What matters to patients? A systematic review of preferences for medication-associated outcomes in mental disorders

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ABSTRACT

Objective: To investigate patients’ preferences for outcomes associated with psychoactive medications.

Setting/design: Systematic review of stated preference studies. No settings restrictions were applied.

Participants/eligibility criteria: We included studies containing quantitative data regarding the relative value adults with mental disorders place on treatment outcomes. Studies with high risk of bias were excluded.

Primary and secondary outcome measures: We restricted the scope of our review to preferences for outcomes, including the consequences from, attributes of, and health states associated with particular medications or medication classes, and process outcomes.

Results: After reviewing 11 215 citations, 16 studies were included in the systematic review. These studies reported the stated preferences from patients with schizophrenia (n=9), depression (n=4), bipolar disorder (n=2) and attention deficit hyperactive disorder (n=1). The median sample size was 81. Side effects and symptom outcomes outnumbered functioning and process outcomes. Severe disease and hospitalisation were reported to be least desirable. Patients with schizophrenia tended to value disease states as higher and side effects as lower, compared to other stakeholder groups. In depression, the ability to cope with activities was found to be more important than a depressed mood, per se. Patient preferences could not consistently be predicted from demographic or disease variables. Only a limited number of potentially important outcomes had been investigated. Benefits to patients were not part of the purpose in 9 of the 16 studies, and in 10 studies patients were not involved when the outcomes to present were selected.

Conclusions: Insufficient evidence exists on the relative value patients with mental disorders place on medication-associated outcomes. To increase patient-centredness in decisions involving psychoactive drugs, further research—with outcomes elicited from patients, and for a larger number of conditions—should be undertaken.

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INTRODUCTION

To respect and respond to patient preferences is a crucial aim in patient-centred healthcare and a persistent ideal in evidence-based medicine, clinical practice guidelines and shared decision-making. Integrating patient preferences is increasingly advocated in health technology assessments, drug development and market approval and reimbursement. Yet to allow patient preferences to guide healthcare decisions remains to become common practice.

In the mental health field, healthcare decisions frequently involve medications: one in five Americans and one in eight western Europeans are prescribed psychotropic drugs. The psychopharmacological dilemmas faced by clinicians and patients are often preference-sensitive, and involve trade-offs of conflicting, multiple outcomes. Systematic reviews and meta-analyses have summarised whether patients prefer pharmacological or psychological treatment, and

Strengths and limitations of this study

- This is the first systematic review on patients’ relative, stated preferences for outcomes of psychopharmacological treatments across methods and disorders.
- We summarised patients’ preferences for hypothetical associations with medications and excluded preferences for specific medications or treatment domains, which are amenable to misconceptions. The treatments per se do not give value to the user; it is their outcomes that give value.
- We tested and applied a broad, peer reviewed search strategy, but we might have overlooked or missed studies. Study quality was rigorously and comprehensively assessed.
- Owing to the heterogeneity of methods and outcomes we could not perform quantitative summaries of the relative strengths of preferences.
the effect of matching the treatment to the patient’s preferred option.\textsuperscript{17} \textsuperscript{18} However, in trade-off dilemmas, studies on patients’ preferred options might be less informative than studies on their preferences for the outcomes of the options. Knowledge about the relative strengths of preferences for treatment outcomes, representative for populations, can be gained with stated preference methods. A range of techniques is available.\textsuperscript{19}--\textsuperscript{21} Systematic reviews of studies applying the techniques to elicit patient preferences for outcomes of psychotropic drugs are lacking. The current void of knowledge on the outcomes patients value the most and least, and what those outcomes should be,\textsuperscript{22} strikes the foundation of patient-centred care and suggests missed opportunities for more patient-centred decisions.

For these reasons we conducted a systematic review of studies on patients’ valuations of outcomes associated with psychoactive medications. The main goal was to summarise what is known on the relative strengths of preferences. We also reviewed:

- Whether patient perspectives were part of the purpose and construction of outcomes
- Which outcomes were addressed
- The feasibility of stated preference methods for patients with mental disorders
- Correlations between patient preferences and demographic or disease variables
- Differences between patients’ preferences and those of other stakeholders

**METHODS**

This study followed the PRISMA reporting guidelines (see online supplementary appendix 10): http://www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.1000097

**Eligibility criteria**

Studies applying stated preference methods to elicit the relative values patients place on outcomes of pharmacological treatments, using quantitative methods, were eligible for inclusion. Studies that included rating scales only were excluded due to doubts about whether the techniques adequately measure strength of preference.\textsuperscript{19} No publication date, context or publication status restrictions were imposed.

We included studies on adult patients with direct experience of the mental disorder specified in the study, currently diagnosed with or at risk of recurrence of the disease. Trials addressing patients with substance-related and addictive disorders were excluded.

Patient preferences can be defined as “statements made by individuals regarding the relative desirability of a range of health experiences, treatment options, or health states”.\textsuperscript{23} We restricted the scope of our review to preferences for outcomes, including the consequences from, attributes of, and health states associated with particular medications or medication classes and process outcomes. Studies on patients’ preferences for specific medications, medication classes, or treatment domains, or for health states detached from a medication context, were not included. Studies measuring health-related quality of life were excluded unless they elicited patients’ relative valuations of outcomes.\textsuperscript{24} Studies calculating preferences by mapping life quality scales to utility scores were not included. Owing to the heterogeneity of the field, we did not specify the outcome measures in detail before the study.

**Search strategy**

We searched Medline, Embase, PsycINFO, CENTRAL, SveMed+, The Health Technology Assessment Database, the NHS Economic Evaluation Database and grey literature databases from inception to September 2013. We piloted our strategies in a test search and modified the use of keywords and indexed terms. A PRESS (Peer Review of Electronic Search Strategies) review was undertaken and the strategies revised. In the revised search, we used a combination of subject headings, subheadings and text words. The bibliographies of the included studies were hand searched for additional studies. Online supplementary appendix 1 details the search strategies.

**Study selection**

Two review authors (KN, BFL) independently reviewed all identified titles and abstracts (figure 1). Full text articles were obtained for potentially relevant trials and examined in detail by the same authors. Disagreements were discussed with the principal author (OE) and resolved by consensus.

**Quality assessment**

Standardised criteria for methodological quality and risk of bias in stated preference studies have not been established.\textsuperscript{25} \textsuperscript{26} To enable critical appraisal, we constructed a checklist based on criteria proposed for assessment of stated preference research in eight methodological reviews and evaluation tools.\textsuperscript{19} \textsuperscript{27}--\textsuperscript{33} The resulting inventory consisted of 31 quality criteria within five domains: external validity, presentation of outcomes, minimisation of irrelevant variance, reporting and analysis, and other aspects (see online supplementary appendix 2). Two authors (KN, OE) independently assessed all studies considered for inclusion on the 31 items. Studies given an overall intermediate or high quality rating were included. Inconsistencies were resolved by discussion.

**Data collection**

We developed, piloted and revised a data extraction form consistent with the goals of the review. Two reviewers (KN, OE) independently extracted data on the study, study population, preference elicitation aspects and preference results (see online supplementary appendix 3).
RESULTS
Of 11 215 unique citations, 54 proceeded to full text review. We excluded 39 studies, the most frequent reason being lack of quantitative data on the relative strengths of the preferences (see online supplementary appendix 4). This left 16 studies for our systematic review. We present the results in descriptive and tabular form.

Study characteristics
Sixteen studies in 16 papers included 1785 patients with a median sample size of 81 (range 20–469). Nine studies had assigned patients with schizophrenic disorders, four had depressive disorders, two had bipolar disorders and one had ADHD (attention deficit hyperactive disorder). The range of reported mean ages was 39–46 and the median percentage of female participants 55. In the seven studies reporting ethnicity, the median percentage of Caucasians was 86. Ten studies included only outpatients, one inpatients and outpatients, and five did not report hospitalisation status. Twelve of the 16 studies were partly or fully conducted in the USA. Preference elicitation was the main or part of the main objective in 15 studies. Preferences were elicited from patients with the standard gamble (SG) method in six studies, conjoint analysis (CA) and pair-wise comparison (PC) in two studies each, discrete choice experiment (DCE) and willingness-to-pay (WTP) in two, and time trade-off (TTO) in one (table 1). Basic descriptions of the methods are provided in box 1.

Study quality
A frequently used quality criterion for stated preference studies is whether the outcomes are presented to the participants in adequate detail.28 The level of detail varied in the included studies, from short text descriptions to info-graphics and videos with actors enacting symptoms and side effects. All included studies minimised threats on validity from factors irrelevant to the represented outcomes using measures such as precomprehension or postcomprehension tests.

Non-random recruitment procedures limited the external validity in all studies. Four studies included less than 50 participants. In six studies, data were not reported for participants who did not complete the procedures. Authors generally provided incomplete information on study design, and five studies lacked measures.

Figure 1 Flow chart of study selection.
| Study                        | Condition                                      | Country               | Number* Included/Completed | Number of women (%) | Mean age (years) | Caucasian (%) | Clinical setting                  | Method                      | Relevant medication                  | Funding from pharmaceutical company | Outcomes                              |
|-----------------------------|-----------------------------------------------|-----------------------|---------------------------|---------------------|-----------------|---------------|------------------------------------|-----------------------------|-------------------------------------|--------------------------------------|---------------------------------------|
| Morss et al                 | Schizophrenia                                 | USA                   | 33                        | 2 (6)               | 43              | 75            | Inpatient and outpatient           | VAS, PC, SG                 | Antipsychotics                      | Yes                                  | Side effects                          |
| Revicki et al               | Schizophrenia                                 | UK, USA               | 49                        | 12 (24.5)           | 39              | 94            | Outpatient                         | Rating scale, PC             | Psychopharmacological treatment      | Yes                                  | Symptoms, process related, functioning |
| Lenert et al                | Schizophrenia, schizoaffective disorder       | USA                   | 22                        | Not reported        | 46              | Not reported | Outpatient                         | VAS, PC, SG                 | Antipsychotics                      | No                                   | Side effects                          |
| Lee et al                   | Schizophrenia                                 | USA                   | 20                        | 12 (55)             | Range: 18–60    | 40            | Mental health centre               | VAS, SG                     | Antipsychotics                      | Yes                                  | Symptoms, side effects                |
| Lenert and Kaplan           | Schizophrenia                                 | USA                   | 148                       | 49 (33)             | 98%≤60          | Not reported† | Centres and practice organisations | VAS, SG                     | Antipsychotics                      | Yes                                  | Symptoms, side effects                |
| Shumway                     | Schizophrenia                                 | USA                   | 50                        | 17 (34.5)           | 42              | 69            | Outpatient                         | Rating scales, CA, VAS, TTO   | Antipsychotics                      | No                                   | Symptoms, functioning, side effects, other |
| Briggs et al                | Schizophrenia, schizoaffective disorder       | UK                    | 50/49                     | 27 (55)             | 44              | 94            | Outpatient                         | Self-explicated method         | Prescribed treatments              | Yes                                  | Symptoms, functioning, process related, other |
| Bridges et al               | Schizophrenia                                 | USA, Germany          | 105/97                    | 50†                 | 44              | Not reported | Outpatient                         | CA                          | Antipsychotics                      | Yes                                  | Symptoms, functioning, side effects, other |
| Kinter et al                | Schizophrenia                                 | USA, Germany, New Zealand | 101/100                  | 40 (40)            | 43/42           | Not reported | Outpatient                         | Antipsychotics               | Yes                                  | Symptoms, functioning, side effects, other |
| O’Brien et al               | Mild or moderate depression                   | Canada                | 95                        | 69 (73)            | 41              | Not reported | Outpatient                         | VAS, WTP                      | Antidepressants                      | Yes                                  | Side effects, costs                   |
| Revicki and Wood            | Major depressive disorder                     | USA, Canada           | 70                        | 54 (77)            | 42              | Not reported | Outpatient                         | VAS§, SG                     | Antidepressants                      | Yes                                  | Symptoms, side effects                |
| Morey et al                 | Major depressive disorder                     | USA                    | 104                       | 77 (74)            | 40              | Not reported | Outpatient                         | WTP                          | Antidepressants                      | No                                   | Side effects, costs, process related |
| Zimmermann et al            | Depression                                    | Germany               | 255/227                   | 140 (82)           | Not reported‡   | Not reported | Outpatient                         | CA                          | Antidepressants                      | Yes                                  | Symptoms, functioning, side effects, process related |
| Revicki et al               | Bipolar disorder type I                      | USA                    | 96/92                     | 51 (55.5)          | 42              | Not reported | Community hospital, research centre and health centre | VAS, SG | Mood stabilisers, antipsychotics | Yes                                  | Symptoms, side effects, process related |
| Johnson et al               | Bipolar disorder                              | USA                    | 469                       | 295 (63)           | 43              | 86            | Members of a web-based chronic illness panel | DCE**                         | Bipolar medications                  | Yes                                  | Symptoms, side effects                |
| Glennärd et al              | ADHD                                          | Sweden, Denmark, Norway | 116                      | 66 (57)            | Not reported   | Not reported | Centres DCE                         | Stimulants                   | Yes                                  | Functioning, side effects, process related, costs |

*Patient participants only.
†31% African American or Hispanic.
‡Approximate percentage.
§VAS was used as a training exercise.
¶Largest age group 50–59 years.
**Choice-format trade-off questions.
CA, conjoint analysis; DCE, discrete choice experiment; PC, pairwise comparison; SG, standard gamble; TTO, time trade-off; VAS, visual analogue scale; WTP, willingness to pay.
of variance. The use of statistical techniques was deemed appropriate in all studies. Only two studies were given an overall ‘high quality’ rating (see online supplementary appendix 5).

**Purposes**

Seven studies related their results to potential benefits for individual patients, for instance to tailor adherence programmes, to be helpful in medical decision-making or to promote concordance between patients and psychiatrists. Although 13 of the studies received funding from a pharmaceutical company, only five studies suggested or performed economic analyses from an industry perspective. Eight studies discussed how their preference results could be used in public evaluation and prioritisation contexts (see online supplementary appendix 6).

**Outcome sources**

In 10 of the 16 studies, input from patients was sought when outcomes were selected and constructed. In 10 of the 16 studies, input from patients was not. Outcome sources varied systematically from those of other stakeholders in the five studies published after 1997, and the magnitude of the differences varied from modest to considerable. People with schizophrenia valued disease states higher than other stakeholder groups. The preferences of family members were closer to those of patients, compared to psychiatrists and laypeople, in studies that performed relevant comparisons. Other stakeholders did not value functioning or symptoms significantly

**Feasibility and validity**

The studies reported that patients were able to provide usable preference measures for the six methods applied, generally comprehended the tasks and gave sufficiently consistent answers. A total of 92–100% of the participants completed the procedures.

Three of the nine studies with patients with schizophrenia reported moderate or major problems. In the first, a small SG study, 30% of the patients did not understand the survey well and 56% had inconsistent rank ordering. In the second, also a SG study, patients made more logical errors than others and mostly, in contrast to other stakeholders, preferred not to correct their mistakes. In one of the two studies applying conjoint analysis, patients reported lower levels of understanding and more difficulty with the task compared to other participants. Minor or no problems were reported in the two schizophrenia studies applying TTO and self-explicated methods.

The studies including patients with depression, bipolar disorder and ADHD reported minor or no feasibility problems, but feasibility and validity were less focused on compared to the schizophrenia studies (see online supplementary appendix 7).

**Correlations with patient characteristics**

Eleven studies investigated whether patient preferences correlated with demographic or disease variables, with negative or conflicting findings.

Three studies found that preferences correlated with age, whereas five found no significant association. Gender correlated with preferences in one study, but did not correlate in four. Possible correlations with living arrangement, education, employment-status and income level were investigated with negative or mixed results. Severity of disease correlated with preferences for hypothetical health states and the impact of a side effect on utility. Two studies found that disease severity did not correlate with preferences, and one study reported mixed results.

**Comparison with other stakeholder groups**

Eight studies, all on schizophrenia, compared the preferences of patients with those of other stakeholder groups. Patients’ preference values differed systematically from those of other stakeholders in the five studies published after 1997, and the magnitude of the differences varied from modest to considerable. Extrapyramidal side effects (EPS) were given a lower value or deemed more important, compared to clinicians, except in one study. The preferences of family members were closer to those of patients, compared to psychiatrists and laypeople, in studies that performed relevant comparisons. Other stakeholders did not value functioning or symptoms significantly

**Box 1  Stated preference methods in healthcare**

- The **standard gamble** elicits the value of outcomes by asking patients to choose between a certain outcome and a gamble.
- **Willingness to pay** is the maximum amount a patient is willing to offer to obtain good, or to avoid undesirable, outcomes.
- In **conjoint analysis**, patients place weights on different features of a health option.
- In **pairwise comparison**, patients compare health options in pairs to find which is preferred, or which has the largest amount of a measurable aspect.
- In **discrete choice experiments**, patients state their preference over alternative scenarios, such as health states.
- In **time trade-off**, patients are asked to choose between living in a suboptimal state for a certain period of time, versus living a healthier life for a shorter time.

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and/or consistently different from what patients did (see online supplementary appendix 8).

**Strengths of preferences**

Stated preference methods elicit different preference measures. WTP represents the value that an individual places on a commodity, SG and TTO estimate a utility, most often on a scale where 0 is death and 1 perfect health. CA and DCE measure the relative importance or value of different outcomes.19

**Schizophrenia**

‘Positive’, ‘acute’ or ‘psychotic’ symptoms figured consistently among the least desirable outcomes to patients.36 40 45 Negative symptoms such as reduced capacity for emotion were found more desirable or less important than positive symptoms.36 45 48

Independency was rated highly,36 45 and being an inpatient, lowly.48 Cognitive36 42 and social36 42 45 functions were moderately or highly important compared to other outcomes. The importance of capacity for work and for daily living was intermediate.36 42.45

EPS was included in seven studies. Two small studies39 46 both reported that the disutility of Parkinsonism was larger than the disutility of akathisia and tardive dyskinesia. The presence of EPS reduced the utility by 12–21%. Pseudoparkinsonism reduced the utility with 5–7% in two other studies.28 44 In three additional studies the relative importance of EPS was moderate or high, compared to other outcomes.40 42 45 Health states with weight gain had a higher utility than states with EPS in the only schizophrenia study including side effects other than EPS.40

**Depression**

Severe, untreated depression reduced the utility from 1.0 (perfect health) to 0.3, and 25% of patients considered this state equivalent to or worse than death.47 Patients’ reduced ability to start and cope with activities on their own, due to fatigue, was more important than depressed mood in one large, well-performed study.35 The same study found that side effects after 2 weeks also were more important than depressed mood.35

The simultaneous presence of weight gain and no orgasm reduced the WTP from USD 686 per month for an antidepressant without side effects, to USD 227.41 One study found very small differences in side effect utilities.47 Patients were willing to pay more to avoid tremor and sleepiness than to avoid dry mouth and sweating, according to one study.38

**Bipolar disorder**

The inpatient state, inpatient mania and severe depression had lower utilities than the outpatient, stable state in one study.43 The relative strengths of preferences for mania versus depression were conflicting in two studies.34 45 Cognitive effect and severity of depression were equally important in one study.34

Weight gain within 3 months was found to be equally important to cognitive impairment and severity of depression, and three times more important than serious side effects.34 A weight gain of more than 2.3 kg reduced the utility with 0.07.45

**ADHD**

Patients were willing to pay 74% more for functioning well in the morning and school/workday, compared to functioning well in the afternoon/evening in one study.37 Table 2 and online supplementary appendix 9 contain additional details on all the conditions.

**DISCUSSION**

**Principal findings**

Benefits to patients and clinical practice were part of the purpose in a minority of the 16 studies included in this review. Most authors had not involved patients when they selected and developed the outcomes in their studies. Side effect and symptom outcomes outnumbered functioning and process outcomes, and only a limited selection of potentially important outcomes were presented to patients. The stated preference methods were generally found to be feasible across different conditions and disease severities, but patients with schizophrenia experienced more problems with the tasks than other patient groups, in particular for SG. The patients’ preferences did not vary consistently with age, gender, disease severity or other demographic or disease variables. The relative preferences of patients with schizophrenia differed systematically from those of other stakeholders in most studies. Patients valued disease states higher than did other groups and perceived side effects more negatively than clinicians did. Patients with schizophrenia desired acute and psychotic symptoms least of all outcomes, and valued independency highly. Functioning occupied a middle ground; social function tended to be more important than vocational function. The importance of EPS was moderate or high. For patients with depression, severe disease greatly reduced utility, though the ability to cope with activities, and presence of side effects, appeared more important than a depressed mood, per se. Patients with bipolar disorder valued inpatient mania and severe depression lowly, and reported weight gain to be important. In ADHD, patients reported that functioning in the morning and during daytime was most important.

**Strengths and weaknesses of the review**

This is the first systematic review on patients’ relative, stated preferences for outcomes of psychopharmacological treatments across methods and disorders. The review accords with the PRISMA guidelines (see online supplementary appendix 10) and the protocol was registered in the PROSPERO database prior to conduction (see online supplementary appendix 11).
| Study                  | Condition                      | Outcomes                                                                 | Results, patients’ preferences only                                                                 |
|-----------------------|--------------------------------|---------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------|
| Morris et al<sup>16</sup> | Schizophrenia                  | 3 side effects: akathisia, tardive dyskinesia, parkinsonism                | 33 patients with chronic schizophrenia gave their preferences for three side effects, using VAS scales, PC and SG. 78% of the patients had at least one of the three side effects themselves. The SG disutilities for the three side effects reduced the expected quality of life by 12–16%. The expected mean value of life for akathisia and for tardive dyskinesia using the SG method was 0.88, while parkinsonism reduced the value to 0.84. Patients reported parkinsonism to be the worst side effect, using VAS and PC. The VAS method yielded significantly lower values than the SG method. |
| Revicki et al<sup>48</sup>     | Schizophrenia                  | 5 health states: (1) inpatient, acute positive symptoms, (2) outpatient, negative symptoms, (3) outpatient, moderate function, (4) outpatient, good function, (5) outpatient, excellent function | 49 patients with schizophrenia used CRS and PC. The patients had relatively little psychopathology and cognitive impairment. Five hypothetical health states were presented to the patients. In the SG, patients valued being hospitalised and having acute positive symptoms the lowest (0.19), followed by the outpatient state with negative symptoms (0.30), and outpatient with moderate (0.49), good (0.57) and excellent (0.77) function. SG utilities in the current study were significantly higher than the CRS preferences for all health states. |
| Lenert et al<sup>46</sup>     | Schizophrenia and schizoaffective disorder | 3 side effects: akathisia, tardive dyskinesia, parkinsonism                | 22 patients with schizophrenia or schizoaffective disorder used VAS, PC and SG methods. The same three side effects as in Morris 1993 were presented to patients. The SG disutilities for each of the three side effects reduced the expected quality of life by 13–21%. The expected mean value of life using the SG method was 0.87 for akathisia and 0.88 for tardive dyskinesia, and 0.79 for parkinsonism. Parkinsonism was rated the worst side effect using the VAS scale. The VAS method yielded significantly lower values than the SG methods. |
| Lee et al<sup>44</sup>       | Schizophrenia                  | 2 patterns of mental health impairment (less severe/more severe), based on 4 dimensions and 1 side effect: hostility/suspiciousness, anxiety/depression, withdrawal/retardation and thought disorder, and pseudo-parkinsonism | 20 patients with schizophrenia were included in the study, which used VAS and SG methods. Less and more severe health states based on four “dimensions” were presented to patients. Pseudoparkinsonism reduced the average SG values with 0.07, and using VAS: 0.08. The utilities of the four dimensions were not reported. |
| Lenert and Kaplan<sup>28</sup> | Schizophrenia                  | 6 health states with different degrees of symptoms (mild or moderate levels), with or without pseudo-parkinsonism, based on four symptom domains: thought disorders and disorders of cognition, withdrawal (negative symptoms), anxiety/depression and hostility | 148 patients with schizophrenia from geographically and clinically diverse environments were included in the study. The SG disutilities for hypothetical health states representing four symptom domains similar to those in Lee et al, using VAS and SG methods. The reduction in utility between states without and with pseudo-parkinsonism was found to be approximately 0.07 (SG) and 0.14 (VAS) for milder states, and 0.05 (SG) and 0.07 (VAS) for more severe states (values based on figure in original article). Mild disease symptoms with pseudoparkinsonism was equally preferable to moderate symptoms without side effects. VAS scores were systematically higher than SG scores were. The utilities of the four symptom domains were not reported. |
| Shumway<sup>45</sup>          | Schizophrenia                  | 16 health states including 7 outcomes: positive symptoms, negative symptoms, extrapyramidal symptoms, tardive dyskinesia, social function, independent living, vocational function | 50 patients with schizophrenia in an outpatient setting rated 16 health states using rating scales and CA. Preference weights for seven outcome domains were computed using a CA procedure. The highest mean preference weight was found for social function (16.9), followed by, in descending order, positive symptoms (15.0), independent living and tardive dyskinesia (both 14.5), vocational function (14.1), extrapyramidal symptoms (13.5) and negative symptoms (11.5). There were no statistically significant differences between the ranked preferences. |
| Briggs et al<sup>40</sup>     | Schizophrenia and schizoaffective disorder | 7 health states: stable disease, relapse and 5 side effects: weight gain, hyperprolactinaemia, diabetes, EPS and negative symptoms | 50 outpatients with schizophrenia or schizoaffective disorder rated health states directly on a preference assessment rating scale and then completed a TTO task for each health state. The highest mean utility was given to the stable schizophrenia state (0.92), followed by weight gain (0.83), hyperprolactinaemia (0.82), diabetes (0.77) and EPS (0.72). Relapse had the lowest mean utility (0.60). |
| Study          | Condition                      | Outcomes                                                                 | Results, patients’ preferences only                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|---------------|--------------------------------|--------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Bridges et al | Schizophrenia                  | 20 treatment goals: decreased/increased depressive thoughts and feelings, cognition, satisfaction, performance, self-independence, physical health, psychotic symptoms, anxiety, social contacts, activities of daily living, capacity for work, self-confidence, family relationships, restlessness, visits to the doctor/hospital, improved communication, mistrust/hostility, irritability, capacity for emotion, sexual pleasure | 105 outpatients with schizophrenia ranked and stated 20 treatment goals in a self-expliquid method study. The product of the ranking and rating (scale 0–100) revealed that decreased depressive thoughts and feelings was valued highest (58.5), followed by, in descending order, improved cognition (55.9), improved satisfaction (54.4), improved performance (52.6), improved self-independence (51.3), improved physical health (50.1), decreased psychotic symptoms (49.9), decreased anxiety (46.6), improved social contacts (45.3), improved activities of daily living (45.1), improved capacity for work (43.5), improved self-confidence (42.4), improved family relationships (38.9), decreased restlessness (36.9), decreased visits to the doctor/hospital (36.8), improved communication (35.9), decreased mistrust/hostility (31.9), decreased irritability (30.8), improved capacity for emotion (28.9) and improved sexual pleasure (24.2) |
| Kinter et al  | Schizophrenia                  | 7 attributes, defined over 2 levels including: disease symptoms, relapse, clear thinking, social activities, extrapyramidal symptoms, daily activities, and support | 101 patients diagnosed with schizophrenia participated in this methodological study that compared two different CA designs. Seven patient-oriented attributes, each defined over two levels, were presented. The parameter estimate for the outcomes, using a D-efficient design, were in descending order, disease symptoms (0.553), relapse (0.415), clear thinking (0.394), social activities (0.394), extrapyramidal symptoms (0.196), daily activities (0.196) and disease symptoms (0.107). All parameter estimates except disease symptoms were statistically significant within the model. Using the orthogonal design, disease symptoms (0.756) and daily activities (0.623) also had the highest estimates, followed by clear thinking (0.454), support (0.446), social activities (0.313), and disease symptoms (0.269) and relapse (0.095). All parameter estimates except relapse were statistically significant within the model. The results of the two models were not statistically different |
| O’Brien et al | Mild or moderate depression    | 7 side effects: blurred vision, tremor, sleepiness, dizziness, constipation, sweating, dry mouth | 95 patients with mild or moderate depression ranked and rated seven adverse effects. The maximum WTP per month (CAD) for a reduction in the incidence of each adverse effect was highest for blurred vision (21.9), followed by (in descending order) tremor (19.4), sleepiness (18.6), dizziness (16.8), constipation (15.9), sweating (13.9) and dry mouth (11.4). There was a statistically significant difference between the two extremes of blurred vision and dry mouth |
| Revicki       | Major depressive disorder      | 11 health states, with varying depression severity, functioning and well-being, medication treatment, 8 side effects | Utilities for 11 hypothetical health states from 70 patients with major depressive disorder were obtained in this VAS and SG study. Severe, untreated depression had the lowest mean utility (0.30). 25% rated this state as worse or equal to death. The highest score was found for remission and no treatment (0.86), followed by depression in remission and maintenance treatment (0.72–0.83). The observed mean differences in utility for side effects compared to their absence ranged from 0.12 points for nervousness and light-headedness, to 0.01 points for dry mouth and nausea. Point values for sedation, headache, constipation and tension were not reported. The only side effect showing a statistically significant reduction in utility when present was light-headedness |
| Morey et al   | Major depressive disorder      | Different treatment characteristics presented in 40 states (20 choice pairs) varying the treatment characteristics of effectiveness, side effects (weight gain, little or no interest in sex, inability to achieve orgasm), money costs, hours of psychotherapy per month and use of antidepressants | 104 patients with major depressive disorder were included in the study. Using a willingness to pay (WTP) approach, treatment characteristics were varied in 20 different choice-pairs presented to patients. The monthly expected WTP was highest for “antidepressants with no side effects” and the combined treatment of “anti-depressants and 2 hrs therapy” (both $686 for a RI). WTP decreased if the antidepressant treatment had the side effect of no orgasm (WTP for an RI $478), weight gain of 5% (WTP for an RI $409) or both these side effects (WTP for an RI $227) |

Continued
| Study                  | Condition                        | Outcomes                                                                 | Results, patients' preferences only                                                                                                                                                                                                                     |
|-----------------------|----------------------------------|--------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Zimmermann et al      | Depression                       | 18 hypothetical treatment outcome scenarios, differing in 8 attributes: depressed mood, loss of interest and enjoyment, loss of energy/fatigue, sleep disturbance, feelings of guilt, depression-related pain, treatment duration, side effects after 2 weeks | 227 patients with self-reported depression, currently or recently on antidepressants, used a choice-based conjoint analysis. 18 pairs of hypothetical treatment outcome scenarios differing on 8 attributes were presented. Loss of energy/fatigue was the most important outcome attribute (relative importance 18.5%), differing significantly from all other attribute importance values. The relative importance of side effects after 2 weeks was 14.2%, loss of interest and enjoyment 13.5%, depression-related pain 12.0%, sleep disturbance 12.0%, feelings of guilt 11.5%, and duration of treatment 9.9%. Least important was assigned to depressed mood: 8.5%. The factor levels most strongly affecting the utility scores for "loss of energy/fatigue" were "Can start and cope with all activities on his/her own" (utility score + 10.9) and "Cannot start or cope with any activities on his/her own" (-11.7). The factor level most strongly affecting the utility of "loss of interest and enjoyment" was "Has no interest in previous leisure activities" (-10.0). Standard deviations were given for factor levels but not for the attributes. |
| Revicki et al         | Bipolar disorder I               | 55 health states differing in side effects, symptom severity, functioning, well-being and mono-/combination therapy | 96 patients in a VAS and SG study were presented hypothetical health states describing combinations of symptom severity, functioning, well-being and side effects. Mean utilities (0 anchored as death, 1 anchored as complete health) were calculated for inpatient states (0.12–0.33), inpatient mania states (0.23–0.26), severe depressive state (0.29), outpatient mania states (0.29–0.64), stable tardive dyskinesia (0.76) outpatient stable states with few clinical symptoms and no weight gain (0.58–0.83). A weight gain of more than 2.3 kg demonstrated an average 0.066 decrease in health state utilities. Patients preferred mono-therapy to combination therapies. The difference for weight gain was statistically significant. The difference in utilities for the outpatient and inpatient mania state was not statistically significant. |
| Johnson et al         | Bipolar disorder                 | 8 medication attributes including: frequency and severity of mania or depression episodes, side effects such as weight gain, cognitive deterioration, fatigue and the risk of developing an unspecified, but potentially life-threatening, side effect | 469 patients in a DCE gave their importance weights for eight medication attributes. Patients considered weight gain within 3 months to be most important (0.20), followed by cognitive impairment (0.185) and changes in the severity of depression (0.184). These outcomes were statistically significantly more important than a fatigue effect (0.11), mania severity (0.09), mania frequency (0.08), depression frequency (0.08) and risk of serious side effects (0.06). The values are approximate and based on the figures in the original article. |
| Glenngård et al       | ADHD                             | 5 health states: health state morning/workday (effectiveness), health state afternoon/early evening (effectiveness), side effects, dosing frequency per day, and price (cost of treatment per month) | 116 patients, all currently on ADHD, participated in DCE, presenting a combination of five hypothetical medication attributes, including attribute levels. Functioning in the morning and during school/workday was most important (WTP per month 252), followed by functioning during the afternoon/evening (WTP 145), number of dosages per day (WTP -43) and side effects (WTP -98). |

CA, conjoint analysis; CRS, categorical rating scale; DCE, discrete choice experiment; PC, pairwise comparison; RI, representative individual; SG, standard gamble; TTO, time trade-off; VAS, visual analogue scale; WTP, willingness to pay.
We summarised patients’ preferences for outcomes associated with medications and excluded preferences for specific medications or treatment domains, which are amenable to misconceptions. The treatments do not give value to the user, per se; it is their outcomes that give value. In a trade-off situation, the best option reflects the partial valuations and probabilities of those outcomes.

Preference studies are not archived in reference databases with common subject headings and keywords that allow a highly sensitive and specific retrieval. We tested and applied a broad, peer reviewed search strategy, but we might have overlooked or missed studies.

We rigorously and comprehensively assessed study quality. Several included studies risked multiple biases and stricter criteria could have been applied. However, quality criteria for preference studies can conflict and methodological rigour must be balanced with the cognitive effort demanded from participants.

Owing to the heterogeneity of methods and outcomes, we could not perform quantitative summaries of the relative strengths of preferences, as is common in systematic reviews on preference studies. Our review includes studies that were not powered to provide statistically significant differences for strengths of preferences. Preferences for outcomes were elicited from varying and often small numbers of participants, with heterogeneous disorders.

The end of the search period was September 2013, thus at the time of publication the search is relatively old in comparison to the median for systematic reviews.

Stated preference studies elicit preferences in hypothetical choices, and the outcome preferences in a real setting might be different. The reliability and validity of specific patient preference methods is debated, and the techniques and quality standards are likely to change in the future.

**Results in context**

The call for outcomes that are meaningful and important to patients is increasing. Patient-centred outcomes are often contrasted to clinical outcomes such as symptom control and side effects. They assess the impact of illness and therapy from patients’ perspectives, and should be those that patients notice and care about.

In contrast to this aim, we found that outcomes presented for preference elicitation were mostly selected and described without input from patients. Other systematic reviews on stated preferences confirm this finding. In a review of experiences of healthcare delivery, few outcomes were worded from patients’ perspectives. In a review on diabetes care, only 3 of 14 studies had employed focus groups in the outcome selection process. Disease-specific reviews often do not report on patient involvement. In line with this lack of patient-centredness and similar to our findings, symptom outcomes and adverse effects are most frequently included in preference studies, at the expense of other outcomes.

Suggested patient-centred outcomes in mental disorders include social and vocational functioning, body image, reduced stigma, recovery and reduced burden to caregivers. In schizophrenia alone, 194 non-traditional outcomes have been suggested. We found that side effects and in particular EPS and weight gain were important to patients, both relative to other outcomes and to other stakeholders. Side effects have an impact on health status, but to patients, their effect on physical attractiveness and the associated status, self-esteem and social opportunity might be more important. When the functional consequences of adverse events and no treatment are similar, people value avoiding the adverse effects most.

In addition to side effects, severe symptoms were highly important to patients, whereas functioning was moderately important. The claim that patients value functioning higher than symptom-oriented, ‘textbook’ outcomes, was therefore not supported.

We found significant differences in how patients and non-patients valued outcomes. This topic is currently debated. Accordant with our findings, the most comprehensive meta-analysis to date concluded that patients value health states higher than the general public. The difference was small to moderate, and notably the valuations differed less when both groups valued descriptions of health states, instead of patients valuing their actual health. A possible explanation for a difference is that people adapt when they become ill: we develop skills, adjust activities and expectations, and redefine what is good health and a good life. Notably, different valuations of one-dimensional health states do not necessarily translate to differing partial utilities of health states and to process outcomes.

Concerns have been raised that cognitive impairment, limited self-insight and distortions of reality impede patients’ use of stated preferences methods, and could leave the results meaningless, in particular in schizophrenia. The results of the studies in this review indicate that several stated preference methods might be feasible for identifying relative outcome preferences from patients with mental disorders, and that validity is comparable to other stakeholder groups. In a systematic review, the practicality of TTO and CV (contingent valuation) was found to be generally good in patients with depression and schizophrenia. Two of the four studies in the review reported that patients with schizophrenia had some difficulties with the SG tasks. The need to improve the techniques persists.

**Meaning of study**

Patients report that being told the risks and benefits of treatments is one of the 10 most important aspects of healthcare. However, which risks and benefits clinicians communicate to patients is a matter of choice. This review highlights outcomes and outcome priorities clinicians should consider bringing into their conversations with patients when they discuss and decide between psychotropic drug options.
Our findings could inform on the benefits and harms to include in patient decision aids, which are tools designed to help patients participate in making choices among healthcare options.²⁸

It has been suggested that authors of clinical guidelines should conduct a systematic review on patient preferences in the relevant content area.²⁸ ⁵¹ The stated preferences presented in this review could be used as an early point of reference when guidelines are developed for schizophrenia, depression, bipolar disorder and ADHD.

In situations where stakeholder groups have different values, spotlighted in this review, a main question is whose preferences should be accommodated? Proponents of the patients’ preferences argue that people with the relevant disease are the best judges of their own welfare, and that true preferences require experience with the outcome. Opponents claim that the judgments of non-patients are more appropriate, because decisions affecting resource allocation for one group of patients affect the provision for other groups.⁵⁵ The dilemma is not empirical, but normative, and the answer depends on the decision context.⁵⁵ ⁷³

In economic assessments, the relative preferences from patients reported in this review might inform regulatory benefit-risk assessments and be used in direct comparisons of drugs,⁹ but in this field, the preferences of the general population is currently the norm.⁷⁴

Unanswered questions and implications for research

Although many studies have addressed ‘what matters’ to patients with mental disorders, few have investigated the relative preferences for medication outcomes. Current knowledge is fragmented and exists for a limited number of aspects and conditions only. Surprisingly, only a minority of the studies have been performed from patients’ perspectives. The evidence does not allow firm conclusions on what outcomes of psychotropic medications matter most to patients, and there is an obvious need for more research.

Insufficient reporting in stated preference studies is widespread.⁵¹ ⁵² ⁶⁰ Concise reporting of all study dimensions, including variance, study design and the outcome descriptions presented to patients, is necessary. Although the studies in this review generally found that stated preference methods were feasible for patients with mental health disorders, challenges were also exposed, demonstrating that the techniques need to be improved and tailored to the relevant populations.

CONCLUSION

Despite the widely declared prominence of patient preferences in healthcare, knowledge on which medication-related outcomes matter most to patients with mental health disorders has been largely absent. Clinicians and policymakers should be aware that patients’ priorities might be different from theirs and that they cannot reliably be inferred from patients’ demographic characteristics or health status. To improve health outcomes for patients, we need more evidence on the relative importance patients place on relevant outcomes. In clinical practice, knowledge on group-level preferences can be a starting point, but to know what matters most to the person in front of you, you have to ask.

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Contributors OE was involved in study design, systematic search, pilot of data extraction form, title/abstract scanning, determining eligibility of articles, quality assessment of articles, data extraction, data synthesis, data interpretation, literature search, and writing and revising paper and appendices. BFL was involved in title/abstract scanning, determining eligibility of articles, obtaining full text and revising manuscript. EA was involved in systematic search, writing the article and see online supplementary appendix 2. MN was involved in study design, data synthesis, data interpretation and revising the manuscript. GS was involved in study design, determining eligibility of articles, quality checks of included articles and appendices, and revising the paper. KN was involved in study design, title/abstract scanning, pilot of data extraction form, determining eligibility of articles, quality assessment of articles, data extraction, data synthesis/analysis, data interpretation, literature search, and writing and revising the paper and appendices. All authors had full access to the data, approved the final draft, and take responsibility for the accuracy of the analysis and the integrity of the data. OE and KN are guarantors.

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Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement Full data sets and technical appendices are available with open access from corresponding authors.

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Appendix 1: Search strategies

Bibliographic databases:
- Medline (Ovid) (1946 to September 27th, 2013);
- Embase (Ovid) (1974 to September 27th, 2013);
- PsycINFO (Ovid) (1967 to September 27th, 2013);
- Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library; Issue 8 of 12, September 2013);
- SveMed+ (Karolinska Institutet, 1977 to September 27th, 2013);
- The Health Technology Assessment Database (The Cochrane Library; Issue 8 of 12, September 2013)
- The NHS Economic Evaluation Database (The Cochrane Library; Issue 8 of 12, September 2013)

Grey literature databases:
- Science.gov
- Scitation
- OAISTER
- REPEC
- Science Research
- WHOLIS
- Conference papers
- 176 sources in Grey Matters
- Google Scholar

Strategies
postfix .tw.= textword (same terms across all databases)
prefix “exp” designates exploded MeSH term, Emtree term or PsychTree term.

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R)
1. "likert scale".tw.
2. "conjoint analysis".tw.
3. "simple ranking exercise".tw.
4. "rating scale".tw.
5. "qualitative discriminant process".tw.
6. "cardinal ranking".tw.
7. "ordinal ranking".tw.
8. "constrained choice".tw.
9. "schedule for the evaluation of individual quality of life " or SEIQoL).tw.
10. "semantic differential technique" or SDT).tw.
11. "guttman scale".tw.
12. SERVQUAL.tw.
13. "simple choice exercise".tw.
14. "random paired scenario" or RPD).tw.
15. "choice based question".tw.
16. "analytic hierarchy process" or AHP).tw.
17. "standard gamble".tw.
18. "time trade-off" or TTO).tw.
19. "person trade-off" or PTO).tw.
20. "willingness to pay" or WTP).tw.
21. "open ended".tw.
22. "bidding game".tw.
23. "payment card".tw.
24. "closed ended".tw.
25. "measure of value" or MoV).tw.
26. "allocation of points".tw.
27. "direct rating".tw.
28. (SMART or SWING or CROC).tw.
29. "likert scale$".tw.
30. "patient participation".tw.
31. (satisf$ adj4 survey$).tw.
32. Decision Making.mp. or exp decision making/
33. Motivation.mp. or exp motivation/
34. Quality of Life.mp. or exp "quality of life"/
35. Health Behavior.mp. or exp health behavior/
36. Questionnaires.mp. or exp questionnaire/
37. Multivariate Analysis.mp. or exp multivariate analysis/
38. questionnaires.mp. or exp Questionnaires/
39. Choice Behavior.mp. or exp Choice Behavior/
40. Decision Support Techniques.mp. or exp Decision Support Techniques/
41. consumer satisfaction.mp. or exp Consumer Satisfaction/
42. patient satisfaction.mp. or exp Patient Satisfaction/
43. Patient Acceptance of Health Care.mp. or exp "Patient Acceptance of Health Care"/
44. psychiatric status rating scales.mp. or exp Psychiatric Status Rating Scales/
45. Socioeconomic Factors.mp. or exp Socioeconomic Factors/
46. treatment outcome.mp. or exp Treatment Outcome/
47. Activities of daily living.mp. or exp "Activities of Daily Living"
48. patient centered care.mp. or exp Patient-Centered Care/
49. cost benefit analysis.mp. or exp Cost-Benefit Analysis/
50. multivariate analysis.mp. or exp Multivariate Analysis/
51. mental disorders.mp. or exp Mental Disorders/
52. Psychopharmacology.mp. or exp Psychopharmacology/
53. dt.fs.
54. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31
55. 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50
56. 52 or 53
57. 51 and 54 and 55 and 56
58. limit 57 to ("young adult (19 to 24 years)" or "adult (19 to 44 years)" or "young adult and adult (19-24 and 19-44)" or "middle age (45 to 64 years)" or "middle aged (45 plus years)" or "all aged (65 and over)" or "aged (80 and over)"") and (danish or english or french or german or norwegian or spanish or swedish)

Embase
1. "likert scale$".tw.
2. "conjoint analysis".tw.
3. "simple ranking exercise$".tw.
4. "rating scale$".tw.
5. "qualitative discriminant process$".tw.
6. "cardinal ranking$".tw.
7. "ordinal ranking$".tw.
8. "constrained choice$".tw.
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11. "guttman scale$".tw.
12. SERVQUAL.tw.
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15. "choice based question$".tw.
16. ("analytic hierarchy process$" or AHP).tw.
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18. ("time trade-offs" or TTO).tw.
19. ("person trade-offs" or PTO).tw.
20. ("willingness to pay" or WTP).tw.
21. "open ended".tw.
22. "bidding game$".tw.
23. "payment card$".tw.
24. "closed ended".tw.
25. ("measure of value" or MoV1).tw.
26. "allocation of points".tw.
27. "direct rating$".tw.
28. (SMART or SWING or CROC).tw.
29. "likert scale$".tw.
30. "consumer satisfaction".tw.
31. (satisf$ adj4 survey$).tw.
32. "patient satisfaction".tw.
33. Decision Making.mp. or exp decision making/
34. exp decision support system/ or Decision support system.mp.
35. Patient Compliance.mp. or exp patient compliance/
37. Motivation.mp. or exp motivation/
38. Patient attitude.mp. or exp patient attitude/
39. Psychological rating scales.mp. or exp psychological rating scale/
40. Socioeconomics.mp. or exp socioeconomics/
41. Treatment Outcome.mp. or exp treatment outcome/
42. Quality of Life.mp. or exp "quality of life"/
43. Attitude to Health.mp. or exp attitude to health/
44. Health Status.mp. or exp health status/
45. Health Behavior.mp. or exp health behavior/
46. Daily life activity.mp. or exp daily life activity/
47. Outcome Assessment.mp. or outcome assessment/
48. Questionnaires.mp. or exp questionnaire/
49. Patient care.mp. or exp patient care/
50. Multivariate Analysis.mp. or exp multivariate analysis/
51. Cost-Benefit Analysis.mp. or exp "cost benefit analysis"/
52. Mental disease.mp. or exp mental disease/
53. Depression.mp. or exp depression/
54. major depression.mp. or exp major depression/
55. Psychopharmacology.mp. or exp psychopharmacology/
56. dt.fs.
57. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33
58. 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51
59. 52 or 53 or 54
60. 55 or 56
61. 57 and 58 and 59 and 60
62. limit 61 to ((danish or english or french or german or norwegian or spanish or swedish) and (adult <18 to 64 years> or aged <65+ years>))

PsycINFO
1. "likert scale$".tw.
2. "conjoint analysis".tw.
3. "simple ranking exercise$".tw.
4. "rating scale$".tw.
5. "qualitative discriminant process$".tw.
6. "cardinal ranking$".tw.
7. "ordinal ranking$".tw.
8. "constrained choice$".tw.
9. ("schedule for the evaluation of individual quality of life " or SEIQoL).tw.
10. ("semantic differential technique$" or SDT).tw.
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15. "choice based question$".tw.
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19. ("person trade-off" or PTO).tw.
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35. exp decision support system/ or Decision support system.mp.
36. Motivation.mp. or exp motivation/
37. Psychological rating scales.mp. or exp psychological rating scale/
38. Quality of Life.mp. or exp "quality of life"/
39. Health Behavior.mp. or exp health behavior/
40. Questionnaires.mp. or exp questionnaire/
41. Multivariate Analysis.mp. or exp multivariate analysis/
42. Treatment compliance.mp. or exp Treatment Compliance/
43. exp Compliance/ or compliance.mp.
44. rating scales.mp. or exp Rating Scales/
45. Socioeconomic status.mp. or exp Socioeconomic Status/
46. Treatment Outcomes.mp. or exp Treatment Outcomes/
47. daily activities.mp. or exp Daily Activities/
48. questionnaires.mp. or exp Questionnaires/
49. client centered therapy.mp. or exp Client Centered Therapy/
50. exp "Costs and Cost Analysis"/ or cost analysis.mp.
51. mental disorders.mp. or exp Mental Disorders/
52. major depression.mp. or exp Major Depression/
53. bipolar disorder.mp. or exp Bipolar Disorder/
54. psychopharmacology.mp. or exp Psychopharmacology/
55. drug therapy.mp. or exp Drug Therapy/
56. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33
57. 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50
58. 51 or 52 or 53
59. 54 or 55
60. 56 and 57 and 58 and 59
61. limit 60 to ("300 adulthood " or 320 young adulthood or 340 thirties or 360 middle age or "380 aged " or "390 very old ") and (danish or english or french or german or norwegian or spanish or swedish))

SveMed+
Identical to Medline search strategy

The Cochrane Library
- Trials (CENTRAL)
- Methods Studies
- Technology Assessments
- Economic Evaluations

#1 MeSH descriptor: [Choice Behavior] explode all trees
#2 MeSH descriptor: [Decision Making] explode all trees
#3 MeSH descriptor: [Decision Support Techniques] explode all trees
#4 MeSH descriptor: [Patient Satisfaction] explode all trees
#5 MeSH descriptor: [Patient Participation] explode all trees
#6 MeSH descriptor: [Quality of Life] explode all trees
#7 MeSH descriptor: [Consumer Satisfaction] explode all trees
#8 MeSH descriptor: [Patient Compliance] explode all trees
#9 MeSH descriptor: [Motivation] explode all trees
#10 MeSH descriptor: [Patient Acceptance of Health Care] explode all trees
#11 MeSH descriptor: [Psychiatric Status Rating Scales] explode all trees
#12 MeSH descriptor: [Socioeconomic Factors] explode all trees
#13 MeSH descriptor: [Treatment Outcome] explode all trees
#14 MeSH descriptor: [Attitude to Health] explode all trees
#15 MeSH descriptor: [Health Status] explode all trees
#16 MeSH descriptor: [Health Behavior] explode all trees
#17 MeSH descriptor: [Activities of Daily Living] explode all trees
#18 MeSH descriptor: [Outcome Assessment (Health Care)] explode all trees
#19 MeSH descriptor: [Questionnaires] explode all trees
#20 MeSH descriptor: [Patient-Centered Care] explode all trees
#21 MeSH descriptor: [Multivariate Analysis] explode all trees
#22 MeSH descriptor: [Cost-Benefit Analysis] explode all trees
#23 MeSH descriptor: [Mental Disorders] explode all trees
#24 MeSH descriptor: [Depressive Disorder] explode all trees
#25 MeSH descriptor: [Drug Therapy] explode all trees
#26 MeSH descriptor: [Psychopharmacology] explode all trees
#27 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or
#19 or #20 or #21 or #22
#28 #25 or #26
#29 #23 or #24
#30 "simple ranking exercise"
#31 "conjoint analysis"
#32 "rating scale"
#33 "qualitative discriminant process"
#34 "direct rating scale"
Grey literature databases

- Science.gov
- Scitation
- OAISTER (Books)
- REPEC (Economic papers).
- Science Research
- WHOLIS (WHO)
- Conference papers

(simple ranking exercise OR conjoint analysis OR rating scale OR qualitative discriminant process OR direct rating scale OR cardinal ranking OR ordinal ranking OR constrained choice OR likert scale OR semantic differential technique OR guttman scale OR satisfaction survey OR simple choice exercise OR random paired scenario OR choice based question OR analytic hierarchy process OR standard gamble OR time trade-off OR person trade-off OR willingness to pay OR open ended OR bidding game OR payment card OR closed ended OR measure of value OR allocation of points OR direct rating)

AND

(Choice Behavior OR Decision Making OR Decision Support Techniques OR Patient Satisfaction OR Patient Participation OR Consumer Satisfaction OR Patient Compliance OR Motivation OR "Patient Acceptance of Health Care" OR Psychiatric Status Rating Scales OR Socioeconomic Factors OR Treatment Outcome OR "Quality of Life" OR Attitude to Health OR Health Status OR Health Behavior OR "Activities of Daily Living" OR "Outcome Assessment (Health Care)" OR Questionnaires OR Patient-Centered Care OR Multivariate Analysis OR Cost-Benefit Analysis)

AND

(Mental Disorders OR Depressive Disorder)

AND (Drug Therapy)

Grey Matters

(Choice Behavior OR Decision Making OR Decision Support Techniques OR Patient Satisfaction OR Patient Participation OR Consumer Satisfaction OR Patient Compliance OR Motivation OR "Patient Acceptance of
Health Care” OR Psychiatric Status Rating Scales OR Socioeconomic Factors OR Treatment Outcome OR "Quality of Life" OR Attitude to Health OR Health Status OR Health Behavior OR "Activities of Daily Living” OR "Outcome Assessment (Health Care)” OR Questionnaires OR Patient-Centered Care OR Multivariate Analysis OR Cost-Benefit Analysis)
AND
(Mental Disorders OR Depressive Disorder) AND (Drug Therapy OR Pharmacology)

Google Scholar
1. (simple ranking exercise OR conjoint analysis OR rating Scala OR qualitative discriminant process OR direct rating scale OR cardinal ranking OR ordinal ranking OR constrained choice OR likert scale OR semantic differential technique OR guttman scale OR satisfaction survey OR simple choice exercise OR random paired scenario OR choice based question OR analytic hierarchy process)
AND
(Mental Disorders OR Depressive Disorder)
AND Drug Therapy)

2. (standard gamble OR time trade-off OR person trade-off OR willingness to pay OR open ended OR bidding game OR payment card OR closed ended OR measure of value OR allocation of points OR direct ratings OR SMART OR SWING OR CROC)
AND
(Mental Disorders OR Depressive Disorder)
AND Drug Therapy)

3. (Choice Behavior OR Decision Making OR Decision Support Techniques OR Patient Satisfaction OR Patient Participation OR Consumer Satisfaction OR Patient Compliance OR Motivation OR "Patient Acceptance of Health Care” OR Psychiatric Status Rating Scales OR Socioeconomic Factors)
AND
(Mental Disorders OR Depressive Disorder)
AND Drug Therapy)

4. (Treatment Outcome OR "Quality of Life” OR Attitude to Health OR Health Status OR Health Behavior OR "Activities of Daily Living” OR "Outcome Assessment (Health Care)” OR Questionnaires OR Patient-Centered Care OR Multivariate Analysis OR Cost-Benefit Analysis)
AND
(Mental Disorders OR Depressive Disorder)
AND Drug Therapy)

Additional details on the search strategies are available on request.
Appendix 10: PROSPERO protocol

What matters to patients? A systematic review of patient preferences in psychopharmacological decisions.

Øystein Eiring, Kari Nytrøen, Endre Aas, Brynjjar Landmark, Glenn Salkeld

Citation
Øystein Eiring, Kari Nytrøen, Endre Aas, Brynjjar Landmark, Glenn Salkeld. What matters to patients? A systematic review of patient preferences in psychopharmacological decisions.. PROSPERO 2013:CRD42013005685 Available from http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42013005685

Review question(s)
What is known from quantitative research methods about preferences relevant for medication choices, from adult patients with a mental disorder?

Searches
Embase, Medline, PsycINFO, SveMed+, The Cochrane Central Register of Controlled Trials, The Health Technology Assessment Database, the NHS Economic Evaluation Database, International Pharmaceutical Abstracts. Google Scholar.

Types of study to be included
Studies using quantitative patient preference methods will be included. These are usually classified as ranking, rating or choice-based methods.
Studies using qualitative methodology only will be excluded.

Condition or domain being studied
Mental disorders

Participants/ population
Adult patients with direct experience of mental disorder, currently diagnosed with the disease or at risk for the relevant disease.
Children/adolescents are excluded.

Intervention(s), exposure(s)
We will review the outcomes of studies applying quantitative patient preference methodologies to elicit patient preferences relevant in decisions involving pharmacotherapeutic interventions. Studies in which the scope is not mental disorder are excluded.

Comparator(s)/ control
There are no comparator(s)/control.

Context
No restrictions regarding study setting.

Outcome(s)
Primary outcomes
The outcomes are quantitative measures of patient preferences in psychopharmacological treatments.

Secondary outcomes
None

Data extraction, (selection and coding)
Two researchers (OE and KN) will independently evaluate all the identified titles and abstracts for inclusion. If both researchers agree, articles will be included or eliminated accordingly. In cases of disagreement, the full article will be retrieved and discussed until consensus is achieved. All the remaining included abstracts will move to full text review by the same two researchers. In cases of discrepancy the researchers will discuss the article and try to reach consensus. If not, a third reviewer will be consulted.

We will develop and pilot a data extraction form on a few randomly selected studies from the inclusion list. A manual recording of the potential amendments and or/corrections to the data extraction form will be kept for future reference.

Items in the data extraction form will include:
- General information about the publication
- Study characteristics (objective, study design, inclusion/exclusion criteria, recruitment procedures)
- Participant characteristics (number, age, gender, disease)
- Intervention and setting (clinical setting, treatment options or attributes, decision problem, timing, preference elicitation method)
- Outcome data and results

Risk of bias (quality) assessment
There is no gold standard method for quality assessment and evaluation of risk of bias in patient preference elicitation studies. We will consider risk of bias by using well-known elements for quality assessment and evaluate factors such as: appropriateness of study design; validity; reliability; internal consistency; outcome reporting bias; acceptability and generalisability.

Strategy for data synthesis
Due to the variability of the outcome measures and heterogeneity of included studies found in comparable patient preference systematic reviews, we do not plan to conduct a meta-analysis, but we will summarise the results in narrative and tabular form.

Analysis of subgroups or subsets
We will summarise the research on preferences for the individual disorders if the data permits.

Dissemination plans
The results of the review will be prepared for publication in an international peer-reviewed journal and the results will also be presented at national and international conferences.

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Collaborators

Anticipated or actual start date
05 August 2013

Anticipated completion date
30 December 2013

Funding sources/sponsors
1) Southern and Eastern Norway Regional Health Authority
2) Norwegian Electronic Library of Health
3) Norwegian Research Council

Conflicts of interest
None known

Language
English

Country
Norway

Subject index terms status
Subject indexing assigned by CRD

Subject index terms
Decision Making; Humans; Patient Preference

Stage of review
Ongoing

Date of registration in PROSPERO
16 September 2013

Date of publication of this revision
16 September 2013

Stage of review at time of this submission
| Activity                                         | Status |
|-------------------------------------------------|--------|
| Preliminary searches                             | Yes    |
| Piloting of the study selection process          | No     |
| Formal screening of search results against eligibility criteria | No     |
| Data extraction                                  | No     |
| Risk of bias (quality) assessment                | No     |
| Data analysis                                    | No     |
Appendix 2: Assessment of methodological quality

To enable critical assessment of patient preference studies across methodologies we followed the approach recommended by Streiner and Norman, and constructed a practical tool. We performed a rapid review and identified seven relevant methodological reviews:

- An overview of techniques used to elicit public preferences on the provision of healthcare and a discussion of their weaknesses and strengths.
- An appraisal of stated preference valuation techniques and criteria for how studies should be designed from the perspective of competition in the market.
- A summary and discussion of approaches to assess and compare the validity of methods in cost-utility analysis.
- A review of methods for economic evaluation of healthcare and a checklist for assessing methods.
- Critical appraisal principles for cost-effectiveness and cost-utility studies in healthcare.
- Critical appraisal criteria for systematic reviews.

We identified an initial list of 75 possible items. Two researchers (OE, KN) piloted the items on four methodologically different studies. Based on our experiences on practicality and usefulness, we reduced the number of items to 50 and then applied the tool to 25 stated preference studies. The agreement of the reviewers on the overall quality of the studies was 80% (20/25). Formal tests on the consistency and construct validity were not performed. Three studies were removed due to not meeting inclusion criteria. After the initial review we simplified the checklist to 31 items within five categories. The final version of the tool is presented below.

1. What is the external validity of the study? (High/medium/low)

The population included in the study should be representative of patients with the relevant condition.

1. Is the patient population in the study clearly described?
   a. Disease or condition
   b. Age group(s)
   c. Gender distribution
   d. Ethnicity
   e. Socio-economic status
   f. Inclusion and exclusion criteria
   g. Clinical setting
   h. Common comorbidities

2. What was the sample size and is it robust? No guidelines have been established for sample size calculations for stated preference studies. For simple surveys a minimum total sample size of 400 and a size of each cell of interest of at least 75 has been recommended.

3. Did the recruitment procedures ensure generalizability?

4. Was randomisation and/or stratification applied to avoid selection bias?

5. Consider the number of participants enrolled in the study and how many participants were included in the analysis. What was the completion rate? Poor completion may cause non-response error because those who do not respond are different from those who do.
   a. Consider how empty cells, such as questions not replied to in a questionnaire, are treated. Are empty cells given zero value, replaced with the mean or excluded from analysis?
   b. Are the reasons for refusals, attritions, withdrawals, exclusions and re-inclusions reported? If refusals are reported, are they representative of the population?

6. If a decision problem was presented, to what extent did the problem take into account the real decision-making context and involve a constrained choice?

2. What is the quality of construct representation in the study? (High/medium/low)

Construct underrepresentation occurs when "a stimulus presented to a judge fails to fully represent the depth and complexity of information required in actual judgments". In preference studies, construct
underrepresentation threatens validity when options, health states, attributes or health state/attribute levels presented for preference elicitation are inadequate, ambiguous, vague, non-meaningful, unrealistic or incomprehensive.

1. Were all important and relevant options, attributes and attribute levels relevant to the main objective of the study identified? If options were presented to participants, were all relevant alternatives included? Important comparators such as non-pharmaceutical alternatives, do-nothing or the opt-out option should not be excluded.

2. Are the sources used in the construction of options, attributes and attribute levels for the preference elicitation accounted for and are they appropriate? Constructs might be based on systematic literature reviews, patient focus groups and clinician interviews.

3. Were options, attributes and attribute levels presented with sufficient detail and accuracy?
   a. Were attribute levels appropriate and plausible to respondents? Attribute levels should neither be too wide nor too narrow.
   b. If time periods were presented to participants, were the periods clearly stated and appropriate?
   c. If costs were presented to participants, were the measurement units clearly described? Are the sources for the costs clearly referenced?
   d. Were consequences that occur in the future discounted when required?

3. To what extent was the risk of construct-irrelevant variance minimised? (To a high/moderate/small degree)

Construct-irrelevant variation threatens the validity of a study when factors irrelevant to preferences influence measurements of utilities. Construct-irrelevant variance may be caused by a number of factors such as impairments in the cognitive abilities of the participants, numeracy skills, emotions and prejudices, and the elicitation procedure.

1. Was the study piloted?
2. Was a pre-test procedure performed to ensure that participants understood all the questions, and/or were post-test diagnostic questions included to explore the extent to which the respondents understood their tasks?
3. Was a "cheap talk" script included? A cheap talk script is a script that explicitly highlights the hypothetical bias problem before participants make a decision.
4. Is there evidence of starting point bias, e.g. resulting from an anchoring on initial stated values?
5. Were the questions neutral in tone? A negative or positive tone in the questions can result in framing effects.
6. If an interviewer was present - what was the possible influence on the respondent’s answers?
7. Is there evidence of high cognitive load, resulting in fatigue and frustration bias?
8. Were tests or parts of tests repeated for different subjects? With repetition, a subject’s ability to express his or her preferences can improve, and result in changes in the responses.
9. Is there evidence that emotions, hidden prejudices or reduced cognitive abilities and skills impaired the judgement of the participants?
10. For analogue scaling methods, consider the risk of sequencing effects. For rating scales, consider whether the values obtained influenced the appearance of the scale. For standard gamble and time trade-off, consider how the gamble was framed, the bottom anchor of the gamble, and the procedure used to find a subject’s indifference point. For standard gamble methods, consider the specific probabilities used. For time trade-off, consider the duration of survival in the base case.

4. What is the quality of the reporting and analysis? (High/medium/low)

1. How complete are the outcome data? Are all pre-specified measures reported? Selective reporting such as extensive use of sub-group analysis, use of data from participants with consistent results only, and the deletion of outliers or extreme values can lead to reporting bias.
2. Is there a tendency for the assessments to take a few discrete values? Are the data skewed or normally distributed?
3. What statistical techniques were used and are they appropriate? This aspect of quality should be assessed by a health economist or statistician with experience in the field.
4. Is allowance made for uncertainty in the estimates?
5. Is heterogeneity and patient subgroups analysed when relevant?

5. Do other aspects strengthen or weaken the study? (Strengthen/no difference/weaken)
   1. Were formal tests of internal validity performed and what were the results?
   2. To what extent are well-defined, answerable research questions stated and answered?
   3. Was more than one assessment method used? If so, is the rank ordering of preferences for health states consistent?  
   4. Do the authors outline how their piece of work compares and adds to the current evidence base? If so, are allowances made for potential differences in study methodology?
   5. Is the protocol or supplementary information about the study available? If so, examine the assessment protocol.
   6. Which limitations and weaknesses of the study are cited by the authors themselves?
   7. Are there other aspects of the study that strengthen or weaken the quality?

6. Based on the above, what is the overall quality of the study? (High/medium/low)

References
1. Streiner DL NG. Health measurement scales: A practical guide to their development and use. 3rd ed. Oxford: Oxford University Press, 1995.
2. Ryan M, Scott DA, Reeves C, et al. Eliciting public preferences for healthcare: a systematic review of techniques. Health technology assessment (Winchester, England) 2001;5(5):1-186.
3. Review of stated preference and willingness to pay methods. London: Accent and RAND Europe, April 2010. URL: http://webarchive.nationalarchives.gov.uk/+/http://www.competition-commission.org.uk/our_role/analysis/summary_and_report_combined.pdf
4. Lenert L, Kaplan RM. Validity and interpretation of preference-based measures of health-related quality of life. Medical care 2000;38(9 Suppl):Ii138-50.
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7. Higgins JPT, Altman DG. Assessing Risk of Bias in Included Studies. Cochrane Handbook for Systematic Reviews of Interventions: John Wiley & Sons, Ltd, 2008:187-241.
8. CRD AJ. Systematic Reviews: CRD’s guidance for undertaking reviews in health care: Centre for Reviews and Dissemination, University of York, 2009.
Appendix 3: Data extraction form

General
• First author, year
• Date of extraction and assessment
• Origin of study (all countries)
• Publication year
• Funding from pharmaceutical industry (fully, partly, or no funding from pharmaceutical industry, unknown)

Study population
• Disease/condition
• Age groups (mean)
• Gender distribution
• Ethnicity distribution
• In-/outpatient
• Sample size

Aspects of the preference elicitation
• Objective of the overall study (Main, secondary/supporting, other)
• Medication(s) involved
• Purpose of the preference elicitation (Economic assessment in public policy/ economic assessment in pharmaceutical industry, benefit to individual patients, research prioritisation, other)
• Sources used in attribute, health state or option selection and construction (researcher, research, clinician, patient, other)
• Preference elicitation method(s)
• Categories presented for preference elicitation (treatment options/treatment attributes/health states/health domains/other)

Results
• Main conclusions of the study
• Outcomes included in the study
• Preference rankings
• Relative strengths of preferences
• Heterogeneity of patients’ preferences. If sub-group analysis was performed: results for each subgroup
• Comparative results for different stakeholder group preference weightings
• Feasibility measures, results, and conclusions
• Correlations between patient preferences and demographic/disease variables: results
• Other main findings as reported by authors
## Appendix 4: Excluded studies

| Study | Reason for exclusion | Exclusion type |
|-------|----------------------|----------------|
| 1     | Absence of quantified relative preferences data | 1 |
| 2     | Substance-related disorder | 1 |
| 3     | One outcome only | 1 |
| 4     | Absence of quantified relative preferences data | 1 |
| 5     | Absence of quantified relative preferences data | 1 |
| 6     | Low study quality | 2 |
| 7     | Absence of quantified relative preferences data | 1 |
| 8     | Absence of quantified relative preferences data | 1 |
| 9     | Preference data not specified for medication | 1 |
| 10    | Rating scale only | 1 |
| 11    | Low study quality | 2 |
| 12    | Absence of quantified relative preferences data | 1 |
| 13    | Absence of quantified relative preferences data | 1 |
| 14    | Outcomes not associated with medication | 1 |
| 15 | Hamann J, Kruse J, Schmitz FS, Kissling W, Pajonk FG. Patient participation in antipsychotic drug choice decisions. *Psychiatry research* 2010;178:63-7. | Outcomes not associated with medication | 1 |
| 16 | Han SS, Lee SC. Effecting factors on depression in patients with fibromyalgia. *Taehan Kanho Hakhoe chi* 2005;35:87-94. | Absence of quantified relative preferences data | 1 |
| 17 | Hellewell JSE, Kalali AH, Langham SJ, McKellar J, Awad AG. Patient satisfaction and acceptability of long-term treatment with quetiapine. *Int J Psychiatry Clin Pract* 1999;3:105-113 | Absence of quantified relative preferences data | 1 |
| 18 | Herbild L, Bech M, Gyrd-Hansen D. Estimating the Danish populations' preferences for pharmacogenetic testing using a discrete choice experiment. The case of treating depression. *Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research* 2009;12:560-7. | Patients not included | 1 |
| 19 | Hodge K, Jespersen S. Side-effects and treatment with clozapine: a comparison between the views of consumers and their clinicians. *International journal of mental health nursing* 2008;17:2-8. | Absence of quantified relative preferences data | 1 |
| 20 | Hummel MJ, Volz F, van Manen JG, Danner M, Dintsios CM, Ijzerman MJ, et al. Using the analytic hierarchy process to elicit patient preferences: prioritizing multiple outcome measures of antidepressant drug treatment. *The patient* 2012;5:225-37. | Low study quality | 2 |
| 21 | Kinter ET, Schmeding A, Rudolph I, dosReis S, Bridges JF. Identifying patient-relevant endpoints among individuals with schizophrenia: an application of patient-centered health technology assessment. *International journal of technology assessment in health care* 2009;25:35-41. | Absence of quantified relative preferences data | 1 |
| 22 | Kocsis JH, Leon AC, Markowitz JC, Manber R, Arnow B, Klein DN, et al. Patient preference as a moderator of outcome for chronic forms of major depressive disorder treated with nefazodone, cognitive behavioral analysis system of psychotherapy, or their combination. *The Journal of clinical psychiatry* 2009;70:354-61. |Preferences for options only | 1 |
| 23 | Kwan BM, Dimidjian S, Rizvi SL. Treatment preference, engagement, and clinical improvement in pharmacotherapy versus psychotherapy for depression. *Behaviour research and therapy* 2010;48:799-804. |Preferences for options only | 1 |
| 24 | König HH, Gunther OH, Angermeyer MC, Roick C. Utility assessment in patients with mental disorders: validity and discriminative ability of the time trade-off method. *PharmacoEconomics* 2009;27:405-19. |Rating scales only | 1 |
| 25 | Maczka G, Siwek M, Skalski M, Dudek D. Patients' and doctors' attitudes towards bipolar disorder - do we share our beliefs?. *Psychiatria polska* 2009;43:301-12. |Absence of quantified relative preferences data | 1 |
| 26 | Muhlbacher AC, Rudolph I, Lincke HJ, Nubling M. Preferences for treatment of Attention-Deficit/Hyperactivity Disorder (ADHD): a discrete choice experiment. *BMC health services research* 2009;9:149. |Adult patients not included | 1 |
| 27 | Osborne RH, Dalton A, Hertel J, Schrero R, Smith DK. Health-related quality of life advantage of long-acting injectable antipsychotic treatment for schizophrenia: a time trade-off study. *Health and quality of life outcomes* 2012;10:35. |Patients not included | 1 |
| 28 | Patel SR, Simpson HB. Patient preferences for OCD treatment. *The Journal of Clinical Psychiatry* 2010;71:1434-39 |Preferences for options only | 1 |
| 29 | Pedersen RD, Pallay AG, Rudolph RL. Can improvement in well-being and functioning be distinguished from depression improvement in antidepressant clinical trials? *Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation* 2002;11:9-17. |Absence of quantified relative preferences data | 1 |
| 30 | Pyne JM, Fortney JC, Tripathi S, Feeny D, Ubel P, Brazier J. How bad is depression? Preference score |One outcome only | 1 |
|   | Estimates from depressed patients and the general population. *Health services research* 2009;44:1406-23. | Absence of quantified relative preferences data | 1 |
|---|---|---|---|
| 31 | Rettenbacher MA, Hofer A, Eder U, Hummer M, Kemmler G, Weiss EM, et al. Compliance in schizophrenia: psychopathology, side effects, and patients' attitudes toward the illness and medication. *The Journal of Clinical Psychiatry* 2004;65:1211-8. | Low study quality | 2 |
| 32 | Rosenheck R, Stroup S, Keefe RS, McEvoy J, Swartz M, Perkins D, et al. Measuring outcome priorities and preferences in people with schizophrenia. *The British journal of Psychiatry : the Journal of Mental Science* 2005;187:529-36. | Absence of quantified relative preferences data | 1 |
| 33 | Sevy S, Nathanson K, Schechter C, Fulop G. Contingency valuation and preferences of health states associated with side effects of antipsychotic medications in schizophrenia. *Schizophrenia bulletin* 2001;27:643-51. | Low study quality | 2 |
| 34 | Shumway M, Saunders T, Shern D, Pines E, Downs A, Burbine T, et al. Preferences for schizophrenia treatment outcomes among public policy makers, consumers, families, and providers. *Psychiatric services* 2003;54:1124-8. | Quantified relative preference data not related to medication | 1 |
| 35 | Tsevat J, Keck PE, Hornung RW, McElroy SL. Health values of patients with bipolar disorder. *Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation* 2000;9:579-86. | Patients not included | 1 |
| 36 | Voruganti LN, Awad AG, Oyewumi JK, Cortese L, Zirul S, Dhawan R. Assessing health utilities in schizophrenia. A feasibility study. *PharmacoEconomics* 2000;17:273-86. | Patients not included | 1 |
| 37 | Wilder CM, Elbogen EB, Moser LL, Swanson JW, Swartz MS. Medication preferences and adherence among individuals with severe mental illness and psychiatric advance directives. *Psychiatric services* 2010;61:380-5. | Preferences for options only | 1 |
| 38 | Wittink MN, Cary M, Tenhave T, Baron J, Gallo JJ. Towards patient-centered care for depression: conjoint methods to tailor treatment based on preferences. *The patient* 2010;3:145-57. | Patients not included | 1 |
| 39 | Wittink MN, Morales KH, Cary M, Gallo JJ, Bartels SJ. Towards personalizing treatment for depression : developing treatment values markers. *The patient* 2013;6:35-43. | Patients not included | 1 |

Exclusion type: 1=Inclusion criteria, 2=quality criteria
Appendix 5: Summary of quality domain scores in included studies

| Study                | External validity | Construct representation | Minimisation of construct-irrelevant variance | Reporting and analysis | Other aspects | Overall |
|----------------------|-------------------|--------------------------|---------------------------------------------|------------------------|--------------|---------|
| Morss 1993<sup>39</sup> | 2                 | 1.75                     | 3                                           | 1.75                   | 1            | 2       |
| Revicki 1996<sup>48</sup> | 2                 | 2                        | 2                                           | 2                      | 2            | 2       |
| Lenert 1997<sup>49</sup> | 1.5               | 2                        | 2                                           | 2                      | 2            | 2       |
| Lee 2000<sup>54</sup>    | 2                 | 2.5                      | 2                                           | 2                      | 1.5          | 2       |
| Lenert 2000<sup>55</sup> | 2                 | 2.5                      | 2.5                                         | 3                      | 3            | 3       |
| Shumway 2003<sup>33</sup> | 2                 | 2                        | 2                                           | 2.5                    | 2.5          | 2       |
| Briggs 2008<sup>40</sup>  | 2                 | 2.5                      | 3                                           | 3                      | 2            | 2       |
| Bridges 2013<sup>36</sup> | 2                 | 2                        | 2                                           | 2.5                    | 2.5          | 2       |
| Kinter 2012<sup>42</sup>  | 1.5               | 2                        | 2                                           | 2.25                   | 1.5          | 2       |
| O’Brien 1995<sup>38</sup> | 2                 | 2.5                      | 2                                           | 3                      | 2            | 2       |
| Revicki 1998<sup>47</sup>  | 2                 | 2                        | 2                                           | 2.25                   | 2            | 2       |
| Morey 2007<sup>41</sup>   | 1.5               | 1.5                      | 2                                           | 3                      | 2.5          | 2       |
| Zimmermann 2013<sup>35</sup> | 2            | 3                        | 3                                           | 3                      | 3            | 3       |
| Reviick 2005<sup>43</sup>  | 2                 | 2.25                     | 2.5                                         | 2                      | 2            | 2       |
| Johnson 2007<sup>44</sup>  | 1.5               | 2.5                      | 2                                           | 2.25                   | 2.5          | 2       |
| Glenngård 2013<sup>47</sup> | 2                 | 2                        | 2                                           | 2                      | 1            | 2       |

1=low quality; 2=medium quality; 3=high quality
Appendix 2 includes descriptions of the quality domains. Additional details on the assessments are available on request. The reference numbers refer to the reference list in the main article.
## Appendix 6  Aspects of preference elicitation

| Study     | Purpose of study                                      | Outcome sources                  | Outcomes                                |
|-----------|-------------------------------------------------------|-----------------------------------|-----------------------------------------|
| Morss 1993 | Economic assessment; public policy and industry perspective. | Research/literature, patients     | Side effects                            |
| Revicki 1996 | Economic assessment; public policy.                   | Research/literature, clinicians   | Symptoms, process related, functioning  |
| Lenert 1997 | Individual patient. Research*                        | Not reported                      | Side effects                            |
| Lee 2000   | Economic assessment; public policy.                   | Research/literature               | Symptoms, side effect                   |
| Lenert 2000 | Economic assessment; public policy                    | Research/literature, clinicians   | Symptoms, side effect                   |
| Shumway 2003 | Research.                                             | Research/literature               | Symptoms, functioning, side effects, other |
| Briggs 2008 | Economic assessment; public policy and industry perspective. | Research/literature, patients, laypersons | Symptoms, side effects, other |
| Bridges 2013 | Individual patient.                                   | Research/literature, patients     | Symptoms, functioning, process related, other |
| Kinter 2012 | Research.                                             | Research/literature, patients     | Symptoms, functioning, side effects, other |
| O’Brien 1995 | Economic assessment; industry perspective.            | Research/literature               | Side effects, costs                     |
| Revicki 1998 | Economic assessment; public policy. Individual patient. | Research/literature, clinicians   | Symptoms, side effects                  |
| Morey 2007  | Economic assessment; public policy and industry perspective. Individual patient. | Not reported                      | Side effects, costs, process related    |
| Zimmermann 2013 | Individual patient. Research.                     | Research/literature, clinicians, patients | Symptoms, functioning, side effects, process related |
| Revicki 2005 | Economic assessment; public policy. Research.         | Research/literature, clinicians, patients | Symptoms, side effects, process related |
| Johnson 2007 | Individual patient.                                   | Research/literature, clinicians   | Symptoms, side effects                  |
| Glenngård 2013 | Economic assessment; industry perspective. Individual patient. | Caregivers                        | Functioning, side effects, process related, costs |

* Research guidance, methodology or prioritisation

Reference numbers refer to the reference list in the main article.
## Appendix 7: Feasibility of the preference methods

| Study       | Condition                  | Method*                  | Tests and conclusions                                                                                                                                                                                                                                                                                                                                 | Problems reported |
|-------------|----------------------------|--------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|
| Morss 1993  | Schizophrenia              | VAS, PC, SG              | 92% of the multiple-choice clarity questions were answered correctly. On average, patients reported that they understood the survey "pretty well" (mean = 3.9, where 5 = "very well"), and were only a little confused. Patients’ answers were internally valid and consistent (74% internal consistency). The authors’ concluded that their techniques were useful, and allow effective patient education and elicitation of useful values, even in subgroups with cognitive impairments. | Minor             |
| Revicki 1996| Schizophrenia              | Rating scale, PC         | Patients with schizophrenia were able to complete categorical rating scales and paired comparisons. The rank ordering of health states was consistent across the choice-based preference measures, indicating that people with schizophrenia were capable of assigning preferences for different hypothetical health states. The authors concluded that patients are able to make meaningful preference ratings. | None              |
| Lenert 1997 | Schizophrenia, schizoaffective disorder | VAS, PC, SG             | 70% of the patients indicated that they understood the survey well. 44% had consistent rank ordering among PC and VAS. The internal consistency in their SG ratings was 61%, and in their VAS ratings 33%. 18 of the 22 patients completed the survey. Authors found that it was "feasible to collect data on preferences in patients with severe mental illness and to automate the process of utility elicitation in healthy volunteers using a computer interview". | Medium            |
| Lee 2000    | Schizophrenia              | VAS, SG                  | 20% of persons with schizophrenia had inconsistent results, slightly higher, but not significantly different from other groups. 19 out of 20 patients completed the study. "This study demonstrates the feasibility of having patients use self-administered computer instruments and confirms the feasibility of using the more complex "gold standard" standard gamble method for preference assessment in persons with schizophrenia". "Preference ratings (...) showed that (...) persons with schizophrenia, could readily distinguish between states and were internally consistent". | Minor             |
| Lenert 2000 | Schizophrenia              | VAS, SG                  | 77.4% of patients made logical errors, compared to 62.5% of family members and 26.3% of health professionals. Logical errors in preference ratings were similar in SG and VAS assessments. Only 44% of the patients chose to repair errors, compared to 100% of providers and 86% of family members. 50% of patients had illogically ordered responses and did not satisfy procedural invariance. 72.5% of family members and 94.5% of health care providers’ responses were logically ordered. | Major             |
| Shumway 2003| Schizophrenia              | Rating scales, CA        | All participants completed the preference assessment interview, but the patient group had more difficulty with the task than the other stakeholder groups, and reported a significantly lower level of understanding. All groups found the task challenging. Group differences were examined in a series of one-way analyses of variance where stakeholder group was the classification variable and the measures of comprehension and acceptance were the dependent variables. Overall, preference assessment task was found to be acceptable to all stakeholder groups. The authors concluded that "although patients’ task comprehension was clearly lower than that of the other stakeholder groups, there are some indications that their comprehension was sufficient to yield valid preference valuations". | Medium            |
| Reference | Condition | Methodology | Sample Size | Notes |
|-----------|-----------|-------------|-------------|-------|
| Briggs 2008<sup>40</sup> | Schizophrenia, schizoaffective disorder | VAS, TTO | Patients and laypersons showed equal ability to complete the questionnaire, and all 49 patients completed the utility interview. Interviewers reported no problems in understanding within the patient population. Authors concluded that the study results suggest that "stable patients are capable of participating in studies designed to elicit the quality of life impact of schizophrenia and its treatment". | None |
| Bridges 2013<sup>36</sup> | Schizophrenia | Self-explicated method | 97 out of 105 patients completed all choice tasks. By incorporating both ordinal and cardinal aspects of preference the authors found that the self-explicated method was superior to either the rating or ranking method alone. The authors found that complex choice tasks could be used in patients diagnosed with schizophrenia. | Minor |
| Kinter 2012<sup>22</sup> | Schizophrenia | CA | Only one out of 101 patients was excluded from analysis because of an abnormal response. | Minor |
| O’Brien 1995<sup>38</sup> | Mild or moderate depression | VAS, WTP | Authors concluded that "...the WTP approach is a potentially valuable tool that requires more development for use in healthcare economic evaluation". | None |
| Revicki 1998<sup>47</sup> | Major depressive disorder | VAS, SG | The authors found that it was feasible to elicit utilities using the SG technique in patients recently recovered from a depression episode. 3% of the patients could not complete the SG interview. The authors concluded that health state utility scores can be provided by patients with depression. | Minor |
| Morey 2007<sup>71</sup> | Major depressive disorder | WTP | "105 individuals completed the survey and provided usable data". | None |
| Zimmermann 2013<sup>35</sup> | Depression | CA | 227 out of 255 participants completed the online interview including the CA module and provided valid information at all stages of the interview. Choice-based CA was able to reveal preferences for treatment outcomes and revealed consistent underlying preference patterns of the subjects. | Minor |
| Revicki 2005<sup>41</sup> | Bipolar disorder type I | VAS, SG | 92 out of 96 patients provided complete utility interview data. Health state had consistent rank orderings. The authors concluded that patients with bipolar disorder are capable of participating in utility assessment and providing ratings for hypothetical health states associated with different mood stabilizer treatments. Stable individuals with bipolar disorder were found to provide meaningful preference ratings for different hypothetical health states. | Minor |
| Johnson 2007<sup>24</sup> | Bipolar disorder | DCE | In a test-retest experiment, 20% of subjects reversed their preference between the first and last question in the sequence. The failure rate was around 7% and 8% for the first and second logit test. Patients with bipolar disorder performed better than patients with diabetes in a referenced stated preference survey. | Minor |
| Glenngård 2013<sup>37</sup> | ADHD | DCE | "The results suggest that DCE is a method that can be used to value not only hypothetical scenarios but also can be used to value and distinguish between real-life scenarios". | None |

VAS=visual analogue scale; PC=pairwise comparison; SG=standard gamble; TTO=time trade-off; WTP=willingness to pay; DCE=discrete choice experiment; CA=conjoint analysis.

*Methods used in the initial piloting of the methods, in some of the studies, are not included.

Reference numbers refer to the reference list in the main article.
## Appendix 8: Comparison of patient preferences with other stakeholder groups

| Study       | Condition                          | No of patients | Stakeholder groups in addition to patients | Summary                                                                                                                                                                                                 |
|-------------|------------------------------------|----------------|--------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Mors 1993   | Schizophrenia                      | 33             | Psychiatrists                              | The preference values obtained from patients and psychiatrists were relatively equivalent, but patients ranked the three side effects in the opposite order of psychiatrists. Patients rated akathisia highest, followed by tardive dyskinesia and then parkinsonism, which was the worst side effect and ranked lowest. There were no statistically significant differences between psychiatrists’ and patients’ ranking. |
| Revicki 1996 | Schizophrenia                      | 49             | Psychiatrists, caregivers                  | The preferences were strongly correlated between the groups. Caregivers rated six out of six states higher than the patients. Psychiatrists’ preferences for hypothetical states were not statistically significantly different from those of patients. The hospitalised state was rated the worst by all three groups. No differences in patients’ and caregivers’ preferences were found, that were both statistically significant and consistent across the two methods applied. |
| Lenert 1997  | Schizophrenia, schizoaffective disorder | 22             | Healthy volunteers                         | No statistically significant differences were found in preferences for side effects (parkinsonism, tardive dyskinesia and akathisia) between patients and healthy volunteer subjects.                                             |
| Lee 2000    | Schizophrenia                      | 20             | Family members, health providers and community members | Persons with schizophrenia valued the disease states higher and placed more negative significance on the effects of pseudo-parkinsonism than the other groups. Pseudo-parkinsonism resulted in a larger decrease in the desirableness of health states for patients compared to family members, health providers and community members (p=0.024). Ratings by health professionals and community members tended to be lower for the health states. Family members had very similar preference ratings to those of the patients. Differences between patients and community volunteers were statistically significant for the disease states and for the effect of pseudo-parkinsonism. |
| Lenert 2000  | Schizophrenia                      | 148            | Family members, health professionals      | The differences in preferences between the groups were systematic, but the magnitude of the differences was modest. Patients’ and family members’ utilities for health states averaged from 0.10 to 0.15 units higher than those of health professionals, and the difference between the groups was statistically significant. The disutility placed on pseudo-parkinsonism was less for health professionals than patients and family members. Differences between groups for pseudo-parkinsonism were statistically significant. Health professionals tended to prefer control of disease above prevention of adverse drug effects. Health professionals preferred states with mild symptoms and pseudo-parkinsonism to moderate symptoms without the side effect, whereas patients and family members found the two states equally preferable. The differences between the groups were statistically significant. Family members had values that were more similar to those of patients, compared to those of health professionals. |
| Shumway 2003 | Schizophrenia                      | 50             | Clinicians, family members, members       | Patients rated extrapyramidal symptoms as more important than clinicians, family members, and members of the general public. Clinicians rated social functioning as more important than patients.                                                                 |

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### Notes

- **Mors 1993**
  - 39 patients
  - Psychiatrists

- **Revicki 1996**
  - 49 patients
  - Psychiatrists, caregivers

- **Lenert 1997**
  - 22 patients
  - Healthy volunteers

- **Lee 2000**
  - 20 patients
  - Family members, health providers and community members

- **Lenert 2000**
  - 148 patients
  - Family members, health professionals

- **Shumway 2003**
  - 50 patients
  - Clinicians, family members, members
of the general public and family members did. Clinicians and family members rated vocational functioning as more important than patients and the general public did. The differences were statistically significant. All stakeholders rated positive symptoms and social functioning as more important than negative and extrapyramidal symptoms.

| Reference | Disease | Population | Stakeholder | Health State | Utility Values |
|-----------|---------|-------------|-------------|--------------|----------------|
| Briggs 2008 40 | Schizophrenia, schizoaffective disorder | 50 | Laypersons | The utility values varied considerably according to the population from which the values were derived. Patients with stable schizophrenia were less willing to trade years of life to avoid schizophrenia-related symptoms, compared to laypersons. Patients reported significantly higher utilities than laypersons for stable schizophrenia (0.92 vs. 0.87), EPS (0.72 vs. 0.57) and relapse (0.60 vs. 0.48). The ranking of the health states by patients and laypersons was similar. |
| Bridges 2013 36 | Schizophrenia | 105 | Psychiatrists | There was a significant difference between patients and psychiatrists regarding their valuation of treatment goals. Psychiatrists tended to focus on "textbook" outcomes, while patients were more concerned with functioning and living a normal life. Psychiatrists overvalued improved capacity for emotion by 63%, improved sexual pleasure by 45%, decreased mistrust/hostility by 37%, decreased irritability by 25% and improved self-confidence by 20%. The psychiatrists undervalued improved activities for daily living (21%), improved capacity for work (18%), improved satisfaction (16%), improved self-independence (15%) and decreased depressive thoughts and feelings (13%). |

Reference numbers refer to the reference list in the main article.
### Appendix 9 (Table A–C): Quantified relative strengths of preferences

#### Table A: Schizophrenia

| Study* | Morris 199339 | Revicki 199648 | Lenert 199746 | Lee 200044 | Lenert 200048 | Shumway 200345 | Briggs 200840 | Bridges 201146 | Kinter 201242 |
|--------|---------------|---------------|---------------|-------------|-------------|--------------|--------------|--------------|---------------|
| Method | VAS, PC, SG** | Rating scale, PC | VAS, PC, SG | VAS, SG | VAS, SG | Rating scales, CA | VAS, TTO | Self-explicated method | CA (two method variants) |
| Unit | SG utility | Interval scale | SG utility | Average reduction in SG utility | Reduction in utility | Preference weights | Mean utility | Ranking/rating product | Parameter estimates (D/O) |
| Scale | 0-1 | 0-1 | 0-1 | 0-1 | 0-100 | 0-1 | 0-100 | 0-1 |
| Outcome domain | Outcome type | Outcome |
| Disease related outcomes | Symptoms | Cognitive impairment/ cognition | 55.9 (SE 30.5) |
| | | Clear thinking | 0.33 (SE 0.12) / 0.45 (SE 0.13) |
| | Inpatient, acute positive symptoms† | 0.19 |
| | Outpatient with negative symptoms | 0.30 |
| | Severity of schizophrenia | N/A | N/A |
| | Positive symptoms | 15.0 (SD 9.5) |
| | Decreased psychotic symptoms | 48.9 (SE 30.9) |
| | Negative symptoms | 11.5 (SD 9.0) |
| | Improved capacity for emotion | 28.5 (SE 23.8) |
| | Decreased depressive thoughts and feelings | 58.5 (SE 31.7) |
| | Improved self confidence | 42.4 (SE 25.0) |
| | Decreased anxiety | 46.6 (SE 29.7) |
| | Decreased irritability | 30.8 (SE 25.6) |
| | Improved sexual pleasure | 24.2 (SE 25.6) |
| | Disease symptoms | 0.11 (SE 0.09) / 0.27 (SE 0.13) |
| | Decreased restlessness | 36.9 (SE 27.5) |
| | Stable schizophrenia | 0.92 (SE 0.02) |
| | Relapse | 0.60 (SE 0.04) |
| | Decreased restlessness | 0.20 (SE 0.09) / 0.10 (SE 0.09) |
| Quality of life | Improved satisfaction | 54.4 (SE 30.8) |
|   |   |   |   |   |
|---|---|---|---|---|
| Autonomy | Improved self-independence |  |  | 51.3 (SE 29.0) |
|   | Independent living |  |   | 14.5 (SD 11.0) |
| Functioning | General | Outpatient, moderate function | 0.49 |   |
|   | Outpatient, good function | 0.57 |   |   |
|   | Outpatient, excellent function | 0.77 |   |   |
|   | Improved performance |   |   | 52.6 (SE 29.2) |
| Social | Social function | 16.9 (SD 12.2) |   | 0.36 (SE 0.09) / 0.31 (SE 0.13) |
|   | Social activities |   |   |   |
|   | Support |   |   | 0.45 (SE 0.15) / 0.45 (SE 0.10) |
|   | Improved communication |   |   | 35.9 (SE 26.6) |
|   | Decreased mistrust/hostility |   |   | 31.9 (SE 25.7) |
|   | Improved social function |   |   | 45.3 (SE 27.3) |
|   | Improved family relationships |   |   | 38.9 (SE 27.3) |
| Work | Improved capacity for work | 14.1 (SD 11.8) |   | 43.5 (SE 33.5) |
| Daily living | Improved activities for daily living |   |   | 45.1 (SE 27.4) |
|   | Daily activities |   |   | 0.52 (SE 0.14) / 0.62 (SE 0.15) |
| Physical health | Improved physical health |   |   | 50.1 (SE 28.6) |
| Intervention related | Side effects | Weight gain of 5% | 0.83 (SE 0.03) |   |
|   | EPS | 13.5 (SD 9.0) | 0.72 (SE 0.04) | 0.55 (SE 0.15) / 0.76 (SE 0.16) |
|   | Tardive dyskinesia (EPS) | 0.88 | 0.88 | 14.5 (SD 11.4) |
|   | Akathisia (EPS) | 0.88 | 0.87 |   |
|   | Parkinsonism (EPS) | 0.84 | 0.79 |   |
|   | Pseudo-parkinsonism (EPS) |   | 0.07 | 0.05 - 0.07 |
|   | Hyperprolactinemia |   |   | 0.82 (SE 0.03) |
|   | Diabetes |   |   | 0.77 (SE 0.04) |
| Process related | Decreased visits to doctor/hospital |   |   | 36.8 (SE 27.3) |
|   | Inpatient, acute positive symptoms† |   |   | 0.19 |

* Taxonomy in tables is modified from Opmeer et al.*
* All reference numbers refer to the reference list in the main article.
**When several designs are used including a SG design, only SG utilities are given.
†Combined outcome categorised under two outcome domains in table.
CA, conjoint analysis; D-efficient and Orthogonal design used in CA; EPS, extrapyramidal symptoms; N/A, not applicable; PC, pair-wise comparison; SD, standard deviation; SE, standard error; SG, standard gamble; TTO, time trade-off; VAS, visual analogue scale.

**Table B** Depression

| Study* | Revicki 1998 | Zimmermann 2013 | O’Brien 1995 | Morey 2007 |
|--------|-------------|-----------------|-------------|------------|
| Method | SG          | CA              | WTP         | WTP        |
| Unit   | SG utility  | Relative        | CAD         | USD        |
| Scale  | 0-1         | 0-100           | 0-N/A       | 0-N/A      |

| Outcome domain | Outcome type | Outcome |
|----------------|--------------|---------|
| Disease related outcomes | Symptoms | Severe, untreated depression | 0.30 (SD 0.28) |
| | | Loss of interest and enjoyment | 13.5** |
| | | Depression-related pain | 12.0 |
| | | Sleep disturbance | 12.0 |
| | | Feelings of guilt | 11.5 |
| | | Depressed mood | 8.5 |
| | | Loss of energy/fatigue | 18.5** |
| | | Remission, maintenance treatment | 0.72 (SD 0.17) to 0.83 (SD 0.13) |
| | | Remission, no treatment | 0.86 (SD 0.16) |
| | | Current health | 0.74 (SD 0.22) |
| Functioning | Loss of interest and enjoyment | 13.5** |
| | Loss of energy/fatigue | 18.5** |
| Intervention related | Side effects | Side effects after 2 weeks | 14.2 |
| | | Weight gain of 5% | 409 (min-max: 19-1547) |
| | | Sedation | 0.75/0.69† |
| | | Nervousness | 0.76/0.64† |
| | | Headache | 0.75/0.65† |
| | | Constipation | 0.74/0.68† |
| | | Tension | 0.74/0.71† |
| | | Dry mouth | 0.74/0.73† |
| | | Nausea | 0.74/0.73† |
| | | No orgasm | 478 (min-max: -1-1480) |
| | | Tremor | 19.4 (CI 13.2-25.6) |
| | | Dizziness | 16.8 (CI 11.6-32.0) |
| | | Lightheadedness | 0.75/0.63‡ |
| | | Sleepiness | 18.6 (CI 14.2-23.0) |
| | | Sweating | 13.9 (CI 9.6-18.2) |
| | | Blurred vision | 21.9 (CI 16.3-27.5) |
### Table C  ADHD and bipolar disorder

| Study*          | Method   | Unit                  | Outcome domain | Outcome type | Outcome |
|-----------------|----------|-----------------------|-----------------|--------------|---------|
| ADHD            |          |                       | Disease related|              |         |
| Bipolar disorder|          |                       |                 |              |         |
| Johnson 2007    | DCE      | Importance weight     | Symptoms        | Heroin-free time (3-24 months) | 0.185   |
| Revicki 2005    | SG       | SG utility score      | Cognitive impairment / cognition | 0.184 |
| Glenngård 2012  | DCE      | Estimated WTP in EUR  | Severity of depression | 0.29 (CI 0.16-0.42) |
|                 |          |                       | Severe depression | 0.23 (CI 0.19-0.34) to 0.26 (CI 0.16-0.31) |
|                 |          |                       | Outpatient, mania | 0.29 (CI 0.13-0.44) to 0.64 (CI 0.52-0.76) |
|                 |          |                       | Inpatient mania† | 0.09 |
|                 |          |                       | Severity of mania | 0.23 (CI 0.19-0.34) to 0.26 (CI 0.16-0.31) |
|                 |          |                       | Outpatient, stable | 0.58-0.83 (CI 0.45-0.74) |
|                 |          |                       | Fatigue effect | 0.11 |
|                 |          |                       | Current health | 0.80 (SD 0.22) |
| Risk of recurrence|          |                       | Relapse | 0.08 |
|                 |          |                       | Mania frequency | 0.08 |
|                 |          |                       | Depression frequency | 0.08 |
| Functioning|          |                       | Functioning morning/day | 252 |
|               |          |                       | Functioning afternoon/evening | 145 |
| Intervention related|          |                       | Side effects | Side-effects (not specified) | 0.20 |
|                 |          |                       | Weight gain of 5% | 0.066** |
|                 |          |                       | Serious side effect | 0.06 |
|                 |          |                       | Tardive dyskinesia | 0.76 (CI 0.64-0.88) |
| Patient related|          |                       | Costs | In WTP |
| Process related|          |                       | Treatment schedule | Number of dosages per day | 0.43 |
|                 |          |                       | Mono- or combination therapies | Monotherapy preferred |

**Composite outcomes including factor levels for functioning, categorised simultaneously as "symptoms" and "functioning" outcome.
†Patients with/without the side effect. SG values estimated from figure 2 in paper. Non-significant difference.
‡Patients with/without the side effect. SG values estimated from figure 2 in paper. Statistically significant difference.
CAD=canadian dollars; CI, 95% confidence interval; N/A, not applicable; SD, standard deviation; SG, standard gamble; USD=US dollars; WTP=willingness to pay.
| Healthcare provider                  | Hospitalisation (inpatient) | 0.12 - 0.33 |
|-------------------------------------|-----------------------------|-------------|
| Inpatient mania†                    |                             | 0.23 (CI 0.19-0.34) to 0.26 (CI 0.16-0.31) |
| Presence of case management         |                             |             |

Taxonomy in tables is modified from Opmeer et al. *All reference numbers refer to the reference list in the main article.

†Composite outcome categorised simultaneously as "symptoms" and "functioning" outcome.
CI, 95% confidence interval; DCE=discrete choice experiment; EUR=euros; SD, standard deviation; SG, standard gamble; USD, US dollars; WTP, willingness to pay.