those with BD (80% vs 97%). Our results confirm previous research indicating that MSM during hospitalisation increased the autonomy, confidence, self-reliance, appreciation and satisfaction of patients [13, 19]. According to previous studies, most patients who have experienced MSM during hospitalisation are satisfied with their experiences and would choose to do so again, but those who have never experienced MSM are more likely to choose nurse administration [13, 20].

Many of the patients in our study stated that they would be likely to take their medication more correctly if MSM was allowed. These findings were in line with those of previous research indicating that training in MSM was beneficial for to adherence in patients with severe psychiatric disorders [21, 22]. Habit-based interventions that examined the daily routines of patients and then linked medication management to these have also been particularly effective.

Some patients in our study also perceived MSM as an opportunity to learn how to take medication correctly. This might affect medication-related problems after discharge [23].

There is a huge contrast between inpatient and outpatient treatment. During the inpatient treatment, all medication is administrated and prepared, while at home the patient is often on his own. Patients suddenly must be able to read their medication schedule, pick up the prescribed drugs at the pharmacy, and prepare and take them at the right time [24, 25].

Patients reported receiving sufficient support to take their medication correctly during their hospital admission and during their follow-up treatment plans after hospitalisation. The majority of patients (82%) had followed complete MSM at home, in contrast to during hospitalisation (20%). These findings are in line with previous research [4] indicating that 21% of hospitalised patients self-managed their medication. Most of these units involved in that study were medical and surgical units, with a minority being psychiatric units [4]. The literature reveals a sharp contrast between the prevalence of MSM amongst inpatients and outpatients. It is important for patients to be able to self-manage their medications successfully during hospitalisation, as they will often be expected to do after their ad-

mission. To this end, healthcare providers should help patients to take responsibility for their medicines and to self-manage their conditions. Most of the patients in our study had already taken responsibility for their own medication prior to admission and had shared this responsibility with family members or significant others. The literature reveals a sharp contrast between the willingness towards MSM during hospitalisation in psychiatric units. Most patients believed MSM during hospitalisation increased their autonomy, confidence, self- reliance, appreciation, and satisfaction [13].

Although the literature clearly demonstrates that patients tend to be positive towards MSM, not all patients would be willing to participate in MSM during a future hospitalisation. This may reflect the current culture in hospitals, in which patients expect to assume a more passive role and healthcare providers expect to assume responsibility for the medical care of their patients, regardless of their level of involvement in their own care prior to admission [26].

Allowing patients to begin MSM during their hospitalisation would provide a several days during which to observe the way in which they manage their medication. This could enable healthcare providers to detect, respond to and intervene in case of errors in the medication routines of patients.

Willingness to participate in medication self-management during hospitalisation

Willingness to participate in MSM was positively associated with the extent of support provided by significant others during and after hospitalisation. These findings are in line with those of previous research. External support from relatives or significant others is desirable, given the positive impact that a familiar carer may have on a patient's willingness to participate in MSM [26-28]. In addition, significant others can communicate with healthcare providers in case of ambiguities concerning treatment or possible problems. Some family members had too little insight into medications initiated in hospital [28]. Inviting patients' significant others to unit rounds can be a possible means by which healthcare providers can inform them about medication changes and providing opportunities for more proactive care.

Shared decision-making

While patients have expressed a desire to be involved in decisions about their treatment, they often report that they are not sufficiently involved in decision-making concerning medication [5, 7]. Shared decision-making has the potential to alleviate problematic aspects of current medication man-

agement. It may enhance the customisation of medication to the needs, preferences and lifestyle of patients, as well as their stage of disease, with knock-on effects for health and social functioning. In general, patients are more likely to adhere to treatment plans with which they are satisfied or for which they feel that they have been involved in the decision-making process. In the clinical practice of mental healthcare, however, shared decision-making remains an exception rather than the norm [29].

Attitudes towards medication

Most of the patients in our study were positive concerning their medication. They agreed that their future health status depends on their medication, and they were concerned about the long-term effects of their medicines. These results are partially in line with the literature, which reports that outpatients and long-term care in patients had more positive attitudes about medication than did patients with acute illness [30-32]. In contrast to literature, however, we did not find any statistically significant correlations between medication attitude scores and any of the socio-demographic and clinical variables. Most previous studies have identified previous psychiatric hospitalisations and polypharmacy as factors that do not promote a positive attitude towards medication treatment [33-36]. In addition to a positive attitude towards medication, patients should be enabled to recognise their medication and to organise its' intake autonomously in full self-responsibility. The literature indicates patients' medication knowledge and disease insight increase with MSM, nevertheless it is not clear which aspects significantly improve (e.g. medication knowledge on name, dosage, side effects...) [26]. Medication schedules tailored to the patient's needs and Cleary as possible is highly recommended.

Prerequisites for medication self-management

The results of our study indicate that patients are likely to be willing to participate in MSM under specific conditions. The majority of patients indicated that they needed to be motivated to take their medication correctly and to understand the benefits of their medication. Furthermore, they acknowledged the importance of regularly evaluating their ability to continue MSM during hospitalisation. These findings are in line with previous research indicating that evaluation is necessary to the objective assessment of a patient's actual competences. Such assessment should consider several aspects, including the specific conditions of patients, their mental and physical condition, and any possible side-effects of their current medication [19]. In addition, patients should be hospitalised or be followed at

home for a sufficient period to allow for the assessment of their competences.

Several existing programs for MSM incorporate a tool for evaluating the competences of patients. One such tool, the Self-Administration of Medication (SAM) instrument, has been validate in two studies and takes an average of eight minutes per patient to administer [26]. This tool is intended to provide an objective means of determining the extent to which patients are able to self-manage their own medication [37, 38]. Taken together, the findings of our study confirm the need for further research on the validation of tools for use in psychiatry, as this topic currently represents a gap in the literature.

6.4.2. Strengths and limitations

One strength of this study was the random inclusion of several units in one university psychiatric hospital and two general psychiatric hospitals, which ensured the inclusion of a diversity of patients in the study sample. The sample size was adequate, as indicated by a test of statistical power, and it included almost equal proportions of participants with schizophrenia spectrum and bipolar disorders (52% vs 48%). This enhances the generalisability of our study results. Unfortunately, the response rate could not be calculated exactly.

We cannot rule out the possibility of selection and participation bias. It is possible, however, that patients with a more outspoken opinion on MSM were more likely to complete the survey. Therefore, the results of this study are therefore likely to reflect the willingness and attitudes of patients receiving long-term treatment in an inpatient setting with good clinical compensation, as opposed to outpatients or severely ill hospitalised patients. Further investigation is needed to explore the willingness and attitudes of severely ill inpatients and outpatients concerning MSM. We are convinced that the insights provided by our study provide concerning how patients look at MSM could be used as input in the development and implementation of future strategies.

6.4.3. Future prospects

Future research should focus on the development of a feasible MSM procedure that begins with the assessment of a patient's willingness to participate in shared decision-making. Processes of shared decision-making emphasise patients as people, taking into consideration their preferences, needs, beliefs and concerns about treatment, while incorporating

their experiential knowledge. Ongoing medication counselling and regular consultations help build confidence and understanding that could help patients adhere to their treatment plans.

We also strongly recommend the development of a patient assessment tool for determining whether patients are capable of MSM and for regularly evaluating their ability to participate in MSM during and after hospitalisation. In addition, regular screening for the needs of individual patients with regard to treatment and their attitudes towards medication in inpatient and outpatient settings is needed in order to anticipate possible relapses. Furthermore, it is important to involve the significant others of patient both during and after hospitalisation. They could assist nurses in screening patients and following up on them after hospitalisation. Future research should therefore focus on what significant others need in order to assist and support patients in their treatment.

6.5. Conclusion

Most of the patients were willing to self-manage their medication during hospitalisation, however, under specific conditions. Patients needed to be motivated to take their medication correctly and to understand the benefits of their medication. Furthermore, they acknowledged the importance of regularly evaluating their ability to continue MSM during hospitalisation. The majority of patients stated that they would be likely to take their medication more correctly if MSM were to be allowed. Additionally, patients agreed that their future health status depends on their medication, and they were concerned about the long-term effects of their medicines.

6.6. References

1. Parnell M. Medicines at the bedside. Am J Nurse. 1959;59:1417-8.
2. Xiao J, Mi W, Li L, Shi Y, Zhang H. High relapse rate and poor medication adherence in the Chinese population with schizophrenia: results from an observational survey in the People's Republic of China. Neuropsychiatr Dis Treat. 2015;11:1161-7.
3. Sendt KV, Tracy DK, Bhattacharyya S. A systematic review of factors influencing adherence to antipsychotic medication in schizophrenia-spectrum disorders. Psychiatry Res. 2015;225(1-2):14-30.
4. Vanwesemael T, Van Rompaey B, Petrovic M, Boussery K, Dilles T. SelfMED: Self-Administration of Medication in Hospital: A Prevalence Study in Flanders, Belgium. Nurs Scholarsh. 2017;49:277-85.
5. Zisman-Ilani Y, Barnett E, Harik J, Pavlo A, M. OC. Expanding the concept of shared decision making for mental health: systematic search and scoping review of interventions. Mental Health Review Journal. 2017;22:14.

6. Charles C, Gafni A. Decision-making in the physician-patient encounter: revisiting the shared treatment decision-making model. Soc Sci Med. 1999;49:61.
7. Moncrieff J, Azam K, Johnson S, Marston L, Morant N, Darton K, et al. Results of a pilot cluster randomised trial of the use of a Medication Review Tool for people taking antipsychotic medication. BMC Psychiatry. 2016;16:205.
8. Zisman-Ilani Y, Shern D, Deegan P, Kreyenbuhl J, Dixon L, Drake R. Continue, adjust, or stop antipsychotic medication: developing and user testing an encounter decision aid for people with first-episode and long-term psychosis. BMC Psychiatry. 2018;18:12.
9. Zisman-Ilani Y, Lysaker PH. Shared risk taking: shared decision making in serious mental illness. Psychiatr Serv. 2021;72:10.
10. Formby F. Medication self-administration by patients: a way to prevent errors? . Medical Journal of Australia. 2008;189(8).
11. Furlong S. Do programmes of medicine self-administration enhance patient knowledge, compliance and satisfaction? Journal of advanced nursing. 1996;23:9.
12. Garfield S, Bell H, Nathan C, Randall S, Husson F, Boucher C, Taylor A, Lloyd J, Backhouse A, Ritchie L, Franklin B. A quality improvement project to increase self-administration of medicines in an acute hospital. Int J Qual Health Care. 2018;30(5):12.
13. Loots E, Leys J, Proost S, Morrens M, Glazemakers I, Dilles T, Van Rompaey B. Medication Self-Management in Hospitalised Patients with Schizophrenia or Bipolar Disorder: The Perceptions of Patients and Healthcare Providers. Int J Environ Res Public Health 2022, 19, 4835
14. Vanwesemael T, Boussery K, Van den Bemt P, Dilles T. The willingness and attitude of patients towards self-administration of medication in hospital. her Adv Drug Saf. 2018;9 (6):309-21.
15. Müller M. What is the value or harm of Cronbach's alpha? . Pflege, 26(2), 143 2013.
16. Kim HY. Statistical notes for clinical researchers: Assessing normal distribution, using skewness and kurtosis. Restor Dent Endod. 2013;38:52–4.
17. Arend MG ST. Statistical power in two-level models: a tutorial based onmonte carlo simulation. Psychol Methods 2019;24(1):1–19.
18. Thissen D, Steinberg L, Kuang D. Quick and Easy Implementation of the Benjamini-Hochberg Procedure for Controlling the False Positive Rate in Multiple Comparisons. Journal of Educational and Behavioral Statistics. 2002;27(1):7.
19. Vanwesemael T. Proefschrift voorgelegd tot het behalen van de graad van Doctor in de Medische Wetenschappen aan de Universiteit Antwerpen. In: Faculteit geneeskunde en gezondheidswetenschappen. Universiteit Antwerpen. 2018:95-109.
20. Wright J, Emerson A, Stephens M, Lennan, E. Hospital inpatient self-administration of medicine programmes: a critical literature review. Pharm World Sci. 2006;28(3):140-51.
21. Zhou B, Gu Y. Effect of self-management training on adherence to medications among community residents with chronic schizophrenia: a singleblind randomized controlled trial in Shanghai, China. Shanghai Arch Psychiatry. 2014;26(6):332-8.
22. Valenstein M, Kavanagh J, Lee T, Reilly P, Dalack GW, Grabowski J, et al. Using a pharmacy-based intervention to improve antipsychotic adherence among patients with serious mental illness. Schizophr Bull. 2011;37(4):36.
23. Conn VS, Ruppar TM. Medication adherence interventions that target subjects with adherence problems: systematic review and meta-analysis. Res Social Adm Pharm. 2016;12:218–46.
24. Richard AA, & Shea, K. Delineation of self-care and associated concepts. J Nurs Scholarsh. 2011;43(3):255-64.

25. Davis A, Muir P, Allardice J, Clark K, Groves J, Molenaar M, Robson G. SHPA Guidelines for Self-Administration of Medication in Hospitals and Residential Care Facilities. Journal of Pharmacy Practice and Research, 32(4), 324-325. 2002.

26. Richardson SJ, Brooks H, Bramley, Coleman J. J. Evaluating the effectiveness of self-administration of medication (SAM) schemes in the hospital setting: a systematic review of the literature. PLoS One. 2014;9(12).

27. Loots E, Goossens E, Vanwesemael T, Morrens M, Van Rompaey B, Dilles T. Interventions to Improve Medication Adherence in Patients with Schizophrenia or Bipolar Disorders: A Systematic Review and Meta-Analysis. Int J Environ Res Public Health 2021, 18, 10213

28. Manias E. Communication relating to family members' involvement and understandings about patients' medication management in hospital. Health Expectations. 2013;18:850–66.

29. Morant N, Kaminskiy E, Ramon S. Shared decision making for psychiatric medication management: beyond the micro-social. . Health Expect. 2016;19 (5):1002-14.

30. Balestrieri M, Di Sciascio G, Isola M. Drug attitude and subjective well-being in antipsychotic treatment monotherapy in real-world settings. Epidemiol Psichiatr Soc 2009;18(2):114–8.

31. Medina E, Salvà J, Ampudia R, Maurino J, J. L. Short-term clinical stability and lack of insight are associated with a negative attitude towards antipsychotic treatment at discharge in patients with schizophrenia and bipolar disorder. . Patient Prefer Adherence. 2012;6:623–9.

32. Rej S, Schuurmans J, Elie D, Stek ML, Shulman K, A. D. Attitudes towards pharmacotherapy in late-life bipolar disorder. Int Psychogeriatr. 2016;28(6):945–50.

33. Di Lorenzo R, Sagona M, Landi G, Martire L, Piemonte C, C. DG. The revolving door phenomenon in an Italian acute psychiatric ward: a 5-year retrospective analysis of the potential risk factors. J Nerv Ment Dis. 2016;204(9):686–92.

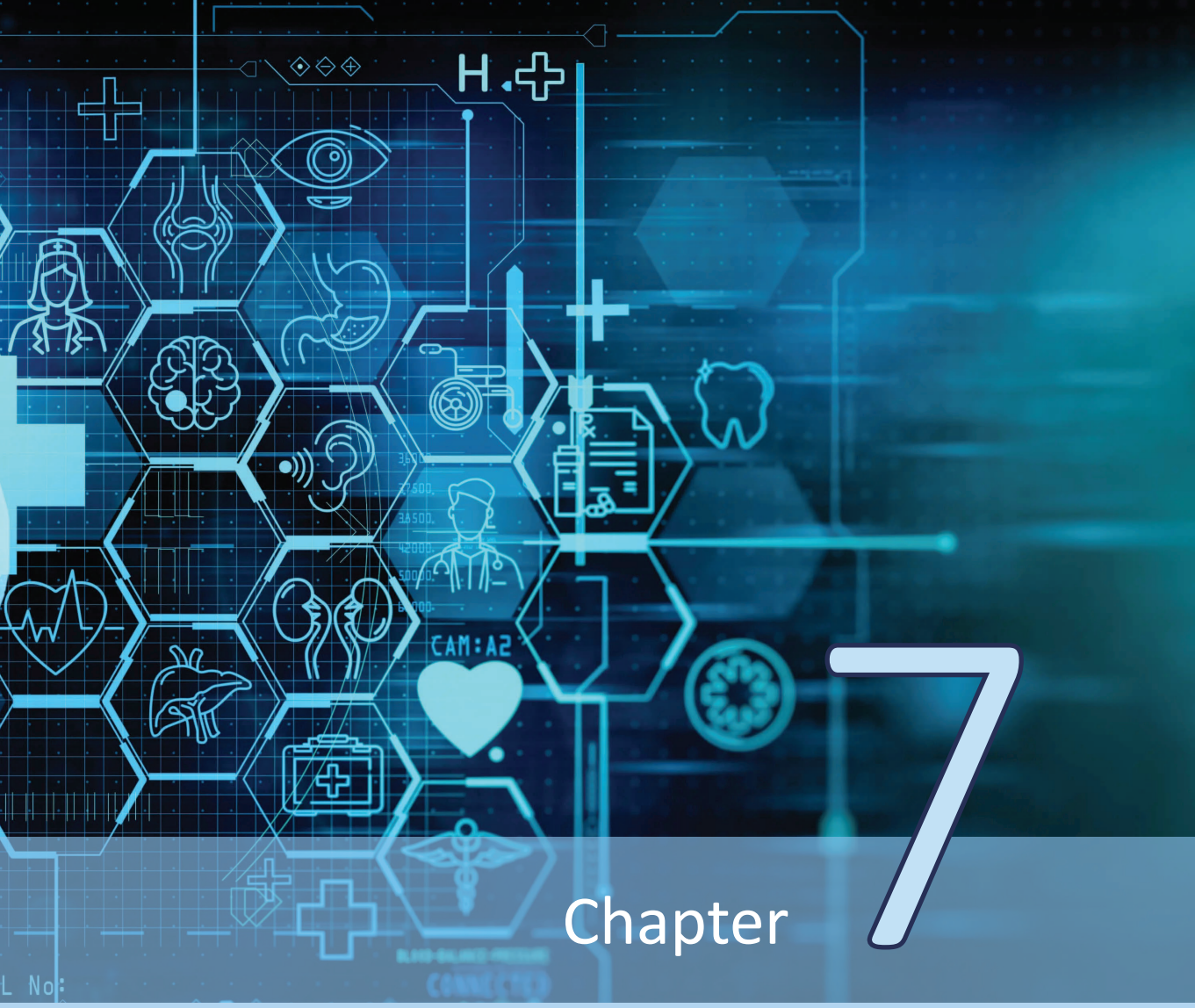
34. Haddad P, Brain C, Scott J. Nonadherence with antipsychotic medica- tion in schizophrenia: challenges and management strategies. Patient Relat Outcome Meas. 2014;5:43–62.

35. Hong J, Reed C, Novick D, Haro JM. Clinical and economic consequences of medication non-adherence in the treat- ment of patients with a manic/mixed episode of bipolar disorder: results from the European Mania in Bipolar Longitudinal Evaluation of Medication (EMBLEM) study. Psychiatry Res. 2011;190(1):110–4.

36. García S, Martínez-Cengotitabengoa M, Lopez-Zurbano S, Zorilla I, Lopez P, Vieta E, Gonzalez-Pinto A. Adherence to antipsychotic medication in bipolar disorder and schizophrenic patients. A systematic review. J Clin Psychopharmacol. 2016;36(4):355–71.

37. Anderson J, Manias E, Kusljic S, Finch S. Testing the validity, reliability and utility of the Self-Administration of Medication (SAM) tool in patients undergoing rehabilitation. Res Social Adm Pharm 10 (1), 204-216. 2014.

38. Manias E, Beanland C, Riley R, Hutchinson A. Development and validation of the self-administration of medication tool. Ann Pharmacother 40 (6), 1064-1073. 2006.



Chapter 7

General discussion, practical implications, recommendations and conclusion

Chapter 7: Contents

7.1. General discussion

7.1.1. Overall aim

Schizophrenia Spectrum (SSD) and Bipolar Disorders (BD) are severe major psychiatric disorders that are often complicated by recurring psychotic relapses requiring hospitalisation [1-3]. Next to stressful life events and substance abuse, non-adherence, to medication is an important and the most common risk factor for relapse[4-7]. Importantly, patients interrupting or discontinuing their medication are five times more likely to relapse [7, 8].

This doctoral study summarized the findings of studies aimed at improving medication adherence in patients with SSD and BD. Because of its expected positive impact on medicines adherence, we studied patients' and health care providers' opinions regarding allowing patients to self-manage their medicines during hospitalization.

Firstly, the impact of different interventions to tackle non-adherence, in patients with SSD or BD were evaluated (Chapter 2). Secondly, to map the current situation, prevalence rates of medication self-management (MSM) in Flemish psychiatric hospitals in patients with SSD or BD. If MSM was present, the way MSM was organised, were described (Chapter 3). Finally, we explored all involved stakeholders' perceptions concerning MSM during hospitalisation in patients with SSD or BD, their general attitude towards MSM in hospital, concerns and prerequisites for implementation to define their willingness to support the implementation (Chapters 4, 5 and 6).

7.1.2. Main findings

Interventions for improving medication adherence

First, we provided a synthesis of the effectiveness of interventions improving medication adherence in patients with SSD or BD (Chapter 2). The extensive literature concerning effectiveness of different interventions improving medication adherence showed to be heterogeneous in its findings and hampered by its mixed methodological quality. Most of the studies were based on single sites, limiting generalisability, limiting interpretation, and only a handful had a follow-up assessment after six months or more (n=14). Short-term follow-up makes it difficult to ascertain whether interventions with promising adherence-improving effects can safeguard and maintain their effects over time.

The main conclusion was that successful interventions typically used a

combination of educational and behavioural strategies (moderate to very large effect sizes). Implementing motivational interviewing with both family members and patients, coupled with personalized education, home-based medication reminders, and targeted educational sessions covering diagnosis, symptoms, medication, and relapse were found to significantly enhance patients' adherence to their treatment plans. Additionally, problems with adherence are recurrent, and therefore repeated sessions are needed to maintain adherence. Extensive follow-up periods are important, as researchers need to measure the immediate effects of their intervention(s) on adherence, but also intermediate and long-term effects.

As a MSM intervention was deemed to be the most effective (Chapter 2), follow-up research as part of this doctoral study focussed on revealing the fundamental pillars for the development of a MSM intervention to prevent non-adherence and relapse rates in this population.

MSM as intervention in patients with SSD or BD during hospitalisation

MSM is becoming an increasingly important element in rehabilitation programs. As patients are not capable of MSM, aid is often required. Healthcare providers can support and coach patients towards self-management of their medication. Patients who are not able to self-manage their medication, but are expected to do MSM after discharge, should be given the opportunity to learn to self-manage their medication whilst in hospital. MSM during hospitalisation aims to improve patient understanding of their medicines, allow healthcare providers to assess adherence, improve patient's confidence, minimise medication problems when patients are discharged and allows the patient to maintain their independence. Chapter 3 revealed that only 4% of the hospitalised patients were on MSM during the inclusion period with 84% of the total medication amount being self-administered. Therefore, with a prevalence of only 1 patient in 5 a stronger implementation would be possible. Additionally, only 15% of the units had an available procedure and screening tool to assess the MSM competences of the patients. The results of this study confirmed the need for a unified policy and a MSM procedure. However, because medicine pose a risk to patients if they are used incorrectly and pose a risk of theft and abuse, MSM can only occur when closely controlled and monitored. A clear policy sets out how MSM can happen on hospital units with the minimum of risk to patients, staff and visitors [9-11]. For example, the Joint Commission International (JCI) has established a standard focused on Medication Management and Use (MMU). Furthermore, JCI permits self-management, provided it is governed by established policies and procedures [12].

Evidence on the implications of MSM during hospitalisation

MSM during hospitalisation potentially has important implications for patients and healthcare providers. Two systematic reviews clearly describe that patients who self-manage their medication in hospital were statistically significant more adherent in treatment compared to patients who do not MSM [13, 14]. According to Richardson [13] medication error rates during hospitalisation are ranging from 3% - 8%. Previous research in a non-psychiatric setting, demonstrated that most patients were successful in self-managing medication, and patient characteristics, setting, or medication factors might be related to this success. There was some weak evidence that patients with greater cognitive function were more likely to be successful [15, 16].

The effect of MSM on the knowledge of patients on their own treatment was tested in multiple studies. The literature indicates patients' medication knowledge and disease insight increase with MSM, nevertheless it is not clear which aspects significantly improve (e.g. medication knowledge on name, dosage, side effects...) [13]. Additionally, differences between the education provided (type of counselling), made it difficult to draw conclusions [13, 14]. The literature reveals a sharp contrast between patient's satisfaction towards MSM during hospitalisation. Most patients who have experience in MSM during hospitalisation are satisfied with their experiences and would choose to do so again, but some literature suggest that patients who have never experienced MSM are more likely to choose nurse administration in the belief that it was more convenient for the nurse and saved time. Additionally, nurse administration of medication can offer patients with severe psychiatric disorders a sense of support, safety, and structure during their hospital admission, which may contribute to their preference for this method of administration [14]. Literature clearly described nurses, hospital pharmacists, and patients believed that MSM could be beneficial to the hospital due to the potential positive experiences and higher patient satisfaction. They believed MSM during hospitalisation increased patients' autonomy, confidence, self-reliance, appreciation, and satisfaction [17].

Context for implementation

Psychiatric healthcare providers' and patients' attitude towards MSM (willingness, prerequisites for implementation, prerequisites, benefits, risks) during hospitalisation was described (Chapters 5 and 6).

Overall, all stakeholders were positive towards MSM under specific prerequisites: 1) MSM abilities should be evaluated on a regular basis during hospitalization, 2) patients

should be motivated to take their medication correctly and to understand the benefits of their medication, 3) Additionally, patients need to show to be willing to facilitate and perform MSM in daily practice and 4) patients should be willing to train their MSM skills (Chapters 4, 5 and 6). Healthcare providers were concerned about losing track of or control over the actual medication intake or perhaps overlooking errors, overdoses, and/or misuse. All stakeholders stated that MSM during hospitalisation can result in several positive patient-related outcomes as an increased patients' autonomy, confidence, self-reliance, more structure for the patients, preparation for discharge, and an improvement of their health literacy, adherence and satisfaction (Chapters 5 and 6).

This doctoral study showed the effectiveness of various interventions which are promising to improve medication adherence. MSM in hospitalised patients with SSD or BD is currently not widely implemented in Flemish psychiatric hospitals. However, stakeholders are willing to support the implementation if the prerequisites are fulfilled.

7.1.3. Discussion in a broader context

Shared decision-making concerning in hospital treatment: The elephant in the room

Literature specific focusing on patients with severe psychiatric disorders revealed that patients were insufficiently involved in decision-making concerning their treatment, such as MSM during their hospital admission [18-23]. The underlying belief is that patients with severe psychiatric disorders can be unable to understand their needs for treatment [24]. The literature indicates that about 25% of people with severe mental illnesses, such as SSD or BD, do not retain the capacity to make decisions about their treatment (e.g. MSM during their hospitalisation) [22, 25, 26]. Brief repeated interventions aimed at disease insight and medication training can improve patients to make adequate decisions about their treatment [26]. The literature strongly recommended shared decision-making (SDM), in which the emphasis is on the patient as a person, considering the patient's preferences, needs, beliefs and concerns about treatment in general. SDM has potential to improve treatment decisions and health outcomes [27, 28]. SDM is defined as the process by which a physician cooperates with the patient to make a decision about medical [29]. Approaching patients as active partners in their treatment during hospitalisation is supported by the World Health Organization, as demonstrated by the Framework on Integrated People-Centred Health Services and the Orem Self- Care Theory [30, 31]. SDM can lead to an improvement of adherence to treatment [32-34]. Several studies have shown that most patients with SSD and BD would like to be involved in decision making [35, 36], and are able to participate [37-40].

This doctoral study clearly revealed all stakeholders tend to be positive towards MSM (Chapters 4, 5 and 6). Unfortunately, MSM in patients with SSD or BD is only implemented in a minority of Flemish psychiatric hospitals (Chapter 3). First, this may reflect the current paternalistic culture in hospitals. Patients assume a more passive role and healthcare providers expect to assume responsibility for the medical care of their patients, regardless of their level of involvement in their own care prior to admission [13, 20, 22, 23, 41].

Upon hospitalisation, there is 'ritual confiscation' of patients' medication, where the nursing staff confiscates patient's medication and stores it in a locked medication box in the nursing station, despite patients are managing this aspect of their care whilst at home [21, 42, 43]. These processes unfortunately reflect the dominance of the 'medical model' within mental

health practice, a term first coined by Laing in the early 1970s [44]. There is a focus on psychiatric diagnosis, disease management and prognosis, with the balance of power firmly lying with the healthcare provider that manages the individuals' care [44].

The effect of psychiatric medication

The relationship between patients with severe psychiatric disorders and psychiatric medication is often complicated [45]. Although many patients with SSD or BD see psychiatric medication as helpful, a dilemma often emerges [46, 47]. Many patients report that the adverse effects of psychiatric medication are worse than the mental disorder itself [47-49].

Additionally, lack of disease insight and treatment in patients with SSD is a significant clinical concern. The literature reveals that between 50% and 80% of patients with SSD had characterized by poor disease insight [50-52], which is believed to be associated with patients' non-adherence and adverse disease progression, serving as an indicator of an unfavourable prognosis [50, 53]. Various patients may perceive the necessity for treatment solely due to external pressures exerted by significant others. Conversely, some individuals may acknowledge the presence of symptoms but resist embracing the categorization of a mental disorder, attributing these symptoms to alternative causal factors [54, 55]. Enhancing medication adherence involves acquiring insights into the attitudes and underlying factors contributing to suboptimal medication compliance. This knowledge informs the development of judicious management strategies aimed at ameliorating adherence issues [56].

Recent literature in Flanders revealed that patients appeared to understand the need for their medication. However, when reporting physical complaints to the psychiatrist related to medication use, some patients experienced that their complaints were minimized and ignored [57]. This could place patients in a difficult impasse. Despite their efficacy, antipsychotic medications are linked to various adverse effects, encompassing weight gain, metabolic disturbances, sedation or somnolence, sexual dysfunction and neurological symptoms such as parkinsonism or akathisia. These side effects may exacerbate the overall burden of the underlying illness [58-60]. The impact of these adverse reactions on daily functioning is significant for many individuals [61, 62], leading to suboptimal medication adherence and potential treatment discontinuation, patterns observed across diverse prerequisites [61, 63]. Overall, patients with SSD and BD agree that oral antipsychotic medications were effective at managing their symptoms [46, 61, 64, 65].

Potential hurdles for MSM during hospitalisation

The need for a validated policy

There are no Royal Decrees in Belgium that describe MSM during hospitalisation. The formulation of policies in this regard falls within the purview of the individual hospitals.

If MSM occurs, this has to be noted in the patient's personal medical file and it has to be clearly described which medication is self-managed and which is administered by nurses. The Belgian Royal Decree of March 4th 1991 states all medicines for providing a diagnosis or treatment of hospitalized patients should be delivered by the hospital pharmacist. The dispensing process is expected to employ unit dose medication, with the number of dispensed doses limited to a treatment duration not exceeding five days, which facilitate MSM on the hospital unit [66].

Healthcare providers have a duty of care and a duty of surveillance during hospitalisation. If any problems occur during MSM, these problems have to be noted in the patient's medical file.

Nevertheless, the Care Inspection of the Flemish Division of Wellbeing, Public Health and Family provided rules to be adhered to. Therefore, relevant aspects on Belgian healthcare regulation related to MSM were presented below [66].

This doctoral study revealed the need for a validated policy with a standardised procedure for MSM during hospitalisation.

According to literature, a standardized procedure for MSM defines three levels of supervision within the scheme for MSM [9-11, 67]:

- The nurse dispenses medications from the pharmaceutical cart.
- Under nurse supervision, the patient self-administers medication sourced from the pharmaceutical cart.
- The patient independently self-administers medication and assumes responsibility for the key to their medication box.

The policy delineates the procedures pertaining to the management of patients' medications upon hospitalisation, the evaluation of these medications for patient use during their hospitalisation, and the facilitation of self-administration. Additional provisions encompass the procurement of supplementary medication as required, including the acquisition of novel pharmaceuticals requested by patients [9-11, 67, 68].

MSM during hospitalisation entails inherent risks because medicine pose a risk to patients if they are used incorrectly and pose a risk of theft

and abuse; however, these can be mitigated through meticulous patient selection for the program, vigilant oversight by involved staff to ensure adherence to the established policy, and accurate record-keeping in accordance with the specified protocols [9-11, 67].

Workload

Healthcare providers may be concerned over increased workload due to MSM, such as preparing medication and medication schedules and educating patients (chapters 4 and 5). To date, there appears to be a lack of studies on the workload of healthcare providers due to MSM. Only one systematic review provided a synthesis of evidence concerning the possible effects on workload [13]. Although more nursing time was needed in early levels, time was saved on later ones, but it is unclear whether timings quoted are based on empirical data. Unfortunately, a clear methodology was not described. To date, research into the actual time investment spent on education or facilitating MSM during hospitalisation is lacking.

Patient safety and accountability

One of the most discussed barriers for MSM during hospitalisation is the concern about patient safety and accountability (Chapter 4). Our results are partially in line with literature reporting that the perception of increased medication errors, medication intoxication, suicide (attempt), and medication abuse with eventual medical damage to the patient's health, to others, and to the environment can also be possible barriers to implement MSM during hospitalisation [13, 65, 69].

Assessing patients' eligibility for MSM

Many healthcare providers were concerned about the difficulty of correctly assessing patients' eligibility for MSM (Chapters 4 and 5). The literature clearly describes that an assessment is necessary to objectively evaluate the actual competencies of the patient. This assessment should consider various aspects, such as patients' specific prerequisites, mental and physical condition, and possible side-effects of their current medication [17, 65, 68]. Other important competencies are the ability to take medication out of a blister, adherence to treatment, being able to communicate with caregivers concerning the medication and the ability to orient in time and place. These results are partially in line with the literature, reporting that potential hurdles for patients are the difficulties in comprehending the importance of managing the medication regimen correctly [13, 16, 65, 70], reading the medication schedule [13, 16, 68, 71-73], sort-

ing or administering their medications [16, 73], and physically opening pill containers [68]. Several existing programs for MSM incorporate a tool for evaluating the competences of patients. One such tool, the Self-Administration of Medication (SAM) instrument, has been validated in two studies and takes an average of eight minutes per patient to complete [13]. This tool is intended to provide an objective means of determining the extent to which patients can self-manage their own medications and have a good internal consistency with a Cronbach's alpha of 0.899. The tool has two question sections. The first section asked questions about the desire to self-administer medications and an overall competency. The second section is based on the discharge planning and the patient's desire and ability to self-administer medications at home [74, 75].

Feasibility

The current Belgian structure of the residential mental healthcare, with its emphasis on rapid discharge procedures and the reduction of long-term hospitalizations, presents challenges for the implementation of MSM. However, a strategic and integrated approach is necessary to make MSM successful. This approach requires prioritizing MSM from the beginning of hospitalization, utilizing intensive guidance, technological tools, and a well-coordinated transition to outpatient care. By combining these elements, we can better prepare patients for discharge and enhance their ability to manage their medication independently and effectively at home. Ultimately, even within a rapidly evolving healthcare environment, MSM offers a valuable opportunity to improve the quality of care and empower patients to take greater control of their own health.

7.1.4. Methodological strengths and limitations of this doctoral study

One of the notable strengths of the research undertaken in this doctoral dissertation is the use of a multi-methods approach, integrating both quantitative and qualitative approaches. Achieving a profound comprehension of the needs of all involved stakeholders necessitates the exploration of diverse layers of information. Combining quantitative and qualitative methodologies, a comprehensive portrayal of all involved stakeholders' the perceptions, willingness and attitudes towards MSM in patients with SSD or BD during hospitalization. An additionally strength of this doctoral study is the sufficient stakeholder variation. We included stakeholders (patients, attending physicians, nurses and pharmacists) from different settings and generations. In addition, all healthcare providers had relevant experience in clinical practice. This doctoral study contributes to broad fundament

of new knowledge, allowing to develop a MSM intervention. A particular strength of this doctoral study was the inclusion of vulnerable and hard-to-reach patients with SSD or BD. We focused on one of the most vulnerable populations in our society hence contributing to the understanding of the unmet needs in this population. There is evidence that most vulnerable individuals within society have a lower likelihood of active participation in research [76, 77], notwithstanding endeavours to maximize inclusivity. Stigma, anxiety, and mistrust have consistently been identified as barriers in mental health research, so attempts to address these are also likely to increase recruitment [77]. Enhancing transparency in the study and providing a clear explanation of patients' expectations could significantly reduce anxiety and distrust. Furthermore, it is meaningful to involve patients' significant others, as they often play key roles in patients' decision-making processes. This approach may assuage anxieties held by patients and their significant others regarding the research's impact on patients' health status and potential benefits [77]. Another notable methodological aspect of this doctoral dissertation is the variation in definitions of MSM throughout the chapters. The variation in definitions was applied deliberately to align with the specific focus of each chapter. For example, in some chapters, the definition of MSM emphasized the role of healthcare providers (Chapter 4), while in others it focused more on the patients (Chapters 5 and 6) or on the organizational factors of the care process (Chapter 3). This context-specific approach was intended to tailor the concept to the thematic content and focus of each chapter. Another limitation of this doctoral study is the exclusion of stakeholders in the outpatient setting whereas non-adherence is situated in a wider context. These stakeholders have remained under the radar and were not selected. Unfortunately, we cannot rule out the possibility of selection and participation bias, which may affect the generalizability of the results. It is possible, however, that stakeholders with a more outspoken opinion on MSM were more likely to participate in the research. Therefore, the results of this study likely reflect the willingness and attitudes of patients receiving long-term treatment in an inpatient setting with good clinical compensation, as opposed to outpatients or severely ill hospitalised patients. Additionally, comorbid substance use and involuntary commitment were not explicitly addressed, which may represent a limitation. The omission of these factors could potentially influence the results, as they are known to affect both the clinical outcomes and treatment trajectories in psychiatric populations. Future research should consider incorporating these variables to provide a more comprehensive understanding of the issues at hand. These limitations give an incomplete view of the

current situation in clinical practice. Another point of consideration is the inclusion of patients from resocialization units and chronic psychosis units. While this allowed for in-depth analysis of a well-defined and relevant subpopulation, it may limit the generalizability of the findings to broader patient populations, such as patients with a first-episode psychosis.

We were able to include several hospitals, in rural and urban areas in Flanders and the willingness to participate in our research was high. A clear view of the current prevalence rates and organization of MSM in in Flemish psychiatric hospitals in patients with SSD or BD was obtained. Unfortunately, we do not have denominator data of the number of patients hospitalised during the inclusion period. Therefore, determining the prevalence of patients on MSM during hospitalisation was impossible.

7.2. Recommendations for a future MSM intervention

This doctoral study revealed the essential fundamental components and needs necessary for the development of a MSM program. A MSM program should include the following aspects:

1. Assessment for patients' eligibility for MSM.
2. Assessment of patients' MSM competences of problems.
3. Patient information leaflet prior to commencing MSM.
4. Tools for patient education and support throughout MSM.
5. Procedures for monitoring progress, adherence to medication and feedback to healthcare providers.

Patients should know their prescribed medication; such as, the names of the medicines, the packages, the doses, the required schedule for medication intake. Also, they should learn to prepare their medication in advance in a weekly dispenser containing the prescribed tablets in separate compartments for each time of intake. A training manual should be developed, describing the levels of autonomy in the use of medication and the required skills. For each level, the objectives of the training have to be defined. The training program is conducted in one-to-one lessons with a healthcare provider.

The preparation of the medication follows a flowchart, describing all necessary steps and the criteria for an upgrade to the next step or, if problems occur, a downgrade.

Step 1 focuses on the scheduled medication intake.

Step 2 covers the arrangement of the next day's medication coached by a healthcare provider.

Step 3, the dispenser will be in the patient's room, and the next day's medication is arranged autonomously by the patient.

Finally, in step 4, the patient arranges the medication for one week in a dispenser, which remains in the patient's room.

To obtain high-quality outcomes, we recommend starting with a pilot study for the MSM intervention. Analysing the feasibility and safety prior to performing an intervention study on a larger scale can be highly advantageous for this purpose. The pilot study will be the first step of the entire research protocol and will be performed on a small-sized study assisting in planning and modification of the main intervention study.

7.3. Practical implications

7.3.1. Implications for clinical practice

Shared decision-making

This doctoral study revealed important implications for practice. These findings indicated that some aspects for the development of a MSM procedure are lacking. The importance of giving patients the choice to participate in MSM during hospitalisation is central and is then discussed with the attending psychiatrist and the nursing team. The literature highlighted the importance of not being paternalistic and empowering patients to coordinate their own care.

The effect of psychiatric medication

Explore and address any concerns the patient may have about the medication. This could include misconceptions about the necessity of treatment or distrust of medications.

When side effects are problematic, adjusting the dosage of the antipsychotic medication may be considered. Lowering the dose can sometimes alleviate side effects while maintaining symptom control. If side effects persist, switching to a different antipsychotic with a different profile of side effects may be an option. Some patients may tolerate one medication better than another. Encouraging and supporting a healthy lifestyle can mitigate some side effects. This includes regular exercise, a balanced diet, and adequate sleep. Avoiding substances like alcohol and recreational drugs

can also help minimize negative effects. Another implication may be to consider using long-acting or depot medications when appropriate. These medications require less frequent administration, reducing the burden on the patient and potentially improving adherence [78]. Schedule regular follow-up appointments to monitor medication intake and assess the patient's response to treatment. Furthermore, use these appointments to address any issues or concerns the patient may have and adjust the treatment plan as needed. Providing education to the patient and their significant others about potential side effects can empower them to recognize and manage these effects at an early stage. This can include information about what to expect and when to seek medical attention [45, 79]. Literature showed that, in general, minority management approaches are supported by strong evidence, with recommendations often based at least in part on expert opinion. In addition, literature suggest that adverse effects are not the main reason why patients discontinue their antipsychotic medication [79].

Need for assessments and procedures

It is important to respond to the individual needs of the patient regarding the MSM training during hospitalisation. Given the fact that not all patients seem to benefit from 'one size fits all' interventions, the effectiveness of the MSM programme might substantially increase by tailoring programs. Secondly, regular screening for the needs of individual patients with regard to treatment in inpatient and outpatient settings is needed in order to anticipate possible relapses. Thirdly, there is a need for an assessment tool to objectively evaluate the actual MSM competencies of the patient. Fourthly, a regularly evaluating of the patients' ability to continue MSM during and after hospitalisation is necessary. First, recognizing the importance of monitoring the medication intake during MSM, it is essential to consider the ABC-taxonomy, which categorizes medication adherence into three distinct phases: initiation, implementation, and persistence. While this taxonomy offers a nuanced understanding of adherence, the definition of nonadherence as taking "less than 80% of prescribed doses" can complicate this framework.

This quantitative threshold may not fully capture the complexities inherent in each phase of adherence. For instance, a patient might initiate treatment but struggle with implementation or persistence due to various factors. Therefore, it is vital to interpret adherence not merely as a binary measure but as a dynamic process that reflects individual patient experiences and circumstances. This complexity underscores the necessity of

continuous monitoring, as it allows healthcare providers to identify specific challenges that patients may encounter at different stages of their medication regimen.

Secondly, different tools and measurements have been developed and validated in order to effectively and accurately assess adherence. Each has advantages and disadvantages that should be thoroughly taken into consideration when designing and choosing a suitable method [80-83]. No single measurement method can be regarded as the best available approach given the various patient-related factors. Hence, the use of multiple measurement methods of adherence is highly recommended [82-84]. The literature identifies three categories of adherence assessment, including (i) direct measures, such as blood serum levels, (ii) indirect measures such as pill counts, electronic monitoring, prescription refill rate, and (iii) subjective measures such as patients' and nurses' self-report adherence rating scales or interviews [80-83].

Additionally, it is important to involve the significant others of the patient both during and after hospitalisation. They could assist nurses in assessing patients and monitoring the medication intake by following up on them after hospitalisation. An important possible obstacle for MSM is related to the medication delivery. During hospitalisation, it is mandatory that the medication will be delivered by the hospital pharmacy; therefore, patients would receive medication from the present medicines formulary of that specific hospital. It is also a well-known problem in hospital pharmacies to make sure that medication arrived on time on the units. Hence, problems on stock shortages or rare medications were common [17, 85].

In addition, literature indicates the importance of a procedure including the medication logistic and delivery for every hospital or unit when self-managing medication.

Communication to the primary care

Literature showed that general practitioners in Flanders needed access to an up-to-date medication list and clear communication about somatic problems, such as abnormal blood results, with an active referral of the patient to the general practitioner. There was agreement between the physicians that major changes, problems or medication adjustments should always be communicated. In general, cooperation and communication between general practitioners and psychiatrists was perceived as being variable and dependent on the care professional or institutions involved [57]. To improve collaboration and communication between psychiatrists and general practitioners, the co-location of services or community liaison

services should be recommended. The development of multidisciplinary guidelines could promote better collaboration and task distribution, as well as shared patient records. In addition, enlarging nurses' tasks could increase the quality of care after hospitalisation, screening patients' MSM competences and follow-up after hospitalisation.

7.3.2. Implications for primary care

While the primary focus of this doctoral study was on MSM during hospitalization, the literature emphasizes broader challenges related to medication non-adherence that exacerbated during the transitions of care, particularly within primary care settings. This aligns with existing evidence highlighting the significant role of the primary care in addressing the non-adherence challenges, thereby informing the following recommendations.

Prevention for relapse

Primary care can ensure correct early diagnosis, treatment and referral for patients with severe mental disorders [23]. The general practitioner plays an essential role in the prevention of relapse and is often the first contact person in case of health-related problems and patient follow-up. Additionally, general practitioners reach a wide group including more complex or insecure target groups who have little or no access to more specialised healthcare services. Clinical reports of patients should be given to the general practitioner as well. In addition, the general practitioner is often more oriented outside the scope of mental healthcare, which can decrease stigma and promote patients' social integration. About 30% of the Belgian patients with mental health disorders is searching professional support [86, 87] of which 30% consults a general practitioner and 43% contacts a general practitioner and a psychiatrist. This implies that in 73% the general practitioner is involved in the detection, diagnosis or treatment of patients with mental health disorders [88].

The importance of outreach teams

About 50% of patients with severe mental disorders reported to have regular contacts with their general practitioner; hence suggesting that treatment by an outreach team can improve general practitioner involvement [89]. Outreach teams ought to proactively establish collaborations with general practitioners and primary care nurses. The incorporation of screening patients' MSM competences and subsequent follow-up should constitute a formal component of these collaborative efforts.

A majority (81%) of the patients with severe mental disorders in Flan-

ders were personally responsible for their medication management at home. Additionally, 15% were supported by the pharmacist; 13% by primary care home nurses and 8% by significant others. In 15% of the cases a combination of different possibilities was used [89].

7.3.3. Implications for future research and policy makers

Implications for research

Given that the initial phase of Participatory Action Research (PAR), 'Phase 1: Knowledge and Needs', has already been undertaken and fulfilled through the findings of this doctoral study, the next logical step is to advance this work by continuing with subsequent phases of PAR. This approach will ensure that the research remains grounded in the real-world needs and perspectives of the stakeholders involved.

Literature confirmed that action research is useful in any context that aims to improve aspects of health [90]. From a methodological perspective, it is crucial to emphasize that although there are different approaches to action research [91],the results of a recent systematic review indicated that in the field of mental health the most used method is PAR [90]. This could be attributed to the necessity of adopting a participatory approach, with researchers and stakeholders side by side to address a shared concern being the driver of the process of change [92]. Another noteworthy facet, from a methodological standpoint, was that most of the studies described the cyclical designs used which made it possible to elaborate on a classification of the common stages identified. Previous research delineated two primary focal points wherein the action research method was applied within the domain of mental health: enhancing patient-centred models of care and refining shared decision-making procedures [90].

We highly recommend the following steps in Participatory Action Research (PAR) to emphasise collaboration and active involvement of stakeholders in the research process with the aim of facilitating MSM implementation and promoting a process of collaborative enquiry [90, 92, 93]. PAR is a methodology that creates transformative change by actively engaging stakeholders and focusing on their attitudes. Research evidence indicates that PAR has the capacity to cultivate favourable attitudes, particularly concerning organizational citizenship, as evidenced in healthcare contexts. Moreover, its implementation has been associated with heightened perceptions of self-worth and professional competence among clinicians [90, 93].

Recently, three important key points to improve the effectiveness and

quality of the use of PAR in mental healthcare were revealed [94-96].

1. The perspective of all stakeholders should be incorporated throughout the research process, from design to the reporting of results. PAR includes the participation of all stakeholders and, therefore, incorporates a collaborative approach both in the problem identification and in the actions to foster change. In this regard, it facilitates heightened awareness among all stakeholders to become aware of the issue of interest, directly applying knowledge in practice and obtaining satisfaction and empowerment. Unfortunately, currently, in the context of mental healthcare, stakeholders are not representatively included in projects and all their phases.
2. A comprehensive description of the cycles and stages constituting the entire process is imperative, accompanied by a delineation of the objectives slated for accomplishment at each stage.
3. Clarity in reporting is essential to the knowledge generated and the change produced throughout the action research process.

We suggest a three-phase process to guide stakeholders in the improvement of MSM after hospitalisation [97]. PAR is uses throughout the three phases of knowledge and needs, intervention, and evaluation, complemented by quantitative assessments of MSM outcomes such as adherence to treatment. Firstly, measuring the number of patients who achieve medication adherence to the regimen as prescribed could be used to evaluate the effectiveness of a MSM intervention. It may, however, be more important to identify patients as involved stakeholders not achieving desired therapeutic outcomes and considering strategies to remove barriers that are preventing this in the future.

Phase 1: Knowledge and needs

In this doctoral study, we conducted the first phase. The aim of this phase was to map out and understand the needs and knowledge of all involved stakeholders, namely patients, mental healthcare providers, patients' significant others, pharmacists and primary care healthcare providers. This phase was intended to identify the needs, knowledge and current available resources.

Within this phase, we conducted the following methods:

1. Research consisting of reviewing our previous findings related to improve patients' MSM competences.
2. Semi-structured interviews with all involved stakeholders. The aim of

this phase is to understand the current experiences of stakeholders and tools used for supporting MSM and exploring elements that could inform the development of MSM.

Phase 2: Intervention

The aim of this phase is to develop and implement a MSM intervention to establish priorities for action that improve MSM.

Using the baseline understandings gathered from the previous phase, the research team can create several scenarios depicting stakeholders at high risk for possible problems and needs due to MSM after hospitalisation. A workshop with mixed groups of all stakeholders can review the scenarios. Each group will assign a scenario where they can create a description of a need, a tool or process that would enhance MSM as described in their scenario. We recommend a participatory, learning and action (PLA) approach to the intervention would be an ideal structure [98-100]. PLA is a specific approach to community interventions that fosters stakeholder engagement in the identification of problems and threats to their health, the design and implementation of solutions to tackle these problems, and reflecting on their success (Fig 7.1). Incorporating theoretical frameworks, such as the COM-B model [107] and the MRC framework [108], can sig-

Figure 7.1: Participatory, learning and action (PLA) approach.

nificantly enhance the effectiveness of this intervention phase. The COM-B model can guide the identification of specific barriers and facilitators affecting patients' capability, opportunity, and motivation regarding MSM, allowing for a more tailored intervention design. The MRC framework can function as a comprehensive guide for the systematic development (and evaluation) of the MSM intervention, facilitating the integration of evidence-based practices and the implementation of continuous feedback mechanisms to enhance the intervention's effectiveness.

Phase 3: Evaluation

The evaluation phase involves reflection, analysis, and registration to understand how the intervention has contributed to the desired change and to inform improvements and future actions [101]. We suggest facilitating structured reflection sessions with the participants to gather their insights, experiences, and feedback on the entire research process, from problem identification to action implementation. The predetermined outcomes on the MSM intervention will be evaluated. We highly recommend to assess the degree to which the whole research process has contributed to the empowerment and capacity building of the participants. This could involve changes in knowledge, medication self-management skills, and confidence among individuals. Additionally, to the identification of possible areas where further empowerment or capacity building may be needed. The involvement of engaged stakeholders is recommended in the decision-making about the next steps, ensuring their ongoing involvement in the process.

Implications for policymakers

The majority of patients with severe mental disorders retain the capacity to make decisions about their treatment, whereas up to a third of non-psychiatric patients do not [22, 25, 26, 102]. Having a comprehensive framework for monitoring and evaluating quality indicators of healthcare services would provide an integrated framework linking service data collection with national data sets such as relapse rates and medication non-adherence. Implementing of these two quality indicators will improve the quality of care (e.g. more evidence-base work, by improved enhancing partnership throughout multidisciplinary teams, etc.) and may serve as indicators for financing.

Additionally, healthcare providers stressed the need for multidisciplinary teams and intersectoral collaborations [103]. A majority of the patients with SSD or BD receive care from multiple sources that are often not

coordinated, which can be confusing for both the patient and the healthcare providers. Mental health care should also be tailored to a patients' needs, however, healthcare providers admitted that in practice they are too often bound by non-flexible procedures and trajectories. Healthcare providers stated that currently far too little is done about prevention, partly because the need for curative care is high and budgets and time are limited [23, 103, 104]. Additionally, the needs for continuity of care and recovery- oriented care were stressed. For patients who are hard to reach or avoid mental health care, healthcare providers consider more primary care through outreach teams is needed [103]. Although outreach teams are still being developed in Belgium, literature indicates this as a good and promising practice if its capacity is further increased [89, 103]. A multidisciplinary guideline tailored to this population and to the context of Belgian healthcare can be valuable in supporting healthcare providers. Recent literature revealed the importance of efficient interdisciplinary care pathways and referral options, from both primary and secondary care [105]. We propose that the role of nurses' responsibilities be broadened and defined more specifically within healthcare plans or protocols. In Belgium, recently, nurses have been working more commonly in general practices. Research revealed several positive effects of the implementation of primary care nurses in the medication management of patients with severe psychiatric disorders, after receiving sufficient training and education [106].

7.4. General conclusion

This thesis provides a synthesis of the effectiveness of interventions improving medication adherence in patients with SSD or BD. As the most efficacious intervention, a MSM intervention was identified. MSM during hospitalisation offers patients the opportunity to train their MSM skills and facilitates assistance when needed. Additionally, MSM aims to improve patient understanding of their medicines, allow healthcare providers to assess adherence, improve patient's confidence, minimise medication problems when patients are discharged and allows the patient to maintain their independence. MSM in hospitalised patients with SSD or BD is currently not widely implemented in Flemish psychiatric hospitals. However, stakeholders are willing to support the implementation of MSM if the prerequisites are fulfilled. Patients' individual MSM abilities should be evaluated on a regular basis during hospitalization, 2) patients should be motivated to take their medication correctly and to understand the benefits of their medication, 3) Additionally, patients need to show to be willing to facilitate

and perform MSM in daily practice and 4) patients should be willing to train their MSM skills. In addition, the minority of the hospital units have an available procedure and screening tool to assess the MSM competences of the patients. The results of this study confirmed the need for a unified policy and a MSM procedure.

7.5. References

1. World Health Organization. The global economic burden of non-communicable diseases. World Economic Forum, Geneva, Switzerland. Mental health atlas. 2011.
2. Kebede D, Alem A, Shibire T, Deyassa N, Negash A, Beyero T, et al. Symptomatic and functional outcome of bipolar disorder in Butajira, Ethiopia. J Affect Disord. 2006;90(2-3):239-49.
3. Robinson D, Woerner MG, Alvir JM, Bilder R, Goldman R, Geisler S, et al. Predictors of relapse following response from a first episode of schizophrenia or schizoaffective disorder. Arch Gen Psychiatry. 1999;56(3):241-7.
4. Pitanupong J, Ratanaapiromyakij P, Teetharatkul T. Factors Associated with Low Relapse Rates of Schizophrenia in Southern Thailand: A University Hospital-Based Study; Research Square: Durham, NC, UAS. 2021.
5. Sendt KV, Tracy DK, Bhattacharyya S. A systematic review of factors influencing adherence to antipsychotic medication in schizophrenia-spectrum disorders. Psychiatry Res. 2015;225(1-2):14-30.
6. Xiao J, Mi W, Li L, Shi Y, Zhang H. High relapse rate and poor medication adherence in the Chinese population with schizophrenia: results from an observational survey in the People's Republic of China. Neuropsychiatr Dis Treat. 2015;11:1161–7.
7. Xiao J, Mi W, Li L, Shi Y, Zhang H. High relapse rate and poor medication adherence in the Chinese population with schizophrenia: results from an observational survey in the People's Republic of China. Neuropsychiatr Dis Treat. 2015;11:1161-7.
8. Rzewuska M. Drug maintenance treatment compliance and its correlation with the clinical picture and course of schizophrenia. Prog Neuro-Psychopharmacol Biol Psychiatry. 2002;26:811–4.
9. Broadhead A. Self-administration of medicines by adult patients policy in English NHS hospitals. 2012.
10. Flint H. Self-administration of Medicines (SAM) UHL Policy in English NHS hospitals. 2023.
11. West S. Policy for Self Administration of Medicine on Solent NHS Trust Inpatient Wards. 2016.
12. Joint Commission International accreditation standarts for hospitals-standarts. Oak Brook. 2013;5th edition.
13. Richardson SJ, Brooks, H. L., Bramley, G., & Coleman, J. J. Evaluating the effectiveness of self-administration of medication (SAM) schemes in the hospital setting: a systematic review of the literature. PLoS One. 2014;9(12).
14. Wright J, Emerson A, Stephens M, & Lennan E. Hospital inpatient self-administration of medicine programmes: a critical literature review. Pharm World Sci. 2006;28(3):140-51.
15. Taylor M, Hajek V. Self-medication on a rehabilitation unit. Archives of Physical Medicine and Rehabilitation 6. 1984: 612–3.
16. Tran T, Taylor SE, Woodward MC. A self-administration of medications program to identify and address potential barriers to adherence in elderly patients. Annals of Pharmacotherapy. 2011;45:201–6.

17. Vanwesemael T, Boussery K, Manias E, Petrovic M, Fraeyman J, Dilles T. Self-management of medication during hospitalisation: Healthcare providers' and patients' perspectives. J Clin Nurse. 2018;27 (3-4): 753-68.

18. Moncrieff J, Azam K, Johnson S, Marston L, Morant N, Darton K, et al. Results of a pilot cluster randomised trial of the use of a Medication Review Tool for people taking antipsychotic medication. BMC Psychiatry. 2016;16:205.

19. Zisman-Ilani Y, Shern D, Deegan P, Kreyenbuhl J, Dixon L, Drake R. Continue, adjust, or stop antipsychotic medication: developing and user testing an encounter decision aid for people with first-episode and long-term psychosis. BMC Psychiatry. 2018;18:12.

20. Pelto-Piri V, Engström K, I E. Paternalism, autonomy and reciprocity: ethical perspectives in encounters with patients in psychiatric in-patient care. BMC Medical Ethics 2013;14(49).

21. Murray A. The implementation of a self-administration of medication programmes within Older Persons Mental Health. Journal of Psychiatriac Mental Health Nursing. 2011;18(2).

22. Okai D, Owen G, McGuire H, Singh S, Churchill R, M H. Mental capacity in psychiatric patients: Systematic review. The British Journal of Psychiatry. 2007;191(4):7.

23. Mistiaen P, Cornelis J, Detollenaere J, Devriese S, Farfan-Portet M, Ricour C. Organisation of mental health care for adults in Belgium. Health Services Research (HSR) Brussels: Belgian Health Care Knowledge Centre (KCE). KCE Reports. 2019;318.

24. Høyer G, Kjellin L, Engberg M, Kaltiala-Heino R, Nilstun T, Sigurjónsdóttir M, et al. Paternalism and autonomy: a presentation of a Nordic study on the use of coercion in the mental health care system. International Journal of Law and Psychiatry. 2002;25(2).

25. Spencer B, Shields G, Gergel T, Hotopf M, Owen G. Diversity or disarray? A systematic review of decision-making capacity for treatment and research in schizophrenia and other non-affective psychoses. Psychol Med. 2017;47(11):22.

26. Calcedo-Barba A, Fructuoso A, Martinez-Raga J, Paz S, Sánchez de Carmona M, E V. A meta-review of literature reviews assessing the capacity of patients with severe mental disorders to make decisions about their healthcare. BMC Psychiatry. 2020;June 30(20).

27. Charles C, Gafni A, T. W. Decision-making in the physician-patient encounter: revisiting the shared treatment decision-making model. Soc Sci Med. 1999;49:61.

28. Zisman-Ilani Y, Barnett E, Harik J, Pavlo A, M. OC. Expanding the concept of shared decision making for mental health: systematic search and scoping review of interventions. Mental Health Review Journal. 2017;22:14.

29. Towle A, Godolphin W. Framework for teaching and learning informed shared decision making. BMJ. 1999;18;319(7212):5.

30. Orem D. Nursing: Concepts of practice (6th edition). St. Louis, MO: Mosby. 2001.

31. Meleis I. Theoretical Nursing : Development & Progress (5th ed.): Philadelphia : Wolters Kluwer. 2012.

32. Raue P, Schulberg H, Heo M, Klimstra S, Bruce M. Patients' depression treatment preferences and initiation, adherence, and outcome: a randomized primary care study. Psychiatric Service. 2009;60(3).

33. Stewart M. Effective physician-patient communication and health outcomes: a review. CMAJ. 1995;May 1;152(9):33.

34. Stewart M, Brown J, Boon H, Galajda J, Meredith L, Sangster M. Evidence on patient-doctor communication. Cancer Prevention Control. 1999;3(1):5.

35. Park S, Derman M, Dixon L, Brown C, Klingaman E, Fang L, et al. Factors associated with shared decision-making preferences among veterans with serious mental illness. Psychiatric Service. 2014;65(12).

36. Velligan D, Roberts D, Sierra C, Fredrick M, Roach M. What Patients With Severe Mental Illness Transitioning From Hospital to Community Have to Say About Care and Shared Decision-Making. Issues in Mental Health Nursing. 2016;Jun;37(6).

37. Aoki Y, Furuno T, Watanabe K, Kayama M. Psychiatric outpatients' experiences with shared decision-making: A qualitative descriptive study. Journal of Communication in Healthcare. 2019a;12(2):9.

38. Aoki Y, Takaesu Y, Inoue M, Furuno T, Kobayashi Y, Chiba H, et al. Seven-day shared decision making for outpatients with first episode of mood disorders among university students: A randomized controlled trial. Psychiatric research. 2019b;281.

39. Duncan E, Best C, Hagen S. Shared decision making interventions for people with mental health conditions. Cochrane Database of Systematic Reviews. 2010;20(1).

40. LeBlanc A, Herrin J, Williams M, Inselman J. Shared Decision Making for Antidepressants in Primary Care: A Cluster Randomized Trial. JAMA Intern Med. 2015;175(11).

41. Lazcano-Ponce E, Angeles-Llerenas A, Rodríguez-Valentín R, Salvador-Carulla L, Domínguez-Esponda R, Astudillo-García C, et al. Communication patterns in the doctor– patient relationship: evaluating determinants associated with low paternalism in Mexico. BMC Medical Ethics. 2020;21(125).

42. Loots E, Van Rompaey B, Morrens M, Dilles T. Medicatie zelfmanagement in Vlaamse psychiatrische ziekenhuizen: Een prevalentiestudie bij gehospitaliseerde patiënten met een schizofrenie spectrum of bipolaire stoornis. Nursing. 2023;38(2):14-21

43. Schirmer UB, Steinert T, Flammer E, Borbe R. Skills-based medication training program for patients with schizophrenic disorders: a rater-blind randomized controlled trial. Patient Prefer Adherence. 2015;9:9.

44. Beveridge A. R.D. Laing Revisited. Psychiatric Bulletin. 1998;22(7).

45. Stroup TS, Gray N. Management of common adverse effects of antipsychotic medications. World Psychiatry. 2018;17(3):341-56.

46. Loots E, Dilles T, Van Rompaey B, Morrens M. Attitudes of patients with schizophrenia spectrum or bipolar disorders towards medication self-management during hospitalisation. Journal of Clinical Nursing. 2023;0536.

47. Moncrieff J, Cohen D, Porter S. The psychoactive effects of psychiatric medication: the elephant in the room. J Psychoactive Drugs. 2013;45(5):409-15.

48. MacKenzie NE, Kowalchuk C, Agarwal SM, Costa-Dookhan KA, Caravaggio F, Gerretsen P, et al. Antipsychotics, Metabolic Adverse Effects, and Cognitive Function in Schizophrenia. Front Psychiatry. 2018;9:622.

49. Hirsch L, Yang J, Bresee L, Jette N, Patten S, Pringsheim T. Second-Generation Antipsychotics and Metabolic Side Effects: A Systematic Review of Population-Based Studies. Drug Saf. 2017;40(9):771-81.

50. Lincoln TM, Lüllmann E, Rief W. Correlates and long-term consequences of poor insight in patients with schizophrenia. A systematic review. Schizophr Bull. 2007;33(6):1324-42.

51. Amador XF, Flaum M, Andreasen NC, Strauss DH, Yale SA, Clark SC, et al. Awareness of illness in schizophrenia and schizoaffective and mood disorders. Arch Gen Psychiatry. 1994;51(10):826-36.

52. Jablensky A, Sartorius N, Ernberg G, Anker M, Korten A, Cooper JE, et al. Schizophrenia: manifestations, incidence and course in different cultures. A World Health Organization ten-country study. Psychol Med Monogr Suppl. 1992;20:1-97.

53. Goodman C, Knoll G, Isakov V, Silver H. Insight into illness in schizophrenia. Compr Psychiatry. 2005;46(4):284-90.

54. David AS. Insight and psychosis. Br J Psychiatry. 1990;156:798-808.

55. Mintz AR, Dobson KS, Romney DM. Insight in schizophrenia: a meta-analysis. Schizophr Res. 2003;61(1):75-88.

56. Chandra IS, Kumar KL, Reddy MP, Reddy CM. Attitudes toward Medication and Reasons for Non-Compliance in Patients with Schizophrenia. Indian J Psychol Med. 2014;36(3):294-8.

57. Martens N, De Haeck E, Van De Vondel E, Destoop M, Catthoor K, Dom G, et al. Physical Healthcare for People with a Severe Mental Illness in Belgium by Long-Term Community Mental Health Outreach Teams: A Qualitative Descriptive Study on Physicians', Community Mental Health Workers' and Patients' Perspectives. Int J Environ Res Public Health. 2023;20(1).

58. Doane MJ, Bessonova L, Friedler HS, Mortimer KM, Cheng H, Brecht T, et al. Weight gain and comorbidities associated with oral second-generation antipsychotics: analysis of real-world data for patients with schizophrenia or bipolar I disorder. BMC Psychiatry. 2022;22(1):114.

59. Haddad PM, Wieck A. Antipsychotic-induced hyperprolactinaemia: mechanisms, clinical features and management. Drugs. 2004;64(20):2291-314.

60. Grande I, Berk M, Birmaher B, Vieta E. Bipolar disorder. Lancet. 2016;387(10027):1561-72.

61. Doane MJ, Sajatovic M, Weiden PJ, O'Sullivan AK, Maher S, Bjorner JB, et al. Antipsychotic Treatment Experiences of People with Schizophrenia: Patient Perspectives from an Online Survey. Patient Prefer Adherence. 2020;14:2043-54.

62. Bessonova L, Velligan DI, Weiden PJ, O'Sullivan AK, Yarlas A, Bayliss M, et al. Antipsychotic treatment experiences of people with bipolar I disorder: patient perspectives from an online survey. BMC Psychiatry. 2020;20(1):354.

63. Kahn RS, Fleischhacker WW, Boter H, Davidson M, Vergouwe Y, Keet IP, et al. Effectiveness of antipsychotic drugs in first-episode schizophrenia and schizophreniform disorder: an open randomised clinical trial. Lancet. 2008;371(9618):1085-97.

64. Doane MJ, Raymond K, Saucier C, Bessonova L, O'Sullivan AK, White MK, et al. Unmet needs with antipsychotic treatment in schizophrenia and bipolar I disorder: patient perspectives from qualitative focus groups. BMC Psychiatry. 2023;23(1):245.

65. Loots E, Leys J, Proost S, Morrens M, Glazemakers I, Dilles T, Van Rompaey B. Medication Self-Management in Hospitalised Patients with Schizophrenia or Bipolar Disorder: The Perceptions of Patients and Healthcare Providers. . Int J Environ Res Public Health 2022, 19, 4835 https://doiorg/103390/ijerph19084835. 2022.

66. FOD. Public Health and Family, personal communication. 2015.

67. University PH. Self-administration of medicine policy in English NHS hospitals. 2023.

68. Vanwesemael T. Proefschrift voorgelegd tot het behalen van de graad van Doctor in de Medische Wetenschappen aan de Universiteit Antwerpen. In: Faculteit geneeskunde en gezondheidswetenschappen. Universiteit Antwerpen. 2018:95-109.

69. Manias E, Beanland C, Riley R, Baker L. Self-administration of medication in hospital: patients' perspectives. J Adv Nurs. 2004;46 (2):194-203.

70. Loots E, Goossens E, Vanwesemael T, Morrens M, Van Rompaey B, Dilles T. Interventions to Improve Medication Adherence in Patients with Schizophrenia or Bipolar Disorders: A Systematic Review and Meta-Analysis. International Journal of Environmental Research and Public Health. 2021;18.

71. Fenton, D. Simplifying the system: Assessing drug administration methods. Professional Nurse: 315–317. 1995.

72. Lowe C RD, Courtney EA, Purvis J, Teale C. Effects of self-medication programme on knowledge of drugs and compliance with treatment in elderly patients. British Medical Journal. 1995;310:1229–31.

73. Dijkstra N, Sino C, Schuurmans M, Schoonhoven L, Heerdink E. Medication self-management: Considerations and decisions by older people living at home. Research in Social and Administrative Pharmacy. 2022;18(3):2410-23.

74. Anderson J, Manias E, Kusljic S, Finch S. Testing the validity, reliability and utility of the Self-Administration of Medication (SAM) tool in patients undergoing rehabilitation. Res Social Adm Pharm 10 (1), 204-216. 2014.

75. Manias E, Beanland CJ, Riley R.G., Hutchinson, A.M. Development and validation of the self-administration of medication tool. Ann Pharmacother 40 (6), 1064-1073. 2006.

76. Dowrick C, Gask L, Edwards S, Aseem S, Bower P, Burroughs H, et al. Researching the mental health needs of hard-to-reach groups: managing multiple sources of evidence. BMC Health Serv Res. 2009;9:226.

77. Woodall A, Morgan C, Sloan C, Howard L. Barriers to participation in mental health research: are there specific gender, ethnicity and age related barriers? BMC Psychiatry. 2010;10:103.

78. McEvoy JP. Risks versus benefits of different types of long-acting injectable antipsychotics. J Clin Psychiatry. 2006;67 Suppl 5:15-8.

79. Lieberman JA, Stroup TS, McEvoy JP, Swartz MS, Rosenheck RA, Perkins DO, et al. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. N Engl J Med. 2005;353(12):1209-23.

80. Anghel LA, Farcas AM, Oprean RN. An overview of the common methods used to measure treatment adherence. Med Pharm Rep. 2019;92(2):117-22.

81. Farris KB, Phillips BB. Instruments assessing capacity to manage medications. Ann Pharmacother. 2008;42(7):1026-36.

82. Kwan YH, Weng SD, Loh DHF, Phang JK, Oo LJY, Blalock DV, et al. Measurement Properties of Existing Patient-Reported Outcome Measures on Medication Adherence: Systematic Review. J Med Internet Res. 2020;22(10):e19179.

83. Lam WY, Fresco P. Medication Adherence Measures: An Overview. Biomed Res Int. 2015;2015:217047.

84. Loots E, Goossens E, Vanwesemael T, Morrens M, Van Rompaey B, Dilles T. Interventions to Improve Medication Adherence in Patients with Schizophrenia or Bipolar Disorders: A Systematic Review and Meta-Analysis. Int J Environ Res Public Health 2021, 18, 10213 https://doiorg/103390/ijerph181910213. 2021.

85. Preece DP, R. Tthe problem of medicines shortages in hospitals across Europe: The European Association of Hospital Pharmacists (EAHP) survey. Eur J Hosp Pharm Sci Pract 21, A174–A175. 2014.

86. Alonso J, Angermeyer M, Bernert S, Bruffaerts R, Brugha T, Bryson H. Prevalence of mental disorders in Europe: results from the European Study of the Epidemiology of Mental Disorders 29 (ESEMeD) project. Acta Psychiatrica Scandinavica. 2004;420.

87. Alonso J, Ferrer M, Romera B, Vilagut G, Angermeyer M, Bernert S. The European Study of the Epidemiology of Mental Disorders (ESEMeD/MHEDEA 2000) project: rationale and methods. Int J Methods Psychiatr Res. 2002;11(2).

88. De Lepeleire J. De bijdrage van huisartsgeneeskunde in de geestelijke gezondheidszorg. Tijdschrift voor Geneeskunde. 2010;66(7):21.

89. Martens N, Destoop M, Dom G. Physical Healthcare, Health-Related Quality of Life and Global Functioning of Persons with a Severe Mental Illness in Belgian Long-Term Mental Health Assertive Outreach Teams: A Cross-Sectional Self-Reported Survey. Int J Environ Res Public Health. 2022;19(9).

90. Moreno-Poyato AR, Subias-Miquel M, Tolosa-Merlos D, Ventosa-Ruiz A, Pérez-Toribio A, El Abidi K, et al. A systematic review on the use of action research methods in mental health nursing care. J Adv Nurs. 2023;79(1):372-84.

91. Rowell L, Bruce C, Shosh J, Riel M. The Palgrave international handbook of action research. Palgrave Macmillan US. 2017.

92. Kemmis S, Mctaggart R. Participatory action research. In Y. S. L. Norman & K. Denzin (Eds.), Strategies of qualitative inquiry (3rd ed., pp. 271–330). Sage Publications. 2008.

93. Cordeiro L, Soares CB. Action research in the healthcare field: a scoping review. JBI Evidence Synthesis. 2018;16(4):1003-47.

94. Abayneh S, Lempp H, Hanlon C. Participatory action research to pilot a model of mental health service user involvement in an Ethiopian rural primary healthcare setting: study protocol. Res Involv Engagem. 2020;6:2.

95. Chen HT, Pan H-LW, Morosanu L, Turner N. Using Logic Models and the Action Model/Change Model Schema in Planning the Learning Community Program: A Comparative Case Study. Canadian Journal of Program Evaluation. 2018;33(1):49-68.

96. Trickett E, Rasmus S, Allen J. Intervention fidelity in participatory research: a framework. Educational Action Research. 2019;28:1-14.

97. Burgess R, Dedios Sanguineti MC, Maldonado-Carrizosa D, Fonseca L, Vera San Juan N, Lucumí D, et al. Using participatory action research to reimagine community mental health services in Colombia: a mixed-method study protocol. BMJ Open. 2022;12(12):e069329.

98. Fottrell E, Jennings H, Kuddus A, Ahmed N, Morrison J, Akter K, et al. The effect of community groups and mobile phone messages on the prevention and control of diabetes in rural Bangladesh: Study protocol for a three-arm cluster randomised controlled trial. Trials. 2016;17.

99. Harris-Fry H, Azad K, Younes L, Kuddus A, Shaha S, Nahar T, et al. Formative evaluation of a participatory women's group intervention to improve reproductive and women's health outcomes in rural Bangladesh: A controlled before and after study. Journal of epidemiology and community health. 2016;70.

100. MacFarlane A, O'Donnell K, Mair F, de Brún M, de Brún T, Spiegel W, et al. REsearch into implementation STrategies to support patients of different ORigins and language background in a variety of European primary care settings (RESTORE): Study protocol. Implementation science : IS. 2012;7:111.

101. Mackenzie J, Tan PL, Hoverman S, C B. The Value and Limitations of Participatory Action Research Methodology. Journal of Hydrology. 2012;474.

102. Raymont V, Bingley W, Buchanan A. Prevalence of mental incapacity in medical inpatients and associated risk factors: cross-sectional study. Lancet. 2004;364:6.

103. Rens E, Dom G, Remmen R, Michielsen J, Van den Broeck K. Unmet mental health needs in the general population: perspectives of Belgian health and social care professionals. Int J Equity Health. 2020;19(1):169.

104. Cornelis J, Detollenaere J, Devriese S, Mistiaen P, Ricour C. Acceptability of possible recommendations for future mental health care organisation in Belgium: a stakeholder survey. Organisation of mental health care for adults in Belgium. Health Services Research (HSR) Brussels: Belgian Health Care Knowledge Centre (KCE). 2019;318.

105. Firth J, Siddiqi N, Koyanagi A, Siskind D, Rosenbaum S, Galletly C, et al. The Lancet Psychiatry Commission: a blueprint for protecting physical health in people with mental illness. Lancet Psychiatry. 2019;6(8):675-712.

106. Bury D, Hendrick D, Smith T, Metcalf J, Drake RE. The Psychiatric Nurse Care Coordinator on a Multi-disciplinary, Community Mental Health Treatment Team. Community Ment Health J. 2022;58(7):1354-60.

107. Michie, S., van Stralen, M.M. & West, R. The behaviour change wheel: A new method for characterising and designing behaviour change interventions. *Implementation Sci* 6, 42 (2011).

108. Skivington K, Matthews L, Simpson SA, Craig P, Baird J, Blazeby JM, Boyd KA, Craig N, French DP, McIntosh E, Petticrew M, Rycroft-Malone J, White M, Moore L. A new framework for developing and evaluating complex interventions: update of Medical Research Council guidance. BMJ. 2021 Sep 30;374:n2061.

Appendix

Supplementary Table S1: Characteristics of included studies

Appendix: Contents

Aho-Mustonen 2011

Methods	Study design: Exploratory RCT Methods of randomisation: Block randomisation. Follow-up: Baseline and 3 months post treatment. Setting: An inpatient psychiatric hospital in Finland. Date it was conducted: Participants were recruited in January 2006. No specific information. Source of funding: Not reported. Conflict of interest: Not reported.	
Participants	Inclusion/exclusion criteria: All forensic patients with a primary diagnosis of schizophrenia of schizoaffective disorder were candidates for inclusion. Exclusion criteria were evidence of organic brain syndrome, primary diagnosis of delusional disorder and earlier participation in a psychoeducational group. Sample size: 39 (IG=19, TAU=20) Gender: 35 (90%) were men. Age: The mean age was 38.6 years (SD 14.0) in the intervention group and 40.6 (SD 8.5) in the control group.	
Interventions	Type of intervention: Educational. The psychoeducation programme (intervention group) consisted of 8 group sessions which were conducted once a week; they were 45-50 minutes long (3-8 participants in each group).	
Outcomes	Primary outcome measured: (1) knowledge, (2) insight illness, (3) adherence, (4) drug attitude, (5) symptoms of mental disorder, (6) ward behaviour, (7) self-reported depressive symptoms, (8) self-esteem, (9) quality of life, (10) stigma The nursing staff assessed adherence at post-treatment and 3-month follow-up with the Compliance Rating Scale.	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Block randomisation was reported.
Allocation concealment (selection bias)	High risk	Patients were specifically asked not to tell the interviewer anything about their group allocation but two patients in condition did.
Blinding of participants and personnel (performance bias) all outcomes	High risk	Blinding of patients was not possible. Data collection blinding failed.
Blinding of outcome assessment (detection bias) all outcomes	Unclear risk	Insufficient information to permit clear judgement.
Incomplete outcome data (attrition bias) all outcomes	Low risk	No missing outcome data are reported. Three patients dropped out at 3 months follow-up. ITT analysis was performed.
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available. No adherence results were found in the text è only in a table.
Other bias	High risk	The risk may be explained by limited follow-up. Self-reported responses can be affected by desirability biases and the small sample size could increase the likelihood of a type II error and other bias.

Awan Riaz 2017

Methods	Study design: RCT Methods of randomisation: Randomisation was done using a computer-generated method. Follow-up: Baseline and 3 months. Setting: Inpatient psychiatric hospital in Pakistan. Date it was conducted: February 2015 – August 2015. Source of funding: Not reported. Conflict of interest: Not reported.	
Participants	Inclusion/exclusion criteria: Patients who fulfilled the ICD-10 diagnostic criteria for schizophrenia were included. Patients who were not able to respond or communicate and with any other psychiatric co morbidity like severe psychical problem were excluded. Sample size: 103 patients were recruited: 53 in the intervention group and 50 in the control group. Gender: 80 (78%) were men. Age: The mean age was 30.6 years (SD 9.5) in the intervention group and 30.4 (SD 9.4) in the control group.	
Interventions	Type of intervention: Educational. One session/month; during 3 months. The intervention had four parts, first part was about giving simple explanations of possible causal factors, second section focused on the nature of schizophrenia describing common symptoms and behaviours in terms of thinking, feelings and behaviour. The third section described the function of the relevant psychiatric services and the role of neuroleptic medication, fourth section was concerned with helping relatives to identify support services in terms of hospital and community resources available. The control group received the treatment provided by the psychiatrist in routine clinical care (antipsychotic medication).	
Outcomes	Primary outcome measured: Adherence. The Compliance Rating Scale was administered on baseline and on three-month follow-up to check the patient's adherence to treatment.	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation was reported.
Allocation concealment (selection bias)	Unclear risk	No information on concealment was reported.
Blinding of participants and personnel (performance bias) all outcomes	Unclear risk	No information on blinding was reported.
Blinding of outcome assessment (detection bias) all outcomes	Unclear risk	No information on blinding was reported.
Incomplete outcome data (attrition bias) all outcomes	High risk	Missing outcome data were reported. Seven participants were lost to follow-up in the intervention group and 14 participants in the control group. No information on dealing with missing data strategies was reported.

Selective reporting (reporting bias)	Unclear risk	The study protocol is not available. Limited results related to adherence.
Other bias	High risk	The risk may be explained by limited follow-up, self-reported responses can be affected by desirability biases and gender bias.

Barkhof 2013

Methods	Study design: RCT Methods of randomisation: Randomisation was done using a computer-generated cluster method. Follow-up: Baseline, 6 and 12 months. Setting: In- and outpatients in three mental health care institutions in Amsterdam. Date it was conducted: 2012 Source of funding: Dr. Paul Janssen Foundation. Conflict of interest: Not reported.	
Participants	Inclusion/exclusion criteria: All patients with a primary diagnosis of schizophrenia of schizoaffective disorder, an age of 18-65 years, experienced a recent (<1 year) psychotic relapse and/or a clinical deterioration, both the following nonadherence to antipsychotic treatment resulting in hospitalisation were candidates for inclusion. Exclusion criteria were an organic disease with a possible etiological relation to the psychotic disorder and/or a severe intellectual dysfunction. Sample size: 114 patients were recruited: 55 in the motivational interviewing group and 59 in the health education group. Gender: 91 (80%) were men. Age: The mean age was 37 years (SD 1.4) in the motivational interviewing group and 34.7 (SD 1.4) in the health education group.	
Interventions	Type of intervention: Behavioural versus educational. Motivational interviewing comprised 4 phases. The phases involved introduction and engagement; exploring attitudes and beliefs toward treatment, exploring patient's own personal goals and the "readiness for change". In the next phase, information was provided and ambivalences were amplified along which favourable attitudes and beliefs toward change were reinforced. The last phase was committed to evaluation and consolidation of the motivation to change. Health education comprised individual lectures on general health topics like food and physical exercise. Within a period of 26 weeks, participants were offered eight sessions of either motivation interviewing of health education. Less than five sessions were counted as a dropout. The sessions duration varied between 20 and 45 minutes.	
Outcomes	Primary outcome measured: Adherence. Medication adherence was assessed with the Medication Adherence Questionnaire (MAQ). Before starting the intervention, a baseline assessment was performed. Participants were interviewed again after the intervention was completed and after six-month follow-up.	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated cluster randomisation with blocks of codes for every 6 consecutive inclusions which were 1 by 1 revealed to the study coordinator was reported.

Allocation concealment (selection bias)	Low risk	Participants were allocated to either the motivational interviewing or the health education group by a computerised cluster randomisation program which were one by one revealed by the coordinating researcher. Patients were not informed about the intervention groups.
Blinding of participants and personnel (performance bias) all outcomes	Low risk	The psychologists, psychiatrics and community health nurses were blinded.
Blinding of outcome assessment (detection bias) all outcomes	Low risk	The assessors were blinded.
Incomplete outcome data (attrition bias) all outcomes	High risk	Missing outcome data were reported and were likely to be related to true outcome.
Selective reporting (reporting bias)	Low risk	The study protocol is not available but the authors are transparent in the abstract, results, discussion and conclusion concerning the results.
Other bias	High risk	Self-reported responses can be affected by desirability biases.

Bäuml 2016

Methods	Study design: RCT Methods of randomisation: Block randomisation. Follow-up: 24 months and 84 months. Setting: Three psychiatric hospitals in Munich, Germany. Date it was conducted: 1990 - 1994. Source of funding: The first two years of the study were supported by a grant from the Bundesministerium für Forschung und Technologie (BMFT); the long-term follow-up was supported by a grant from the DORIST- Fond, in Kreuzlingen, Switzerland. Conflict of interest: Not reported.
Participants	Inclusion/exclusion criteria: The inclusion criteria were patients with a schizophrenic or schizoaffective disorder (DSM III-R: 295.10-94; 297.10/ International Classification of Diseases (ICD)-10: F 20, F22, F25), an indication of antipsychotic relapse prevention for a period of at least 12 months, age between 18 and 65 years, patients' acceptance of an outpatient treatment in the study centre and patients' agreement to involve a key relative or a friend. *Exclusion Criteria were* a distance between home and hospital of more than 150 kilometres, less than 30 minutes contact per week with the key relative, drug addiction during the past six months prior to admis- sion, pregnancy, IQ < 80, insufficient knowledge of the German language and no remission of the psychotic symptoms during the last two years despite a sufficient therapy. Sample size: 41 (IG=21, TAU=20). Gender: In the intervention group were 48% men and in the control group 35%. Age: The mean age was 38 years (SD 7.9) in the intervention group and 41 (SD 9.4) in control group.

Interventions	Type of intervention: Educational. There were 4 weekly sessions of 60 minutes each; afterwards, 4 additional monthly sessions were held. Relatives were also invited to 8 weekly sessions, each lasting 90 minutes. The groups were headed by therapists who had not been involved in the routine treatment. In both settings the same psychoeducational modules were presented. Apart from improvement of coping by discussing similar experiences, considerable attention was paid to the interactive evaluation of illness relevant information. The take-home message of the psychoeducational program was: schizophrenic psychoses are provoked by biological factors in combination with psychosocial stress; therefore, they have to be treated with medication and psychotherapeutic interventions. Patients' empowerment can only be developed successfully on the basis of a sufficient medication and long-term psychosocial treatment elements. Above all, the patients were trained to report their side effects to their therapists immediately and to look together with them for the most suitable medication.
Outcomes	Primary outcome measured: (1) adherence; (2) type of medication; (3) mean number of consumed CPZ-units; (4) neuroleptic side effects of medication. Adherence was rated by the treating psychiatrists on a four-step ordinal scale (1 = very good/ 2 = good/ 3 = moderate/ 4 = bad). Plasma drug level measurements were performed in order to validate the psychiatrists' adherence ratings.

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Block randomisation was reported. The randomisation list was generated by computerised random sampling.
Allocation concealment (selection bias)	Unclear risk	No information on concealment was reported.
Blinding of participants and personnel (performance bias) all outcomes	Unclear risk	No information on blinding was reported.
Blinding of outcome assessment (detection bias) all outcomes	Unclear risk	No information on blinding was reported.
Incomplete outcome data (attrition bias) all outcomes	High risk	Missing outcome data were high (60 patients dropped out) and were likely to be related to true outcome.
Selective reporting (reporting bias)	Low risk	The study protocol is not available but it is clear that the published reports include all expected outcomes.
Other bias	Low risk	The small sample size could increase the likelihood of a type II error.

Beebe 2014

Methods	Study design: RCT Methods of randomisation: Ad random (using a table of random numbers to one of three groups). Follow-up: Baseline and 3 months. Setting: An outpatient community mental health centre in the Southeastern United States. Date it was conducted: Not reported. Source of funding: Not reported. Conflict of interest: The authors report no conflicts of interest.	
Participants	Inclusion/exclusion criteria: Inclusion criteria were age between 21-68 years, receiving outpatient care, chart diagnosis of schizophrenia or schizoaffective disorder and English speaking. Exclusion criteria were chart documentation of mental retardation or developmental delay, hearing loss prohibiting telephone communication or vision or dexterity problems prohibiting texting. Sample size: 30. Gender: 11 (37%) were men. Age: The mean age was 48.7 years (SD 11.6).	
Interventions	Type of intervention: Behavioural (electronic interventions). Three intervention arms: (1) weekly telephone-intervention only; (2) daily text messages only and (3) combination of weekly telephone interventions and daily text messages 1. Telephone call intervention: A weekly telephone call during three months with problem solving strategies (medication, appointments, symptoms, cravings) to provide weekly support. 2. Texting intervention: The participants in this group received a daily text message for three months. The topics are the same as the telephone call intervention. 3. Combined telephone intervention and texting intervention: Participants in this group received weekly phone calls and daily text messages as described in the telephone call and texting intervention for three months.	
Outcomes	Primary outcome measured: Adherence. A measure of adherence was generated by pill counts.	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Participants were randomly assigned (using a table of random numbers) to one of the three groups.
Allocation concealment (selection bias)	High risk	The principal investigator was blinded as to group assignment when conducting the baseline assessment. Afterwards the principal investigator was aware of the allocation because he was responsible for performing the intervention.
Blinding of participants and personnel (performance bias) all outcomes	Unclear risk	Insufficient information to permit clear judgement.
Blinding of outcome assessment (detection bias) all outcomes	Unclear risk	Insufficient information to permit clear judgement.

Incomplete outcome data (attrition bias) all outcomes	Low risk	Only 2 patients dropped out during the three months follow-up.
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available but the non-significant results were minimized and only the beneficial results were showed.
Other bias	High risk	The small sample size and low power could increase the likelihood of a type II error. The risk also may be explained by limited follow up.

Beebe 2016

Methods	Study design: RCT Methods of randomisation: Convenience sample. Follow-up: Baseline and 3 months. Setting: An outpatient community mental health centre in the Southeastern United States. Date it was conducted: Not reported. Source of funding: Agency for Healthcare Research and Quality. Conflict of interest: The authors report no conflicts of interest.	
Participants	Inclusion/exclusion criteria: Inclusion criteria were chart diagnosis of schizophrenia or schizoaffective disorder, not hospitalised for psychiatric illness within the past six months and English speaking. Exclusion criteria were a chart of diagnosis of coexisting mental retardation, neurological disorders or head injury. Sample size: 140 Gender: 80 (57%) were men. Age: The mean age was 46.1 years (SD 12.9).	
Interventions	Type of intervention: Behavioural (electronic interventions). Telephone call intervention: A weekly telephone call during three months with problem solving strategies (medication, appointments, symptoms, cravings) to provide weekly support.	
Outcomes	Primary outcome measured: (1) Medication adherence; (2) Schizophrenia symptoms The Medication Adherence Rating Scale was used to measure self-reported medication adherence.	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit clear judgement.
Allocation concealment (selection bias)	Unclear risk	No information on concealment was reported.
Blinding of participants and personnel (performance bias) all outcomes	Unclear risk	No information on blinding was reported.

Blinding of out-come assessment (detection bias) all outcomes	Unclear risk	No information on blinding was reported.
Incomplete outcome data (attrition bias) all outcomes	Unclear risk	No missing outcome data are reported.
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement due to a lack of details provided on the methodology and results.
Other bias	High risk	The risk may be explained by limited follow-up. Self-reported re-sponses can be affected by desirability biases.

Çetin 2018

Methods	Study design: RCT with pre and post-test Methods of randomisation: A simple random sampling. Follow-up: Not reported. Setting: Community Mental Health Centres (CMHC) located in Balıkesir and Eskişehir provincial centres, Turkey. Date it was conducted: February 2016 – May 2016. Source of funding: Not reported. Conflict of interest: Not reported.
Participants	Inclusion/exclusion criteria: The inclusion criteria were to be between 18 and 65 years of age, to be literate, to be open to communication and cooperation, to have been diagnosed with schizophrenia according to DSM-IV criteria for the last one year. Patients with acute exacerbations, active alcohol or psychoactive substance use, mental condition which makes impossible the communication and cooperation like mental retardation or de- mentia were excluded from the study. Sample size: 135 (IG=55, TAU=80). Gender: In the intervention group were 67% men and in the control group 69%.

Interventions	Type of intervention: Educational A total of 8 sessions were held twice a week on Mondays and Fridays so that home works and exercises could be done by the participants in the psychoeducation program. A total of 55 experimental group patients was divided into 8–12 people for psycho-education groups according to the session configuration of mindfulness therapy. Throughout the entire program, patients were provided with the opportunity to participate in psycho-therapy interactively in the form of questions and answers. Each session was held for a total of 70 min with a break of 10 min, divided into 2 with a 30 min interval taking into account the situation of the patients. During the entire psychoeducation program and after each session, counselling and support were provided by interviewing patients who had additional questions. In the study, the meditation techniques of the Mindfulness Therapy constituted the backbone/framework of the psychoeducation program and were used as a means to increase insight and medication adherence in patients. Body and breath, body scanning, mindfulness movement and three-minute respiration techniques were practiced during the psychoeducation program, practically every session in accordance with the researchers' directives. The body, breath, and three-minute respiration meditation were practiced while the patient was seated on the chair with comfortable clothes, the body scanning and mindfulness movement was performed on the yoga mattress. They were also asked to perform these techniques in the form of homework at home through a meditation CDs distributed by the researcher. By using these meditation techniques, it was aimed that the patients are able to focus their attention on the present moment, to observe their own experiences, bodies, emotions and thoughts internally, to behave unprejudiced and leisurely, to accept themselves as they are, to discover their own physical and spiritual boundaries, to recognize and describe the symptoms, process, treatment and effects on their lives of disease, and develop their ability to cope with the disease. In this way, it was aimed to in- crease the insight and medication adherence of the schizophrenic patients.
Outcomes	Primary outcome measured: (1) Insight; (2) Medication adherence The Morisky and Medication Adherence Scale were used to measure self-reported medication adherence.

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	A simple randomisation but not random allocation was reported.
Allocation concealment (selection bias)	Unclear risk	No information on concealment was reported.
Blinding of participants and personnel (performance bias) all outcomes	Unclear risk	No information on blinding was reported.
Blinding of outcome assessment (detection bias) all outcomes	Unclear risk	No information on blinding was reported.

Incomplete outcome data (attrition bias) all outcomes	High risk	Missing outcome data were reported and were likely to be related to true outcome. High drop-out rates and no information concerning how to deal with missing data.
Selective reporting (reporting bias)	Low risk	The study protocol is not available but it is clear that the published reports include all expected outcomes.
Other bias	High risk	The risk may be explained by the unclear follow-up and the self-reported assessment tool.

Chien Tong 2015

Methods	Study design: RCT Methods of randomisation: A set of computer-generated random numbers provided by an independent statistician. Follow-up: Baseline, immediately post intervention and 6 months post intervention. Setting: One Community Psychiatric Nursing Service. Date it was conducted: December 2012 – January 2014. Source of funding: Financial support by the Health and Medical Research Fund, Food and Health Bureau, the Government of Hong Kong. Conflict of interest: Not reported.
Participants	Inclusion/exclusion criteria: Patients were included if they were aged between 18 and 60 years, Hong Kong residents speaking in Mandarin or Cantonese, having a primary diagnosis of schizophrenia in the past five years and had poor adherence to medication. Exclusion criteria were those patients who had regular depot or intramuscular injections only, co-morbidities of learning disability, organic brain disease and/or cognitive impairments, previous participation in any medication management program and/or hostel residents supervised by mental health workers to take their medication. Sample size: 114 (IG=57, TAU=57). Gender: In the intervention group were 51% men and in the control group 53%. Age: The participants had a mean age of 28 to 29 years (range 18-49).
Interventions	Type of intervention: Behavioural. Motivational interviewing techniques concerning cognitive, motivational, insight inducing and behavioural training in 8 sessions during a four-month program. The first phase (two sessions) aimed to engage participants in addressing their needs for, and concerns with medication adherence, facilitating goal and action setting for changes in medication adherence. The second phase (three sessions) focused on education about the mental illness and its treatment and, then explored participants' strengths and barriers to adherence, assisting them in recognising social stigma and family support, and developing coping strategies in medication management over months. The third phase (three sessions) aimed to rationalize patient's beliefs and concerns, manage their perceived of experienced social stigma, and enhance family and social support networks, thus improving relapse prevention and integration into the community.
Outcomes	Primary outcome measured: (1) Medication adherence; (2) Symptom severity; (3) Insight into treatment; (4) Hospitalisation rate; (5) Functioning It is not clear which instrument was used. They reported only the measurement concerns a self-reported five-point Likert scale. The questions were based on the MARS, MAQ, DAI and CRS but it is unclear which questions were used.
Risk of bias	

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation was reported.
Allocation concealment (selection bias)	Low risk	Participants were allocated to either the motivational interviewing or the TAU group by a computerised cluster randomisation program which were one by one revealed by an independent statistician, who was blind to the patient list.
Blinding of participants and personnel (performance bias) all outcomes	Low risk	The psychiatrists and assessing nurses were blinded.
Blinding of outcome assessment (detection bias) all outcomes	Low risk	Research assistants and community nurses were blinded for outcome assessments.
Incomplete outcome data (attrition bias) all outcomes	Low risk	The attrition rate was 3.5% and balanced in numbers across groups with similar reasons for missing data. ITT analysis was performed.
Selective reporting (reporting bias)	Low risk	The study protocol is not available but it is clear that the published reports include all expected outcomes.
Other bias	Low risk	The risk may be explained by the unclear assessment tool.

Dahan 2016

Methods	Study design: RCT Methods of randomisation: Randomly assigned via lottery drawing. Follow-up: After the intervention. Setting: An active open unit in a Mental Health Centre in Tel-Aviv. Date it was conducted: January 2009 and April 2010. Source of funding: Not reported. Conflict of interest: Not reported.
Participants	Inclusion/exclusion criteria: Hospitalised patients diagnosed with schizophrenia and aged between 18 and 60 yrs. Sample size: 63 (IG=31, TAU=32). Gender: Twenty-four (80%) were men in each group. Age: The mean age was 36.1 years (SD 8.9) in the intervention group and 39.67 (SD 10.6) in control group.
Interventions	Type of intervention: Mixed The intervention combined psycho-education, cognitive-behavioural strategies and motivational interviewing. Each participant in the intervention group attended an average of 6 sessions spread over once to twice a week and lasting approximately 20-40 minutes. The sessions were one on one with the same nurse. 1. The psycho-education aimed to promote understanding of the disease process and improve attitude toward treatment. 2. The cognitive-behavioural strategies aimed problem solving techniques for increasing attention and decreasing forgetfulness. 3. Motivational interviewing aimed at exploring the patient's perspective on the illness and placing it into a coherent life narrative.

Outcomes	Primary outcome measured: (1) Medication adherence; (2) Drug attitude inventory The Visual Analog Scale for Assessing Treatment Compliance was used to measure self-reported medication adherence.	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	Randomly assigned via lottery drawing was reported. It was unclear how the lottery drawing was done.
Allocation concealment (selection bias)	Unclear risk	No information on concealment was reported.
Blinding of participants and personnel (performance bias) all outcomes	Unclear risk	No information on blinding was reported.
Blinding of outcome assessment (detection bias) all outcomes	Unclear risk	No information on blinding was reported.
Incomplete outcome data (attrition bias) all outcomes	Low risk	There was no drop-out.
Selective reporting (reporting bias)	Low risk	The study protocol is not available but it is clear that the published reports include all expected outcomes.
Other bias	High risk	The risk may be explained by the unclear follow-up. Self-reported responses can be affected by desirability biases.

Eker 2012

Methods	Study design: Semi-experimental study, pre and post-test with IG and CG. Methods of randomisation: Not reported. Follow-up: 2,5 months. Setting: University Hospital Mood Disorders Outpatient Clinic in Turkey. Date it was conducted: April 2009 – May 2009. Source of funding: No funding. Conflict of interest: No conflicts of interest.
Participants	Inclusion/exclusion criteria: Patients were included if they were having the diagnosis of Bipolar Affective Disorder, were able to learn the defined concepts in every learning activity and would stay calmly during the sessions. Sample size: 71 (IG=36, TAU=35). Gender: In the intervention group were 46% men and in the control group 47%. Age: The mean age was 34.6 years (SD 11.3) in the intervention group and 36.64 (SD 10.6) in control group.
Interventions	Type of intervention: Educational. The psycho-education program consisted of six sessions lasted 90-120 minutes, groups of 10-12 persons and were held once a week. In every session, learning objectives and aims were stated: interactive teaching methods like role playing, question and answers, discussion and presentation.

Outcomes	Primary outcome measured: Adherence. The Medication Adherence Rating Scale was used to measure self-reported medication adherence.	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No information on randomisation was reported.
Allocation concealment (selection bias)	Unclear risk	No information on concealment was reported.
Blinding of participants and personnel (performance bias) all outcomes	Unclear risk	No information on blinding was reported.
Blinding of outcome assessment (detection bias) all outcomes	Unclear risk	No information on blinding was reported.
Incomplete outcome data (attrition bias) all outcomes	Low risk	The drop-out rates were 5 patients in the IG and 3 patients in the CG. Two types of analysis were performed (1) analysis of completers only; (2) last observation carried forward (LOCF).
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available and not much results details provided.
Other bias	High risk	The risk may be explained by limited follow-up. Self-reported responses can be affected by desirability biases.

Ertem 2017

Methods	Study design: RCT Methods of randomisation: Randomisation (simple numbers table). Follow-up: Baseline, immediately post intervention, 3 and 6 months follow-up. Setting: University hospital psychiatry outpatient clinic in Turkey Date it was conducted: December 2014 – October 2015. Source of funding: No funding. Conflict of interest: There is no conflict of interest between the authors.
Participants	Inclusion/exclusion criteria: Patients were included if they were aged between 18 and 65 years, the diagnosis of schizophrenia, able to read and write Turkish, as were willing and able to be interviewed. Exclusion criteria were history of chronic physical disease, a history of substance use (except caffeine and nicotine) and a history of mental retardation. Sample size: 40 Gender: In the intervention group were 70% men and in the control group 50%. Age: The mean age was 43.2 years (SD 10.5) in the intervention group and 40.1 (SD 10.9) in control group.
Interventions	Type of intervention: Behavioural. The intervention program consists of 6 semi-structured, interconnected interviews. All the interviews were interconnected with themselves because of providing topic integrity. Each interview lasted 40-60 minutes on average and the process was completed in a total of 6 by weekly interviews.

Outcomes	Primary outcome measured: Adherence. The Morisky scale was used to measure self-reported medication adherence.	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomisation (simple numbers table) was reported.
Allocation concealment (selection bias)	Unclear risk	No information on concealment was reported.
Blinding of participants and personnel (performance bias) all outcomes	Unclear risk	No information on blinding was reported.
Blinding of outcome assessment (detection bias) all outcomes	Unclear risk	No information on blinding was reported.
Incomplete outcome data (attrition bias) all outcomes	Low risk	No missing outcome data are reported. ITT analysis were performed.
Selective reporting (reporting bias)	High risk	The study protocol is not available and risk for multiple testing.
Other bias	Low risk	Self-reported responses can be affected by desirability biases.

Guo 2015

Methods	Study design: RCT Methods of randomisation: 1:1 randomisation. Follow-up: 12 months. Setting: 10 clinical outpatient psychiatric clinics in China. Date it was conducted: 1 January 2005 – 31 October 2007. Source of funding: National Key Technologies R&D Program of China and National Natural Science Foundation of China. Conflict of interest: Funding organizations played no role in the design, conduct, analysis or interpretation of the research in any aspect of preparation or approval of the manuscript.
Participants	Inclusion/exclusion criteria: The inclusion criteria were aged 18 to 50 years, a diagnosis of schizophrenia or schizoaffective disorder within the past five years, living with family members who could be involved in the patient's care, Positive and Negative Syndrome Scale total score of 60 or less, receiving maintenance treatment with one antipsychotics. Patients were excluded if they were prescribed two or more antipsychotics or long-acting injectable antipsychotics, participating in other therapy programs, pregnant or diagnosed as having a serious and unstable medical condition. Sample size: 1268 (IG=633, TAU=635). Gender: In the intervention group were 344 (54%) men and in the control group 354 (56%). Age: The mean age was 26.1 years in the intervention group and 26.4 in control group.

Interventions	Type of intervention: Mixed. The intervention consists of psycho-education, family intervention, skills training and cognitive behaviour therapy administered during 48 group sessions. Participants were seen 12 times (once per month for 12 months), receiving each of the 4 group treatments on the same day, for a total of 48 one-hour sessions.
Outcomes	Primary outcome measured: (1) Relapse Secondary outcome measured: (1) Insight; (2) medication adherence; (3) Quality of life; (4) Social functioning. The psychiatrists assessed participants monthly for medication adherence on appointment adherence. It is unclear which instrument was used.

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit clear judgement.
Allocation concealment (selection bias)	Unclear risk	No information on concealment was reported. ((cfr. to be checked later in paper of 2007, not accessible on 16/12/2019).
Blinding of participants and personnel (performance bias) all outcomes	Low risk	The clinicians were blinded.
Blinding of outcome assessment (detection bias) all outcomes	Low risk	The assessors were blinded.
Incomplete outcome data (attrition bias) all outcomes	High risk	High drop-out rates. Only 60% of patients completed one year follow-up. No information provided about dealing with missing data.
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available and raw data results concerning the intervention improved adherence were unclear.
Other bias	Low risk	The risk may be explained by the unclear assessment tool.

Javadpour 2013

Methods	Study design: RCT Methods of randomisation: Randomly with equal sets of odd and even numbers in a sealed envelope and send to the researcher. Follow-up: 18 months (baseline, 6-8-12 months follow-up). Setting: Hospital in Shiraz, Iran. Date it was conducted: June 2010 – November 2011. Source of funding: Shiraz University of Medical Science. Conflict of interest: None declared.
Participants	Inclusion/exclusion criteria: Patients were included if they were having the diagnosis of Bipolar Affective Disorder, were aged between 18 and 60 and had a history of at least two episodes of relapse in the past two or three episodes in last five years. Sample size: 108 (IG=54, TAU=54). Gender: In the intervention were 22 and the control group were 20 men. Age: Not reported.

Interventions	Type of intervention: Educational. Participants in the intervention group received individual psycho-education. The program consisted of 8 sessions each consisting of a 50 min session per week including: understanding bipolar disorder and its aetiology, familiarisation with symptoms of mania and hypomania, understanding signs of depression and other episodes, awareness of causes and prognosis, education about the functions, types and adverse side effects of antimanic and antidepressant medications. Participants also received information about the risk of discontinuation of these medications, learning how to detect any future episodes of relapse as well as strategies and plans on which to base early detection of symptoms and for being self-directed towards new situations. After the sessions of face to face individual education, the intervention continued using scheduled monthly telephone contact to remind the participants of their next appointment. Each telephone contact consisted of a 10 min question and answer.
Outcomes	Primary outcome measured: (1) Quality of life; (2) Symptoms of relapse; (3) Medication adherence. The Medication Adherence Rating Scale was used to measure self-reported medication adherence.

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomly with equal sets of odd and even numbers in a sealed envelope and send to the researcher.
Allocation concealment (selection bias)	Unclear risk	No information on concealment was reported.
Blinding of participants and personnel (performance bias) all outcomes	High risk	The psychiatry resident could not be blinded because he performed the sessions. Blinding of patients is not possible.
Blinding of outcome assessment (detection bias) all outcomes	Low risk	The assessor was blinded.
Incomplete outcome data (attrition bias) all outcomes	High risk	High drop-out rates; 33% of the IG and 24% of the CG. No information on dealing with missing data strategies was reported.
Selective reporting (reporting bias)	Low risk	The study protocol is not available but it is clear that the published reports include all expected outcomes.
Other bias	Low risk	Self-reported responses can be affected by desirability biases.

Jones 2015

Methods	Study design: RCT Methods of randomisation: Randomised by an independent clinical trials unit. Follow-up: Baseline, 6, 12 and 15 months post intervention. Setting: Community mental health and outpatient clinics. Date it was conducted: 9 February 2011 – 19 January 2012. Source of funding: National Institute for Health Research, England. Conflict of interest: Not reported.

Participants	Inclusion/exclusion criteria: Patients were included if they were having the diagnosis of Bipolar Affective Disorder with onset in past five years, were aged between 18 and 65 years, sufficient understanding of written and spoken English in order to provide consent and engage with interviews and use the intervention. Exclusion criteria included: manic, hypomanic and depressed or mixed episode currently or in the past four weeks. Sample size: 67 (IG=34, TAU=33). Gender: In the intervention group 25 (76%) were female and 22 (64%) in the control group. Age: The mean age was 38.3 years (SD 12.8) in the intervention group and 39.9 (SD 10.4) in the control group.
Interventions	Type of intervention: Behavioural. The intervention group received an 18 hour delivered therapy over approximately 6 months at client's homes or mental health facilities, according to personal preference. Initial sessions were weekly and typically lasted 45-60 minutes. The following elements are included: meaning and relevance of diagnosis, identification of recovery-informed therapy goals, initial formulation of relationships between mood experiences and progress towards recovery goals, identification and application of CBT techniques to address and facilitate positive coping and considering of wider functioning issues in relation to recovery.
Outcomes	Primary outcome measured: (1) Level of recruitment in the trial; (2) Retention of patients into both study arms; (3) Adherence to the intervention; (4) Completion of the intervention. Secondary outcomes measured: (1) Bipolar relapse; (2) Observer-rated mood; (3) Recovery; (4) Clinical measures; (5) Medication adherence. The Stephenson Medical Adherence Questionnaire was used to measure self-reported medication adherence.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Individuals were randomised by an independent clinical trials unit with minimisation on the number of previous episodes, current mood symptoms and mania, all significant predictors of therapy outcome.
Allocation concealment (selection bias)	Low risk	Participants were allocated to either groups by an independent clinical trials unit.
Blinding of participants and personnel (performance bias) all outcomes	Low risk	The clinicians, researchers and patients were blinded.
Blinding of outcome assessment (detection bias) all outcomes	Low risk	The assessors were blinded. In total, 79% of pts had masked assessments throughout and 95% of all assessment sessions were confirmed as definitely masked.
Incomplete outcome data (attrition bias) all outcomes	Low risk	Recruitment and follow-up rates within 10% of pre-planned targets for 12 months follow-up was achieved. Missing data were assumed to be missing at random (ignorable) and automatically allowed for in fitting the random-effects or analysis of covariance models

Selective reporting (reporting bias)	Low risk	The study protocol is not available but it is clear that the published reports include all expected outcomes.
Other bias	High risk	The small sample size could increase the likelihood of a type II error. The risk also may be explained to Self-reported responses can be affected by desirability biases.

Kopelowicz 2012

Methods	Study design: RCT Methods of randomisation: Randomisation was done using a computer-generated method. Follow-up: Baseline, 4, 8, 12, 18 and 24 months. Setting: Two community mental health centres in Los Angeles, California. Date it was conducted: April 2003 – January 2007. Source of funding: National Institute of Mental Health (Dr. Kopelowicz). Conflict of interest: Not reported.	
Participants	Inclusion/exclusion criteria: Patients were included if they were aged between 18 and 50 years, the diagnosis of schizophrenia, spoke Spanish, had been without antipsychotic medication without medical authorisation for one continuous week in the month prior to study enrolment, lived with their family of origin and had least one family member willing to participate in the family treatment. Sample size: 174 (MFG-A=64, MFG-S=53, TAU=57). Gender: In the intervention groups 67% and 68% were men and in the control group 57% were men. Age: Not reported.	
Interventions	Type of intervention: Educational versus mixed intervention. Three arms: MFG-A (educational), MFG-S (mixed) and care as usual. The MFG-A was focusing on specific obstacles to maintaining medication adherence. The MFG-S consisted of 3 components: 3 sessions separately with each family, a one day (6 hour) multifamily educational workshops and multifamily group sessions. There were 24 sessions total spread over 12 months (twice monthly). The sessions consisted a formal discussion of the illness, discussing how schizophrenia had affected each of their lives and teaching problem-solving skills. Members were free to select any problem, regardless of its relevance to medication adherence.	
Outcomes	Primary outcome measured: Adherence. The psychiatrists assessed participants monthly for medication adherence on appointment adherence with a five point Likert scale. It is unclear which instrument was used.	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation was reported.
Allocation concealment (selection bias)	Unclear risk	No information on concealment was reported.
Blinding of participants and personnel (performance bias) all outcomes	Unclear risk	No information on blinding was reported.

Blinding of outcome assessment (detection bias) all outcomes	Low risk	The research assistant was blinded for the outcome assessment.
Incomplete outcome data (attrition bias) all outcomes	High risk	Missing outcome data was 26% immediately after the baseline assessments.
Selective reporting (reporting bias)	Low risk	The study protocol is not available but it is clear that the published reports include all expected outcomes.
Other bias	Low risk	The risk may be explained by the unclear assessment tool.

Menon 2018

Methods	Study design: RCT. Methods of randomisation: Randomisation was done using a computer-generated method. Follow-up: 3 months. Setting: Department of Psychiatry of the Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Puducherry, India. Date it was conducted: December 2015 – July 2017. Source of funding: This review received no specific grant from any funding. Conflict of interest: No conflict of interest has been declared by the authors.
Participants	Inclusion/exclusion criteria: The inclusion criteria were aged between 18 and 65 years, diagnosed with Bipolar I Disorder (BD-I) on the Diagnostic and Statistical Manual of Mental Disorders – fifth edition (DSM -5) (American Psychiatric Association, 2013). All patients were on a stable drug/dose regimen for at least the past one year. Patients with Hamilton Depression Rating Scale (HDRS) scores ≥ 7 and Young Mania Rating Scale (YMRS) scores ≥ 8 were excluded as were patients/caregivers without access to mobile phones and patients/caregivers who were unable to read either English or the regional language (Tamil). Sample size: 132 (IG=62, TAU=70). Gender: In the intervention group were 55% men and in the control group 50%. Age: The mean age was 37 years (SD 9.6) in the intervention group and 38.7 (SD 11.6) in control group.
Interventions	Type of intervention: Behavioural. The intervention group received identical twice-weekly, text SMS reminders. The SMS messages greeted the recipient, reminded the recipient about taking medications at the times and doses prescribed, and ended with a positive message such as “Have a nice day”. During monthly follow up visits, and in the first three months of the study, intervention group patients were asked (by an investigator who was not involved in outcome measurement) whether they were receiving the SMS messages regularly. The TAU group received TAU alone for the entire duration of the six-month study. TAU included both pharmacologic treatment (with medications such as mood stabilizers and/or anti- psychotics) and psychosocial treatment strategies, as indicated.
Outcomes	Primary outcome measured: Adherence. The Morisky scale was used to measure self-reported medication adherence. Secondary outcomes measured: (1) Treatment attitudes; (2) Quality of life.
Risk of bias	

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Computer-generated randomisation was reported. No further details were available.
Allocation concealment (selection bias)	Unclear risk	No information on concealment was reported.
Blinding of participants and personnel (performance bias) all outcomes	Unclear risk	No information on blinding of participants and personnel was reported.
Blinding of outcome assessment (detection bias) all outcomes	Low risk	The assessors were blinded (rater-blinded assessments).
Incomplete outcome data (attrition bias) all outcomes	Low risk	By the end of the intervention phase, 16 participants had dropped out of the trial (3 and 13 in the intervention and control groups), and by the end of the subsequent 3-month follow- up phase, the cumulative study drop out was 32 (10 and 22 in the intervention and control groups). Complete data were unavailable for all study completers. ITT analyses were conducted, missing data were imputed by LOCF and sensitivity analyses examined completer samples.
Selective reporting (reporting bias)	Low risk	The study protocol is not available but it is clear that the published reports include all expected outcomes.
Other bias	Low risk	Self-reported responses can be affected by desirability biases. Power analysis was performed, including a 10% attrition/non-participation rate; estimated 60 pts per group.

Moncrieff 2016

Methods	Study design: RCT Methods of randomisation: Cluster randomisation based on an internet randomisation service (sealed envelope) using block size. Follow-up: 1 and 3 months post intervention. Setting: Community recovery, North East London. Date it was conducted: Not reported. Source of funding: National Institute for Health Research. Conflict of interest: No conflict of interest.
Participants	Inclusion/exclusion criteria: Patients had to be over the age of 18, have a diagnosis of psychosis, schizophrenia or schizoaffective disorder or a mood disorder with psychotic symptoms and be currently taking antipsychotic medication. Patients were required to have an allocated health professional who was usually a nurse, social worker or occupational therapist from the participant's clinical team. They also needed to have a consultation with their psychiatrist pending within the next three months. Patients who could not speak English or lacked capacity to consent were excluded from the study. Sample size: 60 (IG=31, TAU=29). Gender: In the intervention group were 74% men and in the control group 69. Age: The mean age was 45 years in the intervention group and 39 in control group.

Interventions	Type of intervention: Educational. The Medication Review Tool and website was designed to provide information about psychotic conditions including schizophrenia, types of antipsychotic medication and points for people to consider when discussing and making decisions about medication with professionals. It included links to external sites for users to access more detailed information.
Outcomes	Primary outcome measured: Self-confidence Secondary outcomes measured: (1) Client Satisfaction; (2) Drug Attitude; (3) Medication side effects; (4) Positive and negative syndromes; (5) Medication Adherence The Morisky scale was used to measure self-reported medication adherence.

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Cluster randomisation based on an internet randomisation service (sealed envelope) using block size.
Allocation concealment (selection bias)	Low risk	The allocation list was held by an independent administrator.
Blinding of participants and personnel (performance bias) all outcomes	High risk	Participants and health professionals were not blinded due to the nature of the intervention and the data collection.
Blinding of outcome assessment (detection bias) all outcomes	High risk	The data collection was not blinded due to the fact there was only one principal researcher assigned to the study.
Incomplete outcome data (attrition bias) all outcomes	Low risk	Missing outcome data balanced in numbers across groups with similar reasons for missing data.
Selective reporting (reporting bias)	Low risk	Statistical analyses were conducted blind.
Other bias	High risk	The risk may be explained by limited follow-up. Self-reported responses can be affected by desirability biases.

Montes 2012

Methods	Study design: RCT Methods of randomisation: Group assignment was based on a 1:1 randomisation scheme. Follow-up: Baseline, 3 and 6 months post intervention. Setting: Psychiatric Centres in Spain. Date it was conducted: April 2009 – February 2010 Source of funding: AstraZenca Spain. Conflict of interest: Two authors are employees of AstraZenca Spain.

Participants	Inclusion/exclusion criteria: Patients were included if they were aged between 18 and 65 years, a diagnosis of schizophrenia, clinically stable in the last six months, a single oral antipsychotic medication, follow-up as an outpatient, at least one affirmative answer (indicating suboptimal medication adherence) to the Morisky Adherence Questionnaire and availability of a cell phone capable of receiving SMS messages. Those patients receiving long-acting injectable antipsychotic treatment were excluded. Sample size: 254 (IG=100, TAU=154). Gender: In the intervention group were 65 (65%) men and in the control group 104 (67.5%). Age: The mean age was 38.6 years (SD 10.2) in the intervention group and 40.6 (SD 11.5) in control group.
Interventions	Type of intervention: Behavioural. Participants assigned to the intervention received daily SMS reminders on their cell phones to take their medication for three months.
Outcomes	Primary outcome measured: Adherence. The Medication Adherence Questionnaire was used to measure self-reported medication adherence.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Group assignment was based on a 1:1 randomisation scheme. Randomisation codes were computer-generated by statistician and sealed in envelopes labelled with consecutive numbers, envelopes were opened by the investigator in an ascending order and patients were allocated to intervention and control groups.
Allocation concealment (selection bias)	High risk	Open labelled study.
Blinding of participants and personnel (performance bias) all outcomes	High risk	Open labelled study.
Blinding of outcome assessment (detection bias) all outcomes	High risk	Open labelled study.
Incomplete outcome data (attrition bias) all outcomes	Low risk	Missing outcome data balanced in numbers across groups with similar reasons for missing data.
Selective reporting (reporting bias)	Low risk	The study protocol is not available but it is clear that the published reports include all expected outcomes.
Other bias	Low risk	Self-reported responses can be affected by desirability biases.

Pakpour 2017

Methods	Study design: RCT Methods of randomisation: Randomisation was done using a computer-generated method. Follow-up: Baseline and 6 months post intervention. Setting: Ten academic centres in Iran. Date it was conducted: September 2014 – October 2016. Source of funding: Not reported. Conflict of interest: Not reported.
Participants	Inclusion/exclusion criteria: Patients were included if they were 18 years or older, a diagnosis of Bipolar disorder I or II, being treated with a mood stabiliser and were not attending weekly or biweekly psychotherapy. Patients were excluded if they had a diagnosis of drug or alcohol misuse disorders, showed evidence of severe borderline personality, needed to change the type and/or the dose of a mood stabiliser, were pregnant or planned to be pregnant in the next year, had any organic cerebral cause for bipolar disorder or had an intellectual disability. Sample size: 270 (IG=134, TAU=136). Gender: In the intervention group were 60 (45%) men and in the control group 67 (49%). Age: The mean age was 41.8 years (SD 8.4) in the intervention group and 41.2 (SD 6.4) in control group.
Interventions	Type of intervention: Mixed. The multifaceted intervention included two components: psychoeducation for the participants and their family members and motivational interviewing.
Outcomes	Primary outcome measured: Adherence. The Medication Adherence Rating Scale was used to measure self-reported medication adherence. Adherence was also assessed using objective indices like plasma levels of mood stabilisers. Secondary outcomes measured: (1) Serum levels of mood stabilizers; (2) Clinical symptoms; (3) Quality of life; (4) Measures of intention; (5) Beliefs about medicine; (6) Perceived behavioural control; (7) Automaticity; (8) Action and coping planning; (9) Adverse reactions

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation was reported.
Allocation concealment (selection bias)	Low risk	Assessors, psychologists and psychiatrists were blind to the intervention status of the participants.
Blinding of participants and personnel (performance bias) all outcomes	Low risk	Assessors, psychologists and psychiatrists were blind to the intervention status of the participants.
Blinding of outcome assessment (detection bias) all outcomes	Unclear risk	Assessors, psychologists and psychiatrists were blind to the intervention status of the participants.

Incomplete outcome data (attrition bias) all outcomes	Low risk	Missing outcome data balanced in numbers across groups with similar reasons for missing data.
Selective reporting (reporting bias)	Low risk	The study protocol is not available but it is clear that the published reports include all expected outcomes.
Other bias	Low risk	The study seems to be free of other sources of bias.

Sajatovic 2018

Methods	Study design: RCT Methods of randomisation: Block randomisation. Follow-up: Baseline, 10 weeks, 14 weeks and 6 months. Setting: National Institute of Mental Health, U.S.A. Date it was conducted: October 2012 – July 2017. Source of funding: This study was supported by a grant from the National Institute of Mental Health (NIMH) grant NIMH (PI Sajatovic) and by the Clinical and Translational Science Award (CTSC) Conflict of interest: Dr. Sajatovic has research grants from Alkermes, Pfizer, Merck, Janssen, Reuter Foundation, Woodruff Foundation, Reinberger Foundation, National Institute of Health (NIH), and the Centers for Disease Control and Prevention (CDC). Dr. Sajatovic is a consultant to Bracket, Otsuka, Supernus, Neurocrine, Health Analytics and Sunovion and has received royalties from Springer Press, Johns Hopkins University Press, Oxford Press, and UpToDate.
Participants	Inclusion/exclusion criteria: The inclusion criteria were either type I or type II Bipolar disorder as confirmed by the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID), Bipolar disorder for at least two years, prescribed at least one evidence-based Bipolar disorder medication (i.e. lithium, anticonvulsant, or antipsychotic) for at least six months and ≥ 20% non-adherent as assessed by the TRQ. Only individuals unable to participate in study procedures, unable to provide informed consent, and at high risk of harm to self or others were excluded. Sample size: 184 (Mixed intervention group=92, Education group=92). Gender: In the education group were 36% men and in the mixed intervention group 27%. Age: The mean age was 46 years (SD 10.9) in the education group and 49 (SD 9.8) in the mixed intervention group.
Interventions	Type of intervention: Educational versus mixed intervention The education group had five in-person sessions. Four core sessions were followed by one “booster” session and one phone call between the core and booster sessions. Education addresses bipolar disorder treatment broadly including diagnosis and management, and allows time for questions and therapist interaction as needed. The mixed intervention includes an educational and behavioural approach. These modules are psychoeducation focused on the role of medication in bipolar disorder management, Modified Motivational Enhancement Therapy (MET) to address non- adherence related to substance use, Communication with Providers to facilitate appropriate treatment expectations and optimize side effect management, and Medication Routines intended to incorporate medication-taking into lifestyle. Mixed intervention participants had a core series of up to four in-person one-to-one sessions spaced about one week apart over a four–six week period, and one “booster” session four weeks after the core sessions. There was one follow-up phone call between core session completion and the booster session.

Outcomes	Primary outcome measured: (1) Medication adherence; (2) Bipolar disorders symptoms. Adherence was assessed using the Tablets Routine Questionnaire (TRQ), which derives a proportion (%) of days with missed medication doses in the last week and last month. TRQ scores ranges from perfect adherence (0% missed) to missing all medication (100% missed). The Medication Event Monitoring System (MEMS) supplemented the TRQ. Secondary outcome measured: (1) Depression; (2) Mania; (3) Clinical symptoms.

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Specific details on random sequence generation were missing.
Allocation concealment (selection bias)	Unclear risk	No information on concealment was reported.
Blinding of participants and personnel (performance bias) all outcomes	Unclear risk	No information on blinding of participants and personnel was reported.
Blinding of outcome assessment (detection bias) all outcomes	Unclear risk	No information on blinding of outcome assessors was reported.
Incomplete outcome data (attrition bias) all outcomes	Unclear risk	After randomisation initially 184 enrolled patients and only 148 completed the evaluation.
Selective reporting (reporting bias)	Low risk	The study protocol is not available but it is clear that the published reports include all expected outcomes.
Other bias	Low risk	The study seems to be free of other sources of bias.

Schirmer 2015

Methods	Study design: RCT Methods of randomisation: Randomisation was done using a computer-generated method. Follow-up: 1 month. Setting: Centres for Psychiatry in Zwiefalten and Weissenau and the Clinic for Psychiatry in Reutelingen in the south of Germany. Date it was conducted: October 2008 – September 2010. Source of funding: Centre for Psychiatry, South-Württemberg. Conflict of interest: Not reported.

Participants	Inclusion/exclusion criteria: Inclusion criteria were voluntary, written informed consent, diagnosis of schizophrenia or schizoaffective disorder, age 18-60 years, reachability for home visits, no earlier participation in such a training program and outpatient visits for antipsychotic maintenance treatment after discharge. Exclusion criteria were admission for crisis intervention, absence of written informed consent, high probability that support would be needed for medication intake over a longer period of time and monotherapy with depot antipsychotics. Sample size: 102 (IG=52, TAU=50). Gender: In the intervention group were 27 (52%) men and in the control group 23 (44%). Age: The mean age was 49.8 years in the intervention group and 40.4 in control group.
Interventions	Type of intervention: Mixed. The training program is conducted in one-to-one lessons with skilled nurses. Participants should learn to prepare their medication by themselves during the hospital stay in the same way they are expected to do it autonomously after discharge. The participants are informed using an educational approach: colour, shape and name of the medication. Level 1 focuses on the scheduled intake of medication, level 2 covers the arrangement of the next day's medication coached by a nurse, in level 3 the dispenser is located in the patient's room and the next day's in level 4, the patient arranges the medication for one week in a dispenser which remains in de patient's room in a locked cupboard. The training takes place in a low-stimulus room in one-to-one lessons.
Outcomes	Primary outcome measured: Adherence. Three strategies were chosen for this study; pill count, serum levels of the antipsychotic medication and self-reported of medication intake (unclear assessment tool).

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation was reported.
Allocation concealment (selection bias)	Low risk	The clinician who rated the adherence by means of serum levels of antipsychotics was blinded to allocation.
Blinding of participants and personnel (performance bias) all outcomes	Low risk	The study workers who conducted the interviews were blinded with regard to the intervention and to ensure consistency.
Blinding of outcome assessment (detection bias) all outcomes	Low risk	The assessors were blinded.
Incomplete outcome data (attrition bias) all outcomes	High risk	Missing outcome data were reported and were likely to be related to true outcome. Initially 141 enrolled patients, only 102 completed the evaluation.
Selective reporting (reporting bias)	Low risk	The study protocol is not available but it is clear that the published reports include all expected outcomes.
Other bias	Low risk	The risks may be explained by limited follow-up.

Valenstein 2009

Methods	Study design: RCT Methods of randomisation: Block randomisation. Follow-up: 6 and 12 months. Setting: Four Departments of Veterans Affairs, Detroit. Date it was conducted: November 2002 – September 2005. Source of funding: Department of Veterans Affairs Health Services Research and Development. Conflict of interest: Not reported.
Participants	Inclusion/exclusion criteria: The inclusion criteria were having clinical diagnoses of schizophrenia, schizoaffective or bipolar disorder, a treatment plan that included long-term antipsychotic treatment, antipsychotic medication possession ratios of <0.8 in the prior 12 months. Sample size: 118 (IG=58, TAU=60). Gender: In the intervention group were 98% men and in the control group 95%. Age: The mean age was 49.6 years (SD 11.0) in the intervention group and 50.2 (SD 11.7) in control group.
Interventions	Type of intervention: Educational. The Meds-Help intervention consisted of unit-of-use packaging that included all patient's medications for psychiatric and general medical conditions, a medication and packaging education session, refill reminders mailed two weeks before scheduled refill dates and notification of clinicians when participants failed to fill antipsychotic prescriptions within seven and 10 days of a fill date. The medication education session was conducted by a pharmacist, usually in-person but occasionally by telephone. During this session, the pharmacist reviewed participants' prescribed medications, including treatment indications. The pharmacist also explained unit-of-use medication packaging and plans for interim use of pill boxes when medication changes were made by clinicians before the next shipment of medication packages.
Outcomes	Primary outcome measured: Adherence. Medication adherence was measured by the Medication Possession Ratios (MPR). A more stringent Composite Adherence Measure (CAM) was also assessed. The MPR is the ratio of number of outpatient day's supply of medication that a patient has received during the designated time period divided by the number of day's supply they needed to receive to take their prescribed dose of antipsychotic continuously during non instutionalised days. The MPR was based on data (pharmacy fills). Participants were considered adherent on the CAM only if their MPR during the study time periods was ³ 0.8, they reported they "always" took their antipsychotics or only missed antipsychotics "a couple of times" in response to questions from Schizophrenia Outcome Module and their blood test indicated the presence of some antipsychotic medication. Secondary outcome measured: (1) Psychiatric symptoms; (2) Quality of life; (3) Care satisfaction.

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Blocked randomisation scheme by site based on patient's level of adherence in the prior 12 months.
Allocation concealment (selection bias)	Unclear risk	No information on concealment was reported.

Blinding of participants and personnel (performance bias) all outcomes	High risk	Patients could not be blinded to study assignment and research associated were also not blinded due to the costs and logistics of hiring blinded assessors for each site and the likelihood that assessors would be unblended by patient comments
Blinding of outcome assessment (detection bias) all outcomes	High risk	The assessors were not blinded.
Incomplete outcome data (attrition bias) all outcomes	Low risk	Missing outcome data balanced in numbers across groups with similar reasons for missing data.
Selective reporting (reporting bias)	Low risk	The study protocol is not available but it is clear that the published reports include all expected outcomes.
Other bias	Low risk	The risk may be explained by the unclear assessment tool.

Velligan 2013

Methods	Study design: RCT Methods of randomisation: Randomisation was done using a computer-generated method. Follow-up: 9 months. Setting: Public mental health clinics in Texas. Date it was conducted: Not reported. Source of funding: National Institutes of Health. Conflict of interest: Not reported.
Participants	Inclusion/exclusion criteria: Patients were included if they were aged between 18 and 60 years, the diagnosis of schizophrenia, receiving ongoing treatment with an oral antipsychotic, had primary responsibility for taking their own medications, had missed at least one dose of medication in the preceding week, had a stable residence and were able to understand and complete assessments. Patients were excluded if they were on a depot antipsychotic medication, had a hospitalisation in the past three months, had a documented history of significant head trauma, seizure disorder or mental retardation, had a history of substance abuse or dependence in the past month or had a history of violence in the past six months. Sample size: 142 (Med-eMonitor group=48, PharmCAT group=47, TAU=47). Gender: In the Med-eMonitor group were 55% men, in the PharmCAT group 52% and in the control group 53%. Age: The mean age was 43.0 years (SD 10.1) in the Med-eMonitor group, 43 (SD 11.0) in the PharmCAT group and 42 (SD 9.3) in control group.
Interventions	Type of intervention: Behavioural. The PharmCAT is manual driven and uses environmental supports such as signs, alarms, calendars, checklists and notebooks to record questions for their prescriber, organisation of belonging and pill containers to improve medication adherence. Interventions in PharmCAT are individualised based. Participants in PharmCAT were seen once weekly in their home for 30 minutes. Med-eMonitor treatment consists of a therapist programming prescribing information into the device, setting up the device in the home to fit into the patient's routine (eg, set alarm to take medication, place in a location where he/she is likely to hear the alarm), assisting the patient in accurately filling the device, training the patient how to use the device and providing ongoing trouble shooting. Every three days the therapist was required to check the secure website to determine whether medication was being taken as prescribed and intervene by telephone if patient was missing doses.

Outcomes	Primary outcome measured: Adherence. Two objective measures of medication adherence were obtained: electronic monitor (opening of pill container) and pill counts.	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation was reported.
Allocation concealment (selection bias)	Unclear risk	No information on concealment was reported.
Blinding of participants and personnel (performance bias) all outcomes	Unclear risk	No information on blinding was reported.
Blinding of outcome assessment (detection bias) all outcomes	Unclear risk	No information on blinding was reported.
Incomplete outcome data (attrition bias) all outcomes	High risk	Fourteen patients (30%) dropped out from the Med-eMonitor intervention.
Selective reporting (reporting bias)	Low risk	The study protocol is not available but it is clear that the published reports include all expected outcomes.
Other bias	Low risk	The risk may be explained by the unclear follow-up.

Summary

Schizophrenia Spectrum (SSD) and Bipolar Disorders (BD) represent severe major psychiatric disorders often characterized by recurrent psychotic relapses that necessitate hospitalization. Besides stressful life events and substance abuse, non-adherence to medication stands out as a crucial and frequent risk factor for relapse.

These conditions often lead to recurrent psychotic relapses requiring hospitalisation. Non-adherence to prescribed medication is identified as a chief contributor to these relapses.

We present the first systematic review providing a synthesis of the effectiveness of interventions improving medication adherence in patients with schizophrenia or bipolar disorders, including a meta-analysis. On the basis of a synthesis of 23 studies, a total of 28 different, complex, and heterogeneous interventions were identified. These interventions, which included behavioural, educational, and mixed approaches, were evaluated against usual care or other intervention types. A total of 4238 participants, ranging from 30 to 1268 per study, were included. The interventions with the strongest of body of evidence were interventions combining motivational interviewing techniques with patient-tailored education sessions. These studies had a very low risk of bias, used a combination of two or more adherence measurement tools, including serum levels, and were also promising to be effective on adherence to treatment on long term. These interventions comprising elements of education and motivational interviewing in a medication self-management (MSM) intervention. Motivational interviewing with significant others and patient-tailored education, medication reminders at patients' home, education sessions focused on diagnosis, symptoms, medication and relapse were found to be beneficial for patients' adherence. This study revealed the importance of MSM on patients' adherence. MSM is becoming an increasingly important element in rehabilitation programs. As patients are not capable of self-manage their medication, aid is often required. Healthcare providers can support and coach patients towards self-management of their medication. Patients who are not able to self-manage their medication, but are expect-

ed to do MSM after discharge, should be given the opportunity to learn to self-manage their medication whilst in hospital. Subsequently, a clear view of the current prevalence rates and organisation of medication self-management in Flemish psychiatric hospitals in patients with SSD or BD was obtained in our next multicentre cross-sectional observational study. The results of this study confirmed that MSM is not yet widely implemented in Flemish psychiatric hospitals. MSM was implemented in 11 of the 48 participating units (23%), of which nine units (82%) applied to all oral prescribed medications except for depot medication. Analysis of patients' medical files revealed that only 4% of the included patients were on MSM during the inclusion period of six months with 84% of the total medication amount being self-administered. The decision-making process concerning participation in MSM is largely shared between the treating physician, the nursing team and the patient. Most units applied to all oral prescribed medications except for long-acting injectable (LAI) antipsychotics. In addition, the presence of available procedures and screening tools to assess the competence of the patients to self-manage their medication are very limited. These results created opportunities for the development and implementing of a future evidence-based MSM intervention to prevent non-adherence and relapse rates in patients with SSD or BD. A first important step in this preparation, we aimed to investigate all involved stakeholders' perceptions concerning MSM during hospitalisation in patients with SSD or BD. These first findings were explored in more depth through interviews with three psychiatrists, 18 nurses, two hospital pharmacists, and 26 patients with SSD or BD. Overall, all stakeholders were positive towards MSM under specific prerequisites and show to be willing to facilitate and perform MSM in daily practice. Our next two cross-sectional studies investigated the attitude of mental healthcare providers and hospitalised patients with SSD or BD towards MSM during hospitalisation. We can state they have a positive attitude towards it. Patients should be willing, MSM abilities should be evaluated on a regular basis during hospitalisation, medication monitoring and patients should be motivated to take their medication correctly. Many healthcare providers were concerned about losing an overview or control over the actual medication intake or perhaps not noticing mistakes, overdoses, and/or misuse. All stakeholders stated that MSM during hospitalisation can result in several positive patient-related outcomes as an increased patients' autonomy, confidence, self-reliance, more structure for the patients, preparation for discharge, and an improvement of their health literacy, adherence and satisfaction.

This dissertation offered mental healthcare providers, policymakers and

188

researchers the opportunity to move a big step forward towards improving MSM abilities of patients with SSD or BD.

Samenvatting

Schizofreniespectrum (SSD) en bipolaire stoornissen (BD) zijn ernstige psychiatrische aandoeningen die veelal gekenmerkt worden door aanhoudende of herhaaldelijke psychoses, wat leidt tot herval waarvoor hospitalisatie noodzakelijk is. Naast stressvolle levensgebeurtenissen en middelenmisbruik, is medicatieontrouw een cruciale en veelvoorkomende risicofactor voor herval. Medicatieontrouw wordt geïdentificeerd als een belangrijke oorzaak van herval.

Wij bieden de eerste systematic review met meta-analyse die een synthese weergeeft van de effectiviteit van interventies die medicatietrouw verbetert bij patiënten met SSD of een BD. Op basis van een synthese van 23 studies werden in totaal 28 verschillende, complexe en heterogene interventies geïdentificeerd. Deze interventies, inclusief gedragsmatige, educatieve en gemengde benaderingen, werden geëvalueerd tegenover de gebruikelijke zorg of andere interventietypes. In totaal werden 4238 deelnemers, variërend van 30 tot 1268 deelnemers per studie, geïncludeerd. De interventies met de sterkste evidentie waren die waarin motiverende gesprekstechnieken gecombineerd werden met - op de patiënt afgestemde - educatiesessies. Deze studies hadden een zeer laag risico op bias, gebruikten een combinatie van twee of meer meetinstrumenten om therapietrouw te meten, inclusief serumlevels, en waren ook veelbelovend op vlak van effectiviteit van medicatietrouw op de lange termijn. Deze interventies omvatten elementen van educatie en motiverende gesprekstechnieken in een medicatie zelf-managementinterventie. Motiverende gesprekken met de naasten van de patiënt en - op de patiënt afgestemde - educatie, medicatieherinneringen bij de patiënt thuis, educatiesessies gericht op diagnose, symptomen, medicatie en herval bleken gunstig te zijn voor medicatietrouw van de patiënten. Deze studie duidde duidelijk het belang van medicatie zelfmanagement (MZM) voor de medicatietrouw van patiënten met SSD of een BD. MZM wordt een steeds belangrijker element in herstelgerichte programma's omdat patiënten vaak niet in staat zijn om hun eigen medicatie thuis correct te beheren. Zorgverleners kunnen patiënten ondersteunen en coachen naar zelfmanagement van hun medicatie.

Patiënten die niet in staat zijn hun medicatie zelf te beheren, maar van wie verwacht wordt dat zij dit na ontslag wel doen, moeten de gelegenheid krijgen om dit te leren tijdens hun ziekenhuisopname.

Vervolgens werd een duidelijk beeld geschetst van de huidige prevalentiecijfers en organisatie van MZM in Vlaamse psychiatrische ziekenhuizen bij patiënten met SSD of een BD. De resultaten van deze studie bevestigden dat MZM nog niet breed is geïmplementeerd in Vlaamse psychiatrische ziekenhuizen. MZM werd geïmplementeerd in 11 van de 48 deelnemende afdelingen (23%), waarvan negen afdeling (82%) dit toepasten op alle voorgeschreven medicatie per os behalve voor de intramusculaire depotmedicatie. Analyse van medische dossiers van patiënten toonde aan dat slechts 4% van de opgenomen patiënten tijdens de inclusieperiode van zes maanden aan MZM deden. Bovendien werden 84% van de totale hoeveelheid medicatie in eigen beheer genomen met uizondering van intramusculaire depotmedicatie. Het besluitvormingsproces betreffende deelname aan MZM wordt grotendeels gedeeld tussen de behandelend arts, het verpleegkundigteam en de patiënt. Daarnaast is de beschikbaarheid van procedures en screeningstools om de competentie van de patiënten om hun medicatie zelf te beheren zeer beperkt. Deze resultaten creëerden mogelijkheden voor de ontwikkeling en implementatie van een toekomstige medicatie zelfmanagementinterventie om therapieontrouw en herval bij patiënten met SSD of BD te reduceren en te voorkomen.

Een eerste belangrijke stap in deze voorbereiding was het onderzoeken van de percepties van alle stakeholders betreffende MZM tijdens hospitalisatie bij patiënten met SSD of een BD. Deze eerste bevindingen werden verder uitgediept door interviews met drie psychiaters, 18 verpleegkundigen, twee ziekenhuisapothekers en 26 patiënten met SSD of een BD. Over het algemeen stonden alle stakeholders positief tegenover MZM maar onder specifieke voorwaarden en toonden zij zich bereid om MZM in de dagelijkse praktijk te faciliteren en uit te voeren.

Onze volgende twee studies onderzochten de attitude van geestelijke gezondheidszorgverleners en gehospitaliseerde patiënten met SSD of een BD tegenover MZM tijdens de hospitalisatie. We kunnen duidelijk stellen dat zij hier positief tegenover staan. Patiënten moeten wel zelf bereid zijn, de MZM-vaardigheden moeten regelmatig worden geëvalueerd tijdens de hospitalisatie, medicatie monitoring moet aanwezig zijn en patiënten moeten gemotiveerd zijn om hun medicatie correct in te nemen. Veel zorgverleners maakten zich wel zorgen over overzicht- en controleverlies over de daadwerkelijke medicatie-inname of het mogelijk niet opmerken van fouten zoals over- en onderdoseringen en/of medicatiemisbruik. Alle

192

stakeholders verklaarden wel dat MZM tijdens de hospitalisatie kan resulteren in verschillende positieve patiëntgerelateerde uitkomsten zoals een toegenomen autonomie van patiënten, vertrouwen, zelfredzaamheid, meer structuur voor de patiënten, voorbereiding op het ontslag naar huis en een verbetering van hun gezondheidsgeletterdheid, therapietrouw en tevredenheid.

Dit proefschrift bood geestelijke gezondheidszorgverleners, beleidsmakers en onderzoekers de mogelijkheid om een grote stap voorwaarts te zetten in het verbeteren van MZM-vaardigheden van patiënten met SSD of een BD.

List of tables

List of figures

Curriculum vitae and list of publications

Elke Loots

Date of birth: November 18, 1988

Nationality: Belgian

Telephone: +32 472 45 48 89

E-mail: elke.loots@uantwerpen.be
elke.loots@zas.be

ORCID: 0000-0002-2211-0847

Education

University of Antwerp
2024 Doctor of medical sciences (PhD)

University of Antwerp
2018 Master of Science in nursing and midwifery

AP University of Antwerp
2015 Bachelor in intensive and emergency care

KdG University of Antwerp
2012 Bachelor in nursing

Professional experience

ZAS hospital network in Antwerp
2023 - today
Data manager and Researcher Hospital Outbreak Support Team (80%)

University of Antwerp
2021 – today
Teaching assistant scientific research (Master in nursing and midwifery) (20%):
- Beginselen van onderzoeksmethodologie
- Toepassingen van onderzoeksmethodologie
- Masterproef – opzetten en opstarten
- Masterproef – argumenteren, debatteren en verdedigen
- Masterproef – wetenschappelijke publicatie
- Systematisch literatuuronderzoek
- Kwantitatieve data-analyse

ZNA Middelheim hospital (Antwerp)
2013 – 2023
Intensive Care nurse

Additional academic courses

University of Antwerp (Antwerp Doctoral School)

2018

Writing academic papers (English)
Centrum voor Evidence-Based Medicine (CEBAM)

2020

GRADE for interventions by CEBAM in collaboration with Cochrane Belgium
ESPACOMP

2020

Medication adherence data-analysis

University of Antwerp (StatUa)

2021

Statistical and methodological issues to model the COVID-19 pandemic

2022

- Multivariate data-analysis
- Multiple linear regression and ANOVA
- Introduction to JMP Pro
- Introduction to R

2023

- Statistical analysis in R
- Graphics in R
- Categorical data-analysis using logistic regression
- Flames statistics (online)

2021

- Regression with ordinal variables

2023

- Power and sample size analysis
- Statistical analysis and graphs in R

200

Scientific activities

Conference presentations

Care4, Leuven (Belgium), 2019, oral presentation: Self-management of medication during hospitalisation: Healthcare providers' and patients' perspectives.

Care4, Leuven (Belgium), 2019, poster presentation: An evidence-based procedure for self-management of medication in hospital: development and validation of the SelfMED procedure.

Care4, Leuven (Belgium), 2019, poster presentation: The willingness and attitude of patients towards self-administration of medication in hospital.

Espacomp - International Society for patient medication adherence, Porto (Portugal), 2019, poster presentation: Interventions to improve medication adherence in patients with Schizophrenia or Bipolar Disorders: A systematic review and meta-analysis.

Nurse and Pharmaceutical Care symposium, Antwerp (Belgium), 2020, oral presentation: Interventions to improve medication adherence in patients with Schizophrenia or Bipolar Disorders: A systematic review and meta-analysis.

Espacomp - International Society for patient medication adherence (Online), 2021, oral presentation: Medication Self-Management in Hospitalised Patients with Schizophrenia Spectrum or Bipolar Disorders: The Perceptions of Patients and Healthcare Providers

Espacomp - International Society for patient medication adherence (Online), 2021, oral presentation: Interventions to improve medication adherence in patients with Schizophrenia or Bipolar Disorders: A systematic review and meta-analysis.

Care4, (Online), 2022, oral presentation: Self-Management in Hospitalised Patients with Schizophrenia Spectrum or Bipolar Disorders: The Perceptions of Patients and Healthcare Providers.

Care4, (Online), 2022, oral presentation: The attitude of healthcare providers towards medication self- management in hospitalised patients with Schizophrenia Spectrum or Bipolar Disorders.

Sigma's International Nursing Research Congress, Edinburgh (Scotland), 2022, oral presentation: Interventions to improve medication adherence in patients with Schizophrenia or Bipolar Disorders: A systematic review and meta-analysis.

ISPE - International Conference on Pharmacoepidemiology & Therapeutic Risk Management, Copenhagen (Denmark), 2022, poster presentation: The attitude of healthcare providers towards medication self- management in hospitalised patients with Schizophrenia Spectrum or Bipolar Disorders.

ISPE - International Conference on Pharmacoepidemiology & Therapeutic Risk Management, Copenhagen (Denmark), 2022, poster presentation: Self-Management in Hospitalised Patients with Schizophrenia Spectrum or Bipolar Disorders: The Perceptions of Patients and Healthcare Providers.

Nurses and interprofessional pharmaceutical care, Antwerp (Belgium), 2023, oral presentation: Evidence based interventions to improve the quality of pharmaceutical care.

Publications

Loots,E.; Goossens,E.; Vanwesemael, T.; Morrens, M.; Van Rompaey, B.; Dilles, T. Interventions to Improve Medication Adherence in Patients with Schizophrenia or Bipolar Disorders: A Systematic Review and Meta- Analysis. Int. J. Environ. Res. Public Health 2021, 18, 10213. https://doi.org/10.3390/ ijerph181910213

Loots, E.; Leys, J.; Proost, S.; Morrens, M.; Glazemakers, I.; Dilles, T.; Van Rompaey, B. Medication Self- Management in Hospitalised Patients with Schizophrenia or Bipolar Disorder: The Perceptions of Patients' and Healthcare Providers'. Int. J. Environ. Res. Public Health 2022, 19, 4835. https://doi.org/10.3390/ijerph19084835

Morrens, M.; Overloop, C.; Coppens, V.; Loots, E. et al. The relationship between immune and cognitive dysfunction in mood and psychotic disorder: a systematic review and a meta-analysis. Mol Psychiatry 2022. https://doi.org/10.1038/s41380-022-01582-y

Loots, E.; Hadouchi, S.; Dilles, T.; Van Rompaey, B.; Morrens, M. The attitude of healthcare providers towards medication self-management in hospitalised patients diagnosed with schizophrenia or bipolar disorders. Journal of Psychiatric and Mental Health Nursing 2023, DOI: 10.1111/jpm.12903

Dilles, T.; Mortelmans, L.; Loots, E.; Sabbe, K.; Feyen, H.; Wauters, M.; Haegdorens, F.; De Baetselier, E. People-centered care and patients' beliefs about medicines and adherence: A cross-sectional study, HELIYON (2023), doi:https://doi.org/10.1016/j.heliyon.2023.e15795

Loots, E.; Van Rompaey, B.; Dilles, T.; Morrens, M. Medication self-management in Flemish psychiatric hospitals: A prevalence study in hospitalised patients with schizophrenia spectrum or bipolar disorder. June 2023. Nursing 38(2):14-21. DOI: 10.24078/vpg.1970.1.23426

Loots, E.; Van Rompaey, B.; Dilles, T.; Morrens, M. Attitudes of patients with schizophrenia spectrum or bipolar disorders towards medication self-management during hospitalisation. Journal of Clinical Nursing 2024 Apr;33(4):1459-1469. doi: 10.1111/jocn.16936.

Languages and skills

Dutch: Native

English: Professional working proficiency

Experience in SPSS, R-studio, Qualtrics, RevMan, and MS Office

Organisational activities for scientific conferences

NuPhac Symposium, Antwerp (Belgium), February 2020

NuPhaC Winter Conference, Antwerp (Belgium), December 2021

Memberships

Nurse and Pharmaceutical Care, 2018 – today

Ethics committee of the ZAS hospital network (Antwerp), IRB and CME, 2023 – today

Reviewer for following journals

- BMC Psychiatry
- BMC Medical Informatics and Decision Making
- BMC Medical Education
- BMJ Open
- International Journal of Nursing Studies
- Journal of Psychiatric Research

Dankwoord

Dit proefschrift is het resultaat van jaren hard werken, niet alleen in het kader van onderzoek, maar ook in het balanceren tussen een voltijdse baan, een PhD-traject en een gezin. Ik wil daarom eerst mijn werkgevers ZAS en Universiteit Antwerpen bedanken voor de mogelijkheid tot het combineren van onderzoek, onderwijs en de klinische praktijk. Het combineren van deze verantwoordelijkheden vergde doorzettingsvermogen maar vooral discipline en een groot aanpassingsvermogen. Het maakt deze prestatie voor mij extra waardevol en betekenisvol. De voltooiing van dit proefschrift zorgde ervoor dat ik een belangrijke mijlpaal heb kunnen bereiken na een lange uitdagende reis met persoonlijke en professionele groei.

Deze weg was er een van vallen en opstaan, van veerkracht tonen en telkens weer opstaan om verder te gaan. Elke stap bracht nieuwe inzichten met zich mee en liet me sterker worden, niet enkel op professioneel vlak maar ook als persoon. Het afronden van dit traject was echter niet mogelijk geweest zonder de steun en toewijding van een aantal bijzondere mensen die me onderweg hebben geholpen. Aan hen wil ik mijn oprechte dank uitspreken.

Allereerst ben ik mijn promotoren bijzonder dankbaar voor de begeleiding, niet alleen voor de ondersteuning van mijn academische ontwikkeling, maar ook voor het vertrouwen om mijn grenzen te verleggen. Dankzij hun aanmoediging heb ik geleerd om door te zetten, zelfs in momenten van twijfel. Een welgemeende dankjewel Prof. dr. Tinne Dilles, Prof. dr. Bart Van Rompaey en Prof. dr. Manuel Morrens. Jullie wisten me op precies de juiste momenten de richting te wijzen, vaak nog voordat ik zelf helder wist waar ik naartoe wilde. Dankjewel voor het vertrouwen en de ruimte om mijn ambities te volgen en mij te laten groeien op mijn eigen tempo. Jullie waren niet enkel zeer toegankelijke promotoren maar ook uitstekende coaches. Hoewel jullie begeleidingsstijlen verschillend waren, vulden ze elkaar op een perfecte manier aan en maakten ze het geheel compleet. Jullie wisten precies wat ik op welk moment nodig had en dit gaf me de vrijheid om mijn eigen pad te volgen.

Tinne, ik kan me voorstellen dat het een uitdaging was om een PhD-traject te begeleiden van iemand die daarnaast nog fulltime werkte. Daarbij kwamen ook

nog allerlei verschillende uitdagingen en obstakels die ik tegenkwam. Bedankt voor je begrip voor de bijzondere omstandigheden waarin ik mijn doctoraat uitvoerde. Bij elk overleg wist je me opnieuw gerust te stellen en bevestigde je me dat ik goed bezig was. Die geruststelling met af en toe een duwtje in de rug gaven me telkens de moed om door te zetten. Jouw waardevolle inzichten en kritische blik hebben niet alleen dit werk, maar ook mij als persoon verrijkt. Bedankt dat je deze uitdaging met mij wilde aangaan en mij zoveel hebt bijgebracht.

Ik waardeer enorm het geduld en de tijd die je steeds nam tijdens onze besprekingen en brainstormsessies. Je gaf me nooit het gevoel dat jouw tijd beperkt was, en je hebt me steeds de ruimte gegeven om te groeien als onderzoeker én als persoon, volledig op mijn eigen tempo. In het bijzonder wil ik je bedanken voor je steun in de laatste fase, toen ik het erg zwaar had. Je was er altijd voor me, met een eindeloos geduld en een luisterend oor. Jouw steun en begrip tijdens deze periode hebben me enorm geholpen om door te zetten en dit traject af te ronden. Bedankt dat je me ook tijdens moeilijke momenten hebt bijgestaan.

Bart, je nam altijd de tijd om me als coach te ondersteunen. Je deed dit niet alleen inhoudelijk maar ook op persoonlijk vlak. Je was altijd kritisch tijdens onze meetings en stelde altijd scherpe vragen zoals “En wat nu? Wat moeten we hier nu mee?” waarop ik meestal antwoordde “Daar moet ik eens goed over nadenken”. Jouw manier van kritisch doorvragen hield me scherp en hielp me om telkens de volgende stappen in het onderzoek helder te zien. Je hebt me ook geleerd wat het betekent als je in de flow van het schrijven zit. Ps: dit pas ik nog steeds toe als ik ergens te laat ben doordat ik de tijd uit het oog verloren ben tijdens het schrijven. Ik zit nog steeds op een volledig andere planeet tijdens het schrijven maar dankzij jou heb ik dit gevoel kunnen plaatsen.

In de moeilijke momenten leerde je me vooral te relativeren en eraan te denken mezelf op de eerste plaats te zetten. Jouw directe aanpak was precies wat ik nodig had, en ik ben je dankbaar dat je me op deze manier hebt begeleid.

Manuel, ik wil je graag bedanken voor jouw enorme geduld en coachende rol als promotor. Je hebt mij geleerd om alles stap voor stap te doen in plaats van met alles tegelijk bezig te zijn, en vooral om mijn eigen tempo aan te houden. Je was altijd bereikbaar voor vragen en feedback en jouw kritische en duidelijke adviezen hebben mijn werk echt naar een hoger niveau getild. Het is voor mij een eer om jou als promotor te hebben gehad. Daarnaast was het een uitdaging voor ons beiden dat ik geen gespecialiseerde achtergrond in de geestelijke gezondheidszorg had, maar dankzij jouw geduld en expertise ben ik erin geslaagd om dit project succesvol af te ronden. Bedankt voor je vertrouwen en je inzet om mij door dit traject te loodsen.

206

Mijn oprechte dank gaat uit naar de juryleden, **Prof. dr. Hilde Bastiaens, Prof. dr. Didier Schrijvers, dr. Jasper Vanhoof en dr. Silvio van den Heuvel**. Jullie zorgvuldige beoordeling, waardevolle feedback en stimulerende vragen hebben niet alleen bijgedragen aan dit proefschrift, maar ook aan mijn persoonlijke groei als onderzoeker. Jullie betrokkenheid heeft een grote impact gehad op de richting en kwaliteit van dit werk.

Er zijn drie mensen die een bijzondere plaats in mijn hart verdienen en zonder wie ik nooit zover had kunnen komen: mijn papa, mijn mama en Nick. Jullie zijn mijn vaste basis, mijn grootste steun en de reden dat ik dit traject kon volhouden.

Mama en papa, jullie hebben mij altijd met liefde en toewijding gesteund, ongeacht de keuzes die ik maakte. Jullie geloof in mij en de waarden die jullie me hebben meegegeven, vormen de kern van wie ik ben geworden. Dankzij jullie aanmoediging durfde ik deze uitdaging aan te gaan en vol te houden, ook in de moeilijke momenten. Jullie steun, op elke mogelijke manier, was onmisbaar, en ik ben diep dankbaar dat ik altijd op jullie kon rekenen. Lieve **mama**, jouw zorg en steun zijn in al die jaren onmisbaar geweest. De ontelbare porties soep met balletjes en Mac & Cheese die altijd klaarstonden, waren niet alleen broodnodig op die momenten, maar ook een herinnering aan jouw liefde en zorg, zelfs als ik het druk had en weinig tijd vond om langs te komen. De vakanties die we sinds 2017 samen twee keer per jaar deden - jij aan het zwembad met een spannend boek en ik op verkenning in de diepte van de oceaan - gaven me de broodnodige rust en energie om weer verder te gaan. Bedankt voor alles wat je voor me hebt gedaan, zowel groot als klein – ik had het niet zonder jouw steun gekund. Lieve **papa**, ik wil je van harte bedanken voor je eindeloze steun. Jouw geduld, inzet en bereidheid om steeds voor me klaar te staan betekenen de wereld voor me. Bedankt dat ik altijd op jou kan rekenen, in alles wat ik doe.

Lieve **Nick**, jij hebt altijd alles van dichtbij meegemaakt – de lange dagen, de pieken en dalen, en de momenten van onzekerheid. Jij was er altijd om me op te vangen en moed in te spreken wanneer ik dat het meeste nodig had. Jouw liefde en geduld (vooral heel veel geduld) gaven me de kracht om door te zetten en mijn grenzen te verleggen. Bedankt dat je altijd achter me stond, ook al was dit voor jou niet altijd gemakkelijk, met onvoorwaardelijke steun en vertrouwen.

Aan jullie, papa, mama en Nick: mijn diepste dankbaarheid. Jullie zijn de reden dat ik dit heb kunnen bereiken en ik draag dit werk op aan jullie.

Mijn lieve **familie**, bedankt voor de vele aanmoedigingen en doorvoelde betrokkenheid. Bij jullie kan ik mijn batterijen opladen dankzij de leuke en memorabele familiefeestjes! Ook al kon ik vaak moeilijk uitleggen waar ik precies mee bezig was – omdat ik dit soms eigenlijk zelf niet altijd meer wist - en

waarom het allemaal zo lang duurde, mocht ik bij jullie steeds op veel begrip rekenen. Een welgemeende dankjewel om altijd oprecht interesse te tonen en het regelmatig stellen van de onvermijdelijke vraag: 'Wanneer ga je verdedigen?' Jullie kunnen die vraag nu met een gerust hart laten rusten – en ik denk dat dat voor jullie ook een hele opluchting zal zijn.

Lieve **Kim DH, Sabine, Pam** en **Inez**, mijn ex-collega's van de ICU "den 8B". Jullie hebben dit traject vanaf het begin gevolgd. Jullie oprechte interesse en betrokkenheid hebben me altijd gesteund en gemotiveerd. Jullie belangstelling en steun hebben dit pad een stuk lichter gemaakt. Bedankt dat jullie dit avontuur met mij hebben meegemaakt. Een speciale dank gaat uit naar **Kim DH**, je was letterlijk altijd beschikbaar met goede raad, praktische tips en een luisterend oor. De oneindig vele koffietjes – want "eerst koffie, dan pas klap" - en taartjes die steeds klaarstonden, waren vaak precies wat ik nodig had om even op adem te komen.

Margot, Sara, Kelly VB en **Leslie**, woorden schieten tekort om jullie te bedanken voor de steun en het geduld die jullie me al die jaren hebben gegeven. Jullie waren er altijd, zelfs toen ik vaak weinig tijd had door de drukte van mijn werk in combinatie met dit doctoraat. Op momenten dat ik het moeilijk had en dacht aan opgeven, kon ik steeds bij jullie terecht. Jullie hebben eindeloos gezocht naar momenten om af te spreken, die in mijn schema pasten, en dat betekende ontzettend veel voor mij.

Dank jullie wel voor jullie begrip, geduld en onvoorwaardelijke vriendschap. Jullie aanwezigheid gaf me telkens de moed om door te zetten.

Aan mijn beste vriendin **Kim V**, met wie ik al zo lang een bijzondere vriendschap deel. We kennen elkaar door en door en weten precies wat we nodig hebben en wanneer. Kim, ik wil je bedanken dat je altijd tijd voor me maakte, hoe druk het ook was. Onze koffiedates in die bijzondere roze koffiebars waren momenten van pure steun en ontspanning, waar ik altijd mijn hart kon luchten. Bedankt voor je luisterend oor en je onvoorwaardelijke vriendschap.

Elyne, ik vergeet nooit onze porto-avonturen in Porto. Dankjewel dat je er altijd voor me was, zowel tijdens het PhD-traject als in mijn eerste jaren als assistent WO. Jouw oprechte raad en feedback hebben me echt geholpen en gebracht tot waar ik nu sta.

Kelly, mijn grote voorbeeld. Het was een eer om onder jouw vleugels te mogen werken voor mijn masterproef. Jouw enthousiasme voor onderzoek en statistiek heeft mijn eigen passie alleen maar verder aangewakkerd om dit traject te starten. We hebben samen niet alleen veel serieuze gesprekken gevoerd maar ook ontspannen momenten gedeeld die deze reis zoveel leuker en

waardevoller hebben gemaakt. Bedankt voor je inspiratie en de fijne samenwerking.

Laura, jouw werk binnen ons gezamenlijke onderzoeksveld is inspirerend en heeft mij meer dan eens tot nieuwe inzichten gebracht. Je bent een topper en ik weet zeker dat je het ver gaat brengen. Blijf je dromen volgen!

Maarten, jouw expertise in statistiek en jouw aanmoedigingen hebben me geïnspireerd om zelfstandig R-Studio verder te ontdekken. Door jouw aanmoediging heb ik de stap durven zetten om het zelf allemaal te ontdekken en nieuwe kennis op te bouwen. Bedankt voor je inspiratie en motivatie – het heeft me echt verder gebracht.

Kristel wil ik bedanken voor haar waardevolle ondersteuning tijdens de practica. Jouw expertise in kwalitatief onderzoek heeft me veel nieuwe inzichten gegeven. Ik heb ontzettend genoten van onze gesprekken over onze vakgebieden, ook al komen we uit verschillende onderzoeksparadigma's ;-).

Lien, hoewel we elkaar nog niet lang kennen, ben ik onder de indruk van jouw kennis en de snelheid waarmee je nieuwe dingen opneemt. Het was geweldig om vorig jaar samen responsiecolleges te doen. Bedankt voor de fijne samenwerking en voor je inzet!

Hilde F, dankzij jou ben ik enorm gegroeid als persoon, vooral op het vlak van zelfvertrouwen. Jouw steun en je geloof in mij hebben me geholpen om sterker en zekerder in mijn schoenen te staan. En natuurlijk zal ik jouw wijze les nooit vergeten: "Als er geen naam op staat, dan is het van iedereen!" ;-) Bedankt voor alles wat je me hebt bijgebracht, zowel over het werk als daarbuiten. Ik geniet nog steeds na van de mooie persoonlijke kaartjes die je zelf maakt. Deze betekenen echt veel voor mij.

Eva, ik bewonder je om je inhoudelijke kennis, je manier van doceren en hoe je alles zo goed weet te managen. Jouw voorbeeld is voor mij een grote inspiratiebron. Bedankt dat ik van je mag leren. Jouw bijdrage en begeleiding bij mijn allereerste paper, tot het moment dat hij accepted was, heeft me ontzettend veel geleerd en betekende heel veel voor me. Bedankt voor je inspiratie, steun en de geduldige begeleiding die je me hebt gegeven.

Ook een dankjewel aan mijn UA-collega's **Erik, Filip, Yaël, Luna, Natwarin, Peter, Caroline, Sandrine, Janne, Veerle, Luka, Ina, Denise, Ines, Senne, Hilde P, Noemi** en **Melissa** voor de korte, maar altijd aangename gesprekken in de wandelgangen. Jullie maakten de werkdagen net wat gezelliger en zorgden voor fijne momenten van ontspanning.

Een dankjewel aan **Kristin** voor haar toegankelijkheid en ondersteuning bij al de administratie – vooral de intensievere ondersteuning de laatste maanden. Bedankt, Kristin!

Mijn collega's van **ZAS** verdienen ook een speciale dank. Jullie waren vaak een luisterend oor en boden me de ondersteuning die ik op dat moment nodig had. Bedankt voor alles wat jullie voor me hebben betekend en de aangename wandelingen tijdens de pauzes. Bedankt voor de waardevolle momenten die we hebben gedeeld. Ps: Aanstaande maandag wacht er een kleine verrassing op jullie, boordevol Kinder Bueno's en Kinder Chocolade (en IPC-proof ;-)).

Martine wil ik in het bijzonder bedanken. Je was mijn leidinggevende en jouw steun en begeleiding hebben ontzettend veel voor mij betekend. Je hebt mij ongelofelijk goed opgevangen toen ik bij het team kwam en je liet mij kennis maken met de wondere wereld van IPC. Je was altijd toegankelijk en jouw bemoedigende woorden – dat ik altijd in mezelf moet blijven geloven en trots mag zijn – hebben me enorm deugd gedaan. Martine, jouw vertrouwen, steun en aanmoediging hebben een diepe indruk op me achtergelaten, en ik ben je daar heel dankbaar voor.

Graag wil ik mijn oprechte dank uitspreken aan mijn **ZAS-directie** en aan **Marleen** als bedrijfsleider voor het vertrouwen en de kans die jullie mij bieden voor de toekomst. Jullie geloof in mijn capaciteiten betekent veel voor me en geeft me de motivatie om mezelf verder te ontwikkelen. Bedankt voor deze bijzondere kans en jullie vertrouwen in mij! Ik heb grote plannen binnen ZAS en ik zal jullie niet teleurstellen, dat beloof ik jullie.

Mijn collega's van het **Ethisch Comité**, ik wil jullie graag bedanken voor de betrokkenheid en voor de steeds fijne babbels. We hebben vaak tijd te kort om bij te praten maar de vergaderingen, symposia en etentjes zijn zowel verrijkend als aangenaam.

Ik wil ook graag de **stakeholders** en **deelnemende ziekenhuizen** bedanken. Zonder hun betrokkenheid en ondersteuning zou onderzoek in de medische wetenschappen onmogelijk zijn. Hun bijdrage maakte het verschil en bood ons de kans om belangrijke stappen te zetten in ons vakgebied. Bedankt voor jullie onmisbare steun, hulp en samenwerking.

Aan al mijn collega's van **NuPhaC**: ik heb enorm veel aan onze samenwerking. De jaarlijkse NuPhaC-dagen in Peer zijn inmiddels een mooie traditie geworden, waar ik telkens inspiratie en plezier uit haal. Dat we nog vele jaren mogen samenwerken en deze inspirerende momenten mogen delen!

Mijn dank gaat ook uit naar de masterstudenten die hebben bijgedragen aan dit werk en een interessante thesis hebben geschreven: **Sarah, Shara, Lisa, Josée, Hilde, Jasmijn, Eva** en **Lobke**. Daarnaast wil ik graag alle masterstudenten vermelden die ik tijdens hun opleiding heb mogen begeleiden. Ik kreeg de kans om vele jonge onderzoekers te helpen in hun ontwikkeling en daar heb ik zelf ook enorm veel van geleerd. Bedankt voor de inspirerende samenwerking en de inzichten die jullie mij hebben gegeven.

Dirk van DDW Design, hartelijk dank voor de prachtige vormgeving van dit proefschrift. Jouw creativiteit en oog voor detail hebben ervoor gezorgd dat het eindresultaat er professioneel en verzorgd uitziet. Bedankt voor je harde werk en het fijne samenwerken.

Elke Loots
november 2024

University of Antwerp
Faculty of Medicine and Health Sciences

Antwerp, 2024
Thesis submitted in fulfilment of
the requirements for the degree of
Doctor in Medical Sciences at the
University of Antwerp

Supervisors: Prof. dr. Tinne Dilles
Prof. dr. Bart Van Rompaey
Prof. dr. Manuel Morrens