RC PSYCH
ROYAL COLLEGE OF PSYCHIATRISTS

POMH
PRESCRIBING OBSERVATORY FOR MENTAL HEALTH

The quality of valproate prescribing in adult mental health services

QI programme 20b Re-audit

Prepared by POMH for

East London NHS Foundation Trust

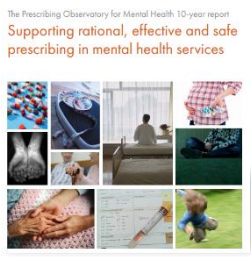
Publication date: May 2023 | Publication no. CCQI 429

Published date: May 2023

Please use the following to cite this report: Prescribing Observatory for Mental Health (2023). Topic 20b: The quality of valproate prescribing in adult mental health services CCQI 429 (data on file).

For further information please contact pomh-uk@rcpsych.ac.uk

About POMH



The Prescribing Observatory for Mental Health (POMH) runs clinical audit-based quality improvement (QI) programmes that focus on discrete areas of prescribing practice. Membership of POMH is open to all NHS, private and not-for-profit providers of mental health services (NHS Trusts/healthcare organisations) in the UK.

The aim is to help mental health services improve prescribing practice by providing benchmarked information on their performance against evidence-based practice standards.

Those interested in learning more about the role of POMH should visit the website: http://www.rcpsych.ac.uk/pomh. A 10-year report (2016) on the work of POMH and a 15-year anniversary report (2020) are also available on the website.

There are also reviews of the POMH 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.

RC PSYCH ROYAL COLLEGE OF PSYCHIATRISTS | POMH PRESCRIBING OBSERVATORY FOR MENTAL HEALTH

Contents

How to read this report

EXECUTIVE SUMMARY p8

PRACTICE STANDARDS p8

The standards against which prescribing practice was measured in this QI programme. These practice standards were derived from evidence-based guidelines and agreed by an expert advisory group.

SUMMARY OF KEY FINDINGS p10

This provides an overview of national performance against the practice standards.

INTRODUCTION p17

CLINICAL BACKGROUND p17

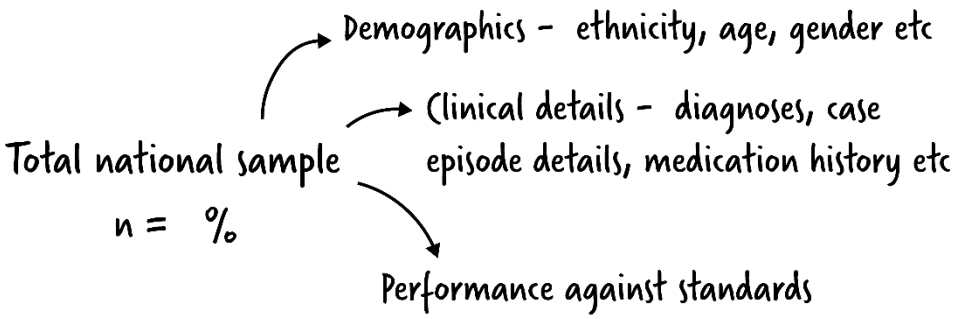
The clinical background to this quality improvement programme

METHOD p18

An outline of the methodology of the quality improvement programme. This includes the nature of the clinical audit data collected and how these were checked.

NATIONAL LEVEL RESULTS p20

The demographic and clinical characteristics of the total national sample are described (TNS). The findings of the data analyses 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 RESULTS ----------p40

The analyses presented in this section allow Trusts to compare the quality of their local practice, in absolute terms, with the practice standards 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 an aspect of prescribing practice across all Trusts individually and the 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 ----------p64

The figures in this section 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 TNS and the bar next to this shows the overall Trust performance.

The results presented in this report allow you to compare your team's/Trust's practice against:

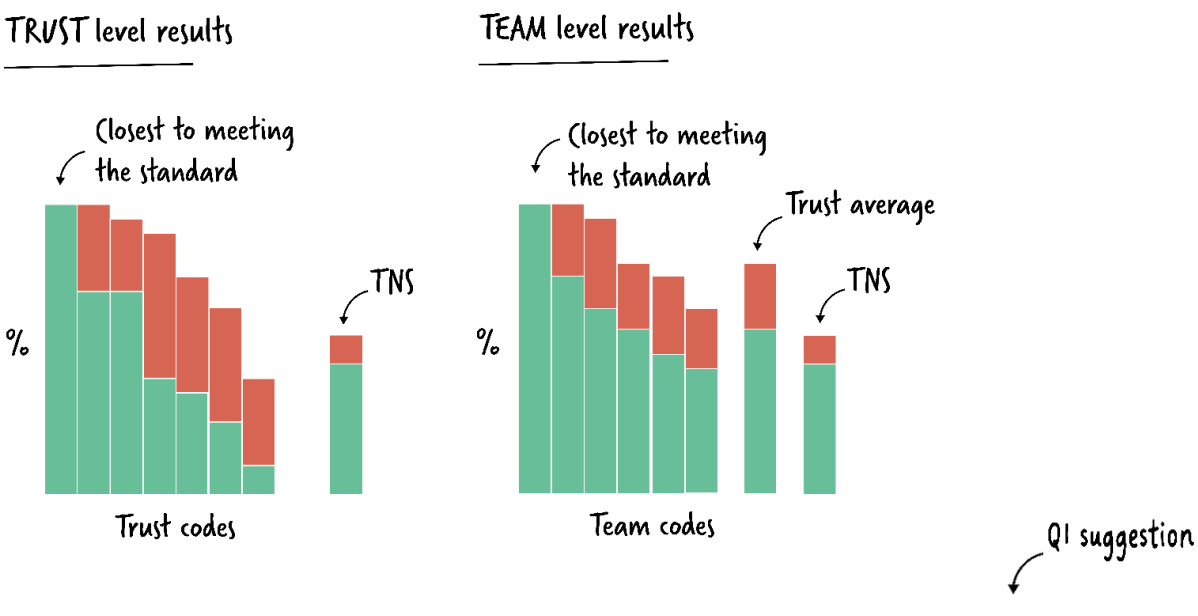
- Treatment recommendations in nationally recognised guidelines, including those published by the National Institute for Health and Care Excellence (NICE) and the British Association for Psychopharmacology (BAP).
- The practice of other participating Trusts.

Further analysis of your Trust's data

An Excel file containing the data submitted by your Trust has been made available to your Local POMH Lead. Please contact this person if you wish to conduct further analyses on your data.

Trust codes

Data from each clinical team or Trust are presented by code only. The POMH Project Team does not know the identity of individual teams. Only the Local POMH Lead for your Trust has the key to team codes for your Trust. You should contact the person if you need to identify data for your own particular team.



These boxes appear throughout the report. They indicate suggested local QI activity that Trusts may wish to consider.

Executive summary

This report presents the results of the re-audit for a quality improvement programme (QIP) addressing valproate prescribing in adult mental health services.

During October to November 2022, 60 NHS Trusts/healthcare organisations (see Appendix B) participated in this re-audit, submitting data for 4662 patients under the care of 725 clinical teams.

Practice standards

Number	Practice standards
	A clinician's reasons for initiating valproate treatment (i.e. target symptoms or behaviour) should be documented in the clinical records.
	If valproate is being prescribed 'off-label', it should be documented that this has been explained to the patient.
	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).
	Review within the first three months of valproate treatment should include: screening for common side effects of the medication (e.g. weight gain, nausea, and tremor) and assessment of the response of the target symptoms/behaviour.
	Patients prescribed continuing valproate treatment should have an annual review of the risk-benefit balance. This should include assessment of therapeutic benefit, adverse effects and medication adherence.
	If valproate is prescribed for a woman of child-bearing age, there should be documented evidence that the conditions of 'prevent', the pregnancy prevention programme, are fulfilled.

In some cases, the evidence for practice recommendations falls short of supporting an audit standard, i.e. being applicable in 100% of cases. However, the evidence may be sufficient to support general guidance for good practice, allowing that deviation may be appropriate in a proportion of cases. For such treatment targets, clinicians may be particularly interested in how their practice benchmarks with their peers.

Treatment target	
	Plasma level monitoring of valproate treatment should not be used unless there is evidence of ineffectiveness, concerns about medication adherence, or dose-related side-effects.

The practice standards and treatment target were derived from:

- *Use of licensed medicines for unlicensed applications in psychiatric practice 2nd ed*. College Report CR210, Royal College of Psychiatrists Psychopharmacology Committee https://www.rcpsych.ac.uk/improving-care/campaigning-for-better-mental-health-policy/college-reports/2017-college-reports/use-of-licensed-medicines-for-unlicensed-applications-in-psychiatric-practice-2nd-edition-cr210-dec-2017

- *Information on the risks of valproate use in girls (of any age) and women of childbearing potential,* Guide for Healthcare Professionals, MHRA, prevent, valproate pregnancy programme, https://www.medicines.org.uk/emc/rmm/1203/Document https://www.gov.uk/guidance/valproate-use-by-women-and-girls

Summary of key findings

Performance against practice standard 1

A clinician's reasons for initiating valproate treatment (i.e. target symptoms or behaviour) should be documented in the clinical records.

The Figure below shows performance against practice standard 1 in the national and your Trust's samples in the 2020 and 2022 audits.

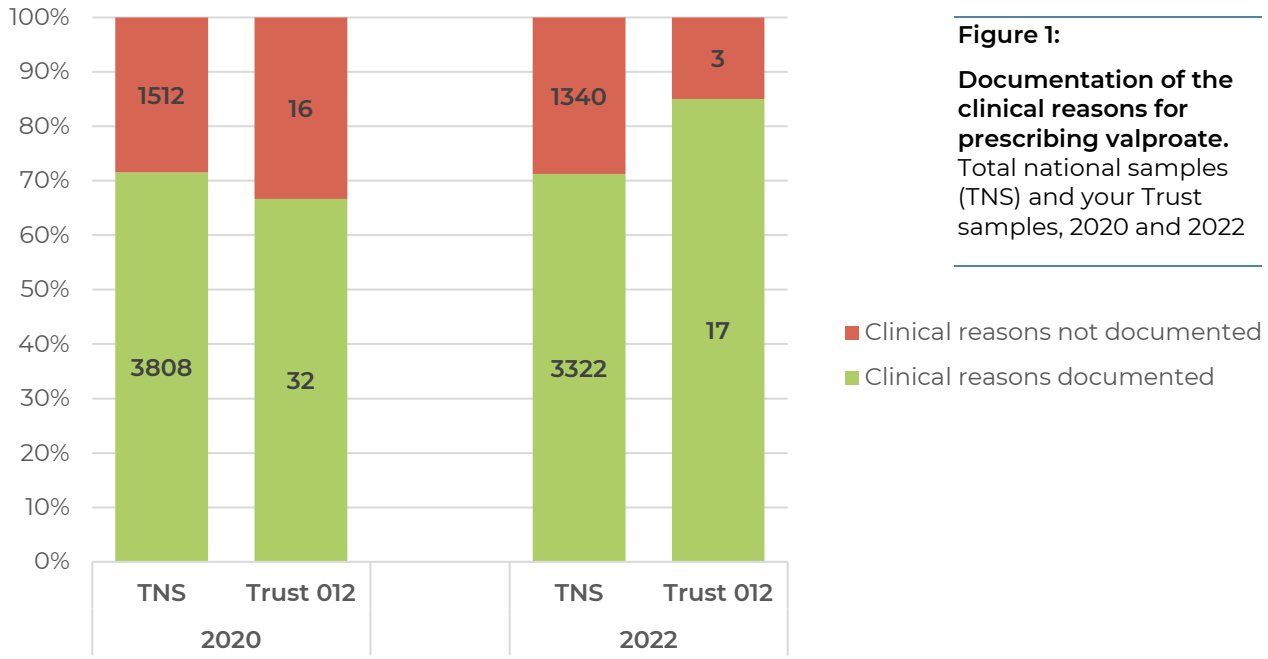


Figure 1:

Documentation of the clinical reasons for prescribing valproate. Total national samples (TNS) and your Trust samples, 2020 and 2022

In 2022, documentation of the clinical reasons for valproate treatment was missing or unclear in more than a quarter of cases in the total national sample. This proportion is unchanged from the 2020 audit.

Given that review of the ongoing effectiveness of valproate treatment becomes challenging if the target symptoms/behaviours for this treatment are unclear, where local practice falls short of this standard, it may benefit from focussed clinical audit.

Performance against practice standard 2

If valproate is being prescribed 'off-label', it should be documented that this has been explained to the patient.

The Figure below shows performance against practice standard 2 in the national and your Trust's subsample of patients prescribed valproate 'off-label', in the 2022 audit.

There was no documented explanation to almost nine out of ten patients that their valproate prescription was 'off-label'.

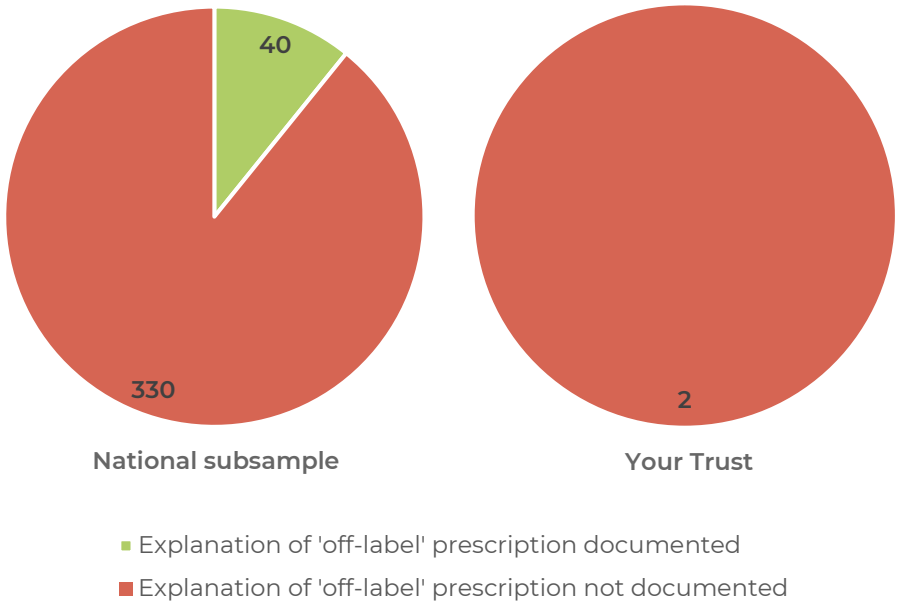


Figure 2:

Documented explanation to patients that valproate prescription is 'off-label'. National subsample and your Trust subsample considered to be prescribed 'off-label' valproate, 2022

Where local practice falls short of this standard, a Trust's medicines management committee (or equivalent) may wish to consider strategies for reminding clinicians of the licensed indications for valproate and also of the paucity of evidence* for the majority of off-label uses.

* Baldwin D & Wieck A. Withdrawal of, and alternatives to, valproate-containing medicines in girls and women of childbearing potential who have a psychiatric illness. Position Statement PS04/18. Royal College of Psychiatrists 2018. https://www.bap.org.uk/pdfs/PS04-18-December2018.pdf
Paton C, Citrome L, Fernandez-Egea E, Rendora O, Barnes TRE. Who is prescribed valproate and how carefully is this treatment reviewed in UK mental health services? Data from a clinical audit. Journal of Psychopharmacology 2022; 12:1-15.

Performance against 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).

The Figure below shows performance against practice standard 3 in the national and your Trust's subsamples of patients treated with valproate for less than a year, in the 2020 and 2022 audits.

Each of the three pre-treatment measures noted in the standard were documented in around two-thirds of patients in both the 2020 and 2022 audits. In the absence of a baseline measure, it becomes more difficult to reliably identify treatment-emergent side effects. While thrombocytopenia and hepatotoxicity are very unlikely to occur, valproate-induced weight gain and related metabolic side effects are far more likely.

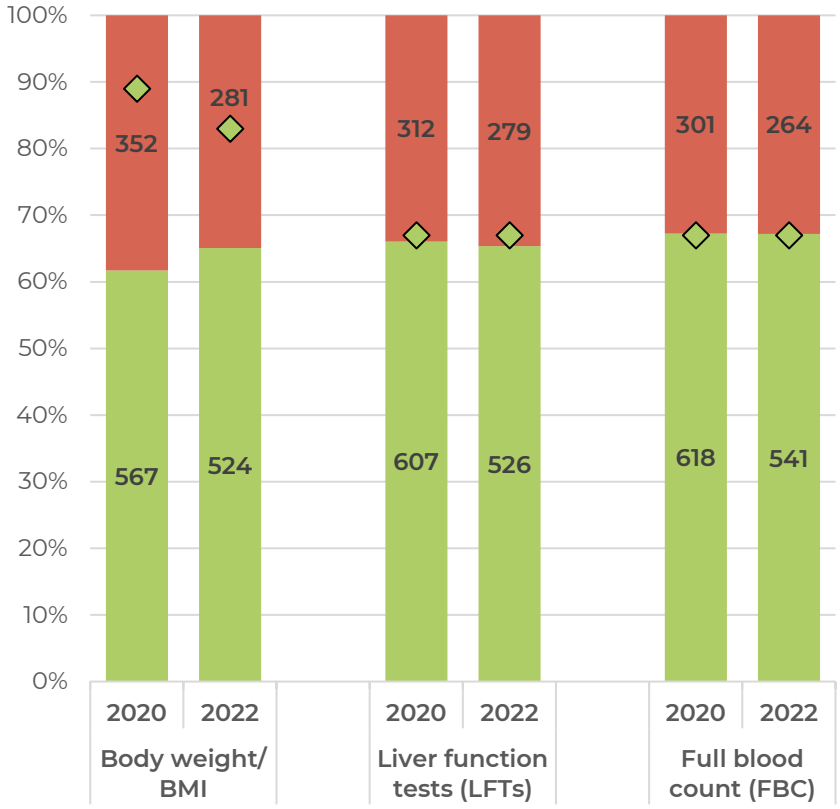


Figure 3:

Documented tests/measures conducted in the three months before valproate medication was started. National subsamples and your Trust subsamples treated with valproate for less than year, 2020 and 2022

Performance against practice standard 4

Review within the first three months of valproate treatment should include: screening for common side effects of the medication (e.g. weight gain, nausea, and tremor) and assessment of the response of the target symptoms/behaviour.

The Figure below shows performance against practice standard 4 in the national and your Trust's subsamples of patients treated with valproate between three months and a year, in the 2020 and 2022 audits.

In 2022, early on-treatment review of therapeutic response and adherence was documented for around three patients in five, while a review of side effects was documented in around half. These proportions are similar to those in 2020.

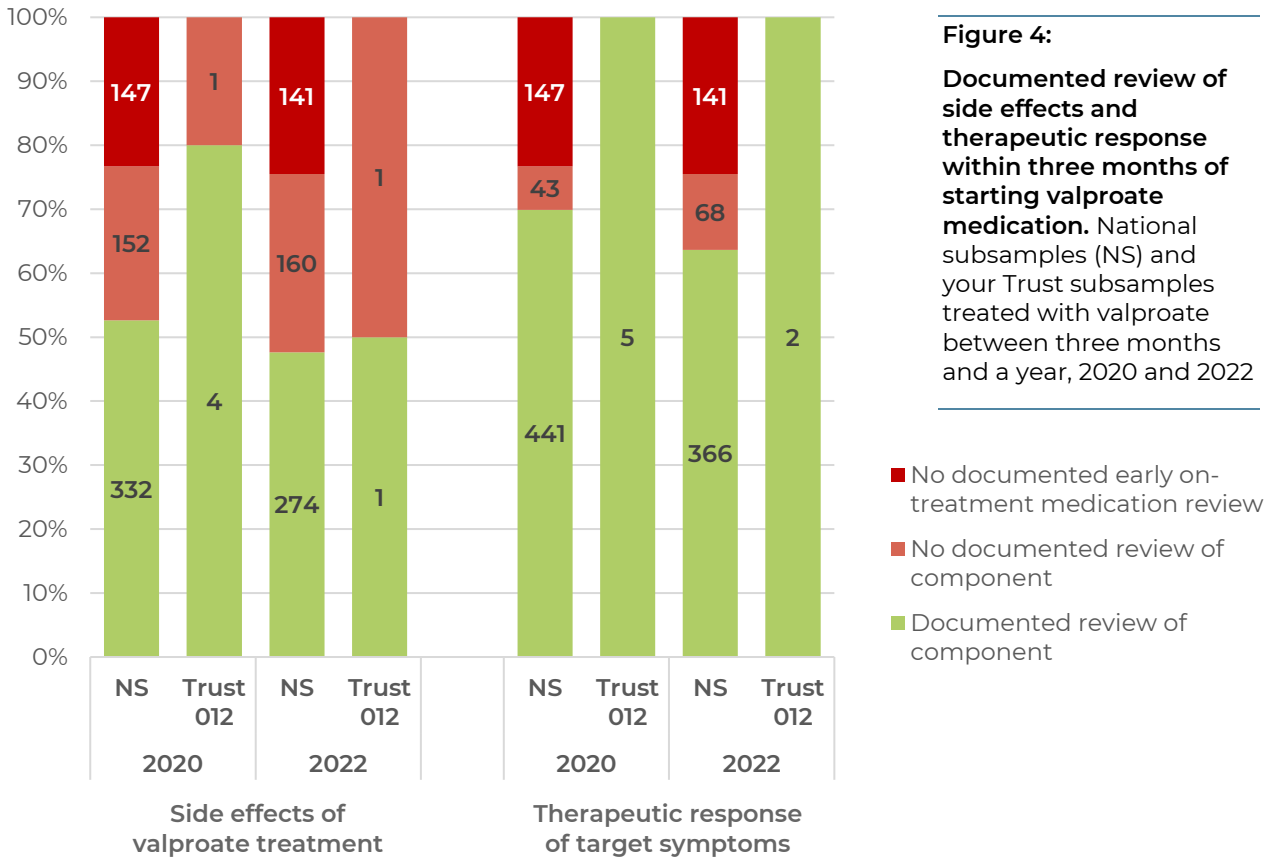


Figure 4:

Documented review of side effects and therapeutic response within three months of starting valproate medication. National subsamples (NS) and your Trust subsamples treated with valproate between three months and a year, 2020 and 2022

Given that early on-treatment review of the risks and benefits of a medication is essential to inform care planning, where practice has fallen short of the standard, Trusts may wish to consider local focussed audits to identify barriers to best practice (e.g., caseload size, interfaces between clinical teams, lack of reminder systems/prompts).

Performance against practice standard 5

Patients prescribed continuing valproate treatment should have an annual review of the risk-benefit balance. This should include assessment of therapeutic benefit, adverse effects and medication adherence.

The Figure below shows performance against practice standard 5 in the national and your Trust's subsamples of patients treated with valproate for more than a year, in the 2020 and 2022 audits.

In 2022, there had been a review in the last year of therapeutic response and medication adherence in around 60% and a review of side effects in around a half of the patients on long-term treatment. These proportions are similar to the 2020 audit.

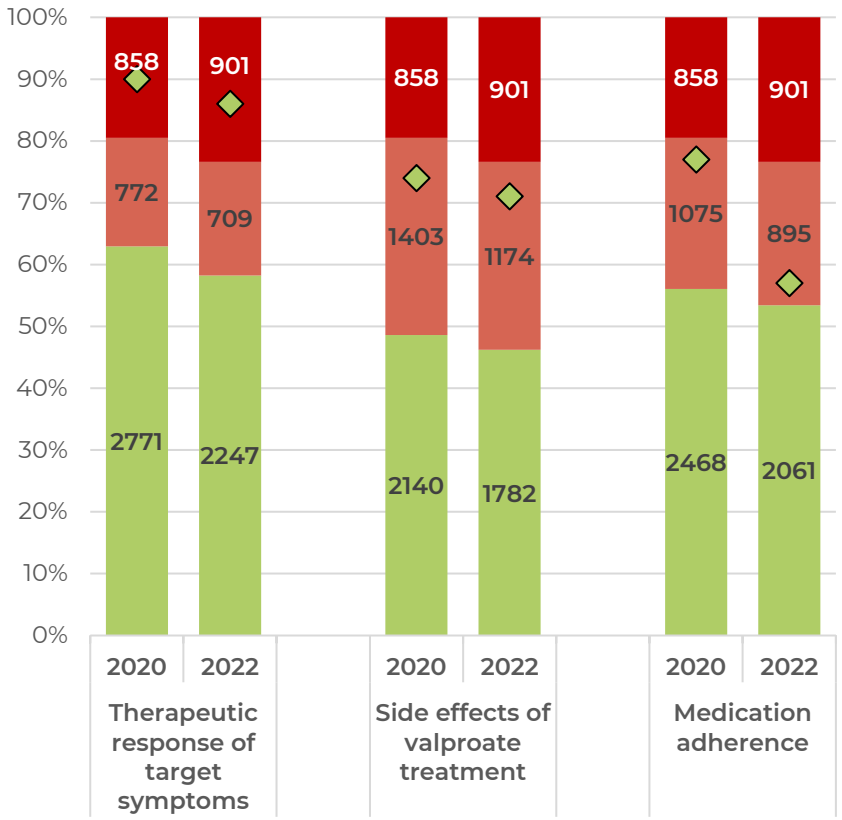
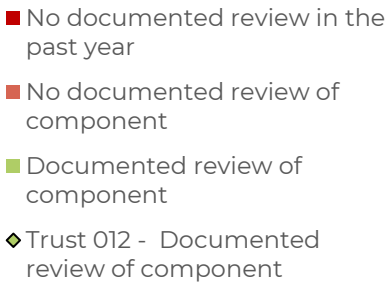


Figure 5:

Documented review of therapeutic response, side effects and adherence in the past year. National subsamples and your Trust subsamples treated with valproate for more than a year, 2020 and 2022



Given that monitoring of the risks and benefits of longer-term medication is essential to inform care planning, where practice has fallen short of the standard, Trusts may like to reflect on local protocols/systems to prompt systematic review, which can then inform decisions such as continuing the medication, at the same or current dosage, or switching to a different medication.

Performance against practice standard 6

Valproate is an established human teratogen also associated with neurodevelopmental problems. In 2018, the Medicines Healthcare products Regulatory Agency (MHRA) mandated that valproate should not be used in girls who were pregnant or women with mental illness or migraine and only prescribed to pregnant women presenting with a severe form of epilepsy that had not responded to other medications. For any women of childbearing potential who were not pregnant, valproate should only be prescribed with the implementation of a specified pregnancy prevention programme.

If valproate is prescribed for a woman of child-bearing age, there should be documented evidence that the conditions of 'prevent', the pregnancy prevention programme, are fulfilled.

The Table below shows performance against practice standard 6 in the national and your Trust's subsamples of females younger than 55 years of age, in the 2022 audit.

Table 1: Implementation of 'prevent' in females prescribed valproate. National subsample and your Trust subsample of females younger than 55 years of age, 2022

Pregnancy prevention programme		Females younger than 55 years of age		Clinical implications
		NS	Trust 012	
		n = 983	n = 5	
		n (%)	n (%)	
'prevent' implemented*		340 (35)	2 (40)	Continue to conduct annual 'prevent' reviews
'prevent' not implemented: documented reason	Documented record that pregnancy was not biologically possible	188 (19)	-	None
	Documented reason for non-permanent protection against pregnancy	78 (8)	1 (20)	The requirements of 'prevent' should be followed for all such patients, as: • personal circumstances may change • contraception needs to be kept under review • there should be reminders about the potential teratogenic and neurodevelopmental consequences of valproate treatment during pregnancy
'prevent' not implemented: no documented reason	Woman 46 years of age or older	205 (21)	2 (40)	Determine if post-menopausal: • if so, this should be documented • if not, 'prevent' should be implemented
	Woman 45 years of age or younger	172 (17)	-	Review these cases individually to: • determine whether the benefits of continuing valproate outweigh the risks • understand why 'prevent' has not been implemented

* 'Prevent' was considered to be implemented if there was an Annual Risk Acknowledgement form dated in the past year.

Treatment target

Plasma level monitoring of valproate treatment should not be used unless there is evidence of ineffectiveness, concerns about medication adherence, or dose-related side-effects.

The Figure below shows performance against the treatment target in the national and your Trust's subsample of patients treated with valproate for more than a year, in the 2022 audit.

Of the 3857 patients treated with valproate for more than a year, a plasma valproate level had been measured in the last year in 256 (7%), a slightly lower proportion than the 10% found in the 2020 audit. Consistent with the 2020 audit, where a valproate level had been measured there was no clear specific clinical rationale documented in almost three-quarters of cases in the total national sample, with marked variation between Trusts.

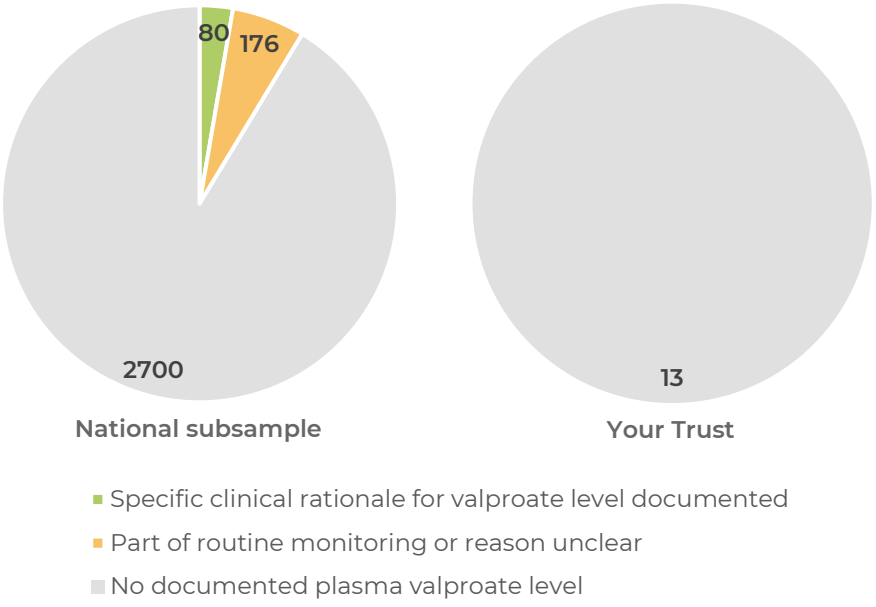


Figure 6:

Measurement of plasma valproate level and documentation of the clinical rationale. National subsample and your Trust subsample treated with valproate for more than a year, with a documented review in the past year, 2022

Where practice fell short of this treatment target, Trusts may wish to consider strategies for informing local clinicians of the limited evidence supporting routine monitoring of valproate levels, for example, presenting a paper on the appropriateness of plasma valproate testing* at a journal club.

* Rathmalgoda et al. Serum sodium valproate testing: is it appropriate? Medical Journal of Australia 2007; 187: 582-4.

Introduction

Clinical background

The clinical background to this QI programme is provided in the Topic 20a 2020 report, and further information on the 'prevent' programme is provided in the Topic 20a 2021 supplementary report, both of which can be found in the members' area of the POMH website:

POMH Members' Areas (rcpsych.ac.uk)

MHRA safety update relating to valproate

Since the 2020 audit, the MHRA has broadened its recommendations to restrict the use of valproate in women of child-bearing potential to include men under the age of 55 years. This advice is based on data that suggest valproate adversely affects fertility in men (this is thought to be reversible). The MHRA are undertaking further work to determine if trans-generational effects, which have been identified in animal studies, are relevant to men who father children and their conclusions are awaited (MHRA 2022).

Current advice is that 'no-one under the age of 55 should be initiated on valproate unless two specialists independently consider and document that there is no other effective or tolerated treatment or the risks do not apply'.

In light of this, we have amended the Figure in Appendix C to show the proportion of men under the age of 55 years in each Trust's sample.

Method

A clinical records audit was conducted for patients prescribed valproate in adult mental health services. A questionnaire/audit tool was sent out to all Trusts/healthcare organisations with instructions that copies should be made available to allow clinical teams to audit prescribing practice for a sample of patients who were currently being treated with valproate medication (see Appendix E).

Submission of data

Each Trust was allocated a code number that was known only to the Trust and POMH. 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. Data coded in this way were entered onto an internet-based form and submitted to POMH via a secure website.

Ownership of data submitted to POMH is retained by the Trust that provided it. See Appendix A for further information on data ownership.

Data collection

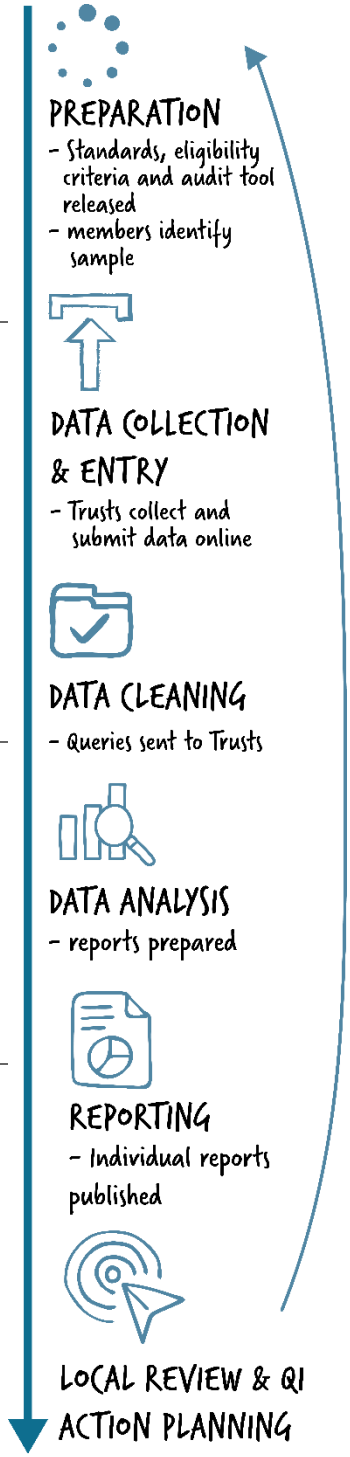
A copy of the data collection tool used for this audit can be found in Appendix E.

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

Data cleaning

Data were collected using FORMIC (electronic survey software).

Data were cleaned to correct instances of obvious data entry error. Details of corrections are held on file by POMH; 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 level.** This section describes the demographic and clinical characteristics of patients in the total national sample. The data relating to prescribing practice were analysed in a variety of ways to facilitate understanding of the national picture and stimulate discussion in participating clinical teams.
2) **Trust level.** The analyses conducted on the national data were repeated for each Trust/healthcare organisation that submitted audit data. This allows Trusts to compare their performance against the practice standards with the performance of the other, anonymous, participating Trusts.
3) **Clinical service level.** This analysis allows Trusts and individual clinical teams to compare their practice with each other and against the national data.

All the figures presented are rounded up (no decimal places) for simplicity, so in some of the Tables and Figures in the report the total percentages may add up to 99% or 101%.

The POMH Lead for each participating Trust will be sent an Excel dataset containing their Trust's data. This allows Trusts to analyse their local data further, should they wish to do so.

National level results

This section includes the demographic and clinical characteristics of the total national sample.

The findings of the data analyses are presented in graphs and tables, primarily to show the extent to which clinical prescribing across the participating services is meeting the practice standards.

60 Trusts/healthcare organisations submitted data on the treatment of 4662 patients who were prescribed valproate and under the care of adult mental health services.

Demographic and clinical characteristics

Of the patients in the 2022 re-audit sample, around three-fifths were male, three-quarters were White/White British, and around three-quarters were age 36-65 years. The overall demographic profile is very similar to the 2020 audit.

Table 2: Demographic characteristics. Total national samples, 2020 and 2022

Key demographic variables			Total national sample	
			2020 n = 5320	2022 n = 4662
			n (%)	n (%)
Sex	Male		3210 (60)	2894 (62)
	Female		2110 (40)	1768 (38)
Ethnicity	White/White British		4022 (76)	3483 (75)
	Black/Black British		379 (7)	332 (7)
	Asian/Asian British		344 (6)	327 (7)
	Mixed or other		282 (5)	231 (5)
	Not collected/stated/refused		293 (6)	289 (6)
Age in years	Median age		49 years	49 years
	Age range		17-90 years	17-92 years
	Age bands	17-18	8 (<1)	6 (<1)
		19-25	230 (4)	245 (5)
		26-35	758 (14)	713 (15)
		36-45	1145 (22)	981 (21)
		46-55	1574 (30)	1290 (28)
		56-65	1204 (23)	1050 (23)
		Over 65	401 (8)	377 (8)

Given the known teratogenic effects of valproate and its association with neurodevelopmental problems, the Medicines and Healthcare products Regulatory Agency (MHRA) has put in place a pregnancy prevention programme. In late 2022, the MHRA also raised concerns about the potential risks for children born to fathers who were taking valproate (Anon, 2022). They have therefore placed restrictions on the use of valproate in all patients younger than 55 years. However, more than two-thirds of the total national sample were in this age category. Individual Trust profiles for age and sex can be found in Appendix C.

The clinical characteristics of the total national sample at re-audit in 2022 were also very similar to the 2020 audit. The data in the Table below show that, on both occasions, almost half had a diagnosis of schizophrenia and around two-fifths a diagnosis of bipolar disorder. More than a quarter had two or more psychiatric diagnoses.

Table 3: Psychiatric diagnoses. Total national samples, 2020 and 2022

Psychiatric diagnoses		Total national sample	
		2020 n = 5320	2022 n = 4662
		n (%)	n (%)
F00-F09: Organic disorder	Neurocognitive problems as a consequence of head injury	29 (1)	30 (1)
	Other organic symptomatic mental disorder	98 (2)	89 (2)
F10 – F19: Disorder due to psychoactive substance use	Alcohol	197 (4)	159 (3)
	Opioids including methadone	26 (<1)	34 (1)
	Cannabis	152 (3)	173 (4)
	Cocaine	63 (1)	64 (1)
	Benzodiazepines	10 (<1)	11 (<1)
	Gabapentinoids	-	2 (<1)
	Novel psychoactive substance	46 (1)	36 (1)
	Mental and behavioural disorder due to use of other psychoactive substance	273 (5)	233 (5)
F20-F29: Schizophrenia spectrum disorder		2442 (46)	2266 (49)
F30-F39: Mood disorder	Bipolar disorder	2183 (41)	1732 (37)
	Other affective disorder	346 (7)	326 (7)
F40-F48: Neurotic, stress-related and somatoform disorders		252 (5)	250 (5)
F50-F59: Behavioural syndromes associated with physiological disturbances and physical factors		14 (<1)	20 (<1)
F60-F69: Personality disorder	Paranoid personality disorder	26 (<1)	20 (<1)
	Dissocial personality disorder	111 (2)	121 (3)
	Emotionally unstable personality disorder	457 (9)	411 (9)
	Other personality disorder	137 (3)	105 (2)
F70-F79: Intellectual disability		176 (3)	199 (4)
F80-F89: Disorder of psychological development		108 (2)	118 (3)
F90-F98: Behavioural and emotional disorders with onset usually occurring in childhood and adolescence	Attention-deficit hyperactivity disorder	60 (1)	79 (2)
	Other behavioural and emotional disorders	16 (<1)	33 (1)
F99: Unspecified disorder		10 (<1)	16 (<1)
One psychiatric diagnosis		3885 (73)	3251 (70)
Two or more psychiatric diagnoses		1371 (26)	1335 (29)
None of the above documented		34 (1)	44 (1)
Information not available		30 (1)	32 (1)

The data in the Table below show the demographic profiles of those patients with only one of the three most common psychiatric diagnoses: schizophrenia spectrum disorder, bipolar disorder or emotionally unstable personality disorder.

Table 4: Demographic characteristics of diagnostic subgroups. National subsamples of patients with a single psychiatric diagnosis: schizophrenia spectrum disorder, bipolar disorder, or emotionally unstable personality disorder, 2022

		National subsamples with a single psychiatric diagnosis		
		Schizophrenia spectrum disorder (F20-29) n = 1584	Bipolar disorder (F31) n = 1253	Emotionally unstable personality disorder (F60.3) n = 121
		n (%)	n (%)	n (%)
Sex	Male	1153 (73)	583 (47)	36 (30)
	Female	431 (27)	670 (53)	85 (70)
Age bands	17-18	1 (<1)	2 (<1)	-
	19-25	78 (5)	35 (3)	9 (7)
	26-35	231 (15)	98 (8)	36 (30)
	36-45	367 (23)	207 (17)	31 (26)
	46-55	441 (28)	372 (30)	32 (26)
	56-65	357 (23)	367 (29)	13 (11)
	Over 65	109 (7)	172 (14)	-

The age profiles of those prescribed valproate suggest that this medication may be more likely to be used in those with established illness, which may reflect its use as an adjunctive treatment for refractory symptoms. The overall profile in 2022 is very similar to that in 2020.

The Table below shows that 86% of patients in the total national sample were under the care of adult mental health services, with community teams providing care in over three-quarters of these cases. Where forensic services were providing care, this was within an inpatient setting in the vast majority of cases, with almost all patients in this setting being subject to mental health legislation.

For those patients who were in hospital and for whom Consent To Treatment legislation applied, treatment with valproate was authorised by a second opinion doctor (SOAD) in just over half of cases.

Table 5: Mental Health Act status. National subsamples of patients under the care of general adult or forensic psychiatric services, 2022

Mental Health Act status	Service providing care					
	General adult n = 3997			Forensic services n = 582		
	Adult acute psychiatric ward n = 729	**Community mental health n = 3074**	**Inpatient rehabilitation services n = 194**	**Forensic psychiatric ward n = 484**	**Forensic community mental health team n = 44**	**Prison psychiatric team n = 54**
	n (%)	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**
Detained in hospital under the MHA and a T2 or equivalent outside England	170 (23)	1 (<1)	44 (23)	222 (46)	4 (9)	N/A
Detained in hospital under the MHA and a T3 or equivalent outside England	179 (25)	-	86 (44)	214 (44)	2 (5)	N/A
Community Treatment Order (CTO) or equivalent outside England	1 (<1)	168 (5)	-	-	9 (20)	N/A
Other mental health legislation	234 (32)	23 (1)	13 (7)	35 (7)	17 (39)	N/A
Not subject to mental health legislation	119 (16)	2882 (94)	43 (22)	4 (1)	12 (27)	N/A

A further 83 patients were under the care of services other than general adult and forensic mental health services, very few of whom were subject to mental health legislation.

Performance against practice standard 1

A clinician's reasons for initiating valproate treatment (i.e. target symptoms or behaviour) should be documented in the clinical records.

Documentation of the clinical reasons for valproate treatment was missing or unclear in more than a quarter of cases in the total national sample. This proportion is unchanged from the 2020 audit.

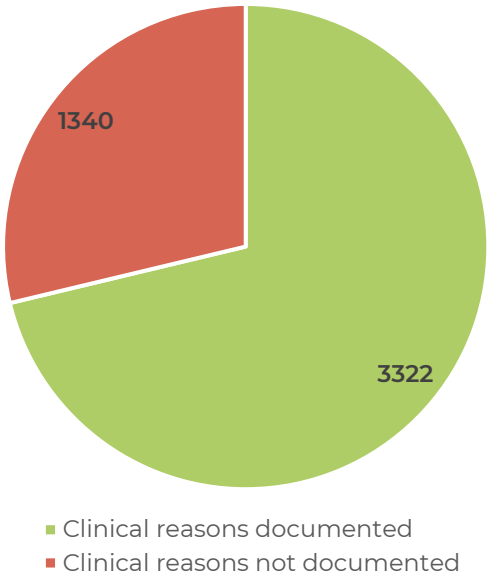


Figure 7:

Documentation of the clinical reasons for prescribing valproate. Total national sample, 2022

Further analysis of the data suggests that the quality of clinical documentation differs modestly with the duration of valproate treatment. For example, the clinical rationale for prescribing valproate was recorded for approximately three-quarters (76%) of those who had started treatment in the past year compared with seven out of every ten (70%) who had been prescribed valproate for more than five years. Whether this is partly because more recent documentation is easier to find is unknown.

Given that review of the ongoing effectiveness of valproate treatment becomes challenging if the target symptoms/behaviours for this treatment are unclear, where local practice falls short of this standard, it may benefit from focussed clinical audit.

Off-label prescribing

Background information on off-label prescribing was included in the 2020 audit report. This is available as an appendix to this report (see Appendix H, page 94).

The Table below shows that only 36% of valproate prescriptions were clearly for a licensed indication. The most common off-label use was to treat mood/affective symptoms/emotional instability in patients with diagnoses other than bipolar disorder. For one patient in seven, the reason for prescribing valproate was unclear. These findings are very similar to the 2020 audit.

Table 6: Valproate prescriptions within the licensed indications or 'off-label' and the common clinical reasons for prescribing. Total national sample, 2022

Category	Total national sample n = 4662 n (%)	Clinical reasons for prescribing valproate within each category	
Licensed indication	n = 1677 (36)	To prevent manic/hypomanic relapse of bipolar disorder	61%
		To treat an acute episode of mania/hypomania	32%
		To treat epilepsy and seizures	20%
		To treat or prevent migraine	1%
Insufficient information to determine	n = 407 (9)	To prevent clozapine-related seizures	32%
		To prevent depressive relapse of bipolar disorder	27%
		To treat an acute episode of bipolar depression	16%
		To treat an acute, mixed affective state	15%
		As a mood stabiliser in bipolar disorder	9%
		To treat rapid-cycling bipolar disorder	7%
Off-label indication	n = 1849 (40)	To treat mood/affective symptoms in schizophrenia/ schizoaffective disorder	66%
		To treat emotional instability	21%
		Adjunctive therapy (i.e. added to antipsychotic medication) for refractory schizophrenia	12%
		To reduce persistent aggression/hostile behaviour	9%
		To reduce impulsivity/poor-impulse control	7%
		To treat agitation/anxiety	6%
		As a mood stabiliser in an affective disorder other than bipolar disorder	6%
		To reduce deliberate self-harming behaviour	2%
		To reduce suicidality	2%
		Other clinical reason	2%
		Patient preference/request	1%
Unclear/not known	n = 729 (16)	Continuation of long-standing valproate prescription: original reason for prescribing not documented/not known	51%
		Unclear why valproate has been prescribed	49%

Given the paucity of evidence for the efficacy of valproate for off-label indications* and the MHRA advice** regarding the risks of valproate treatment in people younger than 55 years of age, Trusts may wish to review their local policy/guidance for the off-label use of medicines to ensure this includes processes specifically relating to the use of valproate.

* Baldwin D & Wieck A. Withdrawal of, and alternatives to, valproate-containing medicines in girls and women of childbearing potential who have a psychiatric illness. Position Statement PS04/18. Royal College of Psychiatrists 2018. https://www.bap.org.uk/pdfs/PS04-18-December2018.pdf
** Medicines and Healthcare Products Regulatory Agency. Drug Safety Update 2022,16:5 https://www.gov.uk/drug-safety-update/valproate-reminder-of-current-pregnancy-prevention-programme-requirements-information-on-new-safety-measures-to-be-introduced-in-the-coming-months

Other psychotropic medicines co-prescribed with valproate

The Table below shows that, in those patients with a single psychiatric diagnosis, most prescriptions for valproate were for off-label indications (i.e. the clinical diagnosis was not bipolar disorder) and that other psychotropic medications were prescribed in combination with valproate in almost all cases. These findings reinforce the earlier observation that valproate use seems to be targeted towards those with more established illness (see page 23) and tends to be used as an adjunct for refractory symptoms (see also page 26). However, the evidence supporting the use of valproate for off-label indications is uncertain (Baldwin & Wieck, 2018; Paton et al, 2022). Further, such use increases the risk of prescribing cascades, where medications are added to manage the side effects of existing medications, which places an additional responsibility on the prescriber to carefully review the benefits and risks of valproate treatment.

The prevalence of regular benzodiazepine prescribing was relatively high across the diagnostic subsamples shown.

Table 7: Regular co-prescription of selected medications with valproate. Four national subsamples with a single psychiatric diagnosis: schizophrenia spectrum disorder, bipolar disorder, other affective disorder, or personality disorder, 2022

Medications co-prescribed with valproate	National subsamples with a single psychiatric diagnosis			
	Schizophrenia spectrum disorder (F20-29) n = 1584	Bipolar disorder (F31) n = 1253	Other affective disorder (F30-39) n = 138	Personality disorder (F60-F69) n = 147
	n (%)	n (%)	n (%)	n (%)
Antipsychotic medication n = 4020	1549 (98)	980 (78)	95 (69)	108 (73)
Antidepressant medication n = 1443	309 (20)	378 (30)	62 (45)	111 (76)
Benzodiazepine n = 975	362 (23)	193 (15)	31 (22)	35 (24)
Lithium n = 356	87 (5)	150 (12)	11 (8)	5 (3)
Lamotrigine n = 177	28 (2)	85 (7)	4 (3)	3 (2)
Gabapentinoids (pregabalin and gabapentin) n = 287	44 (3)	73 (6)	17 (12)	18 (12)
None of the medications above n = 215	21 (1)	105 (8)	7 (5)	12 (8)
Both antipsychotic and antidepressant medications n = 1124	301 (19)	264 (21)	29 (21)	86 (59)

Seven out of every ten patients with a single psychiatric diagnosis of personality disorder who were prescribed valproate were also prescribed antipsychotic medication, a finding that is consistent with the 2020 audit. NICE recommends that psychotropic medicines are not used in the medium to long-term to manage the symptoms/behaviours associated with personality disorder alone (NICE 2009a, 2009b), but such prescribing is common and has been found to be relatively refractory to change, perhaps at least partly due to the overlap of such symptoms with those of mental illness and the perceived need to act when a patient is distressed and/or poses a risk to themselves or others (Paton et al, 2015).

Performance against practice standard 2

In the total national sample, 805 patients had been prescribed valproate for less than a year. In 370 (46%) of these cases, the indication for use was considered to be 'off-label' by Trusts. Performance against standard 2 was therefore assessed in these cases.

If valproate is being prescribed 'off-label', it should be documented that this has been explained to the patient.

The Figure below shows that, where off-label use had been recognised, it was documented that an explanation had been given to the patient in only 11% of cases. While this represents an improvement from the respective proportion of 6% at the 2020 audit, there is no documentation in the clinical records relating to an explanation of off-label use for almost nine patients in every ten.

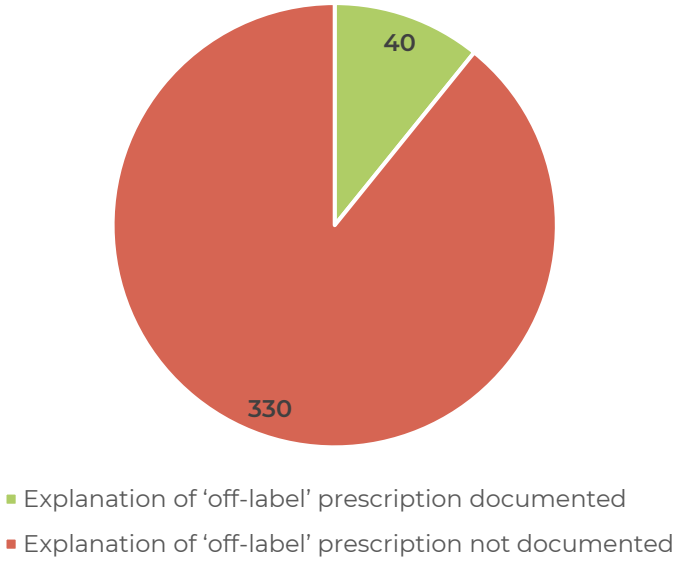


Figure 8:

Documented explanation to patients that valproate prescription is 'off-label'. National subsample considered to be prescribed 'off-label' valproate, 2022

Trust medicines management committees (or equivalent) may wish to consider strategies for reminding clinicians of the licensed indications for valproate and also of the paucity of evidence* for the majority of off-label uses.

* Baldwin D & Wieck A. Withdrawal of, and alternatives to, valproate-containing medicines in girls and women of childbearing potential who have a psychiatric illness. Position Statement PS04/18. Royal College of Psychiatrists 2018. https://www.bap.org.uk/pdfs/PS04-18-December2018.pdf
Paton C, Citrome L, Fernandez-Egea E, Rendora O, Barnes TRE. Who is prescribed valproate and how carefully is this treatment reviewed in UK mental health services? Data from a clinical audit. Journal of Psychopharmacology 2022; 12:1-15.

Performance against practice standard 3

In the total national sample in 2022, 805 patients had been prescribed valproate for less than a year. Performance against practice standard 3 was measured in this subgroup.

> 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 Figure below shows that each of the three pre-treatment measures noted in the standard were documented in around two-thirds of patients in both the 2020 and 2022 audits.

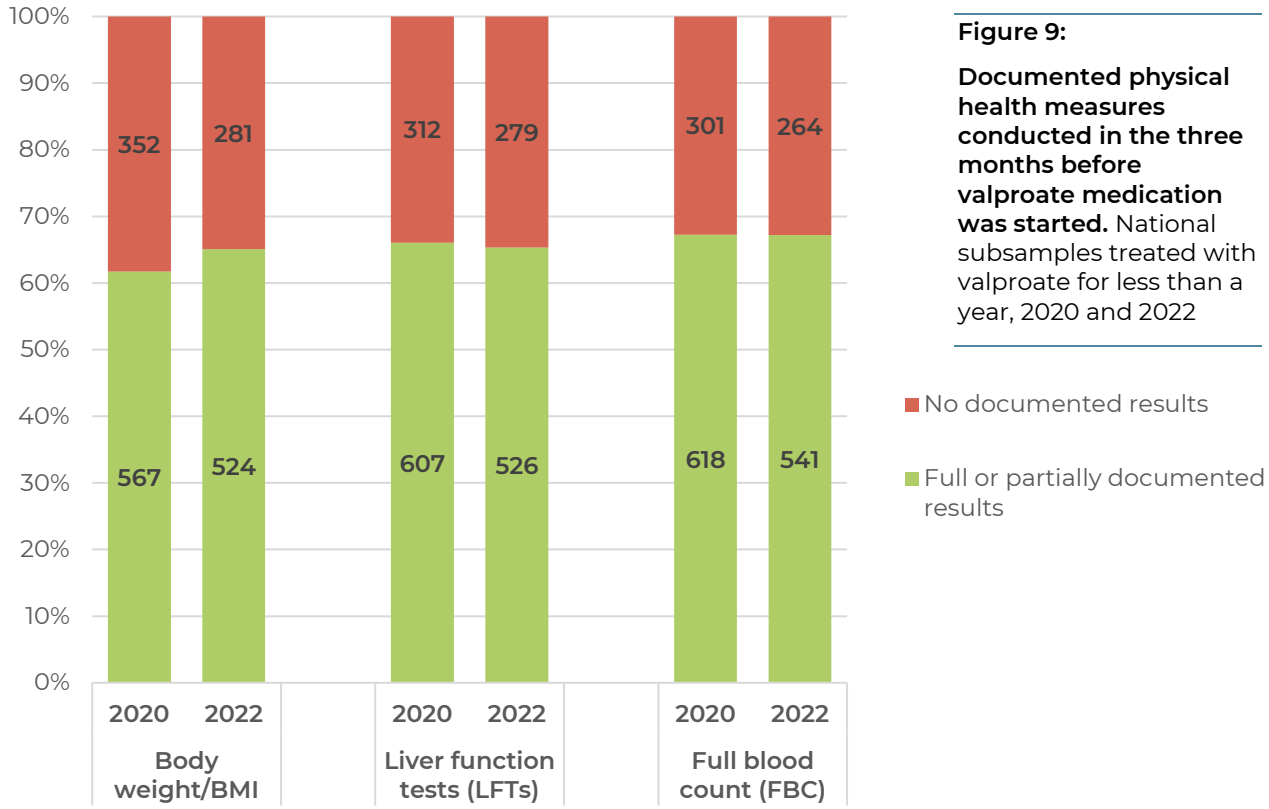


Figure 9:

Documented physical health measures conducted in the three months before valproate medication was started. National subsamples treated with valproate for less than a year, 2020 and 2022

All three measures were documented in 416 (52%) of cases.

Discretionary measures

Each of these three 'metabolic syndrome' measures were documented in around a half to two-thirds of cases.

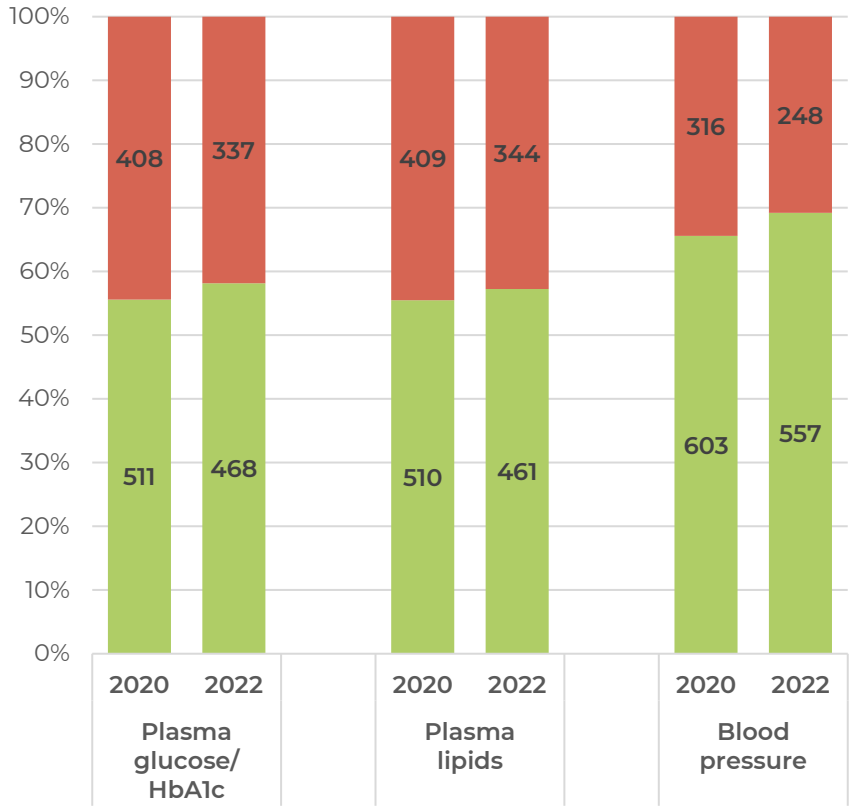


Figure 10:

Documented metabolic tests conducted in the three months before valproate medication was started. National subsamples treated with valproate for less than a year, 2020 and 2022

As can be seen in the Table below, in the vast majority of patients valproate was to be co-prescribed with an antipsychotic medication. In such cases, the pre-treatment physical health measures/ metabolic tests were more likely to be documented, presumably driven by the greater likelihood of side effects with such a medication combination.

Table 8: Documented physical health measures in patients with or without an antipsychotic medication currently co-prescribed. National subsamples treated with valproate for less than a year, 2022

Documented physical health measures/metabolic tests	National subsample treated with valproate for less than a year	
	Antipsychotic co-prescribed n = 705	No antipsychotic co-prescribed n = 100
	n (%)	n (%)
Body weight/BMI	474 (67)	50 (50)
Liver function tests (LFTs)	467 (66)	59 (59)
Full blood count (FBC)	487 (69)	54 (54)
Plasma glucose/HbA1c	418 (59)	50 (50)
Plasma lipids	413 (59)	48 (48)
Blood pressure	502 (71)	55 (55)
All of body weight/BMI, LFTs and FBC	378 (54)	38 (38)

Performance against practice standard 4

In the total national sample in 2022, 575 patients had been prescribed valproate between three months and a year. Performance against practice standard 4 was measured in this subgroup.

Review within the first three months of valproate treatment should include: screening for common side effects of the medication (e.g. weight gain, nausea, and tremor) and assessment of the response of the target symptoms/behaviour.

In 2022, there was a documented review of valproate treatment within three months of initiation in 434 cases (75%).

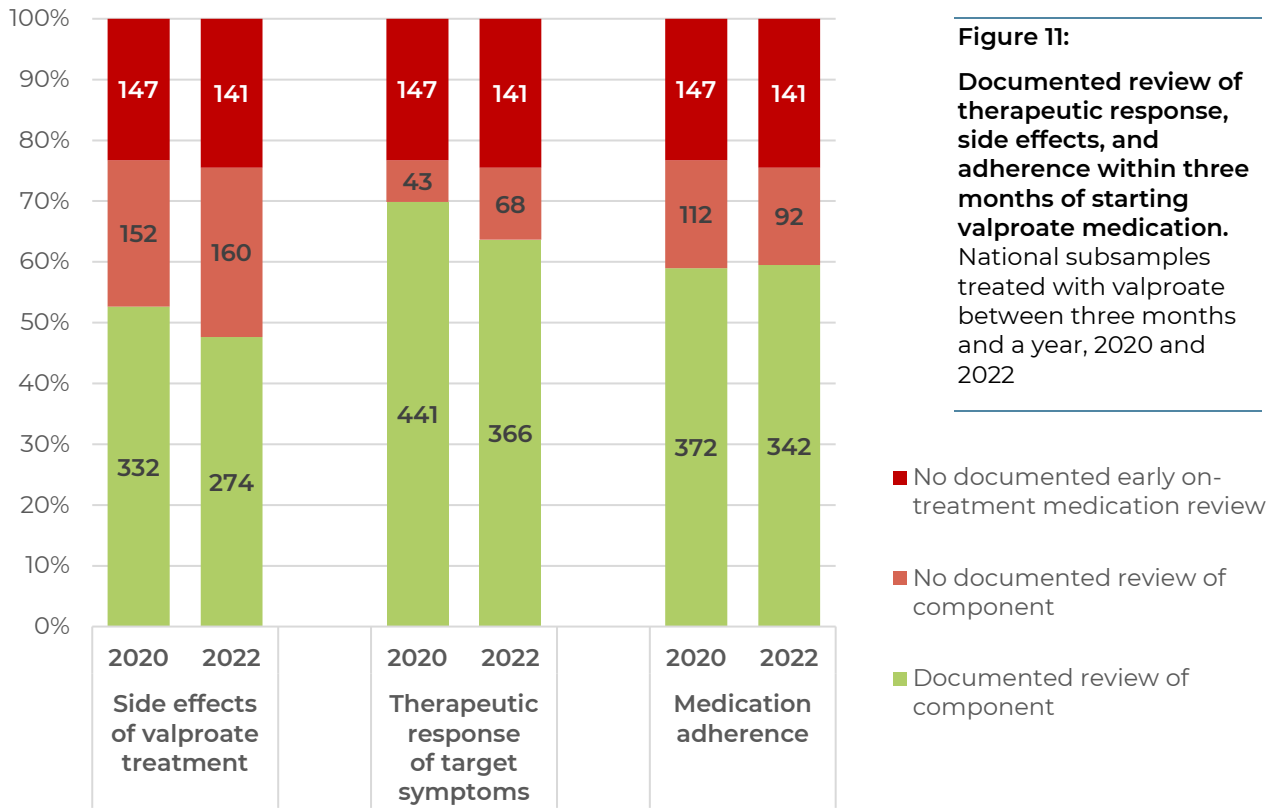


Figure 11:

Documented review of therapeutic response, side effects, and adherence within three months of starting valproate medication. National subsamples treated with valproate between three months and a year, 2020 and 2022

At early on-treatment review, therapeutic response and adherence were documented for around three patients in five, while a review of side effects was documented in around half. These proportions are similar to those in 2020.

Of the 575 patients treated with valproate between three months and a year, 253 cases (44%) had a documented review of both the common side effects and therapeutic response of the target symptoms/behaviours.

Given that early on-treatment review of the risks and benefits of a medication is essential to inform care planning, Trusts may wish to consider local focussed audits to identify barriers to best practice (e.g., caseload size, interfaces between clinical teams, lack of reminder systems/prompts).

The Table below shows the documentation of the physical health measures/metabolic checks that may be indicated for some patients during early on-treatment review. The proportion of patients having such discretionary tests in 2022 is similar to 2020.

Table 9: Documented physical health measures/metabolic tests within three months of starting valproate medication. National subsamples treated with valproate between three months and a year, 2020 and 2022

Documented physical health measures /metabolic tests	National subsample treated with valproate between three months and a year	
	2020 n = 631	2022 n = 575
	n (%)	n (%)
Full blood count (FBC)	244 (39)	259 (45)
Liver function tests (LFTs)	245 (39)	235 (41)
Body weight/BMI	244 (39)	248 (43)
Plasma glucose/HbA1c	193 (31)	201 (35)
Plasma lipids	190 (30)	188 (33)
None of the above	298 (47)	265 (46)

Performance against practice standard 5

In the 3857 patients who have been prescribed valproate for more than a year, there was no documented review of this treatment in just under a quarter.

Patients prescribed continuing valproate treatment should have an annual review of the risk-benefit balance. This should include assessment of therapeutic benefit, adverse effects and medication adherence.

The Figure below shows that there had been a review of therapeutic response and medication adherence in around 60% and a review of side effects in around a half of the patients on long-term treatment. These proportions are similar to the 2020 audit.

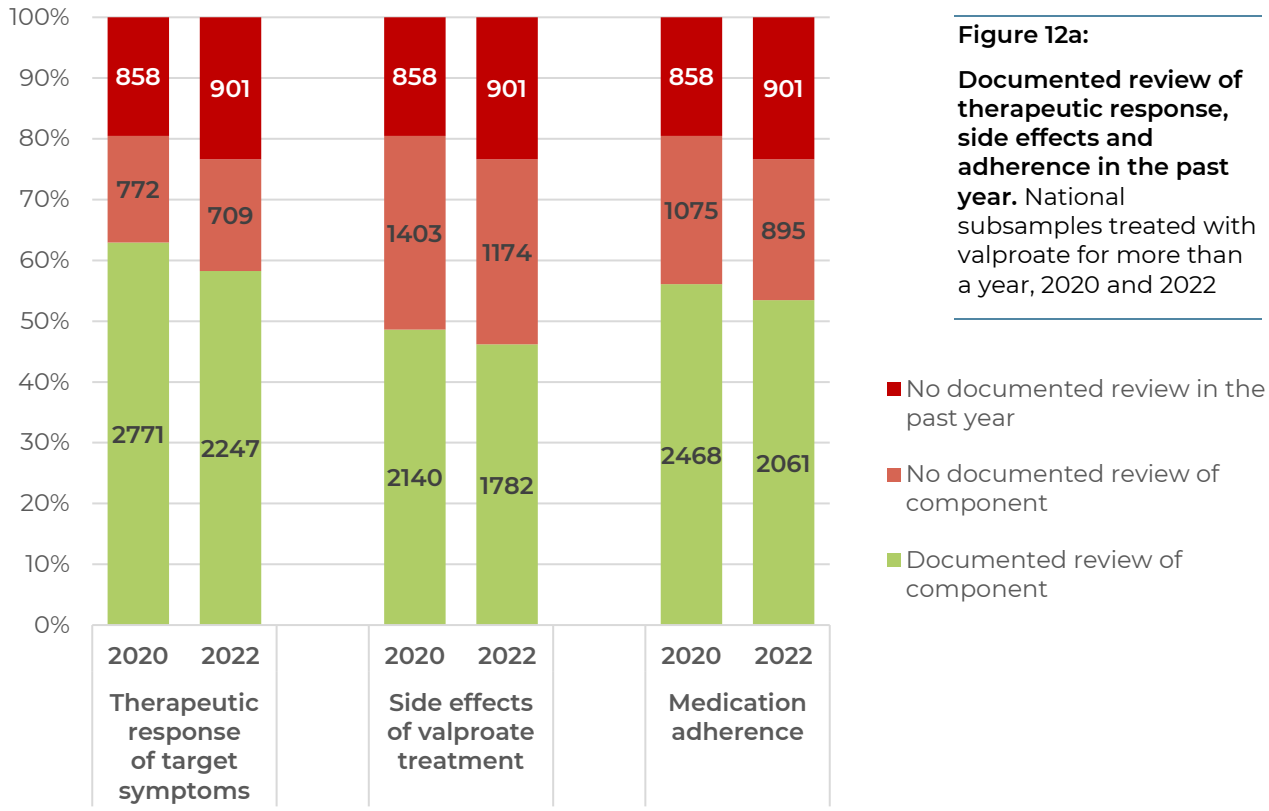


Figure 12a:

Documented review of therapeutic response, side effects and adherence in the past year. National subsamples treated with valproate for more than a year, 2020 and 2022

Given that monitoring of the risks and benefits of longer-term medication is essential to inform care planning, where practice has fallen short of the standard, Trusts may like to reflect on local protocols/systems to prompt systematic review, which can then inform decisions such as continuing the medication, at the same or current dosage, or switching to a different medication.

Monitoring patients on continuing valproate treatment

Each of the physical health tests/measures was documented as having been undertaken in around two-fifths of cases. These proportions are similar to the 2020 audit.

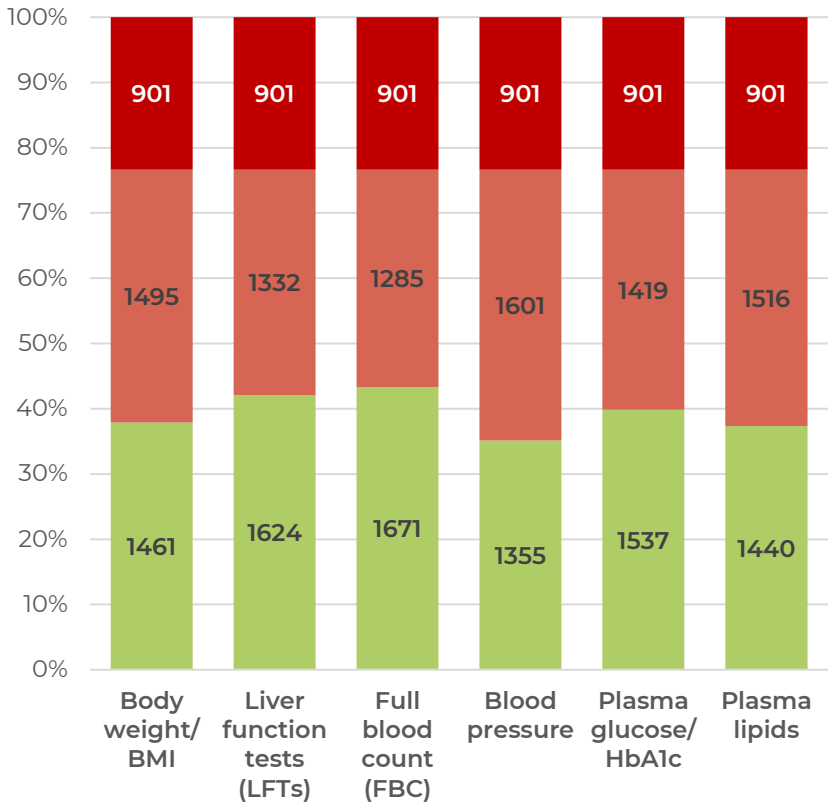


Figure 12b:

Documented physical health tests/measures conducted in the past year. National subsamples treated with valproate for more than a year, 2022

Performance against practice standard 6

In 2018, the MHRA mandated that for any women of childbearing potential who were not pregnant, valproate should only be prescribed with the implementation of a specified pregnancy prevention programme.

If valproate is prescribed for a woman of child-bearing age, there should be documented evidence that the conditions of 'prevent', the pregnancy prevention programme, are fulfilled.

The Table below shows performance against practice standard 6 in the national subsample of females younger than 55 years of age, in the 2020 and 2022 audits. The proportion of women for whom 'prevent' was implemented was higher in 2022 than in 2020. However, the data suggest only a modest fall in the proportion of women for whom 'prevent' was not implemented and there was no documented reason.

Table 10: Implementation of 'prevent' in females prescribed valproate. National subsamples of females younger than 55 years of age, 2020 and 2022

Pregnancy prevention programme		Females younger than 55 years of age		Clinical implications
		2020 n = 1196	2022 n = 983	
		n (%)	n (%)	
'prevent' implemented*		253 (21)	340 (35)	Continue to conduct annual 'prevent' reviews
'prevent' not implemented: documented reason	Documented record that pregnancy was not biologically possible	159 (13)	188 (19)	None
	Documented reason for non-permanent protection against pregnancy	217 (18)	78 (8)	The requirements of 'prevent' should be followed for all such patients, as: • personal circumstances may change • contraception needs to be kept under review • there should be reminders about the potential teratogenic and neurodevelopmental consequences of valproate treatment during pregnancy
'prevent' not implemented: no documented reason	Woman 46 years of age or older	311 (26)	205 (21)	Determine if post-menopausal: • if so, this should be documented • if not, 'prevent' should be implemented
	Woman 45 years of age or younger	256 (21)	172 (17)	Review these cases individually to: • determine whether the benefits of continuing valproate outweigh the risks • understand why 'prevent' has not been implemented

*'Prevent' was considered to be implemented if there was an Annual Risk Acknowledgement (ARA) form dated in the past year.

Further details relating to the completion of the ARA form can be found in Appendix D.

Pregnancy prevention programme: potential QI interventions for local services

Review of the women prescribed valproate, particularly those identified in the **darker red** boxes in Table 10, may prompt consideration of QI interventions.

For example, **would it be helpful if....**

Clinical audit

...the quality of use of valproate in younger women was the focus of a regular monthly snapshot audit of a small number of cases?

Educational materials

...printed copies of the patient guide were available and easily accessible in clinical areas?

...a link to the 'prevent' supporting information was added to the Trust intranet?

...attention was drawn to the fact that the only exception to implementing 'prevent' is that pregnancy is not biologically possible? All other women of child-bearing potential should be kept under review as personal circumstances can change

Clinical policies and procedures

...there were systems in place to ensure that any relevant local policies and procedures incorporated the requirements of 'prevent'?

Clinical roles

...at the point of dispensing, the implementation of 'prevent' was routinely checked by pharmacy staff and a patient-specific prompt provided to the prescriber where needed?

...the implementation (and documentation) of 'prevent' by the responsible service was considered as a subject for clinical supervision of trainee psychiatrists?

Reminders and alerts

...the Trust kept a central electronic register of women prescribed valproate, and their 'prevent' status, that was able to provide patient-specific automatic prompts when reviews were due?

Use of IT/ clinical documents

...the required 'prevent' forms were integrated into the electronic patient record?

...your electronic prescribing system, if you have one, could link directly with the 'prevent' forms?

...there was a naming and dating convention for any uploaded forms so they could be easily identified/ located?

Interface with primary care

...a more detailed review of those patients on Trust caseloads who receive continuing prescriptions for valproate via their GP was conducted to clarify who is responsible for implementing 'prevent' and ensuring that this is done?

...a system was put in place to alert GPs to patients who have an open referral that is restricted to psychology, occupational therapy or social work? Local discussion would be needed to determine who would review the ongoing need for valproate and the implementation of 'prevent'.

‘Prevent’ programme step 2

Where ‘prevent’ was implemented, valproate was prescribed because of failure to respond to or tolerate other treatments in the vast majority of cases.

Table 11: Step 2 reasons given for patients needing valproate where ‘prevent’ was implemented.
National subsamples of females younger than 55 years of age for whom ‘prevent’ was implemented, 2020 and 2022

Step 2: ‘I confirm that the patient needs valproate because:’	National subsample of females younger than 55 years of age for whom ‘prevent’ was implemented	
	2020 n = 253	2022 n = 340
	n (%)	n (%)
Inadequate response to other treatments	210 (83)	266 (78)
Does not tolerate other treatments	150 (59)	202 (59)
Currently switching from valproate to another treatment	116 (46)	171 (50)
Two or more of the above apply	139 (55)	188 (55)
One of the above applies	86 (34)	96 (28)
No reasons stated	28 (11)	56 (16)

The Table below shows the wide range of clinical reasons for prescribing valproate for women in whom the pregnancy prevention programme was implemented.

In more than half of these women, prescribing appeared to be off-label, i.e. outside the licensed indications.

Table 12: Valproate prescriptions within the licensed indications or 'off-label' and the common clinical reasons for prescribing. National subsample of females younger than 55 years of age for whom 'prevent' was implemented and one or more of the step 2 reasons for the patient needing valproate applies, 2022

Category	National subsample for whom one or more of the 'prevent' step 2 reasons for the patient needing valproate applies n = 284 n (%)	Clinical reasons for prescribing valproate within each category	
Licensed indication	n = 117 (41)	To prevent manic/hypomanic relapse of bipolar disorder	76%
		To treat an acute episode of mania/hypomania	28%
		To treat epilepsy and seizures	11%
		To treat or prevent migraine	-
Insufficient information to determine	n = 26 (9)	To prevent depressive relapse of bipolar disorder	42%
		To treat an acute episode of bipolar depression	19%
		To treat rapid-cycling bipolar disorder	19%
		To prevent clozapine-related seizures	12%
		To treat an acute, mixed affective state	8%
		As a mood stabiliser in bipolar disorder	8%
Off-label indication	n = 95 (33)	To treat mood/affective symptoms in schizophrenia/schizoaffective disorder	56%
		To treat emotional instability	41%
		To reduce persistent aggression/hostile behaviour	12%
		To reduce impulsivity/poor-impulse control	8%
		To reduce deliberate self-harming behaviour	8%
		Adjunctive therapy (i.e. added to antipsychotic medication) for refractory schizophrenia	5%
		To treat agitation/anxiety	4%
		As a mood stabiliser in an affective disorder other than bipolar disorder	4%
		To reduce suicidality	4%
		Patient preference/request	2%
		Other	1%
Unclear/not known	n = 46 (16)	Unclear why valproate has been prescribed	59%
		Continuation of long-standing valproate prescription: original reason for prescribing not documented/not known only	41%

Treatment target

Plasma level monitoring of valproate treatment should not be used unless there is evidence of ineffectiveness, concerns about medication adherence, or dose-related side-effects.

Of the 3857 patients treated with valproate for more than a year, a plasma valproate level had been measured in the last year in 256 (7%), a slightly lower proportion than the 10% found in the 2020 audit.

Consistent with the 2020 audit, where a valproate level had been measured, there was no clear specific clinical rationale documented in almost three-quarters of cases in the total national sample, with marked variation between Trusts.

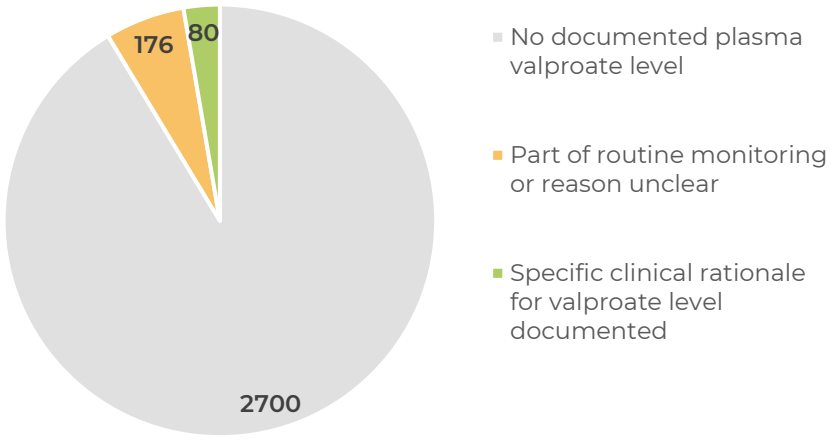


Figure 13:

Measurement of plasma valproate level and documentation of the clinical rationale. National subsample treated with valproate for more than a year, with documented review in the past year, 2022

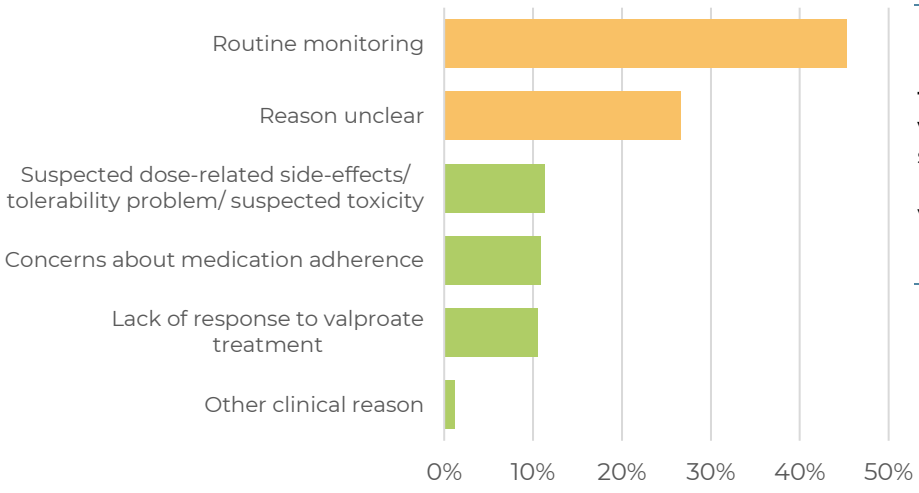


Figure 14:

Documented reasons for measuring plasma valproate level. National subsample with a recorded plasma valproate level in the past year, 2022

Where practice fell short of this treatment target, Trusts may wish to consider strategies for informing local clinicians of the limited evidence supporting routine monitoring of valproate levels, for example, presenting a paper on the appropriateness of plasma valproate testing* at a journal club.

* Rathmalgoda et al. Serum sodium valproate testing: is it appropriate? Medical Journal of Australia 2007; 187: 582-4.

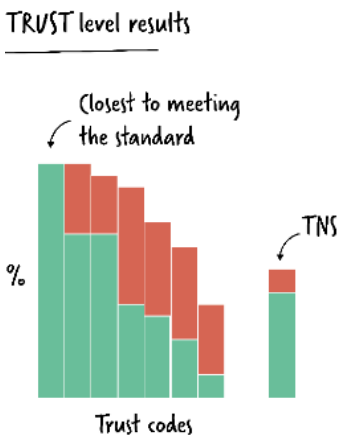
Trust level results

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.



Summary of national participation levels

Table 13: Number of clinical teams and cases submitted by each of the participating Trusts, 2020 and 2022

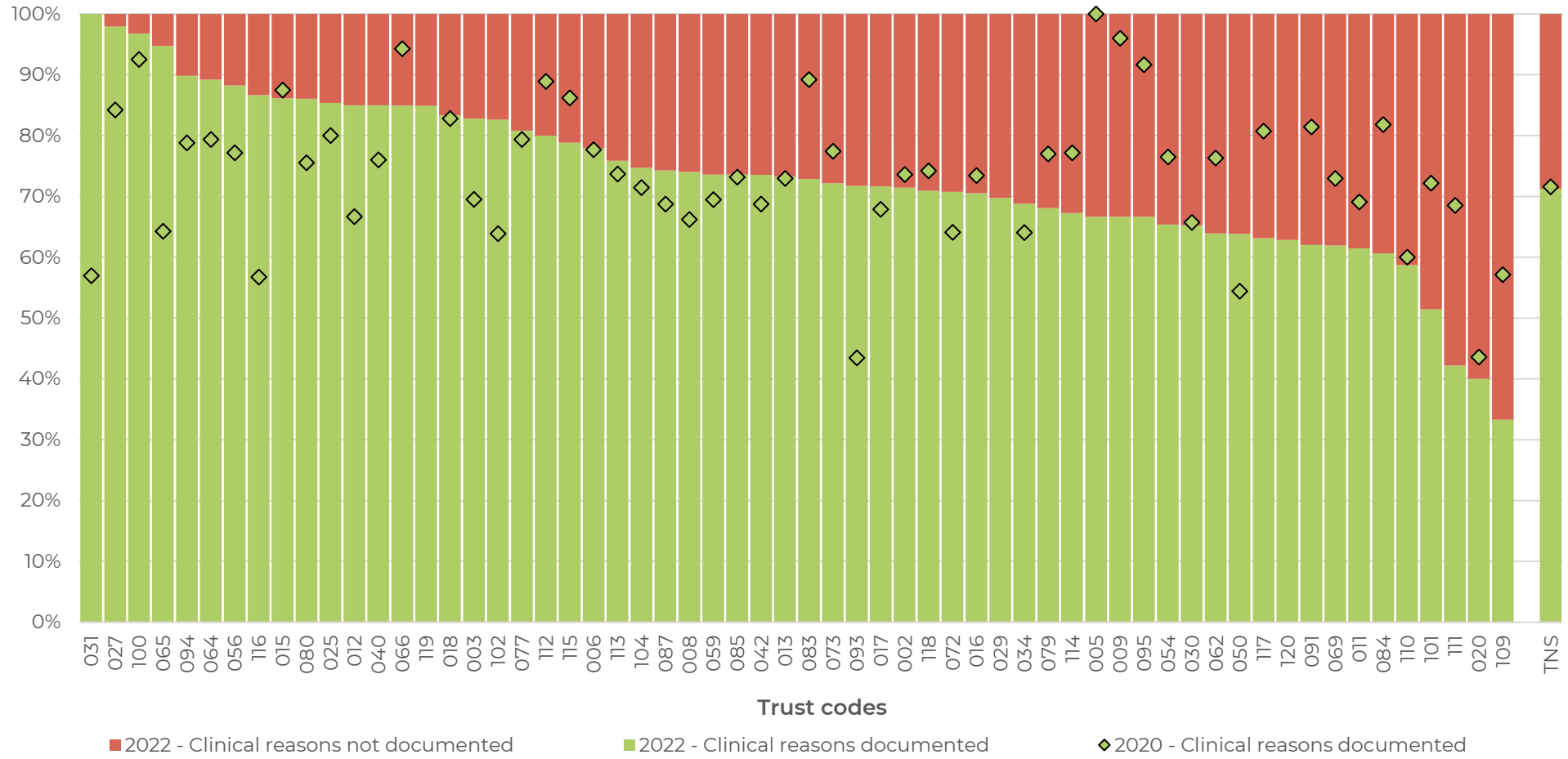
Trust code	2020		2022	
	Number of participating teams	Number of cases	Number of participating teams	Number of cases
002	6	106	6	49
003	15	105	23	93
005	14	28	34	186
006	8	103	6	77
008	8	222	9	154
009	11	25	14	42
011	7	55	9	109
012	30	48	8	20
013	16	281	11	71
015	9	48	10	65
016	14	188	13	163
017	10	112	13	67
018	16	122	30	132
020	8	117	6	100
025	19	60	7	41
027	4	76	3	96
029	-	-	38	182
030	45	143	38	167
031	10	72	1	3
034	18	89	15	77
040	5	25	13	20
042	10	48	1	34
050	42	169	54	249
054	21	68	33	78
056	4	35	5	17

059	36	203	47	197
062	5	38	5	61
064	15	63	14	37
065	2	14	12	38
066	6	87	4	73
069	29	122	27	92
072	5	181	5	147
073	33	93	12	133
077	18	121	9	73
079	34	126	28	94
080	4	49	5	43
083	5	74	6	118
084	1	66	4	94
085	22	123	4	106
087	4	32	9	35
091	16	113	20	108
093	7	23	10	46
094	9	33	15	59
095	1	12	2	15
100	2	40	4	31
101	7	97	10	103
102	3	36	3	69
104	8	35	4	91
109	1	21	2	12
110	13	35	25	63
111	7	162	4	45
112	7	45	2	20
113	7	57	3	29
114	2	35	2	55
115	2	29	10	52
116	7	178	4	15
117	10	140	3	38
118	1	62	1	55
119	-	-	3	53
120	-	-	7	70
TNS	**780**	**5320**	**725**	**4662**

Performance against practice standard 1

A clinician's reasons for initiating valproate treatment (i.e. target symptoms or behaviour) should be documented in the clinical records.

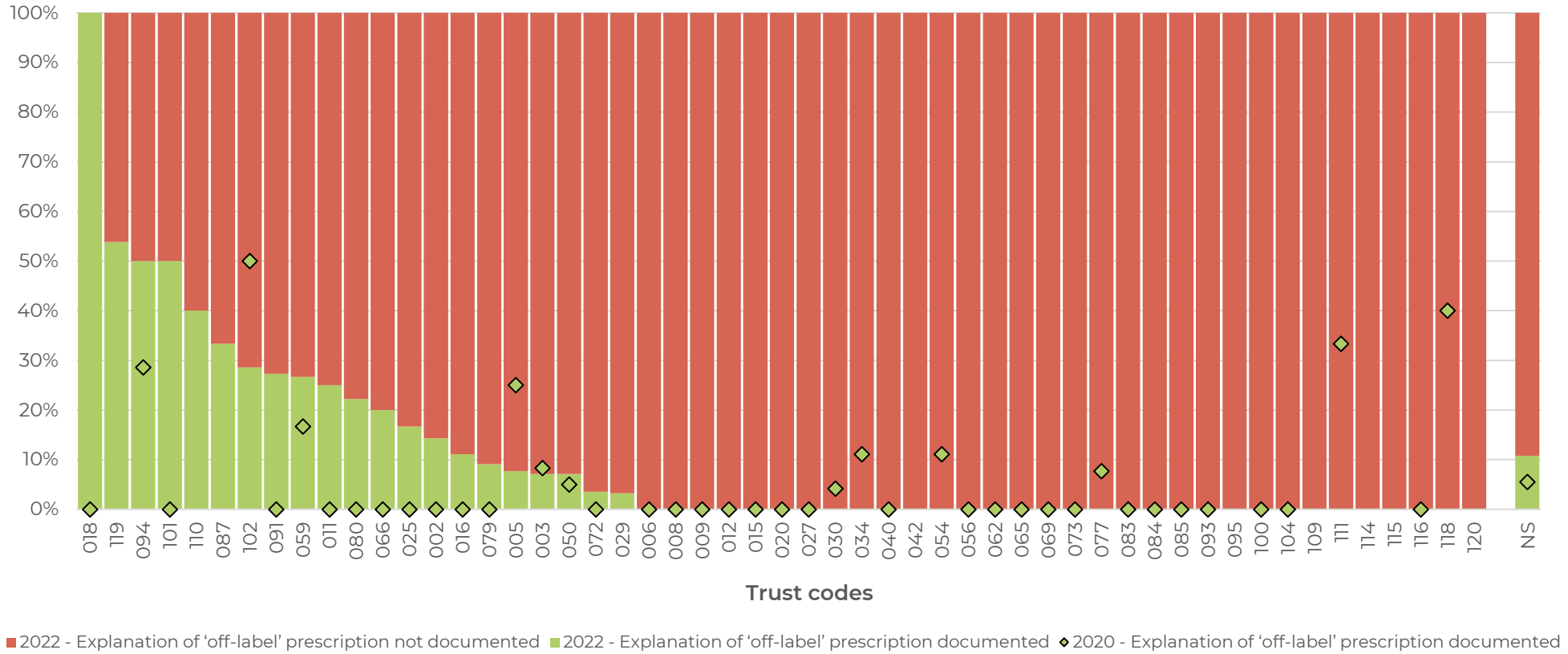
Figure 15: Documentation of the clinical reasons for prescribing valproate. Total national sample and each Trust, 2020 and 2022



Performance against practice standard 2

If valproate is being prescribed 'off-label', it should be documented that this has been explained to the patient.

Figure 16: Documented explanation to patients that valproate prescription is 'off-label'. National subsample considered to be prescribed 'off-label' valproate and each Trust*, 2020 and 2022

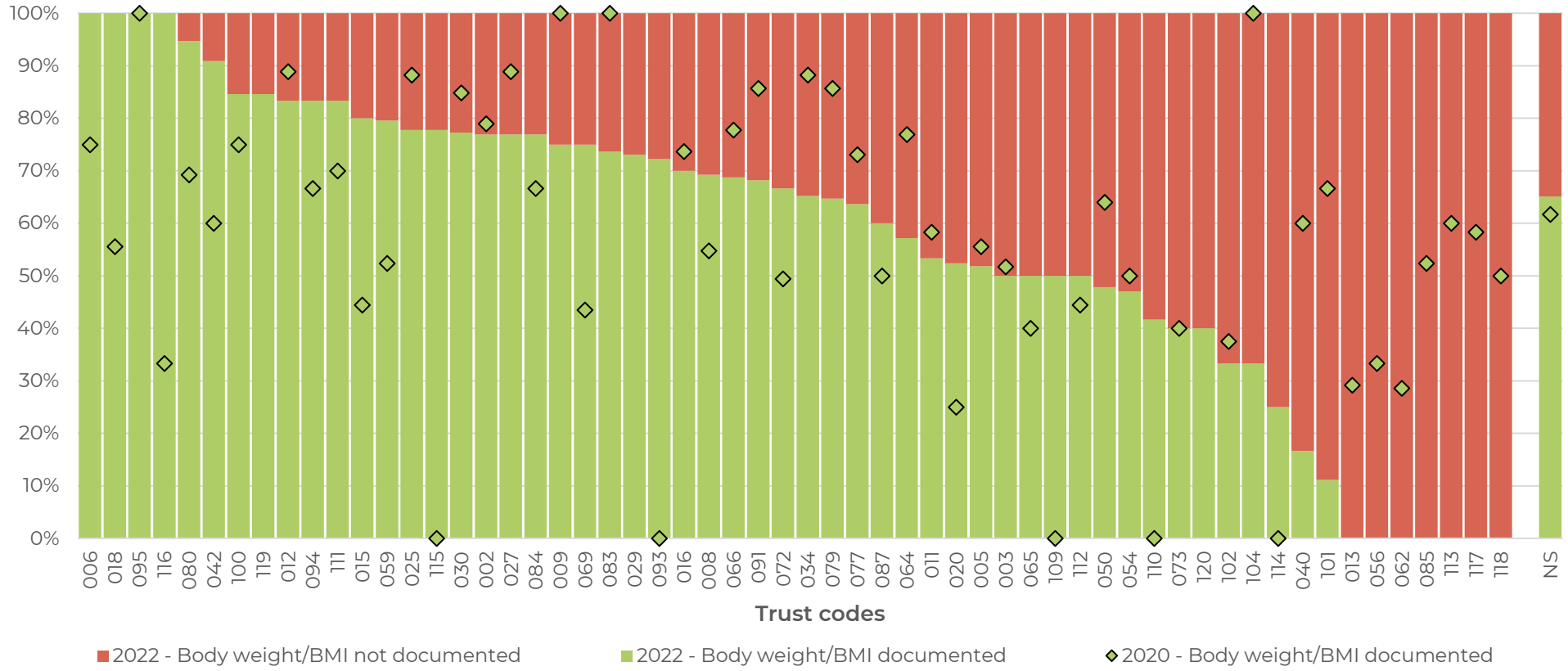


*Trusts that did not submit any data relevant to this standard are not shown in the Figure above.

Performance against practice standard 3

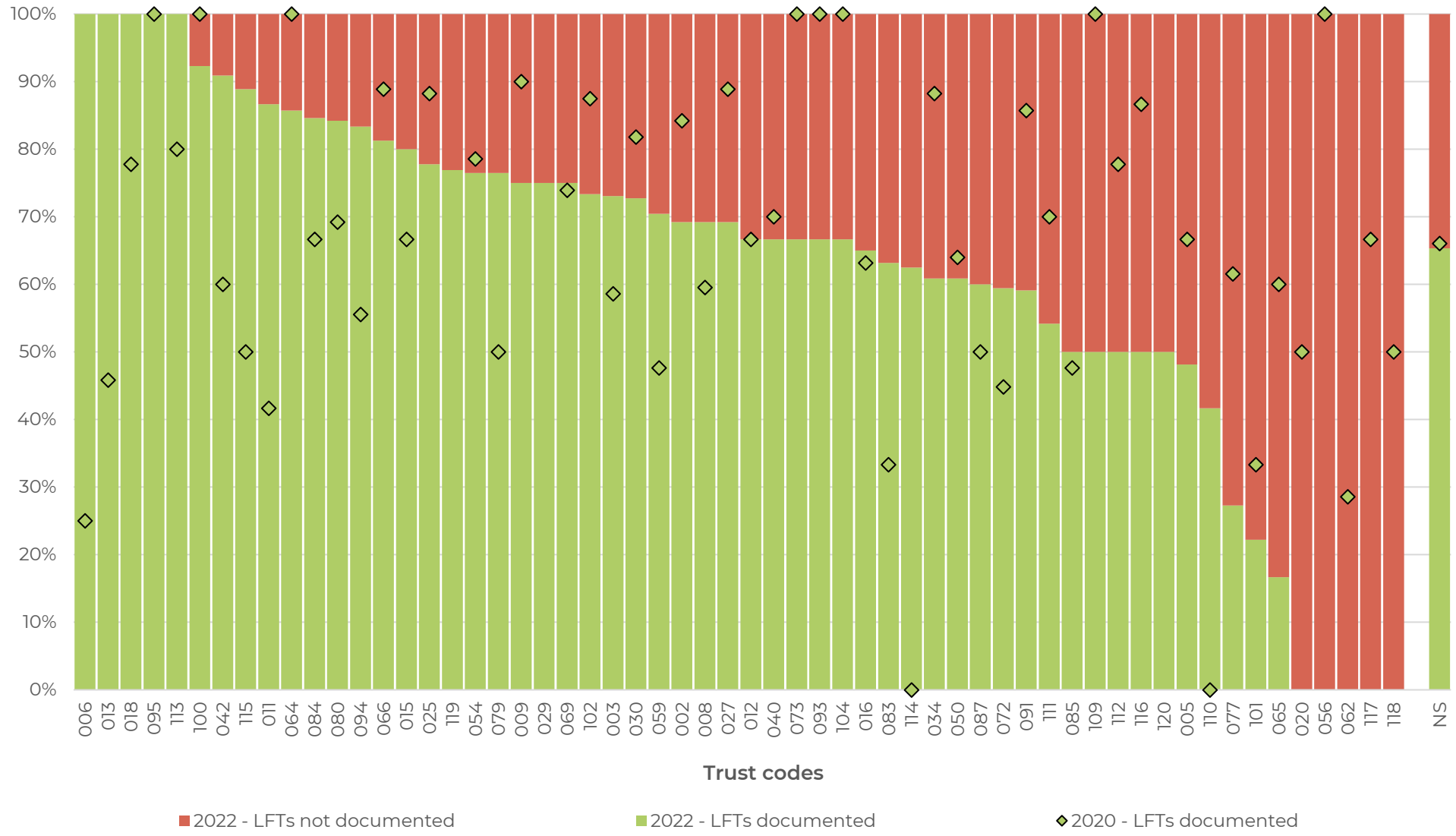
Prior to initiating treatment with valproate, the following should be documented in the clinical records: weight and/or BMI, the results of liver function tests (LFTs), and a full blood count (FBC).

Figure 17: Documented body weight and/or BMI measurement conducted in the three months before valproate medication was started. National subsample treated with valproate for less than a year and each Trust*, 2020 and 2022



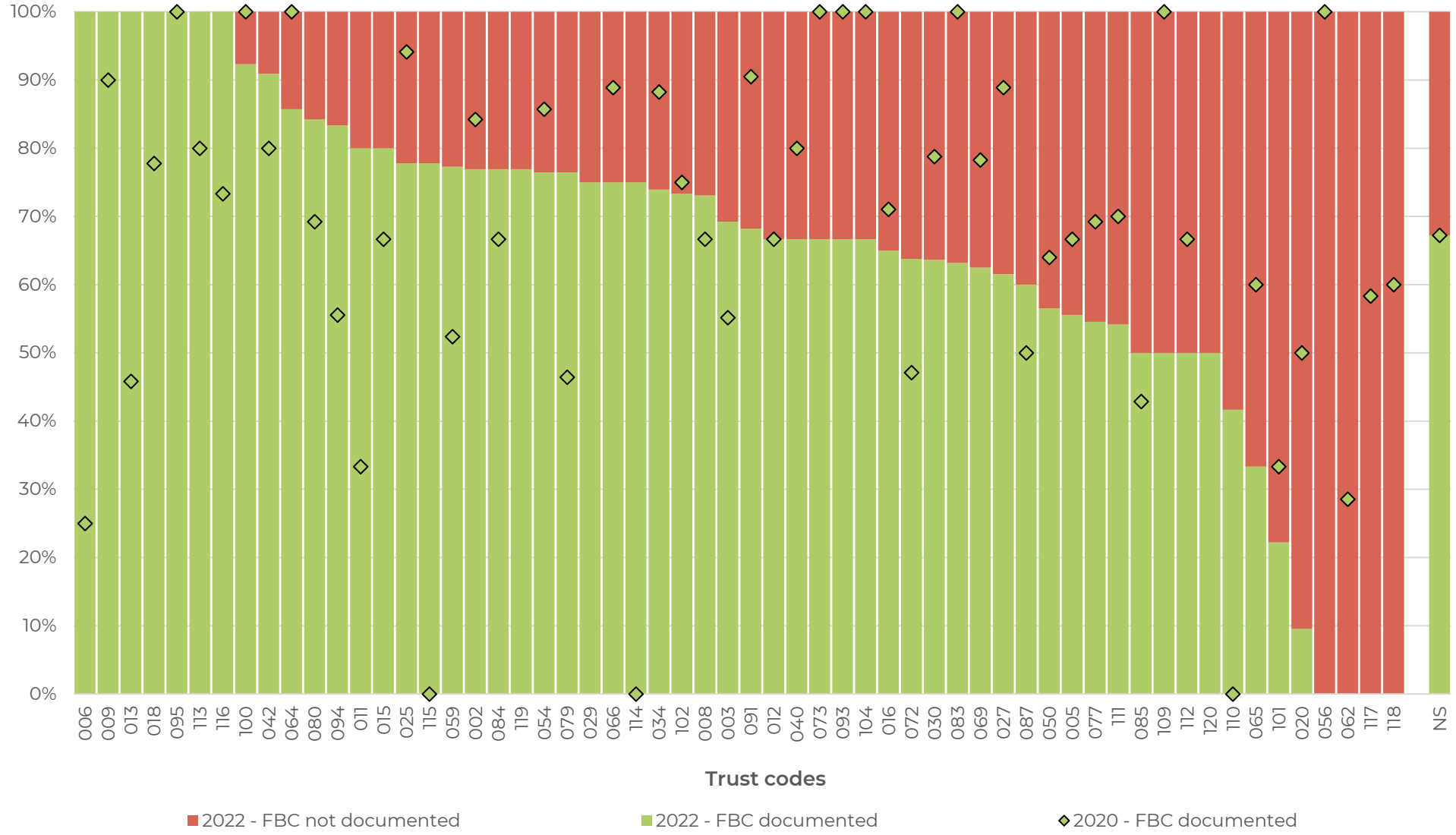
*Trusts that did not submit any data relevant to this standard are not shown in the Figure above.

Figure 18: Documented liver function tests (LFTs) conducted in the three months before valproate medication was started. National subsample treated with valproate for less than a year and each Trust*, 2020 and 2022



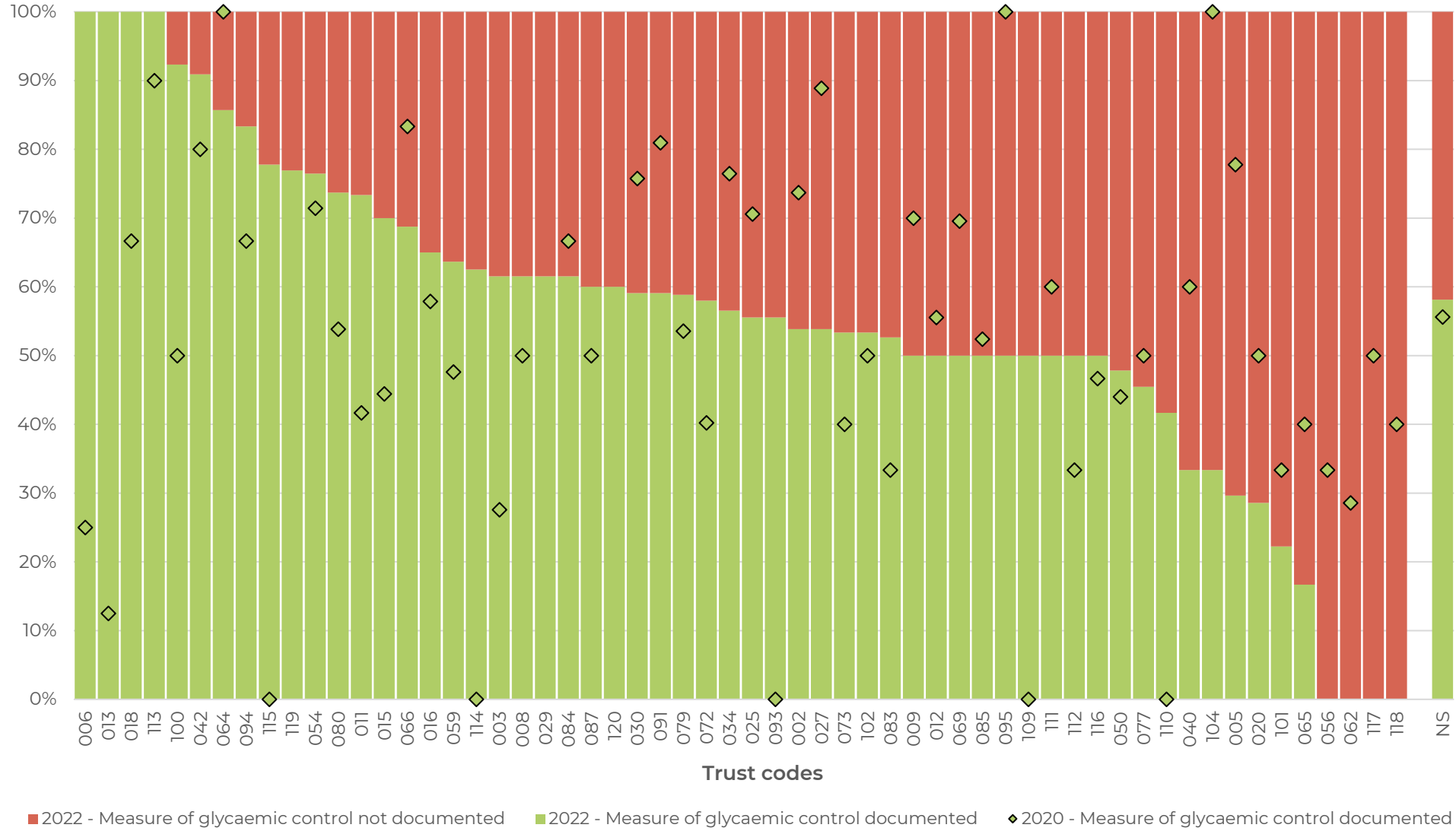
*Trusts that did not submit any data relevant to this standard are not shown in the Figure above.

Figure 19: Documented full blood count (FBC) conducted in the three months before valproate medication was started. National subsample treated with valproate for less than a year and each Trust*, 2020 and 2022



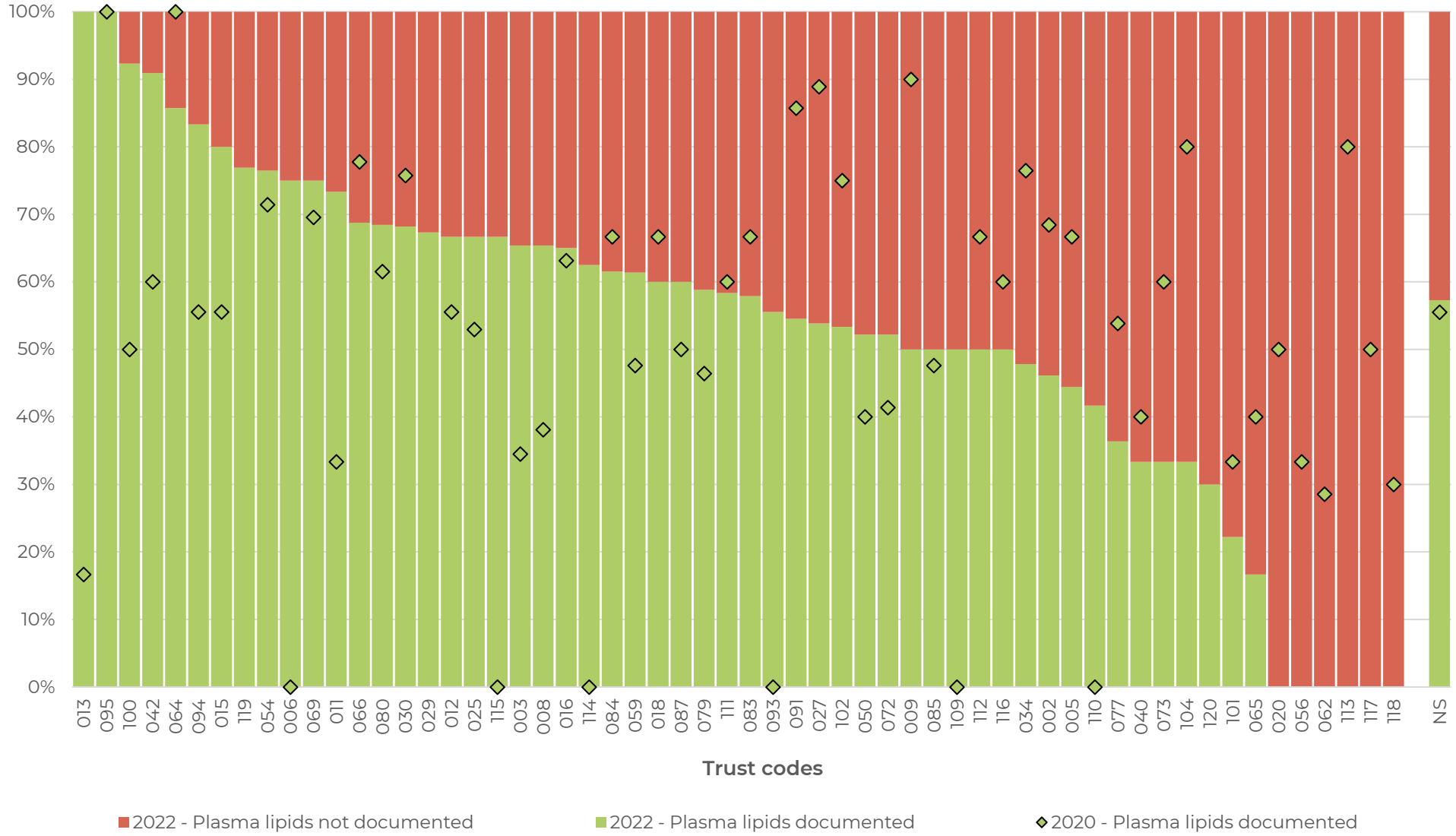
*Trusts that did not submit any data relevant to this standard are not shown in the Figure above.

Figure 20: Documented plasma glucose or HbA1c measurement conducted in the three months before valproate medication was started. National subsample treated with valproate for less than a year and each Trust*, 2020 and 2022



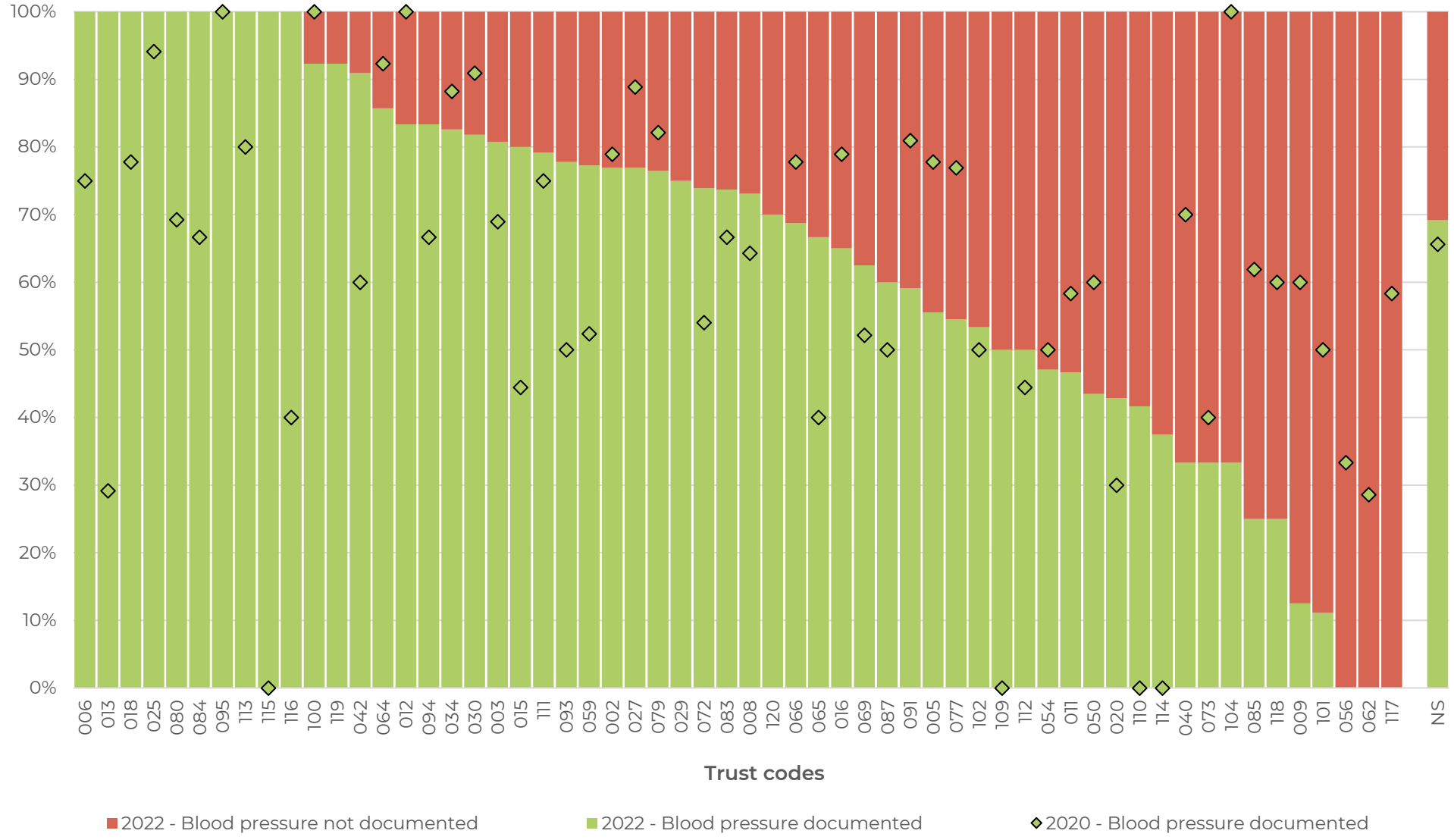
*Trusts that did not submit any data relevant to this standard are not shown in the Figure above.

Figure 21: Documented plasma lipids measurement conducted in the three months before valproate medication was started. National subsample treated with valproate for less than a year and each Trust*, 2020 and 2022



*Trusts that did not submit any data relevant to this standard are not shown in the Figure above.

Figure 22: Documented blood pressure measurement conducted in the three months before valproate medication was started. National subsample treated with valproate for less than a year and each Trust*, 2020 and 2022

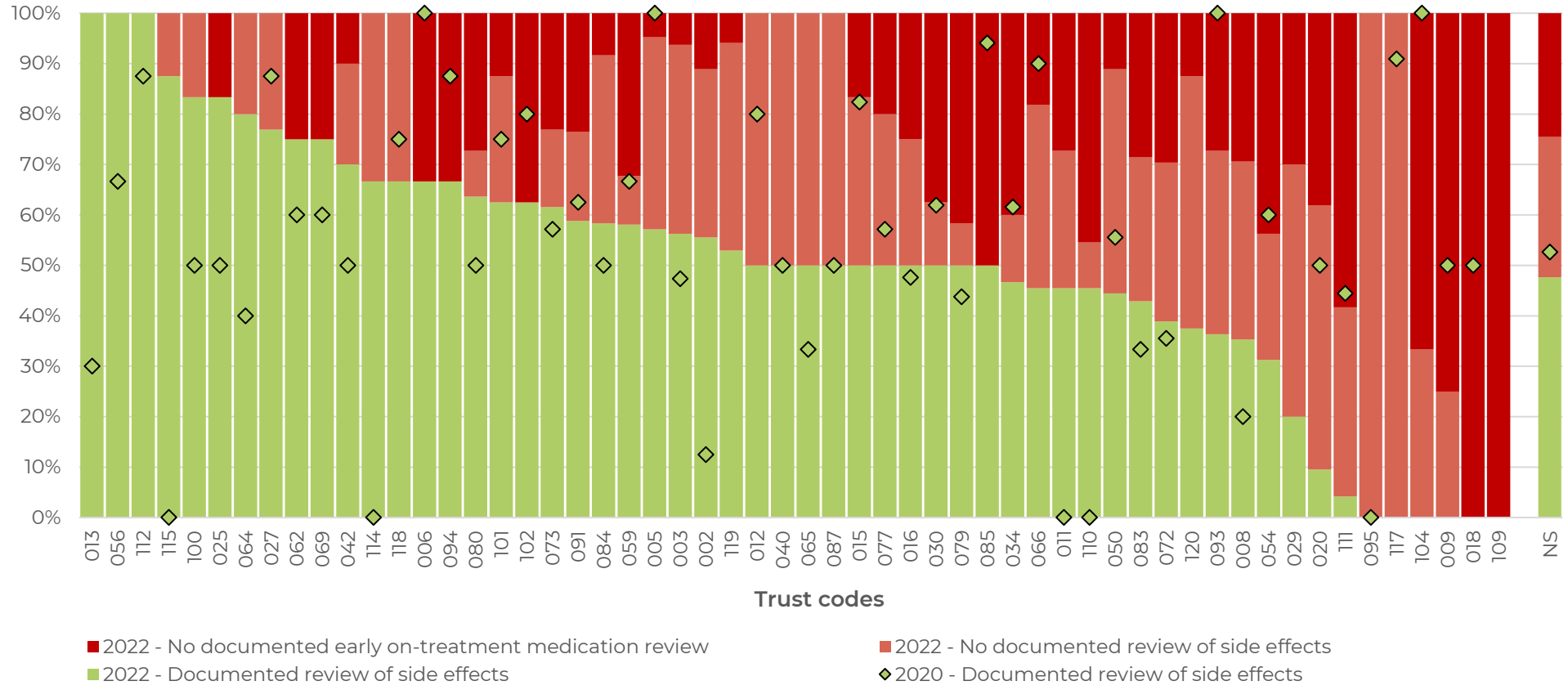


*Trusts that did not submit any data relevant to this standard are not shown in the Figure above.

Performance against practice standard 4

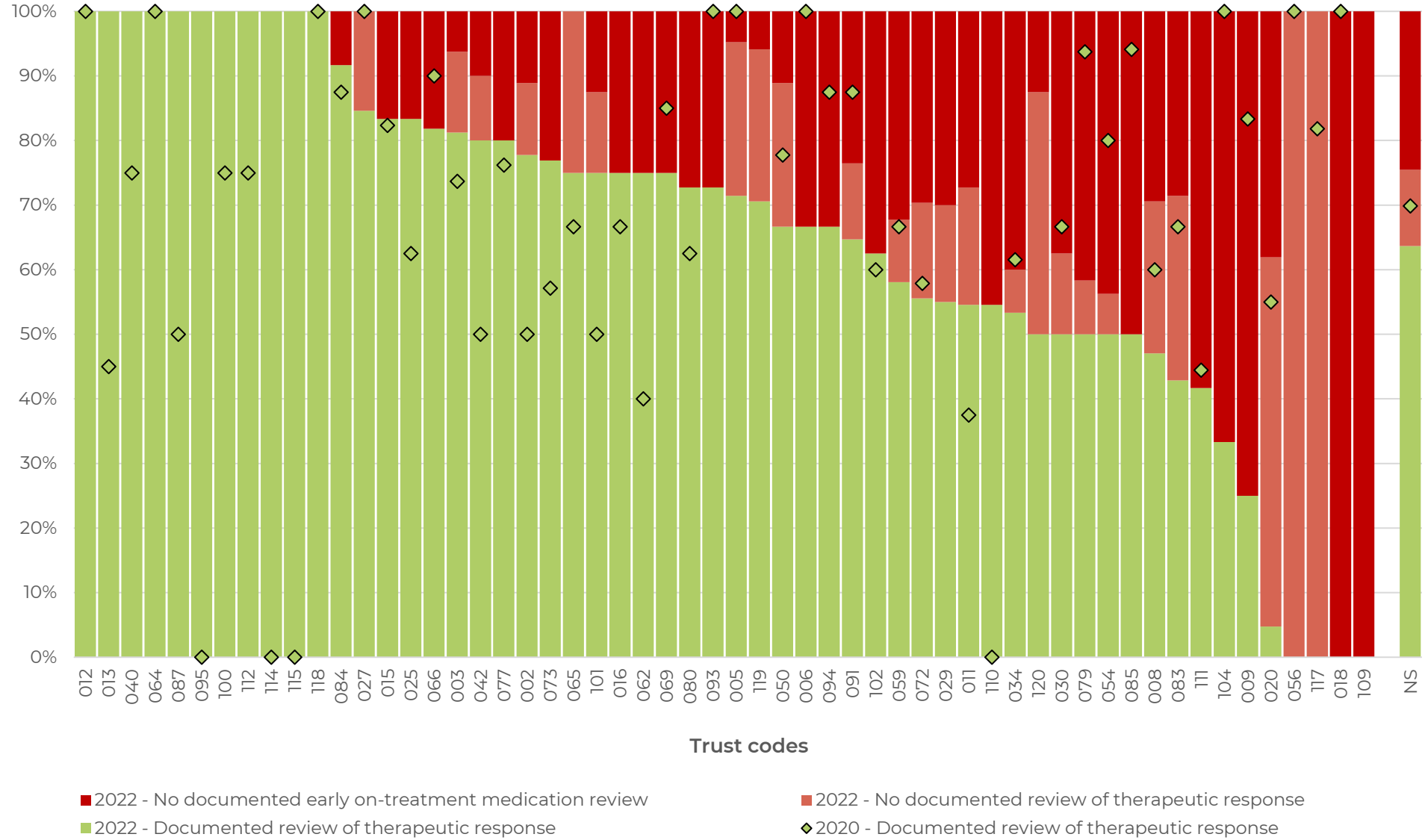
Review within the first three months of valproate treatment should include: screening for common side effects of the medication (e.g. weight gain, nausea, and tremor) and assessment of the response of the target symptoms/behaviour.

Figure 23: Documented review of side effects within three months of starting valproate medication. National subsample treated with valproate between three months and a year and each Trust*, 2020 and 2022



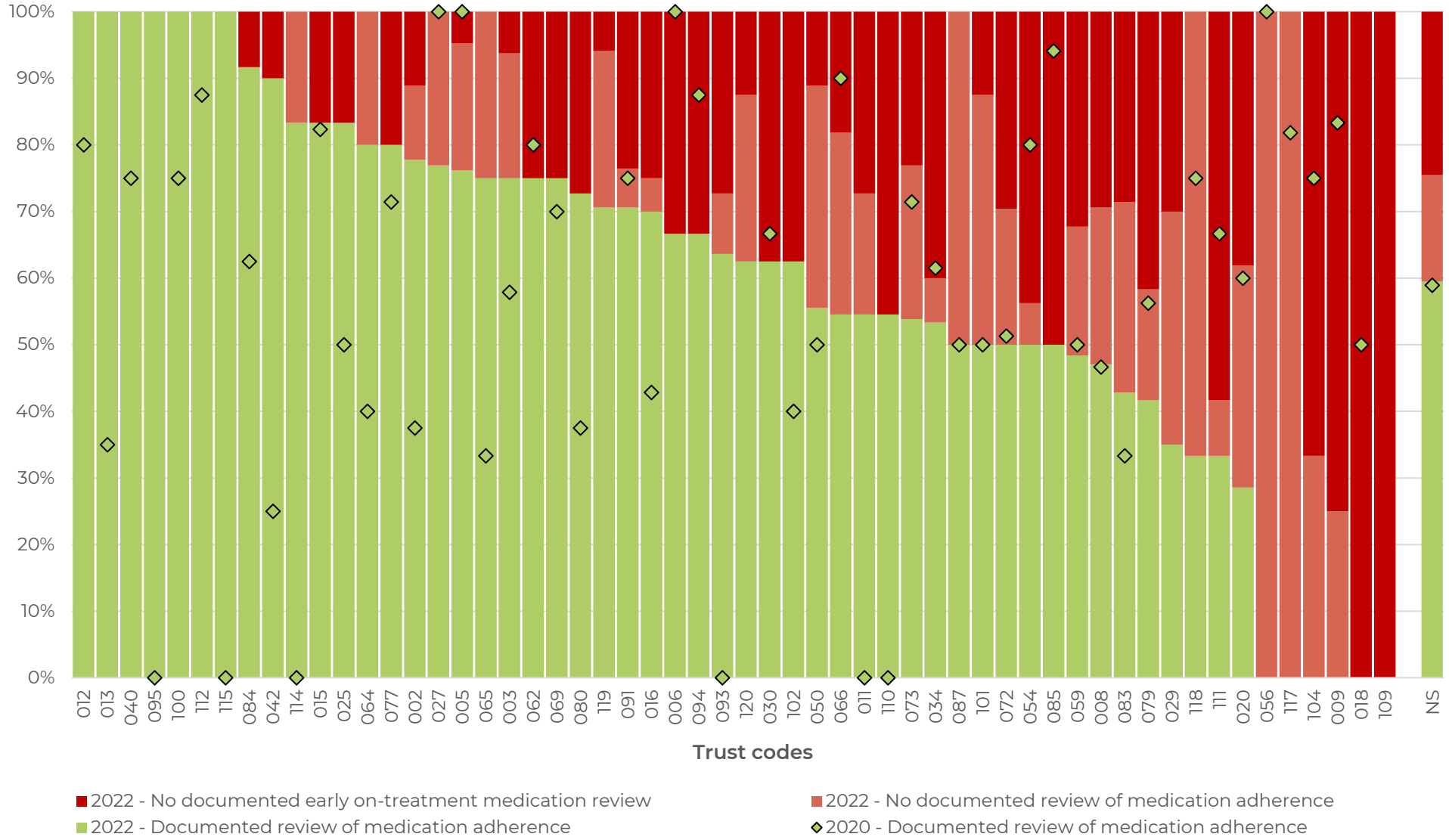
*Trusts that did not submit any data relevant to this standard are not shown in the Figure above.

Figure 24: Documented review of therapeutic response within three months of starting valproate medication. National subsample treated with valproate between three months and a year and each Trust*, 2020 and 2022



*Trusts that did not submit any data relevant to this standard are not shown in the Figure above.

Figure 25: Documented review of medication adherence within three months of starting valproate medication. National subsample treated with valproate between three months and a year and each Trust*, 2020 and 2022



*Trusts that did not submit any data relevant to this standard are not shown in the Figure above.

Performance against practice standard 5

Patients prescribed continuing valproate treatment should have an annual review of the risk-benefit balance. This should include assessment of therapeutic benefit, adverse effects and medication adherence.

Figure 26: Documented review of therapeutic response in the past year. National subsample treated with valproate for more than a year and each Trust, 2020 and 2022

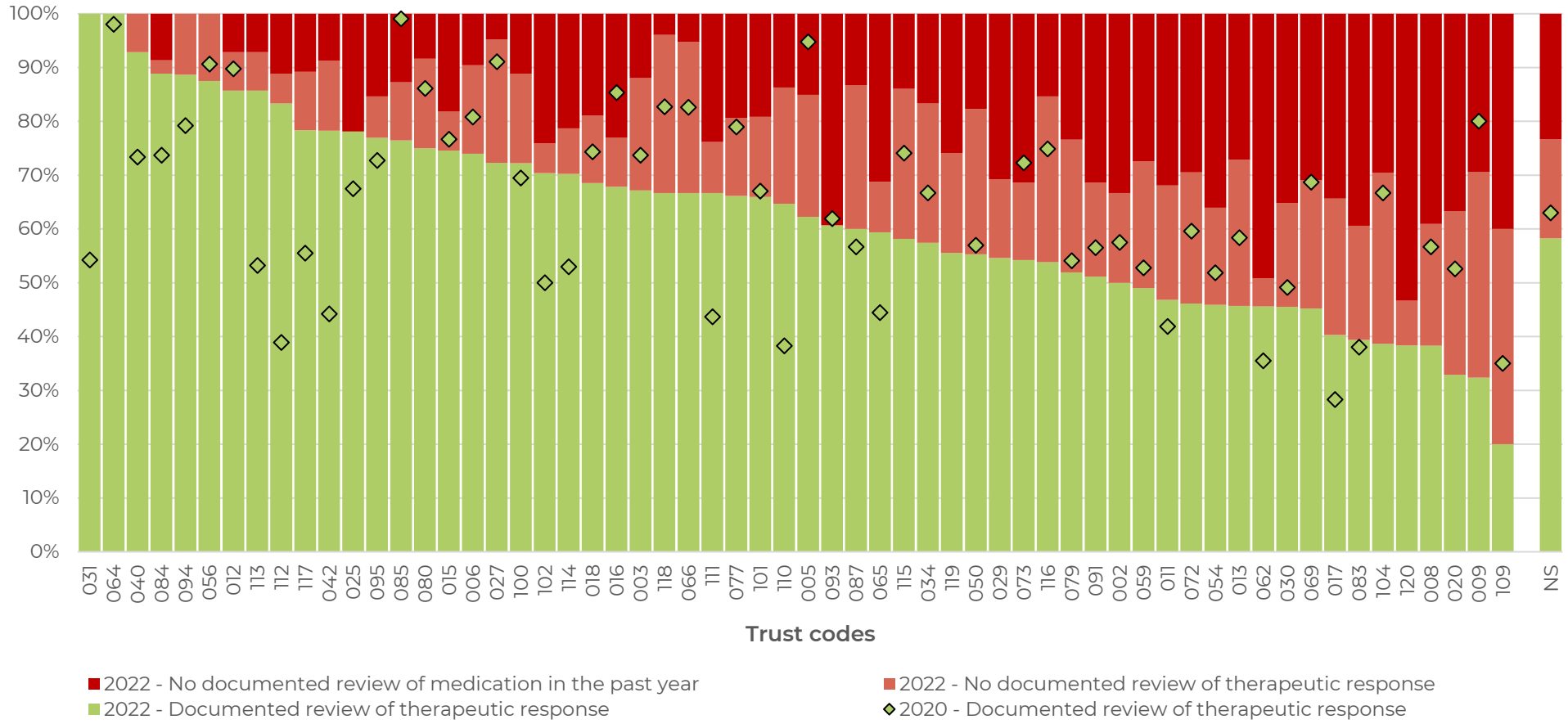


Figure 27: Documented review of side effects in the past year. National subsample treated with valproate for more than a year and each Trust, 2020 and 2022

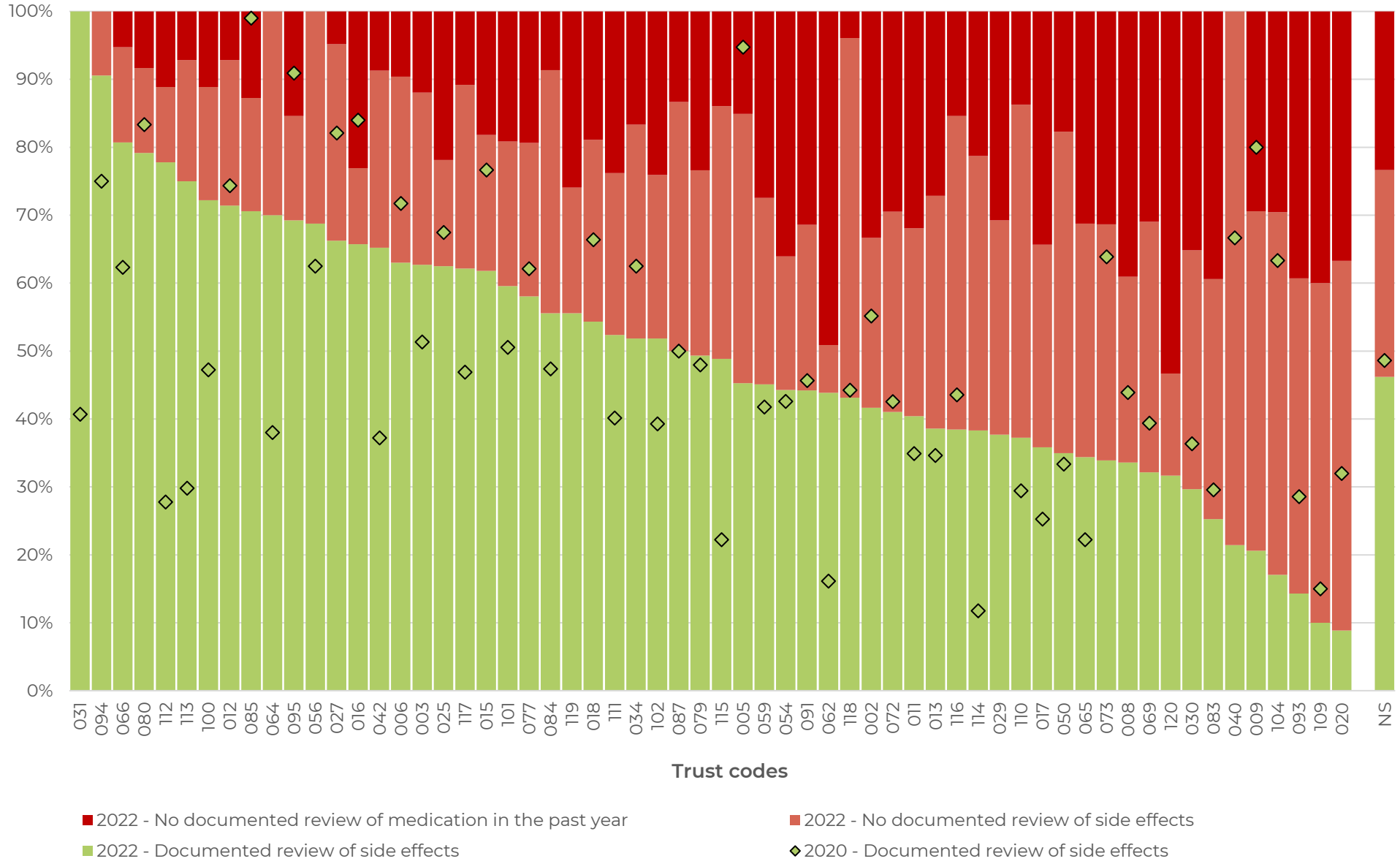


Figure 28: Documented review of medication adherence in the past year. National subsample treated with valproate for more than a year and each Trust, 2020 and 2022

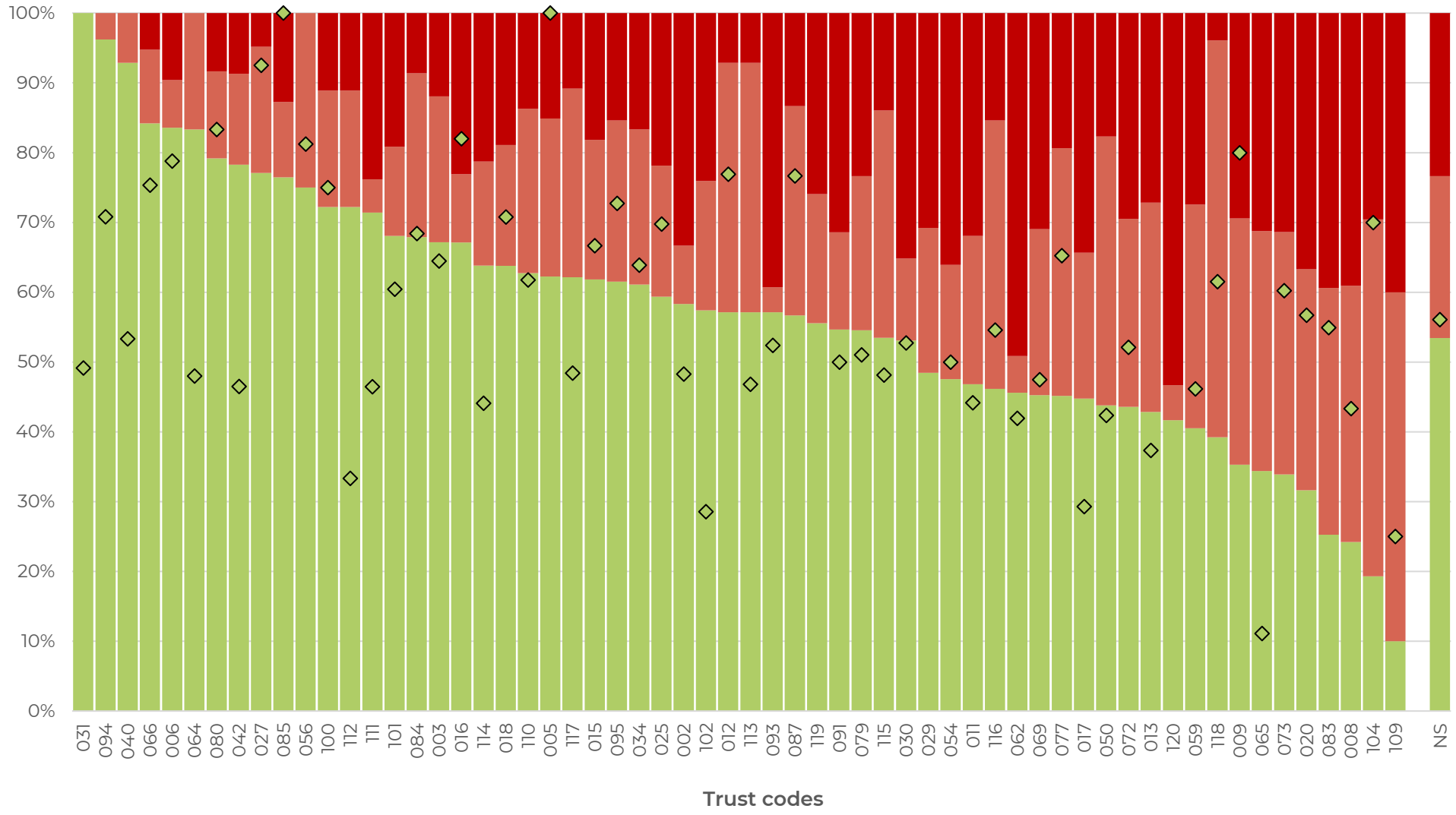


Figure 29: Documented measure of body weight and/or BMI in the past year. National subsample treated with valproate for more than a year and each Trust, 2020 and 2022

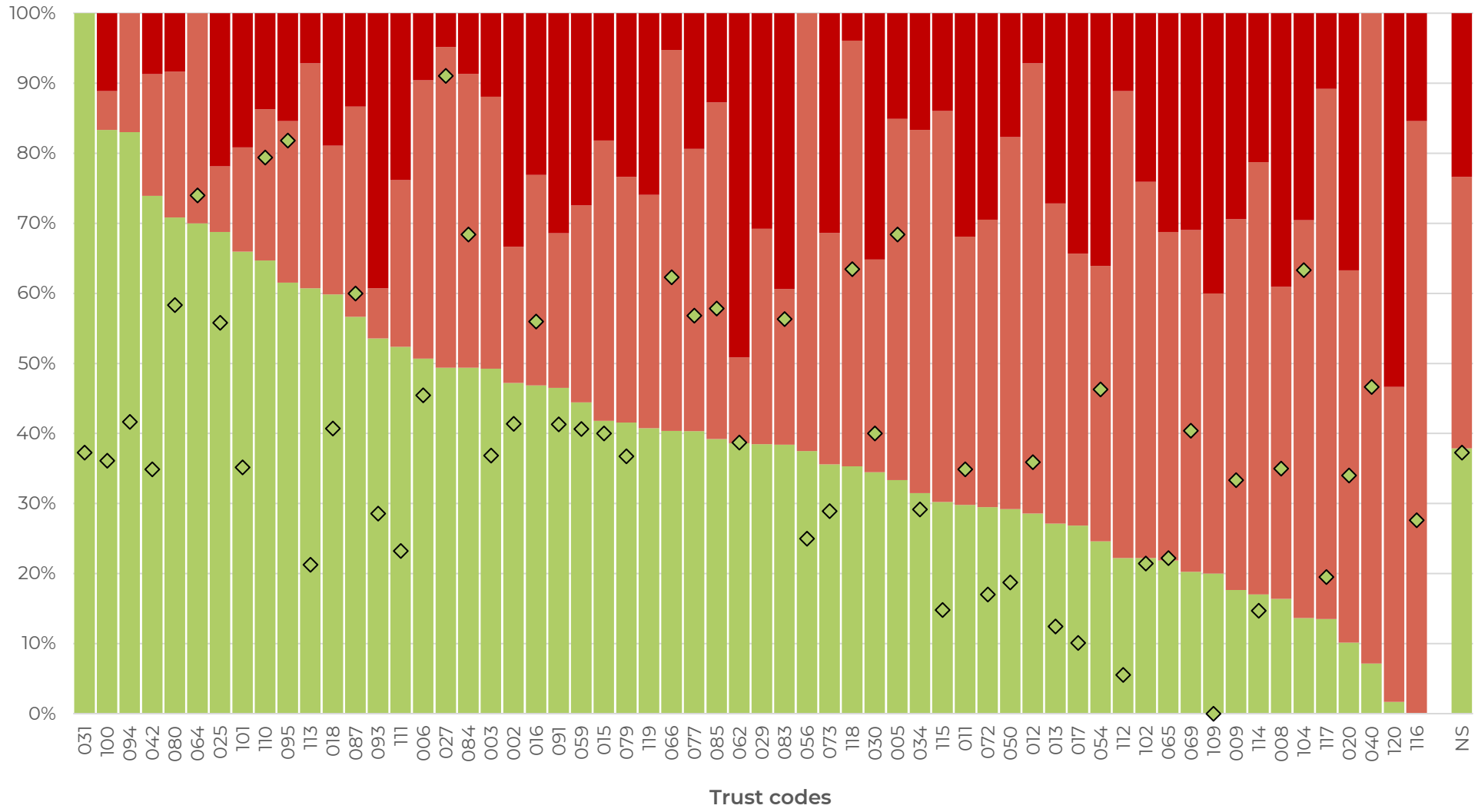


Figure 30: Documented measure of liver function tests (LFTs) in the past year. National subsample treated with valproate for more than a year and each Trust, 2020 and 2022

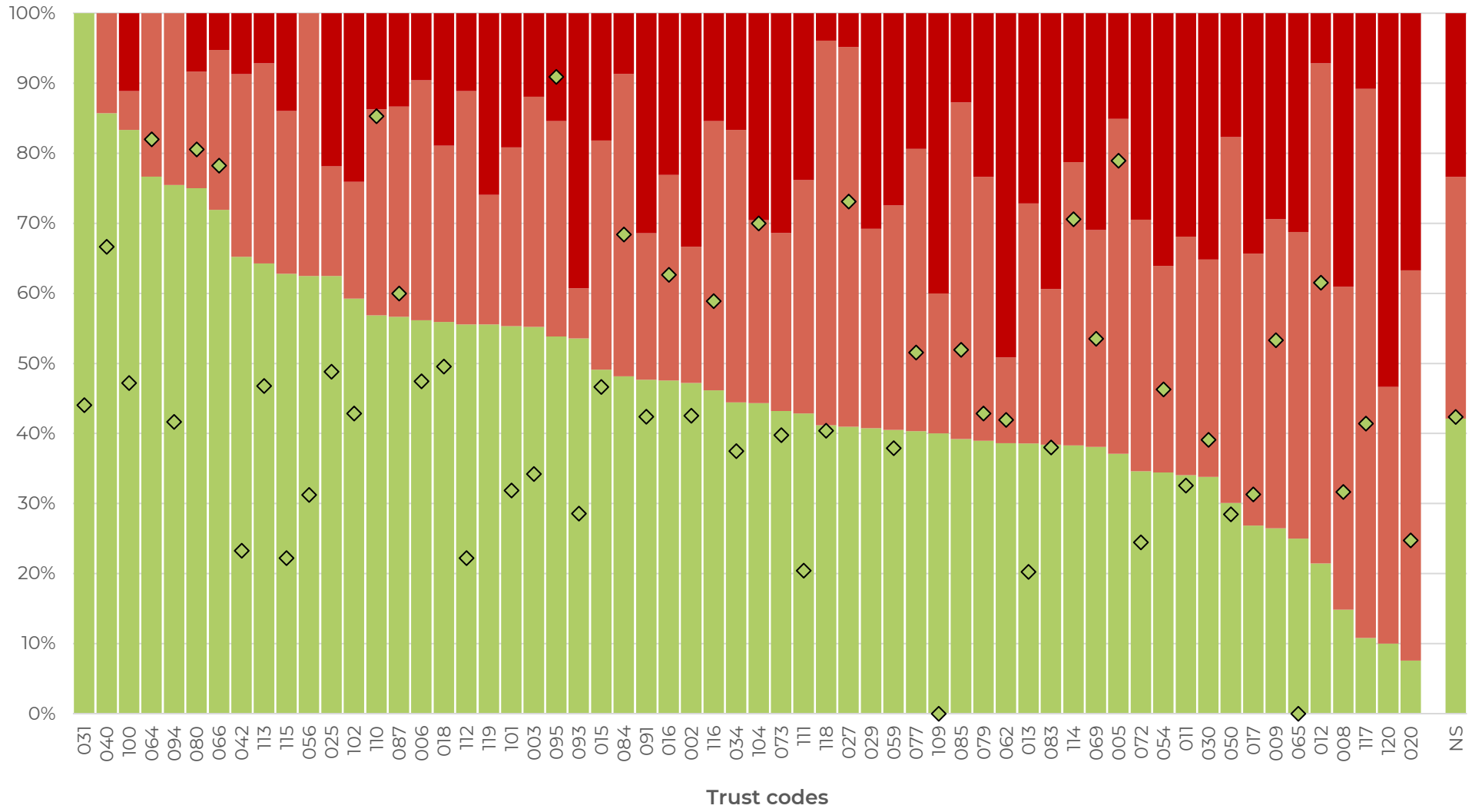


Figure 31: Documented measure of full blood count (FBC) in the past year. National subsample treated with valproate for more than a year and each Trust, 2020 and 2022

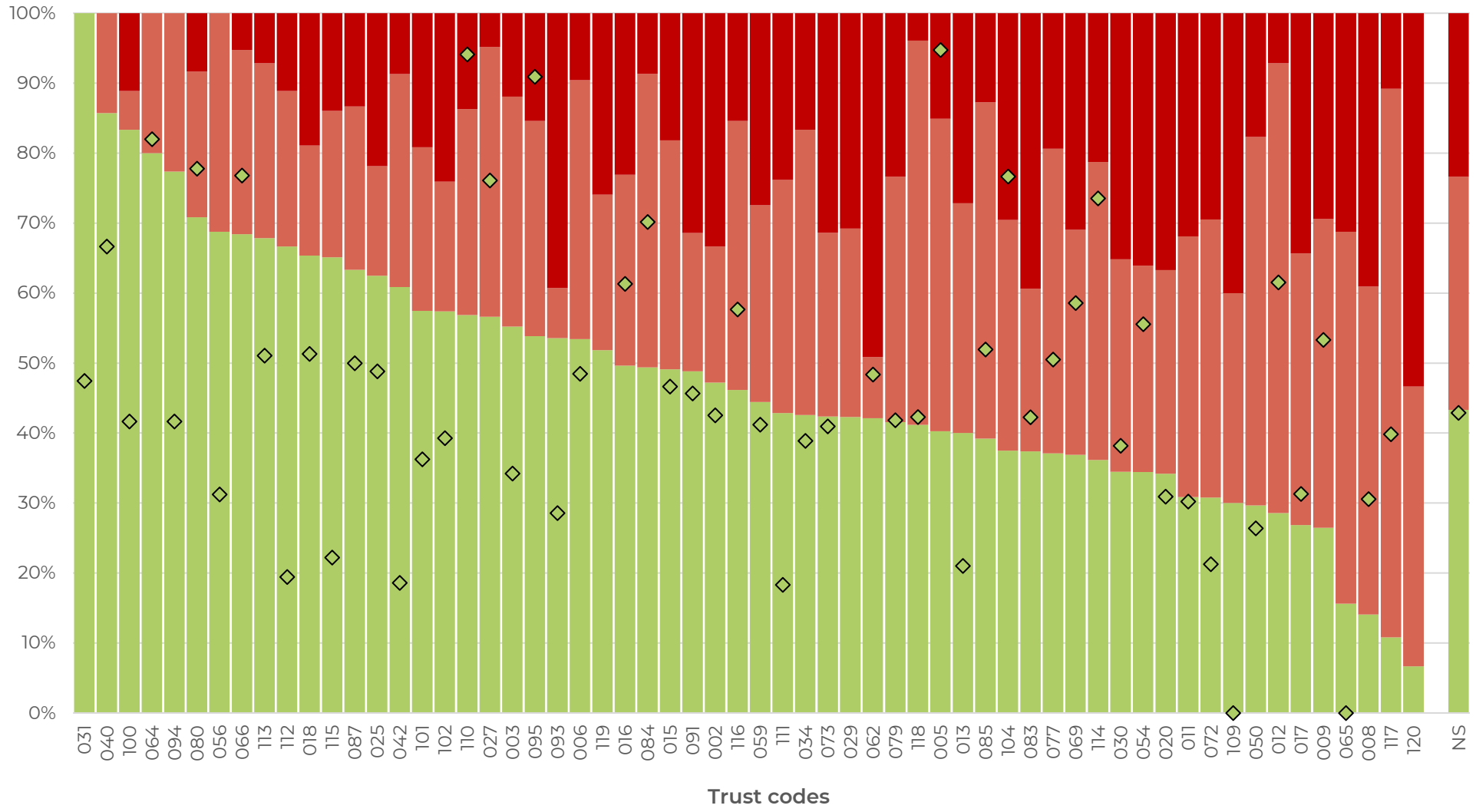


Figure 32: Documented measure of blood pressure in the past year. National subsample treated with valproate for more than a year and each Trust, 2020 and 2022

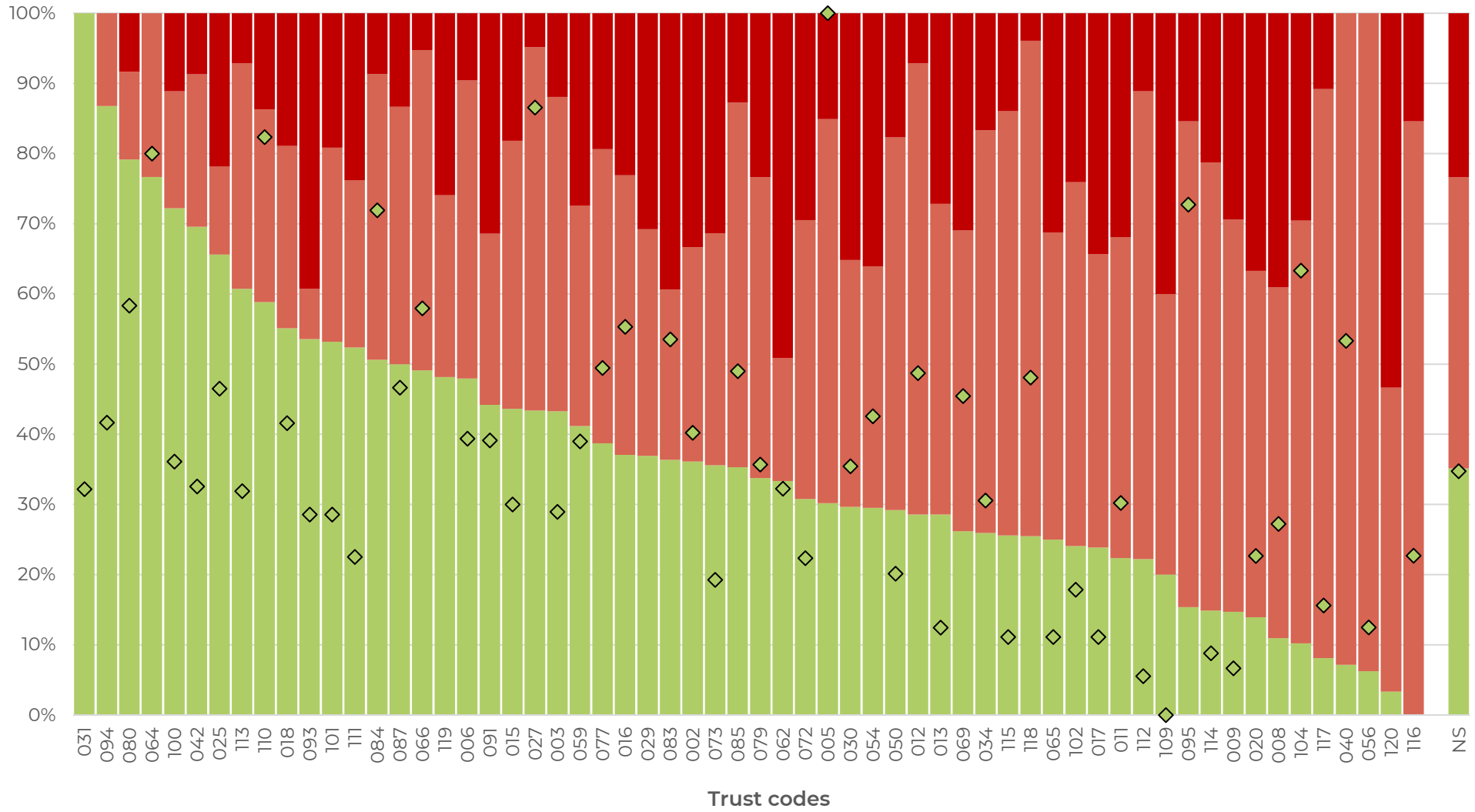


Figure 33: Documented measure of plasma glucose or HbA1c in the past year. National subsample treated with valproate for more than a year and each Trust, 2020 and 2022

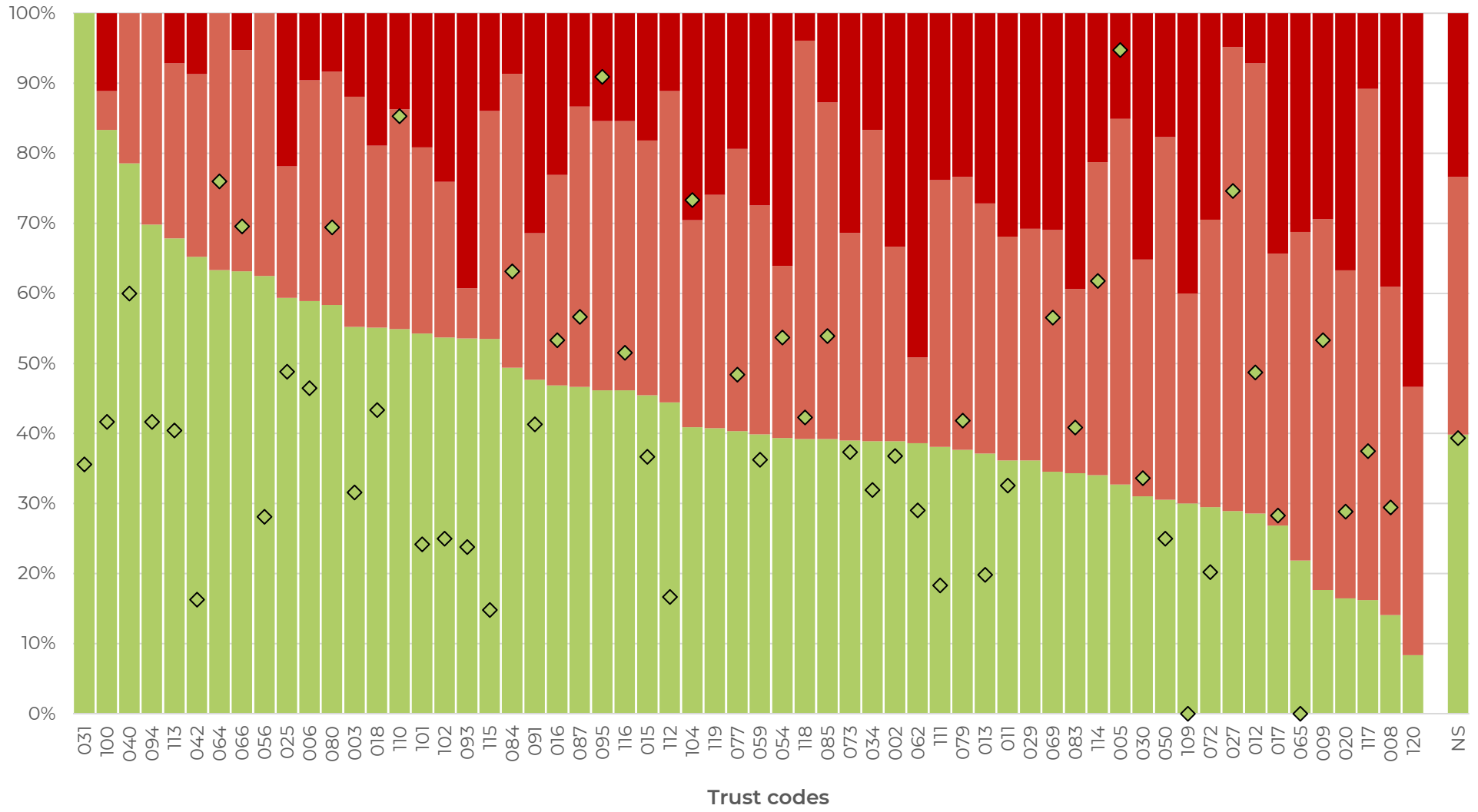
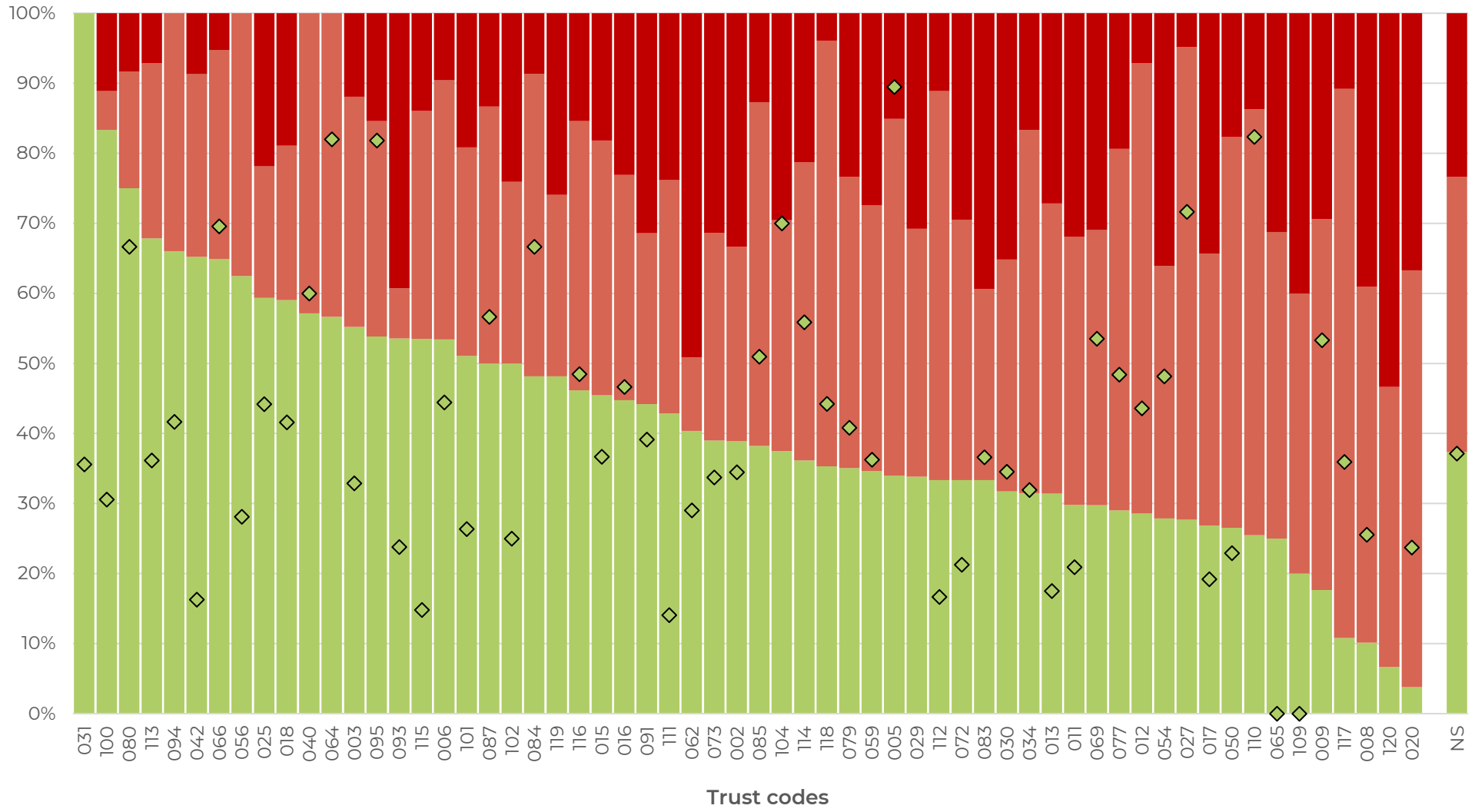


Figure 34: Documented measure of plasma lipids in the past year. National subsample treated with valproate for more than a year and each Trust, 2020 and 2022



Performance against practice standard 6

If valproate is prescribed for a woman of child-bearing age, there should be documented evidence that the conditions of 'prevent', the pregnancy prevention programme, are fulfilled.

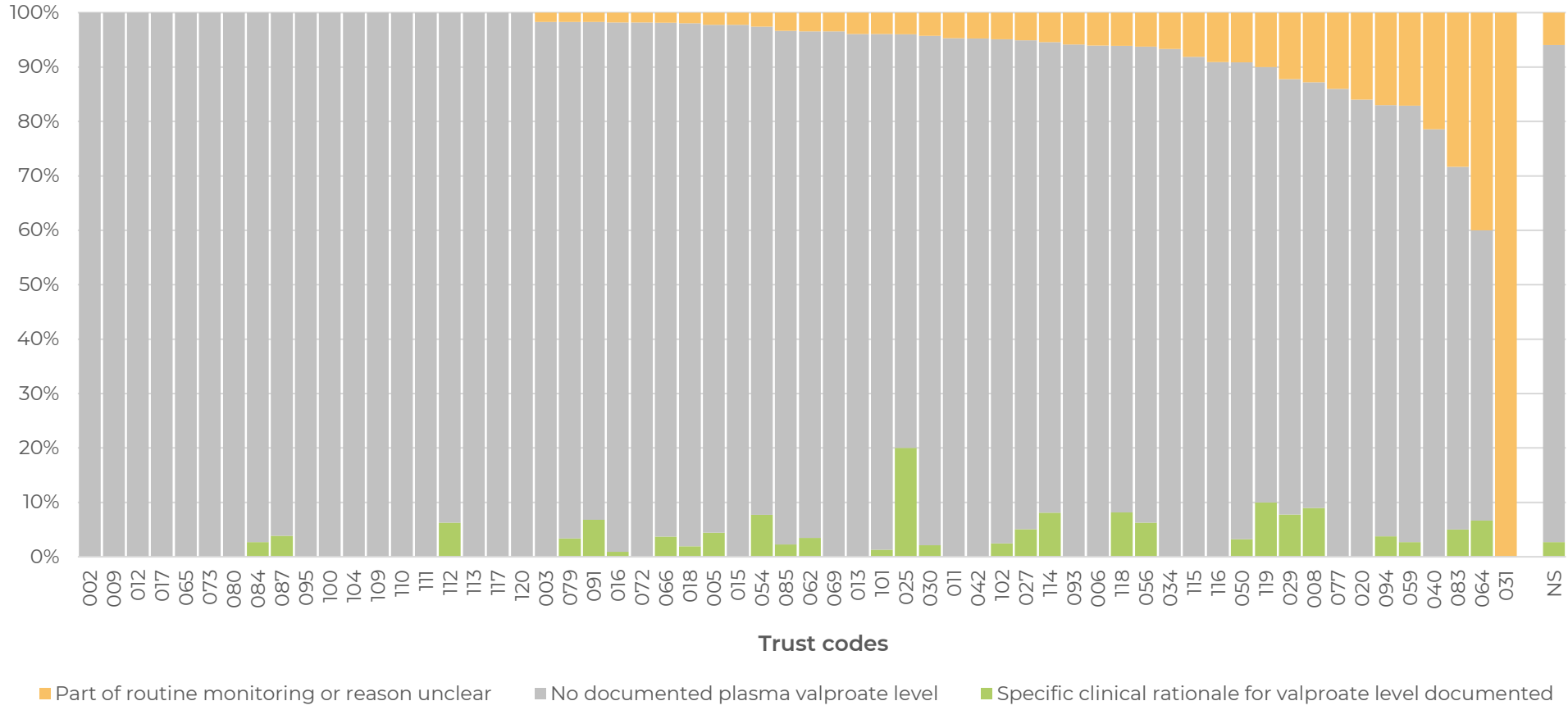
Performance against this practice standard in your Trust can be found in Table 1 in the executive summary.

The numbers of eligible cases in individual Trusts/clinical teams are likely to be very small, limiting the value of benchmarking at this level. If there is a particular aspect of performance against this standard that you wish to look at in more detail within your Trust, you may wish to interrogate the Excel spreadsheet containing your Trust data.

Treatment target

Plasma level monitoring of valproate treatment should not be used unless there is evidence of ineffectiveness, concerns about medication adherence, or dose-related side-effects.

Figure 35: Measurement of plasma valproate level and documentation of the clinical rationale. National subsample treated with valproate for more than a year, with a documented review in the past year, and each Trust, 2022



Clinical team level results

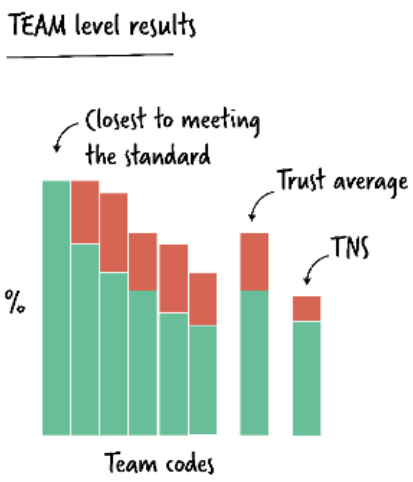
Analyses presented in this section were conducted for each clinical team from your Trust individually, for your total Trust sample and for the total national sample to allow benchmarking.

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

The POMH 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.

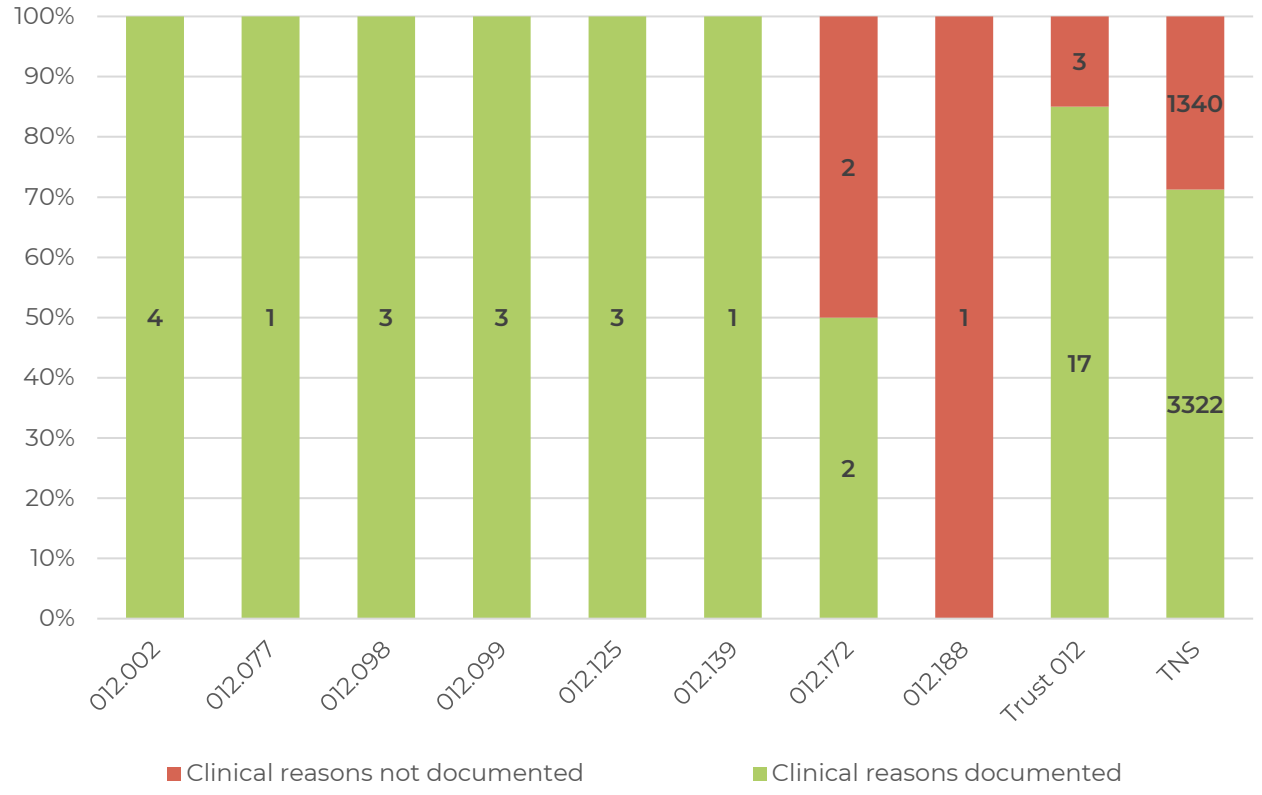
Charts in this section are ordered by frequency of key results and so the position of teams in each figure will vary.



Performance against practice standard 1

A clinician's reasons for initiating valproate treatment (i.e. target symptoms or behaviour) should be documented in the clinical records.

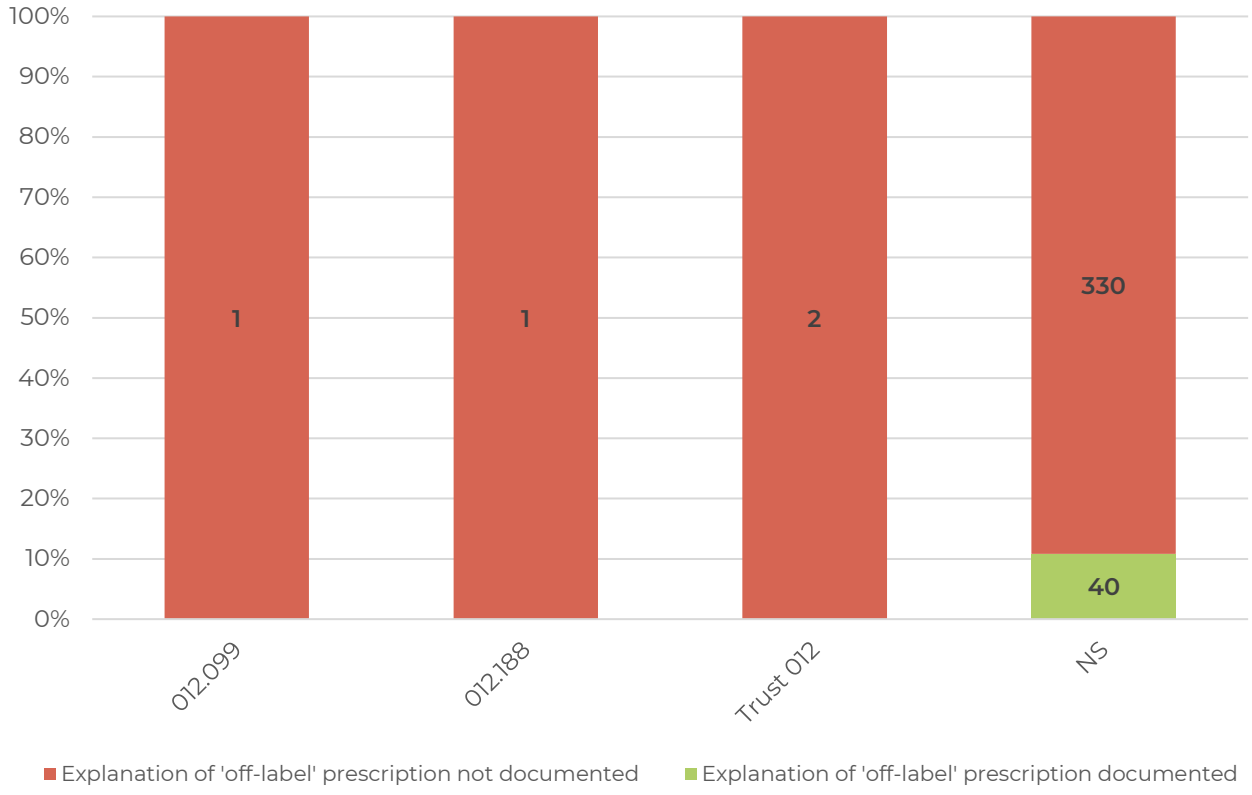
Figure 36: Documentation of the clinical reasons for prescribing valproate. Total national sample and your Trust, 2022



Performance against practice standard 2

If valproate is being prescribed 'off-label', it should be documented that this has been explained to the patient.

Figure 37: Documented explanation to patients that valproate prescription is 'off-label'. National subsample considered to be prescribed 'off-label' valproate and your Trust, 2022



Performance against 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 38: Documented body weight and/or BMI measurement conducted in the three months before valproate medication was started. National subsample treated with valproate for less than year and your Trust, 2022

Figure 39: Documented liver function tests (LFTs) conducted in the three months before valproate medication was started. National subsample treated with valproate for less than year and your Trust, 2022

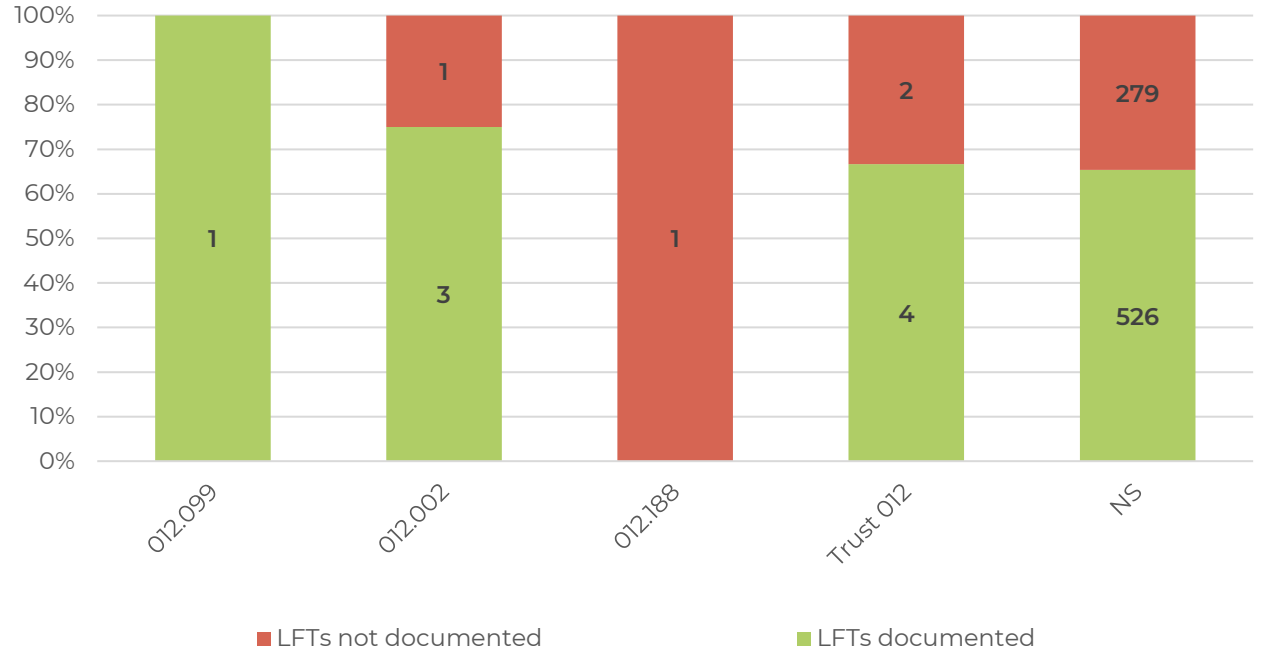


Figure 40: Documented full blood count (FBC) conducted in the three months before valproate medication was started. National subsample treated with valproate for less than year and your Trust, 2022

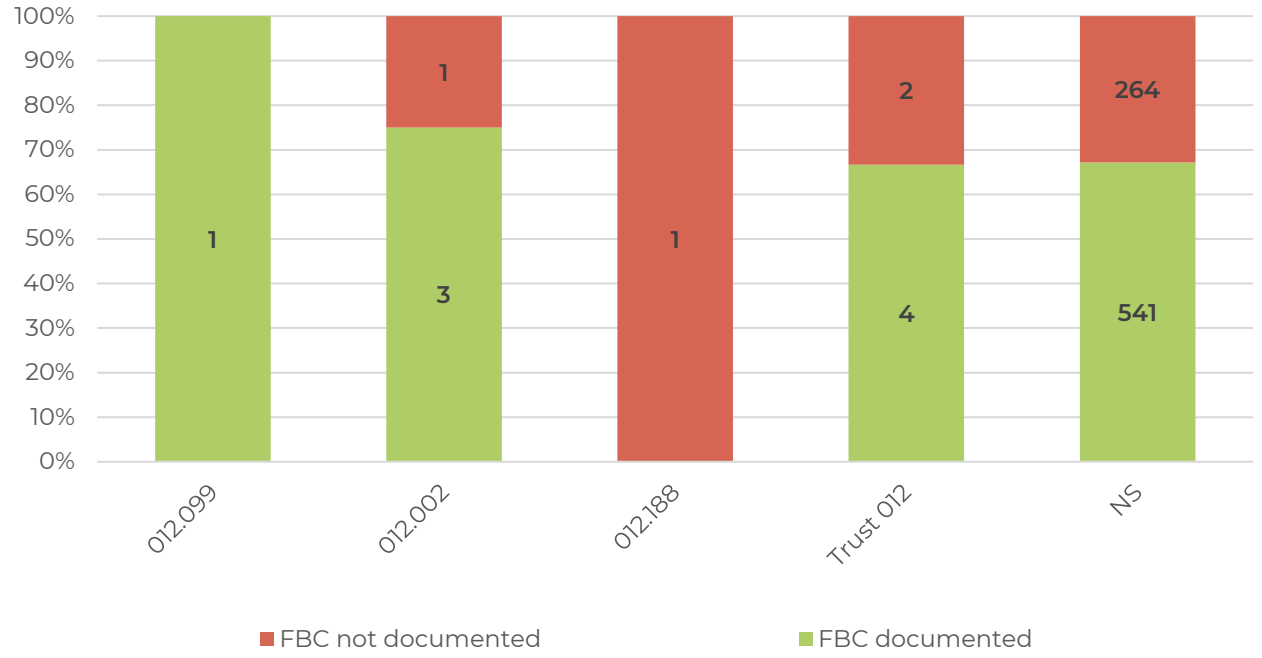


Figure 41: Documented plasma glucose or HbA1c measurement conducted in the three months before valproate medication was started. National subsample treated with valproate for less than year and your Trust, 2022

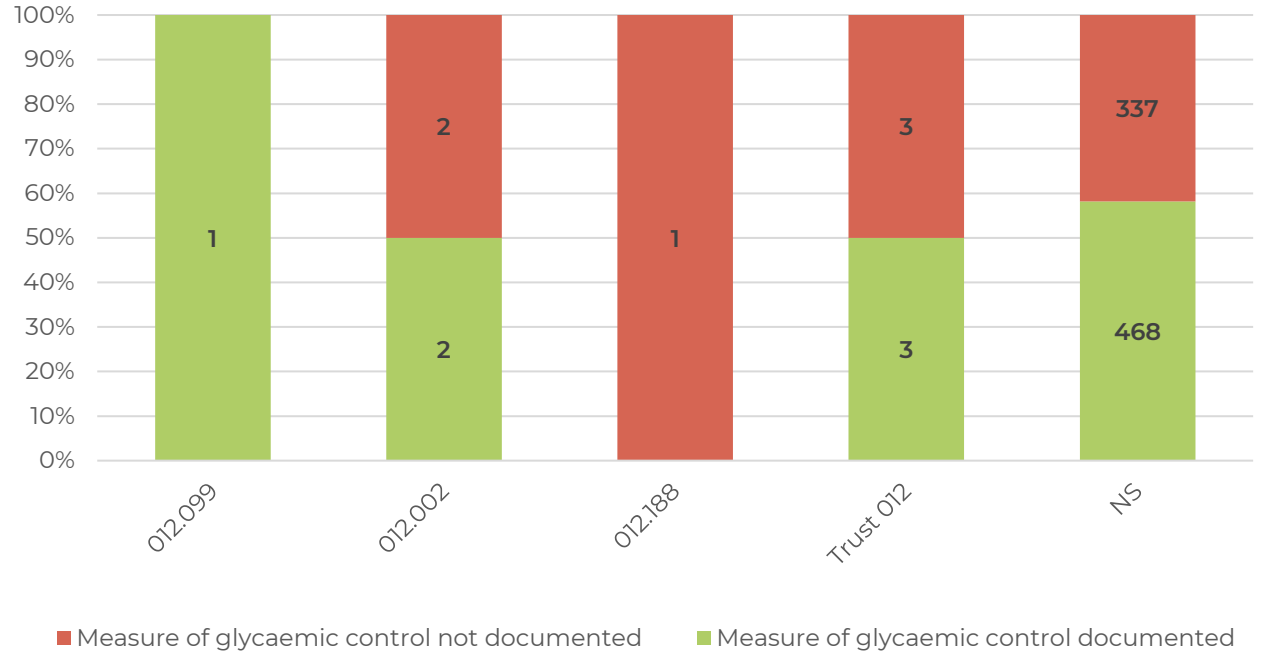


Figure 42: Documented plasma lipids measurement conducted in the three months before valproate medication was started. National subsample treated with valproate for less than year and your Trust, 2022

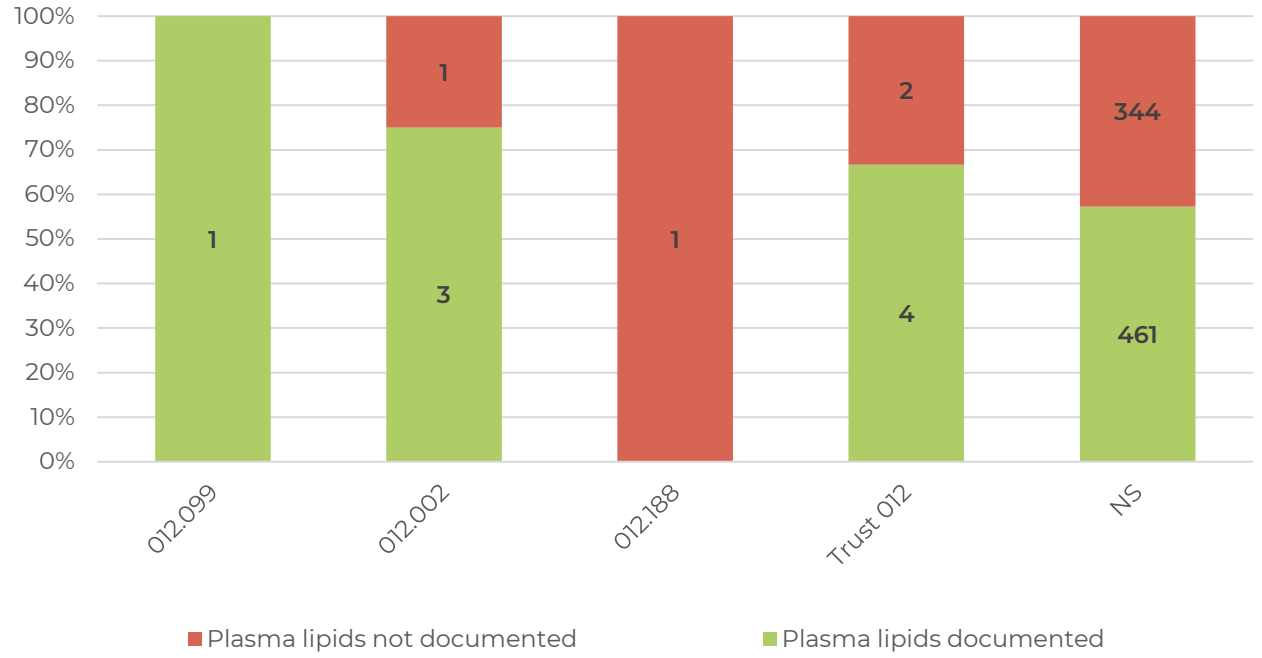
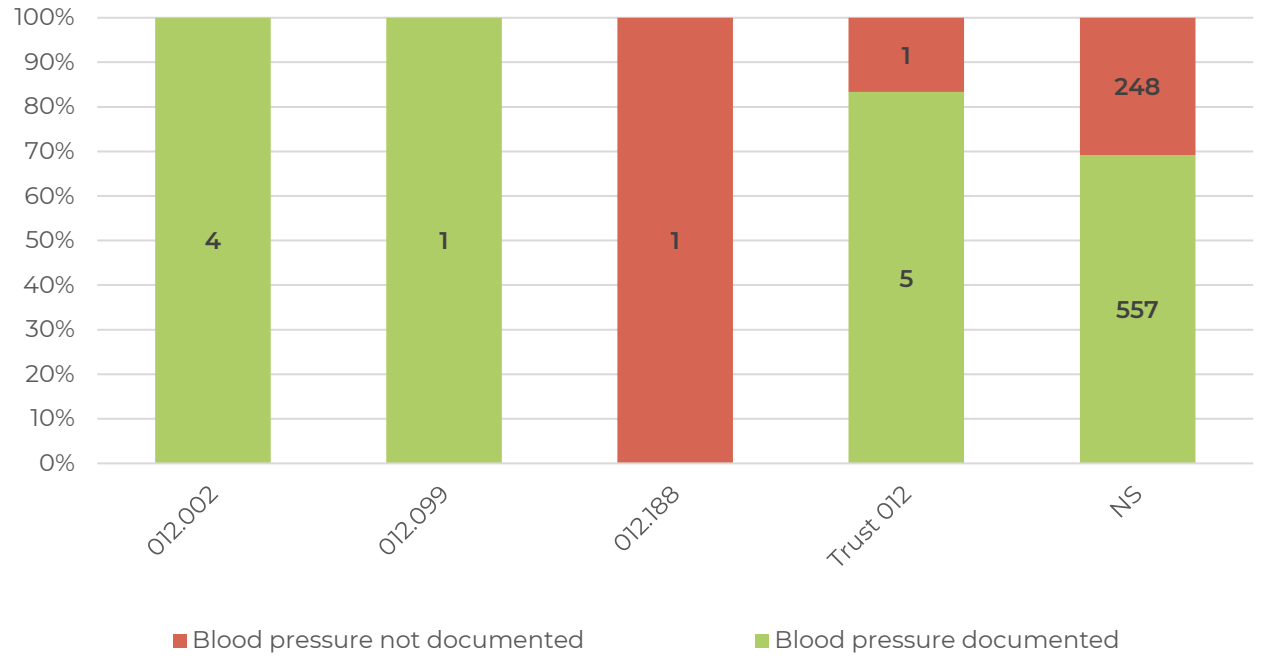


Figure 43: Documented blood pressure measurement conducted in the three months before valproate medication was started. National subsample treated with valproate for less than year and your Trust, 2022



Performance against practice standard 4

Review within the first three months of valproate treatment should include: screening for common side effects of the medication (e.g. weight gain, nausea, and tremor) and assessment of the response of the target symptoms/behaviour.

Figure 44: Documented review of side effects within three months of starting valproate medication.
National subsample treated with valproate between three months and a year and your Trust, 2022

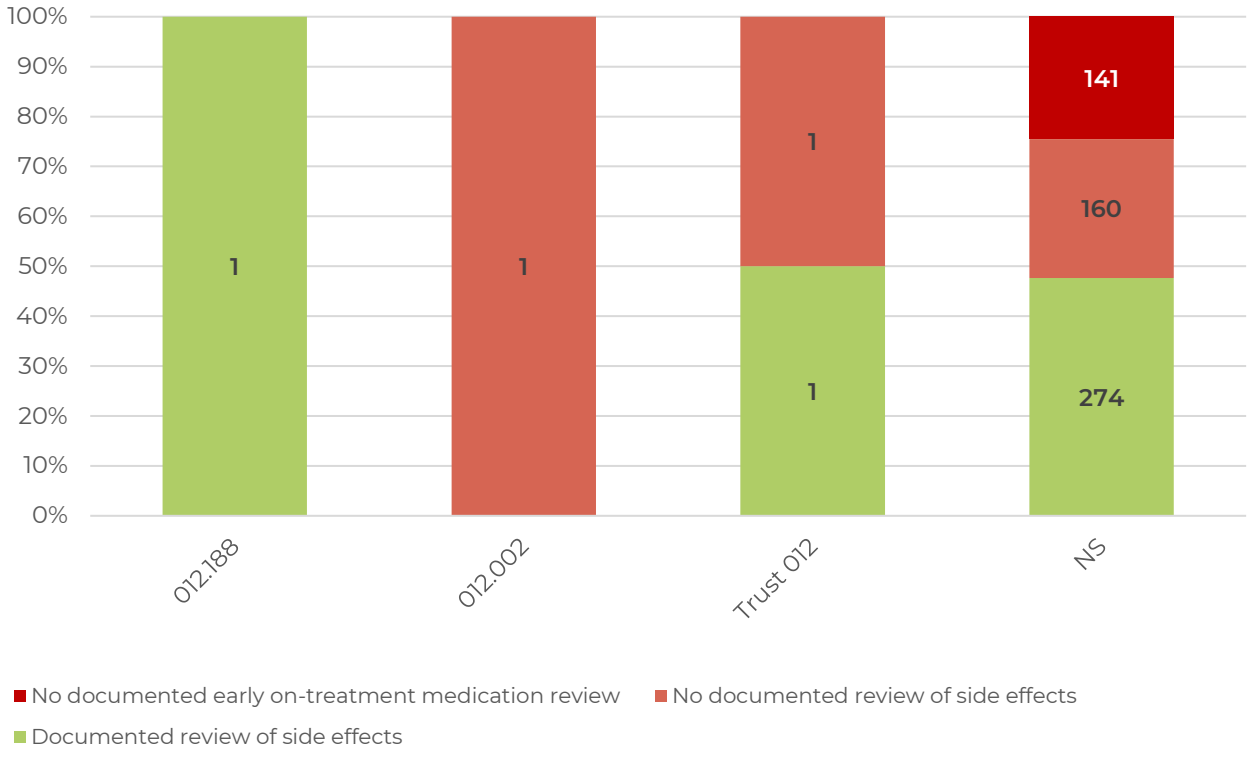


Figure 45: Documented review of therapeutic response within three months of starting valproate medication. National subsample treated with valproate between three months and a year and your Trust, 2022

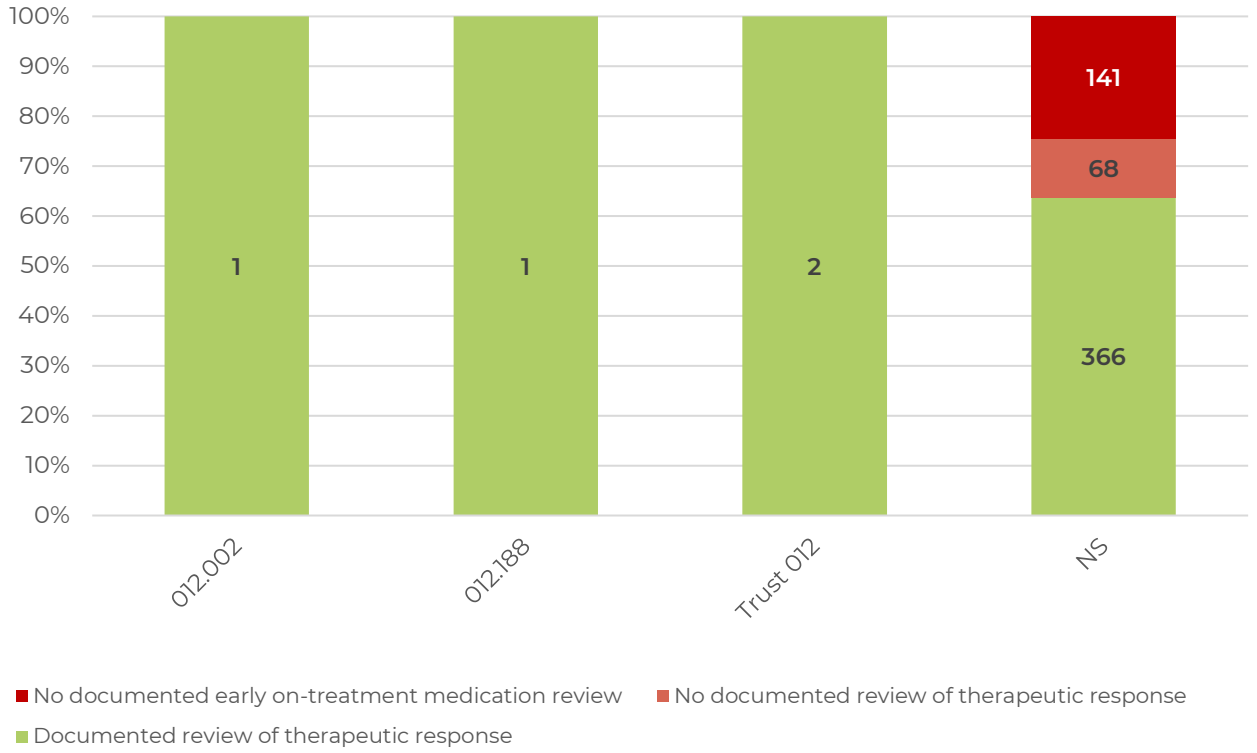
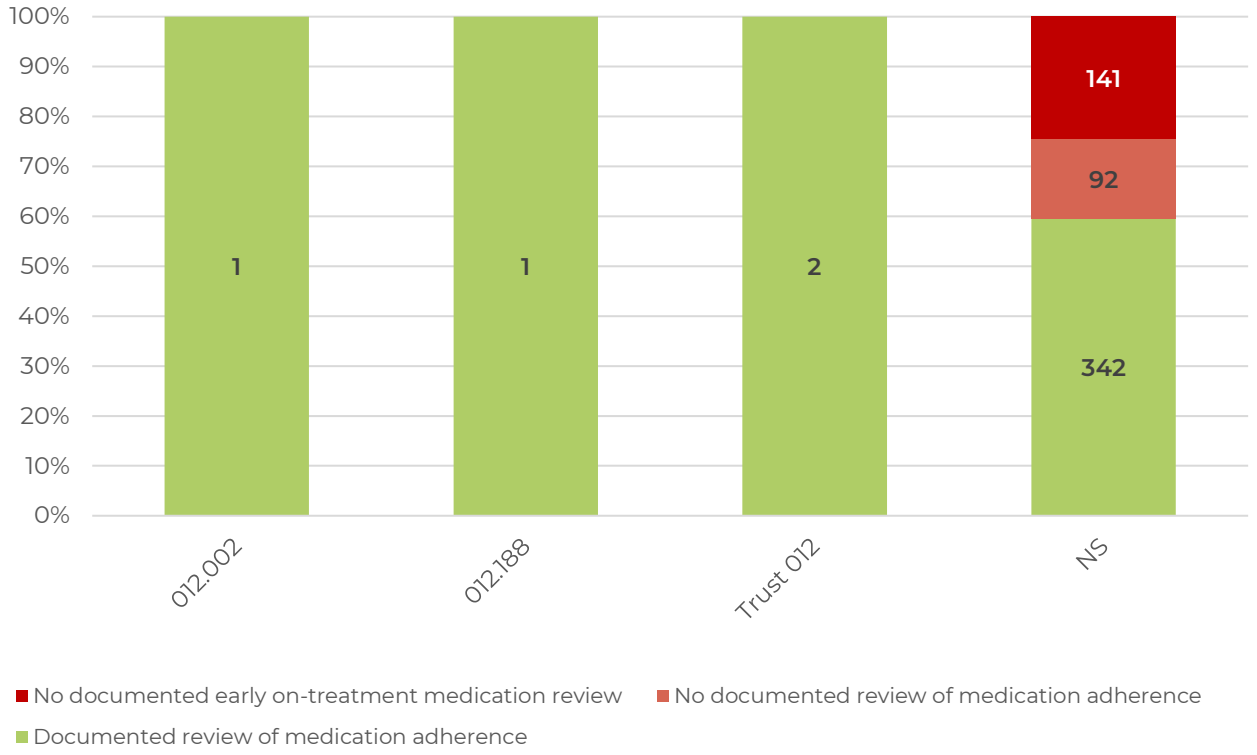


Figure 46: Documented review of medication adherence within three months of starting valproate medication. National subsample treated with valproate between three months and a year and your Trust, 2022



Performance against practice standard 5

Patients prescribed continuing valproate treatment should have an annual review of the risk-benefit balance. This should include assessment of therapeutic benefit, adverse effects and medication adherence.

Figure 47: Documented review of therapeutic response in the past year. National subsample treated with valproate for more than a year and your Trust, 2022

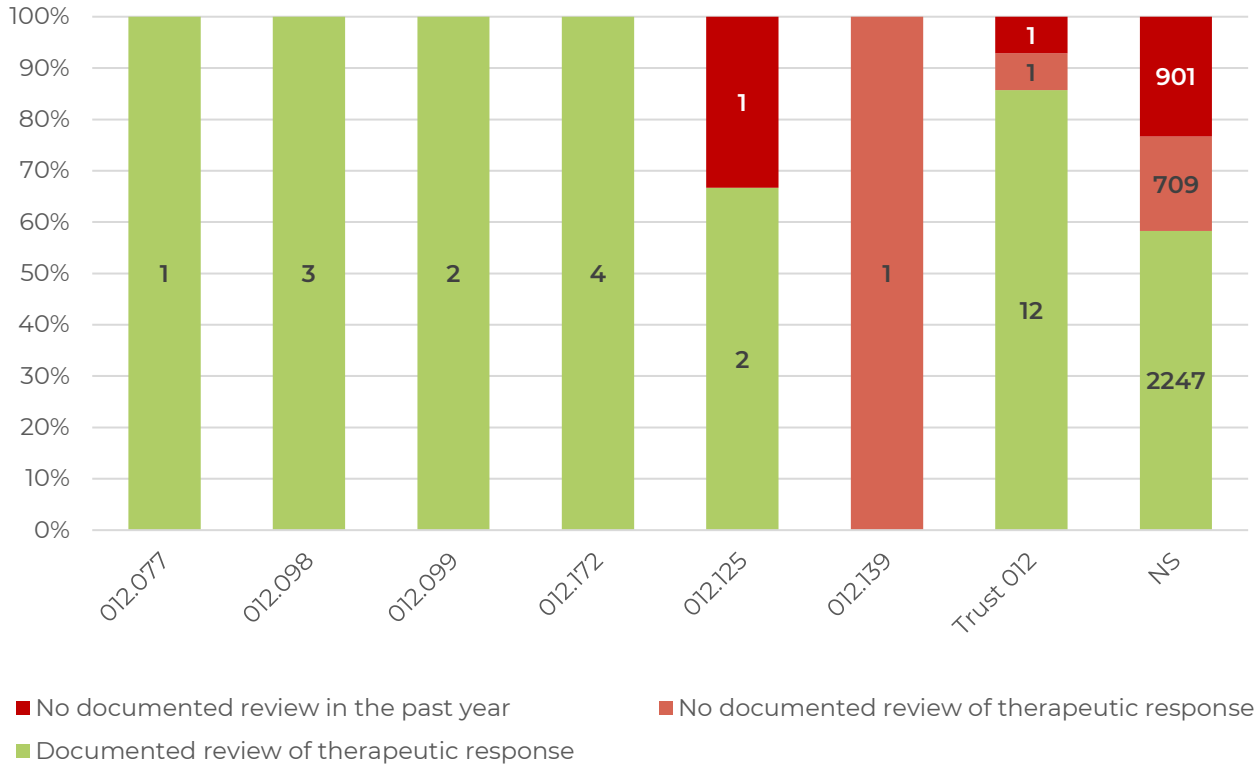


Figure 48: Documented review of side effects in the past year. National subsample treated with valproate for more than a year and your Trust, 2022

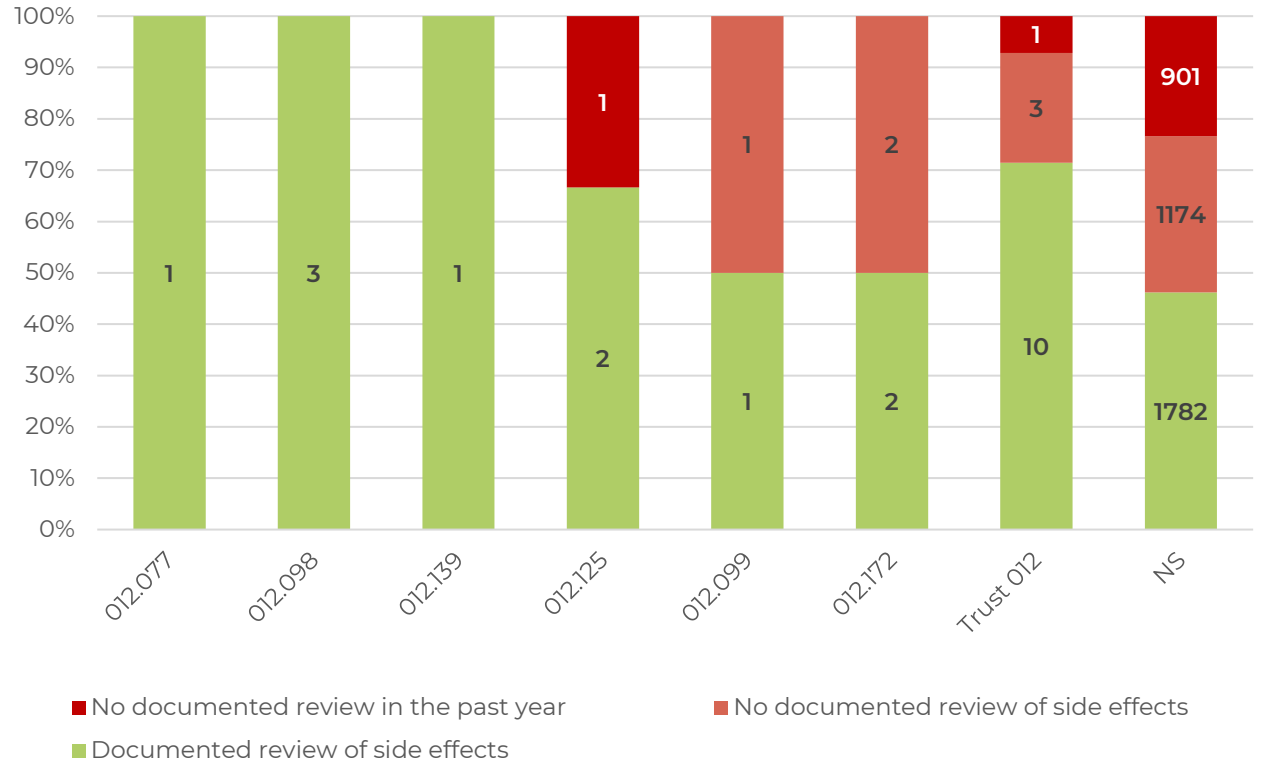
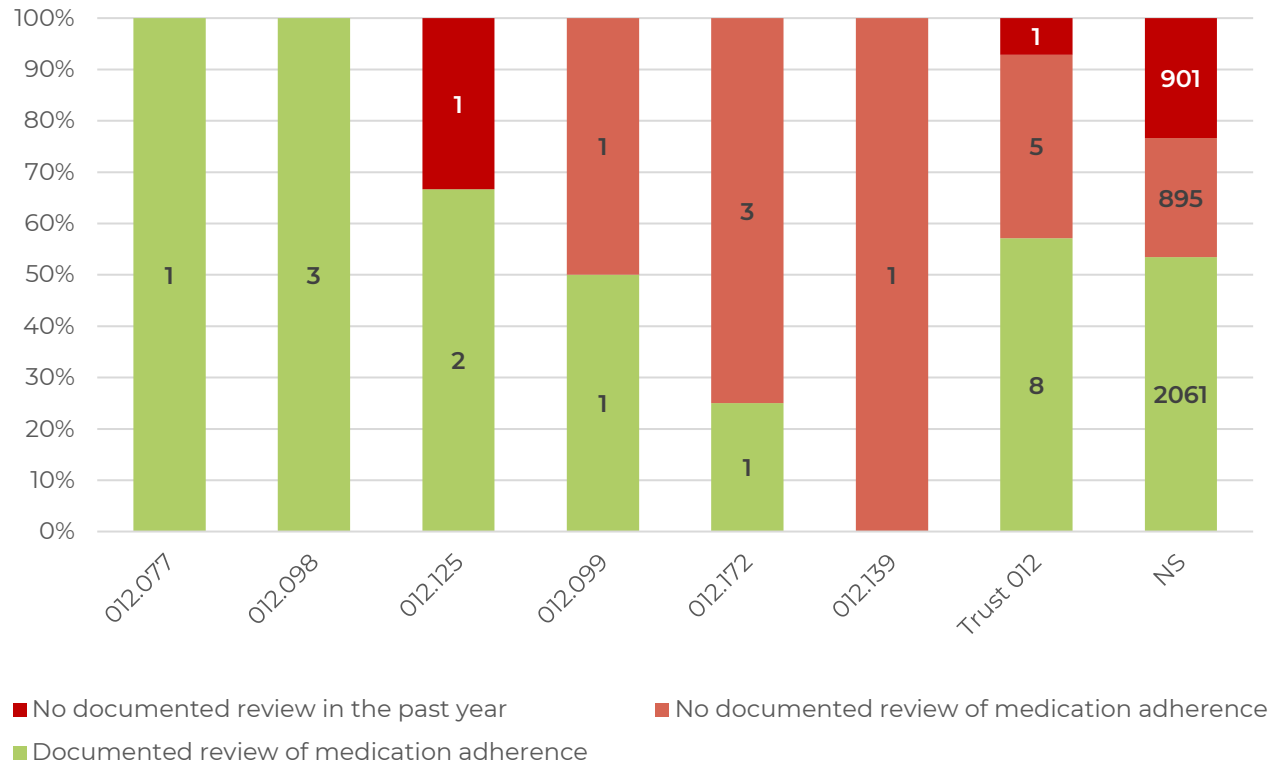


Figure 49: Documented review of medication adherence in the past year. National subsample treated with valproate for more than a year and your Trust, 2022



Performance against practice standard 6

If valproate is prescribed for a woman of child-bearing age, there should be documented evidence that the conditions of 'prevent', the pregnancy prevention programme, are fulfilled.

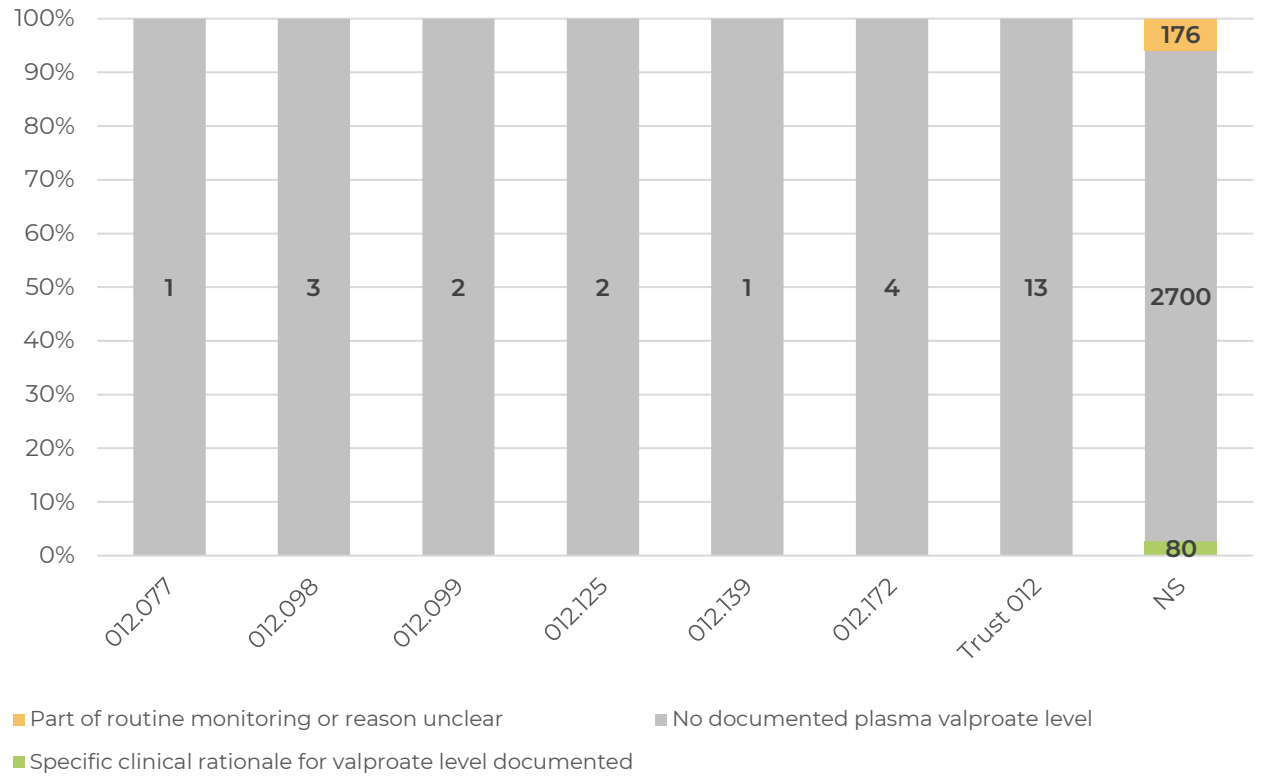
Performance against this practice standard in your Trust can be found in Table 1 in the executive summary.

The numbers of eligible cases in individual Trusts/clinical teams are likely to be very small, limiting the value of benchmarking at this level. If there is a particular aspect of performance against this standard that you wish to look at in more detail within your Trust, you may wish to interrogate the Excel spreadsheet containing your Trust data.

Treatment target

Plasma level monitoring of valproate treatment should not be used unless there is evidence of ineffectiveness, concerns about medication adherence, or dose-related side-effects.

Figure 50: Measurement of plasma valproate level and documentation of the clinical rationale. National subsample treated with valproate for more than a year, with a documented review in the past year, and your Trust, 2022



Appendices

Appendix A: Data use and management

Data control statement for POMH quality improvement programme 20b: Improving the quality of valproate prescribing in adult mental health services.

Data ownership and control

Control of the local data submitted to POMH is retained by the healthcare organisation that submitted them. These data have been made available to POMH in a way that is pseudonymous, with the exception of the identity of the source organisation. The aggregate data from all participating organisations are analysed by POMH to produce our customised reports. These reports summarise 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 to publish the aggregated data on its web site and/or in appropriate scientific journals. Any organisations requesting these audit data will be referred to the POMH 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 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.

Privacy Notice

In accordance with the General Data Protection Regulation (GDPR) we have updated our privacy notice, which provides full details on how we use your data and the data submitted as part of a national clinical audit, along with our legal basis for doing so. Our privacy notice can be found online via the following link:

https://www.rcpsych.ac.uk/aboutthecollege/dataprotection/ccqiprivacynotice.aspx

This privacy notice is provided in addition to POMH's data control statement. The data collected by POMH are pseudonymous.

Appendix B: Participating Trusts

Avon and Wiltshire Mental Health Partnership NHS Trust
Barnet, Enfield and 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 Healthcare NHS Foundation Trust
Bradford District Care NHS Foundation Trust
Cambridgeshire and Peterborough NHS Foundation Trust
Cardiff and Vale University Health Board
Central and North West London NHS Foundation Trust
Cheshire and Wirral Partnership NHS Foundation Trust
Cornwall Partnership NHS Foundation Trust
Coventry and Warwickshire Partnership NHS Trust
Cumbria, Northumberland Tyne and Wear NHS Foundation Trust
Cwm Taf Morgannwg University Health Board
Cygnet Health Care
Derbyshire Healthcare NHS Foundation Trust
Dorset Healthcare University NHS Foundation Trust
East London NHS Foundation Trust
Elysium Healthcare Limited
Essex Partnership University NHS Foundation Trust
Forensic Network (Scotland)
Greater Manchester Mental Health NHS Foundation Trust
Hertfordshire Partnership University NHS Foundation Trust
Humber Teaching NHS Foundation Trust
Kent and Medway NHS and Social Care Partnership Trust
Lancashire and South Cumbria NHS Foundation Trust
Leeds and York Partnership NHS Foundation Trust
Leicestershire Partnership NHS Trust
Lincolnshire Partnership NHS Foundation Trust
Manx Care
Mersey Care NHS Trust
Midlands Partnership NHS Foundation Trust
NAViGO Health and Social Care CIC
Norfolk and Suffolk NHS Foundation Trust
North East London NHS Foundation Trust
North Staffordshire Combined Healthcare NHS Trust
Northamptonshire Healthcare NHS Foundation Trust
Northern Health and Social Care Trust
Nottinghamshire Healthcare NHS 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 NHS Foundation Trust
South Eastern Health and Social Care Trust
South West London and St George's Mental Health Trust
South West Yorkshire Partnership NHS Foundation Trust
Southern Health and Social Care Trust
Southern Health NHS Foundation Trust
St Andrew's Healthcare
St Patrick's Mental Health Services
Surrey and Borders Partnership NHS Foundation Trust
Sussex Partnership NHS Foundation Trust
Swansea Bay University Health Board
Tees, Esk and Wear Valleys NHS Foundation Trust
West London NHS Trust
Western Health and Social Care Trust

Appendix C: Patient demographics and clinical characteristics

Figure 51: Proportion of males and females. Total national sample and each Trust, 2022

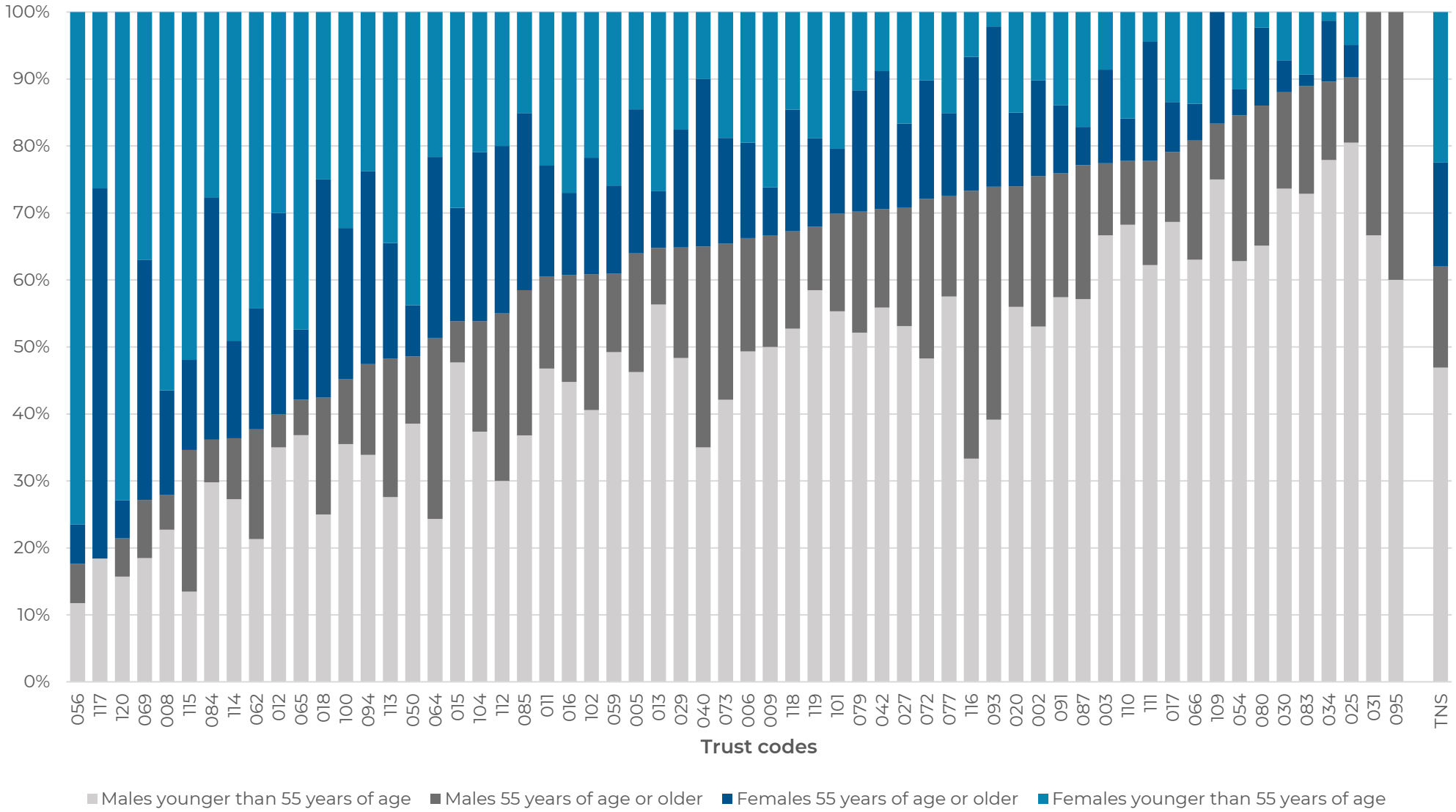


Figure 52: Distribution of ethnicities. Total national sample and each Trust, 2022

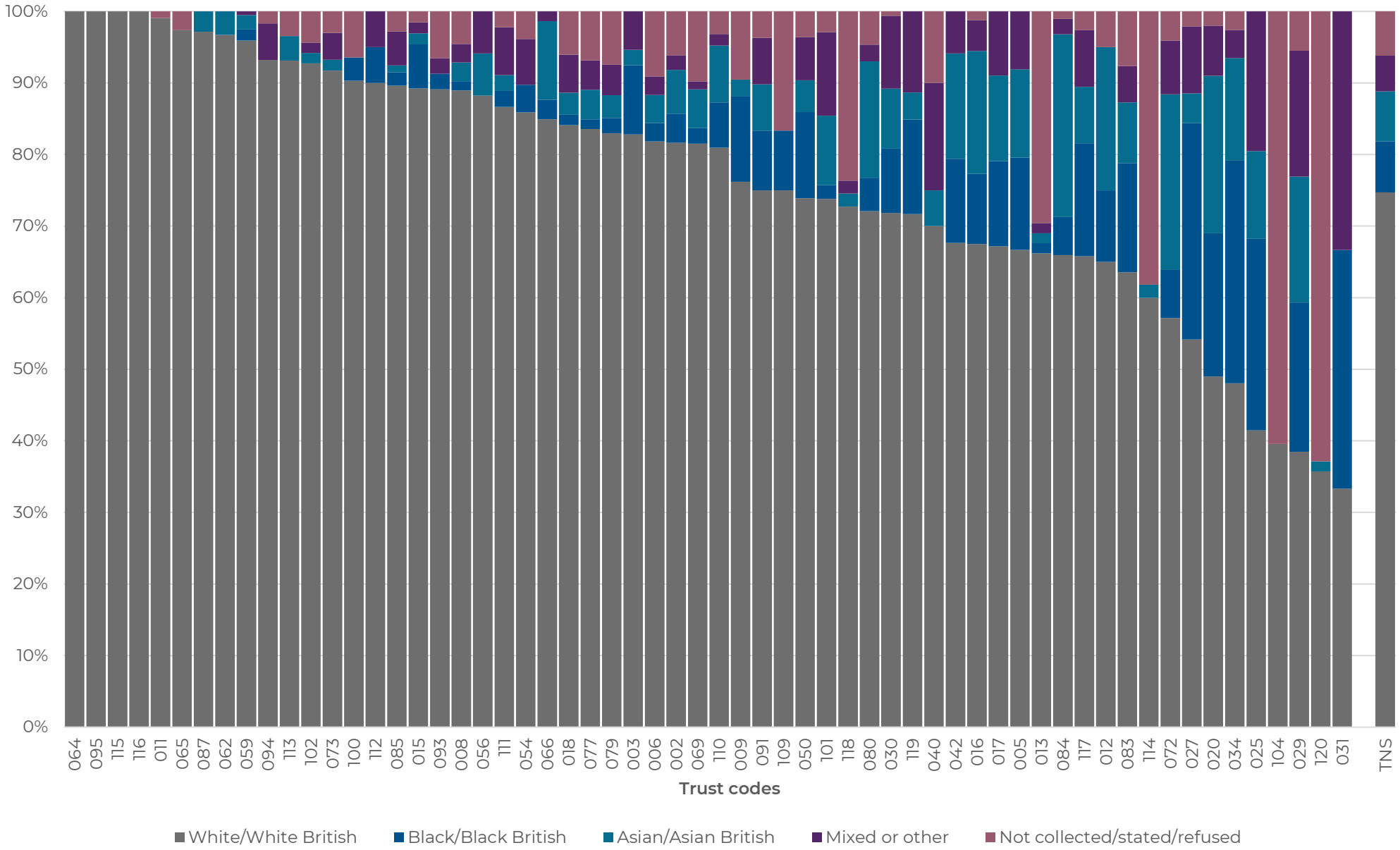
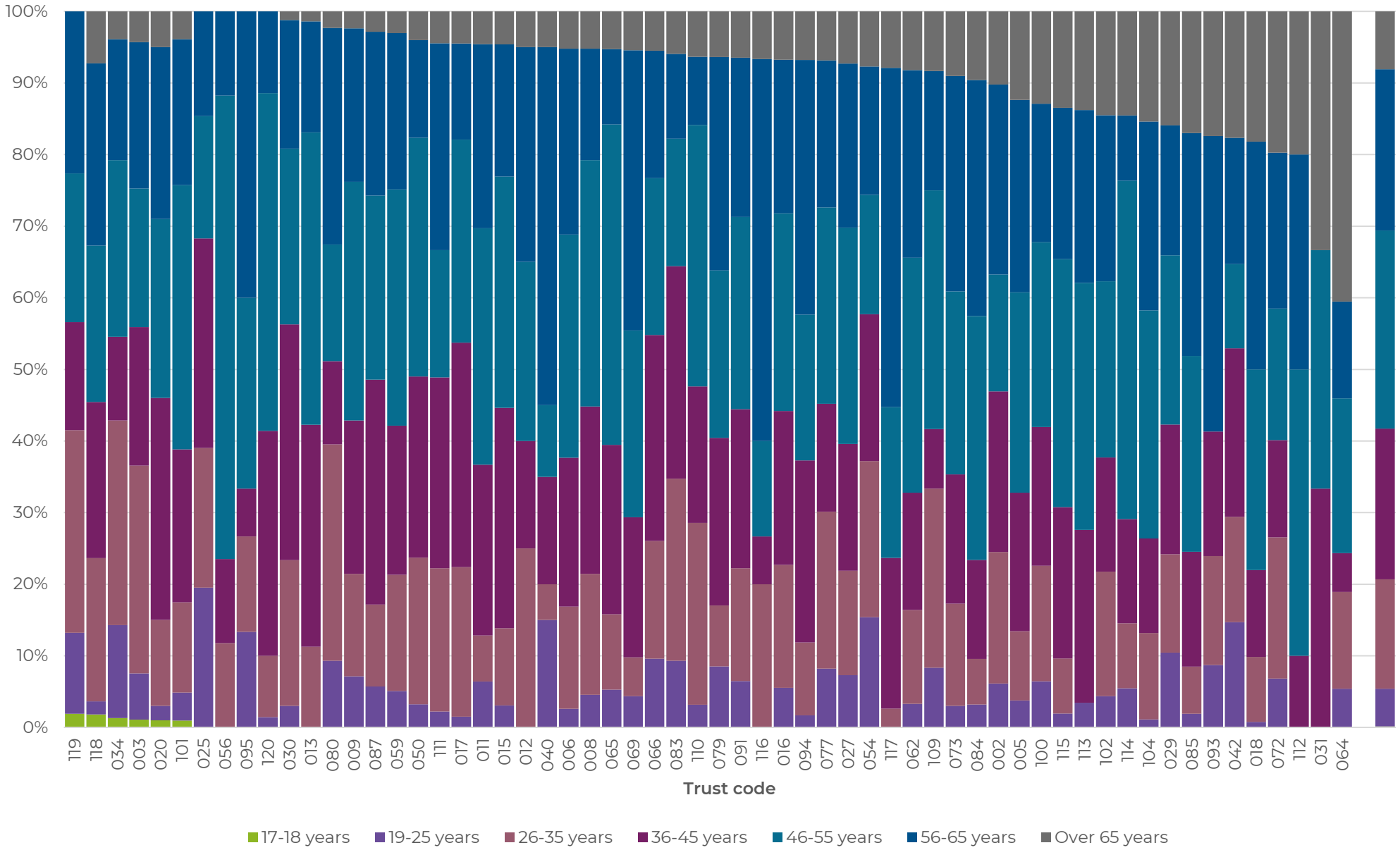
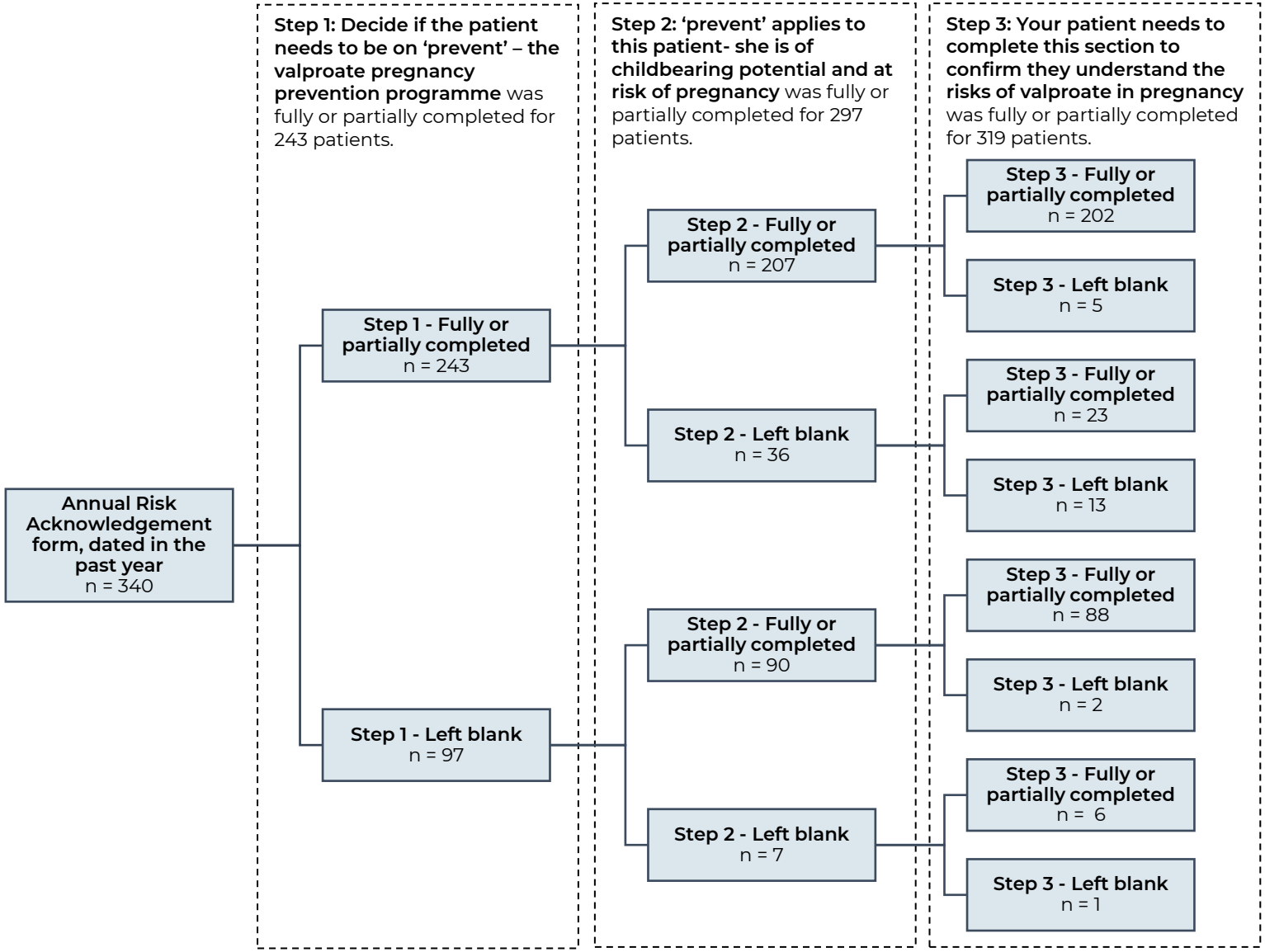


Figure 53: Age bands. Total national sample and each Trust, 2022



Appendix D: Implementation of 'prevent'

Figure 54: Implementation of the Annual Risk Acknowledgement (ARA) form. National subsample with an ARA form dated in the past year, 2022



Appendix E: Audit data collection tool

RC PSYCH ROYAL COLLEGE OF PSYCHIATRISTS | POMH PRESCRIBING OBSERVATORY FOR MENTAL HEALTH

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

Improving the quality of valproate prescribing in adult mental health services

QI Topic 20b

Eligibility criteria

Eligible patients will be **currently prescribed valproate** and under the **care of adult mental health services** (including forensic services), irrespective of age. Patients under the care of other services, such as CAMHS, learning disability and older people's services, should not be included.

Collecting data

To complete this audit form, you should refer to the patient's clinical records. Clinical records include all electronic and paper notes, letters, and other patient information available to the clinical team. Given the nature of the information required to answer some questions, there may be the need to involve a doctor and/or pharmacist.

Before collecting data, please refer to the **Guidance Notes** at the end of this tool.

Submitting data

Data should be submitted online via the POMH Data Entry webpage. You will need your POMH username and password. Before submitting, please read the Guidance for Online Data Submission document, available on the POMH website. If you realise that you have made a mistake in data submission, you will be able to correct this before the data entry period ends. To do this, you will need to ensure you keep a note of the receipt number displayed when the data were submitted. You will not be able to correct your submitted data after the data entry period ends.

To aid the data cleaning process, you may wish to keep a record of the patient ID on the front page of each paper form, for easier identification of cases (you cannot use the submission receipt number).

Data collection & entry: **3 October – 30 November 2022***

Data entry closes: **4pm, 30 November 2022**

**Data collection and entry activities may overlap – members can choose to run data collection and entry at the same time, or as two separate periods within the specified dates.*

Please contact the POMH-UK team if you have any questions or require further assistance.
Email: pomh-uk@rcpsych.ac.uk / Telephone: 0208 618 4010

Please note that this form is intended for use as part of the POMH-UK Topic 20b quality improvement programme only and may not be suitable for other purposes.

No.	Practice Standards	Related questions
1	A clinician's reasons for initiating valproate treatment (i.e. target symptoms or behaviour) should be documented in the clinical records.	19a & 19b
2	If valproate is being prescribed 'off-label', it should be documented that this has been explained to the patient.	22 & 23
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).	21
4	Review within the first three months of valproate treatment should include: screening for the common side effects of the medication (e.g. weight gain, nausea, and tremor) and assessment of the response of the target symptoms/behaviour.	24, 25a & 25b
5	Patients prescribed continuing valproate treatment should have an annual review of the risk-benefit balance. This should include assessment of therapeutic benefit, adverse effects and medication adherence.	26 & 27
6	If valproate is prescribed for a woman of child-bearing age, there should be documented evidence that the conditions of 'prevent', the pregnancy prevention programme, are fulfilled.	30 to 38

Treatment Target	Related questions
Plasma level monitoring of valproate treatment should not be used unless there is evidence of ineffectiveness, concerns about medication adherence, or dose-related side-effects.	28 & 29

References

The practice standards and treatment target were derived from the following:

- *Use of licensed medicines for unlicensed applications in psychiatric practice* 2nd ed. College Report CR210, Royal College of Psychiatrists Psychopharmacology Committee https://www.rcpsych.ac.uk/improving-care/campaigning-for-better-mental-health-policy/college-reports/2017-college-reports/use-of-licensed-medicines-for-unlicensed-applications-in-psychiatric-practice-2nd-edition-cr210-dec-2017
- *Information on the risks of valproate use in girls (of any age) and women of childbearing potential*, Guide for Healthcare Professionals, MHRA, prevent, valproate pregnancy programme, https://www.medicines.org.uk/emc/rmm/1203/Document
  https://www.gov.uk/guidance/valproate-use-by-women-and-girls

Data collection

In accordance with the General Data Protection Regulation (GDPR) we have updated our privacy notice, which provides full details on how we use your data and the data submitted as part of a national clinical audit, along with our legal basis for doing so. Our privacy notice can be found online via the following link:

https://www.rcpsych.ac.uk/about-us/legal/data-protection/pomh-privacy-notice

This privacy notice is provided in addition to POMH-UK's data control statement.

The data collected by POMH-UK are pseudonymous. Please ensure that the data submitted are limited to data specifically requested by this tool and you do **not** supply any personally identifiable data, such as a service user's **name**, **full date of birth** or **NHS number**.

If you have any queries concerning the collection and use of personal data, please contact:

Gavin Herrington, Programme Manager Gavin.herrington@rcpsych.ac.uk

Trust and team information

Q1. Trust identifier
Your Trust identifier is a 3-digit code (e.g. 044)

N	N	N

Q2. Team identifier
Your team codes are known only to your Trust. The POMH-UK team does not know your team code.

N	N	N

Q3. Optional additional identifier
This field gives your Trust the option of identifying data by site, directorate, lead consultant, or any other relevant variable you wish. Your Trust can decide whether or not to use this field.
Enter any assigned numerical code 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.

Q4. 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.

A	A	A

Patient information (complete for ALL patients)

Q5. 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.

N	N	N	N

Q6. Patient's year of birth (YYYY e.g. 1988)

☐ *Patient was born in or before 1967, please enter year of birth:* | Y | Y | Y | Y |

☐ *Patient was born after 1967, please enter year of birth:* | Y | Y | Y | Y |

Q7. Patient's sex *(as recorded in the clinical records)*

☐ *Male* ☐ *Female*

Q8. Patient's ethnicity *(as recorded in the clinical records) (These are the standard NHS ethnic categories currently in use)*

☐ *Asian/Asian British (includes any Asian background e.g. Bangladeshi, Chinese, Indian, Pakistani)*

☐ *White British/Irish (includes any White background)*

☐ *Mixed or multiple ethnic groups (includes any mixed background)*

☐ *Black African, Black British or Caribbean (includes any Black background)*

☐ *Another ethnic group (includes any other ethnic group, e.g. Arab)*

☐ *Unknown/Not documented*

Q9. Patient's current clinical psychiatric diagnoses (ICD-10 categories provided for guidance):

(Please tick all that apply)

F00–F09 Organic, including symptomatic, mental disorders

- ☐ *Neurocognitive problems as a consequence of head injury*
- ☐ *Other organic symptomatic mental disorder (F00-F09)*

F10–F19 Mental and behavioural disorders due to psychoactive substance use

- ☐ *Alcohol (F10)*
- ☐ *Opioids including methadone (F11)*
- ☐ *Cannabis (F12)*
- ☐ *Cocaine (F14)*
- ☐ *Benzodiazepines*
- ☐ *Gabapentinoids (pregabalin, gabapentin)*
- ☐ *Novel psychoactive substance (F19)*
- ☐ *Mental and behavioural disorder due to use of other psychoactive substance (F10-19, Substance not listed above or unknown)*

F20–F29

- ☐ *Schizophrenia, schizotypal, delusional disorders and other non-mood psychotic disorders (F20-29)*

F30–F39 Mood (affective) disorders

- ☐ *Bipolar affective disorder (F31)*
- ☐ *Other affective disorder (F30-39, excluding bipolar disorder)*

F40–F48

- ☐ *Anxiety, dissociative, stress-related, somatoform and other nonpsychotic mental disorders (F40-48)*

F50–F59

- ☐ *Behavioural syndrome associated with physiological disturbance and physical factors (F50-F59)*

F60–F69 Disorders of adult personality and behaviour

- ☐ *Paranoid personality disorder (F60.0)*
- ☐ *Dissocial personality disorder (F60.2)*
- ☐ *Emotionally unstable personality disorder (F60.3)*
- ☐ *Other personality disorder (F60-69, not listed above)*

F70–F79

- ☐ *Intellectual disabilities (F70-79)*

F80–F89

- ☐ *Disorders of psychological development (F80-89)*

F90–F98 Behavioural and emotional disorders with onset occurring in early childhood and adolescence

- ☐ *Attention-deficit hyperactivity disorder (F90)*
- ☐ *Other behavioural and emotional disorders (F91-98)*

F99

- ☐ *Unspecified mental disorder (F99)*

- ☐ ***None of the above diagnoses documented***
- ☐ ***Not known/unclear***

Q10. Which service/clinical team is currently responsible for this patient's care?

*(Tick **one** box only, see guidance notes for further information)*

General adult services	**Forensic psychiatric services**
☐ *Adult acute psychiatric ward*	☐ *Forensic psychiatric ward*
☐ *Community mental health team (includes home treatment and crisis intervention team)*	☐ *Forensic community mental health team*
☐ *Inpatient rehabilitation services*	☐ *Prison psychiatric team*

☐ *Other - please specify:* _____

Patient's current Mental Health Act status

If the patient is currently in hospital answer **Q11a**, if living in the community answer **Q11b**, and if in prison, **Q11c**.

Q11a. If the patient is currently in hospital, select the option that applies *(Tick **one** box only)*

- ☐ *The patient is informal (not detained under the Mental Health Act)*
- ☐ *The patient is detained in hospital under the MHA and a T2 (patient consents to valproate treatment) or equivalent outside England is in place*
- ☐ *The patient is detained in hospital under the MHA and a T3 (a SOAD has consented to valproate treatment on behalf of the patient) or equivalent outside England is in place*
- ☐ *The patient is detained in hospital and valproate is currently administered under Section 62*
- ☐ *The patient is detained in hospital under the MHA and consent to treatment legislation is not yet applicable or does not apply in this case (e.g. valproate prescribed for epilepsy)*
- ☐ *Other - please specify:* _____

11b. If the patient is currently living in the community (including supported accommodation), select the option that applies *(Tick **one** box only)*

- ☐ *A Community Treatment Order (CTO) or equivalent outside England is in place*
- ☐ *Section 41 conditional discharge or equivalent outside England*
- ☐ *The patient is not subject to either of the above*

11c. If the patient is currently in prison, please tick the box below

- ☐ *Patient is in prison*

Psychotropic medication (other than valproate) regularly prescribed

It may be helpful to involve a doctor and/or pharmacist when completing this set of questions

Q12. Please indicate below, any <u>antidepressant</u> medications that are currently regularly prescribed for this patient
(Please tick all that apply)

- ☐ *Agomelatine*
- ☐ *Amitriptyline*
- ☐ *Bupropion*
- ☐ *Citalopram*
- ☐ *Clomipramine*
- ☐ *Dosulepin*
- ☐ *Doxepin*
- ☐ *Duloxetine*
- ☐ *Escitalopram*
- ☐ *Fluoxetine*
- ☐ *Fluvoxamine*
- ☐ *Imipramine*
- ☐ *Isocarboxazid*
- ☐ *Lofepramine*
- ☐ *Mianserin*
- ☐ *Mirtazapine*
- ☐ *Moclobemide*
- ☐ *Nortriptyline*
- ☐ *Paroxetine*
- ☐ *Phenelzine*
- ☐ *Reboxetine*
- ☐ *Sertraline*
- ☐ *Tranylcypromine*
- ☐ *Trazodone*
- ☐ *Trimipramine*
- ☐ *Venlafaxine*
- ☐ *Vortioxetine*
- ☐ ***None of the above is currently regularly prescribed***
- ☐ ***Not documented/unclear***

Q13. Please indicate which of the following <u>oral</u> antipsychotic medications this patient is currently regularly prescribed *(Please tick all that apply)*

- ☐ *Amisulpride*
- ☐ *Aripiprazole*
- ☐ *Asenapine*
- ☐ *Cariprazine*
- ☐ *Chlorpromazine*
- ☐ *Clozapine*
- ☐ *Other antipsychotic medication, please specify:*
- ☐ *Flupentixol*
- ☐ *Haloperidol*
- ☐ *Lurasidone*
- ☐ *Olanzapine*
- ☐ *Paliperidone*
- ☐ *Perphenazine*
- ☐ *Promazine*
- ☐ *Quetiapine*
- ☐ *Risperidone*
- ☐ *Sulpiride*
- ☐ *Trifluoperazine*
- ☐ *Zuclopenthixol*
- ☐ ***No oral antipsychotic medication is currently regularly prescibed***
- ☐ ***Not documented/unclear***

Q14. Please indicate below, whether any <u>depot/LAI antipsychotic</u> medication is currently regularly prescribed for this patient *(Please tick all that apply)*

- ☐ *Aripiprazole*
- ☐ *Flupentixol decanoate*
- ☐ *Fluphenazine decanoate*
- ☐ *Haloperidol decanoate*
- ☐ *Other depot/LAI antipsychotic medication, please specify:*
- ☐ *Olanzapine*
- ☐ *Paliperidone*
- ☐ *Risperidone*
- ☐ *Zuclopenthixol decanoate*
- ☐ ***No depot/LAI antipsychotic medication is currently regularly prescribed***

Q15. Please indicate below, whether any other psychotropic medicines are currently regularly prescribed for this patient

(Please tick all that apply)

- ☐ *One or more benzodiazepine*
- ☐ *Lamotrigine*
- ☐ *Lithium*
- ☐ *Pregabalin*
- ☐ *Gabapentin*
- ☐ *None of the above medicines are currently regularly prescribed*
- ☐ *Other - please specify:*

Details of valproate medication prescribed

Q16. Which preparation of valproate is prescribed?

Ask a pharmacist or a doctor if you are not sure

*(Tick **one** box only)*

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

Q17. How many times a day is valproate prescribed to be taken or administered?

- ☐ *Once*
- ☐ *Twice*
- ☐ *Three times*
- ☐ *Four or more times*

Q18. Please give the current total daily dose of valproate (in mg/day) ☐☐☐☐ mg

Q19a. What are the clinical reasons/indications/target symptoms for valproate treatment?

Ask the clinical team if this is not clear from the clinical records

(Please tick all acute and prophylactic reasons that apply)

- ☐ *To treat an acute episode of mania/hypomania*
- ☐ *To treat an acute episode of bipolar depression*
- ☐ *To treat an acute, mixed affective state*
- ☐ *To treat rapid-cycling bipolar disorder*
- ☐ *To prevent manic/hypomanic relapse of bipolar disorder*
- ☐ *To prevent depressive relapse of bipolar disorder*

- ☐ *To treat mood/affective symptoms in schizophrenia/schizoaffective disorder*
- ☐ *Adjunctive therapy (i.e. added to antipsychotic medication) for refractory schizophrenia*
- ☐ *Prevention of clozapine-related seizures*

- ☐ *To treat emotional instability*
- ☐ *To reduce suicidality*
- ☐ *To reduce persistent aggression/hostile behaviour*
- ☐ *To reduce impulsivity/poor-impulse control*
- ☐ *To reduce deliberate self-harming behaviour*

- ☐ *To treat agitation/anxiety*
- ☐ *To treat epilepsy (see also Q22)*
- ☐ *To treat or prevent migraine (see also Q22)*
- ☐ *Patient preference/request*
- ☐ *Other clinical reason - please specify:*

- ☐ *Continuation of long-standing valproate prescription: the reason for prescribing is not documented/not known **(go to Q20)***
- ☐ *Unclear why valproate has been prescribed **(go to Q20)***

19b. Are the clinical reasons selected in Q19a documented in the clinical records?

- ☐ *Yes*
- ☐ *No*

Q20. How long has this patient been treated with valproate?

- ☐ *Less than 6 months ago* ***(go to Q21)***
- ☐ *6-12 months ago* ***(go to Q21)***
- ☐ *1 to 5 years* ***(go to Q26)***
- ☐ *More than 5 years* ***(go to Q26)***
- ☐ *Not documented/unknown* ***(go to Q26)***

All patients treated with valproate for less than a year

Pre-treatment screening, off-label use and early on-treatment review

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?

(See guidance notes)

	Yes, fully or partially documented results	No documented results
Full blood count	☐	☐
Liver function test (LFTs)	☐	☐
Body weight and or BMI	☐	☐
Plasma glucose or HbA1c	☐	☐
Plasma lipids	☐	☐
Blood pressure	☐	☐

Q22. Is the patient prescribed valproate medication for epilepsy, an episode of mania, relapse prevention in bipolar disorder or migraine?

- ☐ *Yes, valproate was prescribed for epilepsy (see also Q19). This is a licensed indication.* ***(go to Q24)***
- ☐ *Yes, valproate was prescribed for bipolar disorder (for example, treatment of mania or relapse prevention are licensed indications) (see also Q9)* ***(go to Q24)***
- ☐ *Yes, valproate was prescribed for migraine (see also Q19). This is a licensed indication* ***(go to Q24)***
- ☐ *No, valproate was not prescribed for any of the reasons above. Thus, it is prescribed outside the licensed indications (i.e. 'off-label' prescribing)* ***(go to Q23)***

Q23. Is it documented in the clinical records that it was explained to the patient that this was an 'off-label' prescription?

*(Tick **one** box only)*

- ☐ *It is documented in the clinical records that the patient was informed that this is an 'off-label' prescription*
- ☐ *There is no documented evidence that the patient was informed that the valproate prescription was 'off-label'*

Q24. Was a review of valproate medication conducted within three months of starting?

- ☐ *Not applicable as the patient has not yet been treated with valproate for three months* ***(go to Q30)***
- ☐ *There is no documented review of valproate treatment within three months of initiation* ***(go to Q30)***
- ☐ *Yes, there is a documented review of valproate treatment within three months of initiation* ***(go to Q25a)***

Q25a. Is there documented evidence that any of the following were addressed at the early on-treatment review?
(Please tick all that apply)

- ☐ *Therapeutic benefit/response of target symptoms*
- ☐ *Adherence to medication*
- ☐ *Review of side effects of valproate (such as sedation, weight gain, nausea and tremor)*
- ☐ *None of the above*

25b. Discretionary tests that may be carried out, depending on clinical assessment, are listed below. Were the results of any of these tests documented in the clinical records within the first 3 months of starting valproate treatment?
(Please tick all that apply)

- ☐ *Body weight and or BMI*
- ☐ *Liver function tests (LFTs)*
- ☐ *Full blood count (FBC)*
- ☐ *Plasma glucose or HbA1c*
- ☐ *Plasma lipids*
- ☐ *None of the above*

Please go to Q30

All patients treated with valproate for more than a year
Monitoring

Q26. Is there documentation of at least one review of this patient's valproate medication in the past year?

- ☐ *Yes* ***(go to Q27)***
- ☐ *No* ***(go to Q30)***

Q27. If the answer to Q26 was 'yes', is there documented evidence that any of the following were assessed at the review? *(Please tick all that apply)*

- ☐ *Therapeutic benefit/response*
- ☐ *Side effects of valproate treatment*
- ☐ *Medication adherence*
- ☐ *Body weight and/or BMI*
- ☐ *Liver function tests (LFTs)*
- ☐ *Full blood count (FBC)*
- ☐ *Blood pressure*
- ☐ *Plasma glucose or HbA1c*
- ☐ *Plasma lipids*
- ☐ *None of the above*

Q28. Has this patient's plasma valproate concentration been measured in the past year?

- ☐ *No* ***(go to Q30)***
- ☐ *Yes - please provide the plasma level result (mg/L or micrograms/ml):* N N N
- ☐ *Yes – but no plasma level result documented in the clinical records*

Q29. If the answer to Q28 was 'yes', what was the documented reason for measuring the most recent plasma valproate level? *(Please tick all that apply)*

- ☐ *Lack of response to valproate treatment*
- ☐ *Concerns about medication adherence*
- ☐ *Suspected dose-related side-effects/tolerability problem/suspected toxicity*
- ☐ *Routine monitoring*
- ☐ *Other clinical reason:* ____
- ☐ *Reason unclear*

Q30. Is this patient a female born after 1967? (see Questions 6 and 7)

☐ *No* ***(go to end and submit data)***

☐ *Yes* ***(go to Q31)***

Females born after 1967

Q31. Is there documented evidence in the clinical records that pregnancy is not biologically possible for this female?

☐ *Yes, it is recorded that this female has had a surgical sterilisation (e.g. ligation of the fallopian tubes).* ***(Go to the end of this form and finish)***

☐ *Yes, it is recorded that this female has had surgical removal of the uterus (hysterectomy, for whatever reason):* ***(Go to the end of this form and finish)***

☐ *Yes, it is recorded that this female has had surgical removal of the ovaries (oophorectomy, for whatever reason):* ***(Go to the end of this form and finish)***

☐ *Yes, it is recorded that this female is post-menopausal:* ***(Go to the end of this form and finish)***

☐ *No, there is no documented evidence that pregnancy is not biologically possible in this female* ***(go to Q32)***

Q32. Is there a completed Annual Risk Acknowledgment form (MHRA 'prevent' pregnancy prevention programme) in this patient's clinical records?

☐ *Yes, date of completion of the form is in the past year* ***(go to Q34a)***

☐ *Yes, but dated more than a year ago* ***(go to Q33)***

☐ *No* ***(go to Q33)***

Q33. Is there documentation in the clinical records (and/or on a Risk Acknowledgement form that was completed more than a year ago) of the reason(s) that this patient did not need to be on the 'prevent', pregnancy prevention programme?

☐ *No reasons documented for the pregnancy prevention programme being inapplicable* ***(go to end of data collection form and submit data)***

☐ *Yes, the reasons for the pregnancy prevention programme being inapplicable were documented* ***(please specify then go to end of data collection form and submit data)***

Questions 34a-d: Please indicate whether the following boxes on the Annual Risk Acknowledgement form have been ticked (or equivalent electronic verification) for Step 1 (*Decide if the patient needs to be on 'prevent' – the valproate pregnancy prevention programme*):

Q34a. 'Patient has not yet reached menarche (i.e. has not yet had their first menstrual period) and a date for annual review has been set'

☐ *Box for statement above not ticked*

☐ *Box ticked but no future date entered*

☐ *Box ticked and future date entered*

Q34b. 'The absence of pregnancy risk is permanent for the following reasons:'

☐ *Box for statement above not ticked*

☐ *Box ticked but no reason(s) provided*

☐ *Box ticked and reason(s) provided**

**Please provide written details below*

Q34c. 'I consider that sexual activity that could lead to pregnancy would not occur before the next annual review because...'

☐ *Box for statement above not ticked*

☐ *Box ticked but no reason(s) provided*

☐ *Box ticked and reason(s) provided**

**Please provide written details below*

Q34d. 'I have given the patient or responsible person a copy of the Patient Guide'

☐ *Box for statement above not ticked*

☐ *Box ticked*

Q35. Has the Step 1 page been signed (or electronic equivalent) by the patient or their responsible person?

☐ *Yes*

☐ *No*

Please indicate whether the initials of the specialist/clinician (or equivalent electronic verification) have been entered in Step 2 (*'prevent' applies to this patient- a female of childbearing potential and at risk of pregnancy*) of the Annual Risk Acknowledgement form, for the following:

Q36a. *'I confirm that the patient needs valproate because:'*	Box on form initialled	Box on form **not** initialled
Her condition does not respond adequately to other treatments	☐	☐
She does not tolerate other treatments	☐	☐
She is undergoing a treatment change from valproate	☐	☐

'I confirm I have discussed the following with the patient:'	Box on form initialled	Box on form **not** initialled
Q36b. *Valproate must not be used during pregnancy (except in rare situations in epilepsy for patients who are resistant or intolerant to other treatments)*	☐	☐
Q36c. *The overall risks in children exposed to valproate during pregnancy are:* - *An approximately 10% chance of birth defects* - *A 30% to 40% chance of a wide range of early developmental problems that can lead to learning disabilities.*	☐	☐
Q36d. *The conditions of the pregnancy prevention programme must be fulfilled*	☐	☐
Q36e. *The need for regular (at least annual) review of the need to continue valproate treatment by a specialist*	☐	☐
Q36f. *The need for effective contraception, without interruption, throughout treatment with valproate*	☐	☐
Q36g. *The need to arrange an appointment with her specialist as soon as she is planning pregnancy to ensure timely discussion, and a timely switch to an alternative treatment before stopping contraception and conception occurring.*	☐	☐
Q36h. *The need to contact her GP immediately for an urgent review of her treatment in case of suspected or inadvertent pregnancy.*	☐	☐
Q36i. *The need for a negative (ideally serum) pregnancy test result at start and if needed thereafter*	☐	☐
Q36j. *I confirm I have given the patient or responsible person a copy of the Patient Guide*	☐	☐

'In case of pregnancy, I confirm that:'	Box on form initialled	Box on form **not** initialled
Q36k. *We have discussed options for switching treatment*	☐	☐
Q36l. *She is fully aware of the risks of pregnancy, and has had the opportunity for counselling about the risks*	☐	☐
Q36m. *I have given the patient or responsible person a copy of the Patient Guide*	☐	☐

Please indicate whether the Step 3 of the Risk Acknowledgement form has been completed (*Your patient or their responsible person needs to complete this section to confirm they understand the risks of valproate in pregnancy*):

'I have discussed the following with my specialist and I understand:'	Box on form initialled	Box on form **not** initialled
Q37a. *Why I need valproate rather than another medicine*	☐	☐
Q37b. *That I should visit a specialist regularly (at least once a year) to review whether valproate remains the best option for me*	☐	☐
Q37c. *The risks in children whose mothers took valproate during pregnancy are:* - *1 out of 10 children will have physical birth defects* - *3 to 4 out of 10 children will have early developmental problems that can lead to significant learning disabilities*	☐	☐
Q37d. *That I have had a pregnancy test (if advised by my doctor/specialist)*	☐	☐
Q37e. *Why I must use effective contraception, without stopping or interruption, at all times while taking valproate*	☐	☐
Q37f. *The options for effective long-term contraception (or a consultation has been planned with a professional who can give me advice)*	☐	☐
Q37g. *The need to consult my specialist or GP as soon as I start thinking about becoming pregnant. This is to make sure I have time to switch to another treatment before I come off contraception*	☐	☐
Q37h. *That I should request an urgent GP appointment if I think I am pregnant*	☐	☐
Q37i. *I have been given a copy of the Valproate Patient Guide and know where to find more information*	☐	☐

'In case of pregnancy, I confirm that:'	Box on form initialled	Box on form **not** initialled
Q37j. *Options for switching treatment have been considered*	☐	☐
Q37k. *I am fully aware of the risks and have had the opportunity to have counselling about the risks*	☐	☐

Q38. Has the Step 3 page of the Annual Risk Acknowledgement form been signed (or electronic equivalent) by the patient or their responsible person?

☐ *Yes*

☐ *No*

END

Finish and submit data

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

4pm, 30 November 2022

If you realise that you have made a mistake submitting the data on this form online, 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

Q10. Which service/clinical team is currently responsible for this patient's care?

This should be the service/clinical team that is responsible for care on the day the audit data are collected.

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?

'Partially documented results' refers to documentation that a test has been done and the results received and interpreted by a clinician (for example, 'plasma glucose normal') but the actual result is not documented.

Appendix F: POMH team and acknowledgments

POMH central team

Professor Thomas Barnes, Professor Emeritus, Imperial College London: Joint-Head POMH

Carol Paton, Honorary Research Fellow Imperial College London: Joint-Head POMH

Gavin Herrington: Programme Manager

Olivia Rendora: Deputy Programme Manager

Sylvia Ly: Project Officer

Gaia Bove: Project Officer

Expert advisers for this QI programme

Professor Leslie Citrome, Department of Psychiatry & Behavioral Sciences, New York Medical College, New York, USA.

Dr Emilio Fernandez-Egea, Department of Psychiatry and Behavioural and Clinical Neuroscience Institute, University of Cambridge, Cambridge, UK; Cambridgeshire and Peterborough NHS Foundation Trust, Cambridge, UK.

Acknowledgements

Thanks are due to all the clinical and clinical audit staff in the participating Trusts/healthcare organisations who took part in the collection and submission of the audit data.

Appendix G: References

Baldwin DS, Kosky N. Off-label prescribing in psychiatric practice. Adv Psych Treat 2007;13:414-422.

Baldwin D & Wieck A. Withdrawal of, and alternatives to, valproate-containing medicines in girls and women of childbearing potential who have a psychiatric illness. Position Statement PS04/18. Royal College of Psychiatrists 2018. https://www.bap.org.uk/pdfs/PS04-18-December2018.pdf

Barnes TRE, Haddad PM. Working with People with Mental Health Difficulties to Improve Adherence to Medication. In, The Wiley Handbook of Healthcare Treatment Engagement: Theory, Research, and Clinical Practice. Eds., Andrew Hadler, Stephen Sutton, Lars Osterberg. Wiley Online Library, 2020.

Fisher C & Broderick W. Sodium valproate or valproate semisodium: is there a difference in the treatment of bipolar disorder? Psychiatric Bulletin 2003,27;446-8.

General Medical Council. Good practice in prescribing and managing medicines and devices. 2013.

Medicines and Healthcare Products Regulatory Agency. Drug Safety Update 2022,16:5 https://www.gov.uk/drug-safety-update/valproate-reminder-of-current-pregnancy-prevention-programme-requirements-information-on-new-safety-measures-to-be-introduced-in-the-coming-months

National Institute for Health and Care Excellence. Borderline Personality Disorder: recognition and management. Clinical Guideline CG78. NICE, 2009. https://www.nice.org.uk/guidance/cg78

National Institute for Health and Care Excellence. Antisocial Personality Disorder: prevention and management. Clinical Guideline CG77. NICE, 2009. Updated 2013. https://www.nice.org.uk/guidance/cg77

Paton C, Crawford MJ, Bhatti SF et al. The use of psychotropic medication in patients with emotionally unstable personality disorder under the care of UK mental health services. Journal of Clinical Psychiatry 2015, 76:e512-8.

Paton C, Citrome L, Fernandez-Egea E et al. Who is prescribed valproate and how carefully is this treatment reviewed in UK mental health services. Therapeutic Advances in Psychopharmacology 2022,12;1-15

Royal College of Psychiatrists. Use of licensed medicines for unlicensed applications in psychiatric practice. Dec 2017. College Report 2nd edition. CR210.

Sharma AN, Arango C, Coghill D, et al. BAP Position Statement: Off-label prescribing of psychotropic medication to children and adolescents. J Psychopharm 2016;30:416-421

Appendix H: Background information on off-label prescribing

Off-label prescribing

Independent prescribers can prescribe any medication, whether it is licensed, off-label (outside the parameters of the marketing authorisation) or unlicensed; it is the responsibility of the prescriber to ensure that such prescriptions are supported by evidence of benefit and/or a reasonable body of medical opinion. The prescriber should also monitor the effectiveness of any medication they prescribe off-label at least as closely as they would licensed treatments, if not more so. If a prescription is off-label, there is no legal requirement to tell the patient, although such a disclosure is strongly advocated (GMC 2013, Royal College of Psychiatrists 2017). It is generally recommended that a patient should be provided with sufficient information to enable informed consent to any treatment, including an explanation of the off-label nature of any prescription (GMC 2013, Baldwin & Kosky 2007, Sharma et al 2016, Royal College of Psychiatrists 2017). There are good clinical reasons for such a recommendation. Patents may well become aware over time that their medication is being used outside the licensed indications. For example, the information in the package insert will refer only to the use of the medication for its licensed indications, which will be conditions that the patient does not have (the package insert for sodium valproate refers only to its use for the treatment of epilepsy). This realisation may be, at best, confusing for patients and, at worst, cause them to lose trust and confidence in their prescriber. Further, it has long been known that those patients who feel that information about their medication has not been adequately shared with them may be less likely to adhere to their medication regimen (Barnes & Haddad, 2020).

Licensed indications of available valproate preparations

Valproate is available as three different formulations: sodium valproate and valproic acid, both of which are licensed only for the treatment of epilepsy, and a combination of sodium valproate with valproic acid (semi-sodium valproate), which is licensed for both the treatment of manic episodes in bipolar disorder when lithium is contraindicated or not tolerated and the continuation of treatment after a manic episode which has responded to this preparation. It should be noted that the 'active' component of all three formulations is the valproate ion (Fisher & Broderick, 2003). There are no RCTs of sodium valproate in bipolar disorder nor of semi-sodium valproate in epilepsy, so the efficacy and tolerability of these preparations have not been directly compared, although differences would seem unlikely given that the active moiety is the same in all three preparations.

Preparation of valproate prescribed

For the purpose of reporting on off-label use in this QI programme, we took a pragmatic view; the licensed indications of semi-sodium valproate were used and we did not distinguished between valproate formulations.

RC PSYCH
ROYAL COLLEGE OF PSYCHIATRISTS

POMH
PRESCRIBING OBSERVATORY FOR MENTAL HEALTH

POMH

The Royal College of Psychiatrists
21 Prescot Street
London
E1 8BB

RC PSYCH
ROYAL COLLEGE OF PSYCHIATRISTS

CCQI
COLLEGE CENTRE FOR QUALITY IMPROVEMENT