Somatic monitoring of patients with mood and anxiety disorders

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General discussion

INTRODUCTION

Patients with a severe mental illness have a 13-30 year shorter life expectancy compared to the general population.[1] The majority (about 60%) of this excess mortality can be explained by somatic co-morbidities like cardiovascular disease, nutritional and metabolic diseases and pain.[1-3] Several factors may contribute to this increased risk of somatic morbidity and mortality, such as an unhealthy lifestyle and disparities in health care access that are associated with mental illness.[1,4] Psychiatric outpatients often receive both mental and physical care from several health care providers (see Figure 1). Ideally, the continuum of health care providers provides integrated collaborative care to facilitate an efficient and successful treatment for the individual patient. However, evidence suggest that psychiatric patients do not always receive this integrated care in daily clinical practice.

For example, somatic monitoring of psychiatric outpatients, including physical examination, laboratory tests and medication reconciliation, seems to be a fallow area, both in clinical practice and in scientific research. The expected clinical relevance of somatic monitoring in patients with severe mental illness (SMI) is acknowledged, at least to some extent, in monitoring guidelines for specific psychiatric diseases and (classes of) psychotropic drugs. However, adherence to these guidelines is low in daily clinical practice. There is a need for active clinical decision support to implement structural somatic monitoring. In order to address these issues, we implemented the Monitoring Outcomes of Psychiatric Pharmacotherapy (MOPHAR) monitoring program at Mental Health Services (MHS) Drenthe.

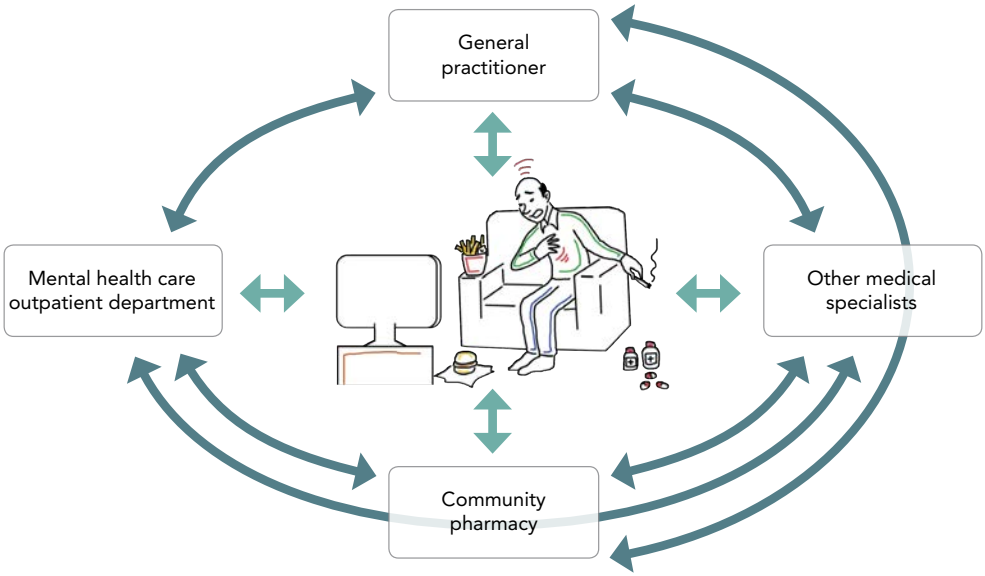

Figure 1. Different health care professionals providing care for psychiatric patients in a patient-centred fashion

In this thesis, we explored the field of somatic monitoring in psychiatry in several themes: the availability of monitoring information in daily care as usual, the added value of implementation of the MOPHAR monitoring program at MHS Drenthe and somatic monitoring parameters beyond MOPHAR. The primary objective of this thesis was to investigate the need for, the construction of and the effects after introduction of a structured somatic monitoring program (MOPHAR) for psychiatric patients visiting an outpatient department of MHS Drenthe. The secondary objectives were to evaluate the criteria for included parameters in MOPHAR and to explore potential new monitoring parameters.

As in the introduction, in this general discussion we will again follow the outpatient during their treatment for a mental illness, this time before and after implementation of MOPHAR at an outpatient department for psychiatry. The results of the individual studies in this thesis will be put into a broader perspective by discussing the following five topics:

- Somatic screening at intake of patients at outpatient departments for psychiatry
- Somatic monitoring during psychiatric outpatient treatment
- MOPHAR: somatic monitoring in a structured monitoring program
- Perspectives for clinical practice
- Perspectives for future research

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SOMATIC SCREENING AT INTAKE OF PATIENTS AT OUTPATIENT DEPARTMENTS FOR PSYCHIATRY

After a new patient is referred to the outpatient department for psychiatry, ideally a large amount of information is available. Apart from a (structured) diagnostic interview to assess patient characteristics and the mental symptoms, also information regarding the physical health status of the patient should be collected, in order to detect cause and consequence of existing side effects and somatic comorbidities. This information includes the medical history of the patient, any current medical diseases and (undiagnosed) symptoms, the actual medication use, up-to-date anthropometric measurements and recent laboratory test results.

Although there is a paucity of specific recommendations for the required elements, a limited number of consensus documents and guidelines suggest a baseline screening should be performed at intake for psychiatric outpatients. It is unclear to what extent these guidelines have been implemented in clinical practice. In 2015, the Dutch guideline on somatic screening in SMI patients was published which suggests an elaborate baseline somatic screening in all SMI patients, irrespective of the specific psychiatric diagnosis.[5] Earlier guidelines have suggested to screen for somatic parameters as part of routine clinical practice in, among others, patients with schizophrenia and bipolar disorder.[6-9] For patients with a (differential) diagnosis of major depressive disorder, in 2011 the first consensus document on safety monitoring was published in which a number of baseline tests are recommended, in part depending on patientcharacteristics.[10,11] Before

implementing MOPHAR, we established a monitoring protocol for the baseline screening with a multidisciplinary working group. We based the recommendations on the available guidelines, expert opinion and experience from clinical practice. The MOPHAR baseline screening serves to screen for existing somatic comorbidities, side effects of (psychotropic) drugs already in use at intake (e.g. metabolic disturbances) and potential (additional) causes of the mental diagnosis (e.g. thyroid dysfunction for depression). In addition, it may serve as a baseline screening if psychotropic drug treatment is started following the intake.

To explore the baseline screening practices in the northern part of The Netherlands, in 2014 we specifically looked at the availability of somatic measurements at intake at outpatient departments for mood and anxiety disorders (**chapter 3**). We found a lack of information on somatic parameters, including anthropometric measurements and laboratory test results. Somatic measurements were unavailable until on a median of 3.8 months after the start of treatment at the outpatient department.[12] These results indicate that a baseline somatic screening is not always daily clinical practice in our sample of four outpatient departments for mood and anxiety disorders, resulting in incomplete information on somatic parameters when the patient for the first time visits his or her mental health care provider.

Our results indicate that outpatients with mood and anxiety disorders are at risk for undetected somatic complications at intake. Baseline somatic screening practices are insufficient and in need of improvement. Reasons for not performing a baseline screening may include limited access to laboratory facilities for physicians and/or patients, insufficiently experienced or educated mental health care professionals or seemingly good somatic health (in young patients).

SOMATIC MONITORING DURING PSYCHIATRIC OUTPATIENT TREATMENT

The 13-30 year shorter life expectancy compared to the general population, predominantly caused by somatic co-morbidities, pleads for structural somatic monitoring during treatment of psychiatric outpatients. Despite the face-validity to monitor known somatic complications of mood and anxiety disorders and adverse effects of psychotropic drugs, the effectiveness of somatic monitoring on treatment outcomes has not been well established.[13]

In order to detect somatic complications and psychotropic drug-induced adverse effects during psychiatric outpatient treatment, several guidelines and consensus documents have suggested to monitor essential somatic parameters as part of routine clinical practice in among others patients with schizophrenia, bipolar disorder and major depressive disorder.[6-8] For patients treated for major depressive disorder, the abovementioned consensus document on safety monitoring recommends a number of baseline and antidepressant-specific follow-up tests, in part depending on patient vulnerability characteristics.[10,11] Similarly, guidelines have been published for somatic monitoring during the use of specific

classes of psychotropic drugs.[6-8,10,14] The previously mentioned 2015 Dutch guideline on somatic screenings in SMI patients suggests a yearly somatic screening in all SMI patients, irrespective of the specific psychiatric diagnosis, plus extra monitoring if the patient starts pharmacotherapy with psychotropic drugs.[5]

The guidelines generally agree that for a correct evaluation of a patient's clinical status and to recognize cause and consequence of side effects, clinicians need to have a complete medication overview. Ideally, this medication overview, which includes current medication use and all medication allergies or intolerances, is obtained by medication reconciliation through the combination of pharmacy records and with patient counseling.[15,16] In a large outpatient population with mood and anxiety disorders, we found that in 95% of the cases, mental health care providers do not have an up-to-date medication overview available for treatment evaluation when their patients visit them (**chapter 2**).[17] This resulted in almost half of all patients in at least one clinically relevant medication discrepancy and warrants the improvement of medication reconciliation processes. Both total number and number of clinically relevant discrepancies were lower in medication overviews from general practitioners and community pharmacies. Moreover, previous studies in both non-psychiatric outpatients[15,18-22] and psychiatric inpatients[23] found substantially lower numbers of medication discrepancies, indicating that this issue may be especially unknown and problematic in psychiatric outpatient settings.

In the same population of outpatients with mood and anxiety disorders, we found scarce performance of somatic monitoring in our evaluation of outpatient monitoring practices (**chapter 3**).[12] Given the high prevalence of somatic co-morbidities, suboptimal monitoring may put these patients at risk for iatrogenic harm, regardless of the specific psychiatric diagnosis. Our naturalistic, non-intervention study showed that, although there were differences between centres, monitoring of somatic parameters at outpatient departments for mood and anxiety disorders is not implemented in daily clinical practice. For almost 60% of all patients, no records of monitoring measurements were available during the median treatment duration of more than seven months. These results are corroborated by several previous research reports, showing poor adherence to monitoring guidelines for psychiatric patients.[24,25] Moreover, the monitoring frequencies of 90-100% for hypertension, diabetes and dyslipidaemia in HIV-patients compared to 40-70% in psychiatric outpatients taking antipsychotics[26], again suggest a particular problem of poor monitoring in psychiatry. The perception that physical health and lifestyle are matters for general practitioners or the belief that patients are uninterested or unwilling to change may be contributing to the lack of physical health care for psychiatric patients.[27-33] However, the low rate of monitoring in psychiatry is in contrast with the SMI patients' perceived need to have their somatic health screened and monitored, as their ability to survey their own physical health interest is reduced.[34] In addition, there is increasing evidence that disparities not only in health care access and utilization, but also in health care provision contribute to the poor physical health outcomes.[27-33]

MOPHAR: SOMATIC MONITORING IN A STRUCTURED MONITORING PROGRAM

The previous two paragraphs suggest that somatic monitoring including medication reconciliation is not part of daily clinical practice for outpatient clinics for psychiatric care. Improvement of monitoring practices provides an opportunity to ensure that somatic complications and adverse drug effects are detected and treated in a timely manner. Unfortunately, the introduction of new guidelines, consensus statements, education materials or (national) quality improvement programs alone have appeared to be only minimally effective in improving monitoring practices.[35-39] An important factor for somatic monitoring may be the attitude of health care providers, which should favour attention to physical health.[40] The basic tools for somatic screening (e.g. weight, waist circumference, blood pressure) are not expensive and most assessments including laboratory tests are routine procedures. The implementation of a more structured monitoring program in which somatic monitoring is ensured as part of routine clinical procedures may be a possible solution to improve monitoring practices.[41]

In **chapter 5** we described how we developed the innovative care path 'Monitoring Outcomes of Psychiatric Pharmacotherapy (MOPHAR)' in the northern part of The Netherlands for implementation at all outpatient departments of MHS Drenthe. In this program, somatic monitoring of psychiatric outpatients is incorporated in routine clinical practice. The primary objective of this program is to prevent, monitor and treat somatic co-morbidities and adverse effects of psychotropic drugs. A nurse conducts and coordinates general somatic screenings with each patient at intake and yearly thereafter. In addition, in the future, recommended monitoring of somatic adverse effects according to pre-specified protocols per psychotropic drug used will be added. Mental health care providers have immediate access to this up-to-date information. As a first check of the implementation of the baseline somatic screening of MOPHAR, we performed an implementation study (**chapter 6**). Of the 24 standard anthropometric and laboratory measurements, on average 21.3 were performed in a one month-margin around the MOPHAR-intake, compared to a median of 3.0 at the time of the original intake at the start of treatment before implementation of MOPHAR – a significant improvement ($p<0.0001$). We concluded that implementation of the MOPHAR monitoring program substantially improved monitoring practices.

The implementation of a monitoring program or physical health checks in other countries has resulted in similar improvements of monitoring practices. In the United Kingdom, by increasing awareness and education in combination with appointments at a mobile physical health clinic increased the number of patients with a physical health check, blood tests and ECG-measurements from 0 to 48%, 6 to 56% and 4 to 24%, respectively.[42] After the introduction of a physical health screening and monitoring protocol at a university psychiatric hospital in Belgium, the proportions of patients receiving somatic medication for specific indications such as hypertension, diabetes and dyslipidaemia as well as

the total somatic medicine increased substantially compared to the pre-intervention period.[40] The results of these studies and the current study justify putting effort, time and money into active implementation of a monitoring program at outpatient departments for psychiatry. Further research should investigate whether these increased monitoring frequencies and the resulting increased number of somatic treatments are associated with improved physical and possibly mental outcomes.

The rate of detected deviating values in the metabolic parameters found during the MOPHAR somatic screening in our implementation study was remarkable. Almost half of all patient met the NCEP ATP-III criteria for the metabolic syndrome. Of note, we could not determine whether these were a result of initiated treatment or were pre-existent. Nevertheless, they confirm the need to monitor these parameters and initiate treatment to prevent further deterioration and subsequent adverse outcomes such as cardiovascular disease.

PERSPECTIVES FOR CLINICAL PRACTICE

We explored only some of the aspects of somatic monitoring in basal studies and found some of these aspects in disagreement with clinical practice standards. We therefore started to implement a monitoring program to overcome these shortcomings and managed to improve monitoring practices. We will now suggest some next steps to further improve the MOPHAR monitoring program.

Integrated collaborative somatic monitoring

Psychiatric patients are often in treatment for both their mental illness and somatic co-morbidities. These comorbidities are sometimes the result of the (psychotropic) drugs in use. Most often several health care providers are involved (Figure 1). Therefore, patient-centred, integrated collaborative care is necessary for a safe and efficient treatment of the individual patient. The results in this thesis show that the care for psychiatric patients seems rather fragmented as shown by low monitoring frequencies and high number of medication discrepancies (**chapters 2 and 3**) and poor transfer of medical information (**chapters 2 and 4**). MOPHAR presents a model for the integration of both mental and somatic monitoring for psychiatric patients (Figure 2). This model provides opportunities for integrated collaborated health care as well. In order to make full use of these opportunities, several aspects have to be addressed: the healthcare provider responsible for performing monitoring measurements, interpretation of measurement results and intervention on aberrances, assurance of protocol-concordance, and communication.

Monitoring results: which health care provider

In order to implement integrated collaborative care, it is crucial that health care providers and the patient use a patient-centred database with data from all relevant sources of information, including health care providers, laboratory and the patient (Figure 2). Although

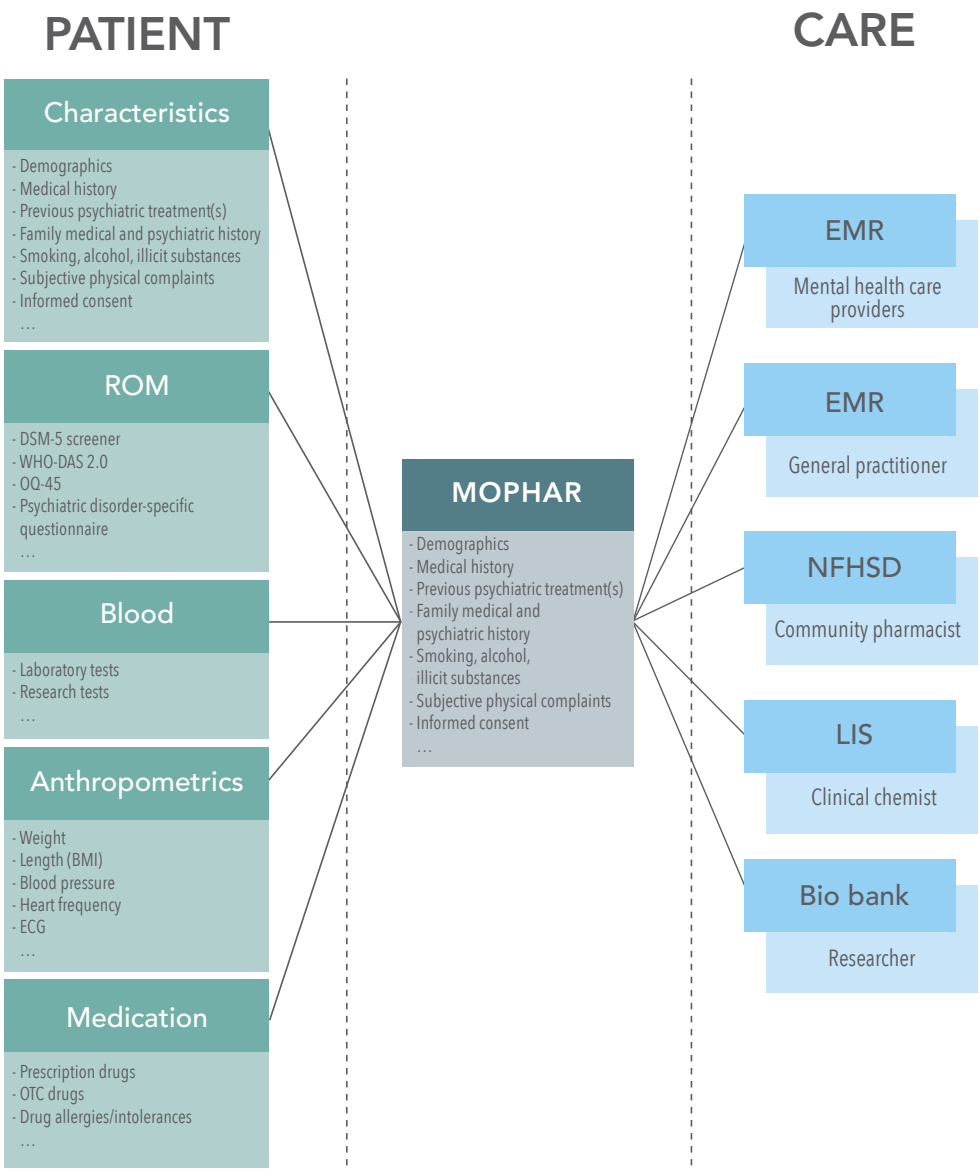

Figure 2. MOPHAR integrated collaborative somatic monitoring care. ROM Routine Outcome Monitoring; DSM Diagnostic and Statistical Manual of Mental Disorders; WHO-DAS World Health Organization Disability Assessment Schedule; OQ Outcome Questionnaire; BMI Body Mass Index; OTC Over The Counter; MOPHAR Monitoring Outcomes of Psychiatric Pharmacotherapy; EMR electronic medical records; NFHSD National First-line Healthcare Shared Database; LIS Laboratory Information System.

MOPHAR is now initiated at the outpatient department for psychiatry, the measurements in the monitoring protocol can be performed by many of the health care providers involved with the psychiatric patient. In many cases, the general practitioner refers the patient to the outpatient department, which may be a good moment for the general practitioner to perform the baseline screening and add the results to the referral. A mental health nurse practitioner at the general practitioner's practice may perform and coordinate the monitoring measurements at baseline and during treatment. An alternative for monitoring during treatment may be the community pharmacy, as psychiatric patients often chronically use psychotropic drugs and have to refill their prescription(s) every three months – a moment that may conveniently coincide with a MOPHAR monitoring consult with a pharmacy technician. Clinical chemical analysts usually draw blood for laboratory tests, but it may be a relatively small extra effort to perform the anthropometric measurements at the same visit to the laboratory. In short, at this moment, it is not yet clear who may be the best health care professional for the monitoring measurements in the near future.

Interpretation of, interventions on and follow-up of (deviating) monitoring results

In MOPHAR, large amounts of monitoring results are generated. A next step in improving the process of the monitoring program is structured interpretation of the results and coordination of the necessary interventions on deviating test results. MOPHAR may then not only cover monitoring, but also the treatment part from the triad of prevention, monitoring and treatment. Depending on who performs the monitoring measurements, the psychiatrist/mental health nursing specialist at the outpatient department or general practitioner/mental health nurse practitioner may receive the results for interpretation. It would be efficient to prepare standard protocols for interventions on specific aberrances, such as the prescription of a statin in case of elevated cholesterol levels (depending on a personalized patient risk-profile) or a lifestyle program in case of the diagnosis of the metabolic syndrome. At this moment, it is unclear which health care provider is responsible for the intervention on monitoring results. Traditionally, the psychiatrist may refer a patient to the general practitioner for treatment of somatic aberrances as determined by a periodic somatic screening. Some general practitioners coordinate and treat these somatic complications, while others are of the opinion that the psychiatrists should treat the psychotropic-induced side effects.[43] The importance of appointing a responsible health care provider for intervening in and follow-up of deviating monitoring results is illustrated by a recent study from the PHAMOUS investigators.[44] Despite prevalences of the metabolic syndrome >50% at three yearly assessments in the PHAMOUS monitoring program, half of the patients were not treated for their metabolic risk.[44] Collaborative monitoring protocols in MOPHAR should determine which health care provider is responsible for the follow-up and intervention of specific deviating monitoring parameters (Figure 2).

Protocol concordance

When implementing a monitoring program, assurance of the conduct of the monitoring protocol is necessary to ensure all measurements are performed. A computer reminder system has been shown to be effective in supporting mental health care providers in laboratory monitoring of psychiatric outpatients using antipsychotics.[45] A similar system may remind the responsible health care provider to perform the other elements of the monitoring program as well. However, in The Netherlands, no digital support system has been implemented yet for somatic monitoring at mental health care institutions. Similarly, digital support could aid in ensuring follow-up aberrances and interventions according to standard protocols or personalized interventions (Figure 2).

Communication

An essential aspect of integrated care is transfer collected information and initiated interventions between the health care providers involved and with the patient. Relevant stakeholders in the model need be kept up-to-date and loss of information and duplicate tests with associated costs as presented in the study on communication of *CYP2D6* genotyping results (**chapter 4**) may be prevented.[46] In our study on medication discrepancies (**chapter 2**), we showed that the medication overview of the outpatient department for mood and anxiety disorders was out-of-date and/or incomplete for almost 95% of the outpatients, indicating poor transmission of medication use data as well.[17] Although we cannot simply generalize these communication practices to other monitoring parameters, these studies serve as an illustration of the need for an efficient communication platform. A digital (web-based) central portal onto which both health care providers and the patient can log on and collect previously generated data, may be a solution. A communication channel may be part of this portal, to facilitate efficient and safe communication between health care provider and patient (Figure 2).

PERSPECTIVES FOR FUTURE RESEARCH

Although somatic monitoring of psychiatric outpatients is increasingly recognized as an invaluable part of treatment of mental illnesses such as mood and anxiety disorders, it is scarcely investigated. We will now suggest some perspectives for future research on somatic monitoring.

Health benefits of somatic monitoring

As stated before, it seems logical to monitor known somatic complications of mental disorders and adverse effects of psychotropic drugs - especially if this can be done by simple, non-invasive and relatively inexpensive measurements such as waist circumference, weight, height, blood pressure and blood sampling. These assessments provide the psychiatrist with useful information for treatment optimization and overall improvement of quality of life for psychiatric patients.[47] However, integration of psychiatric and general

somatic services may at the same time still be one of the most important challenges in mental health care today. More importantly, the effectiveness of somatic monitoring on treatment outcomes has not been well established.[13] Therefore, there is a lack of evidence that somatic monitoring indeed can prevent cases of co-morbidity or mortality. It would be valuable to have evidence of the potential long-term benefits of somatic monitoring with the MOPHAR monitoring program in terms of for example physical and/or mental health, shorter treatment duration, patient satisfaction and quality of life. For this, the 'number needed to monitor' (NNM) would be an interesting outcome to indicate the number of patients that should be monitored (consecutively) to prevent one additional comorbidity or death due to adverse events.

Shaping the MOPHAR monitoring protocol

Shaping the protocol for health care providers

Before implementing MOPHAR, a multidisciplinary working group established monitoring protocols per psychotropic drug (class). The monitoring recommendations were based on relevant guidelines if available. However, since there was a paucity thereof, the protocol was mostly based on clinical experience and expert opinion of the psychiatrists, (hospital) pharmacists and clinical chemist of the working group. Together with other information that was considered necessary to collect for diagnosis and treatment, these monitoring protocols constitute the MOPHAR monitoring program that was implemented in clinical practice. However, the MOPHAR protocol is not perfect yet. There is on ongoing debate regarding the necessity and appropriate frequency of monitoring of parameters such as the electrocardiogram (ECG)[48,49], liver function[50] and blood counts[51]. The protocol therefore needs a regular evaluation in a plan-do-check-act cycle to keep it up-to-date and has to be adjusted to best clinical practices and new guidelines.

The set of monitoring parameters may not be complete. For example, pharmacogenetic determinants are not part of the monitoring program. We investigated the *ABCB1* gene as a potential genetic pharmacokinetic parameter for response to the SSRI paroxetine (**chapter 9**). Ideally, a somatic screening would contain easy-to-determine measurements that reveal whether patients will show clinical response or side effects when treated with specific psychotropic drugs, like antibiotic susceptibility testing for treatment of an infectious disease. In our secondary analysis of data from the DELPHI and DELPHI-SPECT study, we found that two of the four *ABCB1* SNPs showed modification of the relation between paroxetine serum concentration and SERT occupancy, but none of them showed an association with clinical response measured with $HDRS_{17}$. We concluded that at this moment, *ABCB1* genotyping is not yet suitable for individualising psychotropic treatment. Future research should determine whether pharmacogenetics parameters have to be part of the MOPHAR monitoring program.

Future studies on the monitoring protocol may address the optimal efficiency of MOPHAR. An important question to answer is: do we receive the relevant signals in time

with the parameters in the protocol? An important issue that has to be investigated is which patients have to be measured for which parameter and how frequently, which may depend on an a-priori risk-profile instead of a one-size fits all approach. Similarly to the NNM we suggest for assessing the overall benefits of somatic monitoring, NNMs for individual parameters could guide the discussion on their in- and exclusion. For some parameters, we could consider stopping periodic monitoring and instruct the patient to call the psychiatrist if specific symptoms occur as a marker of a specific side effect. An example of such a parameter is a full blood count. Blood dyscrasias, such as agranulocytosis, are rare and they develop rather quickly. As a result, the yield of periodic full blood counts may be low. However, symptoms of a blood dyscrasia, such as haematomas with thrombocytopenia or fever-like sign with agranulocytosis, may be easier to detect and explained to the patient as an alarming symptom, upon which the outpatient department should be contacted. It may be ethically and practically challenging to investigate the need for periodic full blood counts in a (cluster-)randomized controlled trial or otherwise prospective study. Alternatively, long term data from MOPHAR compared to a suitable control/care-as-usual-arm may give more information about these issues. Reducing the number of measurements may relieve the burden on the patients undergoing the measurements, the nurse conducting them and the physician or nurse specialist evaluating them. In addition, costs associated with the somatic screening may be reduced. Therefore, both for individual parameters and the total monitoring program, along with a study on efficiency and health benefits, a cost-effectiveness analysis would be valuable – especially to persuade policy makers, funding agencies and health care insurance companies of the benefits of somatic monitoring.

For many monitoring parameters included in the monitoring program, there is a lack of evidence (for the specific conditions) on which monitoring of the parameter is based. Such specific criteria in recommendations are important in case a parameter is, for example not easily performed at the outpatient department, only informative for a subset of the population or a (surrogate) marker for a complication with a low risk and/or associated with high costs. The ECG for measuring the QTc-interval as a surrogate marker of the risk of potentially lethal cardiac arrhythmias is an example of this. However, as with ECG monitoring, evidence is often lacking as to what are relevant risk factors, what are their relative risks and what are the potential health benefits of monitoring the parameter. Ideally, these questions are answered in a (cluster-)randomized controlled trial or prospective cohort study to provide a definite evidence base for monitoring recommendations. However, again, a randomized controlled trial (RCT) may not always be feasible because of ethical considerations. For our attempt to make evidence-based recommendations on ECG monitoring with antidepressant treatment, we therefore took a different approach. After quantifying the risk of QTc-prolongation by antidepressants (**chapter 7**), we investigated the evidence underlying the risk factors for cardiac arrhythmia and sudden (cardiac) death mentioned in the scarce recommendations on ECG monitoring with antidepressant treatments (**chapter 8**). We could not quantify the relative risks of those risk factors, due to a lack of meta-analyses on this subject. Additional expert opinion

was therefore used to formulate recommendations. This resulted in readily applicable recommendations for clinical practice for selection of high-risk patients for ECG monitoring before and during antidepressant treatment.

The patient

The patient is an important and freely available source of information for somatic monitoring (Figure 2). Mental health treatment should be adjusted to the era of patient empowerment and e-health possibilities. Patients will increasingly be informed by digital sources of varying quality. Mental health care providers can give directions to reliable sources of information if necessary, such as in the case of side effects of psychotropic drugs. E-health solutions like communication through patient portals and self-tests also provide opportunities to more actively involve the patient in somatic monitoring, for example by self-measurement of certain parameters, such as weighing or point-of-care-laboratory tests. The results can be communicated through a patient portal and a notification may be generated when it is time for the next self-measurement according to the protocol. Self-tests and active involvement of the patient in somatic monitoring may relieve the burden for patients of having to go to a laboratory and increase adherence to the monitoring protocols. Although self-management of somatic monitoring by the patient may be a valuable and (cost-)efficient addition to consult-based care, not all patients may be capable of reliable self-management. This may be true for patients with SMI in particular. Therefore, whether the patient can be considered a partner in the somatic monitoring program may depend on specific patient and disease characteristics instead of a one-size-fits-all approach. In addition, not all e-health solutions are effective with self-management for monitoring or treatment purposes in all patients – albeit physically ill or psychiatric patients.[52-55] Furthermore, goals and motives with respect to advice on diet, alcohol consumption, physical activity may differ for patients and their healthcare professionals. Blended interventions, in which face-to-face and internet approaches are combined, usually are more effective in that respect.[56] These issues warrant further research before a definite statement about the role of the patient can be made.

The outcomes from somatic monitoring inform the mental health care provider on relevant side effects and somatic co-morbidities. However, these outcome measures may not reflect the patient's view on his/her clinical status. For that, Patient Reported Outcome Measures (PROMs) may be a better measure, as those measure treatment effect from the patient's perspective. So far, it is unclear which parameter, e.g. their general functioning or quality of life, is valued by psychiatric outpatients as the most important outcome of somatic monitoring. This should be subject of future research and the most relevant PROM(s) should then be added to the MOPHAR monitoring protocol.

Research potential of a MOPHAR-like patient registry of somatic monitoring data

MOPHAR is not a goal in itself but can be considered a means for structured somatic monitoring care in psychiatry. In addition, it provides an infrastructure for scientific

research. The large amounts of information collected in the patient-registry of MOPHAR is of great value in this respect: many questions may be answered in retrospective and prospective studies, including association studies and prediction models on the effects and side effects of psychotropic drugs. By increasing the database as a part of clinical care, MOPHAR will yield sufficient power for many research questions, including genetic studies. Although not performed in a MOPHAR patient sample, the study on *ABCB1* genotyping as a potential application of a pharmacokinetic genetic parameter for predicting clinical response is an example of the studies that can be performed using the extra blood sample in combination with other measurements.

CONCLUSIONS

This thesis explored somatic monitoring of psychiatric outpatients. The limited availability of important medical patient information such as medication use, and monitoring measurements may put psychiatric outpatients at risk for harm. Implementation of a monitoring program brings structure to the somatic monitoring of these vulnerable patients and may ensure that monitoring measurements are performed. The MOPHAR protocol is by no means definite or final but should be evaluated on a regular basis. Nevertheless, a monitoring program such as MOPHAR provides the opportunity to improve patient somatic and at the same time perform a variety of clinical studies that may directly translate to improvements of that same clinical practice. MOPHAR therefore is a vehicle for both improvement of clinical practice and clinical research in psychiatry. Since evidence of the benefits and best practices of somatic monitoring of psychiatric patients is scarce, the exploration of this field should continue.

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