Prescribing valproate for bipolar disorder

POMH-UK Quality Improvement Programme. Topic 15a: baseline audit
Prepared by the Prescribing Observatory for Mental Health-UK for
Northamptonshire Healthcare NHS Foundation Trust

Published date: 26/04/2016

Please use the following to cite this report:
Data control statement for POMH-UK quality improvement programme 15a: Prescribing valproate for bipolar disorder

Data ownership and control

In line with the original memorandum of understanding between POMH-UK and member healthcare organisations (predominantly mental health NHS Trusts), the following statement outlines the agreement regarding ownership of the audit data in this quality improvement programme.

Control of the local data submitted to POMH-UK is retained by the healthcare organisation that submitted them. These data have been made available to POMH-UK in a way that is anonymous, with the exception of the identity of the source organisation. The aggregate data from all participating organisations have been analysed by POMH-UK, to produce this customised report. This report summarises the national results, and local results at organisation and clinical team level, benchmarked anonymously against the other organisations taking part.

Data Sharing

There is a publication strategy allowing POMH-UK to publish the anonymous aggregated data on its web site and/or in appropriate scientific journals. Any organisations requesting these audit data will be referred to the POMH-UK reports appearing in the public domain or provided with a list of member healthcare organisations and asked to approach them individually. It is each organisation’s decision whether, and with whom, to share their data.

Data for Quality Improvement

Given that the data are collected for the purpose of quality improvement they are not necessarily representative of performance across the Trust. The use of data for ranking or judgement at an organisational level may therefore not be appropriate. Participation in POMH QIPs can be considered to indicate engagement in quality improvement. Relative and absolute performance against the practice standards should always be considered with the above caveats in mind.

Reflection by clinical teams on their benchmarked performance is perhaps the most potent element of POMH-UK programmes. In addition to performance against the clinical standards, the audit data include demographic, diagnostic and other relevant clinical information that provide a context for interpretation and understanding of practice, which can inform local strategies and systems to achieve improvement. The data collected are designed to be suitable for this clinical purpose, and not for objective ranking of healthcare organisations, for which they are untested and would not necessarily be appropriate.
How to read this report

The term ‘Trust’ has been used throughout this report to refer to all healthcare organisations that participated.

Executive summary
An executive summary of this report starts on page 5. This provides an overview of national performance against the practice standards and how your Trust compares. It also provides some broader observations relating to national prescribing practice (page 40) that may usefully prompt local reflection and discussion.

Practice standards
Page 5 of this report outlines the standards against which prescribing practice was measured in this quality improvement programme (QIP). These practice standards were derived from evidence-based guidelines and agreed by an expert clinical advisory group.

Method
Page 20 provides an outline of the methodology of the QIP. This includes the nature of the clinical audit data collected and how these were cleaned.

National level results
The section beginning on page 21 describes the demographic and clinical characteristics of the total patient audit sample. The findings of the data analysis are presented in graphs and tables, primarily to show the extent to which clinical prescribing across the participating services is meeting the practice standards.

Trust level section
The analyses presented in this section, starting on page 41, allow Trusts to compare the quality of their local practice, with the practice standards in absolute terms and, in relative terms, with that of the other, anonymous, participating Trusts.

Each of the benchmarked graphs in this section provides evidence of performance on a particular aspect of prescribing practice across all Trusts individually and the total national sample (TNS). In each figure, the Trust(s) on the left hand side is closest to meeting the relevant standard while the Trusts on the right are further away from meeting the standard.

Team level results
This section starts on page 58. The figures allow individual clinical teams in each Trust to compare their practice with each other and against the national data. For each figure, the team(s) on the left hand side is closest to meeting the standard. The bar on the far right shows the total national sample (TNS) and the bar next to this shows the overall Trust performance.
Executive Summary

Background
The Prescribing Observatory for Mental Health (POMH-UK) runs national audit-based quality improvement programmes open to all specialist mental health services in the UK. The aim is to help mental health services improve prescribing practice in discrete areas (‘Topics’).

This report presents the results of the baseline audit for a quality improvement programme (Topic 15a), addressing the use of valproate in bipolar disorder. Data are presented at national, Trust and clinical team level.

Practice standards for audit, derived from NICE guidelines

The practice standards were derived from NICE Clinical Guidance 185*, September 2014.

<table>
<thead>
<tr>
<th>1. Do not routinely prescribe valproate for women of child-bearing age</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. If valproate is prescribed for a woman of child-bearing age, there should be documented evidence that the woman:</td>
</tr>
<tr>
<td>a. is aware of the need to use adequate contraception and</td>
</tr>
<tr>
<td>b. has been informed of the risks that valproate would pose to an unborn baby</td>
</tr>
<tr>
<td>3. Prior to initiating treatment with valproate, the following should be documented in the clinical records: weight and/or BMI, the results of liver function tests (LFTs), and a full blood count (FBC)</td>
</tr>
<tr>
<td>4. Patients prescribed valproate should receive written information about the use of this medicine specifically for treating bipolar disorder</td>
</tr>
<tr>
<td>5. Patients prescribed valproate should have an early, on-treatment review that includes screening for the common side effects of the medication (e.g. weight gain, nausea, tremor)</td>
</tr>
<tr>
<td>6. Body weight and/or BMI, blood pressure, plasma glucose and plasma lipids should be measured at least annually during continuing valproate treatment</td>
</tr>
</tbody>
</table>

Treatment target

| 1. Serum valproate levels should not be routinely monitored unless there is evidence of ineffectiveness, poor adherence or poor tolerability/toxicity |


Sample

During September 2015, fifty-five specialist mental health Trusts (listed in Appendix A) within the UK participated in the baseline audit of this quality improvement programme to address the prescribing of valproate in people with bipolar disorder. Data were submitted for 6,705 patients from 648 clinical teams.
**Practice standard 1:** Do not routinely prescribe valproate for women of child-bearing age

**Practice standard 2:** If valproate is prescribed for a woman of child-bearing age, there should be documented evidence that the woman:

a. is aware of the need to use adequate contraception and  
b. has been informed of the risks that valproate would pose to an unborn baby

Where valproate was newly prescribed for a woman of child-bearing age (50 years of age or younger), there was no documented discussion about the need for contraception in almost half and a similar proportion were not informed about the potential teratogenic effects of this medication. In just over a quarter of these women, there was nothing documented to suggest there had been any discussion at all about the potential benefits or side effects of the newly initiated valproate treatment (see Table 13, page 32).

Women of child-bearing age were prescribed slightly lower doses of valproate than men. However in the vast majority of these women the dose of valproate prescribed is known to be associated with at least a three-fold increase in the risk of having a child with a major congenital malformation (see figure 12, page 33).
The recommended, pre-treatment physical health checks were more likely to be completed in patients initiated on valproate while inpatients compared with those started as outpatients. This may partly reflect easier access to phlebotomy in the former setting.

**Figure 2: Proportion of patients prescribed valproate who had test or measures documented in the 3 months before treatment was initiated in the TNS subsample (inpatient n =189/outpatient n=88) and your Trust (inpatient n=3/outpatient n=1)**

Practice standard 3: Prior to initiating treatment with valproate, the following should be documented in the clinical records: weight and/or BMI, the results of liver function tests (LFTs), and a full blood count (FBC).

There was documented evidence for only a minority of patients that written information about valproate was provided at the point treatment was initiated. The extent to which this reflects actual clinical practice or lack of documentation of what should be a routine clinical activity is unknown (see Figure 14, page 35).

Practice standard 4: Patients prescribed valproate should receive written information about the use of this medicine specifically for treating bipolar disorder.

**Figure 3: Written information about the use of valproate offered to inpatients starting treatment: TNS subsample (n=189) and your Trust (n=3)**
**Practice standard 5:** Patients prescribed valproate should have an early, on-treatment review that includes screening for common side effects of the medication (e.g. weight gain, nausea, tremor).

**Figure 4: Documented treatment review within 3 months of valproate initiation, TNS subsample (n=263) and your Trust (n=7)**

<table>
<thead>
<tr>
<th>Therapeutic response</th>
<th>Weight gain or other common side effects of valproate</th>
<th>FBC and/or LFTs</th>
<th>Medication adherence</th>
</tr>
</thead>
<tbody>
<tr>
<td>No documented evidence</td>
<td>Documented evidence of test/measure</td>
<td>Trust 091</td>
<td>Documented evidence of test/measure</td>
</tr>
</tbody>
</table>

**Practice standard 6:** Body weight and/or BMI, blood pressure, plasma glucose and plasma lipids should be measured at least annually during continuing valproate treatment.

**Figure 5: Documented evidence of test/measures over the past 12 months in the TNS subsample (n=1,976) and your Trust (n=22)**

<table>
<thead>
<tr>
<th>Body weight/BMI</th>
<th>Blood pressure</th>
<th>Plasma glucose</th>
<th>Plasma lipids</th>
</tr>
</thead>
<tbody>
<tr>
<td>No documented evidence</td>
<td>Documented evidence of test/measure</td>
<td>Trust 091</td>
<td>Documented evidence of test/measure</td>
</tr>
</tbody>
</table>

**Treatment target 1:** Serum valproate levels should not be routinely monitored unless there is evidence of ineffectiveness, poor adherence or poor tolerability/toxicity.

Only a small minority (227/1,976; 11%) of the total national sample had a documented valproate serum level in the previous year. This suggests that while valproate levels are not routinely monitored in the majority of patients who receive this treatment for bipolar disorder, up to 1 in 9 may receive such monitoring, often in the absence of a clear clinical rationale (see Figure 19, page 39).
Broader observations on prescribing valproate for bipolar disorder to prompt local discussion

A large, epidemiological community study (Lee et al 2010) suggested that the 12-month prevalence of rapid cycling is around a third of those with a lifetime diagnosis of bipolar disorder. The point prevalence of rapid cycling in this POMH-UK sample is 3%, which is considerably lower than might be expected. One possible explanation is that rapid cycling is under-recognised in clinical practice.

The recommended, pre-treatment physical health checks were more likely to be completed in patients initiated on valproate while inpatients compared with those started as outpatients. This may partly reflect easier access to phlebotomy in the former setting.

The main target symptoms for starting valproate treatment were those of mania and hypomania, and, in the vast majority of such cases, valproate was prescribed alongside an antipsychotic.

Overall, valproate was more likely to be prescribed as part of a drug combination than as monotherapy. For example, more than three-quarters (79%) of the patients prescribed valproate were also prescribed an antipsychotic, most commonly quetiapine or olanzapine.

Valproate was more commonly used than lithium, which was prescribed for a quarter (25%) of patients in the sample. This is despite the robust evidence for efficacy with lithium in bipolar disorder, and may partly reflect avoidance by patients and/or clinicians because of concerns about potential side effects and toxicity and the need for regular biochemical monitoring.

The prevalence of antidepressant prescribing for people with bipolar depression is high relative to the prevalence of prescribing of treatments with an arguably stronger evidence-base, such as quetiapine and lamotrigine. This suggests that clinicians may manage bipolar depression in a similar way to unipolar depression.

Just under a quarter of the women of child-bearing age (50 years of age or younger) were prescribed valproate. The data collected on the subsample of women in whom valproate had been started in the past six months revealed poor compliance with the relevant MHRA recommendations. There was no documentation of any discussion about the potential benefits and side effects of the newly-initiated valproate in just over a quarter. There was no documented discussion about the need for contraception in almost half and a similar proportion had not been informed about the potential teratogenic effects of this medication. Despite the burgeoning evidence for harm with valproate in this context, clinical practice remains some way from the audit standard.

At early on-treatment review and during longer-term monitoring, documentation of the assessment of side effects and consideration of medication adherence was limited.

The reason for measuring serum valproate level was unclear in the majority of cases. With the exception of a small number of patients in whom poor adherence or toxicity was suspected, the result appeared unlikely to inform the pharmacological treatment plan.
What happens next?

- We hope that the data presented in this report will generate local review and discussion of prescribing practice for patients with bipolar disorder. In order to facilitate this, Trusts should consider local practice and systems with respect to aspects of care which their POMH-UK data indicate fall short of the standards, or where the Trust, or teams within the Trust, appear to be outliers in terms of their practice.

- Customised PowerPoint slide sets will be generated for each participating Trust, summarising the benchmarked findings of this audit. This is to help ensure that all participating clinical teams have access to the audit findings relating to their own practice.

- Clinicians who reflect on their performance data and generate and implement action plans as appropriate should be encouraged to submit evidence of this process as part of their CPD, to inform their appraisal and to support revalidation.
Table of contents

Data control statement for POMH-UK quality improvement programme 15a: Prescribing valproate for bipolar disorder .......................................................... 2
How to read this report ........................................................................................................ 3
Executive Summary ........................................................................................................... 5
  Background ......................................................................................................................... 5
  Broader observations on prescribing valproate for bipolar disorder to prompt local discussion ................................................................. 9
What happens next? ............................................................................................................... 10
Table of contents ............................................................................................................... 11
List of Figures ..................................................................................................................... 12
List of Tables ....................................................................................................................... 15
Introduction ......................................................................................................................... 16
  POMH-UK ........................................................................................................................ 16
  Clinical background .......................................................................................................... 17
Method .................................................................................................................................. 20
  Data cleaning ..................................................................................................................... 20
1. National level results ....................................................................................................... 21
  1.1: Patient demographic and clinical characteristics ..................................................... 22
  1.2 Antidepressant prescribing ......................................................................................... 24
  1.3 Antipsychotic prescribing ............................................................................................ 26
  1.4 Prescribing of other mood stabilisers ......................................................................... 28
  1.5 Prescribing valproate for women of child-bearing age .............................................. 32
  1.6 Pre-treatment screening (n=277) ............................................................................... 34
  1.7 Early on-treatment review (n=263) .......................................................................... 37
  1.8 Long-term monitoring (n=1,976) .............................................................................. 38
2. Trust level results ........................................................................................................... 41
  2.1 Pre-treatment screening .............................................................................................. 45
  2.2 Early on-treatment ....................................................................................................... 49
  2.3 Long-term monitoring .................................................................................................. 53
  2.4 Treatment Target ........................................................................................................ 57
3. Clinical team level results ............................................................................................. 58
  3.1 Pre-treatment screening .............................................................................................. 59
  3.2 Early on-treatment ....................................................................................................... 61
  3.3 Long-term monitoring .................................................................................................. 62
References ............................................................................................................................ 64
Appendix A: Participating Trusts ...................................................................................... 66
Appendix B: Audit data collection guide and form ........................................................... 67
Appendix C: Clinical and demographic characteristics of patient sample ............... 73
Appendix D: POMH-UK QIP 15 Advisory Group ............................................................. 76

©2016 The Royal College of Psychiatrists.
List of Figures

Figure 1: Proportion of patients prescribed valproate within the total national sample and your Trust .......................................................... 6

Figure 2: Proportion of patients prescribed valproate who had test or measures documented in the 3 months before treatment was initiated in the TNS subsample (inpatient n=189/outpatient n=88) and your Trust .......................................................... 7

Figure 3: Written information about the use of valproate offered to inpatients starting treatment: TNS subsample (n=189) and your Trust .......................................................... 7

Figure 4: Documented treatment review within 3 months of valproate initiation, TNS subsample (n=263) and your Trust .......................................................... 8

Figure 5: Documented evidence of test/measures over the past 12 months in the TNS subsample (n=1,976) and your Trust .......................................................... 8

Figure 6: Patients prescribed antidepressants and nature of the current phase of bipolar disorder .......................................................... 25

Figure 7: Antipsychotic prescribing and nature of the current phase of bipolar disorder .......................................................... 27

Figure 8: Medications prescribed for patients currently in a depressive episode (n=914) .......................................................... 30

Figure 9: Medications prescribed for patients whose current phase of illness is manic (n=546) .......................................................... 30

Figure 10: Medications prescribed for patients whose current phase of illness is stable, in partial or full remission (n=3,575) .......................................................... 31

Figure 11: Valproate dosage for men younger than 50 years of age (n=648) .......................................................... 33

Figure 12: Valproate dosage for women 50 years of age or younger (n=574) .......................................................... 33

Figure 13: Proportion of patients in the subgroup prescribed valproate who had test or measures documented in the 3 months before treatment was initiated: inpatient n=189/outpatient n=88 .......................................................... 34

Figure 14: Written information about the use of valproate offered to inpatients starting treatment (n=189) .......................................................... 35

Figure 15: Clinical reasons/target symptoms for starting valproate (n=277) .......................................................... 36

Figure 16: Documented evidence of decision to continue treatment with valproate (n=263) .......................................................... 37

Figure 17: Documented evidence of test/measures over the past 12 months in the subsample who had been prescribed valproate for more than one year (n=1,976) .......................................................... 38

Figure 18: Decision to continue valproate documented (n=1,976) .......................................................... 38

Figure 19: Reasons for measuring plasma valproate levels and documented results (n=227) .......................................................... 39

Figure 20: Proportion of patients with bipolar disorder prescribed valproate by Trust .......................................................... 44

Figure 21: Proportion of patients prescribed valproate who had BMI/weight measure documented in the 3 months before treatment was initiated, at Trust level and in the TNS subsample (n=277) .......................................................... 45

Figure 22: Proportion of patients prescribed valproate who had liver function tests (LFTs) documented in the 3 months before treatment was initiated, at Trust level and in the TNS subsample (n=277) .......................................................... 46
Figure 23: Proportion of patients prescribed valproate who had full blood count (FBC) documented in the 3 months before treatment was initiated, at Trust level and in the TNS subsample (n=277)

Figure 24: Proportion of patients who received written information about the use of valproate: inpatients only (n=189)

Figure 25: Documented evidence of review of therapeutic response within 3 months of valproate initiation as part of an early on-treatment review (n=263), by Trust

Figure 26: Documented evidence of weight gain or other common side effects of valproate as part of an early on-treatment review (n=263), by Trust

Figure 27: Documented evidence of undertaking FBC and/or LFTs as part of an early on-treatment review (n=263), by Trust

Figure 28: Documented evidence of information relating to medication adherence as part of an early on-treatment review (n=263), by Trust

Figure 29: Documented evidence that body weight and/or BMI have been measured over the past 12 months (n=1,976), by Trust

Figure 30: Documented evidence that blood pressure has been measured over the past 12 months (n=1,976), by Trust

Figure 31: Documented evidence that plasma glucose has been measured over the past 12 months (n=1,976), by Trust

Figure 32: Documented evidence that plasma lipids have been measured over the past 12 months (n=1,976), by Trust

Figure 33: Reasons for measuring plasma valproate levels (n=1,976), by Trust

Figure 34: Proportion of patients with bipolar disorder prescribed valproate, in the TNS and your Trust

Figure 35: Proportion of patients prescribed valproate who had BMI/weight measure documented in the 3 months before treatment was initiated, in the TNS subsample (n=277) and your Trust

Figure 36: Proportion of patients prescribed valproate who had liver function tests (LFTs) documented in the 3 months before treatment was initiated, in the TNS subsample (n=277) and your Trust

Figure 37: Proportion of patients prescribed valproate who had full blood count (FBC) documented in the 3 months before treatment was initiated, in the TNS subsample (n=277) and your Trust

Figure 38: Proportion of patients who were inpatients and written information about the use of valproate received, in the TNS subsample (n=189) and your Trust

Figure 39: Documented evidence of review of therapeutic response within 3 months of valproate initiation, in the TNS subsample (n=263) and your Trust

Figure 40: Documented evidence of weight gain or other common side effects of valproate, in the TNS subsample (n=263) and your Trust

Figure 41: Documented evidence of information relating to medication adherence as part of an early on-treatment review, in the TNS subsample (n=263) and your Trust

Figure 42: Documented evidence that body weight and/or BMI have been measured over the past 12 months, in the TNS subsample (n=1,976) and your Trust

Figure 43: Documented evidence that blood pressure has been measured over the past 12 months, in the TNS subsample (n=1,976) and your Trust

©2016 The Royal College of Psychiatrists.
Figure 44: Documented evidence that plasma glucose have been measured over the past 12 months, in the TNS subsample (n=1,976) and your Trust ..................................................63

Figure 45: Documented evidence that plasma lipids have been measured over the past 12 months, in the TNS subsample (n=1,976) and your Trust ..................................................63

Figure 46: Proportion of males and females for each Trust and the total national sample ........................................................................................................................................73

Figure 47: Age bands of patients by Trust and in the total national sample .................73

Figure 48: Distribution of the three most common ethnic groups by Trust and in the total national sample ........................................................................................................................................74

Figure 49: Patients’ psychiatric diagnoses by Trust and in the total national sample ......74

Figure 50: Current phase of bipolar disorder by Trust and in the total national sample ..75

Figure 51: Clinical service by Trust and in the total national sample ..........................75
List of Tables

Table 1: Demographic characteristics of the total patient sample and subgroups prescribed and not prescribed valproate ................................................................. 22
Table 2: Proportion of male and female patients 50 years of age or younger across subgroups prescribed and not prescribed valproate ................................................. 22
Table 3: Clinical characteristics of the total patient sample and subgroups prescribed and not prescribed valproate .................................................................................. 23
Table 4: Prevalence of antidepressant prescribing in the total national sample and the subgroups prescribed and not prescribed valproate .................................................. 24
Table 5: Antidepressant medication prescribed in the total national sample and the subgroups prescribed and not prescribed valproate .................................................. 24
Table 6: Prevalence of antipsychotic prescribing in the total national sample and the subgroups prescribed and not prescribed valproate .................................................. 26
Table 7: Antipsychotic medication prescribed in the total national sample and the subgroups prescribed and not prescribed valproate .................................................. 26
Table 8: Prevalence of mood stabilisers other than valproate prescribed, in the total national sample and the subgroups prescribed and not prescribed valproate .............. 28
Table 9: Mood stabilisers prescribed in the total national sample and the subgroups prescribed and not prescribed valproate ................................................................. 28
Table 10: Other medications prescribed ................................................................ 28
Table 11: Patient clinical setting and current phase of bipolar disorder .................. 29
Table 12: Women 50 years of age or younger (n=74) started on valproate in the past six months: documented evidence regarding childbearing potential or use of contraception 32
Table 13: Women 50 years of age or younger (n=74): started on valproate in the past six months: documented evidence of safety issues discussed at initiation of valproate treatment ........................................................................................................ 32
Table 14: Documented evidence review within 3 months of valproate initiation (n=263) .......................................................................................................................... 37
Table 15: Number of clinical teams and patient records submitted by each participating Trust ................................................................................................................. 42
Introduction

POMH-UK
The Prescribing Observatory for Mental Health (POMH-UK) runs national audit-based quality improvement programmes open to all specialist mental health services in the UK. The aim is to help mental health services improve prescribing practice in discrete areas (‘Topics’).

Those interested in learning more about the role of POMH-UK should visit the website: http://www.rcpsych.ac.uk/pomh. There are also reviews of the POMH-UK quality improvement methodology in the following publications:

Barnes TRE, Paton C. The role of the Prescribing Observatory for Mental Health (Editorial). British Journal of Psychiatry 2012; 201: 428-429

Barnes TRE, Paton C. Improving prescribing practice in psychiatry. International Review of Psychiatry 2011; 23: 328-335

This report presents the baseline audit results for a quality improvement programme (Topic 15a) addressing the use of valproate medication in people with bipolar disorder.
Clinical background

“Valproate” is the term that is often used to describe different formulations of valproic acid, the active chemical entity. Sodium valproate has been widely used in epilepsy. Valproate semisodium (also known as divalproex) is a non-covalent dimer molecule which has been studied in bipolar disorder and is licensed in the UK as Depakote® (Goodwin GM et al, 2016).

Efficacy in mania

Valproate has good evidence for efficacy in mania but its use in that condition is relatively infrequent except in the situations discussed below, which the 2014 NICE Guidelines for Bipolar Disorder (NICE CG185, 2014) also endorse. Acute treatment trials support the use of valproate in mania (Yildiz A et al, 2011) but network meta-analysis ranks it below the more efficacious dopamine antagonists; the strong evidence base for the latter has resulted in their acceptance as first line pharmacological treatment for mania. Valproate may be preferred, or instituted together with an antipsychotic drug (Grande I et al, 2015), when the plan is to continue it as long-term treatment. Valproate semisodium is effective in severe mania (Macritchie K et al, 2003) when the dose should be titrated upwards quickly to get control but it is also appropriate for the treatment of less severe manic states.

Patients may already be taking valproate when an episode of mania occurs during long-term treatment. Under these conditions it is recommended to optimise the maintenance treatment and add a dopamine antagonist drug (Ogawa Y et al, 2014). The clearest effect is seen when the antipsychotic is added to valproate and not the reverse. An impact of combination treatment on violence is also seen when antipsychotics are added to mood stabilisers (but not vice versa) in Swedish studies (Fazel S et al, 2014). Valproate dose should be reduced after complete remission of symptoms and preferably after 8 or more weeks of euthymia and tapering off may be preferable to sudden discontinuation (Frankes M et al, 2008).

Efficacy in bipolar depression

In a recent review and meta-analysis, four small studies supported a modest effect of valproate in bipolar depression (Smith LA et al, 2010). A larger, more convincing study is required to establish efficacy (Goodwin GM et al, 2016). The 2014 NICE Guidelines for Bipolar Disorder (NICE CG185) recommended that if a patient develops depression while on valproate consideration should be given to increasing the dose within the therapeutic range before combining it with another drug.

Efficacy in long-term treatment

Valproate is endorsed by the 2014 NICE Guidelines for Bipolar Disorder (NICE CG185, 2014) as a second-line agent after lithium for long-term treatment of bipolar disorder. However data on valproate in long-term treatment are limited. The comparison with placebo is driven by a single RCT of valproate (as valproate semisodium, Depakote®) which showed rates for all relapse of 24% against placebo at 38% (Bowden CL et al, 2000). The absolute risk reduction was statistically non-significant (Goodwin GM et al, 2016). The effect on depressive relapse was higher than that for mania (Cipriani A et al, 2010). The BALANCE trial compared valproate, lithium and the combination in a randomized, non-blind maintenance study with a run-in of the combination treatment to minimise drop-outs after randomization. Lithium alone and in combination with valproate was superior to valproate alone (Geddes JR, 2010).

The main evidence for a positive effect of valproate on the long term outcome of bipolar disorder comes from studies of it in combination with antipsychotics. When acute mania or depression responds to the combination of quetiapine with valproate or lithium, then continuing the combination, versus switching to lithium/ valproate monotherapy, is
associated with a lower rate of relapse of both depression and mania (Vieta E et al, 2008), (Suppes T et al, 2009). For olanzapine (Tohen M et al, 2004) and aripiprazole (Marcus R et al, 2011), RCTs have shown that, when the combination of either drug with lithium or valproate is effective in treating acute mania, then continuing the combination is associated with a lower risk of manic relapse than switching to lithium or valproate alone. The price for continuing the combination versus monotherapy is a greater risk of medication side effects.

Side effects and harms

Common adverse reactions to valproate include gastrointestinal pain, rises in hepatic aminotransferases, tremor, and sedation. Patients with past or current hepatic disease may be at increased risk of hepatotoxicity. Mild, asymptomatic leukopenia and thrombocytopenia occur less frequently and are reversible on drug discontinuation and sometimes with dose reduction. Other adverse reactions include hair loss, increased appetite and weight gain.

Rare, but potentially fatal adverse reactions include irreversible hepatic failure, hemorrhagic pancreatitis and agranulocytosis; patients should contact their physician immediately if severe symptoms develop.

The risk of major congenital malformations in the general population is 2-4% and increases with maternal age. Cohort studies have shown that the risk increases to 11% in valproate-exposed babies (Kaneko S et al, 1999). Valproate is associated with a range of congenital abnormalities, including neural tube defects (incidence 1-2%) (Omtzigt JG et al, 1992) and facial dysmorphia, cleft lip and palate, cardiac defects, digital hypoplasia, and nail dysplasia. The risk of congenital abnormalities with valproate is dose related (blood concentrations over 70 micrograms/ml are implicated). Valproate has been particularly singled out for concern because of apparently higher risks of developmental impairments in children who were exposed to valproate in-utero when compared with children born to mothers who were taking other anticonvulsants (for epilepsy). The problems described include lowered IQ and development disorders (Adab N et al, 2004). Recommendations against its use in women of child bearing potential with bipolar disorder and the need for their informed consent if proposing to do so (NICE CG185, 2014) have been strengthened recently (https://www.gov.uk/drug-safety-update/medicines-related-to-valproate-risk-of-abnormal-pregnancy-outcomes).

Many of the risks for bipolar patients may be unavoidable. 30-50% of pregnancies are unplanned in the general population and this rate may be higher again in patients with mania. Most of the danger for organ development is in the first two months, which may be before a woman is aware that she is pregnant. Consequently, if a female patient of childbearing age has to be on valproate, they should be advised about the importance of effective contraception. Pregnancy should be planned in consultation with the psychiatrist which should include a full explanation of the treatment options and their benefit to harm balance. If valproate has to be continued during pregnancy, prescribing slow-release formulations twice or more times daily can minimize high peak concentrations.

Patients who take valproate during the first trimester should be offered maternal alpha-fetoprotein screening and a high resolution ultrasound scan at 16-18 weeks gestation. Folate supplementation is advised for all pregnant women, but it is unclear whether this reduces the increased risk of neural tube defects associated with valproate (Goodwin GM et al, 2016).

Initial workup, dosing, monitoring and key interactions

A general medical history, with special attention to hepatic, haematological and bleeding abnormalities, should be taken. Physical examination should be carried out and weight recorded. Liver function tests and a pregnancy test should be performed in a woman of childbearing age (NICE CG185, 2014).
Valproate semisodium (divalproex) contains a higher fraction of the valproate moiety than sodium valproate and dosing should reflect this when switching between agents. For hospitalised patients with mania, divalproate semisodium can be administered at an initial dosage of 20 to 30 mg/kg per day in inpatients. A serum valproate concentration between 50 and 125 microg/mL has been associated with an acute response. For outpatients, elderly patients, or patients with hypomania or euthymia, start at 500 mg valproate semisodium at night. Titrate the dose upward by 250 to 500 mg/day every few days, depending on adverse reactions. The SmPC suggests divided doses, but in practice a single dose can often be given at night. The maximum adult daily dosage is 60 mg/kg/day, but all patients taking daily doses higher than 45 mg/kg should be carefully monitored. A total dose of 1,250 mg/day is the highest usually well tolerated by outpatients (Goodwin GM et al, 2016).

Repeat liver function tests may be indicated in the first six months of treatment, although clinical vigilance is more important. Severe complications occur early in treatment and most usually in children.

Valproate displaces highly protein-bound drugs (e.g. carbamazepine, olanzapine) from their protein binding sites. Dosage adjustments will be needed. Valproate inhibits the metabolism of lamotrigine, which must be initiated at half the usual dose when added to valproate. Accordingly, lamotrigine dosage should be reduced when valproate is added to it.

**Conclusion**

Despite limited evidence for its long-term benefits, valproate is relatively widely prescribed in the UK. In a study of 4,700 bipolar patients in a primary care data base in the UK, 24% of the patients were prescribed valproate (Hayes J et al, 2011). Of great concern was the observation made in this study that 34% of women of childbearing age were treated with valproate. The 2014 NICE Guidelines for Bipolar Disorder (NICE CG185, 2014) recommend that valproate is not started in primary care to treat bipolar disorder.

Although valproate is widely prescribed, relatively little is known about the circumstances in which it is prescribed in the UK and details on how frequently precautions are considered, the drug monitored and harms mitigated are similarly lacking. These issues with be the focus of this audit.

For References see page 64.
Method

All Trusts and clinical teams were self-selected in that they chose to participate. All participating Trusts/health care organisations are listed in alphabetical order in Appendix A.

A clinical records audit of the use of valproate in people with bipolar disorder was conducted. A questionnaire/audit tool was sent to Trusts with instructions that copies should be made available to allow clinical teams to audit a sample of patients with a primary clinical diagnosis of bipolar disorder (see Appendix B).

The following data were collected:
- Age, gender, ethnicity, diagnosis of bipolar disorder, current phase of bipolar disorder, co-morbid psychiatric diagnoses and care setting
- Dose and formulation of valproate prescribed
- Other medication prescribed, including antipsychotics, antidepressants and mood stabilisers other than valproate
- The main clinical reasons for prescribing valproate
- Evidence of side effect monitoring
- Evidence of information being given about the use of valproate in bipolar disorder
- Evidence that women of childbearing age were given information about the teratogenic potential of valproate and the need for effective contraception

Data cleaning

Data were collected using FUSION (electronic survey software), and stored and analysed using SPSS.

Data were cleaned to correct instances of obvious data entry error. Details of corrections are held on file by POMH-UK; please contact pomh-uk@rcpsych.ac.uk if you wish to examine these.

All figures presented are rounded to zero decimal places for simplicity. Therefore, the total percentages for some charts or graphs add up to 99% or 101%.

The POMH-UK Lead for each participating Trust will be sent an Excel dataset containing their Trust's data. This allows Trusts to conduct further analyses on their own data should they wish.
1. National level results

Fifty-five specialist mental health Trusts (listed in Appendix A) within the UK participated in the baseline audit of this quality improvement programme to address the prescribing of valproate in people with bipolar disorder. Data were submitted for 6,705 patients from 648 clinical teams.

The analyses presented in this section of the report were conducted on the total national sample (TNS: n = 6,705)

Practice standards

1. Do not routinely prescribe valproate for women of child-bearing age

2. If valproate is prescribed for a woman of child-bearing age, there should be documented evidence that the woman:
   a. is aware of the need to use adequate contraception and
   b. has been informed of the risks that valproate would pose to an unborn baby

3. Prior to initiating treatment with valproate, the following should be documented in the clinical records: weight and/or BMI, the results of liver function tests (LFTs), and a full blood count (FBC)

4. Patients prescribed valproate should receive written information about the use of this medicine specifically for treating bipolar disorder

5. Patients prescribed valproate should have an early, on-treatment review that includes screening for the common side effects of the medication (e.g. weight gain, nausea, tremor)

6. Body weight and/or BMI, blood pressure, plasma glucose and plasma lipids should be measured at least annually during continuing valproate treatment

Treatment target

1. Serum valproate levels should not be routinely monitored unless there is evidence of ineffectiveness, poor adherence or poor tolerability/toxicity
1.1: Patient demographic and clinical characteristics

Table 1 below shows that, compared with women, men who have a diagnosis of bipolar disorder are more likely to be prescribed valproate. However, as can be seen in Table 2, valproate is prescribed for one in four women of child-bearing age (defined as 50 years of age or younger).

The prevalence of valproate prescribing is higher in inpatient than in community settings.

Table 1: Demographic characteristics of the total patient sample and subgroups prescribed and not prescribed valproate

<table>
<thead>
<tr>
<th>Key demographic characteristics</th>
<th>TNS N=6,705</th>
<th>Subgroup prescribed valproate N= 2,416</th>
<th>Subgroup not prescribed valproate N=4,289</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2,648 (40%)</td>
<td>1,186 (49%)</td>
<td>1,462 (34%)</td>
</tr>
<tr>
<td>Female</td>
<td>4,057 (60%)</td>
<td>1,230 (51%)</td>
<td>2,827 (66%)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White/White British</td>
<td>5,159 (77%)</td>
<td>1,850 (77%)</td>
<td>3,309 (77%)</td>
</tr>
<tr>
<td>Asian/Asian British</td>
<td>482 (7%)</td>
<td>198 (8%)</td>
<td>284 (7%)</td>
</tr>
<tr>
<td>Black/Black British</td>
<td>409 (6%)</td>
<td>156 (6%)</td>
<td>253 (6%)</td>
</tr>
<tr>
<td>Mixed or other</td>
<td>655 (10%)</td>
<td>212 (9%)</td>
<td>443 (10%)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age in years (SD)</td>
<td>47 (13)</td>
<td>49 (13)</td>
<td>46 (13)</td>
</tr>
<tr>
<td>Clinical service</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adult community mental health team</td>
<td>5,853 (87%)</td>
<td>2,026 (84%)</td>
<td>3,827 (89%)</td>
</tr>
<tr>
<td>Acute adult psychiatric ward or Psychiatric intensive care unit</td>
<td>539 (8%)</td>
<td>250 (10%)</td>
<td>289 (7%)</td>
</tr>
<tr>
<td>Forensic services</td>
<td>132 (2%)</td>
<td>74 (3%)</td>
<td>58 (1%)</td>
</tr>
<tr>
<td>Adult home treatment team/crisis intervention team</td>
<td>114 (2%)</td>
<td>38 (2%)</td>
<td>76 (2%)</td>
</tr>
<tr>
<td>Adult inpatient rehabilitation services</td>
<td>47 (1%)</td>
<td>22 (1%)</td>
<td>25 (1%)</td>
</tr>
<tr>
<td>Tertiary affective disorders service</td>
<td>20 (&lt;1%)</td>
<td>6 (&lt;1%)</td>
<td>14 (&lt;1%)</td>
</tr>
</tbody>
</table>

Table 2: Proportion of male and female patients 50 years of age or younger across subgroups prescribed and not prescribed valproate

<table>
<thead>
<tr>
<th></th>
<th>≤50 years of age</th>
<th>&gt; 50 years of age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescribed valproate</td>
<td>N=1,490</td>
<td>N=2,364</td>
</tr>
<tr>
<td>Male</td>
<td>648 (43%)</td>
<td>538 (46%)</td>
</tr>
<tr>
<td>Female</td>
<td>574 (24%)</td>
<td>656 (39%)</td>
</tr>
<tr>
<td>Not prescribed valproate</td>
<td>N=1,158</td>
<td>N=1,693</td>
</tr>
<tr>
<td>Male</td>
<td>620 (54%)</td>
<td>1,037 (61%)</td>
</tr>
<tr>
<td>Female</td>
<td>1,790 (76%)</td>
<td>620 (54%)</td>
</tr>
</tbody>
</table>

©2016 The Royal College of Psychiatrists.
The data in the table below suggest that valproate may be particularly used to target episodes of elevated mood. Otherwise, the clinical characteristics of the sub-groups prescribed or not prescribed valproate are similar.

The point prevalence of rapid cycling at 3% of those with a diagnosis of bipolar disorder in our sample seems to be low. For example, the findings of a large epidemiological study suggest that the 12-month prevalence of rapid cycling is around a third of those with a lifetime diagnosis of bipolar disorder (Lee et al, 2010).

Table 3: Clinical characteristics of the total patient sample and subgroups prescribed and not prescribed valproate

<table>
<thead>
<tr>
<th>Key demographic characteristics</th>
<th>Total sample N=6,705</th>
<th>Subsample prescribed valproate N=2,416</th>
<th>Subsample not prescribed valproate N=4,289</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis of bipolar disorder</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICD-10 F31 diagnostic code for bipolar disorder</td>
<td>5,782 (86%)</td>
<td>2,118 (88%)</td>
<td>3,664 (85%)</td>
</tr>
<tr>
<td>No ICD-10 code for bipolar disorder but current clinical diagnosis of bipolar disorder</td>
<td>802 (12%)</td>
<td>259 (11%)</td>
<td>543 (13%)</td>
</tr>
<tr>
<td>No ICD-10 code for bipolar disorder but currently has a provisional or differential diagnosis of bipolar disorder</td>
<td>121 (2%)</td>
<td>39 (2%)</td>
<td>82 (2%)</td>
</tr>
<tr>
<td>Current phase of bipolar</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current episode hypomanic (F31.0)</td>
<td>456 (7%)</td>
<td>190 (8%)</td>
<td>266 (6%)</td>
</tr>
<tr>
<td>Current episode manic (F31.1, F31.2)</td>
<td>546 (8%)</td>
<td>273 (11%)</td>
<td>273 (6%)</td>
</tr>
<tr>
<td>Current episode depressed (F31.3, F31.4, F31.5)</td>
<td>914 (14%)</td>
<td>259 (11%)</td>
<td>655 (15%)</td>
</tr>
<tr>
<td>Current episode mixed affective state (F31.6)</td>
<td>289 (4%)</td>
<td>102 (4%)</td>
<td>187 (4%)</td>
</tr>
<tr>
<td>Current stable, in partial or full remission</td>
<td>3,575 (53%)</td>
<td>1,270 (53%)</td>
<td>2,305 (54%)</td>
</tr>
<tr>
<td>Unclear</td>
<td>583 (9%)</td>
<td>211 (9%)</td>
<td>372 (9%)</td>
</tr>
<tr>
<td>Other</td>
<td>342 (5%)</td>
<td>111 (5%)</td>
<td>231 (5%)</td>
</tr>
<tr>
<td>Rapid cycling</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>220 (3%)</td>
<td>103 (4%)</td>
<td>117 (3%)</td>
</tr>
<tr>
<td>No</td>
<td>6,485 (97%)</td>
<td>2,313 (96%)</td>
<td>4,172 (97%)</td>
</tr>
<tr>
<td>F00-F09</td>
<td>64 (1%)</td>
<td>30 (1%)</td>
<td>34 (1%)</td>
</tr>
<tr>
<td>F10-F19</td>
<td>766 (11%)</td>
<td>331 (14%)</td>
<td>435 (10%)</td>
</tr>
<tr>
<td>F20-F29</td>
<td>285 (4%)</td>
<td>121 (5%)</td>
<td>164 (4%)</td>
</tr>
<tr>
<td>F30, F32-F39 excluding bipolar disorder</td>
<td>188 (3%)</td>
<td>50 (2%)</td>
<td>138 (3%)</td>
</tr>
<tr>
<td>F40-F48</td>
<td>370 (6%)</td>
<td>95 (4%)</td>
<td>275 (6%)</td>
</tr>
<tr>
<td>F50-F59</td>
<td>62 (1%)</td>
<td>19 (1%)</td>
<td>43 (1%)</td>
</tr>
<tr>
<td>F60-F69</td>
<td>556 (8%)</td>
<td>170 (7%)</td>
<td>386 (9%)</td>
</tr>
<tr>
<td>F70-F79</td>
<td>62 (1%)</td>
<td>26 (1%)</td>
<td>36 (1%)</td>
</tr>
<tr>
<td>F80-F89</td>
<td>58 (1%)</td>
<td>30 (1%)</td>
<td>28 (1%)</td>
</tr>
<tr>
<td>F90-F98</td>
<td>43 (1%)</td>
<td>15 (1%)</td>
<td>28 (1%)</td>
</tr>
<tr>
<td>F99</td>
<td>22 (&lt;1%)</td>
<td>7 (&lt;1%)</td>
<td>15 (&lt;1%)</td>
</tr>
<tr>
<td>Other current psychiatric diagnoses within ICD-10 categories(^1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F00-F09</td>
<td>64 (1%)</td>
<td>30 (1%)</td>
<td>34 (1%)</td>
</tr>
<tr>
<td>F10-F19</td>
<td>766 (11%)</td>
<td>331 (14%)</td>
<td>435 (10%)</td>
</tr>
<tr>
<td>F20-F29</td>
<td>285 (4%)</td>
<td>121 (5%)</td>
<td>164 (4%)</td>
</tr>
<tr>
<td>F30, F32-F39 excluding bipolar disorder</td>
<td>188 (3%)</td>
<td>50 (2%)</td>
<td>138 (3%)</td>
</tr>
<tr>
<td>F40-F48</td>
<td>370 (6%)</td>
<td>95 (4%)</td>
<td>275 (6%)</td>
</tr>
<tr>
<td>F50-F59</td>
<td>62 (1%)</td>
<td>19 (1%)</td>
<td>43 (1%)</td>
</tr>
<tr>
<td>F60-F69</td>
<td>556 (8%)</td>
<td>170 (7%)</td>
<td>386 (9%)</td>
</tr>
<tr>
<td>F70-F79</td>
<td>62 (1%)</td>
<td>26 (1%)</td>
<td>36 (1%)</td>
</tr>
<tr>
<td>F80-F89</td>
<td>58 (1%)</td>
<td>30 (1%)</td>
<td>28 (1%)</td>
</tr>
<tr>
<td>F90-F98</td>
<td>43 (1%)</td>
<td>15 (1%)</td>
<td>28 (1%)</td>
</tr>
<tr>
<td>F99</td>
<td>22 (&lt;1%)</td>
<td>7 (&lt;1%)</td>
<td>15 (&lt;1%)</td>
</tr>
<tr>
<td>Number of current psychiatric diagnoses</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bipolar disorder only</td>
<td>4,621 (69%)</td>
<td>1,667 (69%)</td>
<td>2,954 (69%)</td>
</tr>
<tr>
<td>One other</td>
<td>1,735 (26%)</td>
<td>621 (26%)</td>
<td>1,114 (26%)</td>
</tr>
<tr>
<td>Multiple</td>
<td>349 (5%)</td>
<td>128 (5%)</td>
<td>221 (5%)</td>
</tr>
</tbody>
</table>

\(^1\) ICD-10 codes and diagnoses: F00-F09 – Organic, including symptomatic, mental disorders; F10-F19 – Mental and behavioural disorders due to psychoactive substance use; F20-F29 – Schizophrenia, schizotypal and delusional disorders; F30-F39 – Mood (affective) disorders; F40-F48 – Neurotic, stress-related and somatoform disorders; F50-F59 – Behavioural syndromes associated with physiological disturbances and physical factors; F60-F69 – Disorders of adult personality and behaviour; F80-F89 – Disorders of psychological development; F90-F98 – Behavioural and emotional disorders with onset occurring in childhood and adolescence; F99 – Unspecified mental disorder.
1.2 Antidepressant prescribing

Table 4 below shows that compared with patients who are prescribed valproate, those who are not prescribed valproate are more likely to be prescribed an antidepressant. One potential explanation for this finding is that valproate prescribing is more prevalent in those whose current episode is mania/hypomania than in those who are depressed (see Table 3) while antidepressants are more often used in those patients who are currently depressed (see Figure 6).

Table 4: Prevalence of antidepressant prescribing in the total national sample and the sub-groups prescribed and not prescribed valproate

<table>
<thead>
<tr>
<th>Number of antidepressants prescribed</th>
<th>TNS N=6,705</th>
<th>Subgroup prescribed valproate N= 2,416</th>
<th>Subgroup not prescribed valproate N=4,289</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>4,345 (65%)</td>
<td>1,747 (72%)</td>
<td>2,598 (61%)</td>
</tr>
<tr>
<td>One</td>
<td>2,156 (32%)</td>
<td>612 (25%)</td>
<td>1,544 (36%)</td>
</tr>
<tr>
<td>Two or more</td>
<td>204 (3%)</td>
<td>57 (2%)</td>
<td>147 (3%)</td>
</tr>
</tbody>
</table>

This high prevalence of antidepressant prescribing is consistent with other surveys of prescribing practice (Levine et al, 2000). NICE concluded that the available evidence primarily supports the use of fluoxetine (ideally in combination with olanzapine) in the treatment of bipolar depression and is cautious about the use of antidepressants for the prevention of relapse (NICE, 2014).

Table 5 below shows that where an antidepressant is prescribed, clinicians do not preferentially select fluoxetine and that around a third of patients who are currently stable are prescribed antidepressants long-term. This suggests that clinicians may manage bipolar depression in a similar way to unipolar depression.

Table 5: Antidepressant medication prescribed in the total national sample and the sub-groups prescribed and not prescribed valproate

<table>
<thead>
<tr>
<th>Antidepressant prescribed</th>
<th>TNS N=6,705</th>
<th>Subgroup prescribed valproate N= 2,416</th>
<th>Subgroup not prescribed valproate N=4,289</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sertraline</td>
<td>556 (8%)</td>
<td>150 (6%)</td>
<td>406 (9%)</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>457 (7%)</td>
<td>135 (6%)</td>
<td>322 (8%)</td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>384 (6%)</td>
<td>107 (4%)</td>
<td>277 (6%)</td>
</tr>
<tr>
<td>Citalopram</td>
<td>346 (5%)</td>
<td>104 (4%)</td>
<td>242 (6%)</td>
</tr>
</tbody>
</table>

Other antidepressants <5% of TNS includes fluoxetine (n=285) duloxetine (n=105), amitriptyline (n=85), escitalopram (n=77), trazodone (n=59), agomelatine (n=12), bupropion (n=9), clomipramine (n=20), dosulepin (n=24), doxepin (n=4), imipramine (n=11), lofepramine (n=26), moclobemide (n=14), nortriptyline (n=5), paroxetine (n=66), phenelzine (n=7), reboxetine (n=9), tranylcypromine (n=3)
Figure 6: Patients prescribed antidepressants and nature of the current phase of bipolar disorder

NB: as prescribing data were cross-sectional, the point at which antidepressant medication was started is not known. It therefore cannot be assumed that antidepressant medication is being used to target symptoms associated with the current phase of bipolar disorder.
1.3 Antipsychotic prescribing

Although the prevalence of antipsychotic prescribing did not differ across the sub-groups prescribed or not prescribed valproate (just over three quarters), subgroups the choice of antipsychotic medication did differ in that olanzapine was more commonly prescribed in the valproate sub-group and quetiapine in the sub-group who were not prescribed valproate.

One in ten of the total national sample were prescribed a depot antipsychotic which probably reflects the perception by clinicians that non-adherence is a common clinical problem.

Table 6: Prevalence of antipsychotic prescribing in the total national sample and the sub-groups prescribed and not prescribed valproate

<table>
<thead>
<tr>
<th>Number of antipsychotics prescribed</th>
<th>TNS N=6,705</th>
<th>Subgroup prescribed valproate N= 2,416</th>
<th>Subgroup not prescribed valproate N=4,289</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>1,516 (23%)</td>
<td>511 (21%)</td>
<td>1,005 (23%)</td>
</tr>
<tr>
<td>One</td>
<td>4,754 (71%)</td>
<td>1,707 (71%)</td>
<td>3,047 (71%)</td>
</tr>
<tr>
<td>Two or more</td>
<td>435 (6%)</td>
<td>198 (8%)</td>
<td>237 (6%)</td>
</tr>
</tbody>
</table>

Table 7: Antipsychotic medication prescribed in the total national sample and the sub-groups prescribed and not prescribed valproate

<table>
<thead>
<tr>
<th>Antipsychotic prescribed</th>
<th>TNS N=6,705</th>
<th>Subgroup prescribed valproate N= 2,416</th>
<th>Subgroup not prescribed valproate N=4,289</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quetiapine</td>
<td>1,733 (26%)</td>
<td>547 (23%)</td>
<td>1,186 (28%)</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>1,313 (20%)</td>
<td>544 (23%)</td>
<td>769 (18%)</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>755 (11%)</td>
<td>218 (9%)</td>
<td>537 (13%)</td>
</tr>
<tr>
<td>Risperidone</td>
<td>404 (6%)</td>
<td>175 (7%)</td>
<td>229 (5%)</td>
</tr>
<tr>
<td>Any depot</td>
<td>804 (12%)</td>
<td>349 (14%)</td>
<td>455 (11%)</td>
</tr>
</tbody>
</table>

Other antipsychotics < 5% of the TNS: (oral/IM) includes haloperidol (n=168), amisulpride (n=104), chlorpromazine (n=71), clozapine (n=69), zuclopenthixol (n=62), promazine (n=26), fluoxetine (n=25), lurasidone (n=24), zuclopenthixol acetate (n=23), sulpiride (n=21), trifluoperazine (n=18), levomepromazine (n=6), paliperidone (n=4), asenapine (n=3), sertindole (n=2), zotepine (n=2), fluphenazine (n=2)

Other antipsychotics < 5% of the TNS: (depot/long-acting): zuclopenthixol decanoate (n=243), fluoxetine decanoate (n=150), paliperidone palmitate (n=110), risperidone (n=99), haloperidol decanoate (n=83), fluphenazine decanoate (n=42), aripiprazole (n=42), pipotiazine palmitate (n=19) and olanzapine pamoate (n=19).
The prevalence of antipsychotic prescribing was highest in those patients whose current phase of illness was mania and olanzapine was the antipsychotic most often prescribed in this sub-group.

NB: as prescribing data were cross-sectional, the point at which antipsychotic medication was started is not known. It therefore cannot be assumed that antipsychotic medication is being used to target symptoms associated with the current phase of bipolar disorder.
1.4 Prescribing of other mood stabilisers

Lithium is a more effective mood stabiliser than valproate (Geddes, 2010) and is recommended by NICE as a first-line prophylactic agent (NICE, 2014). Valproate was prescribed more frequently than lithium in this audit sample (see Table 9) suggesting that lithium may be under-used in clinical practice. Potential explanations are that clinicians use valproate in preference to lithium, perhaps because of concerns about potential side effects and toxicity or to avoid the need for regular biochemical monitoring. It is also possible that this finding reflects preferential sampling of patients prescribed valproate by Trusts because of the focus of the audit.

Table 8: Prevalence of mood stabilisers other than valproate prescribed, in the total national sample and the sub-groups prescribed and not prescribed valproate

<table>
<thead>
<tr>
<th>Number of mood stabilisers prescribed other than valproate</th>
<th>TNS N=6,705</th>
<th>Subgroup prescribed valproate N=2,416</th>
<th>Subgroup not prescribed valproate N=4,289</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>4,157 (62%)</td>
<td>2,011 (83%)</td>
<td>2,146 (50%)</td>
</tr>
<tr>
<td>One</td>
<td>2,312 (35%)</td>
<td>391 (16%)</td>
<td>1,921 (45%)</td>
</tr>
<tr>
<td>Two or more</td>
<td>236 (3%)</td>
<td>14 (1%)</td>
<td>222 (5%)</td>
</tr>
</tbody>
</table>

Table 9: Mood stabilisers prescribed in the total national sample and the sub-groups prescribed and not prescribed valproate

<table>
<thead>
<tr>
<th>Mood stabilisers prescribed</th>
<th>TNS N=6,705</th>
<th>Subgroup prescribed valproate N=2,416</th>
<th>Subgroup not prescribed valproate N=4,289</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valproate</td>
<td>2,416 (36%)</td>
<td>2,416 (100%)</td>
<td>-</td>
</tr>
<tr>
<td>Lithium</td>
<td>1,669 (25%)</td>
<td>250 (10%)</td>
<td>1,419 (33%)</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>829 (12%)</td>
<td>127 (5%)</td>
<td>702 (16%)</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>259 (4%)</td>
<td>36 (1%)</td>
<td>223 (5%)</td>
</tr>
<tr>
<td>Other mood stabilisers</td>
<td>32 (&lt;1%)</td>
<td>6 (&lt;1%)</td>
<td>26 (1%)</td>
</tr>
</tbody>
</table>
As can be seen from Table 10 below, almost one patient in four was prescribed an anxiolytic and/or hypnotic medicine. Given that the majority of patients in the TNS were in partial or full remission at the time of this audit, this proportion seems high. However this may reflect that anxiety is common in people with bipolar disorder and poor sleep is recognised as a risk factor for relapse.

**Table 10: Other medications prescribed**

<table>
<thead>
<tr>
<th>Other medications prescribed</th>
<th>TNS N=6,705</th>
<th>Subgroup prescribed valproate N= 2,416</th>
<th>Subgroup not prescribed valproate N=4,289</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzodiazepine (daytime use)</td>
<td>894 (13%)</td>
<td>374 (16%)</td>
<td>520 (12%)</td>
</tr>
<tr>
<td>Z-hypnotic</td>
<td>661 (10%)</td>
<td>256 (11%)</td>
<td>405 (9%)</td>
</tr>
<tr>
<td>Benzodiazepine (night time use)</td>
<td>524 (8%)</td>
<td>241 (10%)</td>
<td>283 (7%)</td>
</tr>
<tr>
<td>One or more of the above: benzodiazepine (daytime or night time use) or Z-hypnotic</td>
<td>1,617 (24%)</td>
<td>655 (27%)</td>
<td>962 (22%)</td>
</tr>
</tbody>
</table>

Other medications < 5% of the TNS includes promethazine (n=281), pregabalin (n=209), folic acid (n=86), gabapentin (n=48), fish oils (n=23), melatonin (n=21), triidothyronine T3 (n=8) and tryptophan (n=2)

**Table 11: Patient clinical setting and current phase of bipolar disorder**

<table>
<thead>
<tr>
<th>Current phase of bipolar disorder</th>
<th>Acute (PICU and adult psychiatric ward)</th>
<th>Adult home treatment/crisis team</th>
<th>Adult community mental health team</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypomania (n=456)</td>
<td>75 (16%)</td>
<td>16 (4%)</td>
<td>346 (76%)</td>
</tr>
<tr>
<td>Mania (n=546)</td>
<td>220 (40%)</td>
<td>30 (5%)</td>
<td>273 (50%)</td>
</tr>
<tr>
<td>Depressed (n=914)</td>
<td>81 (9%)</td>
<td>24 (3%)</td>
<td>799 (87%)</td>
</tr>
<tr>
<td>Currently stable (n=3,575)</td>
<td>49 (1%)</td>
<td>25 (1%)</td>
<td>3,412 (95%)</td>
</tr>
</tbody>
</table>
When interpreting the following figures it should be borne in mind that the medications shown may have been started prior to the current episode of illness and therefore it cannot be assumed that they were initiated to treat this episode.

**Figure 8: Medications prescribed for patients currently in a depressive episode (n=914)**

- Any antipsychotic
- Any antidepressant
- Valproate
- Quetiapine
- Lithium
- Lamotrigine
- Fluoxetine
- Quetiapine + Lamotrigine
- Olanzapine + Fluoxetine

**Figure 9: Medications prescribed for patients whose current phase of illness is manic (n=546)**

- Any antipsychotic
- Valproate
- Olanzapine
- Quetiapine
- Lithium
- Any antidepressant
- Haloperidol
- Risperidone
Figure 10: Medications prescribed for patients whose current phase of illness is stable, in partial or full remission (n=3,575)
1.5 Prescribing valproate for women of child-bearing age

**Practice standard 1:** Do not routinely prescribe valproate for women of child-bearing age.

**Practice standard 2:** If valproate is prescribed for a woman of child-bearing age, there should be documented evidence that the woman:

a. is aware of the need to use adequate contraception and
b. has been informed of the risks that valproate would pose to an unborn baby.

Table 2 on page 22 shows that valproate is prescribed less often in women of child-bearing age than in men and older women. Nevertheless, one woman in four who was 50 years of age or younger with bipolar disorder was prescribed valproate; this suggests that not all prescribers may be aware of the teratogenic potential of valproate. The data in the Tables below support this conclusion.

**Table 12: Women 50 years of age or younger (n=74) started on valproate in the past six months: documented evidence regarding childbearing potential or use of contraception**

<table>
<thead>
<tr>
<th>Documented evidence regarding woman’s childbearing potential or use of contraception n=74</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>No documented evidence of protection against pregnancy</td>
<td>48 (65%)</td>
<td>26 (35%)</td>
</tr>
<tr>
<td>Prescribed oral contraceptive</td>
<td>9 (12%)</td>
<td>65 (88%)</td>
</tr>
<tr>
<td>Patient has an IUD/coil fitted</td>
<td>4 (5%)</td>
<td>70 (95%)</td>
</tr>
<tr>
<td>Patient has had an injectable contraceptive or implant fitted</td>
<td>6 (8%)</td>
<td>68 (92%)</td>
</tr>
<tr>
<td>Other contraceptive method documented</td>
<td>6 (8%)</td>
<td>68 (92%)</td>
</tr>
<tr>
<td>Patient has undergone an oophorectomy/hysterectomy/endometrial ablation</td>
<td>1 (1%)</td>
<td>73 (99%)</td>
</tr>
</tbody>
</table>

**Table 13: Women 50 years of age or younger (n=74): started on valproate in the past six months: documented evidence of safety issues discussed at initiation of valproate treatment**

<table>
<thead>
<tr>
<th>Documented evidence of the following:</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>A general discussion regarding side effects and benefits of the treatment</td>
<td>49 (66%)</td>
<td>25 (34%)</td>
</tr>
<tr>
<td>Discussion of the need for adequate contraception during valproate treatment</td>
<td>41 (55%)</td>
<td>33 (45%)</td>
</tr>
<tr>
<td>The woman was informed of the risks to the foetus (teratogenicity, including neural tube defects/spina bifida) when valproate is taken during pregnancy</td>
<td>37 (50%)</td>
<td>37 (50%)</td>
</tr>
<tr>
<td>The woman was informed of the implications for the longer-term cognitive development of the child (for example, neuro-development delay, autistic spectrum disorders) when valproate is taken during pregnancy</td>
<td>18 (24%)</td>
<td>56 (76%)</td>
</tr>
<tr>
<td>The woman was given the MHRA leaflet that outlines the problems associated with valproate in pregnancy</td>
<td>6 (8%)</td>
<td>68 (92%)</td>
</tr>
<tr>
<td>None of the above</td>
<td>20 (27%)</td>
<td>54 (73%)</td>
</tr>
</tbody>
</table>

2 Practice did not differ across inpatient and outpatient settings.
The MHRA (http://www.medicines.org.uk/emc/RMM.420.pdf) has concluded that the teratogenic potential of valproate is greatest at higher doses, which they define as being above 1,000mg (1 gram) daily. They further conclude that the available data do not allow for the identification of a threshold dose below which there is no risk. A large registry study (Tomson et al, 2011) reported that the prevalence of major congenital malformations was 4.2% in neonates whose mothers were prescribed less than 700mg/day valproate during pregnancy. The respective figures for neonates born to mothers who were prescribed daily valproate doses of 700 to 1,499mg and 1,500mg and above were 9% and 23% respectively. Note that the recommended starting dose for valproate is above the lower threshold cited in this study.

The figures below show that women are prescribed slightly lower doses of valproate than men. Nevertheless, the doses of valproate prescribed for the vast majority of women of childbearing age are known to be associated with a substantial risk of harm to an unborn child.

**Figure 11: Valproate dosage for men younger than 50 years of age (n=648)**

![Bar chart showing valproate dosage for men](image1)

**Figure 12: Valproate dosage for women 50 years of age or younger (n=574)**

![Bar chart showing valproate dosage for women](image2)
1.6 Pre-treatment screening (n=277)

**Practice standard 3:** Prior to initiating treatment with valproate, the following should be documented in the clinical records: weight and/or BMI, the results of liver function tests (LFTs), and a full blood count (FBC)

Figure 13 below shows that, compared with outpatient settings, baseline physical health checks were more likely to be carried out in inpatient settings. This may partly reflect easier access to phlebotomy in inpatient settings. In one in four patients in inpatient settings and almost one in two in outpatient settings, there were no documented baseline tests/measures for any of the recommended parameters. This makes it difficult if not impossible to determine whether any abnormalities that are identified later are likely to be associated with valproate treatment or not.

**Figure 13:** Proportion of patients in the subgroup prescribed valproate who had test or measures documented in the 3 months before treatment was initiated: inpatient n=189/outpatient n=88
In almost three quarters of inpatients, there was no documented evidence that information about valproate treatment was offered at the time that treatment was initiated. Where written information was provided, it was mostly in the form of a leaflet that addressed the use of this medicine in bipolar disorder.

It is assumed that all outpatients received, as a minimum, a manufacturer’s patient information leaflet (PIL) as this is packed with the medication and it is a legal requirement for dispensing pharmacists to provide it. However 2 in every 5 outpatients received sodium valproate, a preparation that is licensed for epilepsy but not for bipolar disorder. Therefore, such patients would have received a PIL covering the use of this preparation for epilepsy with no mention of bipolar disorder.

**Figure 14: Written information about the use of valproate offered to inpatients starting treatment (n=189)**

- No documented evidence that written information was provided
- A suitable information leaflet covering the use of valproate in the treatment of bipolar disorder was provided
- Written information provided, but content is unclear
- Manufacturer’s patient information leaflet (PIL) packaged with the medication was provided
- A suitable information leaflet covering the use of valproate in the treatment of epilepsy was provided (and other licensed indications)
In three out of every five patients who recently started treatment with valproate, the target symptoms were those of mania/hypomania. The use of valproate in this phase of illness is consistent with the recommendations in NICE guidelines for the treatment of bipolar disorder.

**Figure 15: Clinical reasons/target symptoms for starting valproate (n=277)**

- Acute manic symptoms
- Hypomanic symptoms
- Long-term relapse prevention/symptom control
- Acute mixed affective state
- Depressive symptoms
- Aggressive behaviour
- Impulsivity/poor impulse control
- Rapid cycling of mood
- Suicidality
- Switched from lithium due to tolerability or safety issues
- Alcohol or other substance use
- Affective instability
- Epilepsy
- Unclear

Number of patients
1.7 Early on-treatment review (n=263)

**Practice standard 5:** Patients prescribed valproate should have an early, on-treatment review that includes screening for the common side effects of the medication (e.g. weight gain, nausea, tremor)

Table 14 and Figure 16 below show that around a quarter of patients did not have an early on-treatment review of the efficacy and tolerability of valproate. Where a review was documented, therapeutic response to valproate was more likely to be assessed than side effects.

**Table 14: Documented evidence review within 3 months of valproate initiation (n=263)**

<table>
<thead>
<tr>
<th>Documented evidence that the following were assessed at review:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapeutic benefit/response</td>
<td>177 (67%)</td>
</tr>
<tr>
<td>Weight gain</td>
<td>60 (23%)</td>
</tr>
<tr>
<td>Other common side effects of valproate</td>
<td>92 (35%)</td>
</tr>
<tr>
<td>Liver function tests (LFTs)</td>
<td>72 (27%)</td>
</tr>
<tr>
<td>Full blood count (FBC)</td>
<td>72 (27%)</td>
</tr>
<tr>
<td>Medication adherence</td>
<td>115 (44%)</td>
</tr>
<tr>
<td>None of the above</td>
<td>72 (27%)</td>
</tr>
</tbody>
</table>

**Figure 16: Documented evidence of decision to continue treatment with valproate (n=263)**

- No documented review of valproate within 3 months of starting
- Yes, valproate to continue at the same dose
- Yes, on a different dose of the same preparation
- Yes, as a different preparation
1.8 Long-term monitoring (n=1,976)

**Practice standard 6:** Body weight and/or BMI, blood pressure, plasma glucose and plasma lipids should be measured at least annually during continuing valproate treatment

In almost half of the total national sample, screening for each of the four cardiometabolic risk factors (obesity, hypertension, elevated plasma glucose, dyslipidaemia) had been undertaken in the previous year. Compared with the sub-group who were not prescribed antipsychotic medication in addition to valproate, these proportions were only modestly higher in the sub-group who were co-prescribed antipsychotic medication. This suggests that a diagnosis of bipolar disorder is a major driver for undertaking the NICE-recommended physical health checks (NICE, 2014).

**Figure 17:** Documented evidence of test/measures over the past 12 months in the sub-sample who had been prescribed valproate for more than one year (n=1,976)

*not included in practice standard 6.

Almost one in four patients who had been prescribed valproate for more than 1 year had no documented review of their treatment in the last year. Where a review had taken place, it addressed therapeutic benefit/response in four-fifths of cases and medication adherence in two-thirds.

**Figure 18:** Decision to continue valproate documented (n=1,976)
Only a small minority (227/1,976; 11%) of the total national sample had a documented valproate serum level in the previous year. This suggests that while valproate levels are not routinely monitored in the majority of patients who receive this treatment for bipolar disorder, up to 1 in 9 may receive such monitoring, often in the absence of a clear clinical rationale. In 72% (164/227) of these cases the test was conducted for reasons other than ineffectiveness of treatment, poor adherence or poor tolerability/side effects.

Where testing had been undertaken, the documented rationale for this and the test results are shown in the Figure below. Where the clinical rationale for testing was suspected non-adherence to treatment, the test results confirm this suspicion in the majority of cases. The pattern of test results associated with all other reasons for testing suggests that, overall, testing is unlikely to helpfully inform treatment plans in these cases.

**Figure 19: Reasons for measuring plasma valproate levels and documented results (n=227)**
2. Trust level results

Analyses presented in this section were conducted for each Trust individually and for the total sample to allow benchmarking

Data from each Trust are presented by code.
Your Trust code is 091

Practice standards

1. Do not routinely prescribe valproate for women of child-bearing age

2. If valproate is prescribed for a woman of child-bearing age, there should be documented evidence that the woman:
   a. is aware of the need to use adequate contraception and
   b. has been informed of the risks that valproate would pose to an unborn baby

3. Prior to initiating treatment with valproate, the following should be documented in the clinical records: weight and/or BMI, the results of liver function tests (LFTs), and a full blood count (FBC)

4. Patients prescribed valproate should receive written information about the use of this medicine specifically for treating bipolar disorder

5. Patients prescribed valproate should have an early, on-treatment review that includes screening for the common side effects of the medication (e.g. weight gain, nausea, tremor)

6. Body weight and/or BMI, blood pressure, plasma glucose and plasma lipids should be measured at least annually during continuing valproate treatment

Treatment target

1. Serum valproate levels should not be routinely monitored unless there is evidence of ineffectiveness, poor adherence or poor tolerability/toxicity
Table 15: Number of clinical teams and patient records submitted by each participating Trust

<table>
<thead>
<tr>
<th>Trust code</th>
<th>Number of clinical teams</th>
<th>Patient records</th>
</tr>
</thead>
<tbody>
<tr>
<td>002</td>
<td>3</td>
<td>74</td>
</tr>
<tr>
<td>003</td>
<td>18</td>
<td>171</td>
</tr>
<tr>
<td>005</td>
<td>24</td>
<td>555</td>
</tr>
<tr>
<td>006</td>
<td>10</td>
<td>122</td>
</tr>
<tr>
<td>008</td>
<td>1</td>
<td>151</td>
</tr>
<tr>
<td>009</td>
<td>10</td>
<td>49</td>
</tr>
<tr>
<td>011</td>
<td>6</td>
<td>23</td>
</tr>
<tr>
<td>012</td>
<td>45</td>
<td>341</td>
</tr>
<tr>
<td>013</td>
<td>6</td>
<td>19</td>
</tr>
<tr>
<td>015</td>
<td>5</td>
<td>60</td>
</tr>
<tr>
<td>016</td>
<td>7</td>
<td>146</td>
</tr>
<tr>
<td>017</td>
<td>11</td>
<td>215</td>
</tr>
<tr>
<td>018</td>
<td>9</td>
<td>60</td>
</tr>
<tr>
<td>019</td>
<td>7</td>
<td>157</td>
</tr>
<tr>
<td>020</td>
<td>41</td>
<td>111</td>
</tr>
<tr>
<td>021</td>
<td>5</td>
<td>94</td>
</tr>
<tr>
<td>022</td>
<td>25</td>
<td>48</td>
</tr>
<tr>
<td>027</td>
<td>17</td>
<td>183</td>
</tr>
<tr>
<td>029</td>
<td>7</td>
<td>422</td>
</tr>
<tr>
<td>030</td>
<td>20</td>
<td>91</td>
</tr>
<tr>
<td>031</td>
<td>24</td>
<td>137</td>
</tr>
<tr>
<td>034</td>
<td>9</td>
<td>288</td>
</tr>
<tr>
<td>040</td>
<td>2</td>
<td>85</td>
</tr>
<tr>
<td>042</td>
<td>11</td>
<td>102</td>
</tr>
<tr>
<td>050</td>
<td>21</td>
<td>65</td>
</tr>
<tr>
<td>051</td>
<td>18</td>
<td>59</td>
</tr>
<tr>
<td>054</td>
<td>8</td>
<td>71</td>
</tr>
<tr>
<td>056</td>
<td>1</td>
<td>102</td>
</tr>
<tr>
<td>059</td>
<td>27</td>
<td>197</td>
</tr>
<tr>
<td>062</td>
<td>4</td>
<td>151</td>
</tr>
<tr>
<td>063</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>066</td>
<td>4</td>
<td>100</td>
</tr>
<tr>
<td>068</td>
<td>2</td>
<td>102</td>
</tr>
<tr>
<td>069</td>
<td>24</td>
<td>45</td>
</tr>
<tr>
<td>073</td>
<td>21</td>
<td>147</td>
</tr>
<tr>
<td>074</td>
<td>1</td>
<td>14</td>
</tr>
<tr>
<td>077</td>
<td>18</td>
<td>66</td>
</tr>
<tr>
<td>079</td>
<td>12</td>
<td>96</td>
</tr>
<tr>
<td>080</td>
<td>5</td>
<td>24</td>
</tr>
<tr>
<td>081</td>
<td>9</td>
<td>151</td>
</tr>
<tr>
<td>083</td>
<td>4</td>
<td>24</td>
</tr>
<tr>
<td>084</td>
<td>3</td>
<td>102</td>
</tr>
<tr>
<td>085</td>
<td>34</td>
<td>395</td>
</tr>
<tr>
<td>087</td>
<td>24</td>
<td>118</td>
</tr>
<tr>
<td>089</td>
<td>9</td>
<td>176</td>
</tr>
<tr>
<td>090</td>
<td>8</td>
<td>60</td>
</tr>
<tr>
<td>091</td>
<td>6</td>
<td>87</td>
</tr>
<tr>
<td>092</td>
<td>2</td>
<td>24</td>
</tr>
<tr>
<td>094</td>
<td>13</td>
<td>123</td>
</tr>
<tr>
<td>098</td>
<td>18</td>
<td>110</td>
</tr>
<tr>
<td>099</td>
<td>10</td>
<td>14</td>
</tr>
<tr>
<td>100</td>
<td>6</td>
<td>77</td>
</tr>
<tr>
<td>101</td>
<td>5</td>
<td>58</td>
</tr>
<tr>
<td>104</td>
<td>6</td>
<td>92</td>
</tr>
<tr>
<td>109</td>
<td>1</td>
<td>145</td>
</tr>
<tr>
<td><strong>TNS</strong></td>
<td><strong>648</strong></td>
<td><strong>6,705</strong></td>
</tr>
</tbody>
</table>
**Practice standard 1:** Do not routinely prescribe valproate for women of child-bearing age

**Figure 20:** Proportion of patients with bipolar disorder prescribed valproate by Trust
2.1 Pre-treatment screening

**Practice standard 3:** Prior to initiating treatment with valproate, the following should be documented in the clinical records: weight and/or BMI, the results of liver function tests (LFTs), and a full blood count (FBC).

Figure 21: Proportion of patients prescribed valproate who had BMI/weight measure documented in the 3 months before treatment was initiated, at Trust level and in the TNS subsample (n=277)
Figure 22: Proportion of patients prescribed valproate who had liver function tests (LFTs) documented in the 3 months before treatment was initiated, at Trust level and in the TNS subsample (n=277)
Figure 23: Proportion of patients prescribed valproate who had full blood count (FBC) documented in the 3 months before treatment was initiated, at Trust level and in the TNS subsample (n=277)
**Practice standard 4:** Patients prescribed valproate should receive written information about the use of this medicine specifically for treating bipolar disorder

**Figure 24:** Proportion of patients who received written information about the use of valproate: inpatients only (n=189)
2.2 Early on-treatment

**Practice standard 5:** Patients prescribed valproate should have an early, on-treatment review that includes screening for the common side effects of the medication (e.g. weight gain, nausea, tremor)

Figure 25: Documented evidence of review of therapeutic response within 3 months of valproate initiation as part of an early on-treatment review (n=263), by Trust
Figure 26: Documented evidence of weight gain or other common side effects of valproate as part of an early on-treatment review (n=263), by Trust

- No documented evidence
- Documented evidence of weight gain or other common side effects of valproate
Figure 27: Documented evidence of undertaking FBC and/or LFTs as part of an early on-treatment review (n=263), by Trust

NB: These tests are not directly referred to in practice standard 5 but Trusts expressed an interest in these data being reported.
Figure 28: Documented evidence of information relating to medication adherence as part of an early on-treatment review (n=263), by Trust
2.3 Long-term monitoring

**Practice standard 6:** Body weight and/or BMI, blood pressure, plasma glucose and plasma lipids should be measured at least annually during continuing valproate treatment

**Figure 29:** Documented evidence that body weight and/or BMI have been measured over the past 12 months (n=1,976), by Trust
Figure 30: Documented evidence that blood pressure has been measured over the past 12 months (n=1,976), by Trust

- **No documented evidence**
- **Documented evidence that blood pressure has been measured over the past 12 months**
Figure 31: Documented evidence that plasma glucose has been measured over the past 12 months (n=1,976), by Trust

No documented evidence

Documented evidence that plasma glucose has been measured over the past 12 months
Figure 32: Documented evidence that plasma lipids have been measured over the past 12 months (n=1,976), by Trust
2.4 Treatment Target

**Treatment target 1:** Serum valproate levels should not be routinely monitored unless there is evidence of ineffectiveness, poor adherence or poor tolerability/toxicity

**Figure 33: Reasons for measuring plasma valproate levels (n=1,976), by Trust**

For interpretation of performance against treatment target 1, see figure 19 on page 39.
3. Clinical team level results

Analyses presented in this section were conducted for each clinical team from your Trust individually, for your total Trust sample and for the total national sample to allow benchmarking.

Data from each Trust clinical team are presented by code only.

The POMH-UK Central Project Team does not know the identity of individual teams.

Only the Local POMH lead for your Trust or organisation has the key to team codes. You should contact this person if you need to identify data for your own particular team.
**Practice standard 1:** Do not routinely prescribe valproate for women of child-bearing age

**Figure 34:** Proportion of patients with bipolar disorder prescribed valproate, in the TNS and your Trust

<table>
<thead>
<tr>
<th>Proportion of patients (%)</th>
<th>0%</th>
<th>20%</th>
<th>40%</th>
<th>60%</th>
<th>80%</th>
<th>100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>091.026</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>091.008</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>091.025</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>091.010</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>091.010</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>091.030</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>091.024</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trust 091</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TNS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**3.1 Pre-treatment screening**

**Practice standard 3:** Prior to initiating treatment with valproate, the following should be documented in the clinical records: weight and/or BMI, the results of liver function tests (LFTs), and a full blood count (FBC)

**Figure 35:** Proportion of patients prescribed valproate who had BMI/weight measure documented in the 3 months before treatment was initiated, in the TNS subsample (n=277) and your Trust (n=4)

<table>
<thead>
<tr>
<th>Proportion of patients (%)</th>
<th>No documented evidence</th>
<th>No, but reference to tests or measures being ordered</th>
<th>Yes, fully or partially documented</th>
</tr>
</thead>
<tbody>
<tr>
<td>091.025</td>
<td>1</td>
<td></td>
<td>137</td>
</tr>
<tr>
<td>091.024</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>091.010</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trust 091</td>
<td>1</td>
<td></td>
<td>32</td>
</tr>
<tr>
<td>TNS</td>
<td>100</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Figure 36: Proportion of patients prescribed valproate who had liver function tests (LFTs) documented in the 3 months before treatment was initiated, in the TNS subsample (n=277) and your Trust (n=4)

![Chart showing proportions of patients with LFTs documented.]

- No documented evidence: 2, 1, 1, 3, 0
- No, but reference to tests or measures being ordered: 1, 1, 3, 0
- Yes, fully or partially documented: 145, 54, 158

Practice standard 4: Patients prescribed valproate should receive written information about the use of this medicine specifically for treating bipolar disorder

Figure 37: Proportion of patients prescribed valproate who had full blood count (FBC) documented in the 3 months before treatment was initiated, in the TNS subsample (n=277) and your Trust (n=4)

![Chart showing proportions of patients with FBC documented.]

- No documented evidence: 2, 1, 1, 3, 0
- No, but reference to tests or measures being ordered: 1, 1, 3, 0
- Yes, fully or partially documented: 161, 51, 161

Figure 38: Proportion of patients who were inpatients and written information about the use of valproate received, in the TNS subsample (n=189) and your Trust (n=3)

![Chart showing proportions of patients with written information.]

- No evidence written information was provided: 1, 1, 1, 3, 0
- Yes, some form of written information was provided but not specific to bipolar disorder: 0, 0, 0, 0, 0
- Suitable information regarding use of valproate in bipolar disorder was provided: 10, 27, 29

©2016 The Royal College of Psychiatrists.
3.2 Early on-treatment

**Practice standard 5:** Patients prescribed valproate should have an early, on-treatment review that includes screening for the common side effects of the medication (e.g. weight gain, nausea, tremor)

Figure 39: Documented evidence of review of therapeutic response within 3 months of valproate initiation, in the TNS subsample (n=263) and your Trust (n=7)

![Therapeutic response graph]

Figure 40: Documented evidence of weight gain or other common side effects of valproate, in the TNS subsample (n=263) and your Trust (n=7)

![Weight gain graph]

Figure 41: Documented evidence of information relating to medication adherence as part of an early on-treatment review, in the TNS subsample (n=263) and your Trust (n=7)

![Medication adherence graph]
3.3 Long-term monitoring

Practice standard 6: Body weight and/or BMI, blood pressure, plasma glucose and plasma lipids should be measured at least annually during continuing valproate treatment

Figure 42: Documented evidence that body weight and/or BMI have been measured over the past 12 months, in the TNS subsample (n=1,976) and your Trust (n=22)

Figure 43: Documented evidence that blood pressure has been measured over the past 12 months, in the TNS subsample (n=1,976) and your Trust (n=22)
**Figure 44:** Documented evidence that plasma glucose have been measured over the past 12 months, in the TNS subsample (n=1,976) and your Trust (n=22)

**Figure 45:** Documented evidence that plasma lipids have been measured over the past 12 months, in the TNS subsample (n=1,976) and your Trust (n=22)
References


Lee S et al. Rapid-cycling bipolar disorder: cross-national community study. BJPsych 2010, 196;217-225

Levine J et al. Psychotropic drug prescription patterns among patients with bipolar 1 disorder. Bipolar disorders 2000,2;120-130


Tomson T et al. Dose-dependent risk of malformations with antiepileptic drugs: an analysis of data from the EURAP epilepsy and pregnancy register. Lancet Neurol 2011,10;609-17


Appendix A: Participating Trusts

The Trusts that participated in this audit are listed below in alphabetical order.

5 Boroughs Partnership NHS Foundation Trust
Abertawe Bro Morgannwg University Health Board
Avon & Wiltshire Mental Health Partnership NHS Trust
Barnet, Enfield & Haringey MH NHS Trust
Belfast Health and Social Care Trust
Berkshire Healthcare NHS Foundation Trust
Birmingham and Solihull Mental Health Foundation Trust
Black Country Partnership NHS Foundation Trust
Bradford District Care Trust
Cambridgeshire and Peterborough NHS Foundation Trust
Camden and Islington NHS Foundation Trust
Central and North West London NHS Foundation Trust
Cheshire and Wirral Partnership Foundation Trust
Coventry and Warwickshire Partnership Trust
Cumbria Partnership NHS Foundation Trust
Derbyshire Healthcare NHS Foundation Trust
Devon Partnership Trust
Dorset Healthcare University NHS Foundation Trust
Dudley and Walsall Mental Health Partnership Trust
East London NHS Foundation Trust
Greater Manchester West Mental Health Foundation Trust
Hertfordshire Partnership University NHS Foundation Trust
Kent and Medway NHS and Social Care Partnership Trust
Lancashire Care NHS Foundation Trust
Leeds and York Partnership NHS Foundation Trust
Lincolnshire Partnership NHS Foundation Trust
Manchester Mental Health & Social Care NHS Trust
Mersey Care NHS Trust
NAViGO Health and Social Care CIC
Norfolk & Suffolk NHS Foundation Trust
North East London NHS Foundation Trust
North Essex Partnership NHS Foundation Trust
North Staffordshire Combined Healthcare NHS Trust
Northamptonshire Healthcare NHS Foundation Trust
Northumberland Tyne and Wear NHS Foundation Trust
Nottinghamshire Healthcare NHS Trust
Oxford Health NHS Foundation Trust
Oxleas NHS Foundation Trust
Partnerships in Care
Pennine Care NHS Foundation Trust
Rotherham, Doncaster and South Humber Mental Health Trust
Sheffield Health & Social Care NHS Foundation Trust
Solent NHS Trust
Somerset Partnership NHS Foundation Trust
South Essex Partnership University NHS Foundation
South London and Maudsley NHS Foundation Trust
South Staffordshire and Shropshire Healthcare NHS
South West London and St George's Mental Health Trust
South West Yorkshire Partnership NHS Foundation Trust
Southern Health NHS Foundation Trust
St Andrew’s Healthcare
Surrey and Borders Partnership NHS Foundation Trust
Sussex Partnership NHS Foundation Trust
Tees, Esk and Wear Valleys NHS Foundation Trust
Worcestershire Health & Care Trust
Appendix B: Audit data collection guide and form

**PRACTICE STANDARDS FOR AUDIT**, derived from NICE guidelines
1) Do not routinely prescribe valproate for women of child-bearing age
2) If valproate is prescribed for a woman of child-bearing age, there should be documented evidence that the woman:
   a) is aware of the need to use adequate contraception and
   b) has been informed of the risks that valproate would pose to an unborn baby
3) Prior to initiating treatment with valproate, the following should be documented in the clinical records: weight and/or BMI, the results of liver function tests (LFTs), and a full blood count (FBC)
4) Patients prescribed valproate should receive written information about the use of this medicine specifically for treating bipolar disorder
5) Patients prescribed valproate should have an early, on-treatment review that includes screening for the common side effects of the medication (e.g. weight gain, nausea, tremor)
6) Body weight and/or BMI, blood pressure, plasma, glucose and plasma lipids should be measured at least annually during continuing valproate treatment

**TREATMENT TARGET**
1) Serum valproate levels should not be routinely measured unless there is evidence of ineffectiveness, poor adherence or poor tolerability/toxicity
### Trust, team and patient information (complete for all patients)

**Q1 Team identifier**
The team identifier is your 3-digit Trust code followed by a 3-digit team code e.g. PAM 008.

**Q2 Optional additional identifier**
This field gives your Trust the option of identifying data by site, lead consultant, or any other variable you wish. Your Trust can decide whether or not to use this field.

**Q3 Initials of data collector**
Enter your own initials in this field (e.g. SB). This will enable your team to identify you should we need to query something about the data that have been entered.

**Q4 Patient identifier**
Please assign a numerical code to each patient whom data are collected, for example 1 (Mrs Bloggs-1), Jane Bloggs-2.

**Q5 Patient year of birth**
YYYY (e.g. 1980)

**Q6 Patient gender** (please use the patient’s self-defined gender)
- Male
- Female

**Q7 Patient self-assigned ethnicity as recorded in case notes**
- White British/English or Other
- Asian/Asian British
- Mixed
- Not stated/missing

**Q8 Which service is currently responsible for this patient’s care?**
- Acute adult psychiatric ward
- Psychiatric intensive care unit
- Adult inpatient rehabilitation services
- Adult home treatment team/crisis intervention team

---

### Diagnosis

**Q9 Diagnosis of bipolar disorder** (tick one response only)
- ICD-10 F31.0 diagnostic code for bipolar disorder
- No ICD-10 code for bipolar disorder but currently has a provisional or differential diagnosis of bipolar disorder
- None of the above: no documented diagnosis of bipolar disorder. This patient is ineligible for this audit. Please finish and do not submit data online.

**Q10 Please indicate the diagnosis of the current phase of bipolar disorder. Please ask a clinician if you are unsure how to answer this question.**
- Current episode hypomanic (may be coded as F31.0)
- Current episode manic (F31.1, F31.2)
- Current episode depressed (F31.3, F31.4, F31.5)
- Current episode mixed affective state (F31.6)
- Currently stable, in partial or full remission
- Unclear
- Other* (e.g. F31.7, F31.8, F31.9)

\*If linked to other above, please specify

**Q11 Does this patient have a rapid-cycling bipolar disorder?** This is usually defined as four or more episodes during a 12-month period. Please ask the patient’s psychiatrist if you are unsure how to answer this question.
- Yes
- No

**Q12 Other than bipolar disorder, does this patient have any other current psychiatric diagnoses?** (please tick all that apply)
- Organic, including symptomatic, mental disorders (F00-F09)
- Mental and behavioural disorders due to psychoactive substance use (F10-F19)
- Schizophrenia, schizoaffective, delusional, and other non-affect psych disorders (F20-F29)
- Mood (affective) disorders (F30, F32-39 excluding bipolar disorder)
- Anxiety, dissociative, stress-related, somatoform and other non-psychotic mental disorders (F40-F83)
- Behavioural syndromes associated with physiological disturbances and physical factors (F90-F99)

---

©2016 The Royal College of Psychiatrists.
Q 15 Is this patient currently prescribed any of the following antidepressant medications?

- Agomelatine
- Amitriptyline
- Bupropion
- Clomipramine
- Citalopram
- Dossulipin
- Dasepin
- Duloxetine
- Escitalopram
- Fluoxetine
- Imipramine
- Lofepramine
- Mirtazapine
- Nortriptyline
- Paroxetine
- Phenelzine
- Reboxetine
- Sertraline
- Tranfluoxetamine
- Trazodone
- Venlafaxine
- No antidepressant prescribed
- Other antidepressant*

*If another antidepressant medication has been prescribed, but is not listed above, please specify the drug name.
### Pre-treatment screening (subsample treated for 6 months or less)

<table>
<thead>
<tr>
<th>Q20 At the time that treatment with valproate was started, was the patient a psychiatric inpatient?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Q21 Were the results of the following tests or measures documented in the clinical records in the three months before treatment with valproate was started?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes, fully or partially documented</td>
</tr>
</tbody>
</table>

- Full blood count
- Liver function tests (LFTs)
- Weight or BMI or waist circumference

<table>
<thead>
<tr>
<th>Q22 Is there documented evidence that, at treatment initiation, the patient was offered written information about the use of valproate? (Tick all that apply):</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes, the manufacturer’s patient information leaflet (PL) packaged with the medication</td>
</tr>
<tr>
<td>Yes, a suitable* information leaflet covering the use of valproate in the treatment of epilepsy (and other licensed indications)</td>
</tr>
<tr>
<td>Written information provided, but the content is unclear</td>
</tr>
<tr>
<td>No evidence that written information was provided</td>
</tr>
</tbody>
</table>

*management or from the records of an appropriate professional organization

<table>
<thead>
<tr>
<th>Q23 What was the clinical reason/indication/target symptom for starting valproate treatment? Ask the clinical team if this is not clear from the clinical records. (Tick all that apply)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute mania symptoms</td>
</tr>
<tr>
<td>Hypo/hypomanic symptoms</td>
</tr>
<tr>
<td>Impulsivity/poor impulse control</td>
</tr>
<tr>
<td>Acute, mixed affective state</td>
</tr>
<tr>
<td>Depressive symptoms</td>
</tr>
<tr>
<td>Suicidality</td>
</tr>
<tr>
<td>To manage rapid cycling of mood</td>
</tr>
<tr>
<td>To provide long-term relapse prevention/symptom control</td>
</tr>
</tbody>
</table>

*If other, please state

<table>
<thead>
<tr>
<th>Q24 Is this patient a woman under 50 years of age?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes - go to Q25 and continue</td>
</tr>
</tbody>
</table>
Prescribing valproate for bipolar disorder

Early on-treatment review
(subsample of patients who have been treated with valproate for 3-12 months)

Q28 Early on-treatment review: Was there a documented review of the valproate medication within three months of starting?
- Yes
- No - finish and go to the end of this form

Q29 If yes to Q28, was there documented evidence that any of the following were assessed at the review? (Tick all that apply)
- Therapeutic benefit/response
- Weight gain
- Other common side effects of valproate (see guidance notes)
- Liver function tests (LFTs)
- Full blood count (FBC)
- Medication adherence
- None of the above

Q30 Was a decision to continue valproate documented?
- Yes, at the same dose
- Yes, on a different dose of the same preparation
- Yes, as a different preparation
- No decision documented

When you have answered Q30, please finish and go to the end of the form

Monitoring
(subsample of patients who have been treated with valproate for a year or more)

Q31 Was there documented evidence that any of the following were measured over the previous 12 months? (Tick all that apply)
- Obesity measure (BMI or body weight or waist circumference)
- Blood pressure
- Measure of plasma glucose/HbA1c
- Measure of plasma lipids
- None of the above

Q32 Was there documented evidence that any other potential side effects of valproate (not covered by the measures in Q31) were assessed during the previous 12 months?
See guidance notes
- Yes
- No

*If yes, please specify: [ ]

Q33 Has there been a documented review of valproate medication in the past year?
- Yes - go to Q34 and continue
- No - go to Q36 and continue
Q4 Was there documented evidence that any of the following were considered in the review? (Tick all that apply)

- Therapeutic benefit/response
- Medication adherence
- Neither of the above

Q5 Was the decision to continue valproate documented?

- Yes, at the same dose
- Yes, on a different dose of the same preparation
- Yes, as a different preparation
- No decision documented

Q6 Has a plasma valproate level been measured in the past year? NICE do not recommend that plasma valproate levels should be routinely monitored. However, such monitoring may be appropriate in some clinical circumstances.

- No. Finish, go to the end of this form
- Yes*
  *If yes, please provide the plasma level result (mg/L or microgram/ml) and then go to Q37

Q7 If yes to Q36, what was the documented reason for measuring the most recent plasma valproate level? (Tick all that apply)

- No reason documented
- Lack of response to valproate treatment
- Perceived poor adherence to valproate treatment
- Suspected dose-related side effects
- Other*
  *If ‘other’ was selected, please specify:

---

Guidance notes

Q29 and Q32: Aside from the adverse effects already covered in Q29, valproate SPCs list the following very common (1/10) or common (1/100 to < 1/10) undesirable effects:

- Very common: nausea, tremor

  Common: gastralgia, diarrhoea, extrapyramidal disorder, stupor, somnolence, convulsion, memory impairment, headache, nystagmus, confusional state, agitation, disturbance in attention, hyponatraemia, hypersensitivity, transient and/or dose related alopecia (hair loss), dysmenorrhea, haemorrhage, deafness.

---

All data should be collected by: 30 Sept 2015

These data should be submitted online to POMH-UK by: 30 Oct 2015

If you realise that you have made a mistake with data submission, you are able to edit submitted data before the data entry period ends. Please refer to the DATA ENTRY GUIDANCE NOTES for instructions on how to do this. You will not be able to correct your submitted data after the data entry period ends.

For further information please contact POMH-UK@psych.ac.uk
© 2015 The Royal College of Psychiatrists.
Appendix C: Clinical and demographic characteristics of patient sample

Figure 46: Proportion of males and females for each Trust and the total national sample

The Trust that submitted data for the highest proportion of males is on the left hand side of the Figure and the Trust with the lowest on the right. In this Figure, and all such subsequent figures, the proportions in the TNS are shown on the far right of the Figure. This Figure allows Trusts to compare the demographic characteristics of their sample of patients against the total national sample.

Figure 47: Age bands of patients by Trust and in the total national sample

The Trust with the highest proportion of patients in the 66 years and over age-band is on the right hand side of the Figure and the Trust with the lowest proportion on the left. This Figure allows Trusts to compare the diagnostic profile of their sample of patients against the total national sample.
Figure 48: Distribution of the three most common ethnic groups by Trust and in the total national sample

The Trusts with the highest proportion of White British/Irish patients are on the left hand side of the Figure and the Trust with the lowest proportion on the right. This Figure allows Trusts to compare the demographic characteristics of their sample of patients against the total national sample. Trust teams may like to compare the ethnic breakdown of their patients with those of their catchment area population.

Figure 49: Patients’ psychiatric diagnoses by Trust and in the total national sample

The Trust with the highest proportion of patients without a co-morbid diagnoses is on the left hand side of the Figure and the Trust with the lowest proportion on the right. This Figure allows Trusts to compare the diagnostic profile of their sample of patients against the total national sample.
**Figure 50: Current phase of bipolar disorder by Trust and in the total national sample**

The Trust with the highest proportion of patients with current episode hypomanic is on the left hand side of the Figure and the Trust with the lowest proportion on the right. This Figure allows Trusts to compare the diagnostic profile of their sample of patients against the total national sample.

**Figure 51: Clinical service by Trust and in the total national sample**

The Trust with the highest proportion of patients from acute adult psychiatric wards is on the left hand side of the Figure and the Trust with the lowest proportion on the right. This Figure allows Trusts to compare the diagnostic profile of their sample of patients against the total national sample.
Appendix D: POMH-UK QIP 15 Advisory Group

**Topic 15a Expert advisors**
Dr John C Cookson
Professor Nicol Ferrier

**POMH-UK Project Team**
Professor Thomas Barnes
Sumera Bhatti
Amy Lawson
Carol Paton
Harold Petkus
Krysia Zalewska