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Branford, David; Sun, James J.; Shankar, Rohit

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## Analysis

# Antiseizure medications prescribing for behavioural and psychiatric concerns in adults with an intellectual disability living in England

David Branford, James J. Sun and Rohit Shankar

## Summary

Antiseizure medications (ASMs) are the second most widely prescribed psychotropic for people with intellectual disabilities in England. Multiple psychotropic prescribing is prevalent in almost half of people with intellectual disabilities on ASMs. This analysis identifies limited evidence of ASM benefit in challenging behaviour management and suggests improvements needed to inform clinical practice.

## Keywords

Epilepsy; challenging behaviour; psychiatric conditions; neuro-developmental; learning disabilities.

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Previously known as anticonvulsants and antiepileptics, antiseizure medications (ASMs) have diverse mechanisms of action. In addition to their value in the treatment of seizures they are prescribed for several psychiatric and neurological conditions.<sup>1</sup>

Most early studies of ASM prescribing in people with intellectual disabilities (PwID; intellectual disabilities are also known as learning disabilities in UK health services) were based on data from institutional cohorts of patients or from specialised epilepsy clinics. They typically have reported 20–30% of the PwID population receiving ASMs. Taken that the most comprehensive systematic review of prevalence studies of epilepsy in PwID estimated it to be between 20% and 25%<sup>2</sup> it is usually assumed that a history of epilepsy is the primary prescribing reason. However, the reasons for ASM prescribing may be more complex. It may be a legacy of seizures experienced in childhood,<sup>3</sup> it may be a psychiatric reason as it is known that some ASMs are psychotropic agents, or it may be to manage challenging behaviours. ASMs are regularly used in a range of psychiatric conditions, with most use being off label.<sup>4</sup> The principal psychiatric conditions to benefit from ASMs, particularly valproate, are bipolar disorder, recurrent aggression and anxiety-related disorders.<sup>5</sup> For some patients, the indication may no longer be clear.<sup>3,6</sup>

The lifetime risk of psychiatric disorders in PwID appears to be considerably higher than in people without intellectual disabilities.<sup>7</sup> The prevalence of bipolar disorder in PwID is at least two times higher than that in the general population.<sup>8</sup> Interestingly, there is no definitive evidence to suggest that epilepsy is associated with increased prevalence of psychiatric disorders in PwID.<sup>9</sup> There is, however, suggestive evidence of ASMs, in the context of high medication burden, causing behavioural distress in PwID and epilepsy, especially older adults.<sup>10</sup>

This paper focuses on the prescribing of ASMs for behavioural and psychiatric indications in PwID. It presents an analysis based on a rapid review of recent published literature about ASM use in PwID for non-seizure management and the available NHS Digital data on national prescribing patterns in England. This analysis does not consider other neurodevelopmental conditions such as autism spectrum disorder or attention-deficit hyperactive disorder, although both conditions are recognised to be significantly comorbid with both intellectual disabilities and epilepsy.

has continued to rise.<sup>11–13</sup> A 2019 Public Health England (PHE) report showed that between 2010 and the end of 2017 the proportion of PwID prescribed an ASM with a recorded recognised indication of epilepsy had fallen from 84.9% to 79.6%.<sup>11</sup> NHS Digital data shows the proportion receiving ASMs continues to rise with age for both those with a history of epilepsy and those without.<sup>12</sup>

Table 1 details 2020–2021 data from NHS Digital of the rate of ASM prescribing for PwID, both for those with epilepsy and those without. For both, the proportion of PwID receiving ASMs continues to rise throughout the age bands.<sup>12</sup> Unfortunately, the NHS Digital data does not indicate the numbers with both epilepsy and mental health conditions.<sup>12</sup>

Multiple ASM use is also seen to increase with age, with a figure of 27.9% in children and young people and 43.3% in adults.<sup>10</sup> A PHE study in 2015 found there was no consistent gender difference in the use of ASMs and that most prescribing (almost 100%) was long term.<sup>13</sup>

## Co-prescribing of ASMs with other psychotropic medications

Data from the 2019 PHE report suggest nearly half of PwID on ASMs are prescribed them in combination with other psychotropic medications (males 46.5%; 95% CI 48.6–44.4; and females 48.8%; 95% CI 51.1–46.4).<sup>11</sup>

Antipsychotic co-prescribing was noted in just over a quarter of females (25.2%; 95% CI 23–27.6) and males (28.5%; 95% CI 26.5–30.7). Approximately a fifth – males 19.8% (95% CI 18–21.7) and females 21.2% (95% CI 19.1–23.4) – were co-prescribed anxiolytics. Nearly a quarter of females were on co-prescribed antidepressants (23.3%; 95% CI 21.2–25.6) compared with approximately one in six males (15.8%; 95% CI 14.1–17.5). Antihypnotic co-prescribing was 6.2% (95% CI 5.1–7.6) in females and 5.7% (95% CI 4.7–6.9) in males.

There is no clear explanation of the high level of co-prescribing with ASMs, however, it is possible that when faced with a prescribing decision for mania or behavioural problems a history of epilepsy may steer the prescriber towards ASMs rather than antipsychotics or antidepressants. Alternatively, ASMs might be used in addition, as some antidepressants and antipsychotics can carry a risk of lowering the seizure threshold.

## Data on the prevalence of ASMs in PwID in England

Recent studies estimate that between one-third and one-fifth of PwID are prescribed ASMs and the percentage of PwID prescribed ASMs

## How complete are the data?

Most studies of ASM use in PwID are based on data generated by general practice prescribing systems. In January 2021 NHS Digital

**Table 1** The age-related rate of antiseizure medication (ASM) prescribing for people with intellectual disability and epilepsy and those with intellectual disability but no epilepsy

Age, years	On ASMs but no epilepsy	% with intellectual disability	On ASMs with epilepsy	% with intellectual disability	Total on ASMs	% with intellectual disability
0 to 9	134	1.37	595	6.10	729	7.48
10 to 17	337	1.64	2040	9.93	2377	11.57
18 to 24	785	3.02	3462	13.33	4247	16.36
25 to 34	1492	4.22	5978	16.91	7470	21.13
35 to 44	1323	5.72	4653	20.10	5976	25.82
45 to 54	1538	7.04	4694	21.49	6232	28.53
55 to 64	1731	8.49	4435	21.75	6166	30.24
65 to 74	793	7.91	1968	19.63	2761	27.54
≥75	287	7.40	522	13.47	809	20.87

Adapted data from NHS Digital.<sup>12</sup>

published data on several aspects of psychotropic and ASM prescribing by general practices for people identified as having intellectual disability along with comparison data for the rest of the registered population.<sup>12</sup> The data are on a large scale and document the years 2015–16 to 2019–20. They were collected as an addition to the data-set called ‘The Health and Care of People with Learning Disabilities’ that was introduced to support ‘Stopping Over-Medication of People with a Learning Disability, Autism or Both’ (STOMP).<sup>12</sup> Unfortunately, this does not give a full picture for England as the data collection process is not supported by one of the large commercial companies providing notes systems for general practice. The solution for bringing together a large single data-set has technical and financial challenges. The overall proportion of patients registered with general practitioners who were included varied over the 5 years from 56.2% to 60.3%. Coverage varied greatly between the current seven NHS regions, ranging from 19.5% to 87.8% in the most recent year, with coverage highest in the North-West, London and the South-East, and lowest in the East of England, the North-East and Yorkshire. There was similarly wide variation between clinical commissioning groups within regions. This means that the total figures quoted do not reflect England proportionately and have a regional bias. The measures used all reflect an end of year (31 March) position.

### The behavioural effects of ASMs

Both positive and negative behavioural effects may be experienced by people with or without epilepsy when taking ASMs.<sup>6</sup> In general, sedating ASMs, such as sodium valproate and carbamazepine, possess anxiolytic, antimanic and sleep-promoting benefits but may cause fatigue, impaired attention and mood problems specifically, depression. Activating ASMs, such as felbamate and lamotrigine, may possess antidepressant and attention-enhancing efficacy but may cause anxiety, insomnia and agitation.

A retrospective, cohort study of 246 PwID and epilepsy at the long-stay department of an epilepsy centre in the Netherlands found a statistically significant lower use of antidepressants when prescribed lamotrigine for epilepsy.<sup>14</sup> They also found significantly less prescriptions of anxiolytics in patients using ASMs with mood-stabilising properties (carbamazepine, valproic acid and lamotrigine).

A study comparing the psychiatric and behavioural side-effects profile of older and newer ASMs in a large specialty practice-based sample of patients diagnosed with epilepsy found that psychiatric and behavioural side-effects occurred in 17.2% of patients and led to lack of tolerance in 13.8% of patients.<sup>15</sup> However, this study was not specific to PwID.

### Association between epilepsy and challenging behaviour in PwID

A 2021 study tried to identify whether there is an association between epilepsy and challenging behaviour in PwID by carrying out a systematic review of published data.<sup>9</sup> They showed no significant association between epilepsy and challenging behaviour. However, the authors warned that the findings were contradictory and must be interpreted with caution because of the difficulty in pooling data from varied studies, which is likely to introduce confounding. Where significant differences were found, effect sizes are small and may not be clinically significant, and there are major methodological flaws in the included studies, which should be addressed in future large-scale properly controlled studies.

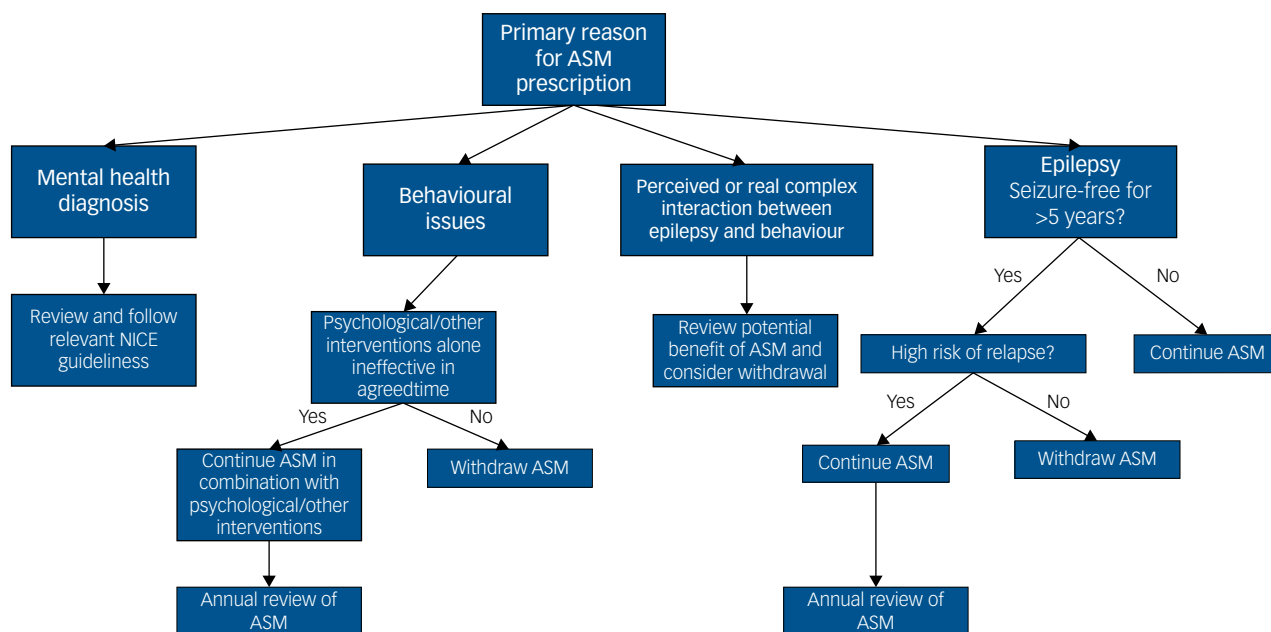
### Prescribing ASMs for the management of challenging behaviours for PwID

A 2008 systematic review of the effectiveness of mood stabilisers and ASMs for the management of behaviour problems in PwID concluded that although there is some support for the use of lithium and some ASMs for the management of behaviour problems in adults with intellectual disability, they could only find one randomised controlled trial (RCT) relating to a non-ASM (lithium) and two non-RCTs, one on lithium and the other on carbamazepine.<sup>16</sup> In addition, one prospective non-controlled trial on sodium valproate and three retrospective case series studies were discovered, of which one considered the efficacy of lithium, one valproate and one topiramate. In the selected studies all the ASMs were add-ons to existing medication.

A recent UK-based 2020 study highlighted significant differences in the understanding, confidence and approaches to managing challenging behaviour in PwID and epilepsy between different professional groups, such as neurologists and psychiatrists.<sup>17</sup> A best practice checklist was proposed to provide a structured framework. The framework outlines various aspects of assessing and managing challenging behaviour in PwID and epilepsy.<sup>17</sup> It gives prompts to enquire into the specifics of domains of biological factors (history taking, clinical examination and physical investigations), psychological and behavioural factors and social factors.<sup>17</sup>

### Why is addressing ASM prescribing in PwID important?

First, the Learning Disability Mortality Review Programme (LeDeR), which is an ongoing national inquiry in England of all deaths in PwID aged 4–74 years, showed one of the most frequently



**Fig. 1** Decision-support flow chart for review of antiseizure medication in people with intellectual disabilities.

prescribed groups of medications were ASMs prescribed to almost half of all PwID who had died prematurely.<sup>18</sup> Around a quarter were on valproate.<sup>18</sup>

Second, PwID on ASMs appear to have high levels of multimorbidity and polypharmacy.<sup>19</sup> In particular, those over 40 years of age are more vulnerable to proportionate increases in polypharmacy and multimorbidity while inversely effected by level of service and care, compared with their younger peers<sup>20</sup>

Third, concerns about long-term side-effects relating to issues such as bone and bowel health need considering.<sup>21,22</sup>

### Who should 'own' the problem?

Any proactive and constructive work to rationalise ASM prescribing needs all key stakeholders across epilepsy, intellectual disability and mental health to collaborate.<sup>23</sup> An unresolved challenge globally has been how should PwID and epilepsy be supported, which is an important challenge to address in order to understand ASM prescribing in this population.<sup>24</sup> Clinical presentations can lead to diagnostic overshadowing leading to a range of situations of neglect, misdiagnosis and overprescribing.<sup>25</sup> There are concerns about unmet training needs across all health and social stakeholder groups which should be inclusive of the needs of this population and require addressing.<sup>26</sup>

### Practice recommendations for review of long-term ASM prescribing

For most PwID the prescribing of ASMs is long term.<sup>3</sup> Ideally where ASMs are being prescribed for an indicated and appropriate condition, for example bipolar or epilepsy, the relevant National Institute for Health and Care Excellence guidance needs to be considered. Specifically, where seizures are an issue clinicians should follow the advice in epilepsy-specific best practice guidelines.

For PwID who receive ASMs solely for behavioural issues (i.e. non-psychiatric indications or in the absence of epilepsy) ASMs

should be initiated or continued only if there is recognised and documented evidence that psychological or other interventions alone did not produce change within an agreed time; treatment for any coexisting mental or physical health problem has not led to a reduction in the behaviour; or the risk to the person or others is very severe (for example, because of violence, aggression or self-injury). The evidence to support this is modest and there needs to be recognition that the aetiology can be diverse, with the best available evidence for aggression being for valproate use for aggressive behaviour in paediatric populations.<sup>27</sup> Further, where possible, ASMs should only be offered in combination with psychological or other evidenced interventions.

For PwID with a history of epilepsy who are taking ASMs and not experiencing any symptoms, consider reducing or discontinuing long-term prescriptions of ASM. This would need to include reviewing the person's condition after reducing or discontinuing a prescription and considering referral to a psychiatrist experienced in working with PwID.

There needs to be annual review and documentation of the reasons for continuing the prescription if it is not reduced or discontinued. [Figure 1](#) provides a decision-support flow chart of the above information for clinicians to consider in practice.

### Conclusion

#### Implications for clinical practice

There is growing recognition that PwID on ASMs are a more vulnerable cohort. Among PwID receiving ASMs there is not only an issue with polypharmacy but an increased tendency for these patients to have a more severe level of intellectual disability.<sup>19,28,29</sup> Issues relating to informed choice are harder for this group.

For many PwID there may be a perceived, or real, complex interaction between either the seizures and psychiatric concerns; seizures and behavioural concerns; seizures with both psychiatric and behavioural issues; or just psychiatric and behavioural issues (without seizures). It is important to comprehensively understand

the relationship between the various aspects of seizures and the psychiatric/behavioural concerns. If the components are unrelated the recommendations above are relevant. However, if the components are linked it is important to understand how the ASM has an impact on that and whether there are benefits. If the benefits are limited, consider ASM withdrawal.

### Implications for policy

For much of the past 50 years the group of psychotropic medications most commonly prescribed for PwID and of most concern has been the antipsychotics. The side-effect profile of antipsychotics (tardive dyskinesia with older antipsychotics and metabolic problems with newer products) and the failure of RCTs to demonstrate benefits indicates that specific attention needs to continue to be on antipsychotic prescribing in this population. Although the current decline in antipsychotic and benzodiazepine prescribing for PwID may have been accelerated by STOMP, the shift to prescribing ASMs, antidepressants and multiple psychotropic medication combinations over the past decade for which there is a limited evidence base, unknown benefits, potential problematic side-effects and difficulty in withdrawal is a matter of concern.<sup>30</sup> It could be STOMP has had unintended consequences that appear to be manifesting in clinicians' practices and which are concerning and may have further long-term consequences as suggested here with the ASM prescribing changes. There needs to be a reappraisal of the role of psychotropic medications in the management of both acute and chronic problems in PwID, and a wider availability of alternatives. There also needs to be suitable examination of policy to focus better on these specific subsets.

### Implications for research

Although there are many antipsychotic withdrawal studies in PwID there is a lack of similar studies for ASMs. The lack of suitable evidence-based strategies to deprescribe or reduce ASMs may make clinicians fear the potential consequences especially if they believe there is too great a challenge in doing so safely. Practical issues such as training and resources need addressing.

In addition, there are concerns about unmasking hitherto undiagnosed or poorly clinically recognised epilepsy and/or mood disorders. With concerns about relapse of seizures there are risks such as sudden unexpected death in epilepsy that need circumnavigating. Clinical confidence to deprescribe ASMs can only be built by a good research evidence base. Given the challenges, and learning from similar projects such as STOMP around the complexities, biases and confounders involved in psychotropic medication deprescribing, it is unlikely gold standard methodologies such as RCTs can help outline best practice of deprescribing in this vulnerable and heterogeneous group. More benefit could come from a large-scale prospective cohort study or a pragmatic clinical trial<sup>31</sup> focusing on stoppage and reduction of ASMs based on best practice recommendations, while ensuring suitable safety measures are in place; this would be a good first step to help build evidence of the specific challenges and barriers.

**David Branford**, Cornwall Intellectual Disability Equitable Research (CIDER), University of Plymouth Peninsula School of Medicine, UK; **James J. Sun**, Royal Free London NHS Foundation Trust, London, UK; **Rohit Shankar** , Cornwall Intellectual Disability Equitable Research (CIDER), University of Plymouth Peninsula School of Medicine, UK; and Cornwall Intellectual Disability Equitable Research (CIDER), Cornwall Partnership NHS Foundation Trust, Bodmin, UK

**Correspondence:** Rohit Shankar. Email: [rohit.shankar@plymouth.ac.uk](mailto:rohit.shankar@plymouth.ac.uk)

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### Data availability

The data that support the findings of this study are available at <https://digital.nhs.uk/data-and-information/publications/statistical/health-and-care-of-people-with-learning-disabilities/experimental-statistics-2019-to-2020>. Further details of analysis are available from the corresponding author upon reasonable request.

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### Author contributions

All authors satisfy the ICMJE guidance by substantially contributing to the design, analysis and interpretation of the work, drafting of the manuscript and final approval of the manuscript, and all agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work is appropriately investigated and resolved.

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