

## **Guideline**

### **Transition between inpatient mental health settings and community and care home settings**

#### **Economics, economic modeling, Appendix 2**

**Title:**

Cost–utility analysis of a 2-year multi-staged psychological intervention for bipolar I patients with their first, second or third hospitalisation (specialised bipolar staff + guideline-based pharmacological treatment + three-staged psychological intervention + 6-week manual-based psychoeducative group therapy for families) vs Generic outpatient treatment of bipolar affective disorders (active treatment as usual)

**Review questions**

Review Question 4: What is the effectiveness of interventions and approaches designed to improve discharge from inpatient mental health settings?

Review Question 5: What is the effectiveness of interventions and approaches designed to reduce or prevent readmissions to inpatient mental health settings?

This report was produced by the Personal Social Services Research Unit at the London School of Economics and Political Science. PSSRU (LSE) is an independent research unit and is contracted as a partner of the NICE Collaborating Centre for Social Care (NCCSC) to carry out the economic reviews of evidence and analyses.

**Authors of the report:**

Marija Trachtenberg and Martin Knapp

## Contents

## 1. IntroductionIntroduction

5

This report presents the economics work undertaken for the guideline, Transition between inpatient mental health settings and community and care home settings.

The economics work is comprised of two main components. The first is the critical appraisal and review of existing cost-effectiveness literature and interpretation of the results to make recommendations for the UK context. These can be found in Appendix C1 and C2 and these are not the focus of this report.

This report addresses the second component: to undertake new economic modelling. New analyses are useful where there is no existing cost-effectiveness evidence available.

The rationale for focusing on this particular intervention is covered in a separate document in Appendix C3.1.

### 2. Aims

### 3. The intervention and the sample

### 4. Background – why the analysis is important

### 5. Methods

5.1. Cost–utility analysis 9

5.2. Data inputs

5.3. Estimating differences in costs and QALYs 10

### 6. Results

### 7. Discussion and limitations

### 8. GC opinions about influential factors in the analysis

### 9. Linking evidence to recommendations

## 10. Bibliography

## **1 Introduction**

This report presents the economics work undertaken for the guideline, Transition between inpatient mental health settings and community and care home settings.

The economics work is comprised of two main components. The first is the critical appraisal and review of existing cost-effectiveness literature and interpretation of the results to make recommendations for the UK context. These can be found in Appendix C1 and C2 and these are not the focus of this report.

This report addresses the second component: to undertake new economic modelling. New analyses are useful where there is no existing cost-effectiveness evidence available.

The rationale for focusing on this particular intervention is covered in a separate document in Appendix C3.1.

## **2 Aims**

This report presents the results of a cost-utility analysis for bipolar I patients with their first, second or third hospital admission, with or without substance misuse (excluding individuals admitted to hospital involuntarily).

The intervention is 2 years long, based in an outpatient clinic staffed by bipolar specialists + guideline-based pharmacological treatment + 3-staged psychological interventions upon discharge from hospital + 6-week manual-based psychoeducative group therapy for families.

This is compared to a generic outpatient treatment of bipolar affective disorders (which is active treatment as usual, which might mean intermittent psychological services). Services in the comparison group might include pharmacological treatment, but prescribing patterns may or may not be based on national guidelines and the provision of psychological therapies may vary in type and duration.

The evaluation is based on a moderately sized RCT from Denmark (n=158) (Kessing et al. 2013) rated as having moderate quality internal validity (+) and good external validity (++)

## **3 The intervention and the sample**

The intervention is staffed by those with specific training in the assessment and management of bipolar disorder. This includes a full-time psychiatrist, psychologist, nurse and social worker. Further detail regarding the intervention is as follows:

1. Discharge. Upon discharge, the individual attends an in-clinic evaluation by the psychiatrist no later than 2 weeks after discharge (Kessing et al. 2013, p213).
  - 1.1. If the patient misses the appointment they would get one or more re-invitations by letter, email, SMS or telephone. House visits were not made as a general rule but if treatment was not attended the GP or psychiatrist was notified. House visits are made only in the event of acute suicidal danger (Personal communication, Kessing 2015).
2. Pharmaceutical treatment. Pharmacological treatment is guideline-based, thereby promoting evidence-based prescribing (Kessing et al. 2013, p213).<sup>1</sup>
3. Provision of evidence-based psychological interventions.
  - 3.1. 'Upon discharge, individuals receive treatment with the aim of moving to the next set [of psychological treatments] when they are partially remitted from symptoms (<14 for mania and depression on the Hamilton Depression Score and the Young Mania Rating Scale). Individuals are usually in this group for a few months up to half a year. The focus of this treatment is to discuss 'current clinical status, beliefs, and experiences in relation to the recent hospitalisation' (Kessing et al. 2013, p4).
  - 3.2. The next stage in treatment is either group psychoeducation or group cognitive behavioural therapy (CBT), decided in collaboration by the individual and clinician. Sessions are 1.5 hours long and provided for 12 weeks, which is then followed by three booster sessions (Kessing et al. 2013).

In either psychoeducation or CBT, 'focus is on knowledge and acceptance of suffering from an affective disorder, identifying affective symptoms from normal reactions, personal identity in relation to suffering from an affective disorder, risk situations, stress management, the need for sustained pharmacological maintenance treatment, adverse events due to treatment, and identification of individual prior early warning signs of upcoming affective episodes' (Kessing et al. 2013, p4). In CBT, additional focus was on 'inter-individual conflicts and cognitive distortions in identity and behaviour' (p.4).
  - 3.3. The final stage in treatment is a 3–6-month training discharge group, preparing the individual for 're-referral to the initially referring physician with the aim of identifying individual early warning signals prospectively in practice and training of how to change upcoming personal conflicts and cognitive distortions' (p4).

---

<sup>1</sup> For contextual purposes it is worth noting that in Denmark pharmaceutical treatment involves 'mood stabilisers, mainly lithium, valproate, lamotrigine, and atypical antipsychotics'.

4. Intervention for families: 'Relatives of patients with bipolar disorder were offered a manual based psychoeducative group course consisting of 2-hours sessions weekly for six weeks' (p4).
5. Staffing of the intervention: 'Six to eight patients and two therapists (psychiatrist, psychologist, or nurse) participate in each group. In CBT, at least one therapist has a formal education in CBT' (p4).

#### **4 Background – why the analysis is important**

##### Significant cost and quality of life implications

There is potential to reduce the substantial costs associated with a bipolar relapse leading to a hospital admission or the use of crisis resolution home treatment teams (CRHTT). If an individual has had a relapse in the last year, there is a 50% chance of a relapse in the next year (CG 185, p43 citing Judd et al. 2008a). However, not all relapses lead to hospital admissions. Based on one small UK study the probability of hospital admission per year is between 10 and 30% (Cheema et al. 2013; Frangou et al. 2006).

A relapse may be manic, depressive, or mixed/cycling. Manic episodes, while less frequent (approximately 20.6% of the time) have a higher chance of leading to inpatient admission (77% of the time) with a mean (median) length of stay of 57 (30) days (CG 185, p147 citing Judd et al. 2008b; CG 185, p147 citing Glover et al. 2006; HSCIC 2015). It is estimated that the remaining 23% of manic relapses are treated through crisis resolution home treatment teams (CRHTT) (CG 185, p147 citing Glover et al. 2006).

Depressive episodes are more prevalent, occurring about 52% of the time but are not as likely to lead to hospital admission (7.7% of the time). It is estimated that 90% of depressive episodes are treated in the community via community mental health teams (CMHTs) and the remaining 2.3% are treated through CRHTTs (CG 185, p147 citing Glover et al. 2006). Length of stay in hospital for a depressive episode is shorter than a manic episode, with a mean (median) of 30 (10) days (HSCIC 2015).

Mixed/cycling bipolar episodes occur 27% of the time. Expert opinion from the Bipolar Guideline Committee (CG 185) assumed that half of these individuals would be treated as if they were having a manic episode and the other half as a depressive episode (CG 185, p147).

In sum, approximately 34% of relapses are likely to be treated as a manic episode and the remaining 66% as depressive episodes.

Relapses leading to an inpatient admission have a significant impact on quality of life. Relapse is associated with a health state utility of 0.44 to 0.47, depending on whether it is a manic or depressive episode. When an individual is free from symptoms, utility scores are around 0.9 and when they are partially recovered, 0.83. These estimates were derived using a combination

of expert opinion from the Bipolar Guideline Committee (CG 185) and the available evidence from one UK study using the EQ-5D instrument (CG 185, p126, 147–9).

#### Positive impacts of similar interventions as indicated from wider literature

CG 185 undertook a meta-analysis of various psychological interventions for bipolar disorder (for individuals and/or families) (CG 185, p248). While the quality of studies varied from low to moderate, and covered a range of time horizons, findings indicate positive impacts on reducing relapse and hospitalisation.

#### Need for cost-effectiveness research

There has been little cost-effectiveness research during discharge or in the post-discharge period. The current economic analysis was also partly motivated by a research recommendation in CG 185: ‘The Guideline Committee recommends research on the “clinical and cost-effectiveness of a specialised collaborative care service for people with bipolar disorder compared to usual treatment delivered by generic care services”’ (CG 185, p48), referring to Kessing et al. (2013).

#### Potential preventative effects

There may be preventative effects for individuals in the early course of bipolar disorder. There is evidence from two studies that psychological therapies become less effective when the number of bipolar episodes increases (Reinares 2014 citing Colom et al. 2010; Scott et al. 2006).<sup>2</sup> However the evidence base is in its early stages and conclusions are not definitive (Reinares 2014, p52).

#### Variation in practice

There may be substantial variation in the provision of psychological therapies in the UK (CG 185, p50). Audits from two trusts indicate that access to structured psychological interventions is very low (7 to 10%) (CG 185, p50). Furthermore, individuals might be receiving services from therapists who have not had specific training for bipolar disorder. Most service configurations for bipolar disorder in England are generic (NICE CG 185, p46). The usual psychological interventions provided are enhanced relapse prevention/ individual psychoeducation (brief intervention), cognitive behavioural therapy and group psychoeducation (CG 185, p49).<sup>3</sup>

Taken together, there is a significant need for cost-effectiveness analysis in this area due to the potential for a recommendation to have a significant impact on resource use, QALYs, and variation in practice.

## **5 Methods**

---

<sup>2</sup> Specifically, interventions become less effective in reducing time until next relapse or the time-spent ill as the number of bipolar episodes increases.

<sup>3</sup> Less commonly provided are interpersonal and social rhythm therapy, and family-focused therapy.



## 5.1 Cost–utility analysis

A cost–utility analysis was conducted. A cost–utility analysis is a type of cost-effectiveness analysis in which the unit of effect is measured in terms of a utility indicator (in this case the quality-adjusted life year (QALY)). The cost-effectiveness of an intervention is then determined by examining the incremental cost ( $C_I - C_C$ ) divided by the incremental effect ( $E_I - E_C$ ), where  $C_I$  and  $C_C$  represent the cost of the intervention and control groups, respectively, and  $E_I - E_C$  represent the outcomes of the intervention and control groups, respectively. The higher the ICER, the less cost-effective the intervention is found to be.

Economic evaluation aims to help decision-makers allocate resources to interventions that provide the best value for money. When the ICER is less than £0 because the intervention delivers cost savings and delivers more benefit, the intervention is generally recommended. From the NICE clinical perspective, the acceptable maximum amount of money to be paid for an additional QALY is where the ICER lies between £0 and £20,000, but NICE advises more caution in concluding something is cost-effective where the ICER is between £20,000 and £30,000. When interventions are above £30,000 per QALY, interventions are generally seen as being not cost-effective, although this is not a strict rule. As in all cost-effectiveness analyses, value judgements are needed.

There is no equivalent threshold in social care economic evaluation. Social care is fundamentally different from clinical care in some important aspects. First, the QALY is a measure of health-related quality of life, and does not reflect outcomes considered important in social care, for example, feeling safe, feeling in control over daily life and activities, feeling comfortable and clean, satisfaction with opportunities to socialise, feeling sufficiently occupied, and maintaining a sense of dignity (see the Adult Social Care Outcomes Toolkit, ASCOT for further examples). For this reason, the QALY is not the agreed-upon outcome on which to base decisions about cost-effectiveness in social care. Secondly, there is no agreed upon value to define or guide a cost-effectiveness threshold in social care.

In spite of the limitations outlined above, a cost–utility analysis is still useful if (i) cost-effectiveness can be demonstrated on the basis of QALYs and (ii) no additional evidence suggests deteriorations in other relevant outcome indicators.

## 5.2 Data inputs

To translate Danish results to a UK context, UK-specific data are needed. To do this, we need baseline UK data for both costs and QALYs, where costs refer to both UK-specific unit costs and the typical pattern of service use of health and social care services.

This section summarises the sources of data used and the costing approach.

The following section (**Error! Reference source not found.**) shows how we estimated cost-effectiveness in more detail.

#### Sources of data

The data used in the model are presented in Table 1. Some of the model parameters were taken from the recent NICE Bipolar Clinical Guideline (CG 185) and updated where appropriate. The rationale for referencing CG 185 is that data would be recent, based on a systematic search, and GC expert opinion was available when assumptions were required. Where information was not available, we took data from other literature.

#### Costing approach

Unit costs are based on national UK estimates using a full-cost approach in line with accepted practice (Curtis 2014). The full-cost approach reflects the long-run average costs.<sup>4</sup> All of the unit costs used in the analysis are also located in Table 1.

#### Price year

All costs reflect 2013/14 price year. Where costs are obtained from older studies these were inflated to 2013/14 using the health and social care community price and pay index (Curtis 2014).

### **5.3 Estimating differences in costs and QALYs**

#### 1. Perspective of the analysis

The analysis takes the perspective of the NHS and personal social services. Outcomes are measured in terms of QALYs. We do not consider the potential impact on service users' employment, housing, or use of legal and criminal justice services nor do we model the potential impact on informal carers.

#### 2. Intervention effect on costs and QALYs

The Danish study is informative but the study does not measure QALYs nor all relevant costs. The study does measure changes in hospitalisation, but does not directly measure changes in community health and social care services; rather, assumptions are made using Danish literature. Those assumptions are not appropriate for the UK context. Also missing from the study is the impact on carers, employment, housing and the legal system. In terms of outcomes, the study does not measure changes in QALYs or clinical outcomes (such as the number of relapses) or social-care related outcomes (such as recovery, hope, sense of control, etc). The study did measure changes in symptoms (manic and depressive) but data are potentially compromised due to low response rates.

#### 3. Treatment effect of the intervention

---

<sup>4</sup> Estimating long-run average costs considers salary, on-costs due to national insurance and pension contributions, qualifications, direct and indirect capital costs and any other indirect time costs (for instance, traveling time).

The findings of the Danish study were favourable for the intervention group, measured over a 30-month time horizon, of which the intervention lasted 24 months:

- Non-statistically significant trend to lower total mean readmissions, Intervention=0.97 (sd=1.74) vs control=1.58 (sd=2.57),  $p=0.11$ , reflecting the lower proportion of individuals in the intervention group admitted to hospital compared to the control group (36%,  $n=26/72$  vs 55%,  $n=47/86$ ).
- Non-statistically significant shorter median length of stay of first readmission to hospital, Intervention=12 days (IQR=3.0–46.5), control = 22 (IQR=4.8–54.8),  $p=0.30$ .
- Statistically significant decrease in time to first admission after adjusting for covariates (Hazard ratio 0.60, 95% CI (0.37 to 0.98),  $p=0.043$ ).
- Statistically significant reductions in the cumulated median duration of all admissions to hospital following randomisation ( $p=0.01$ , median (quartiles), Intervention=33 days (IQR=10.5-133.5), Control = 49 (IQR=21–127.5).

In our economic model we transformed the intervention impact into a relative risk reduction for (i) median cumulative length of stay and (ii) proportion admitted to hospital.

- Relative risk reduction for median length of stay was 0.67. Lower and upper limits were estimated using an assumption because the study did not provide the standard deviation. A conservative approach was used and we assumed lower and upper limits of -0.1 and +0.2 (leading to an assumed interval of 0.57 to 0.87).
- Relative risk reduction for the proportion admitted was 0.66, 95% CI (0.41–1.06), was calculated based on the data provided.

Other outcomes include the use of medication collected by self-report. Completion rates were '77.8% for antipsychotics, 80.4% for antidepressants and 92.4% for mood stabilisers (lithium or anticonvulsant)' (Kessing et al. 2013, p216). The results were:

- Statistically significant higher use of anti-psychotics ( $p=0.02$ ) and mood stabilisers ( $p=0.004$ ) in the intervention group and non-significant difference of antidepressant use between groups ( $p=0.8$ ). However, these results do not seem to be adjusted for baseline use of medications as this information was not collected at baseline. Therefore, it is not clear how to interpret these particular results.

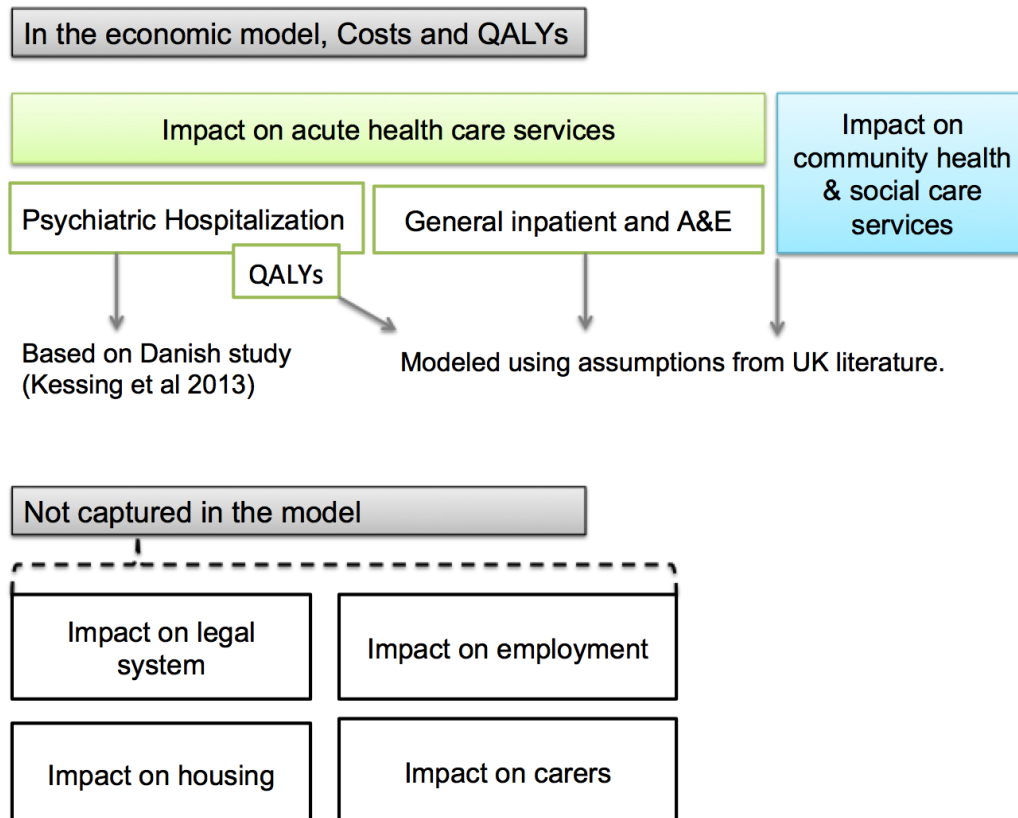
#### Modelling the impact of the intervention in the UK context

The economic analysis is conducted using a Monte Carlo simulation in MS Excel for Mac 2011, Version 14.3.8. Further details about the Monte Carlo simulation is in Section 6 with the results.

The economic analysis models the impact on hospitalisation using the Danish study but to estimate impact on QALYs and changes in health and social care community services, we make assumptions using additional UK literature. This is illustrated in Figure 1.

In estimating QALY gains, we use a conservative approach and do not include the additional QALYs that would be associated with being in the community. This is illustrated in Figure 2.

**Figure 1 Costs and QALYs in the economic model**



**Figure 2 Estimating QALY gains as a result of the intervention**



Gains in QALYs  
Resulting from the reduction in the proportion admitted & reduced duration of stay

4. Use of general acute care and community health and social care services  
Estimates of community health and social care services and general acute care service use were derived from additional UK literature. The data were

identified from CG 185 based on a systematic search which included economic evaluations of psychological interventions.

One UK study was identified comparing cognitive behavioural therapy + standard care vs standard care alone for bipolar I patients (Lam et al. 2005). There are limitations in using this data for our model because the sample characteristics and intervention are not completely comparable and therefore are only partially appropriate for our purposes. Likewise, the institutional context may not be comparable to today as it reflects service patterns from 1999/2000.

In relation to sample characteristics, individuals have a longer history of living with bipolar I disorder (compared to the Kessing sample): a mean of 5–6 hospitalisations and approximately 13 bipolar episodes (either mania, depressive, or hypomania) (Lam et al. 2005).

Another difference is study design. The Lam et al. intervention is individualised and is less intensive: 14 sessions of CBT during the first 6 months with 2 booster sessions in the second 6 months (Lam et al. 2003) (and the time horizon was a total of 30 months). Patients were recruited from an outpatient setting, which is similar to the Danish study, where patients are provided group-based CBT or psychoeducation approximately 6 months after discharge only if the patient is partially remitted from symptoms.<sup>5</sup>

This study found improvements favouring the intervention for clinical outcomes during the 12-month period, including: significantly fewer bipolar episodes and fewer days in a bipolar episode (Lam et al. 2003, 2005), a non-significant trend to fewer hospital admissions (Lam et al. 2005), significantly higher social functioning, fewer mood symptoms on the monthly mood questionnaires, significantly less fluctuation in manic symptoms and better coping with manic prodromes (Lam et al. 2003).

The economic evaluation found that for the first 12 months and the entire 30 months, the intervention group used fewer total health and social care services, but this was not statistically different. Resource use was measured using the Client Services Receipt Inventory (CSRI) at 3-monthly intervals from baseline to 30-month follow-up.<sup>6</sup> Differences in cost were larger for total community health and social care services but were very similar for the use of general acute care for both 12- and 30-month periods. Medication costs were slightly higher for the intervention group. Psychiatric inpatient costs were higher for the control group in the first 12 months and were similar when measured over the total 30-month period.

---

<sup>5</sup> Score of <14 for mania and depression on the Hamilton depression score and the Young Mania Rating Scale (Kessing et al. 2013, p4).

<sup>6</sup> Services included contacts with mental healthcare services (psychiatrists, psychologists, community mental health nurses, day centres, counsellors and other therapists), GPs, social workers, hospital services (outpatient care, day hospital contacts and accident and emergency attendances), support groups and residential care (Lam et al. 2005, p499–500).

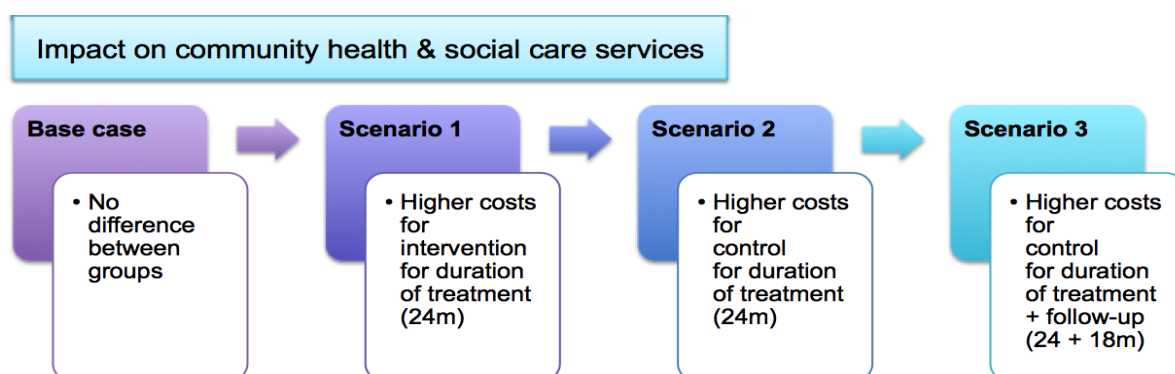
Our economic model used the Lam et al. findings on community health and social care services and general acute care. In line with their findings, our economic model assumed no differences between groups for general acute care services. We were less confident about the impact on community health and social care services, so we conducted several scenario analyses. In the base case scenario we assumed there were no differences between groups (£0). In scenario 1, we assumed that the intervention group had higher community health and social care costs for the duration of treatment (24 months, £2,190) (this will be referred to as the conservative scenario throughout this report). The more optimistic scenarios are scenarios 2 and 3. In scenario 2, we assumed the control group has higher community health and social care costs for the duration of treatment (24 months, £2,190). Scenario 3 is the most optimistic and reflects the findings (not statistically significant) in Lam et al (2005) – it assumes higher health and social care costs for the duration of treatment (24 months, £2,190) plus higher costs in the follow-up period (18 months, £1,590).

We did not incorporate the costs of medication because differences were much smaller and would be marginal to the analysis, especially if generic pharmaceuticals are prescribed, which may be the case today. Excluding medication costs from our analysis is a very minor limitation.

When incorporating community health and social care costs into our economic model we inflated prices from 1999/2000 to 2013/14 using the hospital and community health services pay and price inflators (Curtis 2014).

Figure 3 shows the four scenarios reflecting different assumptions about community health and social care cost differences.

**Figure 3** Community health and social care cost scenarios



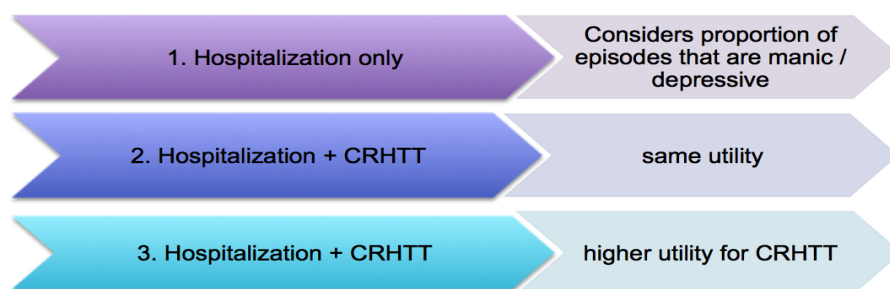
## 5. Structuring the economic model

In the UK, crisis resolution home treatment teams (CRHTTs) are sometimes used as an alternative to hospital. Would the findings from the Danish study have had an impact on the use of CRHTTs? We account for this possibility through additional scenario analyses.

The first scenario assumes an effect on admissions to hospitalisation only. The underlying assumption is that, because the intervention affects only those admitted to hospital, it affects the most acute of relapses. We are assuming that hospitalisations are associated with higher levels of need. We are also assuming the intervention does not have an effect on less acute relapse that might be associated with CRHTTs.

We also assume a second and third scenario where the intervention does affect individuals' use of both CRHTTs and admission to hospital. The scenarios are only different from the perspective of QALYs – in scenario 2; individuals in hospital and those receiving CRHTTs have similar QALYs. In scenario 3, individuals in CRHTTs have higher QALYs assuming that the episode is less severe. The following scenarios are illustrated in Figure 4.

**Figure 4** Structural assumptions about the impact of the intervention



## 6. Estimating QALYs

QALY gains are estimated from the utility of being in psychiatric hospital or receiving treatment from CRHTTs. Data on utilities were obtained from CG 185 and were agreed by that Guideline Committee (p.126, pp147–9). Utility values are different depending on whether the admission is for a manic or depressive episode. Inpatient mania utilities were averaged for moderate and mild symptoms (0.46 and 0.43) for a value of 0.445 whereas a depressive episode had a slightly higher utility value of 0.48.

NICE guidelines prefer the use of EQ-5D in the elicitation of health states. Our utility values do reflect EQ-5D although indirectly by mapping from one non-UK study and therefore our approach has some limitations.<sup>7</sup>

<sup>7</sup> The literature search for CG 185 identified 3 relevant studies. There was only 1 UK study (Hayhurst et al. 2006) that satisfied NICE criteria. It used the EQ-5D and it was based on responses from a representative sample of the general population using a choice-based method (CG 185, p147). However, the UK study did not have utility values for inpatient mania or depression. Therefore, CG 185 referred to data from one non-UK study (Revicki et al. 2005). The elicitation method used in that study was the standard gamble approach based on hypothetical health state vignettes taken from service users in the USA (CG 185, p147). Even though the non-UK study does not meet NICE criteria, it was found that, for similar health states, the non-UK study had consistently lower utilities by 0.20. Therefore, CG 185 decided to create a UK utility for an inpatient individual by adding 0.20 utilities to the non-UK equivalent in an attempt to approximate UK-equivalent values (CG 185, p147).

We did not find utility values for individuals receiving treatment from CRHTTs so we assumed utilities were improved by +0.05. Therefore, scenario 3 assumes that CRHTT values for mania and depression are 0.495 and 0.530 respectively.

## 7. Estimating UK patterns of hospitalisation and CRHTTs

### i. Baseline length of stay in hospital

The Danish study found that the intervention reduced median length of stay in hospital. We used 2013/14 Hospital Episode Statistics.<sup>8</sup> Median length of stay for mania and depressive episodes were 19 and 10 days respectively.

### ii. Baseline contacts with CRHTTs

Using UK data and assumptions from CG 185, individuals had an average of 2 contacts per week with CRHTTs and the duration of contact was of a similar duration to that of an inpatient stay (CG 185, p155 citing Johnson et al. 2005 and McCrone et al. 2009). CG 185 estimates focus on mean length of stay whereas we are focusing on median length of stay (as this is the level of impact taken from the Danish study). Whether the assumptions from CG 185 are transferrable is unclear and therefore our analysis has some limitations; however the implication is that results are conservative rather than optimistic.

### iii. Baseline probability of hospital admission

We initially referred to CG 185 for UK baseline probabilities of admission to psychiatric hospital. We were unable to find data that were recent and from the UK. Therefore we conducted a separate non-systematic search of the literature and found one recent UK study conducting a 3-arm RCT in inner-London (Frangou et al. 2006). Mean baseline inpatient admission rates in each of the three arms of the RCT, in the past 12 months, varied between 0.1 (sd=0.3), 0.2 (sd=0.5), and 0.3 (sd=0.6). We used the value of 0.2 and extrapolated the 1-year probability over a 30-month period, resulting in a 30-month probability of 50% (calculated as 2.5 years x 0.2 probability per year). This explicitly assumes a constant rate over that period: that is, individuals have the same likelihood of being admitted in the first 12 months as they have in the 24th and 30th months.

The Frangou study was based on a three-arm RCT of n=75 individuals (Cheema et al. 2013). The 3 arms did not differ with the exception of the use of antipsychotic medication (p=0.01). There are potentially serious limitations in using this data as it reflects service patterns in England prior to 2006 and it is unclear how similar it is to today's context. Furthermore, the UK sample is slightly different to the Danish sample: the UK sample has a mean of 3 to 4 hospital admissions in their lifetime. However, samples are similar as patients are primarily diagnosed with bipolar I.

### iv. Ratio of hospitalisations due to manic or depressive episodes

---

<sup>8</sup> In particular, we used data generated from the '3-character primary diagnosis'.



Ratio of hospitalisations due to manic or depressive episodes was calculated from estimates provided by GC 185 via published literature (Johnson et al. 2005; Judd et al. 2008b; McCrone et al. 2009) and GC 185 expert opinion. We calculated that 85% of admissions are due to manic episodes.<sup>9</sup>

This is based on information that manic episodes are less prevalent (34.1%) than depressive episodes (65.9%) but depressive episodes are less likely to result in an inpatient admission (7.7%) or receive services from CRHTT (2.3%) than a manic episode (77% and 23% for hospital admission and use of CRHTT) (CG 185, p147–8, 217–18; based on GC expert opinion and Glover et al. 2006).

#### 8. Intervention costs

The costs of the intervention were estimated using the descriptions provided in the study and through personal communication with the author.

The total cost of the intervention is estimated to be £6,791 per person for the duration of treatment (24 months).

The costs of the intervention are based on the direct provision of the therapies, which were provided jointly by the psychiatrist and the mental health nurse. The costing of the intervention considers the in-clinic evaluation of the service user within 2 weeks of discharge, the three-stage group-based psychological interventions, and the group-based intervention for family members only (see Section 3).

Our estimates are based on the assumption that there were on average 7 individuals per group session (authors stated the range was 6 to 8). We did include the indirect costs of administration and patient-related work as a result of a face-to-face contact with the patient or family member.

The outpatient clinic also comprises a social worker and a psychologist, although they did not directly provide the psychological interventions. There was insufficient detail about the collaboration amongst all staff members. We assumed that the social worker and psychologist were involved in the indirect patient-related work that arose after the psychiatrist and nurse delivered the psychological interventions (to both service user and family member). It was our aim to use a conservative approach in our estimates. Therefore, we assumed that after each group session (in total there were 54 sessions) the psychologist and social worker each had 2 hours of patient-related work,

---

<sup>9</sup> Admitted to hospital calculated as:

$$0.84 = ((0.341 * 0.77) / ((0.659 * 0.077) + ((0.341 * 0.77))))$$

This is calculated as the proportion admitted to hospital due to mania as a sum of both probabilities of being admitted for mania and depression.

Admitted to hospital and CRHTT calculated as:

$$0.84 = (0.341 * (0.23 + 0.77)) / ((0.659 * (0.023 + 0.077)) + ((0.341 * (0.23 + 0.77))))$$

This is the proportion admitted to hospital and CRHTT due to mania as a sum of both probabilities of being admitted to hospital and CRHTT for mania and depression.

either through administration or through collaboration with the psychiatrist and nurse. For more detail, see Table 1.

**Table 1 Parameters used in the model.**

<b>TREATMENT EFFECT</b>				
<b>Input parameter</b>	<b>Value</b>	<b>Probabilistic distribution</b>	<b>Notes and sources of data</b>	<b>Guideline Committee confirmation</b>
Impact of intervention on proportion of individuals admitted to hospital	Mean=0.66, 95% CI (0.41–1.06)	<b>Normal distribution.</b> Distribution based on mean and standard deviation.	– Calculated from data provided (Kessing et al. 2013).	<a href="#">Not required.</a>
Impact of intervention on median length of stay	Mean=0.67, 95% CI (0.57–0.87)	<b>Normal distribution.</b> Distribution based on mean and standard deviation.	– Calculated from data provided (Kessing et al. 2013). Distribution based on assumption about lower (-0.1) and upper CI (+0.2).	

<b>HEALTH STATE UTILITIES</b>				
<b>Input parameter</b>	<b>Value</b>	<b>Probabilistic distribution</b>	<b>Notes and sources of data</b>	<b>Guideline Committee confirmation</b>
Relapse inpatient	Mania: 0.445 (SD=0.04)  Depressive: 0.48 (SD = 0.04)	<b>Gamma distribution</b>  Distribution based on mean and standard deviation.	– Estimates reference those used in CG 185 economic model (p147–9). – Estimates derived from EQ-5D using UK data (Hayhurst et al. (2006)) and from non-UK study, Revicki et al. (2005).	<a href="#">CG 185 Guideline Committee confirmed.</a>
Relapse CRHTT	Mania: 0.495 Depressive: 0.53	<b>Gamma distribution.</b> Standard deviation is assumed to be the same as inpatient utility values.	– Assumption that CRHT has higher utility value (+0.05) than inpatient utility (using base values as above).	<a href="#">GC confirmed.</a>  See section 9 for more detail.

RESOURCE USE				
Input parameter	Value	Probabilistic distribution	Notes and sources of data	GC confirmation
Intervention costs per person	£6,791	<b>No distribution</b>	<ul style="list-style-type: none"> <li>- Where group sessions occurred, a mean of 7 patients per session was used in the base-case (range from 6 to 8 individuals). This was applied across all 3 therapies and the family intervention. Costs are based on the direct provision of the therapies, which were provided jointly by the psychiatrist and the mental health nurse.</li> <li>- This does not include the cost of the social worker and the psychologist who also staffed in the clinic. Nor does this include the cost of team collaboration, which was not specified.</li> <li>- INTERVENTION COMPONENTS, cost per person. <ul style="list-style-type: none"> <li>o 2-weeks from discharge, in-clinic evaluation, direct interaction of 1 hour long (Kessing, personal communication) = £320 per contact.</li> <li>o First treatment, group session, 3 to 6 months (Kessing, personal communication). Base case assumes 4.5 months long, 4 times a month, 1 hour per week (total of 18 sessions) = £1,012.</li> <li>o Second treatment, group session, 12 weeks for 1.5 hours per week, either psychoeducation or CBT plus 3 booster sessions (total of 15 sessions) = £1,263.</li> <li>o Third treatment, group session, between 3 to 6 months. Base case assumes 4.5 months, 4 times a month, 1.5 hours per week (total of 18 sessions) = £1,518.</li> <li>o Fourth treatment, family-only group session, 6 sessions, 2 hours per week (total of 6 sessions) = £675.</li> <li>o Cost of social worker and psychologist input either through collaboration with team members or patient-related work. Assumed 2 hours of additional work for each social worker and psychologist per group session. 57 total sessions x 2 hours of work per social worker and psychologist (divided by 7 patients</li> </ul> </li> </ul>	Not required

			<ul style="list-style-type: none"> <li>per group session) = £2,002.</li> <li>○ Total cost per person excluding collaboration with psychologist and social worker = £4,789.</li> <li>○ Total cost per person including collaboration with psychologist and social worker: <ul style="list-style-type: none"> <li>▪ Assumed 2 hours per session = £6,791</li> <li>▪ Assumed 1 hour per session = £5,790</li> </ul> </li> </ul>	
Length of stay in hospital (days)	Mania: Median=19  Depressive: Median=10	<b>Assumption</b> +/- 1 day around the median.	<ul style="list-style-type: none"> <li>- In this economic model, base case data come from the 2013/14 Hospital Episode Statistics using the data from '3-character primary diagnosis'.</li> <li>- We use median length of stay as reported in the Kessing et al. (2013) study.</li> </ul>	Not required
Mean CRHTT contacts per week	2	<b>Assumption</b> 50% have 2 contacts, 40% have 3 contacts, and 10% have 1 contact.	<ul style="list-style-type: none"> <li>- Distribution is assumed.</li> <li>- Mean contacts per week taken from CG 185 (p155) – based on UK data (Johnson et al. 2005; McCrone et al. 2009).</li> </ul>	Not required
Baseline probability of hospitalisation in 30 months	50%	<b>Beta distribution</b> Distribution based on assumption using sample size in the study (n=24)  ( $\alpha=12$ , $\beta=12$ )	<ul style="list-style-type: none"> <li>- Calculated as (2.5 years * 0.2 probability per year)</li> <li>- The data used to estimate mean inpatient admissions in our analysis is based on a 3-arm RCT in inner-London (Frangou et al. 2006). Mean baseline inpatient admission rates in the past 12 months varied from 0.1 (sd=0.3), 0.2 (sd=0.5), and 0.3 (sd=0.6). The range of values is used in our sensitivity analyses. The one year probability was extrapolated over a 30-month period, assumed constant rate over that period. The study was based on a sample of n=75 individuals, a majority of whom have a bipolar I disorder (Cheema et al. 2013). These groups did not differ with the exception of the use of anti-psychotic medication (p=0.01).</li> </ul>	Not required
Proportion of hospitalisation due to mania vs depression	84% due to mania	<b>Beta distribution</b> based on assumption about sample size (assumed to be	<ul style="list-style-type: none"> <li>- Calculated based on estimates provided by GC 185 via published literature and expert opinion, estimated to be 84% in base case scenario. Manic episodes are less prevalent (34.1%) than depressive episodes (65.9%). However, depressive episodes are less likely to result in an</li> </ul>	CG 185 GC confirmed.

Proportion of hospitalisation and CRHTT due to mania vs depression		n=100). ( $\alpha=84$ , $\beta=16$ )	<p>inpatient admission (7.7%) than a manic episode (77%) (CG 185, p147–8, 217–18; based on GC expert opinion and Glover et al. 2006). This analysis used the estimates provided by the GC to reflect UK-specific institutional factors.</p> <ul style="list-style-type: none"> <li>- Distribution is based on assumption using assumed sample size of n=100.</li> </ul> <p>Admitted to hospital calculated as:  <math>((0.341*0.77)/((0.659*0.077)+((0.341*0.77))))</math>.</p> <ul style="list-style-type: none"> <li>- This is the proportion admitted to hospital due to mania as a sum of both probabilities of being admitted for mania and depression.</li> </ul> <p>Admitted to hospital and CRHTT calculated as:  <math>(0.341*(0.23+0.77))/((0.659*(0.023+0.077))+((0.341*(0.23+0.77))))</math></p> <ul style="list-style-type: none"> <li>- This is the proportion admitted to hospital and CRHTT due to mania as a sum of both probabilities of being admitted to hospital and CRHTT for mania and depression.</li> </ul>	
Resource use associated with an episode	<p>Mania: 77% inpatient, 23% CRHTT</p> <p>Depressive: 7.7% inpatient, 2.3% CRHTT</p>	<p><b>Beta distribution</b> based on Glover et al 2006 (<math>\alpha=23</math>, <math>\beta=77</math>)</p> <p><b>Beta distribution</b> using GC expert opinion</p> <p>Inpatient / CRHTT (<math>\alpha=2.3</math>, <math>\beta=7.7</math>)</p>	<ul style="list-style-type: none"> <li>- Resource use associated with an episode references the economic model used in NICE CG 185. The average number of contacts with a crisis resolution home treatment team (CRHTT) was based on data taken from a UK evaluation (Johnson et al., 2005; McCrone et al., 2009) (CG 185, p216–17).</li> <li>- For depressive episodes, the GC estimated 7.7% are treated as inpatients, 2.3% are treated by a CRHTT as an alternative to hospitalisation (with 2x contacts per week), and the remaining 90% receive care from CMHT (comprising 4 visits over a 7-week period).</li> <li>- For mania episodes, the GC estimated that 77% are treated as inpatients and the remaining 23% receive care from CRHTTs for the same period as an inpatient stay but receive 2 contacts per week.</li> </ul>	CG 185 GC confirmed.
Health and social care community cost	<u>Base case scenario:</u> No differences	<b>Gamma distribution</b>  Alpha and beta	<ul style="list-style-type: none"> <li>- Kessing et al. (2013) does not measure use of health and social care service use. Estimates were taken from one UK economic evaluation comparing CBT + standard care vs standard care alone for bipolar I</li> </ul>	GC was unclear which scenario was

<p>difference between intervention and control groups</p>	<p>between groups £0</p> <p><u>Scenario 1:</u> Higher costs for the intervention for duration of treatment (24m) £2,190</p> <p><u>Scenario 2:</u> Higher costs for the control group for duration of treatment (24m) £2,190</p> <p><u>Scenario 3:</u> Higher costs for the control group for the duration of treatment (24m) + additional 18 months £3,780= 2,190 + 1,590</p>	<p>based on mean and assumed standard deviation (standard deviation was assumed to be the same as the mean, which is accepted practice when the true SD is not known (Briggs et al. 2006).</p>	<p>patients (Lam et al. 2005).</p> <ul style="list-style-type: none"> <li>○ Sample characteristics of Lam et al. (2005) are different from Kessing et al. (2013) in that they have a longer history living with bipolar. Individuals had a mean of 5–6 hospitalisations (6) and approximately 13 episodes (either mania, depressive, or hypomania).</li> <li>○ Furthermore, resource use is reflective of the intervention delivered, which was a 6-month CBT programme with two booster sessions in the second 6 months. See main text for more detail.</li> </ul> <p>– Resource use was measured using the CSRI, measured at baseline and every 3 months for 30 months.</p>	<p>more likely than the others.</p> <p>See Section 9 for more detail.</p>
---	---	--	---	---

General inpatient care costs	No differences	<b>No distribution</b>	– Based on Lam et al. (2005). Intervention and control groups had similar use of general inpatient services.	Not required.
Difference between intervention and control groups				

<b>UNIT COSTS</b>				
Inpatient bed day	£274 (SD = 7)	<b>Normal distribution</b>  Assumption after considering lower and upper-value quartiles.	– Inpatient bed day unit costs are based on NHS reference costs 2013/14. Calculated as the weighted average of non-psychotic clusters (3–8), psychosis and affective disorder (difficult to engage (17), patients not assessed or clustered (99). Distribution is assumed based on the upper and lower values (weighted).	Not required
Cost of CRHTT contact	£185	<b>No distribution</b>	– Unit cost of a contact with CRHTT is based on Curtis (2014, p219 citing NHS reference costs).	Not required
Psychiatrist, cost per hour	£320	<b>No distribution</b>	– Consultant, hospital based. Curtis 2013, p.259. – Unit cost per hour includes the assumption of 1.25 additional hours of patient-related work per 1 hour of client contact. – Unit cost without this assumption amounts to £142 per hour. Assuming 1.25 additional hours equates to (£142 * 2.25)=£320 per hour.	Not required
Mental health nurse	£74	<b>No distribution</b>	– Curtis (2013, p188). Unit cost per hour includes the additional patient-related costs due to face-to-face contact.	Not required
Psychologist per hour	£61	<b>No distribution</b>	– Curtis (2013, p183).	Not required
Mental health social worker per hour	£62	<b>No distribution</b>	– Curtis (2010, p175). – Inflated to 2013/14 prices.	Not required



## 6 Results

### Background

Monte Carlo simulations were used to determine the intervention's cost-effectiveness. Monte Carlo simulations are useful when there is uncertainty about the true value of the parameters used in the analysis.

To perform a Monte Carlo simulation, one must know or assume a probabilistic distribution of a particular parameter. In other words, there is a range of values that a parameter can take. In our model we had 3 types of parameter: outcomes, costs and probabilities. An example of a parameter is 'the probability of being hospitalised in 1 year'. This parameter can take a range of values (i.e. the probability could range from 10 to 30%). The mean and standard deviation are used for the probabilistic distribution. In a probabilistic distribution, each value that falls within the standard deviation is associated with a probability of it occurring. The collection of values and its associated probabilities is referred to as the 'probability distribution' for that particular parameter.

A Monte Carlo simulation performs the cost-effectiveness analysis a large number of times and each time, selects a value at random from that probabilistic distribution. In our analysis, Monte Carlo simulations were carried out 2000 times for each scenario.

This type of analysis captures uncertainty in a way that helps us make a decision about whether the intervention is cost-effective or not. The results are presented in two complementary forms. The first result is shown in a scatterplot, illustrating the mean costs and QALYs 2,000 times (**Error! Reference source not found.**). This is then transformed into a cost-effectiveness acceptability curve (CEAC). The CEAC shows the probability that the intervention is cost-effective for different values (i.e. £0 to £20,000) that a decision-maker is willing to pay per additional QALY gained (**Figure 7,**

**Figure 8).**

### Findings from the scatterplot

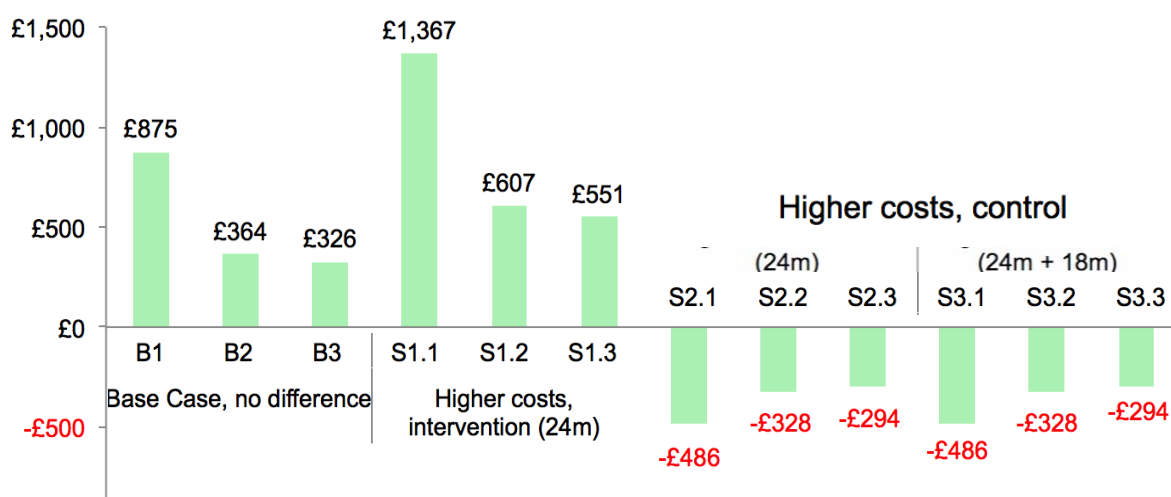
Across each of the scenarios, the minimum and maximum range of mean ICERs is between -£486 and £1,367 (**Error! Reference source not found.** and

1. **Table 2).**
2. In these scenarios, the negative ICER shows that there are cost savings and QALYs gained. The positive ICER shows additional costs for additional QALYs.

**Table 2** Mean QALYs, costs, and cost-effectiveness ratios (ICER)

		Assumptions about H&SC costs between groups			
		Base case	Scenario 1	Scenario 2	Scenario 3
<b>Assumptions about impact</b>		No difference in costs	Intervention has higher costs for duration of treatment (24m)	Control has higher costs for duration of ...	
				Treatment (24 m)	Treatment + follow-up (24 + 18m)
<b>Hospitalisation</b>					
<b>Scenario</b>	<b>B1</b>	<b>S1.1</b>	<b>S2.1</b>	<b>S3.1</b>	
Mean QALYs	4.3	4.3	4.3	4.3	
Mean cost	£3,781	£5,921	-£613	-£2,093	
Mean ICER	£875	£1,367	-£142	-£486	
<b>Hospitalisation + CRHTT</b>					
<b>Same utilities</b>					
<b>Scenario</b>	<b>B2</b>	<b>S1.2</b>	<b>S2.2</b>	<b>S3.2</b>	
Mean QALYs	8.6	8.7	8.7	8.7	
Mean cost	£3,145	£5,282	-£1,093	-£2,839	
Mean ICER	£364	£607	-£126	-£328	
<b>Higher utility for CRHTT</b>					
<b>Scenario</b>	<b>B3</b>	<b>S1.3</b>	<b>S2.3</b>	<b>S3.3</b>	
Mean QALYs	9.6	9.6	9.5	9.6	
Mean cost	£3,125	£5,291	-£1,178	-£2,823	
Mean ICER	£326	£551	-£124	-£294	

**Figure 5** Mean ICERs across various scenarios



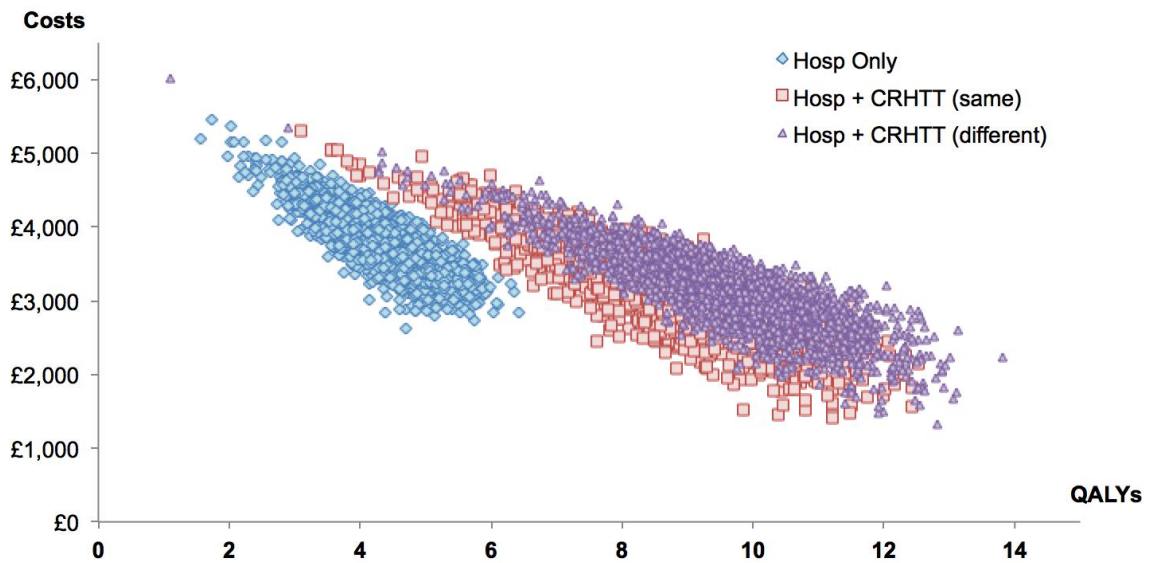
Findings from the scatterplot (continued)

3. The subsequent graphs in Figure 6 show that the ICERs are more optimistic if the impact reduces both hospitalisation and CRHTTs, as a greater number of resources are averted, and consequently a greater number of QALYs are gained.

**Figure 6 Results of the Monte Carlo simulation: costs and QALYs**

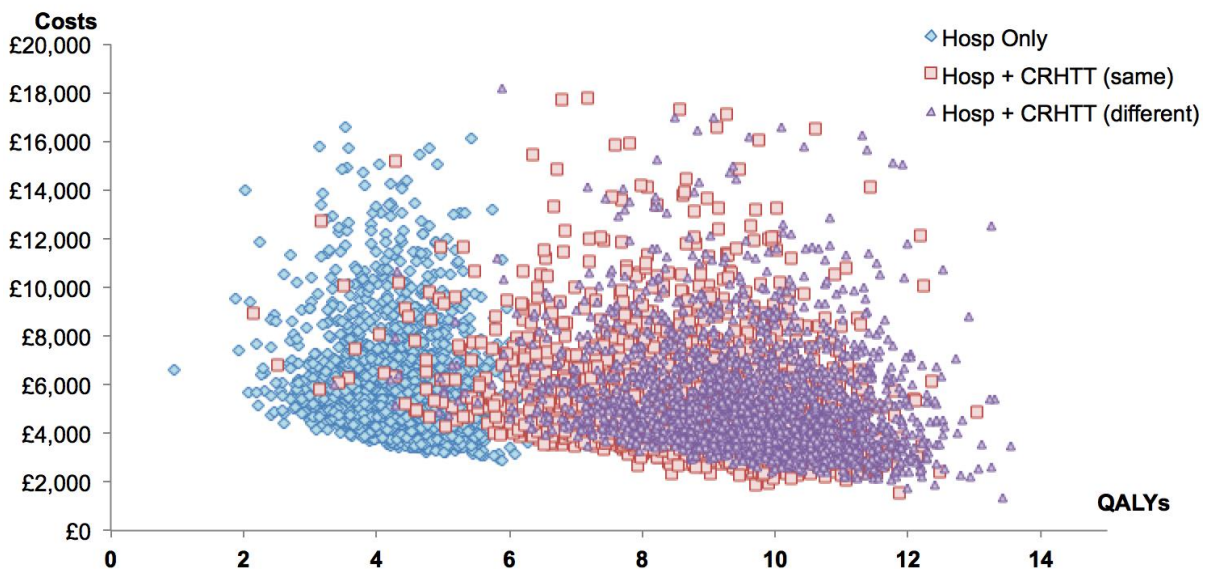
**Base case scenario**

Assumption: No differences in health and social care community costs between groups



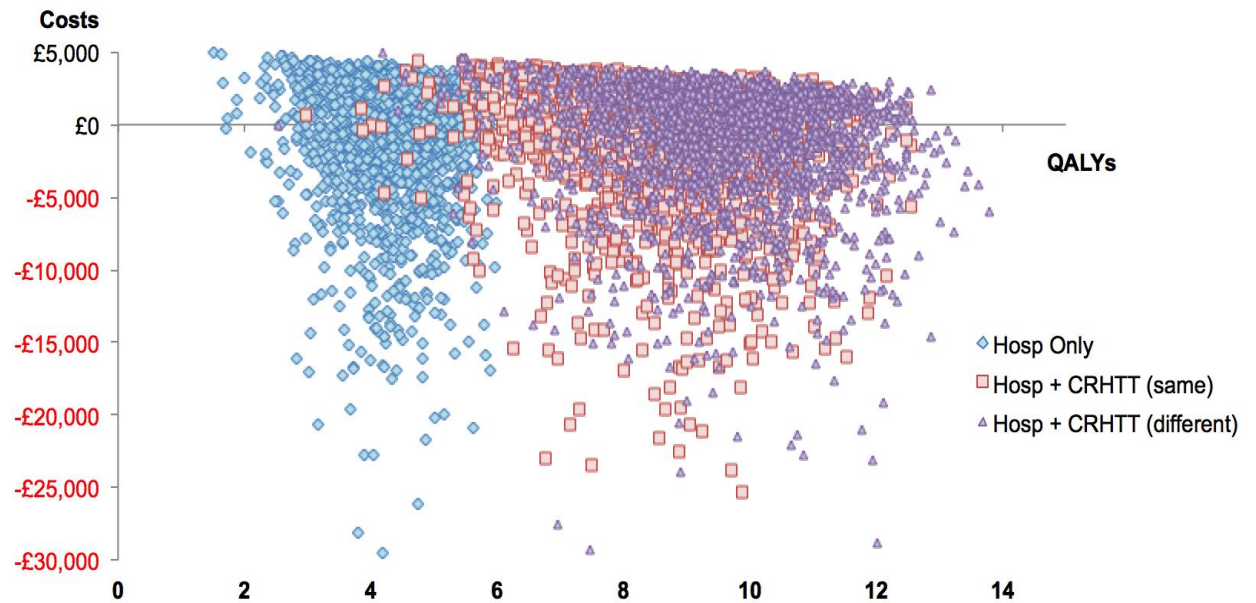
**Scenario 1 (most conservative scenario)**

Assumption: Intervention group has higher H&SC community costs for the duration of treatment (24 months)



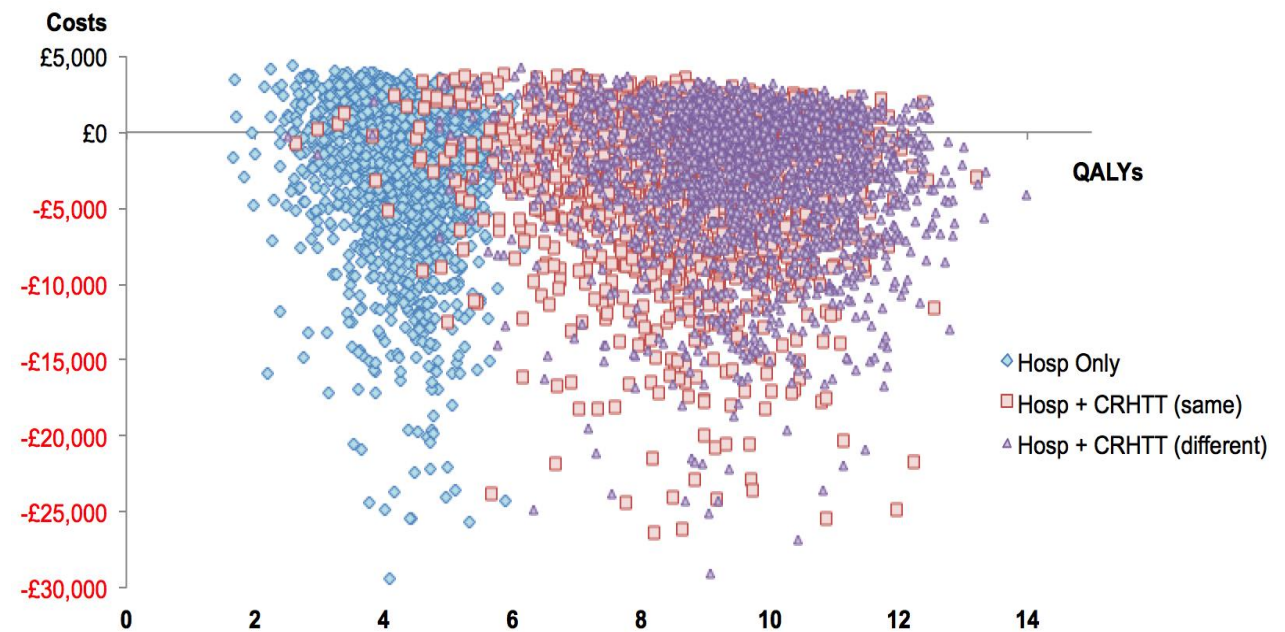
## Scenario 2

Assumption: Control group has higher H&SC community costs for the duration of treatment (24 months)



## Scenario 3 (most optimistic scenario)

Assumption: Control group has higher H&SC community costs for the duration of treatment (24 months) and in the follow-up period (additional 18 months)



Findings from the cost-effectiveness acceptability curve (CEAC)

**Figure 7** presents the cost-effectiveness acceptability curve assuming impact on hospitalisation only.

1. **Figure 8** presents the cost-effectiveness acceptability curve assuming a reduction on both the use of hospital services and CRHTTs. Results are also provided in tabular format (Table 3).
2. There is a 90% probability that the intervention is cost-effective at a willingness-to-pay of £2,200 per additional QALY in the most conservative scenario (scenario 1). In all other increasingly optimistic scenarios, the probability is 100% at a willingness-to-pay of £2,200 (Base case scenario, and scenarios 2 and 3).
3. When the willingness-to-pay per QALY is below £2,200, the assumptions about differences in community health and social care costs are very influential and the probability of the intervention being cost-effective varies.

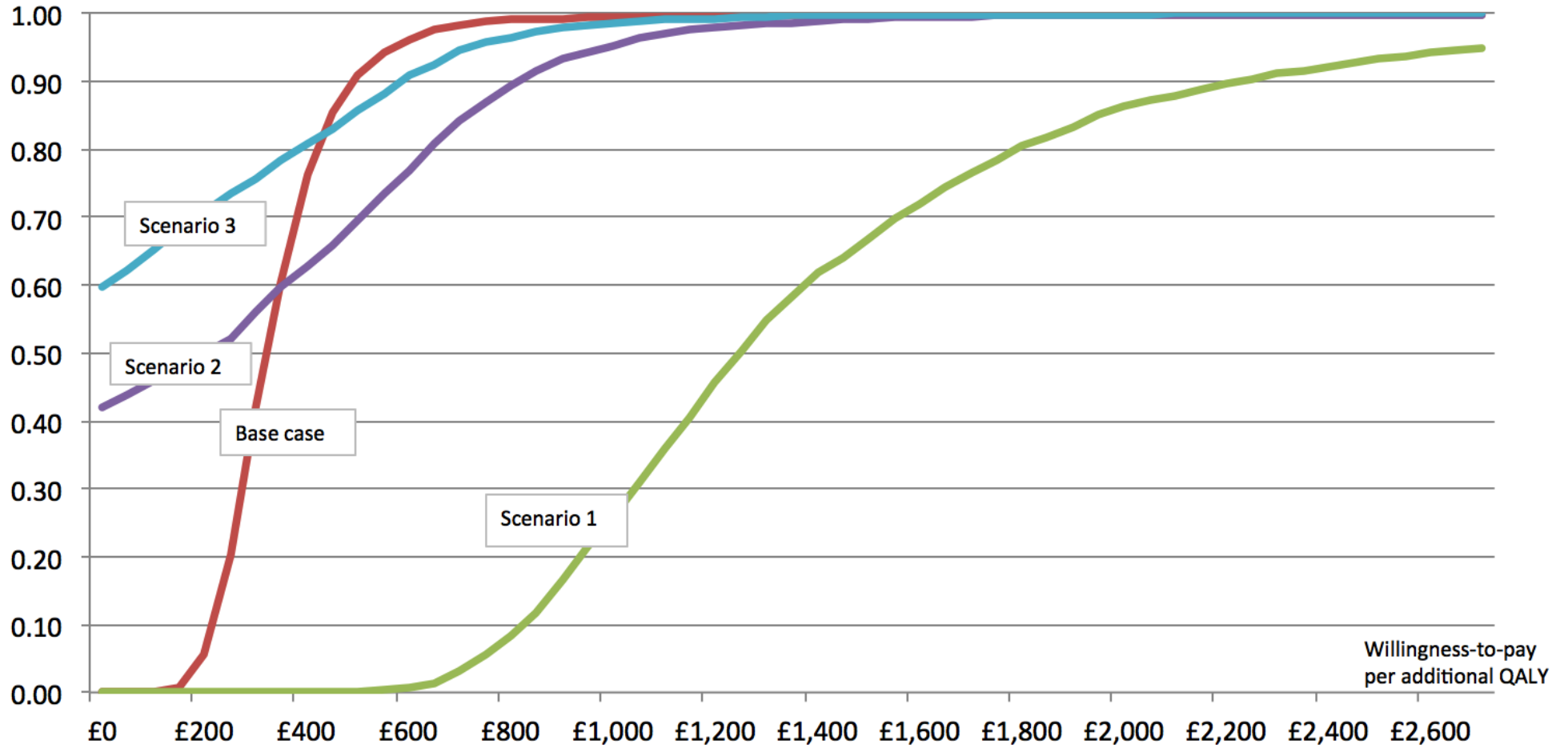
**Table 3** Cost-effectiveness acceptability curves

		<b>Assumptions about H&amp;SC costs between groups</b>			
		<b>Base case</b>	<b>Scenario 1</b>	<b>Scenario 2</b>	<b>Scenario 3</b>
<b>Assumptions about impact</b>		No difference in costs	Intervention has higher costs for duration of treatment (24m)	Control has higher costs for duration of ... Treatment (24m)	Treatment + follow-up (24 + 18m)
	<b>1. Hospitalisation only</b>				
<b>Scenario</b>	<b>B1</b>	<b>S1.1</b>	<b>S2.1</b>	<b>S3.1</b>	
If WTP = £0	0%	0%	42%	60%	
If WTP = £1000	100%	26%	95%	99%	
If WTP = £1,500	100%	67%	100%	100%	
If WTP = £2,000	100%	86%	100%	100%	
If WTP = £2,500	100%	93%	100%	100%	
<b>2. Hospitalisation + CRHTT</b>					
<b>2.1 Same utilities</b>					
<b>Scenario</b>	<b>B2</b>	<b>S1.2</b>	<b>S2.2</b>	<b>S3.2</b>	
If WTP = £0	0%	0%	48%	69%	
If WTP = £1000	99%	88%	100%	100%	
If WTP = £1,500	100%	97%	100%	100%	
<b>2.2 Higher utility for CRHTT</b>					
<b>Scenario</b>	<b>B3</b>	<b>S1.3</b>	<b>S2.3</b>	<b>S3.3</b>	
If WTP = £0	0%	0%	48%	68%	
If WTP = £1000	100%	92%	100%	100%	
If WTP = £1,500	100%	98%	100%	100%	

**Figure 7** Cost-effectiveness acceptability curves across various scenarios. The results reflect the assumption that the intervention only reduces the use of hospital services

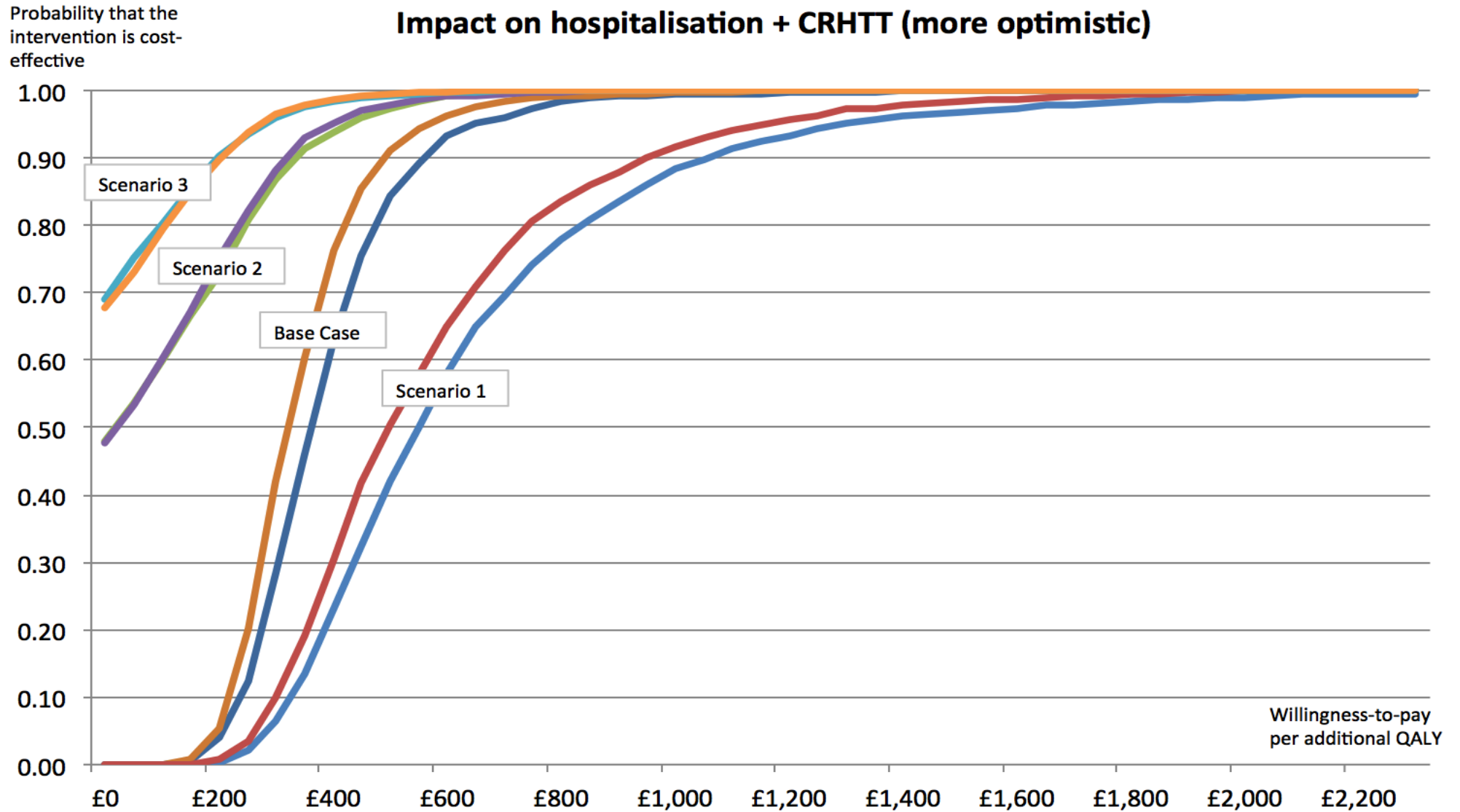
Probability that the intervention is cost-effective

**Impact on hospitalisation only (most conservative scenario)**





**Figure 8** Cost-effectiveness acceptability curves across various scenarios. The results reflect the assumption that the intervention reduces the use of hospital services and CRHTTs. Regarding QALYs, this graph illustrates scenarios where the utilities for hospitalisation and CRHTT are the same or where utilities for CRHTT are higher. Results for both scenarios are similar





### Implications

The implication is that the cost-effectiveness of the intervention is well within the typical thresholds used in clinical decision-making (upper limit being £20,000 per QALY) (see Section 5.1 for a detailed explanation).

### One-way sensitivity analyses

We performed one-way sensitivity analyses with Monte Carlo simulations to determine which parameters were the most influential on the results (Figure 9). We changed values so that they reflected a conservative scenario, varying values by either 50% or 150%.

We conducted one-way sensitivity analyses from the most conservative perspective, which focuses on:

- the base case scenario and scenario 1 (most conservative scenario)
- assuming impact on hospitalisation only.

When we did this, we found that the most influential parameters were:

- the baseline median length of stay in hospital for mania
- the impact of the intervention on reducing median length of stay in hospital
- the impact of the intervention on the proportion of patients admitted to hospital.

For all other parameters, the results are not very different from the original (Figure 9).

Even though baseline median length of stay for mania is **the most** influential, this was the most certain parameter, given that these were taken from current, national data. However, it does illustrate the importance of this parameter in the overall results.

As this study was not a UK-study, the most uncertain parameters are the impact of the intervention on the proportion of patients admitted to hospital and on reducing median length of stay. It is worth noting that by reducing impact by 50% we essentially assumed that the intervention is not different to the control group (see Table 4).

**Table 4** One-way sensitivity analyses, original and new values

<b>Impact of the intervention on ...</b>		
<b>Parameter</b>	<b>Original value</b>	<b>Conservative sensitivity analysis (reducing impact by 50%)</b>
Median length of stay	RR=0.67 Range=0.57 to 0.87	RR=1.01 Range=0.91 to 1.21
Proportion of patients admitted to hospital	RR=0.66 Range = 0.41 to 1.06	RR=0.99 Range=0.41 to 1.06

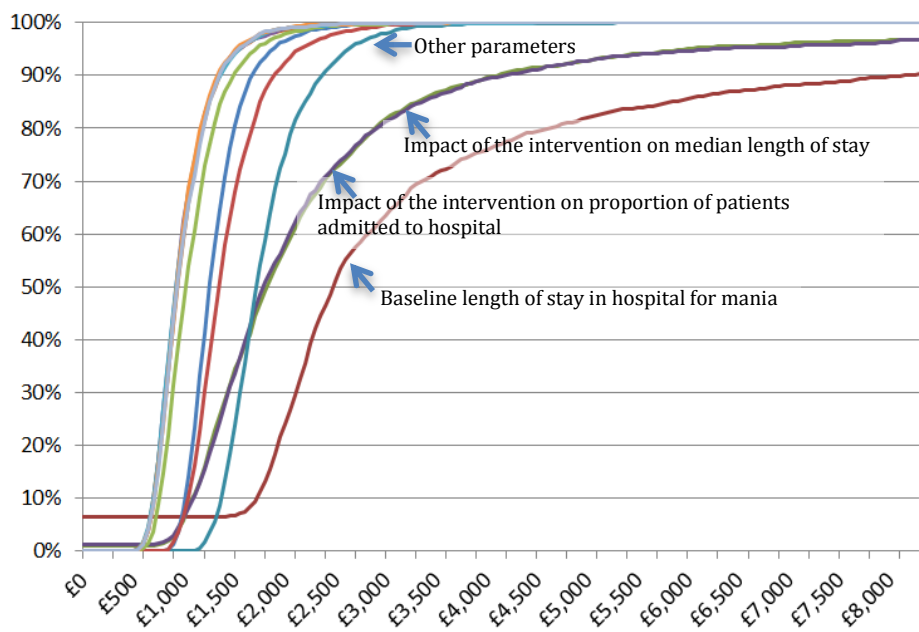
**Figure 9 One-way sensitivity analyses using Monte Carlo simulations on all parameters for base case scenario and scenario 1**

Cost-effectiveness acceptability curves

Assuming impact on hospitalisation only

**Base case scenario**

Assuming no difference in community H&SC costs between groups



**Scenario 1**

Assuming intervention has higher community H&SC costs

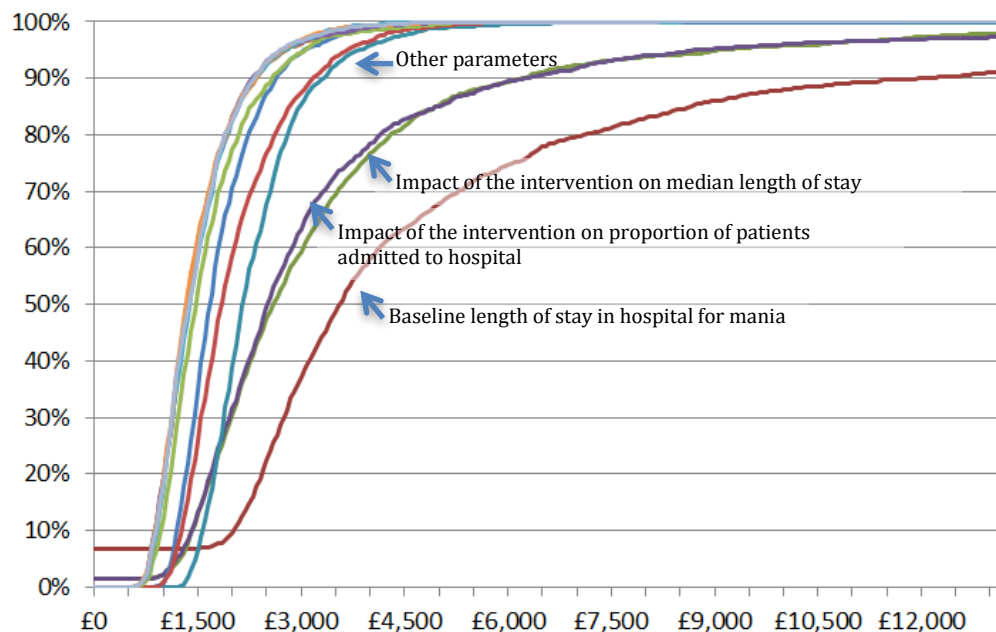
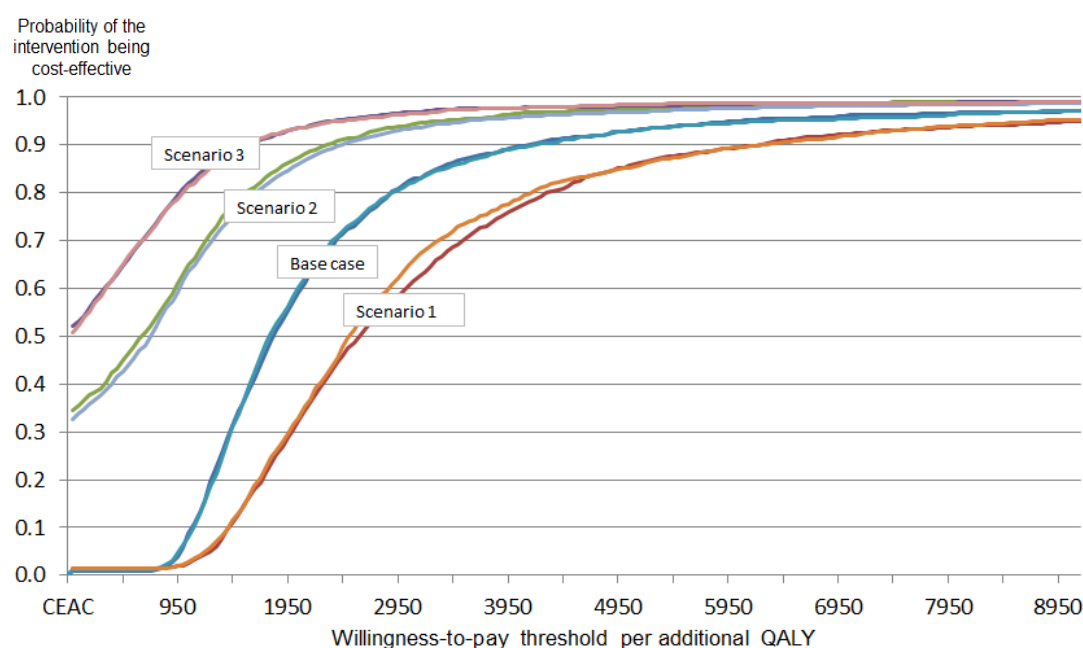


Figure 10 provides a closer look at the sensitivity analysis, focusing on the most uncertain parameters: the impact of the intervention.

- In contrast to Figure 9, we look at all health and social care cost scenarios (base case, scenarios 1–3) and consider impact on both hospitalisation (Figure 10A) and hospitalisation + CRHTT (Figure 10B).

**Figure 10** Impact of the intervention, one-way sensitivity analyses with Monte Carlo simulations

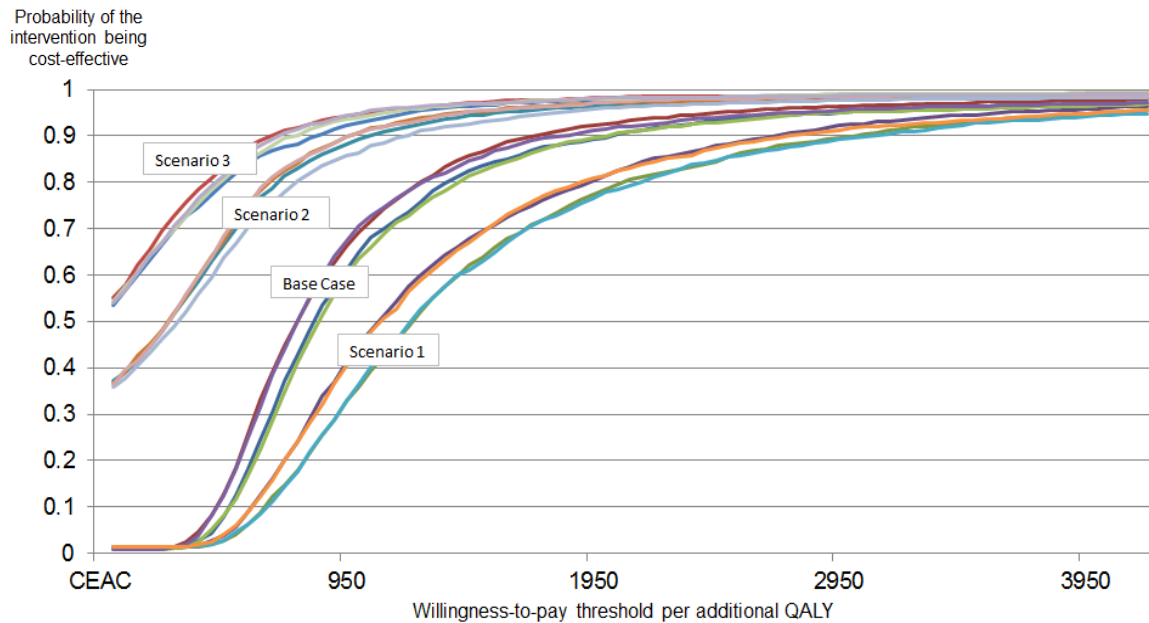
(A) Impact on hospitalization only (conservative scenario)



Using the original data, there was a 100% chance of the intervention being cost-effective at a willingness to pay of £2,200 in the optimistic scenarios (Base case, scenarios 2 and 3) and a 90% chance in the most conservative scenario (scenario 1).

- In contrast to the conservative one-way sensitivity analyses, under the same willingness to pay (at £2,200 per additional QALY), the probability that the intervention is cost-effective varies tremendously between scenarios (scenario 1= 38%, base case = 65%, scenario 2 and 3 = 89% and 94%).
- A 90% chance in the base-case scenario requires an increase in the willingness to pay by almost twice as much: £4,000 per QALY and for Scenario 1, willingness to pay must rise by 3 times as much: £6,050. Even so, it is reassuring that the intervention is still cost-effective by reference to the usual clinical willingness-to-pay threshold.

## (B) Impact on hospitalisation + CRHTT (optimistic scenario)



The results are more favourable in the optimistic scenario when it is assumed that there is an impact on both hospitalisation and CRHTTs.

Using the original data, there was a 100% chance of the intervention being cost-effective at a willingness to pay of £1,000 in the optimistic scenarios (base case, scenarios 2 and 3) and an 88% chance in the most conservative scenario (scenario 1).

- A 90% chance in the base-case scenario requires an increase in the willingness to pay by almost twice as much: £2,000 per QALY and for scenario 1, willingness to pay must rise by 3 times as much: £3,000. Even so, the intervention is still cost-effective by reference to the usual clinical willingness-to-pay threshold.

## 7 Discussion and limitations

There are several limitations to this analysis but we believe that the results are still indicative of the intervention's potential cost-effectiveness in the English context. The main issues relate to assumptions about costs and effects in the analysis.

### Strengths and limitations in the overarching approach

The strength of our analysis is that it takes a conservative approach, including to the estimation of the cost of the intervention and QALY gains. We also deal with some of the uncertainties in the data using both probabilistic analyses (Monte Carlo simulations), conservative one-way sensitivity analyses, and referencing other literature to triangulate findings and fill gaps in information.

The analysis still has some potentially serious limitations, such as not analysing the impact on informal, unpaid carers, or the impact on service users from the perspective of employment, housing and the legal system. However, one might consider that, if anything, results may be underestimated if we assume that positive impacts for service users may, in the best case, positively impact carers, or, at the very least, would not negatively affect them. The same might apply to the impacts on other sectors.

### Strengths and limitations in the data

#### *UK data*

A reassuring finding is that when we carried out sensitivity analyses on less certain UK data, they did not change the results very much. This includes baseline probability of hospital admission, proportion of patients admitted to hospital with mania or depression and the health-state utility of being treated in a CRHTT.

#### *Community health and social care service use*

We had to make assumptions about changes in community health and social care services from an older UK study that was partially comparable in terms of sample characteristics to the people in the intervention study by Kessing et al. However, we addressed this uncertainty through the scenario analyses. We found that the intervention is still cost-effective across these scenarios at very low levels of willingness-to-pay and even in the conservative one-way sensitivity analyses. This is also reassuring.

#### *Structural assumptions about impact*

There are also structural issues. The Danish study measures impact on hospitalisation only, but in the UK context it is unclear whether the intervention would affect not only hospitalisation but also CRHTTs. We also accounted for this uncertainty through scenario analyses. We found that assuming reductions in both hospitalisation and CRHTTs made it much more likely that

the intervention would be cost-effective, even from the perspective of the most conservative scenario (scenario 1).<sup>10</sup>

#### *Impact on hospitalisation*

An important limitation is that the study was not conducted in the UK. Furthermore, results are based on a single study rather than from a meta-analysis. To account for this, we referred to CG 185's meta-analysis of similar psychological interventions (group-based psychological interventions). Results show a positive impact favouring the intervention, reducing hospitalisation and the number of bipolar relapses (CG 185, p257–60). Studies were conducted in European countries. However, the meta-analysis is limited due to the studies being of low quality (as indicated by the GRADE checklist) largely due to imprecision, publication/reporting bias and inconsistency. Furthermore, a slight limitation is that interventions included in the meta-analysis were not completely comparable, but they were similar. The intervention in our analysis is much more intensive (5 components, 24 months long) whereas those in the meta-analysis were single-component interventions lasting 5 to 9 months. We accounted for the uncertainty in effectiveness through conservative one-way sensitivity analyses using Monte Carlo simulations assuming a reduction in impact by 50% (**Error! Reference source not found.**). Even in conservative scenarios, the findings still show that the intervention is cost-effective within clinical thresholds (less than £10,000 per QALY).

#### *Impact on QALYs gained*

We also made assumptions about QALYs gained. QALYs were not directly measured in the study so we estimated gains due to reductions in hospitalisation. We used EQ-5D health-state utility data and found that being in hospital versus other utilities of being in the community were substantially different. However, it is generally unclear whether QALY gains would be different had they been directly measured from the study.

#### Conclusion

In conclusion, the results indicate that the intervention may be cost-effective. Results are dependent on the impact of the intervention on reducing hospitalisation and the corresponding gains in QALYs.

## **8 GC opinions about influential factors in the analysis**

#### Key assumptions in the analysis

Some parameters in the analysis were based on assumptions from the literature. While we considered the full spectrum of possibilities, we wanted to

---

<sup>10</sup> Scenario 1 assumes that H&SC costs are higher for the intervention. If we assume impact on hospitalisation only, mean cost per QALY is £1,367 compared to the assumption that it impacts both hospitalisation and CRHTTs (between £551 and £607 per QALY) (see

**Table 2).**



know whether the Guideline Committee had any strong opinions about choosing one assumption over another.

In particular, the following opinions were sought:

1. Assumptions about differences in community health and social care community costs between intervention and control groups.
  - In the current environment, would individuals who have improved (and who may have fewer needs) use more, fewer or the same services, and if so, which ones?
2. Assumption about utilities.
  - Are utilities for hospitalisation and CRHTTs similar or would individuals using CRHTT have higher utilities?

### Results

The discussion revealed that the GC did not know which health and social care cost scenario was more likely, nor did they know whether health state utilities for hospitalisation or CRHTT would be similar or different.

## **9 Linking evidence to recommendations**

The Guideline Committee was asked whether they wanted to make recommendations based on these findings. In particular, whether to recommend offering the intervention more generally or offered 'in research' to reflect positive but still uncertain findings. The Guideline Committee was initially undecided but then decided to make two recommendations with the support of the economic analysis.

### Recommendation 1.6.4

Consider a staged, group-based psychological intervention for people with bipolar disorder who have had at least 1 hospital admission and are being discharged from hospital. This should include:

- evaluation by a psychiatrist within 2 weeks of discharge
- 3 sequential sets of group sessions led by trained practitioners that focus on, respectively:
  - people's current mental health and recent experiences in hospital
  - psychoeducation or cognitive behavioural therapy
  - early warning signs and coping strategies
- group-based psychoeducation sessions for families and carers.

### Recommendation 1.6.6

During discharge planning offer carers group psychoeducation support. Ensure this is tailored to the specific condition of the person they care for.

## 10 Bibliography

Bauer MS, McBride L, Williford WO, Glick H, Kinosian B, Altshuler L, Beresford T, Kilbourne AM, Sajatovic M (2006) Collaborative care for bipolar disorder: part II. Impact on clinical outcome, function, and costs. *Psychiatr. Serv.* 57: 937–45

Briggs A, Sculpher M, Claxton . (2006) *Decision modelling for health economic evaluation*. New York: Oxford University Press.

Cheema N, Frangou S, McCrone P (2013) Cost-effectiveness of ethyl-eicosapentaenoic acid in the treatment of bipolar disorder. *Therapeutic Advances in Psychopharmacology* 3(2): 73–81

Colom F, Reinares M, Pacchiarotti I, Popovic D, Mazzarini L, Martinez AA, Torrent C, Rosa AR, Palomino-Otiniano R, Franco C, Bonnin CM, Vieta E (2010) Has number of previous episodes any effect on responses to group psychoeducation in bipolar patients? *Acta Neuropsychiatr.* 22: 50–3

Corominas J (2003) A randomized trial on the efficacy of group psychoeducation in the prophylaxis of recurrences in bipolar patients whose disease is in remission. *Arch. Gen. Psychiatry* 60: 402–7

Curtis L (2014) *Unit cost of health and social care 2014*. Canterbury: Personal Social Services Research Unit, University of Kent.

Fajutrao L, Paulsson B, Liu S, Locklear J (2009) Cost-effectiveness of quetiapine plus mood stabilizers compared with mood stabilizers alone in the maintenance therapy of bipolar I disorder: results of a Markov model analysis. *Clinical Therapeutics* 3: 1456–68

Frangou S, Lewis M, McCrone P (2006) Efficacy of ethyl-eicosapentaenoic acid in bipolar depression: randomised double-blind placebo-controlled study. *Br J Psychiatry* 188: 46–50

Gonzalez IA, Echeburua E, Liminana JM, Gonzalez-Pinto A (2012) Psychoeducation and cognitive-behavioral therapy for patients with refractory bipolar disorder: a 5-year controlled clinical trial. *Eur. Psychiatry*, <http://dx.doi.org/10.1016/j.eurpsy.2012.11.002>

Hayhurst HP (2006). Measuring health-related quality of life in bipolar disorder: relationship of the EuroQol (EQ-5D) to condition-specific measures. *Quality of Life Research* 15: 1271–80

HSCIC (2015) *Hospital episode statistics, admitted patient care, England – 2013-14 – national statistics [Excel]* Hospital Episode Statistics, Admitted Patient Care, England – 2013–14: diagnosis. Excel tab title: Primary diagnosis 3 character. <http://www.hscic.gov.uk/catalogue/PUB16719>

Johnson S, Nolan F, Pilling S, Sandor A, Hout J, McKenzie N, et al. (2005) Randomised controlled trial of acute mental health care by a crisis resolution team: the North Islington Crisis Study. *BMJ* 331: 599

Judd LL, Schettler PJ, Akiskal HS, Coryell W, Leon AC, Maser JD, et al. (2008a) Residual symptom recovery from major affective episodes in bipolar disorders and rapid episode relapse/recurrence. *Arch Gen Psychiatry* 65: 386–94

Judd LL, Schettler PJ, Akiskal HS, Coryell W, Leon AC, Maser JD, et al. (2008b) Residual symptom recovery from major affective episodes in bipolar disorders and rapid episode relapse/recurrence. *Archives of General Psychiatry* 65: 386–94

Kessing LV, Hansen HV, Christensen EM, Dam H, Glud C, Wetterslev J (2011) The effects of centralised and specialised combined pharmacological and psychological intervention compared with decentralised and non-specialised treatment in the early course of severe unipolar and bipolar affective disorders – design of two randomised clinical trials. *Trials* 12:32

Kessing L, Hansen H, Hvenegaard A, Christensen E, Dam H, Glud C, Wetterslev J (2013) Treatment in a specialised out-patient mood disorder clinic V. standard out-patient treatment in the early course of bipolar disorder: randomised clinical trial. *The British Journal of Psychiatry* 202: 212–9

Lam, DH, Watkins E, Hayward P, et al. (2003) A randomized controlled study of cognitive therapy of relapse prevention for bipolar affective disorder – outcome of the first year. *Archives of General Psychiatry* 60, 145–52

Lam DH, McCrone P, Wright K, Kerr N (2005) Cost-effectiveness of relapse-prevention cognitive therapy for bipolar disorder: 30-month study. *British Journal of Psychiatry* 186: 500–6

McCrone P, Johnson S, Nolan F, Pilling S, Sandor A, Hout J, et al. (2009) Economic evaluation of a crisis resolution service: a randomised controlled trial. *Epidemiologia e Psichiatria Sociale* 18: 54–8.

NHS Department of Health (2015) NHS reference costs 2013–14. London: Department of Health, <<https://www.gov.uk/government/publications/nhs-reference-costs-2013-to-2014>

Osby U, Brandt L, Correia N, Ekblom A, Sparen P (2001) Excess mortality in bipolar and unipolar disorder in Sweden. *Archives of General Psychiatry* 58: 844–50

Post RM, Leverich GS, Kupka RW, Keck Jr PE, McElroy SL, Altshuler LL, et al. (2010) Early-onset bipolar disorder and treatment delay are risk factors for poor outcome in adulthood. *J Clin Psychiatry* 71: 864–72

- Reinares M, Sanchezz-Moreno J, Fountoulakis KN (2014) Psychosocial interventions in bipolar disorder: what, for whom, and when. *Journal of Affective Disorders* 156: 46–55
- Rosa AR, Gonzalez-Ortega I, Gonzalez-Pinto A, Echeburua E, Comes M, Martinez-Aran A, et al. (2012) One-year psychosocial functioning in patients in the early vs. late stage of bipolar disorder. *Acta Psychiatr Scand* 125: 335–41
- Scott J, Paykel E, Morriss R, Bentall R, Kinderman P, Johnson T, Abbott R, Hayhurst H (2006) Cognitive-behavioural therapy for severe and recurrent bipolar disorders: randomised controlled trial. *Br. J. Psychiatry* 188: 313–20
- Simon GE, Ludman EJ, Bauer MS, Unutzer J, Operskalski B (2006) Long-term effectiveness and cost of a systematic care program for bipolar disorder. *Arch. Gen. Psychiatry* 63: 500–8
- Tohen M, Waternaux CM, Tsuang MT (1990). Outcome in mania. A 4-year prospective follow-up of 75 patients utilizing survival analysis. *Archives of General Psychiatry* 47: 1106–11
- Woodward TC, Tafesse E, Quon P, Kim J, Lazarus A (2009) Cost-effectiveness of quetiapine with lithium or divalproex for maintenance treatment of bipolar I disorder. *Journal of Medical Economics* 12: 259–68
- Woodward TC, Tafesse E, Quon P, Lazarus A (2010) Cost effectiveness of adjunctive quetiapine fumarate extended-release tablets with mood stabilizers in the maintenance treatment of bipolar I disorder. *Pharmacoeconomics* 28: 751–64