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Going beyond cost-effectiveness: analyzing routine mental healthcare data and stakeholders' perspectives to improve depression care

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CHAPTER 8

General discussion

The overall aim of this thesis was to optimize the quality and efficiency of depression care in the Netherlands by learning from past and current practices using routinely collected administrative data on mental healthcare use and patient outcomes, with additionally obtained qualitative data. This thesis covered the efficiency of depression care on patient-level, organizational level, and national policy decision-making level. In the first part of this thesis, we made use of observational mental healthcare data, consisting of treatment (pathway) data and outcome data. These data were used to gain more insight into the clinical effectiveness of treatments (Chapter 2), care utilization and treatment costs in specialist mental healthcare (Chapter 3), and to evaluate a recent change in the Dutch mental health system on a regional level (Chapter 4). In the second part of this thesis, we enriched routinely collected data with qualitative data on stakeholders' values to gain insight into the quality and efficiency of depression care on the policy decision-making level (Chapter 5) and the patient-level and organizational level (Chapter 6, 7).

This final chapter first presents an overview of the main findings of previous chapters. Subsequently, we will reflect and discuss the main findings in a broader context and address the methodologies used with their strengths and weaknesses. Finally, we will discuss the potential clinical implications and recommendations for future research.

OVERVIEW OF MAIN FINDINGS

In Chapter 2, we showed that the overall corroborated remission and response rate of an algorithm-guided treatment program for depression was 36.8% and 23.9% respectively. Within the algorithm-guided treatment program, the remission rates for pharmacotherapy and combination therapy were comparable to remission rates encountered in the literature, although the remission rate of psychotherapy was lower compared to the remission rates found in randomized controlled trials (RCTs). Similarly, response rates were lower for psychotherapy and pharmacotherapy and comparable for combination therapy when compared to response rates observed in efficacy trials. Despite the more heterogeneous patient population, where all patients were treated regardless of their disease duration or severity, we concluded that the effectiveness of the algorithm guided treatment program with strong emphasis on guideline adherence by clinicians, approaches the efficacy reported in RCTs. A similar proportion of patients achieved remission and response both among the "early terminators" and the "completers" of the prescribed number of treatment sessions.

In Chapter 3, we found that in specialist mental healthcare 71.7% of patients diagnosed with major depressive disorder (MDD) had one or more psychiatric comorbidities, among whom 39.7% had a personality disorder (PD). The treatment of patients with MDD and psychiatric comorbidities involved more mental health service

use than treatment of patients with only MDD. Compared with patients with only MDD, costs of patients with additional PD and with or without other psychiatric comorbidities were, respectively, 2.71 and 2.06 times higher. Treatment costs of patients with MDD and comorbidities other than PD were 1.36 times higher compared with patients with only MDD. Next to coexisting psychiatric comorbidities, higher age and first episodes were other drivers of treatment costs.

To realize an effective and appropriate mental healthcare system that would also remain affordable, as of January 1st, 2014, a mental health system change was introduced in the Netherlands. Starting points of the system change were a reduction of inpatient stays by one-third, and the introduction of generalist mental healthcare for the provision of more complex care compared to the former primary mental healthcare. In Chapter 4, we observed a negative trend in average treatment costs per patient per quarter after the system change was implemented in 2014. When accounting for a 1-year transition period (from Q3 2013 to Q3 2014) the analysis revealed a decreasing trend in costs already two quarters before the system change came into force. For the average number of inpatient days, we found that prior to the system change there was already a significant quarter-to-quarter decreasing trend in the average number of inpatient days. The data showed that the system change did not lead to an additional level or slope change in average inpatient days per patient per quarter after the implementation of the system change. We did not find a significant change in average baseline depression severity before and after the system change.

In Chapter 5, we demonstrated a structured approach for eliciting and evaluating a broad range of assessment criteria along with the results of cost-effectiveness analyses by systematically involving key stakeholders. This provides an alternative to the usual deliberative commission approach in healthcare priority setting. From stakeholders' perspectives, two out of the thirteen substitute interventions were deemed acceptable and realistic after considering both the cost-effectiveness criterion and all other relevant criteria. We found that for the majority of the substitute interventions that could improve the cost-effectiveness of depression care, stakeholders expressed one or more concerns. The issues raised were mainly related to workforce capacity, lack of stakeholder support and the need for change in clinicians' attitude. The approach used in this study allows decision makers to prioritize among cost-effective policy options and provided insights into the intended and unintended consequences of using a certain health technology.

In our qualitative study described in Chapter 6, we found that patients and clinicians considered the following treatment outcomes relevant: restoring social functioning and interpersonal relations, regaining quality of life and achieving personal goals. Clinicians also emphasized symptom reduction and patient satisfaction with treatment as relevant, whereas symptom reduction was not an obvious theme for patients. In addition, patients made a clear distinction between outcomes related to first episodes versus recurrent or chronic episodes.

We described the development of a practical decision support tool, the 'Instrument for shared decision-making in depression (I-SHARED)' in Chapter 7. I-SHARED consists of personal information summarized in a patient summary report including an overview of potential successful or unsuccessful treatment options, and treatment option grids summarizing objective treatment information to inform on evidence-based treatment options. The overview of potentially worthwhile treatment options was based on cluster modeling to identify a reference group based on symptoms, functioning, and age. By collaborating with patients, patient organizations and healthcare professionals, the developed tool became a joint effort and explicitly included their preferences and values.

REFLECTION ON THE MAIN FINDINGS

Algorithm-guided treatment

In both Chapter 2 and Chapter 7 algorithms were used to improve care for patients with depression by guiding treatment selection in real-world. In Chapter 2, electronic patient files contained a built-in decision tree reflecting the treatment algorithm, based on the Dutch multidisciplinary guideline for depression treatment¹, to support decision-making in daily practice. For all patients, the treatment recommendation was based on the number of symptoms, disease severity and previous episodes. In Chapter 7, however, a cluster algorithm was part of a decision support tool resulting in tailored treatment recommendations. The clustering algorithm resulted in a personalized overview of potentially worthwhile treatment options based on previously benefited patients with similar characteristics.

While in RCTs and many treatment algorithms treatment durations are often pre-defined, we observed considerable variation in the number of utilized treatment sessions in both our studies. In Chapter 2, we showed that treatment length varied considerably between patients. Some patients achieved remission with fewer treatment sessions while other patients achieved remission after higher numbers of treatment sessions. In Chapter 7, we saw a strongly right-skewed distribution of the average number of treatment contacts per month. It appeared difficult to accurately predict the required number of treatment contacts. Previous dose-response studies indicated different responsiveness for different groups of patients^{2,3}. Based on our findings, further investigation is needed to find the optimal number of treatment sessions, as a pre-defined number of treatment sessions does not seem to suit all individual patients. The outcomes of this assessment may have considerable impact on the resources needed to treat different groups of patients.

We found that treatments provided within an algorithm-guided treatment program for specialized depression treatment in a naturalistic setting can approach the efficacy reported in RCTs. The remission rates found in our study (range: 31-46%, overall:

37%) were higher in comparison with another study in which ROM data were used to assess treatment effectiveness (17-27%)⁴, and comparable to the remission rate for pharmacotherapy in other algorithm-based studies^{5,6}. Although we did not compare our findings with a care as usual setting, previous studies demonstrated improved quality of care and improved outcomes in patients with depression⁷⁻¹¹.

Overall, these findings demonstrate the potential of the using algorithms in clinical practice for (personalized) treatment selection and for improving treatment outcomes by enhancing adherence to guidelines.

Mental healthcare utilization and treatment costs

We addressed mental healthcare utilization and related treatment costs in patients with depression in specialist mental healthcare (Chapter 3), and the changes in mental healthcare utilization and treatment costs that were associated with a mental health system change (Chapter 4). There are some specific findings related to care utilization and treatment costs that are worth mentioning.

Although it is well-known that patients with depression often have other mental disorders^{12,13}, we found it striking that a majority of the patients in specialist mental healthcare suffered a comorbid personality disorder. Previous research found a prevalence of a comorbid personality disorder in patients with depression of 45%, and even 60% in patients with dysthymic disorder¹⁴. A comorbid personality disorder seems to be associated with much more care utilization and treatment costs compared to a patient with only depression.

Our findings confirmed that inpatient care was a major cost component in patients diagnosed with MDD¹⁵ in specialist mental healthcare irrespectively of comorbidities contributing to half of the treatment costs. Policies aiming to substitute inpatient care for ambulant care and care closer to the patient's home seemed to result in less inpatients days and less treatment costs in specialist and generalist mental healthcare (Chapter 4). In our study General Practice (GP) data were not available. However, GP healthcare data should confirm if the overall costs, including the shift to GP care, actually led to costs savings for this specific patient group.

We observed a median treatment duration of ten months. Other epidemiological studies found depressive episode durations of 3-12 months^{16,17}. We also observed that in the specialist mental healthcare setting 23% of the study population remained in treatment. In literature, approximately 20% of patients sampled from the general population, did not recover after two years¹⁷.

Overall, these results suggest that conceptualizing and treating MDD as an isolated disorder may underestimate prognosis and the type of care that is appropriate in patients. Further investigation into the exact costs attributable to combination treatment or more intensive treatment in case of comorbidities and the treatment costs incurred at GPs is needed to be able to draw firm recommendations.

Patients' perspectives and patient-centered care

Recently, provision of patient-centered care received increased attention. Patient-centered care requires provision of care that is respectful of individual patient preferences, values and attitudes towards health and illness^{18,19}. Besides, it ensures that patient values guide clinical decisions. In Chapter 6 and Chapter 7, our findings demonstrated that patients do not only focus on symptom reduction. Social functioning, interpersonal relationships, prevention of future recurrences, managing depression, and achieving personal goals were also considered relevant. These findings indicate that currently used end-points reflect what matters to patients in clinical practice only to a limited extent. Patients may have other goals in treatment, than remission and response, often rarely measured in clinical trials²⁰. A recent study confirmed our findings and showed that outcome domains such as mental pain and capacity for patients to live a family life also matters to patients and other stakeholders²¹. Our findings also indicate that we may need to use different end-points when treating a first episode versus a recurrent or chronic depression. To our knowledge, the gradual modification of treatment goals after experiencing several reoccurrences has not been described elsewhere. Our findings correspond to findings of previous studies that indicate that end-points should reflect all stages of the disease²² and the recommendation to define a secondary outcome, such as daily function, to more broadly inform the results in terms of clinically relevant findings in difficult-to-treat-depression trials²³.

Although previous research identified a range of patients' needs to enhance shared decision making^{24,25}, we started with the identification of patients' needs prior to the development of I-SHARED for our specific setting. Besides, during the entire development and piloting process of I-SHARED we collaborated with MIND, a Dutch umbrella organization that unites different patient and carer organizations in mental health, to ensure a technically sound decision-aid that is appreciated by the end users. We observed that a decision aid should be easy to interpret for both clinicians and patients. Next to the interface of the decision aid, this also holds for the outcomes of the data driven analysis. One should hence keep in mind that the data driven analyses are intuitive. Therefore, not all machine learning approaches are applicable because some approaches are difficult to substantiate in clinical practice. The use of a clustering algorithm was a useful and practical solution, balancing patient relevant aspects, understandability and data requirements.

Overall, only by involving patients in care and research, through inclusion of their experiences and ideas and by co-creating tools meeting their needs, patients may indeed be placed at the center of care. Their input is essential for both the development of treatments that target patients' needs as well as the provision of effective depression care.

Policy decision-making in depression care

Maintaining a comprehensive and affordable healthcare package of high-quality entails difficult choices. In Chapter 5, we discussed that most developed countries apply formal HTAs to substantiate reimbursement decisions. The efficiency criterion plays an important role in most HTA frameworks²⁶. We showed that focusing on the efficiency criterion only, has major limitations because additional criteria relevant to priority setting are less well considered. We suggest that it could be worthwhile to incorporate additional criteria during the appraisal phase. We demonstrated how HTA may be strengthened via a systematic embedded qualitative approach, including diverse stakeholders' views and values. Experts (e.g., clinicians, healthcare professionals) may help to provide important insights into various domains and the context in which technologies are used, while insights and experiences of patients provide an additional perspective into the intended and unintended consequences of using a certain health technology. This is in line with suggestions by Facey et al.,²⁷ who recommend a deliberative decision-making process, to include robust evidence about patients' perspectives next to opinions of experts. Ensuring effective engagement of patients in the entire HTA/appraisal process contributes to a fair deliberative process to strengthen current and future HTA frameworks^{28,29}. Our study demonstrated how our methodology may add to the deliberative commission approach, and how the outcomes can be used for policy decision making.

A substantive finding worth mentioning, is the fact that investment in therapist-guided iCBT and disinvestment in individual CBT appears to be a promising strategy for patients with mild depression. Due to the COVID-19 pandemic many patients participated in online therapy as regular face-to-face contacts were temporarily unavailable. These circumstances provide an opportunity to evaluate the outcomes of widespread use of online therapies in different severity levels of depression using real world data in the future.

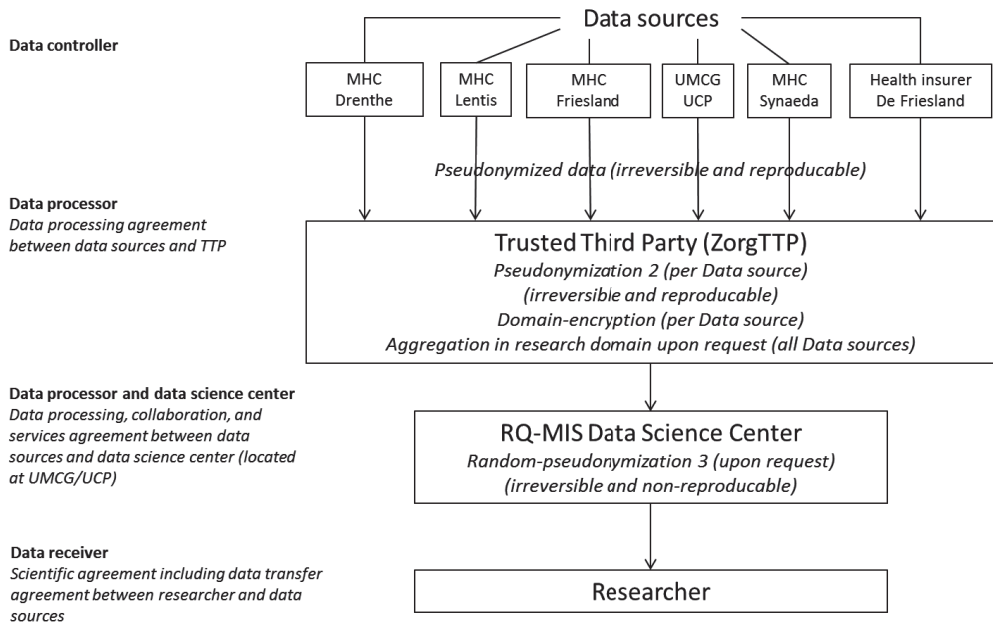
METHODOLOGICAL CONSIDERATIONS

Several strengths and limitations of the studies in this thesis were addressed in each chapter separately. In this section, the most important methodological considerations are discussed, from an aggregated perspective.

In this thesis, most studies were performed using linked routinely collected data sources. The set-up of the data linkage process was a complex and therefore time-consuming process. All parties involved in IMPROVE signed a cooperation agreement to stress their commitment to the IMPROVE project and its main goals³⁰. According to the General Data Protection Regulation (GDPR), the linkage of the different data sources requires a trusted third party (TTP). The TTP facilitated the data linkage

between the different data sources of several parties/care organizations. A repeated pseudonymization and encryption procedure of personal data was used (privacy by design) as shown in Figure 1. Data sources like the mental health organizations and health insurer De Friesland Zorgverzekeraar signed a data processor agreement with the TTP.

Figure 1. Data infrastructure and governance of IMPROVE



MHC: mental healthcare organization
 UMGG: university medical center Groningen
 UCP: university center of psychiatry
 TTP: trusted third party
 RQ-MIS: RoQua Management Information System

Once arranged, the availability of linked data sources on treatment and outcomes provides great opportunities to investigate mental health care utilization and associated costs, treatment effectiveness, and prediction of treatment response related questions. Because the linked data sources contained administrative data, considerable time was needed for data cleaning and data validation.

In the quantitative studies (Chapter 2, 3, 4, and 7), we mainly used observational routinely collected data sources, consisting of treatment data, combined with outcome data and data regarding patient characteristics. Depending on the type of research question, the use of linked observational routinely collected data is highly suitable and provides major advantages. First, it enables the investigation of the real-world

effectiveness of several types of treatments as opposed to efficacy in randomized controlled trials (RCTs), as investigated in Chapter 2. The majority of RCTs include strict inclusion and exclusion criteria, for example for disease severity or other criteria that could make patients ineligible for participation in trials, while in real life all patients are offered some form of treatment regardless of their disease severity (Chapter 2 and 3). Second, a longer follow-up is often available when using or combining several routinely collected data sources. Follow-up periods in RCTs are often limited by budgetary constraints. The observational nature of our data allowed us to investigate the costs of treatment and care utilization of patients with MDD over a long follow-up period, twelve years and seven years respectively in Chapter 3 and Chapter 4. The use of routinely collected time series data over a long period of time is particularly suitable for the evaluation of health policies (Chapter 4). Third, these types of data allow for a relatively large sample size and are relatively inexpensive in comparison to the set-up of RCTs. As depression is highly comorbid with other psychiatric comorbidities, the availability of a relatively large sample size, made it possible to compare care utilization and treatment costs in different groups of patients diagnosed with depression and one or more comorbidities. It provided us with a more complete view on actual care utilization of specific patient groups.

Over the past decades, the use of 'big data' resources also offered novel opportunities for healthcare research, especially the development of diagnostic and prognostic applications. In mental health research, these data are mainly used for epidemiological/etiological research and analyses of treatments and outcomes, especially for medication prescription and monitoring of safety and adverse events³¹. The data allowed us to develop a clinical decision support tool, where we applied a machine learning approach, to provide patients and clinicians with an overview of treatments that have the potential to lead to significant improvement of outcomes based on the patient's characteristics and clinical factors.

Next to the major advantages of using routinely collected data sources, we also ran into several challenges while conducting the studies described in this thesis. In several chapters (Chapter 2, 3), we had to deal with the consequences of the fact that the data we used had not been collected for research purposes. Data regarding patient demographics or medical histories, treatment termination information or medication data were not available in the linked data sources. In addition, after linkage of treatment data (Chapter 2, 7) with routine outcome monitoring (ROM) data, a considerable proportion of data contained non-linkable records. Over the years, routine collection of outcome data has improved. In the studies described in this thesis, we decided to remove the records with missing observations in the key variables and kept a smaller group of patients for the analysis. We investigated the comparability of the study population with the patients that had missing outcomes data. Within the cluster analysis of the I-SHARED tool (Chapter 7) we therefore chose to limit the number of predictive variables. The

predictive value of most tools is hampered by small study sample sizes and therefore the use of large prospective observational studies and comprehensive batteries of self-report data is recommended³². The set-up of the entire data infrastructure where I-SHARED is based upon, is promising for expanding the number of predictors in the algorithm in the future.

Due to the limited number of available patient characteristics in several studies, it was difficult to control for confounding. By either making a comparison with the group of patients with missing data (Chapter 2), or by comparing different patient groups (Chapter 3) we tried to correct for confounding to some extent. Finally, the reliability of the data was based on coding accuracy and practice patterns. This was particularly visible in the DIS treatment data. For example, when healthcare professionals document the type of treatment received by a patient, they have an option to register a 'follow-up contact' instead of the specific type of treatment (e.g., 'interpersonal therapy'). To predict which treatment is most effective for which patients, the registration of the specific type of treatment that is received by the patient is required.

In our studies, different types of depression rating scales were used, as ROM questionnaires used by the different mental health organizations may differ. Therefore, we needed to convert the raw outcomes scores into standardized scores or we ended up with a smaller sample size due to missing outcome data.

In several chapters of this thesis, we used a mixed methods approach, by combining the quantitative data with qualitative data. Qualitative research is particularly suitable to gain an understanding of underlying experiences, motivations, thoughts, and opinions. The outcomes obtained with qualitative research are generally used to provide insights into consequences or to help develop ideas for potential quantitative research. Qualitative techniques provide a unique depth of understanding which is for instance more difficult to gain from quantitative surveys. The conduct of focus group discussions and semi-structured interviews in Chapter 6, provided us with in-depth insights into the perspectives and attitudes of patients and clinicians regarding relevant outcomes of depression treatments. In Chapter 7, patients and clinicians identified gaps in clinical practice, relevant components of a decision-aid, preferences regarding a decision-aid's user interface, and the usability and comprehensibility of the I-SHARED report. In Chapter 5, several stakeholders were involved to elicit information regarding stakeholders' views and values on a wide range of criteria to enable decision makers to make better-informed decisions and appropriate judgments when setting healthcare priorities. By using qualitative research techniques, the participants in the previously mentioned qualitative studies could elaborate freely on the topics, without being guided by pre-defined questionnaires or suggestions from researchers. All studies provided us with crucial in-depth information, which we (as researchers and policymakers) would have missed or overlooked if a non-qualitative approach had been applied. This methodology does require knowledge from the researchers

regarding qualitative research and interview techniques. In each qualitative study conducted, several researchers with knowledge of qualitative research techniques were involved. When considering this method, one should be aware that the methodology requires time for conduct, analyses and reporting. Studies might be limited by the number of participants due to time constraints or one might want to conduct a study more extensively if not limited by budgetary constraints or time constraints. For our studies, we continued data collection until data saturation was reached and we included perspectives of different stakeholders. Furthermore, a good network or collaboration with, among others, patient councils, patient organizations, mental healthcare organizations or other relevant parties, is essential for the recruitment of a heterogeneous group of participants. We were lucky to benefit from the excellent network and collaboration among and between professionals and clients within the mental health organizations of the Rob Giel Research center. Finally, we experienced that all individuals that participated in our interviews and focus group discussions were very willing to share their experiences, views and values. We noticed that some topics were not so obvious to patients. For instance, most patients were not well-versed in health economic rationing or patients did not have a clear idea of a decision-aid that was in the early stages of development. In both cases, we ensured that patients were adequately informed with an oral presentation and explanation prior to the conduct of the focus group discussion. We also provided a couple of examples of existing decision-aids for other disease areas. However, we wanted to minimally influence their own thoughts and ideas, and therefore we did not provide too many examples of decision-aids.

A mixed methods approach was also used in Chapter 7, where we combined qualitative research with quantitative research and a literature review. We started with qualitative research to gain insights into stakeholders' preferences and a literature review to identify predictors of treatment response in patients with MDD. These methods were used together for elaboration, corroboration (hoping for similar outcomes in the methods used) and complementarity. The challenge of using a mixed methods approach is to combine the information into a practical decision-aid. Qualitative results, quantitative results and results of the literature review might lead to contradiction after combining the data. In our study, the outcomes were used as input for the patient summary within the I-SHARED report. Within the patient summary we prioritized the preferences of the end-users and kept in mind the trade-off between the number of questionnaires captured routinely and the expected non-response. A big challenge was to incorporate known predictors into a data driven analysis. We started with using several machine-learning approaches and ended-up with the clustering approach that was intuitive, practical and understandable. Due to our sample size and available variables in the dataset, the data driven analysis is now restricted to a few predictors obtained from the qualitative results and results of the literature review. However,

the set-up of the infrastructure of the decision-aid makes it possible to improve the algorithm and expand the number of predictors because relevant predictors have been added for data collection and more data will become available in the future.

IMPLICATIONS FOR CLINICAL PRACTICE AND POLICY

The findings in this thesis have several implications for clinical practice and policy. In this section we discuss the key implications on different levels of healthcare.

Moving towards a patient-centered approach

The relevance of incorporating the patient's perspective into research is demonstrated in several chapters of this thesis. We found that the traditional end-points used in RCTs only to some extent reflect the outcomes deemed relevant by patients (Chapter 6 and Chapter 7). Adding outcome questionnaires related to aspects that matter to patients would move even further towards value-based care. When treatment effectiveness and efficacy are measured in end-points that are more meaningful to patients, improvement of treatment success rates becomes achievable.

For patient-centered care shared decision making (SDM) is essential. The use of ROM data as source of information is a useful way to enhance the SDM-process between patients and clinicians in the consultation room³³. I-SHARED places the patient at the center of care by providing relevant information to enable the discussion of the patient's complaints, values and preferences regarding treatment. Although the provision of information enables well-informed choices, shared decision making also requires an active role from an individual. Some patients assume that a clinician knows best with regard to the optimal treatment choice for the patient concerned. In addition, the results of the pilot implementation of I-SHARED [not described in this thesis] demonstrated that patients sometimes experience SDM as complicated because they find it difficult to argue against the expertise of the clinician. We would like to stress the importance of not only training health professionals in SDM, but also looking for ways to help patients gain control during the SDM-process. For example, by improving health literacy.

We further advocate to incorporate the patient's perspective into policy decision-making. As patients are most directly affected by the availability or unavailability of technologies and interventions, it is highly relevant to understand patients' values and the impact of a specific technology or intervention on patients' lives. Previous studies showed that patients can contribute to the public argumentation and determination of complex decisions-making matters^{27,34,35}.

Implications for mental healthcare organizations and healthcare professionals

Filling in the number of ROM questionnaires prior to intake may be overwhelming to

some patients. Although broadly seen as an important step forward, using ROM data in the consultation room for shared decision-making processes is not self-evident. Clinicians have an important role to inform patients about the aims of the use of ROM questionnaires, and the outcomes of ROM questionnaires during intake and treatment monitoring. During treatment better monitoring practices of outcomes and progress of treatment can provide opportunities for improving care and outcomes³⁶. Therefore, awareness of the value of ROM data among clinicians for use in clinical practice and for research purposes remains important.

Also emphasized in other studies^{7,9}, adherence to algorithm guided treatment program with a strong emphasis on guideline adherence can approach the efficacy found in RCTs. Algorithms can support clinicians to choose the right type of treatment for the patient concerned (Chapter 2,7) by reducing inappropriate treatment variance between clinicians and enhancing treatment outcomes.

Depression is known to be accompanied by other mental disorders. Specifically, patients with depression and a comorbid personality disorder had more mental healthcare use, longer treatment, and higher treatment costs (Chapter 3). These findings underscore the importance of disease management programs targeting patients with multiple psychiatric disorders. Taking comorbidity into account provides opportunities for future stratified disease management programs, for example by providing integrated treatment or combined treatment instead of several disorder-specific or consecutive treatments³⁷.

Implications for policy decision making

The results of several chapters in this thesis demonstrate that use of linked routinely collected data yields valuable results for policy decision-making. Aggregated data regarding treatment information linked to patient characteristics and outcomes provide insight into how treatment works for a specific patient group. Besides, treatment outcomes can be assessed in a naturalistic setting within a heterogeneous patient population, and such data allow assessing the impact of policy implementations over time. The collection and use of such data are essential to learn from, and enable quality improvements in patients and mental health organizations. For this reason, it is of importance that routine treatment data and outcome data are collected in a structured and consistent manner, also in the future. Although the current ideas of the new mental health funding model (In Dutch: Zorgprestatie model GGZ en FZ, zorgprestatie model.nl), that will come into effect as of January 1st 2022, do not include the registration of type of treatment, it remains crucial to register the treatment type received in one way or another for quality and efficiency improvement purposes.

We found that only three out of ten patients in specialist mental healthcare were diagnosed with depression only (Chapter 3). Therefore, cost-of-illness studies that focus on the isolated costs of depression only, underestimate mental healthcare costs for most

patients with depression in real world. For policy decision makers it is of importance to keep in mind that depressed patients with comorbidities represent the majority of the patient population, and that the associated costs of an additional personality disorder are considerable.

We found treatment endpoints that matter to both patients and clinicians (Chapter 6 and Chapter 7). These findings can be used to develop treatments that are in line with patients' needs. If current treatment outcomes have limited relevance to patients and clinicians, evaluation of treatment effects may be biased, with negative consequences for policy decision making.

We also demonstrated that besides cost-effectiveness other aspects are relevant and should be taken into consideration for priority setting decisions. The use of an explicit and transparent systematic methodology (Chapter 5), by ensuring the disclosure of key stakeholders' values and preferences, can strengthen the current HTA process. It contributes to priority setting decisions, and the deliberative process helps to contextualize technologies to facilitate well-informed priority setting decisions. In our case, findings of the deliberation will be taken into consideration in the coming contract negotiations by a health insurer and a mental healthcare provider.

DIRECTIONS FOR FUTURE RESEARCH

In this thesis we aimed to optimize the quality and efficiency of depression care on several healthcare levels. During the conduct of these studies, we acquired insights into perspectives for future research or obtained knowledge for improved methodologies. In this section we discuss key areas that would merit further investigation.

The improved use of ROM during treatment for better monitoring practices also provides opportunities for future research. In Chapter 2 we showed that a fixed amount of treatment sessions does not seem to suit all individual patients. A part of the patients was in remission with fewer than the amount of recommended treatment sessions while other patients did not reach remission even after receiving more treatment sessions than recommended. Therefore, we recommend the investigation of the optimal treatment length in individual patients by using all ROM information during treatment to predict which individual patients would benefit from shorter treatment durations and which individual patients would benefit from more intensive treatment.

The abundance of data that accumulates after data linkage of patient characteristics data, treatment and outcome data and other sources of data (e.g., claims data, pharmacy data), provides endless possibilities to look into other important matters. Given the available sample sizes of for instance the Psychiatric Case Register North Netherlands, it would be worthwhile to investigate mental healthcare utilization in patients with depression and other psychiatric comorbidities in more detail e.g., anxiety disorder.

Current data linked to claims data or pharmacy data regarding antidepressant medication usage, dosage and type of pharmacological treatment provides opportunities to investigate the real-world (cost-) effectiveness of drugs, drug dosages, or combination of drugs for different groups of patients.

We developed a first version of the I-SHARED decision-aid that is ready for use in clinical practice. During the iterative development process many ideas and possibilities emerged that deserve further investigation. The current version includes social role functioning, interpersonal functioning and symptoms into the clustering model. When data allows, we recommend extension of the cluster model variables with additional predictors, obtained from our literature review and focus group discussions. To enhance this, a selected number of additional variables was added to current ROM. In addition, with the use of pharmacotherapy dosage and tolerability data, I-SHARED can be extended with a prediction of and recommendation on the type of pharmacotherapy based on the effect and tolerability. In the Netherlands, several mental health organizations are working on prediction models that aim to answer the *what works when for whom* question. As data sample size matters when a lot of variables are available, we would also recommend collaboration with several mental health organizations to further improve the algorithms aimed at optimal treatment selection. Data sharing and sharing of knowledge with regard to methodologies make it possible to combine forces and prevent others the effort of reinventing the wheel. When other relevant predictors are added to the model and an improved algorithm is developed, future studies should investigate if the use of the decision aid actually leads to more effective and efficient treatment allocation, improved knowledge and improved shared decision making in patients with depression.

Several studies in this thesis (Chapter 5, 6, 7) demonstrated the value of patient involvement in health research. Patients have unique knowledge and insights about living with a health condition and their needs for treatments can only be taken into consideration by involving them. We advocate co-creation with patients or other relevant stakeholders in future research. To improve outcomes in healthcare, identification of patients' needs is required. Patients are most affected by decisions regarding health, treatment and health technologies.

On the macro level it would be essential to investigate if the alternative explicit and transparent methodology described in this thesis (Chapter 5), by the systematic provision of information relating to other criteria alongside the efficiency criterion, will result in improved decision-making meeting stakeholders' needs and more efficient provision of care for patients with depression.

The studies described in this thesis were performed in the past five years. During the conduct of these studies more observational treatment and outcome data became available over time. With the acquired knowledge of the past five years, I would focus on the following if I would continue working within this field. First, due to the amount of

available data and the lessons learned from the I-SHARED implementation, I recommend developing decision aids for other psychiatric indications as well, next to the expansion of I-SHARED. I learned from the results of Chapter 3 and the feedback obtained from the implementation of I-SHARED that it is important to develop decision aids that take into account comorbidities for example by developing generic decision aids that can be used for more than one indication. Second, I would immediately start co-creating again with patient organizations as our studies demonstrated that their involvement is essential for moving towards patient-centered care. Finally, as observational data are perceived as being less well suited as a basis for effectiveness claims, I would look more into some additional methodologies to reduce the potential bias due to confounding variables that might obscure estimation of treatment effects. Indeed, non-randomized treatment allocation is omnipresent and hence propensity score matching or instrumental variable analysis may improve estimation of causal relations in uncontrolled studies.

CONCLUSIONS

Overall, this thesis demonstrated the potential of using linked administrative data sources regarding patient characteristics, treatment information and treatment outcomes in combination with qualitative research for improving the quality, effectiveness and efficiency of depression care. It provided us with insights regarding real world effectiveness, healthcare utilization and associated costs and the consequences of a mental health system reform. At the same time, this thesis showed the value of the use of algorithms for improving treatment effectiveness and personalized treatment. The findings also highlight the need to increase efforts to incorporate the patient's perspective into several areas of research, especially the value of their perspectives in personalizing treatment and in determining of the acceptability of proposed priority setting decisions. The I-SHARED tool is ready for implementation to support clinicians and patients with depression in shared decision-making concerning treatment choice.

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