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PRESCRIBING OBSERVATORY FOR MENTAL HEALTH-UK

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Prescribing valproate for bipolar disorder

POMH-UK Quality Improvement Programme. Topic 15b: re-audit

Prepared by the Prescribing Observatory for Mental Health-UK for:

East London NHS Foundation Trust

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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 8. 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 14) that may usefully prompt local reflection and discussion.

Practice standards

Page 8 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 16 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 18 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 34, 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 51. 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.

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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 re-audit for a quality improvement programme (Topic 15b) addressing the use of valproate in bipolar disorder. Data are presented at national, Trust and clinical team level.

Practice standards

The practice standards were derived from NICE Clinical Guidance 185[1], September 2014.

Practice standards	
1	Do not routinely prescribe valproate for women of child-bearing age
2a	If valproate is prescribed for a woman of child-bearing age, there should be documented evidence that the woman is aware of the need to use adequate contraception
2b	If valproate is prescribed for a woman of child-bearing age, there should be documented evidence that the woman has been informed of the risks that valproate would pose to an unborn child
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

[1] NICE. Clinical Guideline 185: Bipolar disorder (update): the management of bipolar disorder in adults, children and adolescents in primary and secondary care. London: 2014

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 2017, 56 specialist mental health Trusts (listed in Appendix B) within the UK participated in the re-audit of this quality improvement programme to address the prescribing of valproate in people with bipolar disorder. Data were submitted for 6025 patients from 665 clinical teams.

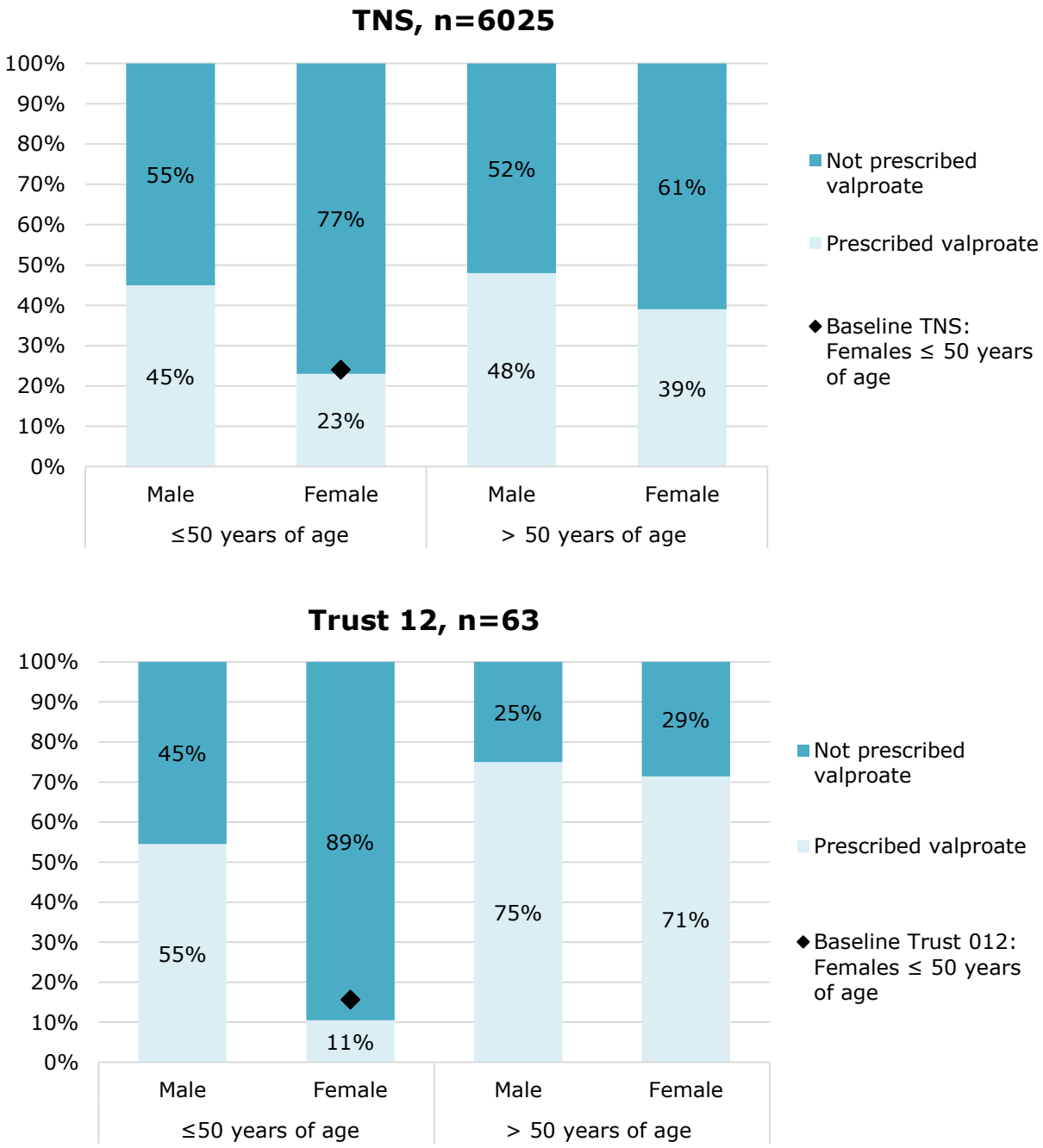
Key national findings

Performance against practice standards

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

At re-audit, valproate was prescribed for nearly 1 in 4 women of child-bearing age (≤ 50 years) in the total national sample. There has been virtually no change since baseline.

Figure 1: Proportion of patients prescribed valproate by gender and age group, at re-audit



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

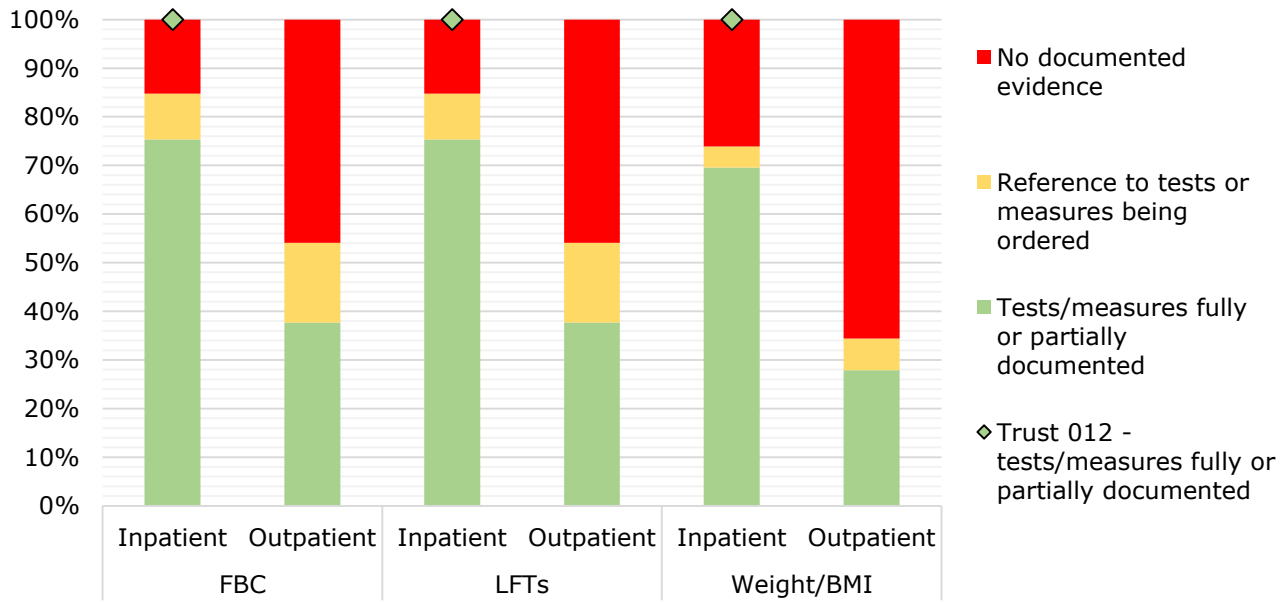
Where valproate was newly prescribed for a woman of child-bearing age (50 years of age or younger), there was no documented discussion about the need for contraception in just under a third and almost a half were not informed about the potential teratogenic effects of this medication. In just over a fifth 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 12, page 26). Performance against this standard in your Trust can be seen in Tables 11 and 12 on pages 25-26.

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 an increased risk of having a child with a major congenital malformation (see figure 8, page 27).

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)

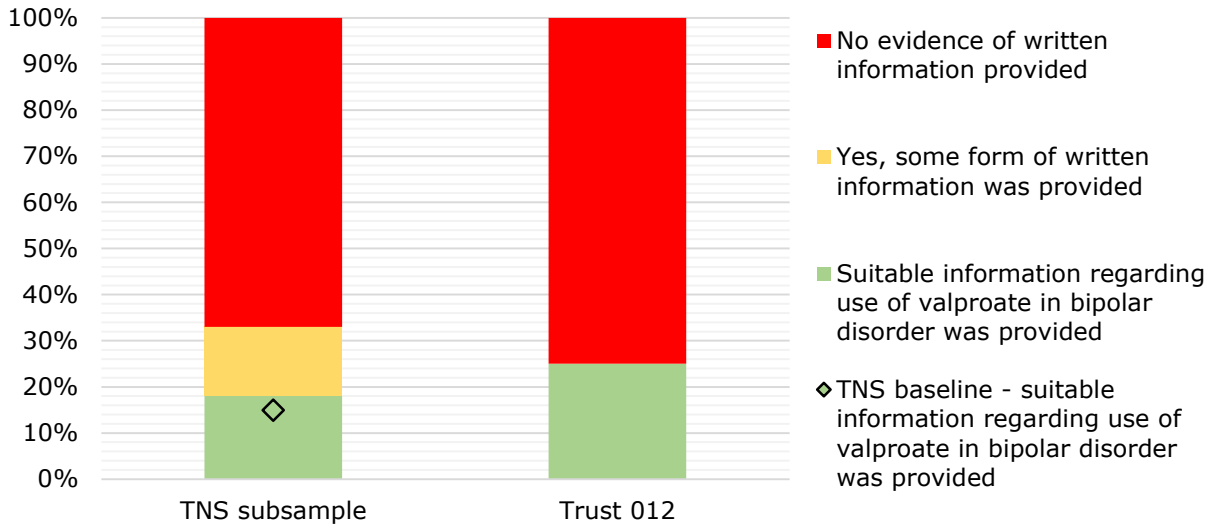
The recommended, pre-treatment physical health checks were more likely to be completed for inpatients initiated on valproate compared with those started as outpatients. This may partly reflect easier access to phlebotomy in the former setting.

Figure 2: Proportion of patients prescribed valproate who had tests or measures, documented in the 3 months before treatment was initiated: national subsample started on valproate in the last 6 months (inpatient n=138/outpatient n=61), and in your Trust (inpatient n=4), at re-audit



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

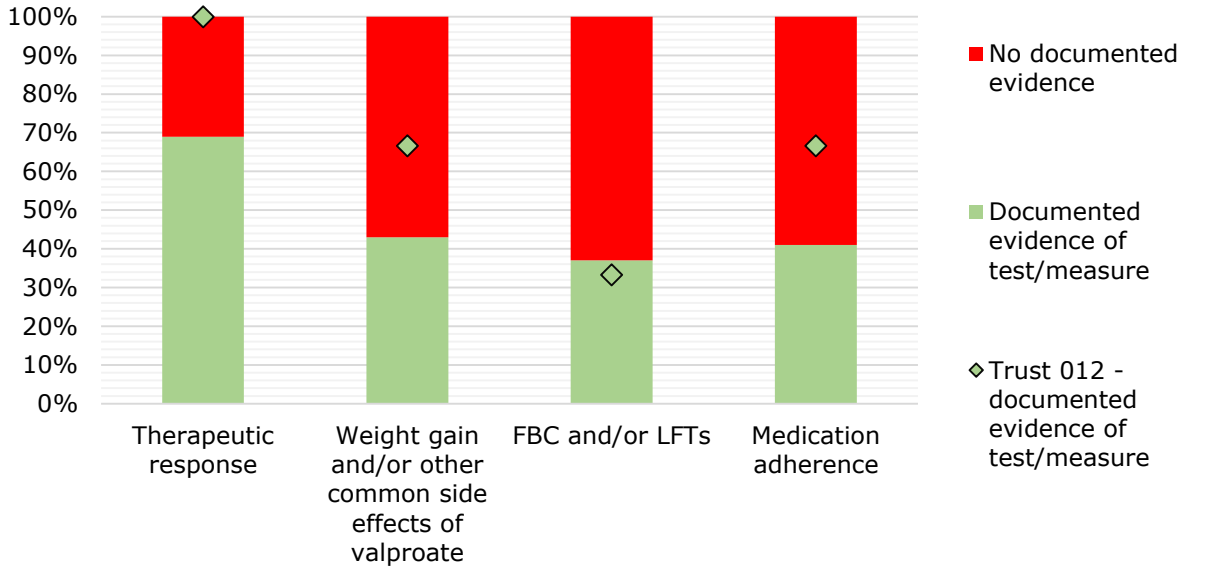
Figure 3: Written information about the use of valproate offered to inpatients: national subsample started on valproate in the last 6 months (n=138) and your Trust (n=4), at re-audit



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 10, page 29).

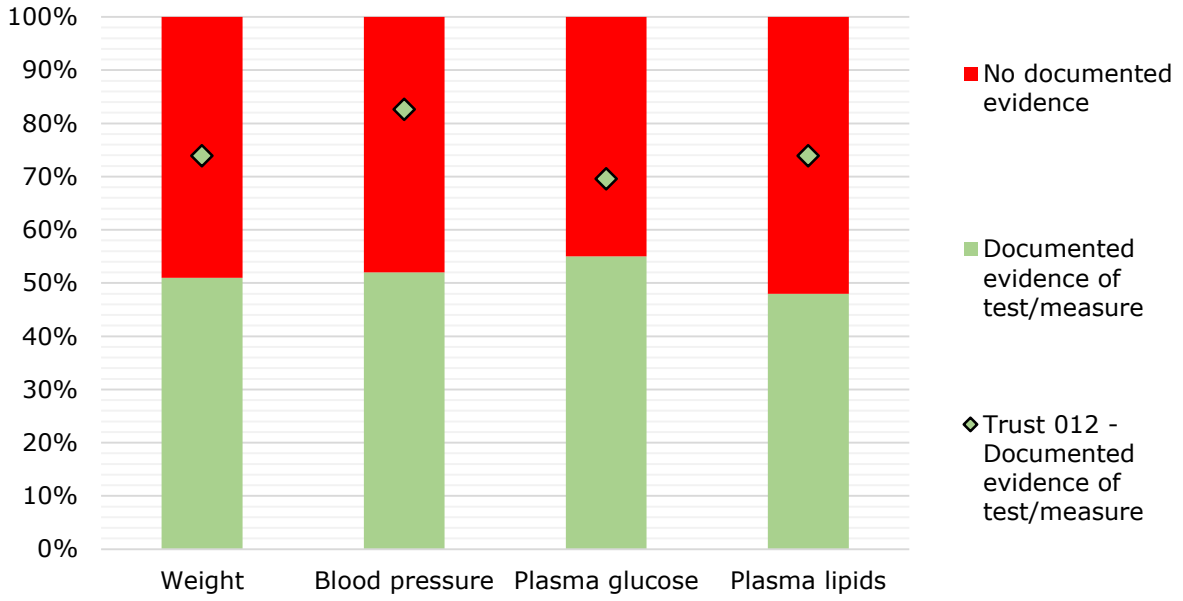
5	Patients prescribed valproate should have an early, on-treatment review that includes screening for the common side effects of the medication (e.g. weight gain, nausea, tremor)

Figure 4: Documented assessments as part of an early on-treatment review: national subsample treated with valproate for 3-12 months (n=235) and your Trust (n=3), at re-audit



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 tests or measures conducted over the past 12 months: national subsample treated with valproate for a year or more (n=1805) and your Trust (n=23), at re-audit



Performance against 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

Only a small minority (136/1805; 8%) 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, around 1 in 12 may receive such monitoring, often in the absence of a clear clinical rationale (see Figure 15, page 33).

Broader observations on prescribing valproate for bipolar disorder to prompt local discussion

As at baseline in 2016, valproate was more commonly prescribed (36%) than lithium (23%) in the total national sample, despite the more robust evidence of efficacy for the latter. This may partly reflect a reluctance to use lithium because of concerns about potential toxicity and the burden of biochemical monitoring.

Practice standards 1, 2 and 3

As at baseline, women with bipolar disorder were less likely than men to be prescribed valproate, although in those women who were 50 years of age or younger (i.e. of child-bearing age), valproate was prescribed for almost a quarter. However, since the baseline audit there have been modest improvements in the proportion of women of child-bearing age starting valproate with whom there was a documented discussion about contraception and/or a record of its prescription and who had been given verbal and/or written information about the teratogenic potential of valproate. Specifically, the recent MHRA patient information leaflet aimed at women of child-bearing age had been given to almost a quarter of the women in this subgroup at re-audit. However, there was no documented evidence of protection against pregnancy in just over a half.

These findings suggest that systems to minimise harm from valproate in women of child-bearing age are not reliably implemented in all mental health services. Such systems may need to take account of the finding that valproate is most commonly started during episodes of hypomania/mania, which has implications for the effective and appropriate communication of risk and the validity of a patient's acknowledgment of this.

Practice standard 5

As at baseline, documentation of the assessment of valproate side effects and consideration of medication adherence at early on-treatment review was limited.

Treatment target

Compared with the baseline findings, performance against the 'treatment target' had improved overall. Of those patients treated for more than a year, there was a small reduction from baseline in the proportion having a serum valproate level measured in the past year. The proportion of such levels that had been carried out as part of routine monitoring or for no documented reason had halved.

Antipsychotic medication

In the total national sample, an antipsychotic medication was prescribed for almost 80% of cases. This was a depot/LAI antipsychotic preparation in almost 10% of cases, which may reflect the perception by clinicians that poor medication adherence is not uncommon.

Antidepressant medication

NICE supports the use of fluoxetine for an episode of bipolar depression, and the use of this medication has increased modestly since the baseline audit.

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

The clinical background to this QIP is provided in the Topic 15a baseline report, which can be found in the members' area of the POMH-UK website: https://www.rcpsych.ac.uk/POMHResources/Login1.aspx.

On the 9th February 2018, the European medication agency issued new restrictions on the use of valproate for women of child-bearing age, including the need for a pregnancy prevention programme: http://www.ema.europa.eu/docs/en_GB/document_library/Referrals_document/Valproate_2017_31/Recommendation_provided_by_Pharmacovigilance_Risk_Assessment_Committee/WC500243552.pdf.

Method

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

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 C).

Submission of data

Each Trust was allocated a code number that was known only to the Trust and POMH-UK. Trusts were asked to allocate codes to participating services and eligible patients and, if they wished to, individual consultants. The key to these codes is held by the Trust and is not known to POMH-UK. Data coded in this way were entered onto an internet-based form and submitted to POMH-UK via a secure website.

Data collection

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 FORMIC (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.

Data analysis

As in previous reports, the data were analysed at three levels:

1. **National data.** This section describes the demographic and clinical characteristics of patients in the total national sample, as well as the prescribing of high-dose and combination antipsychotics. The data were analysed in a variety of ways to facilitate understanding of the national picture and stimulate discussion in participating clinical teams.

2. **Trust level data.** The analyses conducted on the national data were repeated for each Trust. This allows Trusts to compare the demographic and clinical characteristics of their patients, and their performance against the audit standards, with the anonymised data from each of the other participating Trusts and the national data set as a whole.

3. **Team level data.** This allows Trusts and individual clinical teams to compare their practice with each other and against the national data.

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.

Further analysis of your Trust's data

Ownership of data submitted to POMH-UK is retained by the Trust that provided it. See Appendix A for further information on data ownership. An Excel file containing the data submitted by your Trust has been made available to your Local POMH-UK Lead. Please contact this person if you wish to conduct further analyses on your data.

National level results

Patient demographic and clinical characteristics

Fifty-six specialist mental health Trusts (listed in Appendix B) within the UK participated in a re-audit addressing the prescribing of valproate in people with bipolar disorder. Data were submitted for 6025 patients from 665 clinical teams.

Table 1 below shows that, compared with women, men who have a diagnosis of bipolar disorder are more likely to be prescribed valproate. Nevertheless, as can be seen in Table 2, valproate is prescribed for almost one in four women of child-bearing age (defined as 50 years of age or younger) and this proportion has not changed since baseline audit.

The prevalence of valproate prescribing is highest in acute adult inpatient settings and forensic services.

Table 1: Demographic characteristics of the total national samples at baseline and re-audit and the subgroups prescribed and not prescribed valproate at re-audit

Key demographic characteristics		2016 Baseline	2017 Re audit		
		TNS N=6705	TNS N=6025	Subgroup prescribed valproate N=2157	Subgroup not prescribed valproate N=3868
Gender	Male	2648 (40%)	2233 (37%)	1028 (46%)	1205 (54%)
	Female	4057 (60%)	3792 (63%)	1129 (30%)	2663 (70%)
Ethnicity	White/White British	5159 (77%)	4619 (77%)	1614 (35%)	3005 (65%)
	Black/Black British	482 (7%)	330 (5%)	133 (40%)	197 (60%)
	Asian/Asian British	409 (6%)	442 (7%)	208 (47%)	234 (53%)
	Mixed or other	655 (10%)	634 (11%)	202 (31%)	432 (68%)
Age	Mean age in years (SD)	47 (13)	47 (13)	50 (13)	46 (13)
Age bands	16-25 years	372 (6%)	333 (6%)	80 (24%)	253 (76%)
	26-35 years	1061 (16%)	1001 (15%)	252 (25%)	749 (75%)
	36-45 years	1458 (22%)	1269 (21%)	413 (33%)	856 (67%)
	46-55 years	1879 (28%)	1701 (28%)	652 (38%)	1049 (62%)
	56-65 years	1324 (20%)	1247 (21%)	562 (45%)	685 (55%)
	66 years and over	611 (9%)	474 (8%)	198 (42%)	276 (58%)
Clinical service	Adult community mental health team	5853 (87%)	5257 (87%)	1800 (34%)	3457 (66%)
	Acute adult psychiatric ward or Psychiatric intensive care unit	539 (8%)	463 (8%)	219 (47%)	244 (53%)
	Forensic services	132 (2%)	106 (2%)	53 (50%)	53 (50%)
	Adult home treatment team/crisis intervention team	114 (2%)	102 (2%)	43 (42%)	59 (58%)
	Adult inpatient rehabilitation services	47 (1%)	61 (1%)	36 (59%)	25 (41%)
	Tertiary affective disorders service	20 (<1%)	36 (1%)	6 (17%)	30 (83%)

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

Table 2: Proportion of male and female patients 50 years of age or younger across the subgroups prescribed and not prescribed valproate, at re-audit

	≤50 years of age		> 50 years of age	
	Male N=1194	Female N=2252	Male N=1039	Female N=1540
Prescribed valproate	533 (45%)	529 (23%)	495 (48%)	600 (39%)
Not prescribed valproate	661 (55%)	1723 (77%)	544 (52%)	940 (61%)

Table 3 on the following page shows that the clinical characteristics of the subgroups prescribed or not prescribed valproate are similar. The point prevalence of a rapid cycling illness in the audit sample was 4%, which 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 national sample at baseline and re-audit, and the subgroups prescribed and not prescribed valproate, at re-audit

Key demographic characteristics		2016 Baseline	2017 Re audit		
		TNS N=6705	TNS N=6025	Subsample prescribed valproate N=2157	Subsample not prescribed valproate N=3868
Diagnosis of bipolar disorder	ICD-10 F31 diagnostic code for bipolar disorder	5782 (86%)	5310 (88%)	1912 (36%)	3398 (64%)
	No ICD-10 code for bipolar disorder but current clinical diagnosis of bipolar disorder	802 (12%)	117 (2%)	35 (30%)	82 (70%)
	No ICD-10 code for bipolar disorder but currently has a provisional or differential diagnosis of bipolar disorder	121 (2%)	598 (10%)	210 (35%)	388 (65%)
Current phase of bipolar disorder	Current episode hypomanic (F31.0)	456 (7%)	420 (7%)	159 (38%)	261 (62%)
	Current episode manic (F31.1, F31.2)	546 (8%)	597 (10%)	257 (43%)	340 (57%)
	Current episode depressed (F31.3, F31.4, F31.5)	914 (14%)	789 (13%)	231 (29%)	558 (71%)
	Current episode mixed affective state (F31.6)	289 (4%)	262 (4%)	98 (37%)	164 (63%)
	Currently stable, in partial or full remission	3575 (53%)	3071 (51%)	1117 (36%)	1954 (64%)
	Unclear	583 (9%)	567 (9%)	179 (32%)	388 (68%)
	Other	342 (5%)	319 (5%)	116 (36%)	203 (64%)
Rapid cycling	Yes	220 (3%)	220 (4%)	97 (44%)	123 (56%)
	No	6485 (97%)	5805 (96%)	2060 (35%)	3745 (65%)
Other current psychiatric diagnoses within ICD-10 categories[2]	F00-F09	64 (1%)	61 (1%)	29 (48%)	32 (52%)
	F10-F19	766 (11%)	668 (11%)	261 (39%)	407 (61%)
	F20-F29	285 (4%)	302 (5%)	108 (36%)	194 (64%)
	F30, F32-F39 excluding bipolar disorder	188 (3%)	189 (3%)	63 (33%)	126 (67%)
	F40-F48	370 (6%)	410 (7%)	126 (31%)	284 (69%)
	F50-F59	62 (1%)	47 (1%)	11 (23%)	36 (77%)
	F60-F69	556 (8%)	565 (9%)	178 (32%)	387 (68%)
	F70-F79	62 (1%)	75 (1%)	39 (52%)	36 (48%)
	F80-F89	58 (1%)	70 (1%)	27 (39%)	43 (61%)
	F90-F98	43 (1%)	58 (1%)	24 (41%)	34 (59%)
	F99	22 (<1%)	4 (<1%)	0 (<1%)	4 (100%)
Number of current psychiatric diagnoses	Bipolar disorder only	4621 (69%)	4039 (67%)	1453 (36%)	2586 (64%)
	One other	1735 (26%)	1601 (27%)	561 (35%)	1040 (65%)
	Multiple	349 (5%)	385 (6%)	143 (37%)	242 (63%)

[2] 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.

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.

Table 4: Prevalence of antidepressant prescribing in the total national sample and the subgroups prescribed and not prescribed valproate, at re-audit

Number of antidepressants prescribed	TNS N=6025	Subgroup prescribed valproate N=2157	Subgroup not prescribed valproate N=3868
None	3925 (65%)	1537 (71%)	2388 (62%)
One	1918 (32%)	568 (26%)	1350 (35%)
Two or more	182 (3%)	52 (2%)	130 (3%)

This high prevalence of antidepressant prescribing is consistent with other surveys of prescribing practice (Levine et al, 2000). NICE is cautious about the use of anti-depressants for the prevention of relapse (NICE 2014). For the treatment of the episodes of bipolar depression, NICE concluded that the available evidence primarily supports the use of fluoxetine (ideally in combination with olanzapine). However, of the 2,100 patients prescribed antidepressant reduction in our sample (see Table 4), less than a quarter were currently depressed.

Table 5 below shows that where an antidepressant is prescribed, clinicians do not preferentially select fluoxetine, although use has increased since the baseline audit in 2016.

Table 5: Antidepressant medication prescribed in the total national sample and the subgroups prescribed and not prescribed valproate, at re-audit

Antidepressant prescribed[3]	TNS N=6025	Subgroup prescribed valproate N=2157	Subgroup not prescribed valproate N=3868
Sertraline	545 (9%)	174 (8%)	371 (10%)
Mirtazapine	341 (6%)	99 (5%)	242 (6%)
Venlafaxine	331 (5%)	88 (4%)	243 (6%)
Fluoxetine	289 (5%)	84 (4%)	205 (5%)

[3] Other antidepressants <5% of TNS includes citalopram (n=254), duloxetine (n=106), amitriptyline (n=83), escitalopram (n=76), trazodone (n=64), paroxetine (n=51), lofepramine (n=26), clomipramine (n=23), dosulepin (n=13), bupropion (n=8), tranylcypromine (n=8), reboxetine (n=7), imipramine (n=6), nortriptyline (n=5), phenelzine (n=5), doxepin (n=3), agomelatine (n=2), moclobemide (n=2).

Antipsychotic prescribing

Although the prevalence of antipsychotic prescribing did not differ across the subgroups prescribed or not prescribed valproate (four-fifths of both subgroups), the choice of antipsychotic medication did differ in that olanzapine was more commonly prescribed for those on valproate and quetiapine for those who were not.

More than one in ten of the total national sample were prescribed a depot/LAI antipsychotic which probably reflects the perception by clinicians that non-adherence is a common clinical problem; this proportion has fallen slightly since the baseline audit.

Table 6: Prevalence of antipsychotic prescribing in the total national sample and the subgroups prescribed and not prescribed valproate, at re-audit

Number of antipsychotics prescribed	TNS N=6025	Subgroup prescribed valproate N=2157	Subgroup not prescribed valproate N=3868
None	1240 (21%)	427 (20%)	813 (21%)
One	4374 (73%)	1566 (73%)	2808 (73%)
Two or more	411 (7%)	164 (8%)	247 (6%)

Table 7: Antipsychotic medication prescribed in the total national sample and the subgroups prescribed and not prescribed valproate, at re-audit

Antipsychotic prescribed[4]	TNS N=6025	Subgroup prescribed valproate N=2157	Subgroup not prescribed valproate N=3868
Quetiapine	1522 (25%)	436 (20%)	1086 (28%)
Olanzapine	1144 (19%)	477 (22%)	667 (17%)
Aripiprazole	806 (13%)	252 (12%)	554 (14%)
Risperidone	384 (6%)	164 (8 %)	220 (6%)
Any depot (IM)	748 (12%)	318 (15%)	439 (11%)

[4] Other oral antipsychotics prescribed for < 5% of the TNS: (oral/IM) includes haloperidol (n=163), amisulpride (n=100), clozapine (n=71), chlorpromazine (n=49), lurasidone (n=42), promazine (n=28), zuclopenthixol acetate (n=24), flupentixol (n=19), sulpiride (n=13), trifluoperazine (n=12), paliperidone (n=7), levomepromazine (n=6), asenapine (n=4), fluphenazine (n=3), zotepine (n=2), sertindole (n=0).

Depot/LAI antipsychotics all prescribed for < 5% of the TNS: (depot/long-acting): zuclopenthixol decanoate (n=210), paliperidone palmitate (n=126), flupentixol decanoate (n=118), aripiprazole (n=87), risperidone (n=78), haloperidol decanoate (n=76), olanzapine pamoate (n=29), fluphenazine decanoate (n=24) and pipotiazine palmitate (n=9).

Prescribing of other mood stabilisers

Lithium is a more effective mood stabiliser than valproate (Geddes et al 2010, Kessing et al, 2018) and is recommended by NICE as a first-line prophylactic agent (NICE, 2014). But, as at baseline, valproate was prescribed more frequently than lithium in this re-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, 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 subgroups prescribed and not prescribed valproate, at re-audit

Number of mood stabilisers prescribed other than valproate	TNS N=6025	Subgroup prescribed valproate N=2157	Subgroup not prescribed valproate N=3868
None	3770 (63%)	1764 (82%)	2006 (52%)
One	2043 (34%)	374 (17%)	1669 (43%)
Two or more	212 (4%)	19 (1%)	193 (5%)

Table 9: Mood stabilisers prescribed in the total national sample and the subgroups prescribed and not prescribed valproate, at re-audit

Mood stabilisers prescribed	TNS N=6025	Subgroup prescribed valproate N=2157	Subgroup not prescribed valproate N=3868
Valproate	2157 (36%)	2157 (100%)	-
Lithium	1365 (23%)	244 (11%)	1121 (29%)
Lamotrigine	851 (14%)	133 (6%)	718 (19%)
Carbamazepine	223 (4%)	30 (1%)	193 (5%)
Other mood stabilisers	32 (1%)	5 (<1%)	27 (1%)
No mood stabiliser	2006 (33%)	-	2006 (52%)

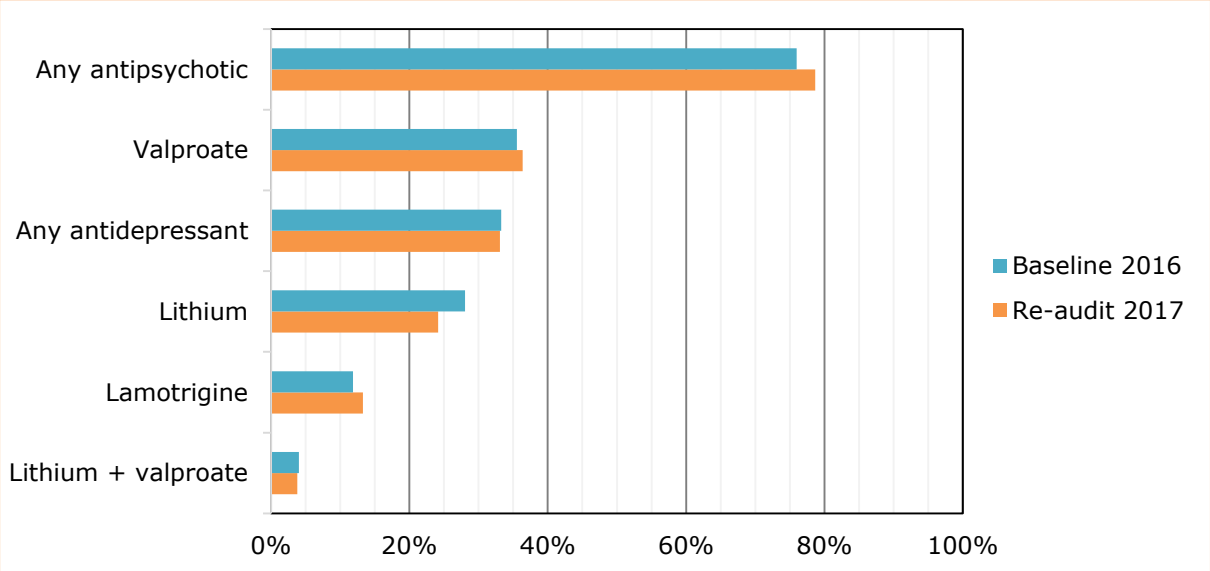
As can be seen from Table 10 below, one patient in four was prescribed an anxiolytic and/or hypnotic medicine. Given that the majority of patients in the TNS were in partial or full remission at the time of this audit, this proportion seems high. However, this may reflect that anxiety is common in people with bipolar disorder and poor sleep is recognised as a risk factor for relapse.

Table 10: Other medications prescribed in the total national sample and the subgroups prescribed and not prescribed valproate, at re-audit

Other medications prescribed[5]	TNS N=6025	Subgroup prescribed valproate N=2157	Subgroup not prescribed valproate N=3868
Benzodiazepine (daytime use)	938 (16%)	380 (18%)	558 (14%)
Z-hypnotic	543 (9%)	203 (9%)	340 (9%)
Benzodiazepine (night time use)	533 (9%)	272 (13%)	281 (7%)
One or more of the above: benzodiazepine (daytime or night time use) or Z-hypnotic	1572 (26%)	638 (30%)	934 (24%)

Figure 6: Medications prescribed for patients whose current phase of illness is stable and <u>in partial or full remission</u>: at baseline and at re-audit (n=3071)

The profile of prescribing for this subgroup at re-audit is very similar to that at baseline, with the exception of a modest decrease in the prevalence of lithium prescribing.



[5] Other medications prescribed includes thyroxine n=354, promethazine (n=323), pregabalin (n=280), folic acid (n=98), gabapentin (n=67), melatonin (n=20), fish oils (n=18), triidothyronine T3 (n=1) and tryptophan (n=1).

Prescribing valproate for women of child-bearing age

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

Table 2 on page 19 shows that valproate is prescribed less often in women of child-bearing age than in men and older women. Nevertheless, almost one woman in four who was 50 years of age or younger with bipolar disorder was prescribed valproate and this proportion has not changed since the baseline audit.

There have however been modest improvements since the baseline audit in the proportion of women for whom contraception has been considered and/or prescribed and who have been given verbal and/or written information about the teratogenic potential of valproate.

Table 11: Women 50 years of age or younger started on valproate in the past six months: documented evidence regarding childbearing potential or use of contraception at baseline (n=74) and re-audit (n=63*)

Documented evidence regarding woman's childbearing potential or use of contraception	2016 Baseline N=74	2017 Re-audit N=63
No documented evidence of protection against pregnancy	48 (65%)	34 (54%)
Prescribed oral contraceptive	9 (12%)	9 (14%)
Patient has an IUD/coil fitted	4 (5%)	-
Patient has had an injectable contraceptive or implant fitted	6 (8%)	6 (10%)
Other contraceptive method documented	6 (8%)	7 (11%)
Patient has undergone an oophorectomy/ hysterectomy/endometrial ablation	1 (1%)	2 (3%)
Yes, patient has undergone surgical sterilisation, e.g. tubal ligation	-	4 (6%)

* including 1 case with missing data

Table 12: Women 50 years of age or younger: started on valproate in the past six months: documented evidence of safety issues discussed at initiation of valproate treatment at baseline (n=74) and re-audit (n=63*)

Documented evidence of the following:	2016 Baseline N=74	2017 Re-audit N=63
A general discussion regarding side effects and benefits of the treatment	49 (66%)	43 (68%)
Discussion with the woman of the need for adequate contraception during valproate treatment	41 (55%)	44 (70%)
The woman was informed of the risks to the foetus (teratogenicity, including neural tube defects/spina bifida) when valproate is taken during pregnancy	37 (50%)	34 (54%)
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	18 (24%)	21 (33%)
The woman was given the MHRA leaflet that outlines the problems associated with valproate in pregnancy	6 (8%)	14 (22%)
None of the above	20 (27%)	13 (21%)

* including 1 case with missing data

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 7: Valproate dosage for men 50 years of age or younger, at re-audit (n=533)

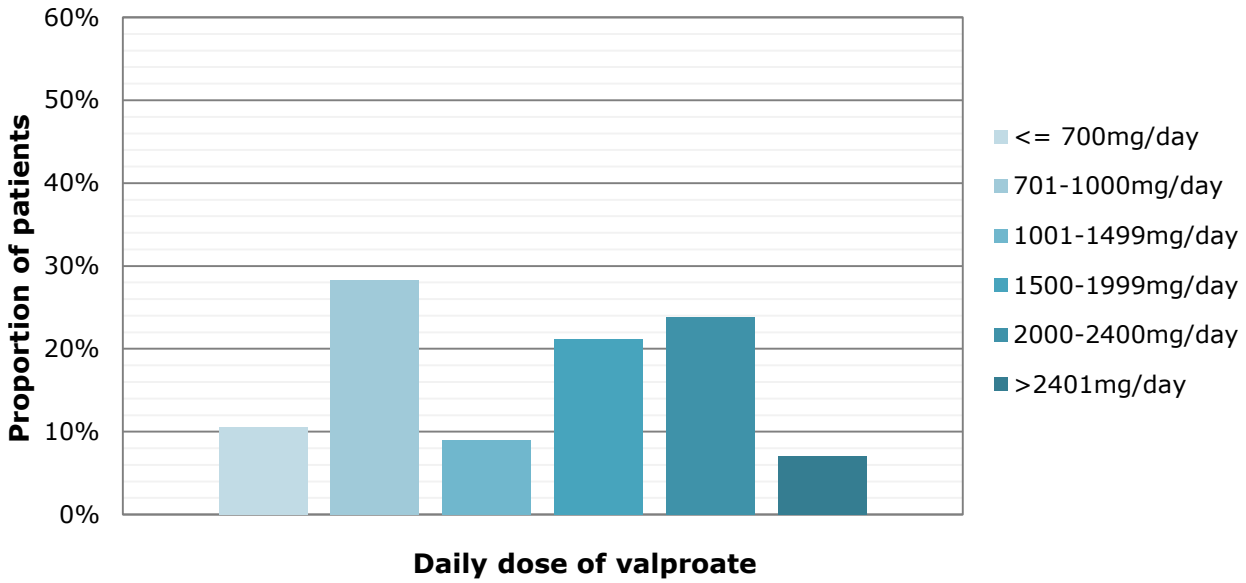
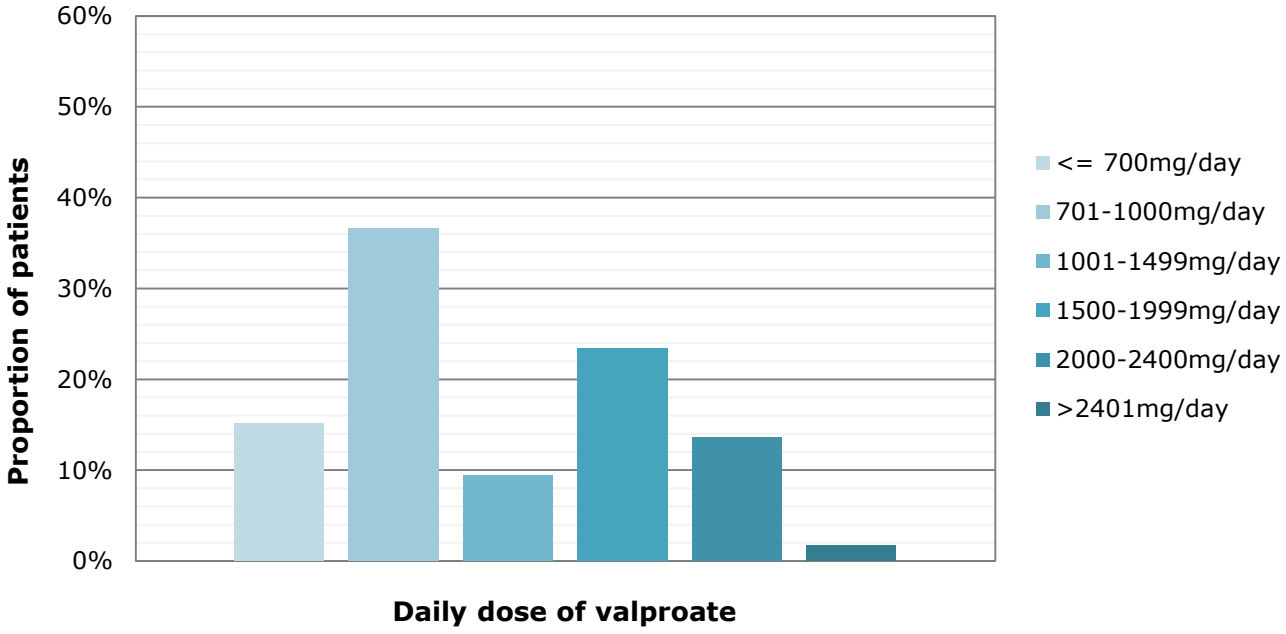


Figure 8: Valproate dosage for women 50 years of age or younger, at re-audit (n=529)

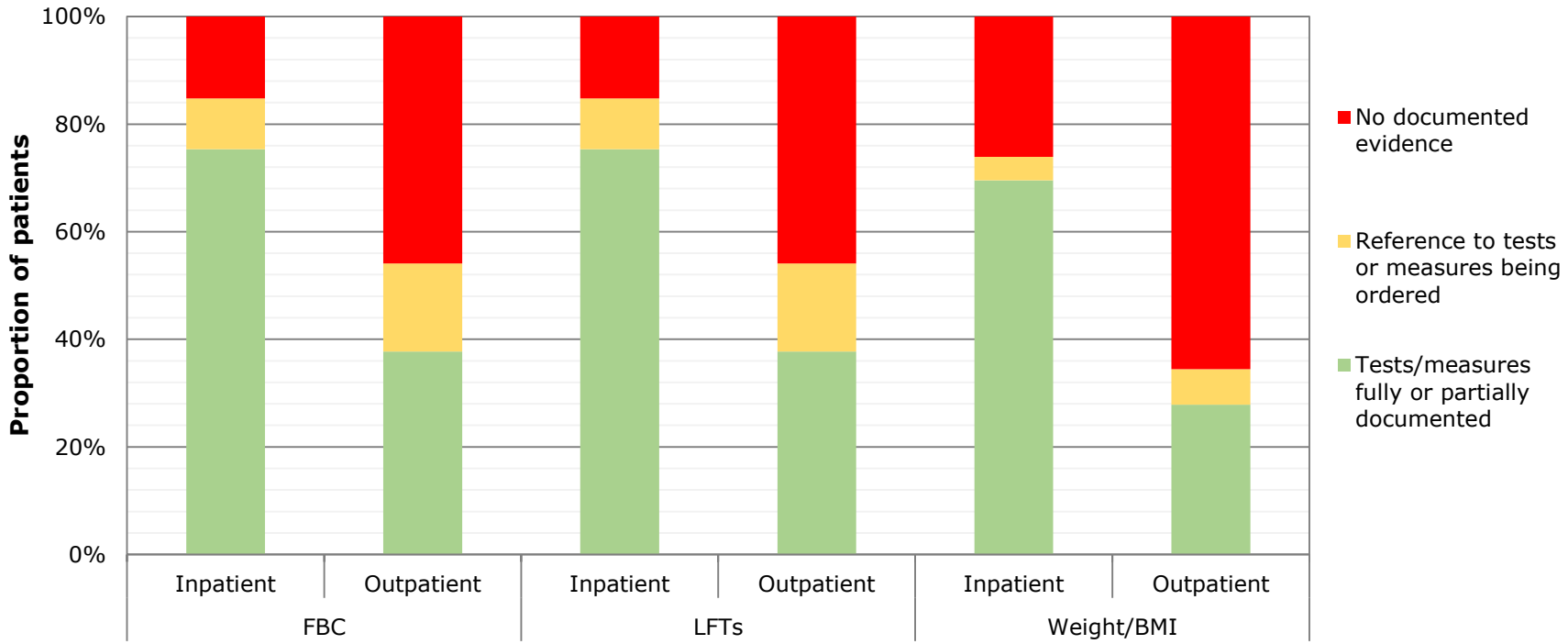


Pre-treatment screening

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 9 below shows that, compared with outpatient settings, physical health checks were more likely to be carried out in inpatient settings. This may partly reflect easier access to phlebotomy in inpatient settings. Prior to starting valproate treatment for 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 9: Proportion of patients prescribed valproate who had tests/results or measures documented in the 3 months before treatment was initiated: in the national subsample started on valproate in the last 6 months (inpatient n=138/outpatient n=61), at re-audit



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

In approximately two-thirds of inpatients, there was no documented evidence that information about valproate treatment was offered at the time that treatment was initiated. This represents a modest improvement from baseline. 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, around two in every five 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.

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 10: Written information about the use of valproate offered to <u>inpatients</u> starting treatment: national subsample started on valproate in the last 6 months (n=138), at re-audit

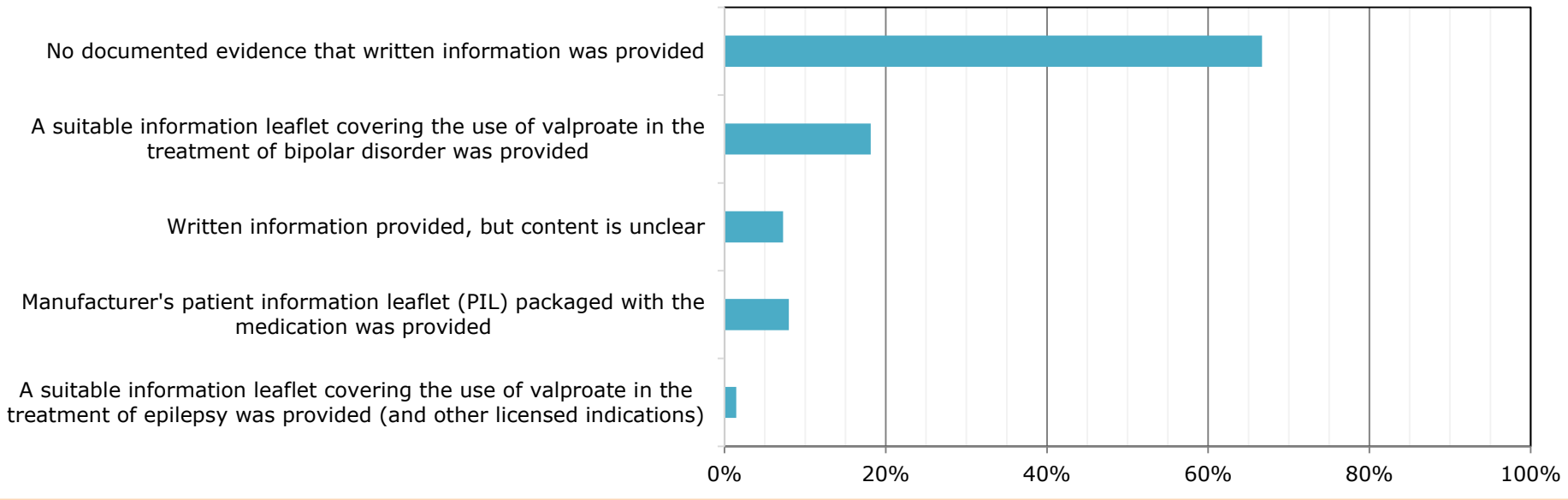
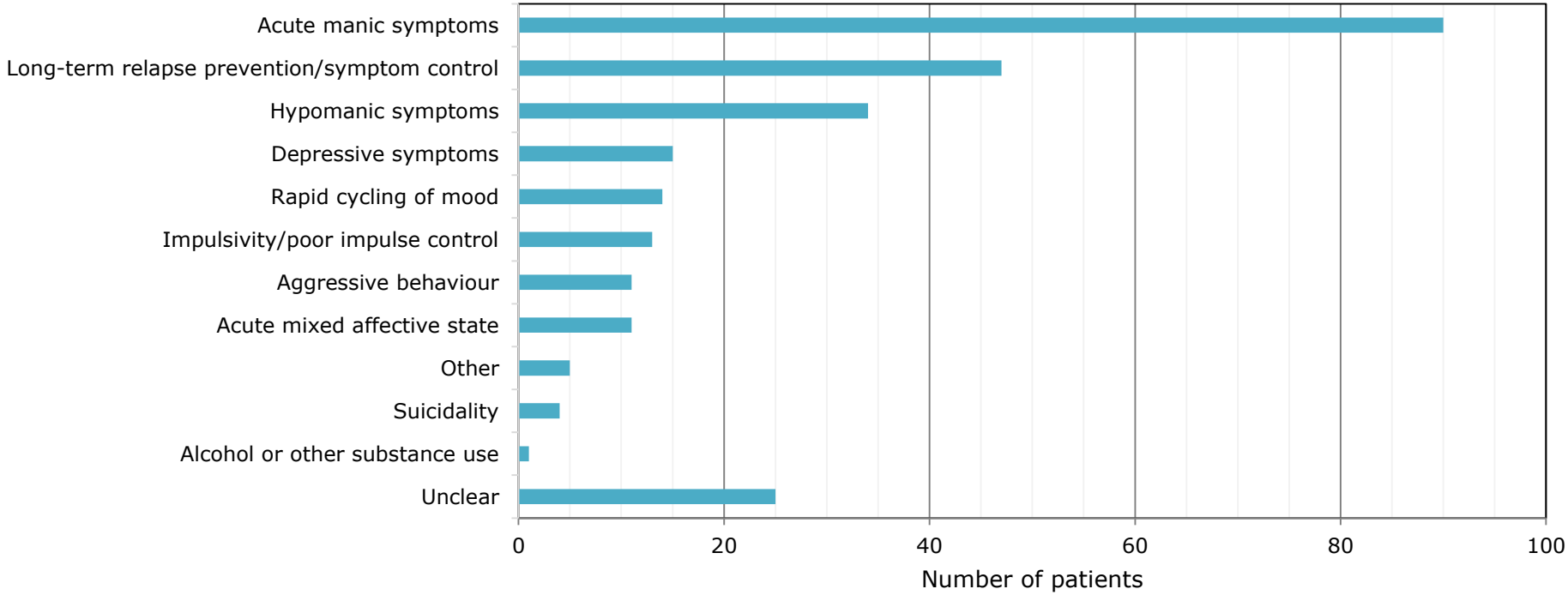


Figure 11: Clinical reasons/target symptoms for starting valproate: in the national subsample of patients started on valproate in the last 6 months (n=199), at re-audit



Early on-treatment review

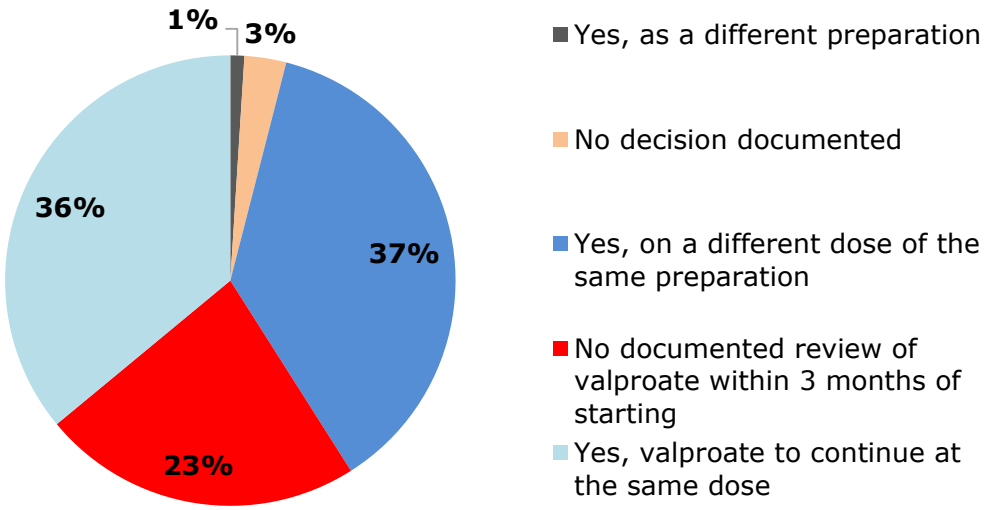
5	Patients prescribed valproate should have an early, on-treatment review that includes screening for the common side effects of the medication (e.g. weight gain, nausea, tremor)

Table 13 below show that almost a quarter of patients did not have an early on-treatment review of the efficacy and tolerability of valproate.

Table 13: Documented assessment of a medication review within 3 months of valproate initiation: in the national subsample treated with valproate for 3-12 months (n=235), at re-audit

Documented evidence that the following were assessed at review:	2016 Baseline N=263	2017 Re-audit N=235
Therapeutic benefit/response	177 (67%)	162 (69%)
Medication adherence	115 (44%)	97 (41%)
Other common side effects of valproate	92 (35%)	84 (36%)
Liver function tests (LFTs)	72 (27%)	81 (34%)
Full blood count (FBC)	72 (27%)	78 (33%)
Weight gain	60 (23%)	57 (24%)
No documented review	63 (23%)	53 (23%)
None of the above	9 (3%)	6 (3%)

Figure 12: Documented evidence of decision to continue treatment with valproate: in the national subsample treated with valproate for 3-12 months (n=235), at re-audit

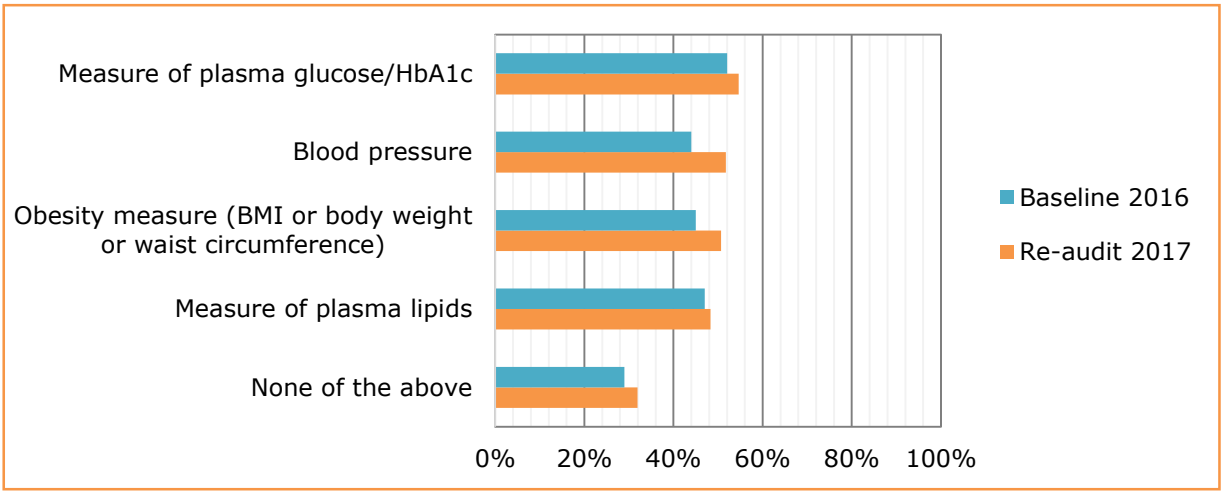


Long-term monitoring

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

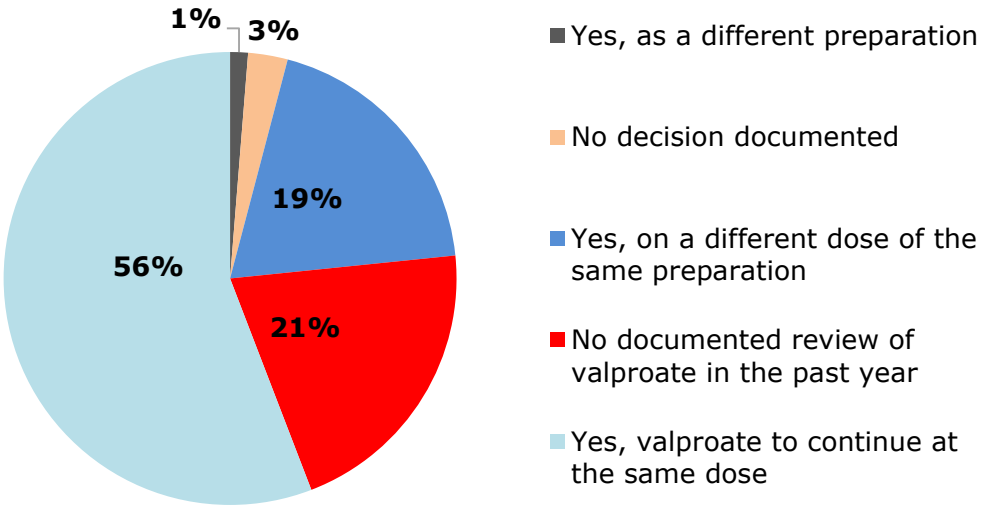
In just over half of the total national sample, screening for each of the four cardiometabolic risk factors (obesity, hypertension, elevated plasma glucose, dyslipidaemia) had been undertaken in the previous year, representing a very modest improvement from baseline.

Figure 13: Documented evidence of tests or measures over the past 12 months: in the national subsample treated with valproate for a year or more (n=1805), at re-audit



Approximately one in five patients who had been prescribed valproate for more than 1 year had not had a documented review of their treatment in the last year. In the sub-sample (n=1430) who had a documented review, it addressed therapeutic benefit/response in more than four-fifths of cases and medication adherence in almost two-thirds of cases.

Figure 14: Decision to continue valproate documented: in the national subsample treated with valproate for a year or more (n=1805), at re-audit



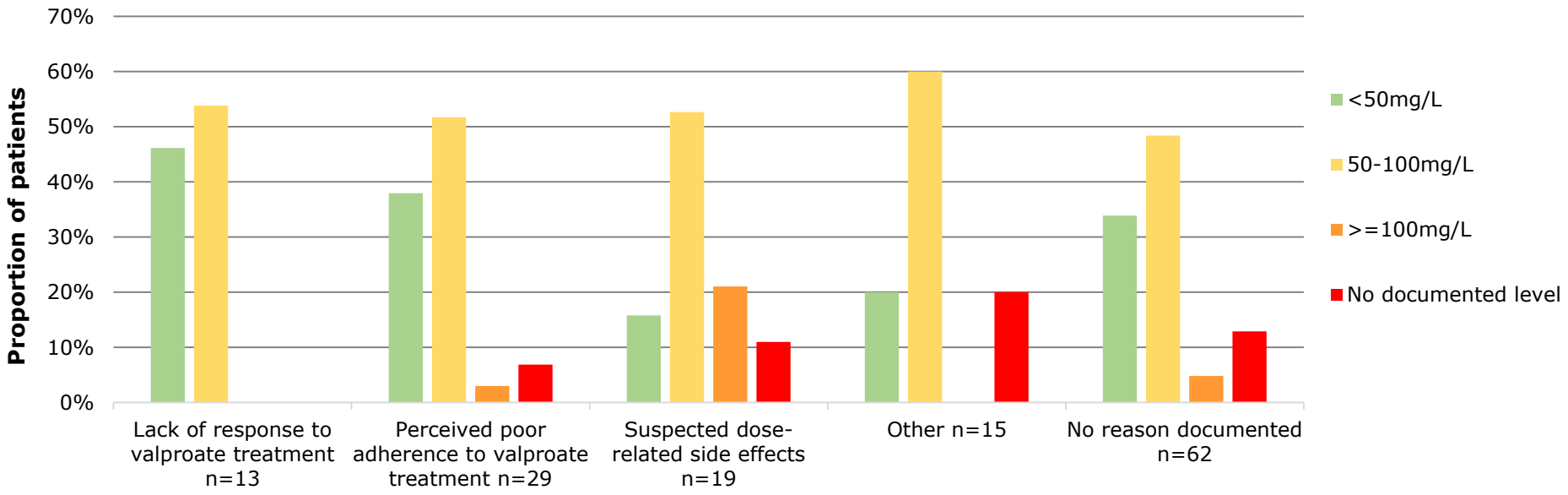
Treatment target

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 (8%) of those patients prescribed valproate had a documented valproate serum level in the previous year.

Where testing had been undertaken, the documented rationale for this and the test results are shown in the Figure below. The pattern of test results suggests that, overall, testing is only likely to helpfully inform treatment plans in a minority of cases.

Figure 15: Reasons for measuring plasma valproate levels and documented results (n=136)*



* For some patients there may have been more than one reason recorded for measuring plasma valproate levels.

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: 012

Charts in this section are ordered by performance against the practice standards so the position of your Trust will vary in each figure relative to other Trusts.

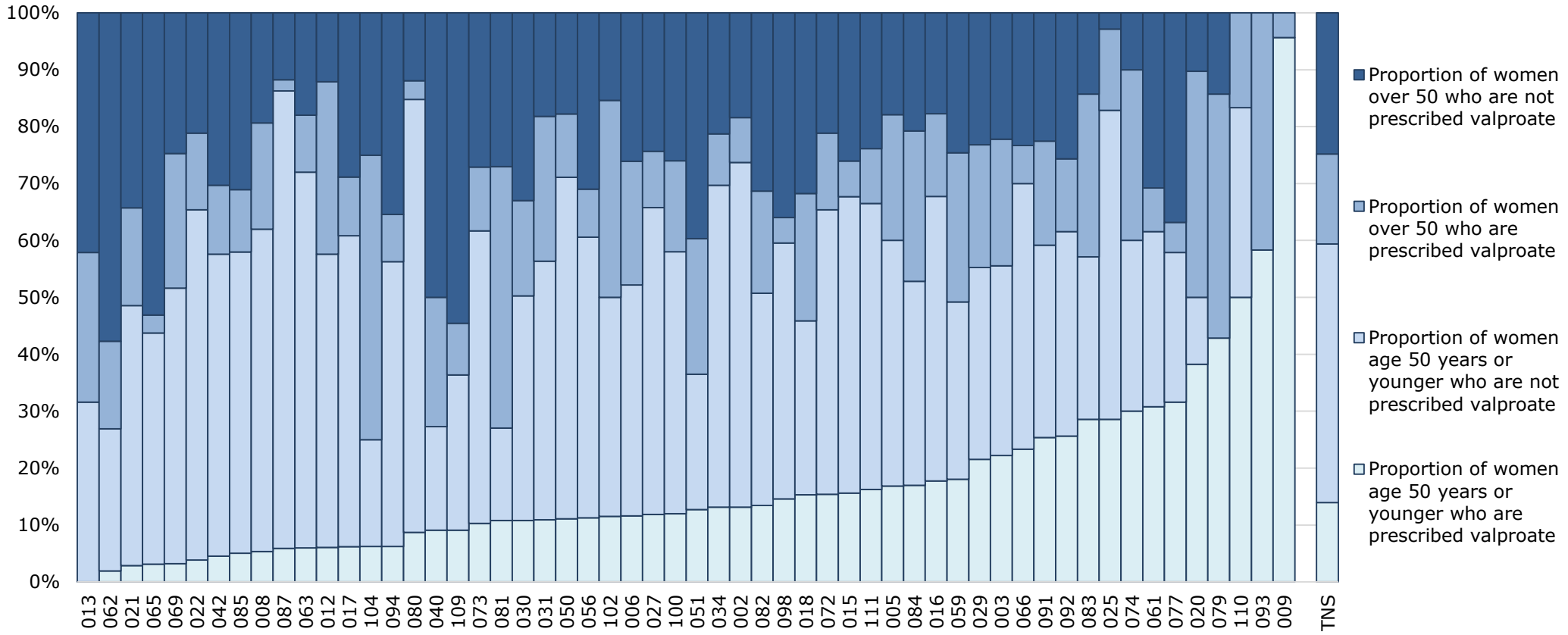
Table 14: Number of clinical teams and patient records submitted by each participating Trust, at baseline and re-audit

Trust code	Clinical teams 2016	Patient records 2016	Clinical teams 2017	Patient records 2017
002	3	74	2	57
003	18	171	8	34
005	24	555	23	324
006	10	122	10	106
008	1	151	13	246
009	10	49	5	23
011	6	23	-	-
012	45	341	15	63
013	6	19	3	23
015	5	60	8	137
016	7	146	7	180
017	11	215	12	154
018	9	60	9	136
019	7	157	-	-
020	41	111	26	97
021	5	94	14	63
022	25	48	44	91
025	-	-	12	63
027	17	183	21	231
029	7	422	6	325
030	20	91	40	306
031	24	137	23	104
034	9	288	15	356
040	2	85	4	45
042	11	102	25	117
050	21	65	4	86
051	18	59	20	90
054	8	71	-	-
056	1	102	1	99
059	27	197	27	190
061	-	-	5	15
062	4	151	4	87
063	1	6	11	77
065	-	-	1	48
066	4	100	5	103
068	2	102	-	-
069	24	45	11	121
072	-	-	3	96
073	21	147	20	180

074	1	14	5	16
077	18	66	9	39
079	12	96	9	12
080	5	24	5	92
081	9	151	8	66
082	-	-	3	109
083	4	24	5	30
084	3	102	2	98
085	34	395	42	187
087	24	118	12	52
089	9	176	-	-
090	8	60	-	-
091	6	87	19	97
092	2	24	6	56
093	-	-	8	16
094	13	123	9	78
098	18	110	22	137
099	10	14	-	-
100	6	77	9	72
101	5	58	-	-
102	-	-	3	33
104	6	92	1	39
109	1	145	1	15
110	-	-	10	14
111	-	-	20	294
TNS	**648**	**6705**	**665**	**6025**

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

Figure 16: Proportion of Trust samples of women with bipolar disorder who are of child-bearing age and are prescribed valproate, at re-audit (n=3792)



Pre-treatment screening

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 17: Proportion of patients prescribed valproate who had a BMI/weight measure documented in the 3 months before treatment was initiated: at Trust level and in the national subsample started on valproate in the last 6 months, at re-audit (n=199)

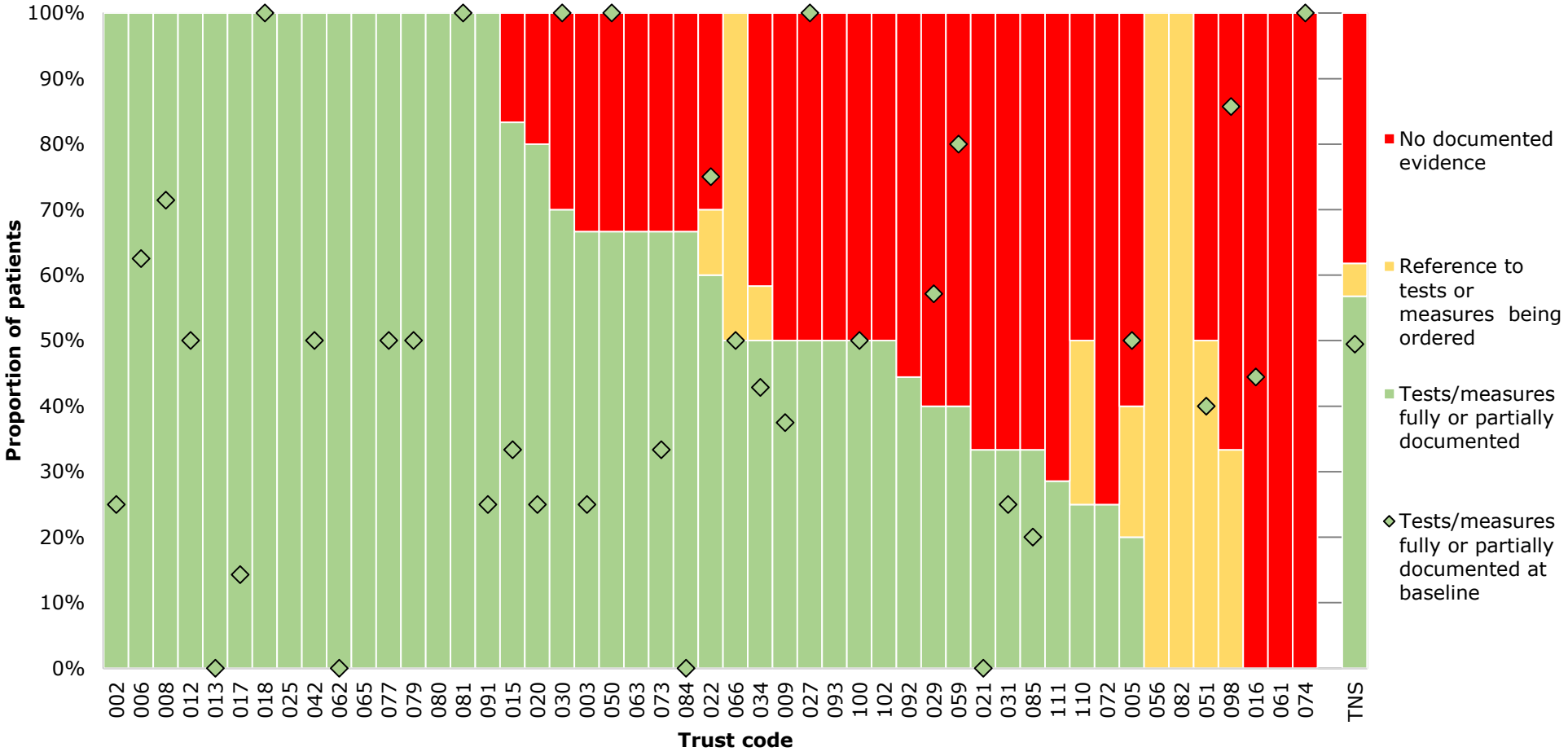


Figure 18: Proportion of patients prescribed valproate who had liver function tests (LFTs) documented in the 3 months before treatment was initiated: at Trust level and in the national subsample of patients started on valproate in the last 6 months (n=199), at re-audit

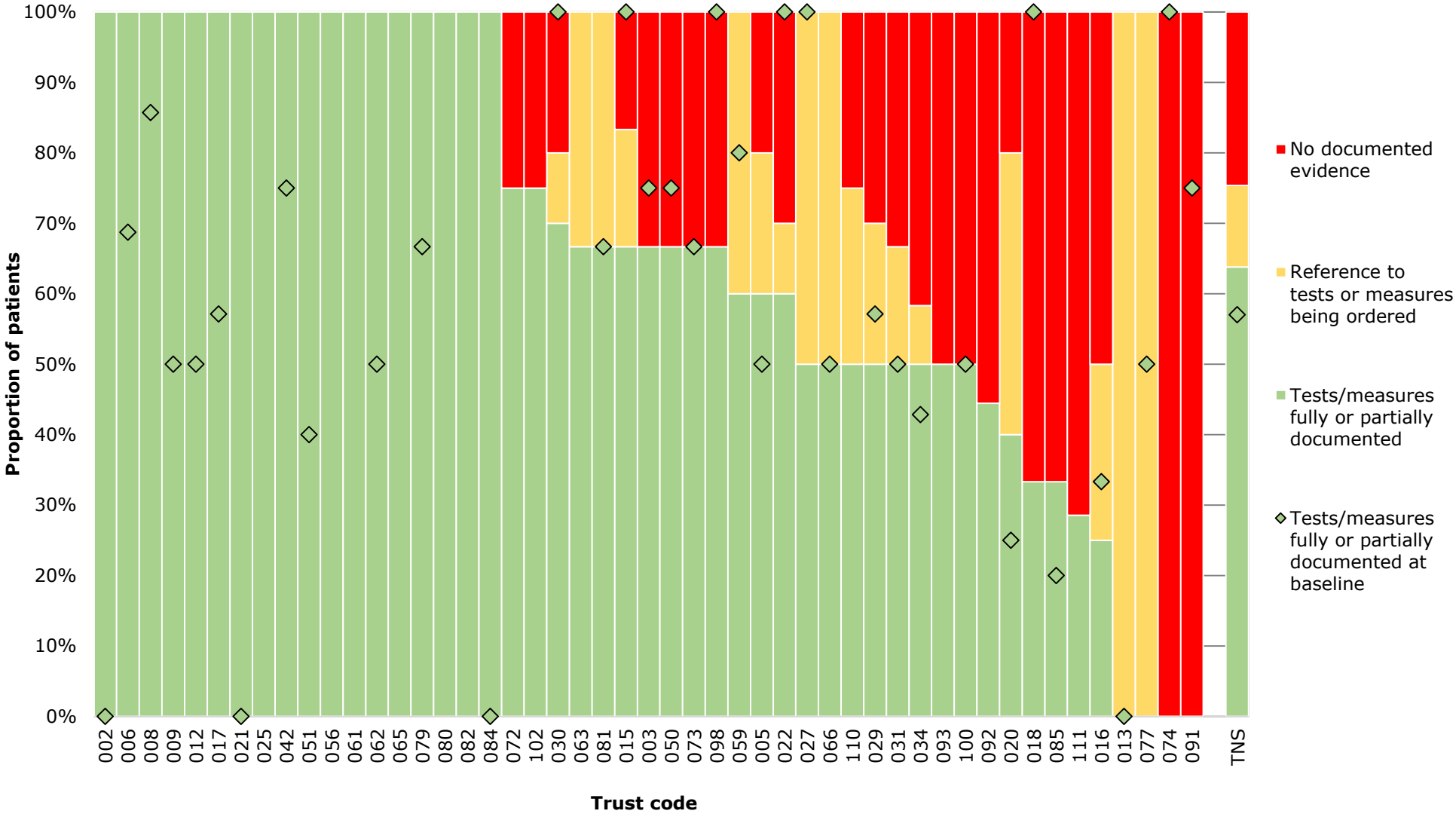
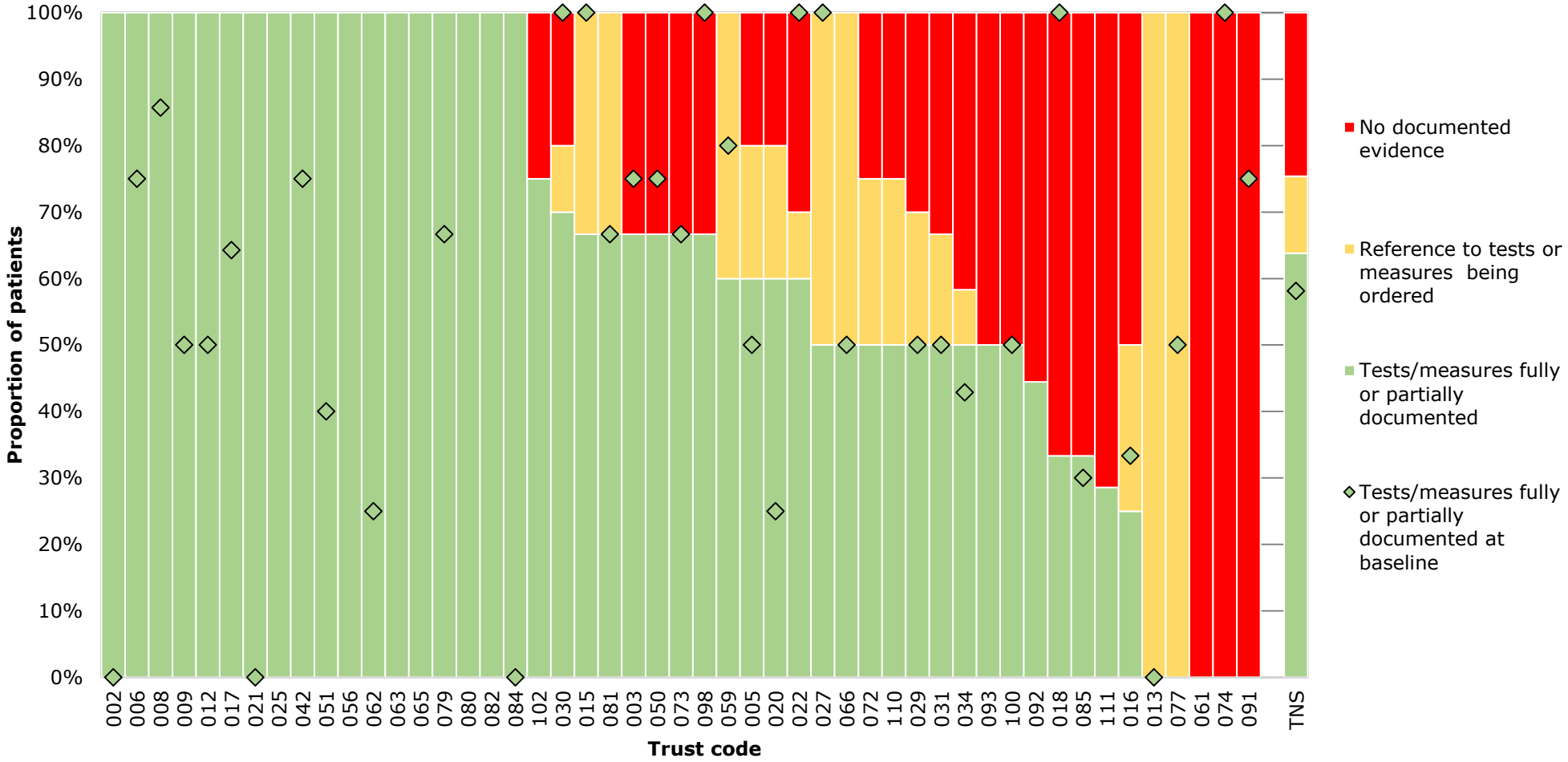
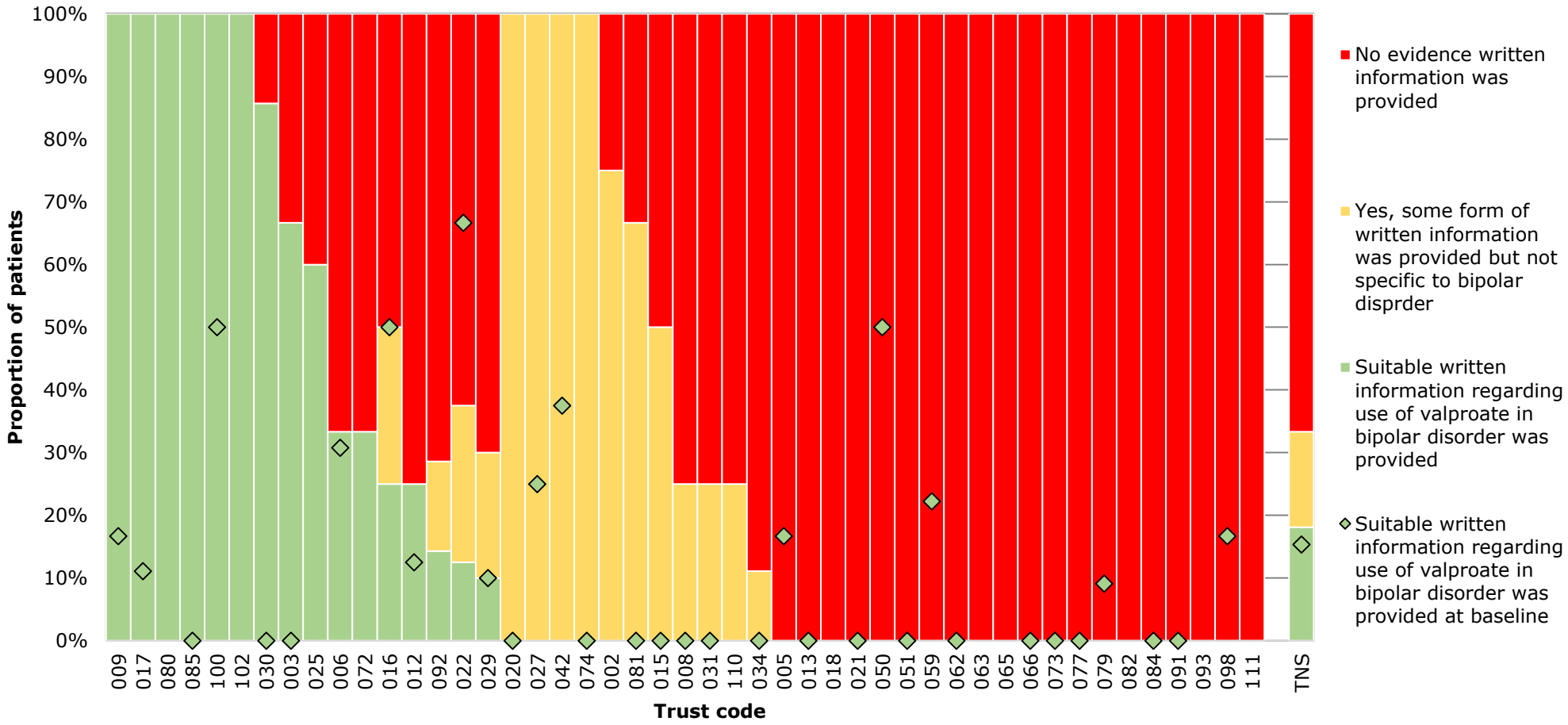


Figure 19: Proportion of patients prescribed valproate who had a full blood count (FBC) documented in the 3 months before treatment was initiated: at Trust level and in the national subsample of patients started on valproate in the last 6 months (n=199), at re-audit



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

Figure 20: Written information about the use of valproate offered to <u>inpatients</u> starting treatment: at Trust level and in the national subsample started on valproate in the last 6 months (n=138), at re-audit



Early on-treatment review

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 21: Documented assessment of therapeutic response as part of an early on-treatment review: at Trust level and in the national subsample treated with valproate for 3-12 months (n=235), at re-audit

Figure 22: Documented assessment of weight gain or other common side effects of valproate as part of an early on-treatment review: at Trust level and in the national subsample treated with valproate for 3-12 months (n=235), at re-audit

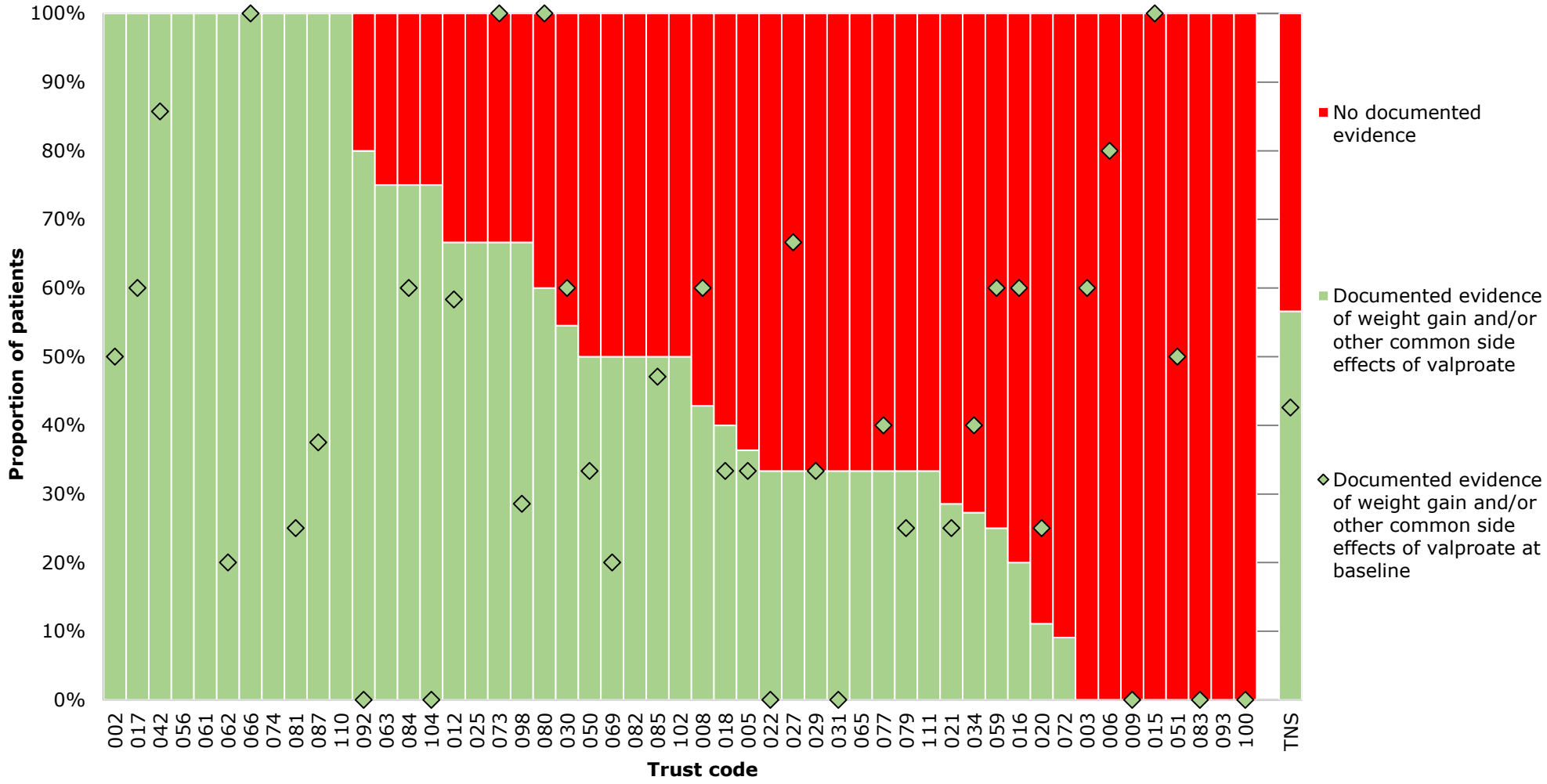


Figure 23: Documented assessment of FBC and/or LFTs as part of an early on-treatment review: at Trust level and in the national subsample treated with valproate for 3-12 months (n=235), at re-audit

NB: These tests are not directly referred to in practice standard 5 but Trusts expressed an interest in these data being reported.

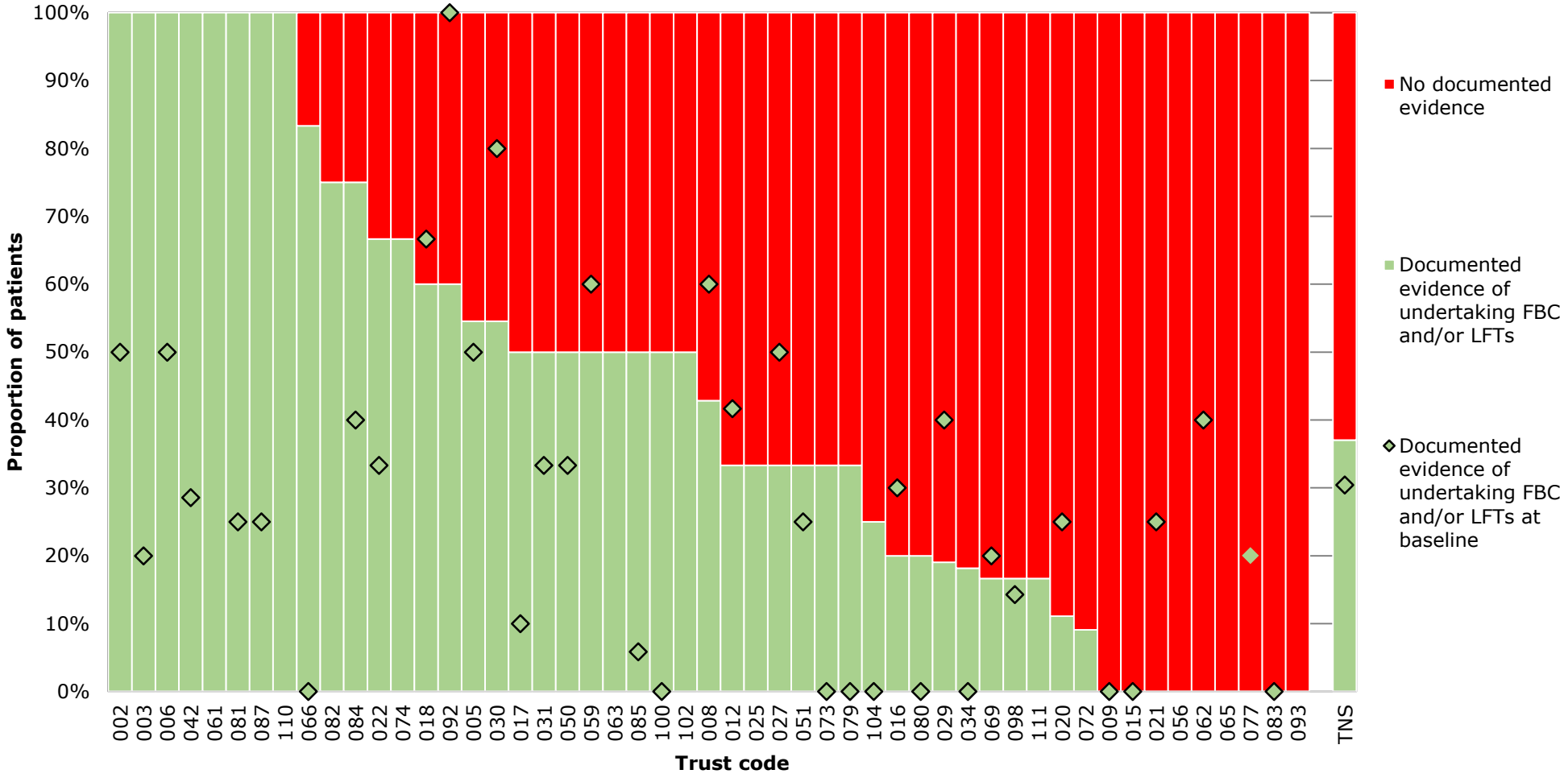
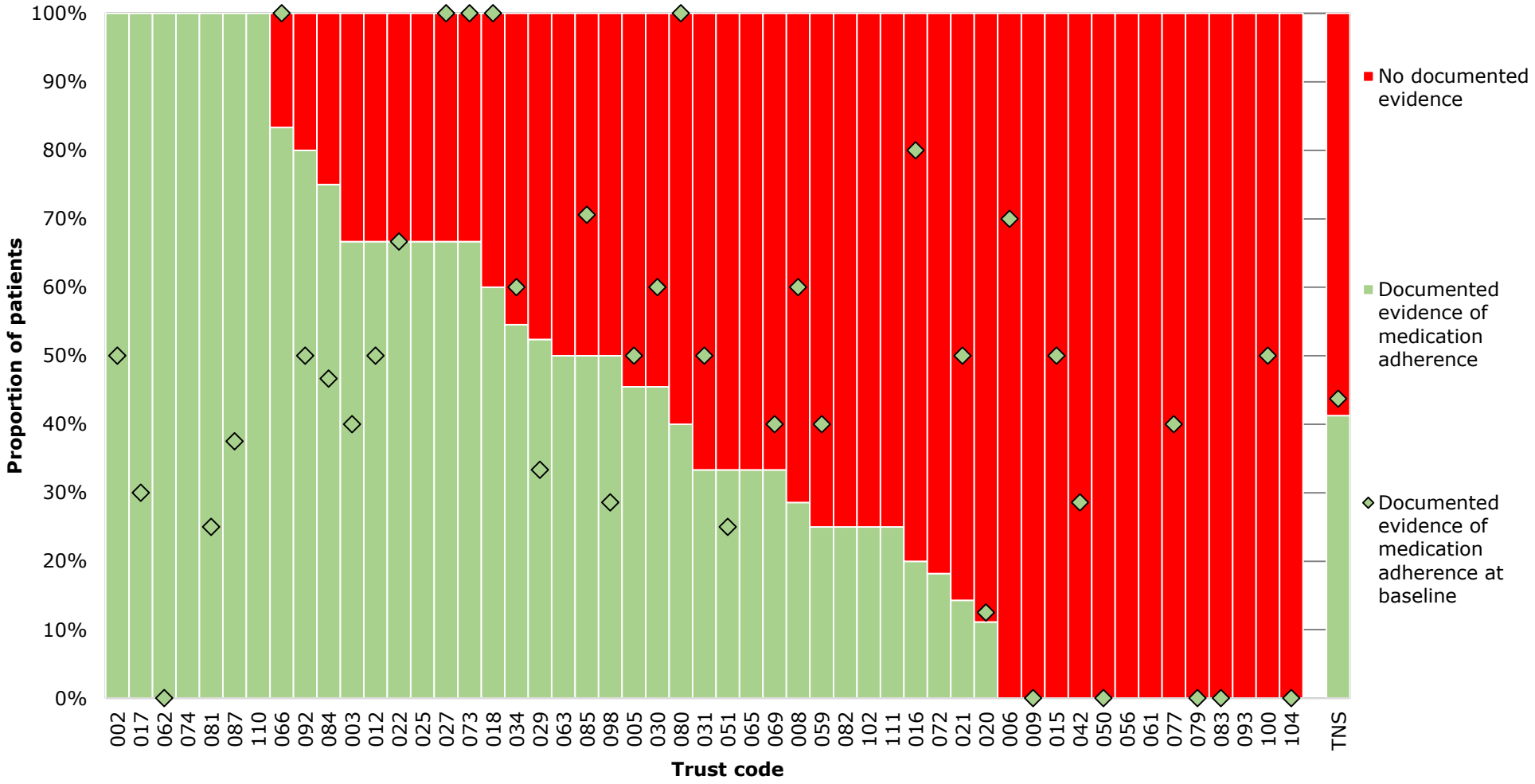


Figure 24: Documented assessment of information relating to medication adherence as part of an early on-treatment review: at Trust level and in the national subsample treated with valproate for 3-12 months (n=235), at re-audit



Long-term monitoring

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

Figure 25: Documented evidence that body weight and/or BMI have been measured over the past 12 months: at Trust level and in the national subsample treated with valproate for a year or more (n=1805), at re-audit

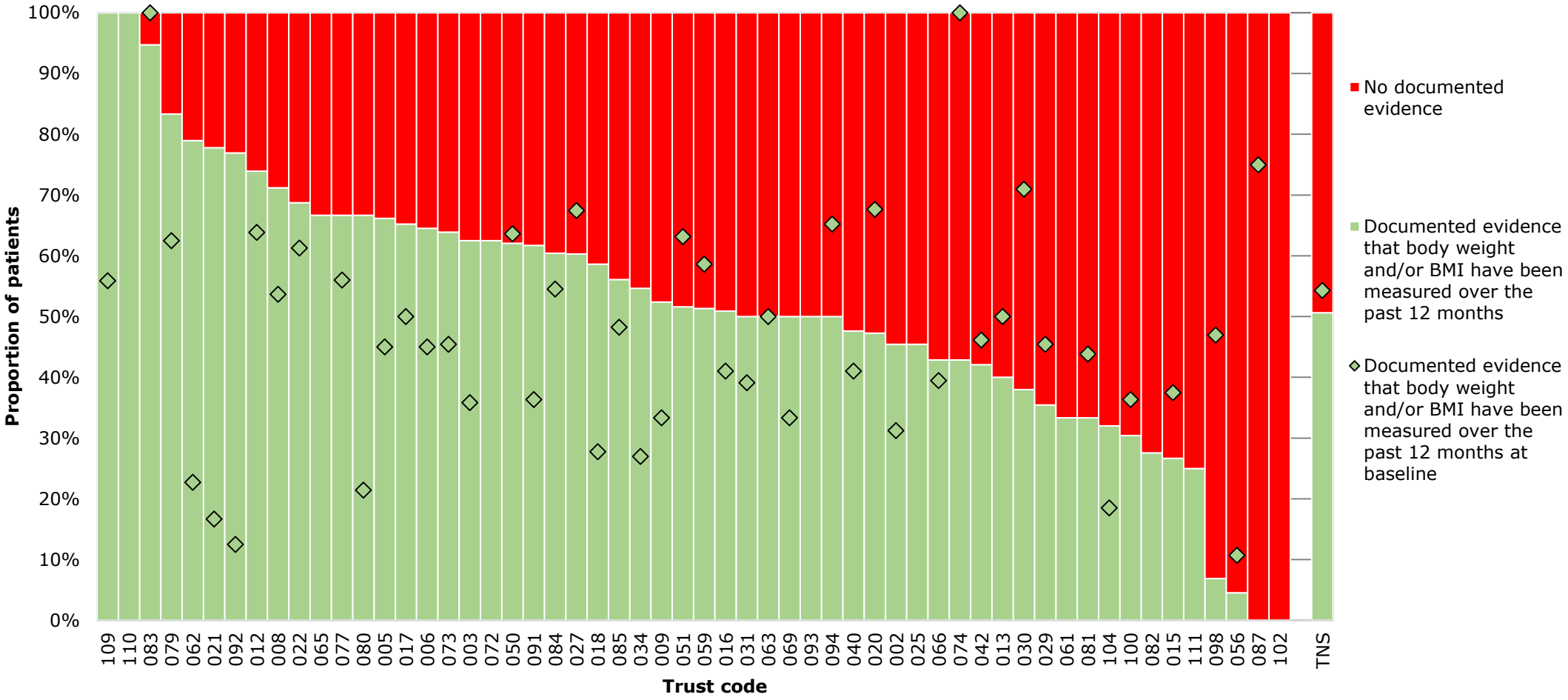


Figure 26: Documented evidence that blood pressure has been measured over the past 12 months: at Trust level and in the national subsample treated with valproate for a year or more (n=1805), at re-audit

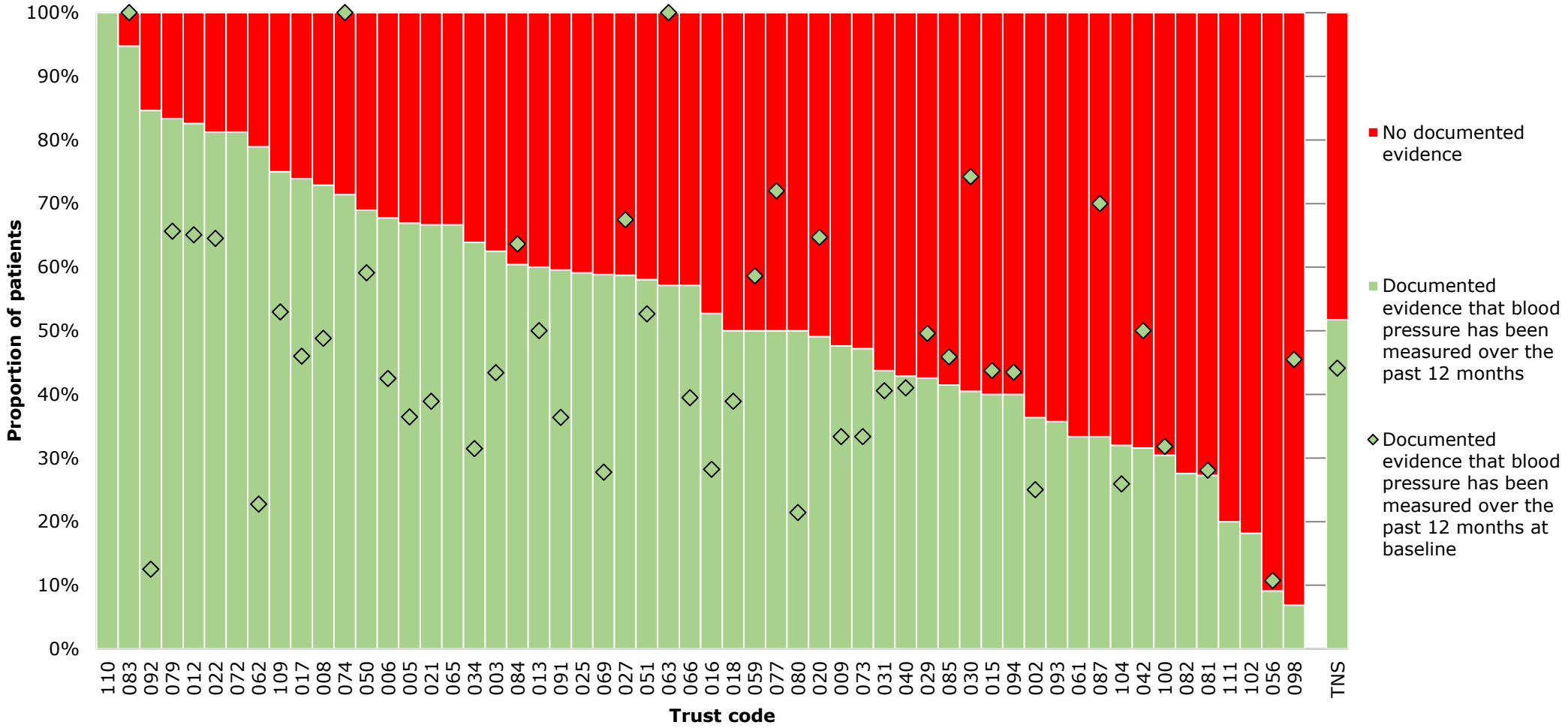


Figure 27: Documented evidence that plasma glucose has been measured over the past 12 months: at Trust level and in the national subsample treated with valproate for a year or more (n=1805), at re-audit

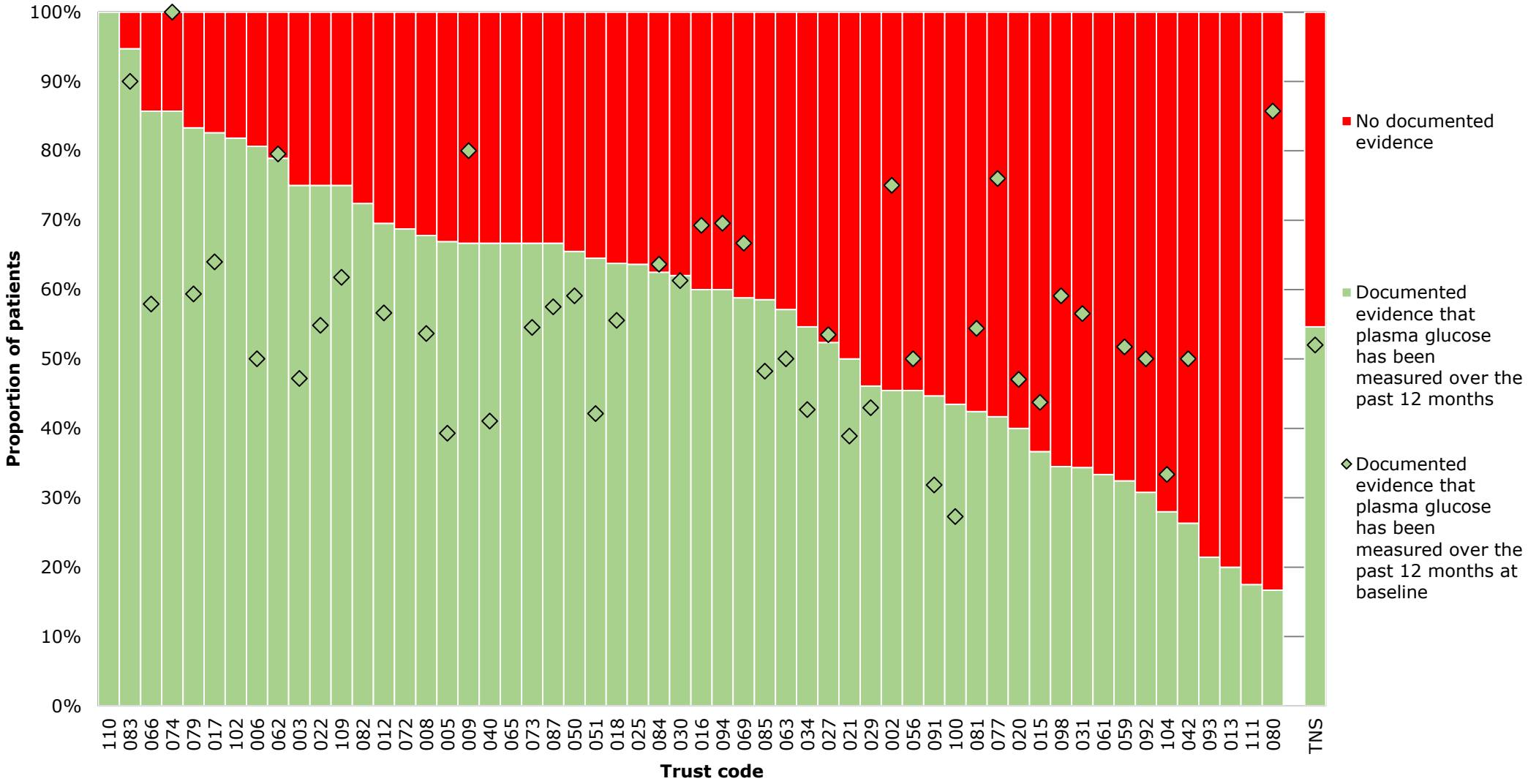
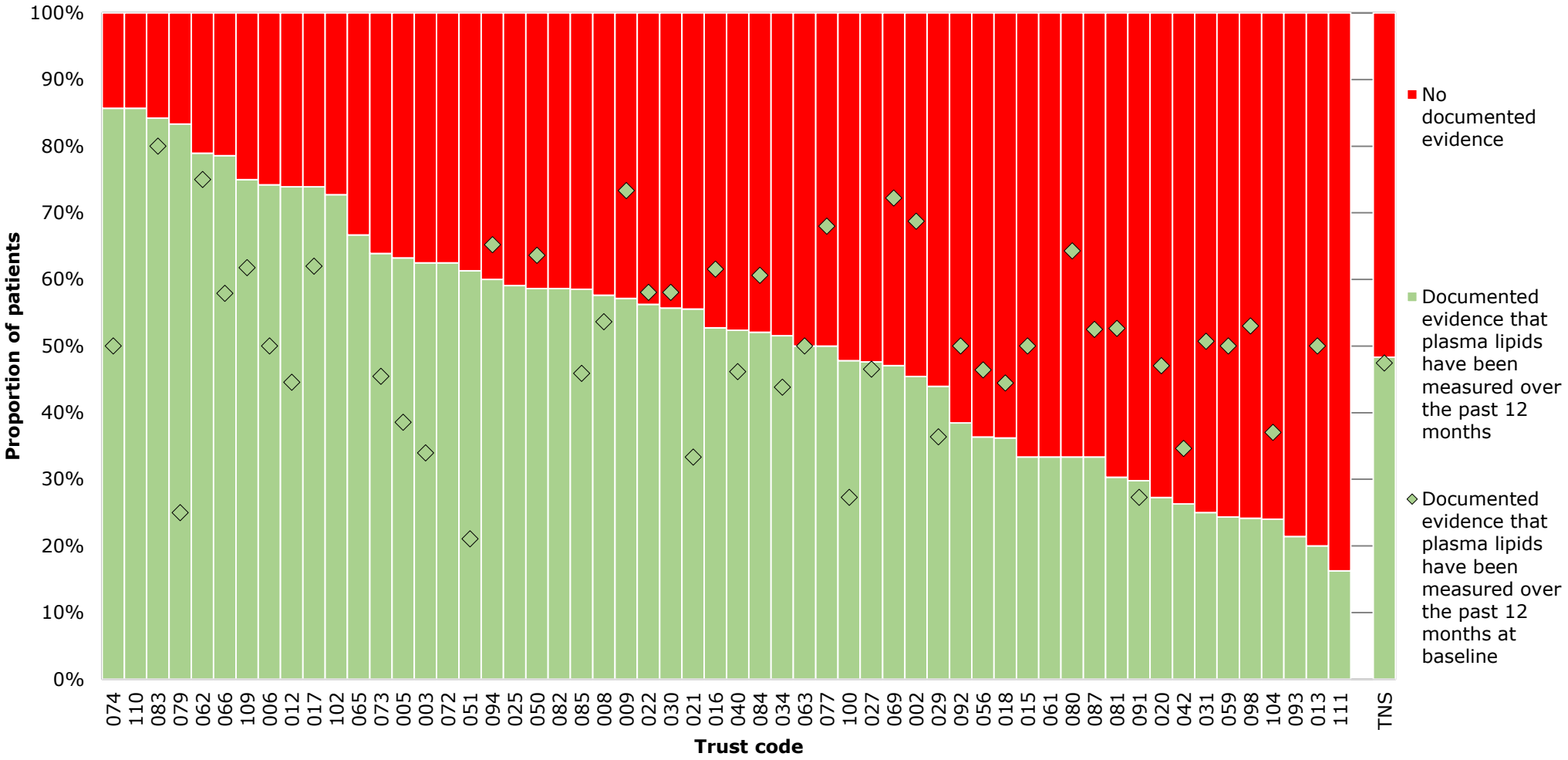


Figure 28: Documented evidence that plasma lipids have been measured over the past 12 months: at Trust level and in the national subsample treated with valproate for a year or more (n=1805), at re-audit

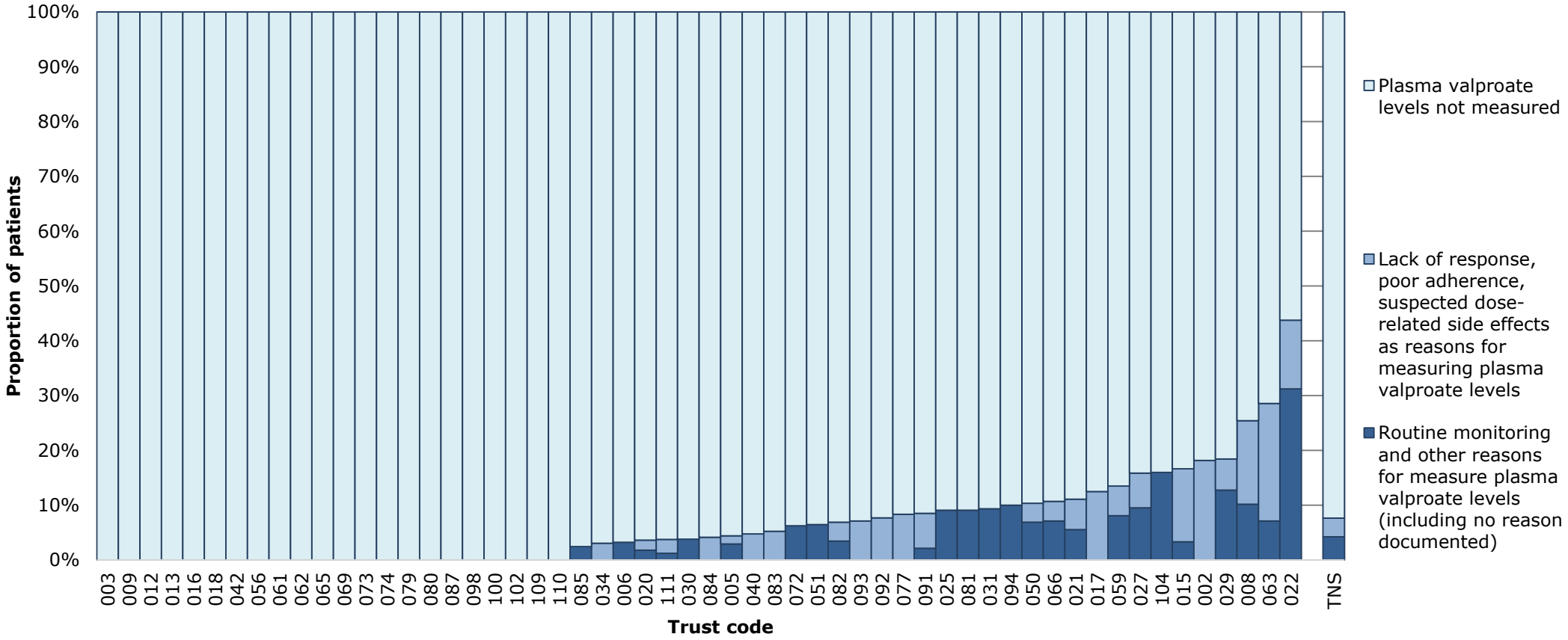


Treatment target

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

Figure 29: Measuring plasma valproate levels and the reasons for doing so (n=136): at Trust level and in the national subsample treated with valproate for a year or more (n=1805), at re-audit

For interpretation of performance against treatment target 1, see figure 15 on page 33.



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.

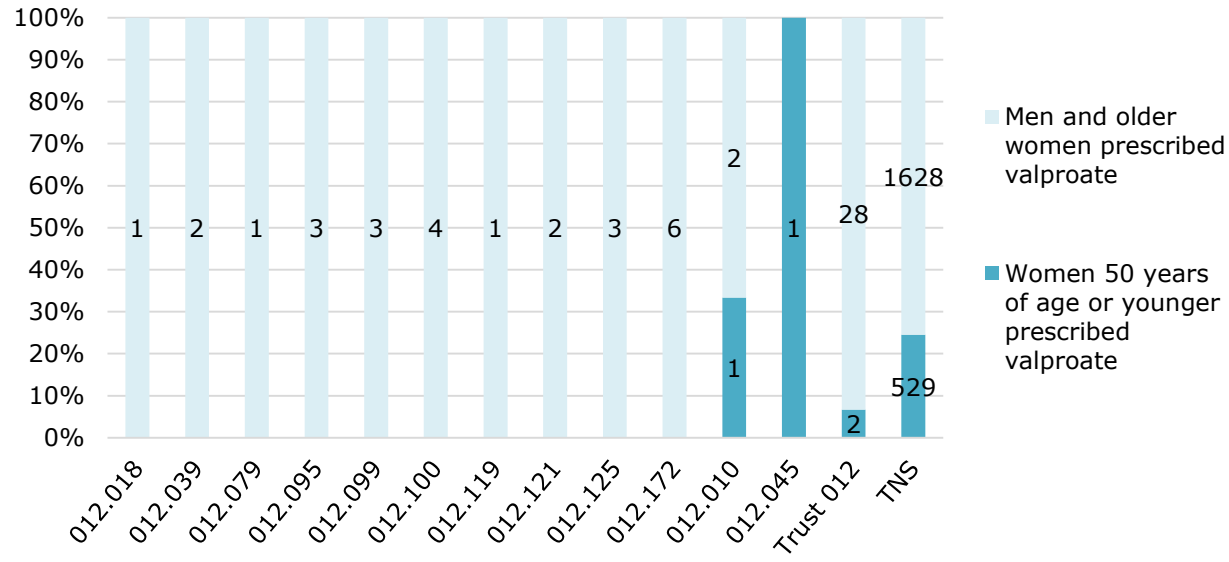
The POMH-UK Central Project Team does not know the identity of individual clinical teams.

Only the Local POMH lead for your Trust or organisation has the key to clinical team codes. You should contact this person if you need to identify data for your own clinical team.

Charts in this section are ordered by frequency of key results and so the position of teams in each figure will vary.

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

Figure 30: Proportion of women 50 years of age or younger prescribed valproate: in the national subgroup prescribed valproate (n=2157) and in your Trust (n=30), at re-audit



Pre-treatment screening

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 31: Proportion of patients prescribed valproate who had BMI/weight measure documented in the 3 months before treatment was initiated: in the national subsample of patients started on valproate in the last 6 months (n=199) and your Trust sample (n=4), at re-audit

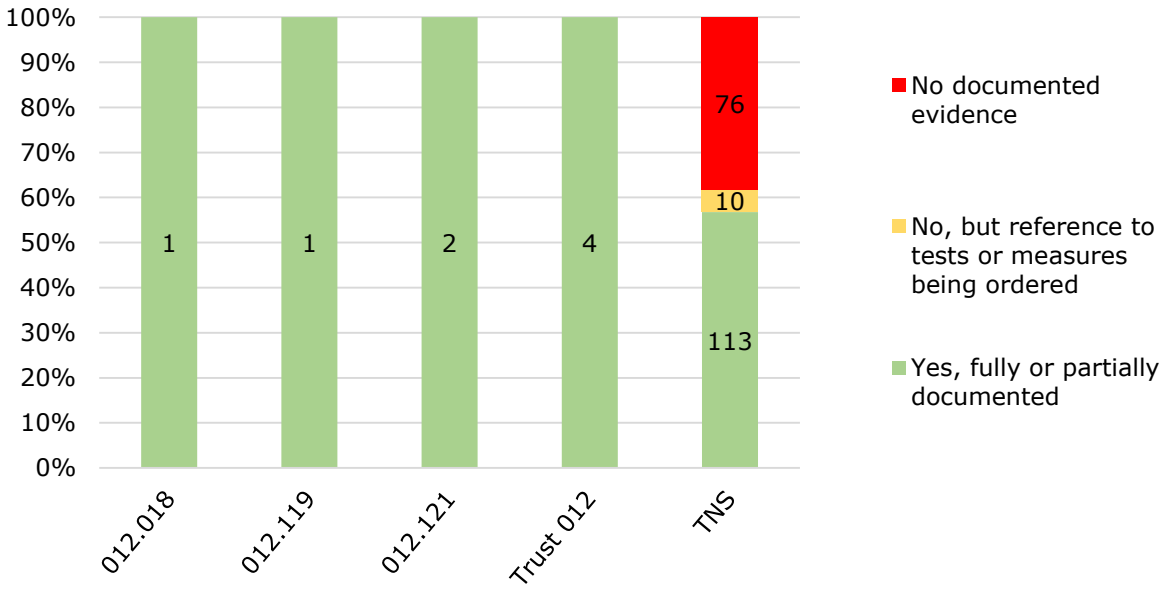


Figure 32: Proportion of patients prescribed valproate who had liver function tests (LFTs) documented in the 3 months before treatment was initiated: in the national subsample of patients started on valproate in the last 6 months (n=199) and your Trust sample (n=4), at re-audit

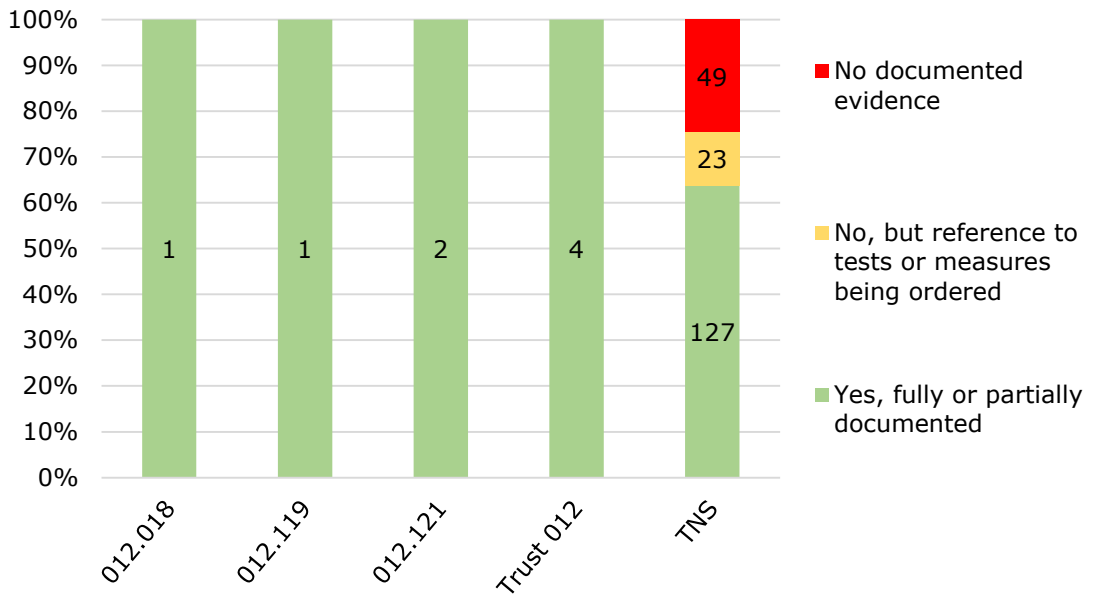
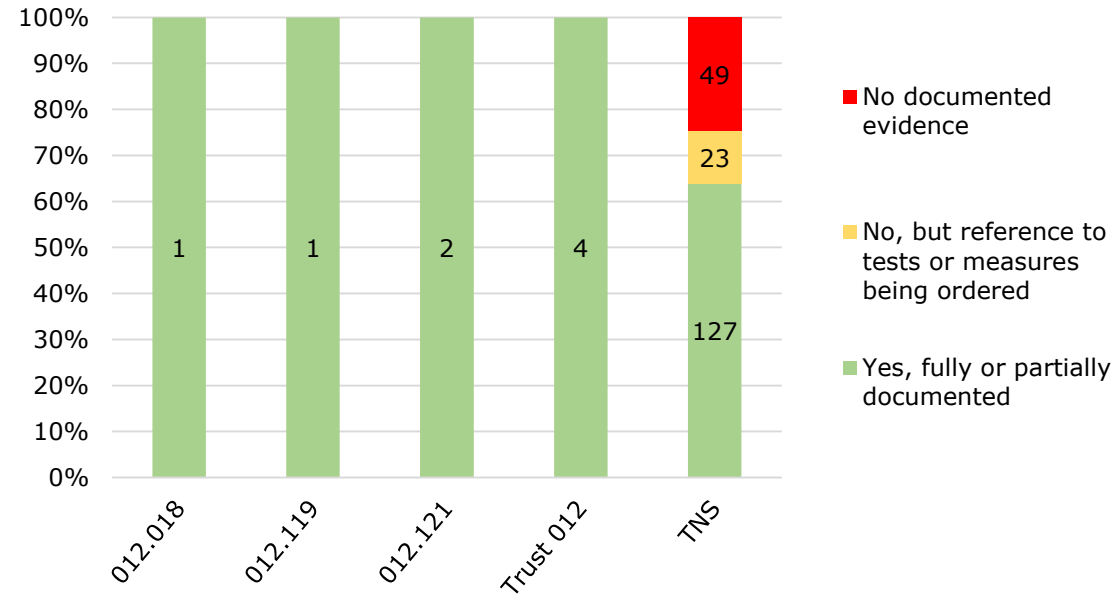
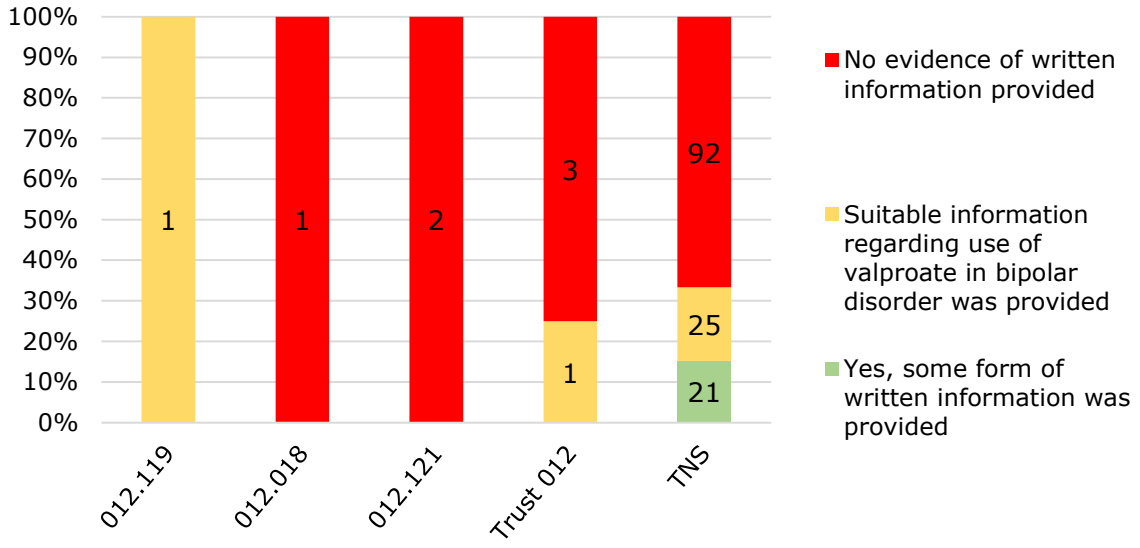


Figure 33: Proportion of patients prescribed valproate who had full blood count (FBC) documented in the 3 months before treatment was initiated: in the national subsample of patients started on valproate in the last 6 months (n=199) and your Trust sample (n=4), at re-audit



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

Figure 34: Written information about the use of valproate offered to inpatients: in the national subsample started on valproate in the last 6 months (n=138) and your Trust sample (n=4), at re-audit



Early on-treatment review

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 35: Documented assessment of therapeutic response as part of an early on-treatment review: in the national subsample treated with valproate for 3-12 months (n=235) and your Trust sample (n=3), at re-audit

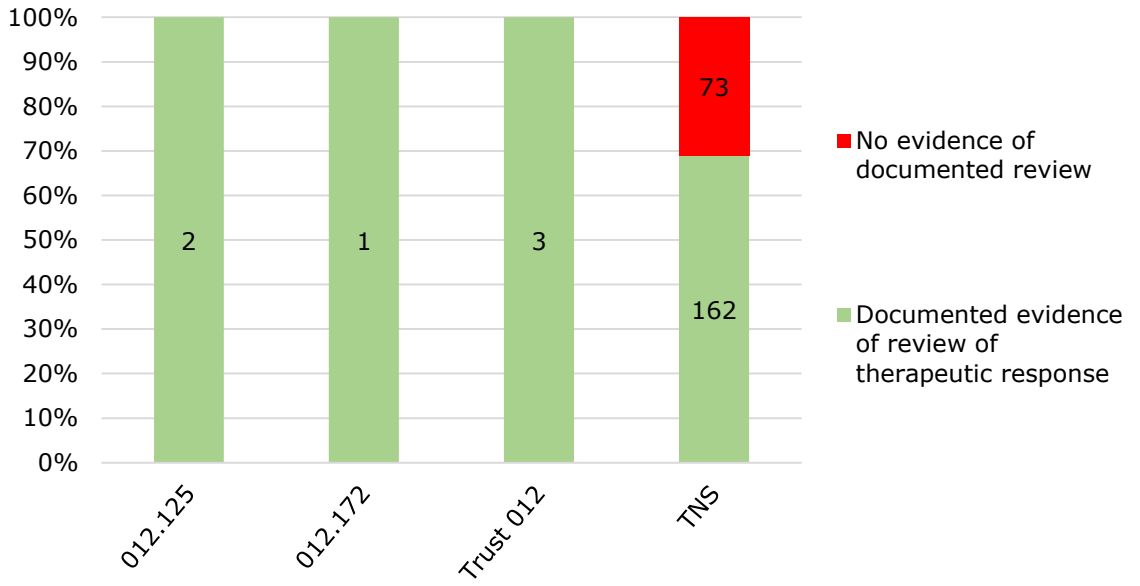


Figure 36: Documented assessment of weight gain or other common side effects as part of an early on-treatment review: in the national subsample treated with valproate for 3-12 months (n=235) and your Trust sample (n=3), at re-audit

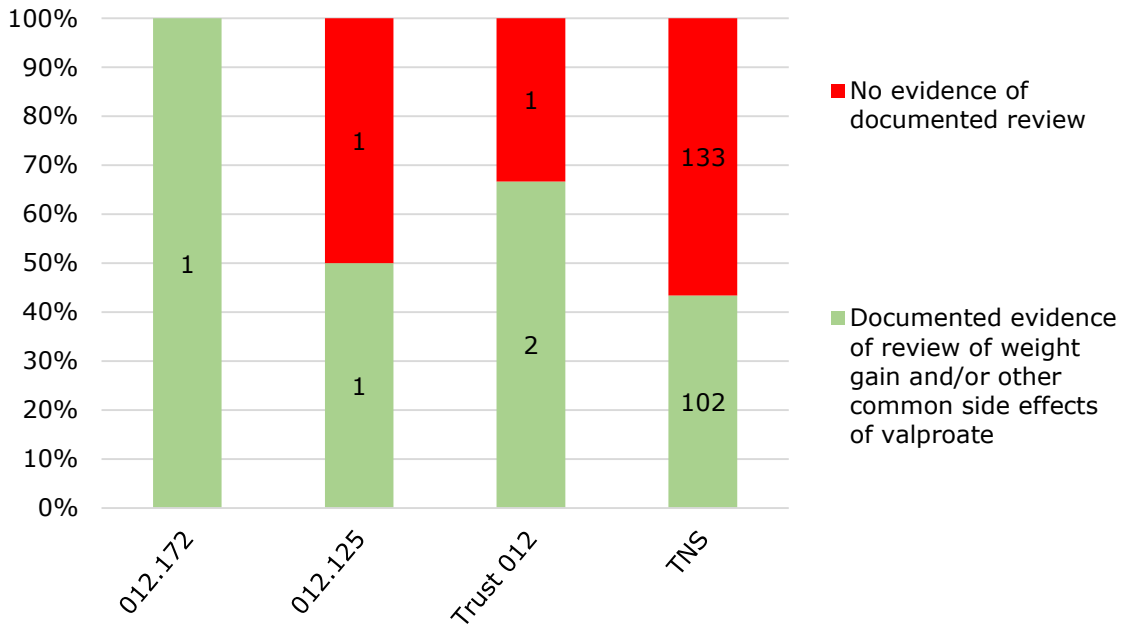


Figure 37: Documented assessment of FBC and/or LFTs as part of an early on-treatment review: in the national subsample treated with valproate for 3-12 months (n=235) and your Trust sample (n=3), at re-audit

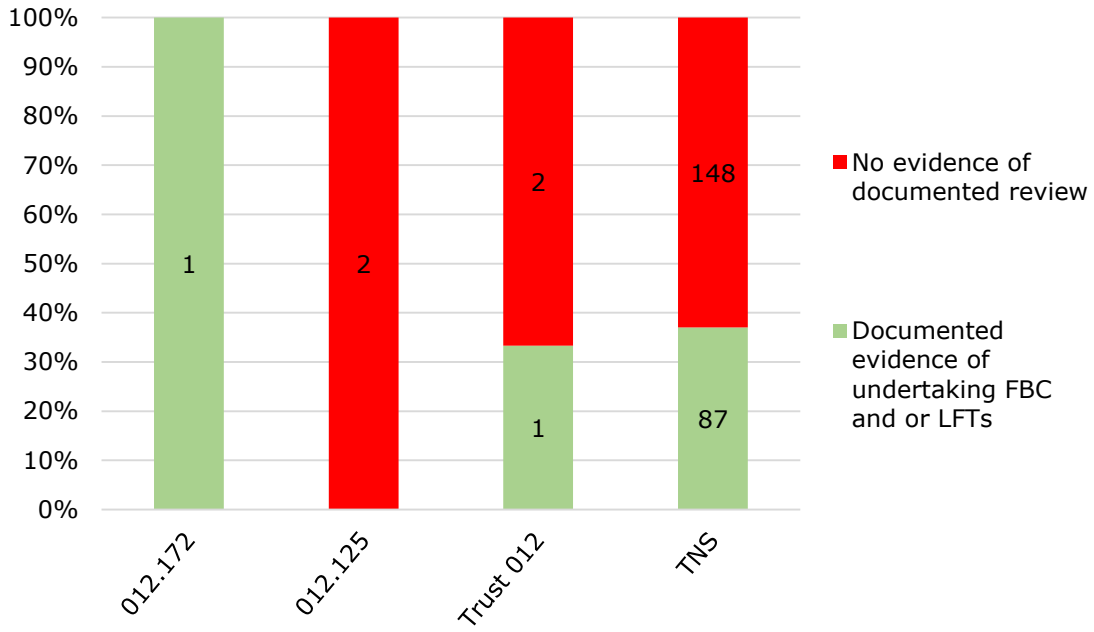
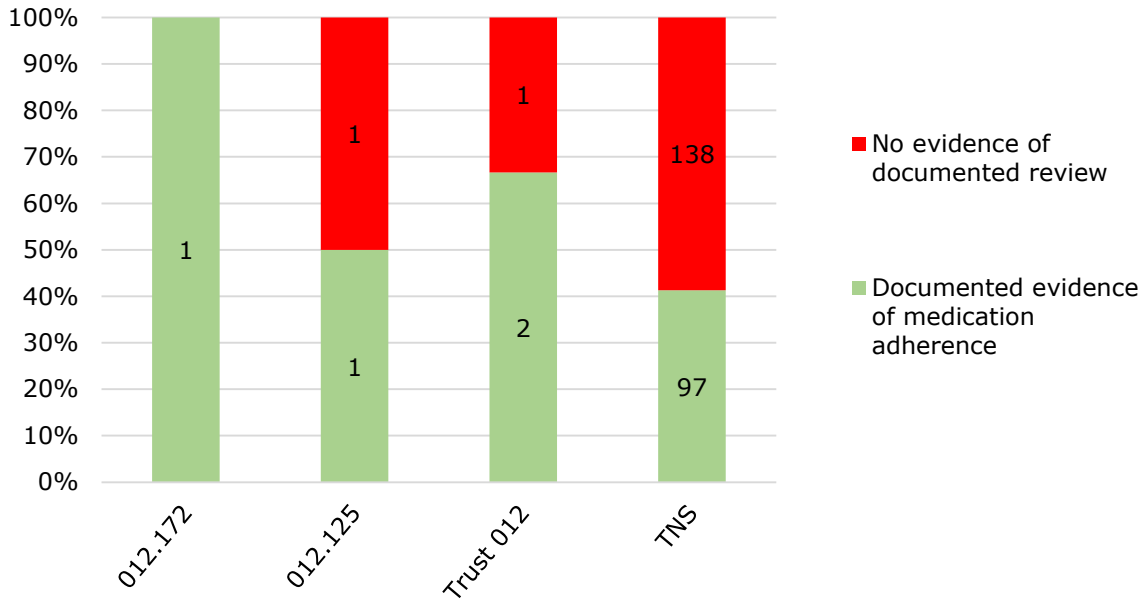


Figure 38: Documented assessment of medication adherence as part of an early on-treatment review: in the national subsample treated with valproate for 3-12 months (n=235) and your Trust sample (n=3), at re-audit



Long-term monitoring

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

Figure 39: Documented evidence that body weight and/or BMI have been measured over the past 12 months: in the national subsample treated with valproate for a year or more (n=1805) and your Trust sample (n=23), at re-audit

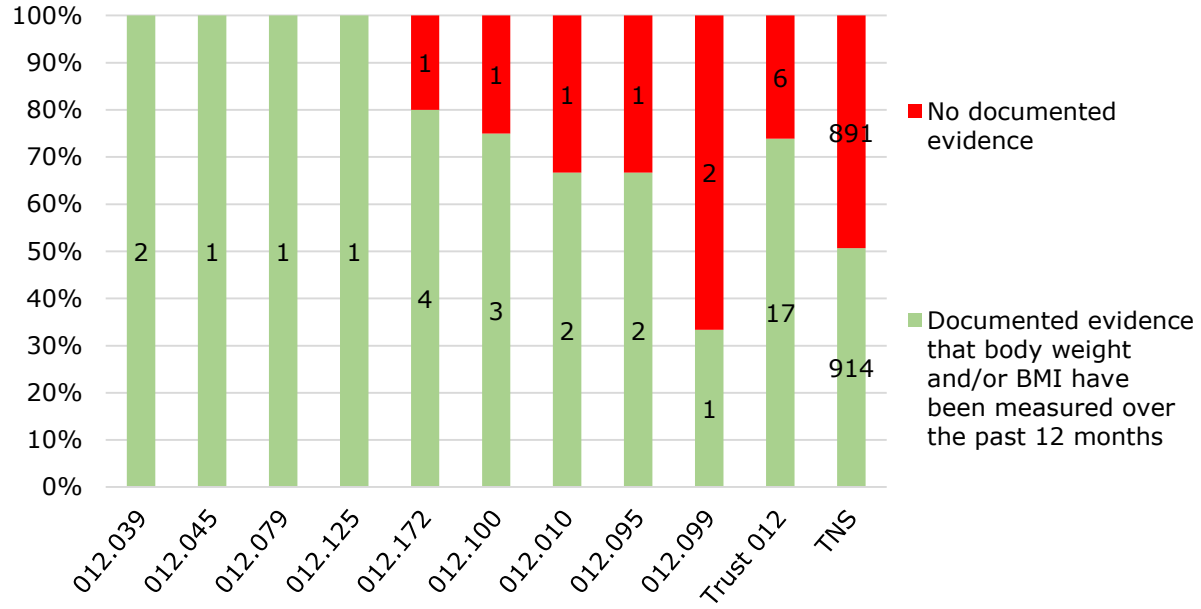


Figure 40: Documented evidence that blood pressure has been measured over the past 12 months: in the national subsample treated with valproate for a year or more (n=1805) and your Trust sample (n=23), at re-audit

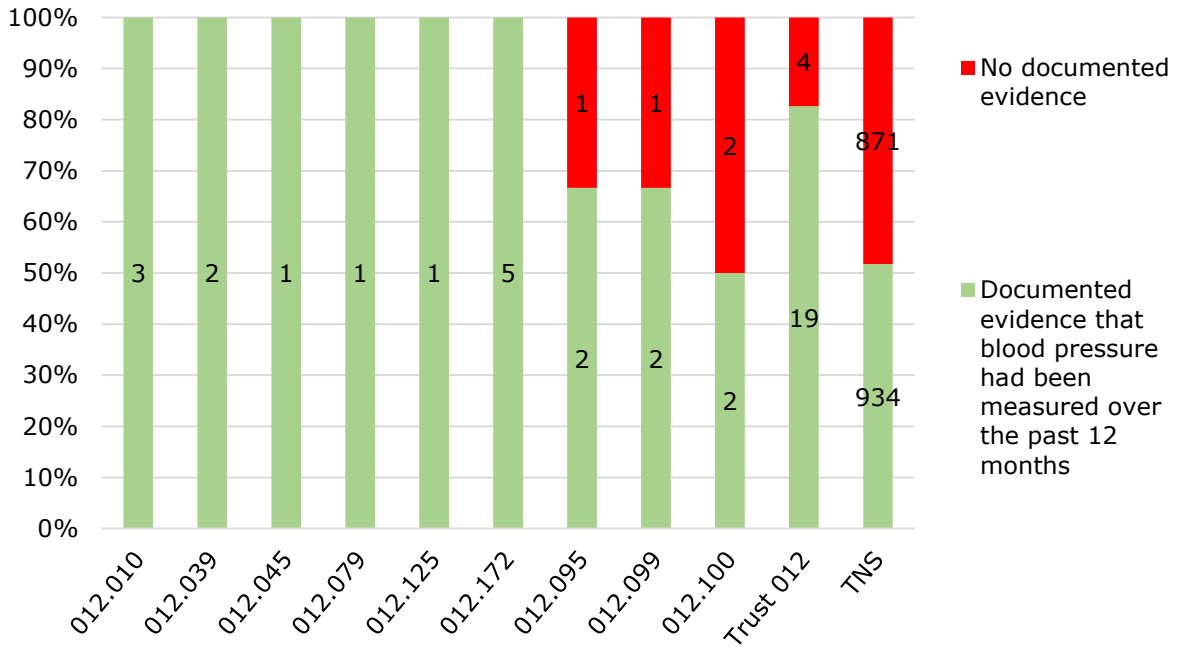


Figure 41: Documented evidence that plasma glucose has been measured over the past 12 months: in the national subsample treated with valproate for a year or more (n=1805) and your Trust sample (n=23), at re-audit

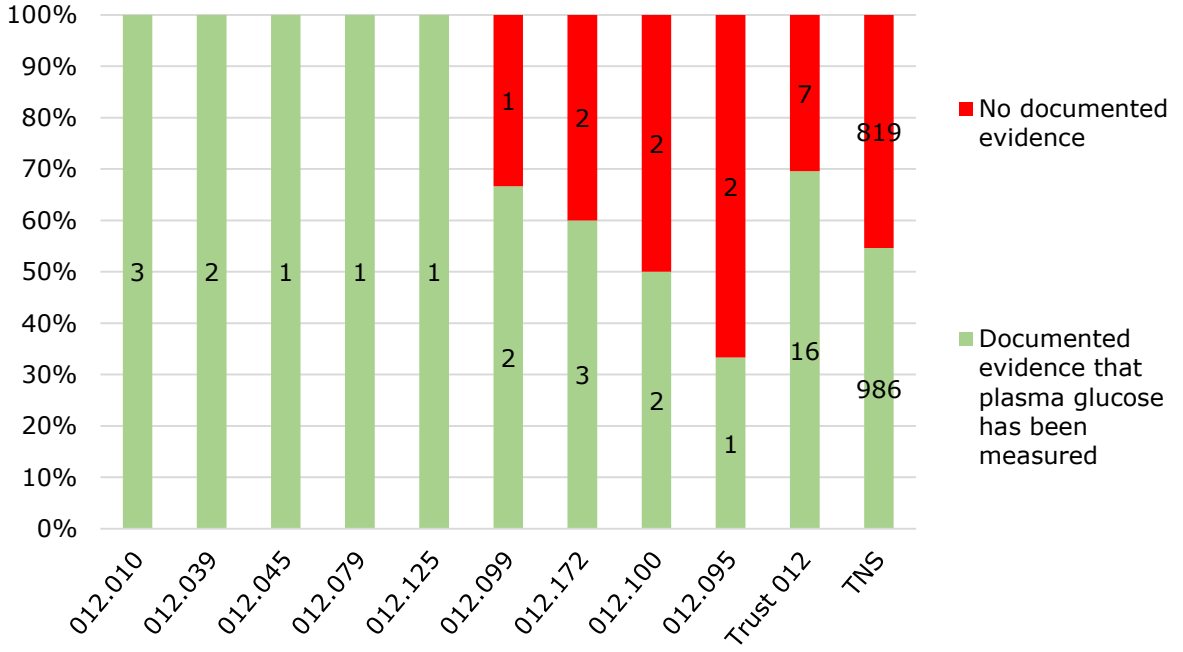
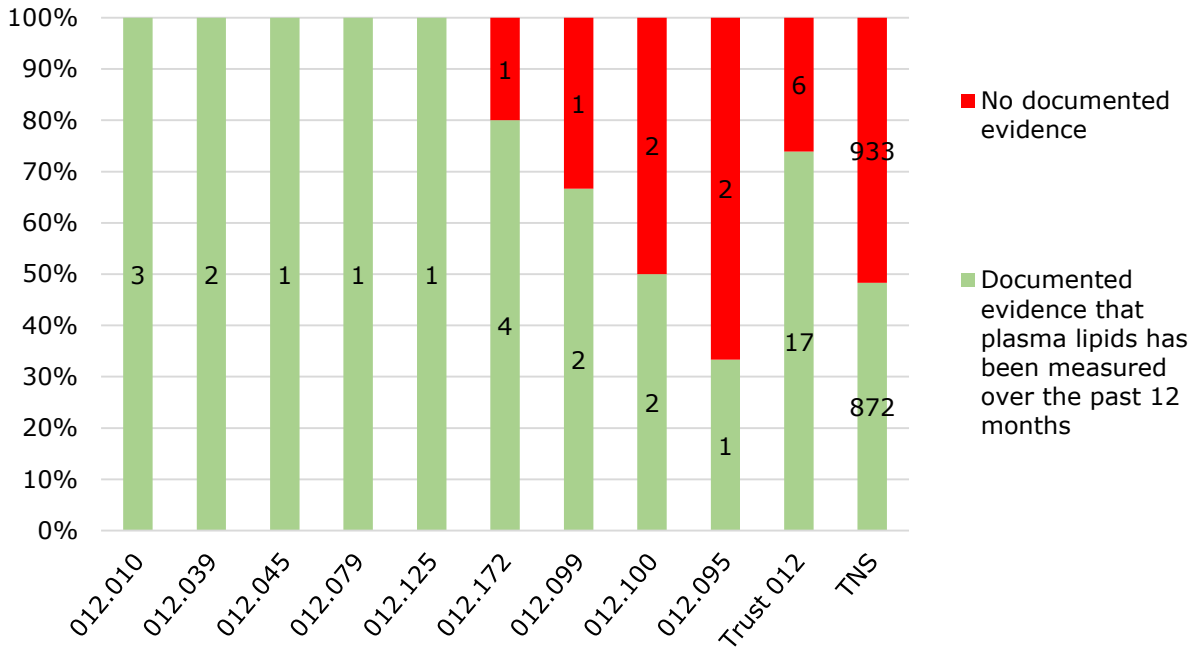


Figure 42: Documented evidence that plasma lipids have been measured over the past 12 months: in the national subsample treated with valproate for a year or more (n=1805) and your Trust sample (n=23), at re-audit



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Appendix A: Data ownership

Data control statement for POMH-UK quality improvement programme 15b: 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.

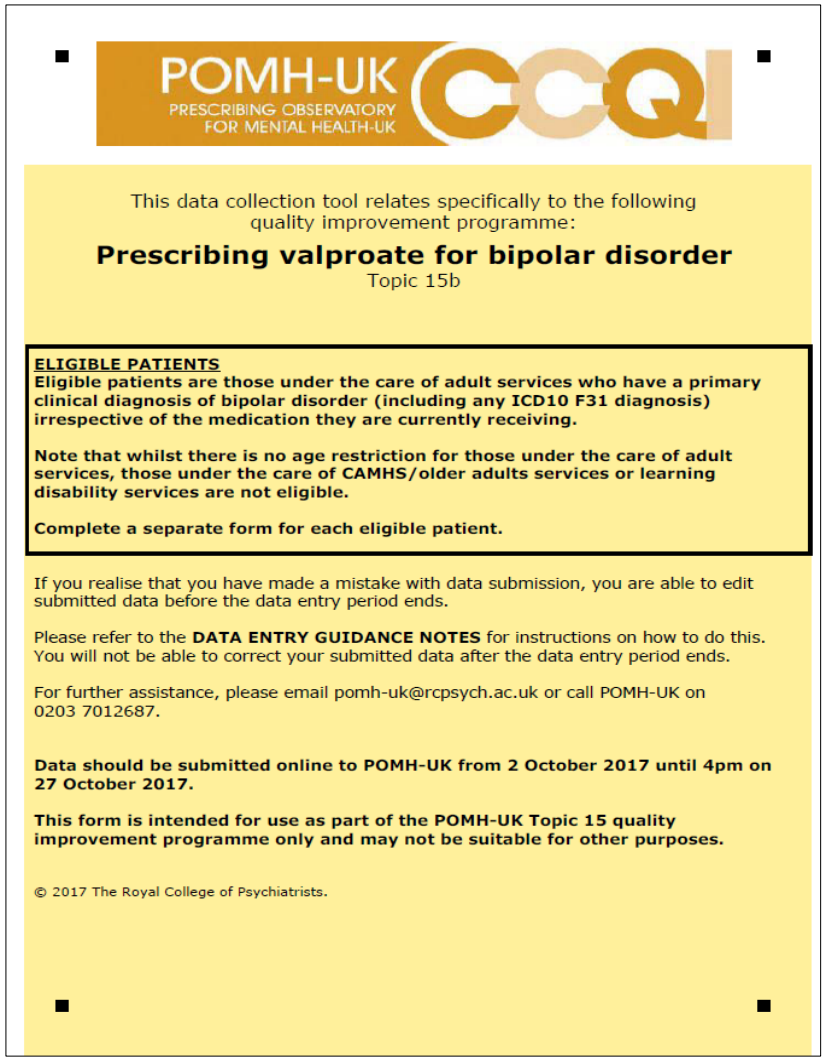
Reflection by clinical teams on their benchmarked performance is perhaps the most potent element of POMH-UK programmes. In addition to performance against the clinical standards, the audit data include demographic, diagnostic and other relevant clinical information that provide a context for interpretation 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.

Appendix B: 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 Mental Health NHS Trust
Belfast Health and Social Care Trust
Berkshire Healthcare NHS Foundation Trust
Betsi Cadwaladr University Health Board
Birmingham and Solihull Mental Health NHS Foundation Trust
Black Country Partnership NHS Foundation Trust
Bradford District Care NHS Foundation 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 NHS Foundation Trust
Cornwall Partnership NHS Foundation Trust
Coventry and Warwickshire Partnership Trust
Cumbria Partnership NHS Foundation Trust
Derbyshire Healthcare NHS Foundation Trust
Dorset Healthcare University NHS Foundation Trust
Dudley and Walsall Mental Health Partnership NHS Trust
East London NHS Foundation Trust
Elysium Healthcare
Essex Partnership University NHS Foundation Trust
Greater Manchester West Mental Health NHS Foundation Trust
Hertfordshire Partnership University NHS Foundation Trust
Humber NHS Foundation Trust
Hywel Dda University Health Board
Isle of Wight NHS Trust
Kent and Medway NHS and Social Care Partnership Trust
Lancashire Care NHS Foundation Trust
Leeds and York Partnership NHS Foundation Trust
Leicestershire Partnership NHS Trust
NAViGO Health and Social Care CIC
Norfolk & Suffolk NHS Foundation Trust
North East London 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
Pennine Care NHS Foundation Trust
Rotherham, Doncaster and South Humber Mental Health NHS Foundation Trust
Sheffield Health & Social Care NHS Foundation Trust
Solent NHS Trust
Somerset Partnership NHS Foundation Trust
South London and Maudsley NHS Foundation Trust
South Staffordshire and Shropshire Healthcare NHS Foundation Trust
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
Sussex Partnership NHS Foundation Trust
Tees, Esk and Wear Valleys NHS Foundation Trust
West London Mental Health NHS Trust
Worcestershire Health & Care NHS Trust

Appendix C: Audit data collection guide and form



POMH-UK
PRESCRIBING OBSERVATORY FOR MENTAL HEALTH-UK

This data collection tool relates specifically to the following quality improvement programme:

Prescribing valproate for bipolar disorder

Topic 15b

ELIGIBLE PATIENTS

Eligible patients are those under the care of adult services who have a primary clinical diagnosis of bipolar disorder (including any ICD10 F31 diagnosis) irrespective of the medication they are currently receiving.

Note that whilst there is no age restriction for those under the care of adult services, those under the care of CAMHS/older adults services or learning disability services are not eligible.

Complete a separate form for each eligible patient.

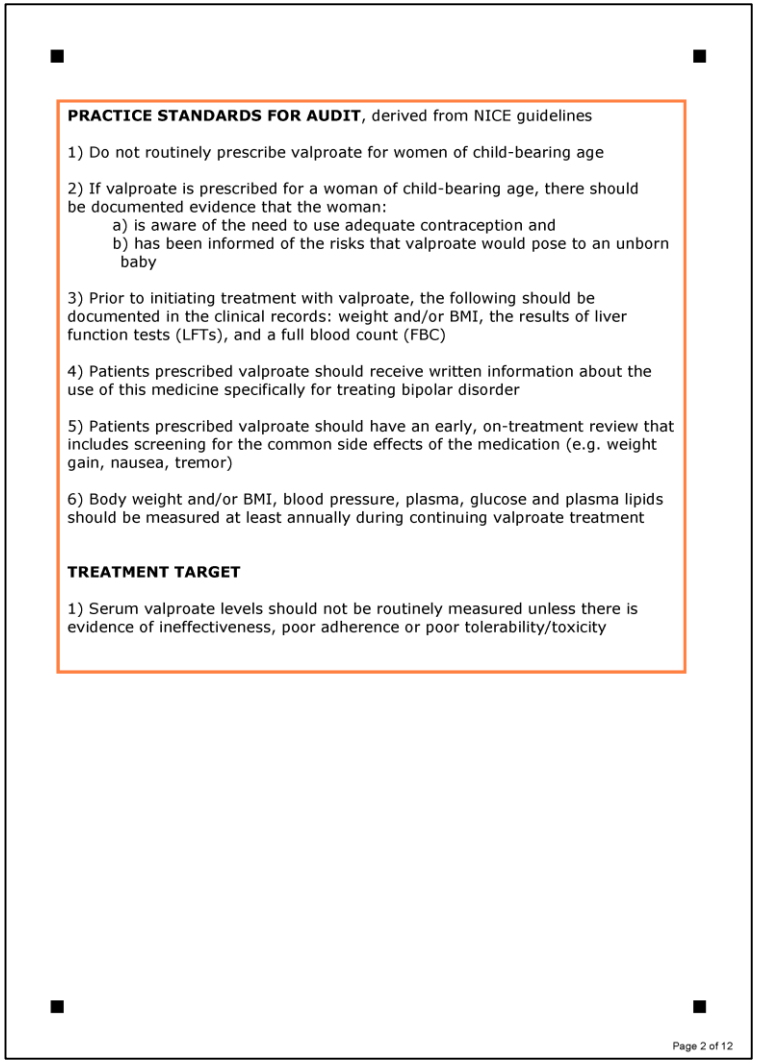
If you realise that you have made a mistake with data submission, you are able to edit submitted data before the data entry period ends.

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 assistance, please email pomh-uk@rcpsych.ac.uk or call POMH-UK on 0203 7012687.

Data should be submitted online to POMH-UK from 2 October 2017 until 4pm on 27 October 2017.

This form is intended for use as part of the POMH-UK Topic 15 quality improvement programme only and may not be suitable for other purposes.



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

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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. 044.006).
Your team codes are known only to your Trust. The POMH-UK team cannot tell you what your team code is.

☐☐☐ . ☐☐☐

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.
Enter any numerical code you like in this field and keep a record for yourselves of what it means.
If you don't want to use an additional identifier, simply leave this field blank.

☐☐☐

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 on whom data are collected, for example Joe Bloggs=1, Jane Bloggs=2.
Keep a record of these codes so you can identify patients should there be data cleaning queries.

☐☐☐

Q5 **Patient year of birth**
(YYYY e.g. 1988)

☐☐☐☐

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/Irish or White Other* ☐ *Asian/Asian British* ☐ *Mixed* ☐ *Not stated/ refused*
☐ *Black/Black British* ☐ *Chinese* ☐ *Other ethnic group* ☐ *Not collected*

Q8 **Which service is currently responsible for this patient's care?**

☐ *Acute adult psychiatric ward*
☐ *Adult community mental health team (includes early intervention, assertive outreach, recovery and rehabilitation teams)*
☐ *Psychiatric intensive care unit*
☐ *Tertiary affective disorders services*
☐ *Adult inpatient rehabilitation services*
☐ *Forensic inpatient services (including low, medium and high secure)*
☐ *Adult home treatment team/crisis intervention team*
☐ *Forensic outpatients*

Diagnosis

Q9 **Diagnosis of bipolar disorder** (tick one response only)

☐ *ICD-10 F31 diagnostic code for bipolar disorder*
☐ *No ICD-10 code for bipolar disorder but currently has a provisional or differential diagnosis of bipolar disorder*
☐ *No ICD-10 code for bipolar disorder but current clinical 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 ticked 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)

N.B. a diagnosis of epilepsy will be recorded later in the audit tool, not in this question.

☐ *Organic, including symptomatic, mental disorders (F00-F09)*
☐ *Mental and behavioural disorders due to psychoactive substance use (F10-F19)*
☐ *Schizophrenia, schizotypal, delusional, and other non-mood psychotic disorders (F20-F29)*
☐ *Mood (affective) disorders (F30, F32-39 excluding bipolar disorder)*
☐ *Anxiety, dissociative, stress-related, somatoform and other nonpsychotic mental disorders (F40-F48)*
☐ *Behavioural syndromes associated with physiological disturbances and physical factors (F50-F59)*
☐ *Disorders of adult personality and behaviour (F60-F69)*
☐ *Intellectual disabilities (F70-F79)*
☐ *Disorders of psychological development (F80-F89)*
☐ *Behavioural and emotional disorders with onset usually occurring in childhood and adolescence (F90-F98)*
☐ *Unspecified mental disorder (F99)*
☐ *None*
☐ *Not known*

Medication

Q 13 **Is this patient currently prescribed any of the following antidepressant medications?**

- Agomelatine ☐
- Amitriptyline ☐
- Bupropion ☐
- Clomipramine ☐
- Citalopram ☐
- Dosulepin ☐
- Doxepin ☐
- Duloxetine ☐
- Escitalopram ☐
- Fluoxetine ☐
- Imipramine ☐
- Lofepramine ☐
- Mirtazapine ☐
- Moclobemide ☐
- Nortriptyline ☐
- Paroxetine ☐
- Phenelzine ☐
- Reboxetine ☐
- Sertraline ☐
- Tranylcypromine ☐
- Trazodone ☐
- Venlafaxine ☐
- No antidepressant prescribed ☐
- Other antidepressant* ☐

**If another antidepressant medication has been prescribed, but is not listed above, please specify the drug name.*

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Q 14 **Is this patient currently prescribed any of the following antipsychotic medications?**

- Amisulpride (oral) ☐
- Aripiprazole (oral/IM) ☐
- Aripiprazole (depot/long-acting injection) ☐
- Asenapine (oral) ☐
- Benperidol (oral) ☐
- Chlorpromazine (oral/IM) ☐
- Clozapine (oral) ☐
- Flupentixol (oral) ☐
- Flupentixol decanoate (depot/long-acting injection) ☐
- Fluphenazine (oral) ☐
- Fluphenazine decanoate (depot/long-acting injection) ☐
- Haloperidol (oral/IM) ☐
- Haloperidol decanoate (depot/long-acting injection) ☐
- Levomepromazine (oral/IM) ☐
- Lurasidone (oral) ☐
- Olanzapine (oral/IM) ☐
- Olanzapine pamoate (depot/long-acting injection) ☐
- Paliperidone (oral) ☐
- Paliperidone palmitate (depot/long-acting injection) ☐
- Pericyazine (oral) ☐
- Perphenazine (oral) ☐
- Pimozide (oral) ☐
- Pipotiazine palmitate (depot/long-acting injection) ☐
- Promazine (oral/IM) ☐
- Quetiapine (oral) ☐
- Risperidone (oral) ☐
- Risperidone (depot/long-acting injection) ☐
- Sertindole (oral) ☐
- Sulpiride (oral) ☐
- Trifluoperazine (oral) ☐
- Zotepine (oral) ☐
- Zuclopenthixol (oral) ☐
- Zuclopenthixol acetate (IM) ☐
- Zuclopenthixol decanoate (depot/long-acting injection) ☐
- None ☐
- Other* ☐

**if an antipsychotic not listed above is prescribed, please write in the name:*

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Q15 **Is the patient prescribed any of the following medications?**

- ☐ *A benzodiazepine (prescribed for day time use)*
- ☐ *A benzodiazepine (prescribed for night time use)*
- ☐ *Fish oils*
- ☐ *Folic acid*
- ☐ *Gabapentin*
- ☐ *Melatonin*
- ☐ *Pregabalin*
- ☐ *Promethazine*
- ☐ *Thyroxine (T4)*
- ☐ *Triidothyronine (T3)*
- ☐ *Tryptophan*
- ☐ *Z-hypnotic*
- ☐ *None of the above*

Q 16 **Is this patient prescribed a 'mood stabiliser'?**

	Yes	No
Carbamazepine	☐	☐
Lamotrigine	☐	☐
Lithium	☐	☐
Topiramate	☐	☐
Valproate	☐	☐
Other 'mood stabiliser'*	☐	☐

**If ticked 'other', please specify. Do not list antipsychotic medication here: tick the appropriate box in Q14*

If the patient is <u>not</u> prescribed valproate, please confirm this by ticking this box and then finish by clicking submit at the end of the page

☐

Q17 **Which preparation of valproate is prescribed?**
<u>Ask a pharmacist or a doctor if you are not sure</u>

- ☐ *Sodium valproate (as Epilim or equivalent)*
- ☐ *Valproic acid (as semi-sodium valproate Depakote or equivalent)*
- ☐ *Valproic acid (as Convulex)*

Q 18 Please give the current **total daily dose of valproate (in mg/day)** ☐☐☐☐ mg

Q 19 **How long has this patient been treated with valproate?**

- ☐ 6 months or less - go to Q20 and continue
- ☐ 7-12 months - go to Q28 and continue
- ☐ More than a year - go to Q31 and continue

Pre-treatment screening (subsample treated for 6 months or less)

Q20 **At the time that treatment with valproate was started, was the patient a psychiatric inpatient?**

☐ *Yes* ☐ *No*

Q 21 **Were the results of the following tests or measures documented in the clinical records in the three months <u>before</u> treatment with valproate was started?**

	Yes, fully or partially documented	No, but reference to tests or measures being ordered	No documented evidence
Full blood count	☐	☐	☐
Liver function tests (LFTs)	☐	☐	☐
Weight or BMI or waist circumference	☐	☐	☐

Q22 **Is there documented evidence that, at treatment initiation, the patient was offered written information about the use of valproate?** (tick all that apply):

- ☐ *Yes, the manufacturer's patient information leaflet (PIL) packaged with the medication*
- ☐ *Yes, a suitable* information leaflet covering the use of valproate in the treatment of epilepsy (and other licensed indications)*
- ☐ *Yes, a suitable* information leaflet covering the use of valproate in the treatment of bipolar disorder*
- ☐ *Written information provided, but the content is unclear*
- ☐ *No evidence that written information was provided*

**Trust-approved or from the website of an appropriate professional organisation*

Q23 **What was the clinical reason/indication/target symptom for starting valproate treatment?** <u>Ask the clinical team if this is not clear from the clinical records.</u> (Tick all that apply)

- ☐ *Acute manic symptoms*
- ☐ *Hypomanic symptoms*
- ☐ *Impulsivity/poor impulse control*
- ☐ *Acute, mixed affective state*
- ☐ *Depressive symptoms*
- ☐ *Suicidality*
- ☐ *To manage rapid cycling of mood*
- ☐ *To provide long-term relapse prevention/symptom control*
- ☐ *Epilepsy*
- ☐ *Prevention of clozapine-related seizures*
- ☐ *Aggressive behaviour*
- ☐ *Part of an alcohol detoxification regimen*
- ☐ *To manage alcohol or other substance use*
- ☐ *To prevent migraine headaches*
- ☐ *Unclear*
- ☐ *Other**

**If other, please state*

Q24 **Is this patient a woman under 50 years of age?**

☐ *Yes* - go to Q25 and continue ☐ *No* - go to Q27 and continue

Q25 **If yes to Q24, at the time valproate treatment was initiated, was there documented evidence in the clinical records of the following:**

	Yes	No
A general discussion regarding side effects and benefits of the treatment	☐	☐
Discussion with the woman of the need for adequate contraception during valproate treatment	☐	☐
The woman was informed of the risks to the foetus (teratogenicity, including neural tube defects/spina bifida) when valproate is taken during pregnancy	☐	☐
The woman was informed of the implications for the longer-term cognitive development of the child (for example, neuro-developmental delay, autistic spectrum disorders) when valproate is taken during pregnancy?	☐	☐
The woman was given the MHRA leaflet that outlines the problems associated with valproate in pregnancy	☐	☐

Q26 **Is there documented evidence in the clinical records regarding this woman's childbearing potential or use of contraception?**

- ☐ *Yes, patient is postmenopausal*
- ☐ *Yes, patient has had an injectable contraceptive or implant fitted*
- ☐ *Yes, patient has undergone an ophorectomy/hysterectomy/endometrial ablation*
- ☐ *Yes, takes oral contraceptive*
- ☐ *Yes, patient has undergone surgical sterilisation (e.g. tubal ligation)*
- ☐ *Yes, other contraceptive method documented*
- ☐ *Yes, patient has an IUD/coil fitted*
- ☐ *No documented evidence of protection against pregnancy*

Q27 **Has this patient been treated with valproate for 3 months or less?**

☐ *Yes* - **finish and go to end of form** ☐ *No - go Q28 and continue*

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*
- ☐ *Other common side effects of valproate (see guidance notes)*
- ☐ *Full blood count (FBC)*
- ☐ *None of the above*
- ☐ *Weight gain*
- ☐ *Liver function tests (LFTs)*
- ☐ *Medication adherence*

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)

Q 31 **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*

Q34 **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*

Q35 **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*

Q36 **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.* **you have finished this form. Press submit**
- ☐ *Yes**

*If yes, please provide the plasma level result (mg/L or micrograms/ml) and then go to Q37

Q37 **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:*

These data should be submitted online to POMH-UK by: 27 Oct 2017

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. Keep a note of the receipt number shown after submission. You will need this to access this submitted form to correct any data entry errors.

You will not be able to correct your submitted data after the data entry period ends.

For further information please contact POMH-UK@rcpsych.ac.uk

Guidance notes

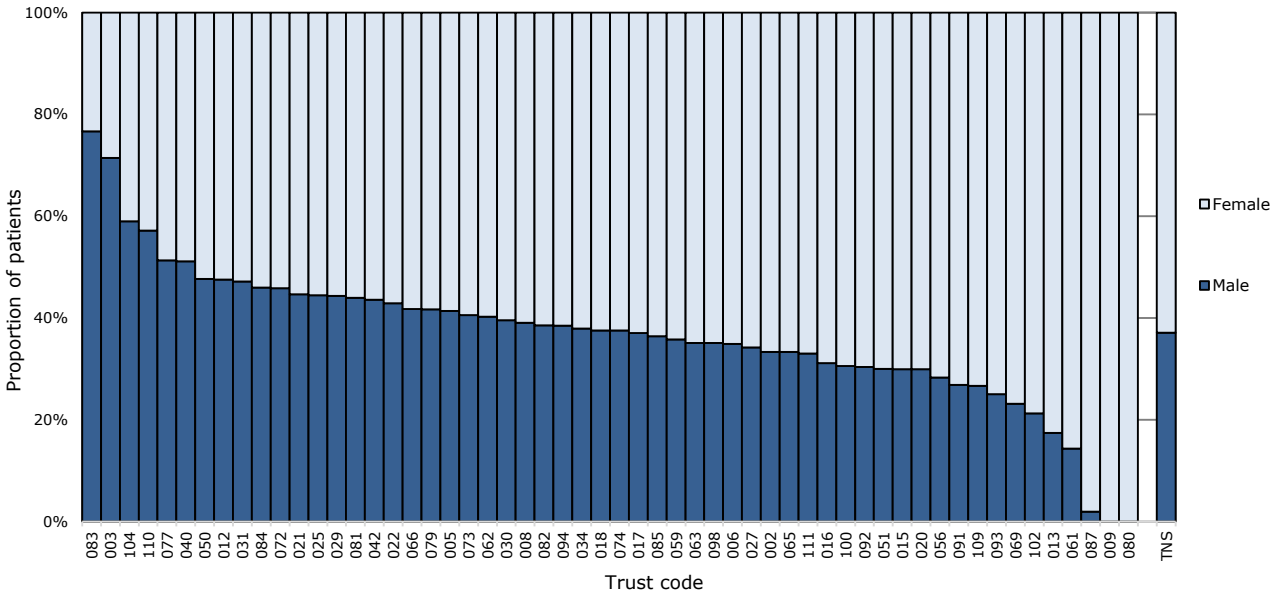
Q29 and **Q32:** Aside from the adverse effects already covered in Q29, valproate SPCs list the following very common (1/10) or common (1/100 to < 1/ 10) undesirable effects:

Very common: nausea, tremor

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

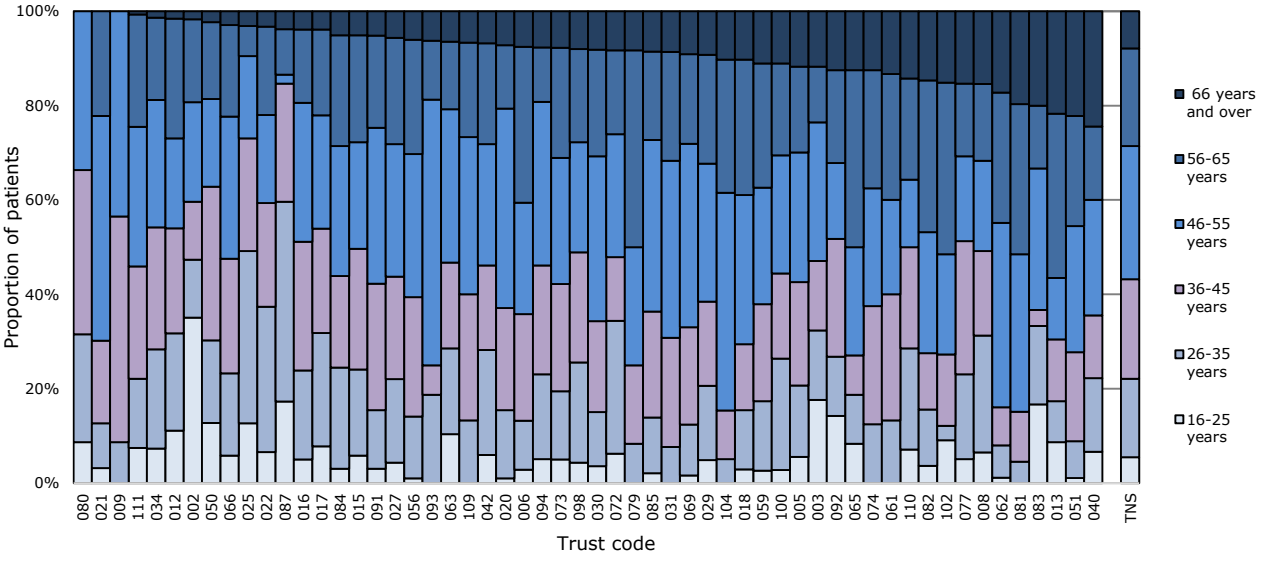
Appendix D: Clinical and demographic characteristics of patient sample

Figure 43: Proportion of males and females for each Trust and the total national sample



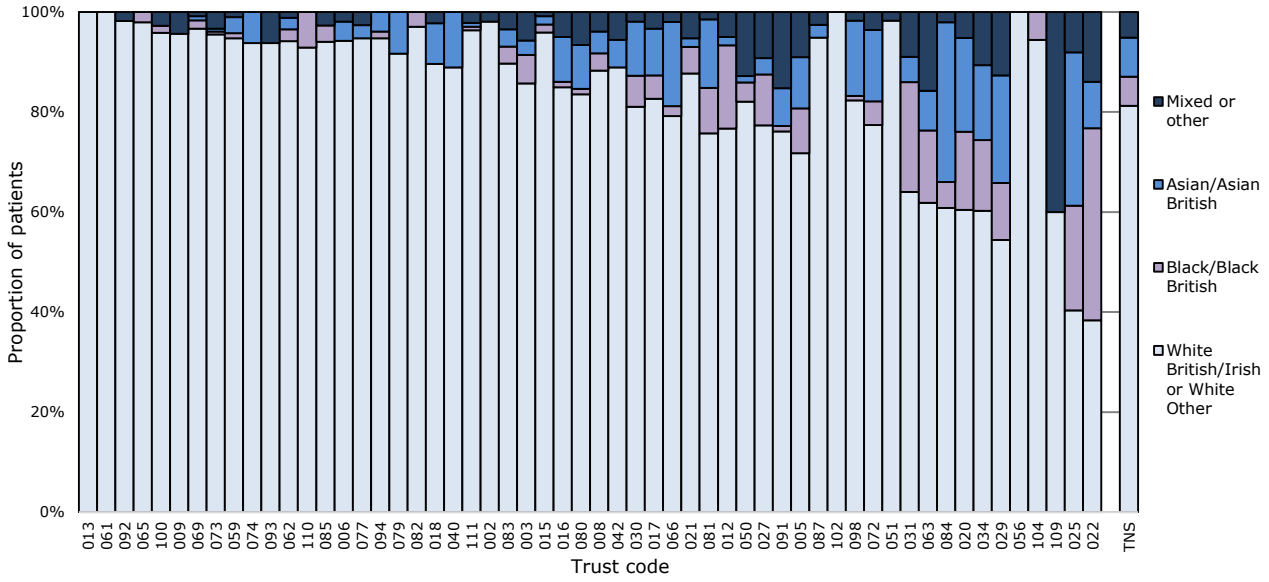
The Trust that submitted data for the highest proportion of males is on the left-hand side of the Figure and the Trust with the lowest on the right. In this Figure, and all such subsequent figures, the proportions in the TNS are shown on the far right of the Figure. This Figure allows Trusts to compare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

Figure 44: Age bands of patients by Trust and in the total national sample



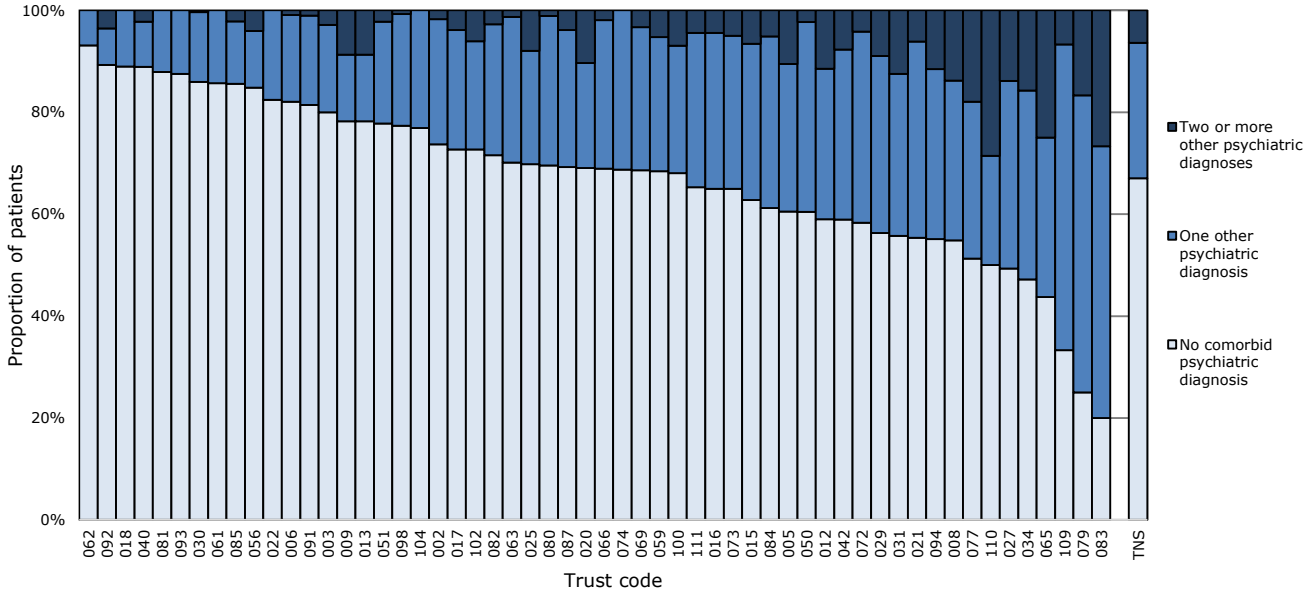
The Trust with the highest proportion of patients in the 66 years and over age-band is on the right-hand side of the Figure and the Trust with the lowest proportion on the left. This Figure allows Trusts to compare the diagnostic profile of their sample of patients against the total national sample.

Figure 45: Distribution of the four most common ethnic groups by Trust and in the total national sample



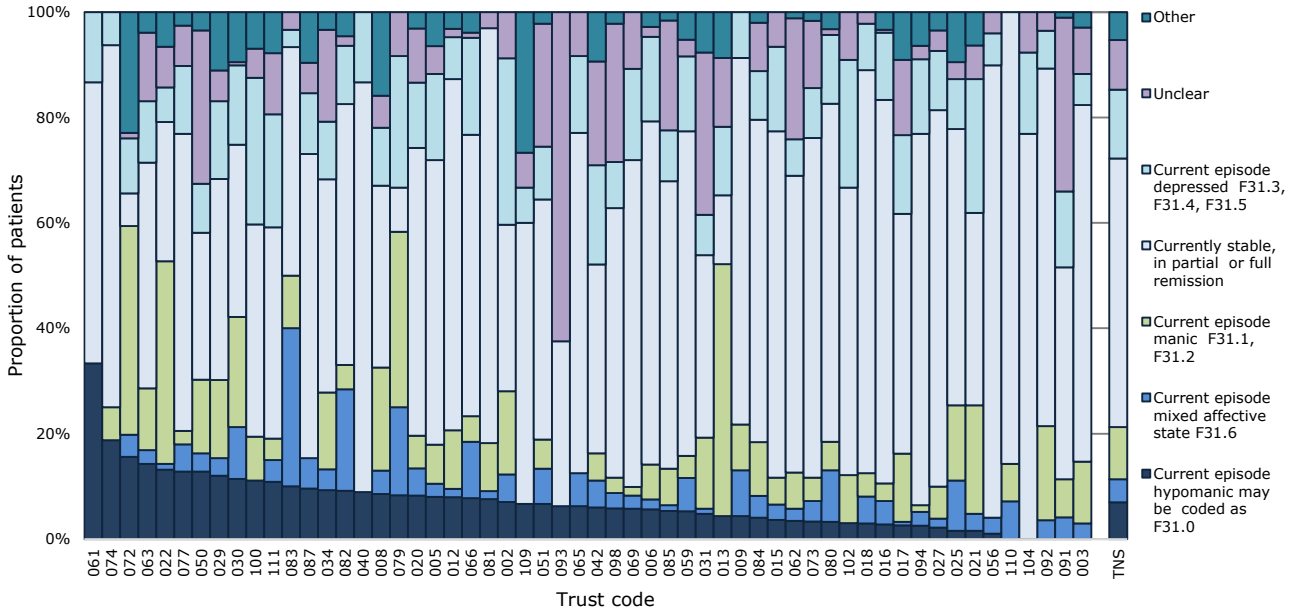
The Trusts with the highest proportion of White British/Irish patients are on the left-hand side of the Figure and the Trust with the lowest proportion on the right. This Figure allows Trusts to compare the demographic characteristics of their sample of patients against the total national sample. Trust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

Figure 46: Patients' psychiatric diagnoses by Trust and in the total national sample



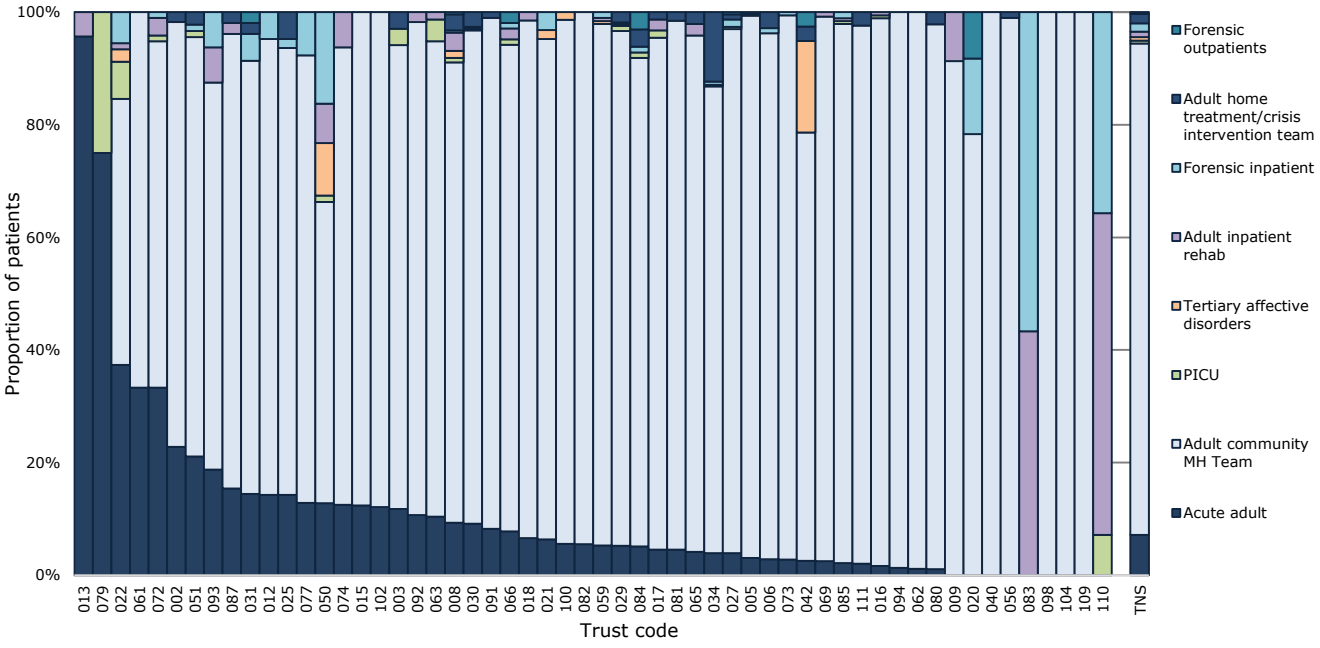
The Trust with the highest proportion of patients without a co-morbid diagnosis is on the left-hand side of the Figure and the Trust with the lowest proportion on the right. This Figure allows Trusts to compare the diagnostic profile of their sample of patients against the total national sample.

Figure 47: 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 48: 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 E: POMH-UK QIP 15 Advisory Group

Topic 15b Expert advisors

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Professor I. Nicol Ferrier

POMH-UK Project Team

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Jenny Bari

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Appendix F: References

BALANCE investigators and collaborators, Geddes JR, Goodwin GM, Rendell J, et al. Lithium plus valproate combination therapy versus monotherapy for relapse prevention in bipolar I disorder (BALANCE): a randomised open-label trial. Lancet 2010;375:385-95

Kessing LV, Bauer M, Nolen WA, et al. Effectiveness of maintenance therapy of lithium vs other mood stabilizers in monotherapy and in combinations: a systematic review of evidence from observational studies. Bipolar Disorder 2018, Feb 14. doi: 10.1111/bdi.12623. [Epub ahead of print]

Lee S, Tsang A, Kessler RC, et al. Rapid-cycling bipolar disorder: cross-national community study. British Journal of Psychiatry 2010;196:217-25.

Levine J, Chengappa KN, Brar JS, et al. Psychotropic drug prescription patterns among patients with bipolar I disorder. Bipolar Disorder 2000;2:120-30.

National Institute of Health and Care Excellence. Bipolar disorder: the NICE guideline on the assessment and management of bipolar disorder in adults, children and young people in primary and secondary care. Updated edition. National Clinical Guideline Number 185, 2014.

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

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