

University of Groningen

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

Kan, Kaying

DOI:
[10.33612/diss.183452704](https://doi.org/10.33612/diss.183452704)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2021

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Kan, K. (2021). *Going beyond cost-effectiveness: analyzing routine mental healthcare data and stakeholders' perspectives to improve depression care*. [Thesis fully internal (DIV), University of Groningen]. University of Groningen. <https://doi.org/10.33612/diss.183452704>

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

CHAPTER 5

More than cost-effectiveness? Applying a second-stage filter to improve policy decision making

Published as:

Kan, K., Jorg, F., Lokkerbol, J., Mihalopoulos, C., Buskens, E., Schoevers, R. A., & Feenstra, T. L. (2021). More than cost-effectiveness? Applying a second-stage filter to improve policy decision making. *Health Expectations*. <https://doi.org/10.1111/hex.13277>

ABSTRACT

Background: Apart from cost-effectiveness, considerations like equity and acceptability may affect health-care priority setting. Preferably, priority setting combines evidence evaluation with an appraisal procedure, to elicit and weigh these considerations.

Objective: To demonstrate a structured approach for eliciting and evaluating a broad range of assessment criteria, including key stakeholders' values, aiming to support decision makers in priority setting.

Methods: For a set of cost-effective substitute interventions for depression care, the appraisal criteria were adopted from the Australian Assessing Cost-Effectiveness initiative. All substitute interventions were assessed in an appraisal, using focus group discussions and semi-structured interviews conducted among key stakeholders.

Results: Appraisal of the substitute cost-effective interventions yielded an overview of considerations and an overall recommendation for decision makers. Two out of the thirteen pairs were deemed acceptable and realistic, that is investment in therapist-guided and internet-based cognitive behavioral therapy instead of cognitive behavioral therapy in mild depression, and investment in combination therapy rather than individual psychotherapy in severe depression. In the remaining substitution pairs, substantive issues affected acceptability. The key issues identified were: workforce capacity, lack of stakeholder support and the need for change in clinicians' attitude.

Conclusions: Systematic identification of stakeholders' considerations allows decision makers to prioritize among cost-effective policy options. Moreover, this approach entails an explicit and transparent priority-setting procedure and provides insights into the intended and unintended consequences of using a certain health technology.

Patient contribution: Patients were involved in the conduct of the study for instance, by sharing their values regarding considerations relevant for priority setting.

INTRODUCTION

Countries have limited public resources to invest in health care. Technological innovations and resource constraints continuously challenges health-care priority setting.¹ Indeed, maintaining comprehensive, high-quality, sustainable and affordable health care packages entails difficult choices. Accordingly, numerous frameworks have been proposed to guide health-care decision making.²⁻⁶

Most developed countries currently apply formal health technology assessments (HTAs), notably for pharmaceuticals, to substantiate reimbursement decisions. Generally, HTAs follow distinct phases: problem definition during a scoping phase, an evaluation according to different assessment criteria during an assessment phase, and an appraisal of all available information by an independent multidisciplinary committee to provide policy recommendations during an appraisal phase.^{7,8}

This organizational structure reflects growing recognition that the evaluation of evidence and public engagement techniques should be incorporated into priority-setting approaches.⁹ HTA can be strengthened by a systematic approach to include robust evidence about patients' perspectives and by ensuring effective engagement of patients in the entire HTA/appraisal process to create a fair deliberative process.¹⁰ Several forms of public or patient engagement (e.g. telephone surveys, questionnaires or public meetings) can occur at various levels of the HTA process.¹¹ For example in the Netherlands, the assessment criteria are set and followed by stakeholder consultation rounds, where medical experts, patients, professional associations or other relevant health-care stakeholders may be consulted during the appraisal. In the UK, the National Institute for Health and Care Excellence (NICE) can consult a citizen council to elicit public perspectives on overarching moral and ethical issues that NICE should consider when providing guidance (e.g. societal values to be considered in decisions about trade-offs between equity and efficiency).¹²

The degree of public engagement (deliberative or non-deliberative participation) differs by country¹³, and the extent to which citizens' or patients' inputs influence the final decision remains unclear.^{11,14} Involving experts such as clinicians and health providers may help to provide important insights into various domains and the context in which technologies are used. However, to improve patient outcomes, and to take into consideration the needs of the group that is affected most by decisions regarding health technologies, requires the involvement of patients. Therefore, a deliberative decision-making process, in which experts and clinicians as well as patients are systematically involved, may be the way forward.^{11,13}

Apart from the regulatory framework, guiding principles or criteria applied within this framework are critical. A World Health Organization survey found that the majority of member states reported using a formal HTA process to inform coverage decisions.¹⁴ The main criteria applied in HTA were safety, clinical effectiveness, and economic and

budgetary considerations. Acceptability to patients and health-care organizations, equity and ethical issues, and feasibility considerations rarely receive systematic attention.¹⁴ Moreover, the findings of HTA-performing organization(s) are considered advisory rather than mandatory for policy decisions. A comparison of criteria applied within international HTA frameworks reveals that some criteria are perceived to be important across systems, but there is no consensus on a universal set of core criteria to inform priority setting.¹⁵

The importance of incorporating a broad range of criteria other than effectiveness and cost-effectiveness in the decision-making process is twofold. First, it is rare that all consequences and costs can be included within technical cost-effectiveness calculations (e.g. informal caregiver impacts are often not considered or valued). Furthermore, there are 'due process' considerations in decision making that do not feature explicitly in estimations of incremental cost effectiveness ratios. For example, parenting interventions designed to prevent anxiety disorders in children appear to provide good value for money.¹⁶ However, several key stakeholders have highlighted issues pertaining to this intervention, including community concerns associated with the stigmatization of positively screened preschool children and parents' reluctance to participate in such interventions.¹⁶

To date, while many studies recommend incorporating additional criteria and perspectives in health-care priority setting, few studies have actually demonstrated how such an approach could be implemented. Importantly, methods for weighing the opinions of different stakeholders, incorporating these opinions, and deciding what criteria to use remain unclear¹⁷. Thus, the aim of this study is to demonstrate a structured methodology for eliciting and weighing additional criteria jointly with the results of cost-effectiveness analyses by systematically involving diverse stakeholders in a different way than having a deliberative commission. We used the principles guiding the 'second-stage filter' approach, derived from the Assessing Cost-Effectiveness (ACE) priority-setting approach,¹⁸ and built onto a set of cost-effectiveness analyses regarding depression treatment, undertaken by Lokkerbol et al.¹⁹ in the Netherlands. We began our qualitative analysis of important criteria, other than cost-effectiveness, with an assessment of the core criteria commonly used in existing ACE studies.^{20,21} Subsequently, we investigated other considerations relevant to the local Dutch mental health-care context for inclusion in the 'second-stage filter analysis'. We have adopted a systematic approach using focus group discussions (FGDs) and semi-structured interviews to elicit information from key stakeholders: health-care professionals, patients, and health provider and health insurer representatives.

METHODS

Study design

We used a case study in depression care to illustrate the application of a structured appraisal methodology using preselected criteria and eliciting additional criteria. Qualitative research techniques were used with key stakeholders to elicit and evaluate criteria other than cost-effectiveness for a list of potential cost-effective substitute interventions.

Cost-effective substitute interventions for depression care

Lokkerbol et al. developed a health economic substitution algorithm to identify pairs of treatment interventions from among those currently in use that could result in a more cost-effective health-care system for patients with major depressive disorders.¹⁹ Intervention pairs were identified via health-care substitution, by (partly) investing in a more cost-effective intervention and simultaneously disinvesting in a less cost-effective intervention. The cost savings from disinvestment would cover the investment in more cost-effective interventions. Comparable economic evaluation approaches that jointly consider investment and disinvestment decisions are called the 'step in the right direction approach', and is also used in program budgeting and marginal analysis.^{22,23} We applied the economic analysis described by Lokkerbol et al.,¹⁹ using regional estimates for the incidence and prevalence of depression in Friesland, a province in the Northern Netherlands. Estimates were based on NEMESIS-2²⁴, and we used updated intervention costs in accordance with the latest Standard of Care for depressive disorders.²⁵

Selection of appraisal criteria

The ACE priority-setting approach was developed in Australia and has been used extensively to support health-care policy in areas not covered by formal HTA. This structured approach is aimed at reducing methodological inconsistencies across economic evaluations. It explicitly considers both formal cost-effectiveness analyses for reducing methodological confounding and 'due-process' decision-making considerations, largely obtained via a Steering Committee of stakeholders. Legitimacy is achieved through explicit discussions of other criteria important to decision-making – commonly referred to as the 'second-stage filter' criteria.

Previous ACE studies have identified the following key criteria essential for decision making: equity and ethical issues, acceptability to key stakeholders, strength of evidence, feasibility considerations, and other important beneficial or harmful effects not captured in the technical analysis.¹⁸ Importantly, these criteria can change according to the requirements of each decision-making context. We used these second-stage filter criteria in our study as a starting point to elicit information from key stakeholders for the list of substitute interventions derived from the model-based cost-effectiveness analysis.¹⁹

Elicitation approach

FGDs and semi-structured interviews were conducted to elicit information on criteria from key stakeholders. While focusing on the above-mentioned criteria, the interview guide also allowed for the inclusion of other relevant issues (for details, see Supplementary Material A). We used a phenomenological approach to obtain stakeholders' views and values on important priority-setting considerations in depression care. This approach elicits individuals' experiences of a certain phenomenon.²⁶ It simultaneously attempts to set aside preconceived assumptions about experiences of a particular situation.

Participants

Key stakeholder participants were patients with depression or a history of depression, health-care professionals who treat depression, the director of the largest regional specialist mental health-care organization and a medical advisor of the health insurer with the largest market share (approximately 61%) in the region.

FGDs with patients stimulated exchanges of knowledge and experiences and their perceptions regarding potential substitute interventions. We conducted semi-structured interviews with the remaining stakeholders. Because of time constraints and logistical issues, five of the ten health-care professionals preferred to fill in a questionnaire covering the same topics.

Patients and health-care professionals were selected through purposive sampling. Patients were eligible to participate in this study if they currently or previously suffered a depressive disorder and underwent several treatments; were willing to provide informed consent; and agreed with the collection and use of audio recorded anonymized data. Health-care professionals were eligible for participation if they had experience in treating patients with depressive disorder and were willing to share their perceptions regarding the substitution pairs. Full details regarding the recruitment of participants are described in Supplementary Material B.

The largest specialist mental health-care organization and health insurer were selected through convenience sampling. The health insurer perspective was represented by the medical advisor in mental health. The director of the mental health-care organization represented the provider perspective. All participants were contacted by telephone or email for an eligibility check. Three patients dropped out of the study due to personal circumstances (a broken toe, a funeral and a hospital admission, respectively) and one interview with a clinician was unusable due to faulty audio equipment.

Data collection and analysis

Data collection took place between December 2017 and August 2018. All interviews were audio recorded and transcribed verbatim. Field notes were taken during the FGDs and semi-structured interviews.

Data were analyzed using ATLAS.ti version 8.2, a qualitative analysis software. One researcher coded the data (K.K.) and two researchers (F.J. and T.F.) participated in peer-debriefing to improve the credibility and validity of the results. Thematic content analysis was performed on the data using the one-sheet-of-paper method.²⁷ Patients and health-care professionals provided feedback on the findings to verify the accuracy of the interpretations of the transcripts. Themes were derived from the data but were mostly driven by the interview guide topics.

We constructed a summary table based on our analysis of the interview data. Subsequently, conclusions on issues identified for each criterion, displayed by colored cells, were converted into appropriate recommendations on each substituted intervention pair for decision makers. Three researchers independently judged the importance of the identified issues. The researchers discussed their differences, eventually reaching consensus. Quotes by different stakeholders were used to illustrate the findings.

RESULTS

Cost-effectiveness analyses

Table 1 presents the intervention substitution pairs using the health economic substitution algorithm. Substitution of an intervention by an alternative can potentially improve cost-effectiveness within the mental health-care system. A detailed description of non-standard interventions is given in Supplementary Material C.

Qualitative data analysis

Data were analyzed for 23 participants: 12 patients, 9 clinicians, 1 director of a mental health-care organization, and 1 medical advisor from the health insurer. The average durations of the FGDs (three in total) and semi-structured interviews were 85 and 45 minutes respectively. We established data saturation, defined as the point when no new information or themes were observed in the data, in May 2018 and June 2018 after conducting three FGDs and ten interviews respectively.

We first elaborate on two specific examples (substitution pairs 1 and 2 in Table 1). Next, we present the salient findings, including judgments, for each of the substitution pairs.

1. Illustration of two examples

Table 2 presents a summary of the findings for substitution pairs 1 and 2: investment in therapist-guided internet-based cognitive behavioral treatment (iCBT) and disinvestment in individual cognitive behavioral therapy (CBT) for (1) mild and (2) moderate depression. Issues identified for each criterion are described in more detail

Table 1. Cost-effective substitute interventions for depression care

No.	Treatment for	Investment in	Disinvestment in
1	Mild depression	therapist-guided internet-based cognitive behavioral treatment	individual cognitive behavioral therapy
2	Moderate depression	therapist-guided internet-based cognitive behavioral treatment	individual cognitive behavioral therapy
3	Moderate depression	pharmacotherapy (3-6 months)	individual cognitive behavioral therapy
4	Severe depression	antidepressant medication (12 months)	individual psychotherapy (8-24 sessions)
5	Severe depression	antidepressant medication (12 months)	combination therapy
6	Severe depression	antidepressant medication + General Practice assistant*	individual psychotherapy (8-24 sessions)
7	Severe depression	antidepressant medication + General Practice assistant*	antidepressant medication (12 months)
8	Severe depression	antidepressant medication + General Practice assistant*	combination therapy
9	Severe depression	combination therapy	individual psychotherapy (8-24 sessions)
10	Prevention: Recurrent depression	mindfulness-based cognitive behavioral therapy	clinical management with maintenance medication (12 months)
11	Prevention: Recurrent depression	mindfulness-based cognitive behavioral therapy	preventive cognitive (behavioral) therapy
12	Prevention: Recurrent depression	interpersonal psychotherapy	clinical management with maintenance medication (12 months)
13	Prevention: Recurrent depression	preventive cognitive (behavioral) therapy	clinical management with maintenance medication (12 months)

* Hypothetical scenario: effectiveness of antidepressant medication with increased adherence rate caused by guidance of General Practice assistant

below, and the findings are illustrated with respondents' quotations (Table 3). Similar tables for all remaining substitution pairs (3–13) are provided in Supplementary Material D.

Level of evidence

Most of the health-care professionals who were unfamiliar with iCBT believed that it could be meaningful for patients who are not severely depressed. They indicated that it should be at least as effective as regular face-to-face CBT. Health-care professionals already familiar with iCBT reported seeing good outcomes and did not have any doubts about the effectiveness in clinical practice (Table 3, quote 1). One health-care professional remarked that some of her colleagues were more reluctant to apply iCBT because they lacked information regarding its effectiveness in clinical practice. The representatives of the mental health-care organization and health insurer felt that iCBT

was worth investing in, and both stakeholders endorsed provision of this intervention and evaluations of its effects on patients with *mild* depression. By contrast, several stakeholders were reluctant to offer therapist-guided iCBT to patients with *moderate* depression because they anticipated limited treatment adherence within this group.

Table 2. Priority setting considerations based on different stakeholders' perspectives on investment in therapist-guided, internet-based cognitive behavioral treatment (iCBT) and disinvestment in individual cognitive behavioral therapy (CBT) for mild and moderate depression

Level of evidence	<ul style="list-style-type: none"> - Clinicians doubt treatment effects in routine practice; not all clinicians have experience in providing internet-based treatments. Clinicians with experience in providing internet-based treatments have no doubts - Evidence of treatment effectiveness is required for mild and moderate depression and for primary care services versus specialized care services
Equity and equality considerations	<p>Potential causes of increased inequalities/inequities are:</p> <ul style="list-style-type: none"> - An aging population, (computer) illiteracy, low socioeconomic status of patients, patients with sight and hearing deficiencies, psychiatric comorbidities, and intellectual disabilities - Treatment effects are more obvious in younger patients. However, for adolescents, in particular, connecting with others could be important in a digital world - Patients are not open to this form of therapy - Treatment is more suitable for patients with mild depression, but its suitability for patients with moderate depression is questionable because of their decreased treatment adherence and difficulties putting things into perspective <p>Potential causes of decreased inequalities/inequities are:</p> <ul style="list-style-type: none"> - Patients' insights - Individual clinicians' increased caseloads and reductions in waiting lists - Less travel time and costs - Insights of patients who experience barriers to therapy sessions and/or patients who have difficulty expressing themselves - Treatment occurs in patients' own environments, and they have opportunities to re-read the information at leisure
Feasibility of implementation	<p>Positive:</p> <ul style="list-style-type: none"> - In organizations that already provide this form of treatment, clinicians are qualified, and no issues are anticipated - Implementation is less intensive for clinicians; whereas a CBT session requires an hour, a therapist-guided internet-based cognitive behavioral treatment requires 30 minutes <p>Neutral:</p> <ul style="list-style-type: none"> - More efficient deployment of staff is required - The recommendation is to start with a pilot initiative to gain some experience <p>Issues:</p> <ul style="list-style-type: none"> - Training of qualified personnel is required regarding to e-health guidance and a different form of contact - The application should be interactive, user-friendly, and catchy - Mental healthcare procurement is dependent on the resources of care organizations - Training is required when intervention is provided as a component of primary care services

Acceptability to stakeholders	<p>Positive:</p> <ul style="list-style-type: none"> - Acceptable in its blended form in combination with face-to-face therapy - Could be more effective: working method is more task-oriented - Good experiences - Structured moments of contact via the internet, during which clinicians can provide supportive and stimulating feedback <p>Neutral:</p> <ul style="list-style-type: none"> - Patients' preferences remain important - Suitable for moderate depression along a continuum (if not too severe); CBT treatment is appropriate for more severe cases <p>Issues:</p> <ul style="list-style-type: none"> - The extent of clinicians' openness and willingness to adapt to this method of interacting with patients - Clinicians' handling of patients' self-responsibility - Suitability and quality of the e-health material (adaptation for different target populations, content tailored for specific patients, and based on CBT principles) and ease of use for both clinicians and patients - Challenges of convincing patients and clinicians to accept the innovative intervention - Requires patients' trust in clinicians (as a precondition) - Requires patients to work independently during treatment, demonstrating self-discipline and responsibility - Not suitable or questionable suitability for patients with moderate depression. Suggestions: begin with medication and then continue with therapist-guided internet-based cognitive behavioral treatment. Requires patient stability and structure in daily routine. Not suitable for patients with suicidal thoughts. More intensive initial treatment, more frequent sessions, or in conjunction with medication - CBT remains important for treating moderate depression - Clinicians' unfamiliarity with this type of treatment - Possible resistance from the older generation of clinicians; doubts about treatment effectiveness
Other effects not captured in modelling	<p>Positive:</p> <ul style="list-style-type: none"> - Patient empowerment - Current waiting lists for CBT are long, and depression can start to resolve (prevention of deterioration) - Antidepressant prescriptions or CBT treatments may be reduced or avoided <p>Negative:</p> <ul style="list-style-type: none"> - Non-verbal communication and interaction is missing in the e-health component; patients' openness to this form of therapy is unclear - Requires a therapeutic relationship prior to implementing the e-health component of the intervention - Physically attending the treatment motivates patients to stay active, and maintains structure in daily routine

Equity and equality

All the stakeholders indicated that the substitute intervention would be justified for the majority of patients with *mild* depression. They all agreed that a minority of patients with mild depression might not prefer this type of intervention for reasons such as (computer) illiteracy or low socio-economic status (Table 3, quote 2). Most stakeholders considered iCBT to be more appropriate for younger patients, as most of them are familiar with digital devices. One patient did not recommend it for adolescents, especially those who needed social connections. Conversely, others believed that iCBT provides a solution for young people who feel ashamed about undergoing psychological treatment. It could reduce no-show in patients who require therapy but whose time is occupied by work/

Table 3. Illustrative quotes for each criterion

Criterion	Quotations for illustration
Level of evidence	Quote 1: 'Good proposal, you are less caught up in the hassle of every day, so to say. You are really putting in a lot more work. I have had good experiences, but I have also noticed, the main practitioners, i.e. the psychiatrists, clinical psychologists, psychotherapists, they often forget that we have that option. So, it is a matter of repeating it during meetings, also consider that option. Because it simply fades away again, people have not yet gotten it into their system.' (Participant 23, woman, age 35)
Equity and equality considerations	Quote 2: 'Maybe you don't reach the entire target group, but that doesn't happen for CBT either. I don't think you should let that stop you because in every form of therapy, you will have people who are making progress and people who are not benefitting, and then you should pay more attention to them [the latter].' (Participant 20, man, age 35)
Feasibility of implementation	Quote 3: 'People always think more eHealth means less staff'. And I ask myself ... that is what I am wondering. Because you also need to properly support eHealth. And yes, you still need the face-to-face contacts anyway. So, the story is about a more efficient use of staff.' (Participant 15, man, age 56)
Acceptability to stakeholders	Quote 4: 'As a clinician, you obviously loose some of the control, you are going to hand more control to the patient. That I really think is a very good development, but for a clinician it may be a bit uncomfortable. I think you need to gain more experience, learning to confide in that system.' (Participant 20, man, age 35) Quote 5: 'So acceptance of the clinicians' side. Them actually taking that step, stepping away from the comfort zone of the treatment room, and switching to a different kind of making contact with the. patients. Uh, it's the suitability of the material, right? So, of the e-health modules that we have.' (Participant 15, man, age 56) Quote 6: 'You miss the non-verbal element of course; but it's just another way of making contact, but I notice that the therapists themselves seem to find it pleasant.' (Participant 23, woman, age 35)
Other effects not captured in modelling	Quote 7: 'And you allow, moreover, in the entire system of the empowering of the patient, you give them the tools to do things. Tools that you can use after the treatment has ended.' (Participant 22, man, age 45-55)

school. Moreover, it could overcome barriers for a certain group of patients, as some patients find it difficult to tell their stories face-to-face.

Some patients and health-care professionals argued that iCBT would not be equivalent to existing therapies for *moderately* depressed patients because some patients find structure in daily routine, discipline, stability, and independent functioning challenging. In such cases, expectations of motivating oneself to participate in an internet-based treatment may not be realistic.

Other important equity and equality considerations included provision of treatment in patients' own environments, which saves travel time and costs. The treatment also elicits patients' insights and the possibility of re-reading the information in patients' own time and pace. Finally, it may increase the productivity of health-care professionals, reducing waiting lists.

Feasibility of implementation

None of the stakeholders expected major implementation issues for patients with either *mild* or *moderate* depression. Some health-care professionals and the director of the mental health-care provider expected that iCBT would require more efficient staff deployment (Table 3, quote 3).

The stakeholders also did not anticipate major implementation issues with an internet-based application that is user-friendly and well integrated within current systems. In organizations yet to offer iCBT and in primary care, proper training of qualified personnel regarding different ways of interacting with patients (e.g., less non-verbal communication in iCBT) is required. The health insurer's medical advisor was very open to iCBT procurement if mental healthcare organizations could provide such interventions.

Acceptability

Stakeholders prioritized investments in iCBT over individual CBT for *mild* depression. One clinician stated that task-oriented interventions like iCBT could even be more effective than CBT for some patients, as treatments are structured and entail regular online contact. In addition, patients regularly receive supportive and stimulating feedback, while non-verbal information can still be conveyed through face-to-face contact. Clinicians experienced in using iCBT have rarely encountered resistance from patients.

Stakeholders mentioned some potential risks for iCBT, which would require patients to be self-disciplined. Moreover, face-to-face contact remains important for maintaining the therapeutic relationship. Patients' acceptance is needed, so the suitability of the intervention requires verification.

Some other challenges were mentioned by health-care professionals and representatives of the health insurer and mental health-care provider: health-care professionals should be open and willing to adapt to a new form of contact with patients, and trust patients to be self-responsible (Table 3, quotes 4, 5, and 6). Furthermore, patients' preferences for treatment types remain important and stakeholders agreed that health care professionals cannot be expected to adopt this treatment easily and immediately. Finally, they mentioned that the e-Health material should be appropriate for the target population, and ease of use for both health-care professionals and patients was considered a necessary condition.

Most stakeholders questioned the suitability of iCBT for treating *moderate* depression, because of patients' decreased concentration and moods. For iCBT to work, patients need a stable environment, structure in daily routine, and they should not be severely depressed. Some stakeholders suggested beginning with a more intensive intervention until the depression stabilizes and subsequently providing iCBT or providing it along with medication. Several stakeholders mentioned that conventional face-to-face CBT remains important in treating moderate depression.

Other relevant non-efficiency considerations

Both patients and health-care professionals felt that patients' trust in therapy and the therapeutic relationship were crucial for good treatment outcomes. For patients without a social network or structured routine, traveling to treatment centers could have benefits, as it promotes some scheduled activities. However, providing more iCBT could lead to a reduced need for antidepressant prescriptions and CBT treatment, thereby saving costs and shortening waiting lists. Finally, patients and health-care professionals felt that iCBT could increase patient involvement in therapy, leading to patients regaining control over themselves more rapidly, with expected consequences for recovery times (Table 3, quote 7).

In sum, for treating *mild* depression, investment in therapist-guided iCBT and disinvestment in individual CBT seems to be a promising potential substitute intervention pair with no major issues anticipated. However, for treating *moderate* depression some concerns remain.

2. Assessment of all substitution pairs incorporating all criteria

Table 4 presents the conclusions for all the assessed substitution pairs incorporating all considerations. Green, orange, and red cells denote no, possible, and considerable issues/concerns, respectively, from the stakeholders' perspectives. The last column depicts policy considerations for each substitution pair.

Key issues regarding the level of evidence criterion were related to clinical effectiveness as opposed to efficacy, and the outcomes for specific target groups. In addition, health-care professionals noted that patients' preferences, which they wished to consider, could sometimes conflict with treatment protocols and guidelines, which were perceived as being rigid. The stakeholders also pointed to equity and equality issues. For example, stakeholders found it inequitable that some people cannot benefit from certain treatment for instance because of computer illiteracy. They also mentioned that several substitute interventions that targeted patients with severe depression were seen as interventions that were too 'light' for the type of depression concerned. For example, as treatment with medication only without psychological treatment does not provide patients any insights or personal behavioral changes stakeholders perceived it as an inequality issue for this specific group of patients. This substitute intervention was found to be more suitable for patients with milder complaints. They preferred more intensive treatment over under-treatment. The main feasibility issue identified was insufficient staff to implement the interventions, for example when investing in mindfulness-based cognitive behavioral therapy for patients with recurrent depressions. For several substitute interventions (e.g. the interventions with support from a General Practice assistant), training of staff is required to increase feasibility of implementation. The main acceptability issues stemmed from the clinicians' work culture, including

Table 4. Summary of the results of the second-stage filter analysis

Number	Treatment Type	Investment in	Disinvestment in	Level of evidence	Equity
1	Mild depression	therapist-guided internet-based cognitive behavioral treatment	individual cognitive behavioral therapy	Yellow	Green
2	Moderate depression	therapist-guided internet-based cognitive behavioral treatment	individual cognitive behavioral therapy	Yellow	Yellow
3	Moderate depression	pharmacotherapy (3-6 months)	individual cognitive behavioral therapy	Green	Yellow
4	Severe depression	antidepressant medication (12 months)	individual psychotherapy (8-24 sessions)	Yellow	Green
5	Severe depression	antidepressant medication (12 months)	combination therapy	Yellow	Green
6	Severe depression	antidepressant medication + General Practice assistant	individual psychotherapy (8-24 sessions)	Red	Yellow
7	Severe depression	antidepressant medication + General Practice assistant	antidepressant medication (12 months)	Red	Yellow
8	Severe depression	antidepressant medication + General Practice assistant	combination therapy	Red	Yellow
9	Severe depression	combination therapy	individual psychotherapy (8-24 sessions)	Green	Green
10	Prevention: Recurrent depression	mindfulness-based cognitive behavioral therapy	clinical management with maintenance medication (12 months)	Green	Yellow
11	Prevention: Recurrent depression	mindfulness-based cognitive behavioral therapy	preventive cognitive (behavioral) therapy	Green	Yellow
12	Prevention: Recurrent depression	interpersonal psychotherapy	clinical management with maintenance medication (12 months)	Green	Green
13	Prevention: Recurrent depression	preventive cognitive (behavioral) therapy	clinical management with maintenance medication (12 months)	Green	Green

Feasibility of implementation	Acceptability to stakeholders	Other effects not captured	Policy considerations
			No major issues anticipated: evidence from routine practice is desirable; equitable for majority of patients
			Some/possible concerns: the appropriateness of the intervention for treating moderate depression
			Some/possible concerns: underlying causes of depression are not resolved; antidepressant medication can have negative health consequences
			Concerns: underlying causes of depression are not resolved; antidepressant medication can have negative health consequences; little support from most stakeholders.
			Concerns: underlying causes of depression are not resolved; antidepressant medication can have negative health consequences; little support from most stakeholders.
			Concerns: evidence of use in treating severe depression; little support from most stakeholders; requires more knowledge and training of General Practice assistants; the suitability of the intervention in severe depression.
			Concerns: evidence of use in treating severe depression; little support from most stakeholders; better than medication only; requires more knowledge and training of General Practice assistants.
			Concerns: evidence of use in treating severe depression; little support from most stakeholders; requires more knowledge and training of General Practice assistants; the suitability of the intervention in severe depression
			No major issues anticipated: however, not all patients require medication
			Some/possible concern: insufficient staff and lack of training for providing mindfulness-based CBT (not offered everywhere); relatively new for some patients; patients' fear of depression recurrence/relapse when not using medication requires attention
			Some/possible concerns: insufficient staff and lack of training for providing mindfulness-based CBT (not offered everywhere); relatively new for some patients
			Some/possible concerns: insufficient staff to provide interpersonal therapy; patients' fear of depression recurrence/relapse when not using medication requires attention
			Some/possible concerns: the CBT waiting list is currently long, and more staff would be required to provide CBT; patients' fear of depression recurrence/relapse when not using medication requires attention

reluctance to pass on patients to their colleagues, who might be better equipped to provide necessary interventions, or to transfer responsibilities to their patients.

Finally, independent of a specific substitute intervention, personalized treatment and shared decision making remain essential, and were prioritized over and above economic considerations by all of the stakeholders. Further, stakeholders noted that patients' social networks or contexts could significantly affect treatment outcomes. Economic evaluations do not usually cover this aspect. From the perspectives of the mental health-care provider and health insurer, the long-term (cost-)effectiveness of interventions and prevention of future recurrences were deemed important.

DISCUSSION

The aim of this study was to demonstrate how the structured approach may add to the deliberative commission approach in that viewpoints on a range of pre-specified domains are elicited from diverse stakeholders, while also leaving room for other domains. Next to the perspectives of experts, the insights and experiences of patients provide an additional perspective into the intended and unintended consequences of using a certain health technology. A large number of patients and other relevant stakeholders can potentially be involved, and their viewpoints processed to provide an overview of perspectives to increase the extent to which their inputs influence final decisions. By understanding the views and values of diverse stakeholders, balanced against the requirements of fair health-care resource distribution, decision makers are facilitated in well-informed health-care priority-setting decisions. The study also demonstrated that incorporating such criteria was possible in an alternative procedure than the ACE-setting, using systematic qualitative research methods.

We found that for the majority of substitute interventions that could improve the cost-effectiveness of depression care, stakeholders addressed one or more concerns. Six substitute interventions showed possible issues/concerns and five substitute interventions showed considerable issues/concerns. Tackling anticipated issues prior to implementing proposed substitute interventions increases the chances of successful implementation and the likelihood of eliciting key stakeholders' support. From the stakeholders' perspectives, two substitute interventions remained promising after considering the cost-effectiveness criterion as well as all other relevant criteria.

In the particular case study discussed here, investment in therapist-guided iCBT and disinvestment in individual CBT appears to be a promising strategy for patients with mild depression. Health-care professionals and patients expressed concerns regarding its suitability for patients with moderate depression due to an anticipated limited treatment adherence. Evidence suggests however that the adherence to therapist-guided iCBT appears to be adequate, equals the adherence to face-to-face CBT²⁸ and

can meet the same outcomes as face-to-face CBT, also in moderate depression.²⁹⁻³¹ After further investigation of the quality and validity of the expressed concerns, any remaining obstacles can be taken away by, for example, informing or educating specific stakeholders. These concerns, biased or not, are however important to take into account when informing HTA recommendations, as they influence acceptability and feasibility of implementation. Interestingly, the 2019-2020 COVID-19 pandemic has compelled clinicians to provide patients with online therapy. Moreover, patients have had to participate in online therapy during the pandemic because of the temporary unavailability of regular face-to-face contact. From clinicians' and patients' perspectives, online therapy, video calling, and chatting appear to offer a possible solution when conventional CBT is not an option.^{32,33} This finding sheds new light on the relative importance of the identified considerations and provides an opportunity to evaluate the outcomes of widespread use of online therapies using real world data in the future.

Using qualitative methodology, we elicited key stakeholders' perspectives on a wide range of criteria. Other methods, such as sending out questionnaires, do not allow stakeholders to elaborate freely, and important considerations may therefore be missed. Recent policies have not captured all of the criteria considered for priority setting.³⁴⁻³⁶ In the Netherlands, the formal assessment criteria applied are necessity, evidence of effectiveness, cost-effectiveness and feasibility.³⁷ Our findings suggest that it could be worthwhile to incorporate additional criteria like acceptability or equity during the appraisal phase by eliciting stakeholder views on these issues.

Although this methodology's implementation requires additional resources and time, we found that its execution was highly feasible. Participants were willing to share their views and values regarding the substitution pairs. Because stakeholders' views and values may conflict, all concerned stakeholders should be represented to enable informed decision making. Apart from carefully selecting criteria for priority setting, we recommend leaving room for other criteria not considered during the interviews, so that crucial issues are not missed.

In our study, the researchers made an overall judgment considering all of the identified issues per substitution pair to demonstrate which substitute interventions could potentially contribute to a cost-effective health-care system. As recommended by Facey et al, professionals experienced in research should be responsible for gathering evidence and its presentation and interpretation in HTA, More intense collaboration between the HTA community and researchers is needed.¹⁰ We recommend that existing national appraisal committees in which all stakeholders are represented should be tasked with the final evaluation process, to ensure a more standardized process.

Our study has several limitations. First, not all stakeholders are equally well represented in terms of numbers. However, we included different stakeholders' perspectives in our analysis to capture the breadth of opinions. In addition, data saturation was reached as the stakeholders independently raised similar issues.

Second, various criteria, defined a priori, were evaluated during the interviews, along with other criteria that the stakeholders considered relevant. However, the stakeholders did not rank the relative importance of the criteria. Nevertheless, the FGDs revealed that patients believed that cost should not be the foremost consideration. For health-care professionals, experience through clinical practice sometimes prevails over research evidence. Further, a shortage of personnel to administer the treatment was considered an important bottleneck. This finding indicates that different stakeholders prioritize different criteria, although practical or logistic impediments were considered to be objective constraints, rather than stakeholders' opinions or preferences.

Finally, although patients were knowledgeable about depression treatments, most patients were not well-versed in health economic rationing. To ensure that patients were adequately informed, we explained the rationale of the study, and economic rationing in general, to them prior to conducting the FGD.

Implications for policy and future research

Recent trends like value based healthcare, but also the long standing tradition of HTA stress that cost-effectiveness is not the only relevant aspect for priority setting decisions. Current policy processes address these broader perspectives mostly in the appraisal phase, using deliberative panels. The current study piloted an alternative approach that adds to deliberative panels by offering a structured approach resulting in an overview of stakeholders' views, and that has the potential to increase the extent to which their inputs influence final decisions.

Because stakeholders' values relating to allocation of care could differ, the process of mapping all of their issues and concerns could contribute to a transparent methodology of informed decision-making. Accordingly, future studies should investigate whether the systematic provision of information relating to other criteria alongside the efficiency criterion results in improved decision-making. Our findings contribute to the growing body of evidence that demonstrates that patients can contribute to public argumentation and may determine the acceptability of proposed decisions.^{10,38,39} Understanding patients' values and the impact of a specific technology/intervention on patients' lives and their visions and requirements concerning the intervention are highly relevant as patients are most directly affected by the technology. It will be most relevant for reimbursement policy concerning treatments that currently lack formal inclusion of cost-effectiveness e.g. in the area of mental health care or prevention.

This systematic methodology can strengthen the HTA process by ensuring the disclosure of key stakeholders' values and preferences. A deliberative process in which diverse stakeholders are included helps to contextualize technologies and enables informed decision making. It highlights interventions that can be easily and quickly rolled out, as well as those that require further consideration before roll-out can be considered. How the findings of current deliberation will inform the final decision-

making process and their impacts on service delivery is not yet clear. However, a major health insurer and a mental health-care provider indicated their intention to take the results presented into account in the coming contract negotiations for multi-year agreements starting from 2022. The application of this methodology requires additional resources and time compared with a cost-effectiveness evaluation alone. However, when smooth implementation follows, this investment may prove worthwhile.

CONCLUSIONS

Improving the health-care system through interventions that meet the efficiency criterion may have limitations because they do not include additional considerations relevant to priority setting. Access to diverse stakeholders' views and values regarding these criteria, via a systematic embedded qualitative approach, enables decision makers to make better-informed decisions and appropriate judgments when setting health-care priorities. It also informs decision makers on issues that could impede successful adoption of the intervention, allowing them to tackle these issues. Furthermore, addressing such criteria in an open and explicit manner increases the transparency of the priority-setting process.

REFERENCES

1. Sabik LM, Lie RK. Priority setting in health care: Lessons from the experiences of eight countries. *Int J Equity Health*. 2008;7:4-9276-7-4.
2. Peacock S, Mitton C, Bate A, McCoy B, Donaldson C. Overcoming barriers to priority setting using interdisciplinary methods. *Health Policy*. 2009;92(2-3):124-132.
3. Morgan RL, Kelley L, Guyatt GH, Johnson A, Lavis JN. Decision-making frameworks and considerations for informing coverage decisions for healthcare interventions: A critical interpretive synthesis. *J Clin Epidemiol*. 2018;94:143-150.
4. Johnson AP, Sikich NJ, Evans G, et al. Health technology assessment: A comprehensive framework for evidence-based recommendations in ontario. *Int J Technol Assess Health Care*. 2009;25(2):141-150.
5. Birch S, Chambers S. To each according to need: A community-based approach to allocating health care resources. *CMAJ*. 1993;149(5):607-612.
6. Honigsbaum F, Calltorp J, Ham C, Holmström S. *Priority setting processes for healthcare*. 1st edition ed. London: CRC Press; 1995. <https://doi.org/10.1201/9781315379777>.
7. National Institute for Health and Care Excellence. Guide to the methods of technology appraisal. 2013.
8. Zorginstituut Nederland. Beoordeling stand van de wetenschap en praktijk. 2015. <https://www.zorginstituutnederland.nl/binaries/zinl/documenten/rapport/2015/01/15/beoordeling-stand-van-de-wetenschap-en-praktijk/Beoordeling+stand+van+de+wetenschap+en+praktijk.pdf>. Accessed 18-04-2019.
9. Drummond MF, Schwartz JS, Jonsson B, et al. Key principles for the improved conduct of health technology assessments for resource allocation decisions. *Int J Technol Assess Health Care*. 2008;24(3):244-58; discussion 362-8.
10. Facey K, Boivin A, Gracia J, et al. Patients' perspectives in health technology assessment: A route to robust evidence and fair deliberation. *Int J Technol Assess Health Care*. 2010;26(3):334-340.
11. Bal R, van de Lindeloof A. Publieksparticipatie bij pakketbeslissingen: Leren van buitenlandse ervaringen. In: *Zicht op zinnige en duurzame zorg*. The Hague: Council for Public Health and Health Care; 2006:169. https://www.parlementairemonitor.nl/9353000/1/j4nvgs5kjg27kof_j9vvij5epmj1ey0/vi3k9g5171yv/f=/blg14649.pdf.
12. National Institute for Health and Care Excellence. Citizen council. <https://www.nice.org.uk/get-involved/citizens-council>. Accessed July, 6, 2020.
13. Hailey D, Nordwall M. Survey on the involvement of consumers in health technology assessment programs. *Int J Technol Assess Health Care*. 2006;22(4):497-499.
14. World Health Organization (WHO). 2015 Global Survey on Health Technology Assessment by National Authorities. Main findings. Geneva, Switzerland, 2015.
15. Ham C. Priority setting in health care: Learning from international experience. *Health Policy*. 1997;42(1):49-66.
16. Mihalopoulos C, Vos T, Rapee RM, et al. The population cost-effectiveness of a parenting intervention designed to prevent anxiety disorders in children. *J Child Psychol Psychiatry*. 2015;56(9):1026-1033.
17. Facey KM. Patient involvement in HTA: What added value? *Pharmaceuticals, Policy and Law*. 2011;13:245-251.
18. Carter R, Vos T, Moodie M, Haby M, Magnus A, Mihalopoulos C. Priority setting in health: Origins, description and application of the Australian assessing cost-effectiveness initiative. *Expert Rev Pharmacoecon Outcomes Res*. 2008;8(6):593-617.

19. Lokkerbol J. *Rationalization of innovation: The role of health-economic evaluation in improving the efficiency of mental health care (dissertation)*. VU University, Amsterdam, 2015.
20. Mihalopoulos C, Vos T, Pirkis J, Carter R. The economic analysis of prevention in mental health programs. *Annu Rev Clin Psychol*. 2011;7:169-201.
21. Ananthapavan J, Sacks G, Brown V, et al. *Assessing cost-effectiveness of obesity prevention policies in australia 2018 (ACE-obesity policy)*. Geelong, Vic., Deakin University, 2018.
22. Birch S, Gafni A. Cost effectiveness/utility analyses. do current decision rules lead us to where we want to be? *J Health Econ*. 1992;11(3):279-296.
23. Pole J. Program, priorities and budgets. *Br J Prev Soc Med.*, 1974;28:191-195.
24. de Graaf R, ten Have M, Tuithof M, van Dorsselaer S. First-incident of DSM-IV mood, anxiety and substance use disorders and its determinants: Results from the netherlands mental health survey and incidence study-2. *J Affect Disord*. 2013;149(1-3):100-107.
25. Akwa GGZ. Zorgstandaard depressieve stoornissen. <https://www.ggzstandaarden.nl/zorgstandaarden/depressieve-stoornissen>. Updated 2018. Accessed April, 28, 2020.
26. Zahavi D. *Husserl's phenomenology*. Stanford, California: Stanford University Press; 2003.
27. Ziebland S, McPherson A. Making sense of qualitative data analysis: An introduction with illustrations from DIPEX (personal experiences of health and illness). *Med Educ*. 2006;40(5):405-414.
28. van Ballegooijen W, Cuijpers P, van Straten A, et al. Adherence to internet-based and face-to-face cognitive behavioural therapy for depression: A meta-analysis. *PLoS One*. 2014;9(7):e100674.
29. Khatri N, Marziali E, Tchernikov I, Shepherd N. Comparing telehealth-based and clinic-based group cognitive behavioral therapy for adults with depression and anxiety: A pilot study. *Clin Interv Aging*. 2014;9:765-770.
30. Ruwaard J, Schrieken B, Schrijver M, et al. Standardized web-based cognitive behavioural therapy of mild to moderate depression: A randomized controlled trial with a long-term follow-up. *Cogn Behav Ther*. 2009;38(4):206-221.
31. Ruwaard J, Lange A, Schrieken B, Emmelkamp P. Efficacy and effectiveness of online cognitive behavioral treatment: A decade of interapy research. *Stud Health Technol Inform*. 2011;167:9-14.
32. Freeman MP. COVID-19 from a psychiatry perspective: Meeting the challenges. *Journal of Clinical Psychiatry*. 2020;81(2):13.
33. Shinn AK, Viron M. Perspectives on the COVID-19 pandemic and individuals with serious mental illness. *J Clin Psychiatry*. 2020;81(3):20com13412. doi: 10.4088/JCP.20com13412.
34. Cromwell I, Peacock SJ, Mitton C. 'Real-world' health care priority setting using explicit decision criteria: A systematic review of the literature. *BMC Health Serv Res*. 2015;15:164-015-0814-3.
35. Aidem JM. Stakeholder views on criteria and processes for priority setting in norway: A qualitative study. *Health Policy*. 2017;121(6):683-690.
36. Guindo LA, Wagner M, Baltussen R, et al. From efficacy to equity: Literature review of decision criteria for resource allocation and healthcare decisionmaking. *Cost Eff Resour Alloc*. 2012;10(1):9-7547-10-9.
37. Zwaap J. Pakketadvies in de praktijk: wikken en wegen voor een rechtvaardig pakket. National Health Care Institute, Diemen, the Netherlands. 2017.
38. Wale J, Scott AM, Hofmann B, Garner S, Low E, Sansom L. Why patients should be involved in health technology assessment. *Int J Technol Assess Health Care*. 2017;33(1):1-4.
39. Stafinski T, McCabe C, Menon D. Determining social values for resource allocation decision-making in cancer care: A canadian experiment. *Journal of Cancer Policy*. 2014;2(3):81-88. doi: <https://doi.org/10.1016/j.jcpo.2014.07.002>.

Supplemental Material A - Interview guide topics

Topics	
Introduction	Familiarity with the different interventions
	General opinion on the use of economic considerations for priority setting
Acceptability / desirability	General opinion on the acceptability of investment and disinvestment of the substitution pair. Pro's and con's
	Desirable changes needed for acceptability
Feasibility of implementation	Consequences for general practice/ mental healthcare procurement / mental healthcare organization
	Changes needed to increase feasibility of implementation
Equity considerations	Suitability substitution pair for entire target population
	Consequences substitution pair for equity and equality
Level of evidence	Importance of level of evidence
	Experiences in practice with regard to effectiveness
Other considerations	Other considerations to take into account

Supplemental Material B - Details of the recruitment of patients and healthcare professionals and the conduct of the focus group interviews and semi-structured interviews in the study

In line with the Dutch Medical Research involving Human Subjects Act, the Medical Ethics Review Board (METc) of the University Medical Center Groningen exempted this research from full review. We obtained a waiver from the METc because there was not an infringement of the physical and/or psychological integrity of the study participants. Prior to the start of the focus groups, written informed consent was obtained from all participants. All participants agreed on audiotaping the interviews and usage for scientific research after anonymization.

Patients were recruited in several mental healthcare organization in the north of the Netherlands connected to the Rob Giel Research center (a collaboration of regional mental healthcare organizations in the northern part of the Netherlands). Mental healthcare organizations provide inpatient, outpatient, and community care treatment to patients with (severe) mental health problems. Client Councils of these mental healthcare organizations distributed the call via flyers and a call was posted on the website of the University Medical Center Groningen (https://www.umcg.nl/NL/UMCG/Afdelingen/Universitair_Centrum_Psychiatrie/Nieuws/Paginas/oproep-improve-studie.aspx).

Similarly, clinicians from various mental healthcare organizations in the northern part of the Netherlands were recruited and interviewed. In the Netherlands, every citizen is mandatory insured with standard health insurance. Citizens have an option to take out additional insurance to cover services not included in the standard package.

Focus group interviews took place in meeting rooms of a mental healthcare organization. Healthcare professionals were interviewed in their consultation room, the member of the Executive Board was interviewed in the mental healthcare organization and the medical advisor of the health insurer was interviewed at the headquarters of the health insurance company. Besides the participants and the researchers, nobody else was present during the conduct of the interviews. After the first interview, we made small adaptations in the interview guide. All participants participated once, and no repeated interviews were carried out.

Supplemental Material C - Description of interventions that may not be frequently used internationally

Intervention	Description of the intervention
Therapist-guided internet-based cognitive behavioral treatment (iCBT) ^{1,2}	iCBT is a web-based, manualized, therapist-assisted cognitive behavior therapy. The therapy consists of patients performing homework assignments that implement common CBT interventions. Therapist guidance consist of feedback and instructions that are tailored by the therapist to the patient's situation using motivational techniques. Treatment duration varies from 5-16 weeks, in which feedback is provided by the therapist two times a week.
Antidepressant medication + General Practice assistant*	In the Netherlands, the mental health system is divided into General Practitioner care including General Practice assistants specialized in mental health, generalist mental healthcare and specialist mental healthcare. Currently, patients with minor psychiatric complaints receive treatment at the GP with assistance from specialized GP assistants. The intervention means that patients receive antidepressant medication and that patients are supported by the specialized GP assistants.

¹ Ruwaard J, Lange A, Schrieken B, Emmelkamp P. Efficacy and effectiveness of online cognitive behavioral treatment: A decade of interapy research. *Stud Health Technol Inform.* 2011;167:9-14.

² Ruwaard J, Broeksteeg J, Schrieken B, Emmelkamp P, Lange A (2010) Web-based therapist-assisted cognitive behavioral treatment of panic symptoms: A randomized controlled trial with a three-year follow-up. *J Anxiety Disord* 24: 387–396.

Supplemental Material D - Findings of the remaining substitution pairs 3-13

Intervention substitution pair 3: Stakeholders' perspectives on investment in pharmacotherapy (3-6 months) and disinvestment in individual cognitive behavioral therapy for moderate depression

Level of evidence	- Questionable long-term effectiveness
Equity and equality considerations	Potential causes of increased inequalities/inequities are: <ul style="list-style-type: none">- Religion; some religions do not allow the use of medication- Medication only may result in under-treatment, and no insights and/or, personal (behavioral) changes are achieved Potential causes of decreased inequalities/inequities are not mentioned
Feasibility of implementation	Positive: <ul style="list-style-type: none">- No major issues anticipated, it is also current practice Issues: <ul style="list-style-type: none">- More psychiatrists needed for prescribing antidepressants- Higher workload for psychiatric nursing specialists and psychiatrists
Acceptability to stakeholders	Positive: <ul style="list-style-type: none">- Some patients respond well to medication only- Acceptable if it is the patients' preference or if patients are not willing to undergo psychological treatment- Desirable in vital depressions Issues: <ul style="list-style-type: none">- Not all patients need medication for a moderate depression- Medication only alleviates depressive symptoms, it does not solve the depression completely- Medication is supportive, in (behavioral) psychotherapy patients learn to deal with underlying/predisposing/persistent factors and patients obtain tools to be able to cope. This would be lacking if investing in pharmacotherapy only- Good and affordable investment on short-term but individual psychotherapy is needed once the depression is more stable- Dependent on the origin/ symptomatology of the depression; in the case of factors within a person, the person must also learn skills by psychological treatment, otherwise there is an increased risk of relapse- Patients' fear for side effects (which can be decreased with psycho-education)
Other effects not captured in modelling	Positive: <ul style="list-style-type: none">- Makes patients more open to other forms of therapy Negative: <ul style="list-style-type: none">- Undesirable addictive effect with negative health consequences- Patients feel like not being themselves, their thinking and reasoning is flattened- Metabolic adverse events; rapid aging, hypertension

Intervention substitution pair 4 and 5: Stakeholders' perspectives on investment in antidepressant medication 12 months and disinvestment in individual cognitive behavioral therapy / combination therapy for severe depression

Level of evidence	<ul style="list-style-type: none"> - Long-term effectiveness of antidepressant medication for 12 months should be well proven - Long-term effects are important
Equity and equality considerations	<p>Potential causes of increased inequalities/inequities are:</p> <ul style="list-style-type: none"> - Results in under-treatment, psychological treatment is needed - Religion; some religions do not allow the use of medication - Patients not willing to take medication <p>Potential causes of decreased inequalities/inequities are:</p> <ul style="list-style-type: none"> - Patients with difficulties in cognitive thinking due to their depression
Feasibility of implementation	<p>Positive:</p> <ul style="list-style-type: none"> - No major issues anticipated, it is also current practice <p>Issues:</p> <ul style="list-style-type: none"> - Proper alignment needed and a clear plan of action - The availability of psychiatrist or other personnel allowed to provide the pharmacological intervention. - Higher workload for psychiatric nursing specialists and psychiatrists - Psychiatrists need to see the patient more frequently, and thereby less able to see more new patients in a day
Acceptability to stakeholders	<p>Positive:</p> <ul style="list-style-type: none"> - Medication provides a boost and makes patients ready to go into therapy in the beginning, thereafter gradually decrease the amount of medication - Effective in case of suicidal thoughts - In minor cases this could work - Not desirable to withhold patients from medication - This is the recommended approach for a vital depression - in severe depression antidepressants are desirable <p>Issues:</p> <ul style="list-style-type: none"> - Medication in severe depression is only supportive, it is not desirable to provide medication only - Medication only alleviates symptoms, makes a depression milder and bearable, psychotherapy, structure in daily routine is crucial - Coaching and support is still needed to work on structure in daily routine and to resume daily activities - Medication does not solve the (cause of) depression, the underlying factors should be tackled. It remains important to obtain tools to cope with depression - Psychiatrists need to see the patient more frequently; uncomplicated depression without psychiatric comorbidities in severe depression is rare - In non-vital depression CBT treatment will be more effective - Combination therapy is common practice, and is the preference of most patients
Other effects not captured in modelling	<p>Positive:</p> <ul style="list-style-type: none"> - Antidepressant use make patients ready to start other forms of therapies <p>Negative:</p> <ul style="list-style-type: none"> - Medication tackles sadness but therapy addresses how to deal with sadness - Addiction to some antidepressant medication - Undesirable addictive effect with negative health consequences - Probability of recurrence - Patients feel like not being themselves, their thinking and reasoning is flattened - (Metabolic) adverse events; rapid aging, hypertension - Long term effects after no use of medication

Intervention substitution pair 6, 7 and 8: Stakeholders' perspectives on investment in antidepressant medication 12 months + General Practice assistant and disinvestment in individual psychotherapy / antidepressant medication 12 months / combination therapy for severe depression

Level of evidence	<ul style="list-style-type: none"> - Questionable effects of a General Practice assistant in severe depression - Evidence of effectiveness of a General Practice assistant in severe depression is important
Equity and equality considerations	<p>Potential causes of increased inequalities/inequities are:</p> <ul style="list-style-type: none"> - Burden for General Practice assistants - Severely depressed patients deserve more knowledgeable and experienced staff - Under-treatment <p>Neutral:</p> <ul style="list-style-type: none"> - Investment in antidepressant medication 12 months + General Practice assistant does not necessarily lead to inequalities <p>Potential causes of decreased inequalities/inequities are:</p> <ul style="list-style-type: none"> - Shorter waiting lists in specialized mental healthcare organization - Decreased workload in specialized mental healthcare organization, General Practice assistants have more time
Feasibility of implementation	<p>Positive:</p> <ul style="list-style-type: none"> - Additional investment in experts by experience might be beneficial - Less provision of specialized mental healthcare <p>Neutral:</p> <ul style="list-style-type: none"> - Need to consider the consequences, patients still get coaching and support and personal attention <p>Issues:</p> <ul style="list-style-type: none"> - Training of General Practice assistants are necessary - General Practice assistants' knowledge is questionable for severe cases - Knowledge of General Practice assistant is currently lacking in most cases, they are not all specialized in mental health, training is needed or psychiatrist in the General Practice office can be a solution - General Practice assistants are not qualified to prescribe medication - If antidepressants are provided by a psychiatrist, communication between psychiatrist and General Practice assistant is difficult in current organizational structure. Not clear who is responsible. In a specialized mental healthcare organization there are multidisciplinary meetings. It requires a different organization of care delivery and funding
Acceptability to stakeholders	<p>Positive:</p> <ul style="list-style-type: none"> - Acceptable in case of experienced General Practice assistants - Good social network is a prerequisite - In cases where patients are relatively stable - Preferred over medication only; some qualified General Practice assistants are experienced and can take into account social contexts and patients' interpersonal relations - Suitable in patients that do not benefit from CBT because they are too depressed - For the first couple of weeks where patients need to get through side effects of antidepressant medication it would be beneficial <p>Issues:</p> <ul style="list-style-type: none"> - Acceptable in milder depressions - In severe depression, combination therapy is preferred to enhance behavioral change and lifestyle adjustments - Not desirable in severe depression; it requires specialized care - Severe depression is often accompanied by comorbidities and increased risk of decompensation, which is not suitable for General Practice assistants
Other effects not captured in modelling	Not mentioned

Intervention substitution pair 9: Stakeholders' perspectives on investment in combination therapy and disinvestment in individual cognitive behavioral therapy for severe depression

Level of evidence	No issues mentioned
Equity and equality considerations	<p>Potential causes of increased inequalities/inequities are:</p> <ul style="list-style-type: none"> - Seeing a psychiatrist can be seen as threatening by patients due to stigma. It requires good coordination in practice - CBT is not suitable for everyone, a certain level of cognitive functioning, insights, and self-reflection is needed <p>Potential causes of decreased inequalities/inequities are:</p> <ul style="list-style-type: none"> - Suitable for the majority of adults
Feasibility of implementation	<p>Positive:</p> <ul style="list-style-type: none"> - Combination therapy is current practice, no issues anticipated - Keep training up to date, which is not different from current practice <p>Issues:</p> <ul style="list-style-type: none"> - The availability of psychiatrists or other personnel allowed to provide the pharmacological intervention.
Acceptability to stakeholders	<p>Positive:</p> <ul style="list-style-type: none"> - Patients have experienced great benefits of combination therapy - Acceptable and preferred and current practice; CBT works well if patients are not severely depressed. If that is the case, medication is important. Eventually CBT is important. Check with patients what is most beneficial - In severe depression medication is almost always necessary - Long-term effects are expected to be better in combination therapy <p>Neutral:</p> <ul style="list-style-type: none"> - For some patients, only CBT is sufficient; in the beginning medication is often needed <p>Issues:</p> <ul style="list-style-type: none"> - A minority of patients are willing to take medication due to side effects
Other effects not captured in modelling	<p>Positive:</p> <ul style="list-style-type: none"> - Clinicians have more control over treatment <p>Negative:</p> <ul style="list-style-type: none"> - Not mentioned

Intervention substitution pair 10: Stakeholders' perspectives on investment in mindfulness-based cognitive behavioral therapy and disinvestment in clinical management with maintenance medication (12 months) for prevention of recurrent depression

Level of evidence	<ul style="list-style-type: none"> - In the treatment of recurrent depressions it is proven effective, and patients with experience in mindfulness-based CBT have good experiences - Patients without experience in mindfulness-based CBT question about evidence - Mindfulness-based CBT does not seem to be implemented as frequently as medication or psychotherapy; or patients had no previous experience
Equity and equality considerations	<p>Potential causes of increased inequalities/inequities are:</p> <ul style="list-style-type: none"> - Familial predisposition necessitating medication, complex comorbidities, vital depressions - Unavailability of personnel to provide the intervention <p>Potential causes of decreased inequalities/inequities are:</p> <ul style="list-style-type: none"> - It requires a different way of intervening; it is more about feeling and experiencing. It can serve a subgroup of patients with difficulty in cognitive functioning and recognition
Feasibility of implementation	<p>Positive:</p> <ul style="list-style-type: none"> - Implementable as group therapy as it requires more mindfulness-based CBT therapists <p>Issues:</p> <ul style="list-style-type: none"> - It requires additional investment in personnel and training <p>Availability of workforce to undertake the intervention is currently unavailable</p>
Acceptability to stakeholders	<p>Positive:</p> <ul style="list-style-type: none"> - Acceptable, patients have good experiences - Clinicians' preference if current episode is in remission - Substantial group of chronic patients in need of medication but open and willing to discontinue medication use. However, there is a need for an alternative treatment <p>Neutral:</p> <ul style="list-style-type: none"> - In the ideal situation provide mindfulness-based CBT and in the meantime reduce medication use or align the need for medication alongside mindfulness-based CBT <p>Issues:</p> <ul style="list-style-type: none"> - Clinicians' willingness to provide the intervention, as it requires a different way of living and investment in clinicians' own life - Dependent on the number of and time between past recurrences and its severity. In chronic depression, it is difficult to discontinue medication use - It requires self-discipline to practice in patients' own environments - Patients' (lack of) openness to this kind of intervention - Some people respond well to medication (biological depression) or in some cases it is desirable to maintain medication for 12 months - Patients cannot stop directly, there is a need for tapering antidepressant use or patients might be unsuccessful in discontinuation of medication due to recurrences - Patients that do not experience side effects are more reluctant to discontinue medication - Clinicians' fear of recurrences in patients with severe depression
Other effects not captured in modelling	<p>Positive:</p> <ul style="list-style-type: none"> - In the long-run, patients acquire effective tools and techniques to prevent recurrent depressions - No side-effects of medication, and in the long-run better for one's health - In today's digital world, mindfulness can help bring one's attention to experiences occurring in the present moment - Reflecting patients' desire to try to quit medication use <p>Negative:</p> <ul style="list-style-type: none"> - Patients fear relapse and are reluctant to discontinue medication - Dependent on patient's social network and patient's environment

Intervention substitution pair 11: Stakeholders' perspectives on investment in mindfulness-based cognitive behavioral therapy and disinvestment in preventive cognitive (behavioral) therapy for prevention of recurrent depression

Level of evidence	<ul style="list-style-type: none"> - Both interventions are effective - Patients with experience in mindfulness-based CBT have good experiences - Patients without experience in mindfulness-based CBT question about evidence - Mindfulness-based CBT does not seem to be implemented as frequently as medication or psychotherapy; or patients had no previous experience
Equity and equality considerations	<p>Potential causes of increased inequalities/inequities are:</p> <ul style="list-style-type: none"> - Unavailability of personnel to provide the intervention <p>Potential causes of decreased inequalities/inequities are:</p> <ul style="list-style-type: none"> - It requires a different way of intervening; it is more about feeling and experiencing. It can serve a subgroup of patients with difficulty in cognitive functioning and recognition
Feasibility of implementation	<p>Positive:</p> <ul style="list-style-type: none"> - Implementable as group therapy as it requires more mindfulness-based CBT therapists <p>Issues:</p> <ul style="list-style-type: none"> - It requires additional investment in personnel and training - The availability of workforce to undertake the intervention is currently unavailable
Acceptability to stakeholders	<p>Positive:</p> <ul style="list-style-type: none"> - Acceptable to the majority of patients - Some patients with underlying persisting factors or comorbidities might benefit more of one than the other intervention - Acceptable, patients have good experiences <p>Issues:</p> <ul style="list-style-type: none"> - Clinicians' willingness to provide the intervention as it requires a different way of living and investment in clinicians' own life - It requires self-discipline to practice in patients' own environment - Patients' (lack of) openness to mindfulness-based CBT
Other effects not captured in modelling	<p>Positive:</p> <ul style="list-style-type: none"> - Most patients who experienced recurrent depressions have already gone through several CBT trajectories; more of the same might not be effective. Mindfulness-based CBT is something different <p>Negative:</p> <ul style="list-style-type: none"> - Dependent on patient's social network, and patient's environment

Intervention substitution pair 12 and 13: Stakeholders' perspectives on investment in interpersonal psychotherapy (IPT) / preventive cognitive (behavioral) therapy and disinvestment in clinical management with maintenance medication (12 months) for prevention of recurrent depression

Level of evidence	<ul style="list-style-type: none"> - Preventive CBT works equally well as clinical management with maintenance medication - The effects of antidepressants stops after discontinuation, preventive C(B)T has a prophylactic effect - Interpersonal Therapy (IPT) is an effective intervention
Equity and equality considerations	<p>Potential causes of increased inequalities/inequities are:</p> <ul style="list-style-type: none"> - Familial predisposition in need of medication, complex comorbidities <p>Potential causes of decreased inequalities/inequities are:</p> <ul style="list-style-type: none"> - Severely depressed, comorbid disorders. Then IPT or preventive C(B)T helps to stay in conversation.
Feasibility of implementation	<p>Positive:</p> <ul style="list-style-type: none"> - Existing interventions, and implementable. No issues anticipated <p>Neutral:</p> <ul style="list-style-type: none"> - Prevention program should be adjusted to the target population <p>Issues:</p> <ul style="list-style-type: none"> - There is a lack of professionals to provide IPT - Waiting list of CBT will become even longer than currently: resulting in higher workload for the therapists - Clinical management with maintenance medication is easier to implement
Acceptability to stakeholders	<p>Positive:</p> <ul style="list-style-type: none"> - Acceptable to patients, it is not desirable to maintain medication use in long-term - Acceptable and clinicians' preference if current episode is in remission - In the long-run, with IPT or preventive C(B)T, patients acquire effective tools and techniques to prevent recurrent depressions - Risks and side effects of medication, and medication does not solve the depression - IPT is especially beneficial in patients with (somatic) health issues - Acceptable from health insurers' point of view - Substantial group of chronic patients in need of medication but open and willing to quit medication use and would welcome an alternative <p>Neutral:</p> <ul style="list-style-type: none"> - In the ideal situation provide mindfulness-based CBT and in the meantime reduce medication use or align the need for medication alongside mindfulness-based CBT <p>Issues:</p> <ul style="list-style-type: none"> - Patients prefer discontinuation of medication but fear recurrent depressive episodes - Some patients have benefits from medication (biological depression) or in some cases it is desirable to maintain medication for 12 months for example in severe depression - Patients cannot stop medication directly, there is a need for tapering antidepressant use - Patients that do not experience side effects are more reluctant to discontinue medication use - Dependent on the number of and time between past recurrences and its severity. In chronic depressions, psychotherapy alone is not desirable if discontinuing medication was unsuccessful - Some patients do not benefit from psychotherapies if they are too severely depressed or have comorbidities. Medication is helpful then, especially in the beginning - Some types of medication are hard to quit due to side effects and risk of recurrence
Other effects not captured in modelling	<p>Positive:</p> <ul style="list-style-type: none"> - In the long-run; patients acquire effective tools and techniques to prevent future depressions - It enhances patient empowerment <p>Negative:</p> <ul style="list-style-type: none"> - Patients fear discontinuation of medication - It is dependent on patient's social network - When patients are in remission, they sometimes find it hard to commit to therapy, some patients already had loads of CBT or IPT sessions

