Patterns of Medication Use Associated with Epilepsy and Comorbid Behavioural and Mental Disorders in Older People with Intellectual Disability

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Discussion

8.1 Principal findings of thesis

This thesis is a thorough investigation of psychotropic medication use in older people with intellectual disability experiencing neurological and psychiatric comorbidity. As little research has been published in the field of epilepsy and intellectual disability to date, this thesis sought to address this dearth of evidence and highlight the significant burden that is associated with a diagnosis of epilepsy and mental health problems in people with intellectual disability in a bid to support policy development. The studies in this thesis in relation to epilepsy are novel, as they explore the association between psychotropic medication use and the physical (seizure frequency) and behavioural effects of such use in older adults with intellectual disability in Ireland.

Objective (a)
To examine demographic and clinical factors relating to the prevalence of epilepsy and use of antiepileptic drugs (AEDs) in a nationally representative sample of older adults with intellectual disability and epilepsy in Ireland.

A high prevalence of epilepsy was found (35.8%), with prevalence strongly associated with living in a residential/campus setting and having a severe/profound intellectual disability. Four in ten participants reported at least one seizure in the last year despite high levels of AED use.

Objective (b)
To investigate AED therapy in people with epilepsy and intellectual disability using three drug utilisation research methods - monotherapy/polytherapy, AED load <2/≥2 and numerical AED load.

Almost half of participants with epilepsy were exposed to AED polytherapy, with over a quarter of participants found to have an AED load ≥2. The mood stabilising AEDs were found to be the most commonly prescribed AEDs in this study. A greater number of participants reporting AED polytherapy and who have an AED load ≥2 reported getting their epilepsy reviewed by a neurologist, compared to participants reporting AED monotherapy or having an AED load <2.

Objective (c)
To examine the use of AEDs and co-prescribed psychotropic medications with the potential to lower the seizure threshold and assess the impact on seizure frequency.

This is the first time that psychotropic medication was categorised according to seizure risk and examined in relation to its effects on seizure frequency in adults with an intellectual disability and epilepsy. We found that participants taking at least one medication classified as moderate/high risk were significantly less likely to report at least one seizure in the last year compared to participants taking no potential seizure threshold-lowering psychotropic medication. Additionally, over three quarters of participants taking two or more potential seizure threshold-lowering psychotropic medications reported no seizures in the last year. This is notable owing to the significant psychiatric comorbidity in this population group and the need for safe and effective treatment.

Objective (d)
To determine the relationship between challenging behaviour and use of antiepileptic drugs and AED load in people with epilepsy.

It is also the first time that potential adverse behavioural effects of AEDs were examined in the context of AED load using the PDD/DDD ratio. The highest median AED load was found in participants exhibiting aggressive/destructive behaviour with the lowest median AED load found in participants exhibiting stereotyped behaviour. We found that participants with a severe/profound intellectual disability exhibiting SIB and aggressive/destructive behaviour had significantly higher median AED loads compared to participants not exhibiting these behaviours. Higher AED load was also found to be associated with exhibiting aggressive/destructive behaviour, adjusting for confounders. These results add to the growing interest of the impact and use of AEDs in challenging behaviour.

Objective (e)
To investigate the demographic characteristics of older adults with intellectual disability reporting a mental health disorder and investigate the patterns and use of psychotropic medication.

Many studies in the intellectual disability population discuss antipsychotics or antidepressants in general terms, quoting overall percentages without seeking to understand the type and dosage of the medication prescribed. Chapter 7 of this thesis investigates the subgroups of these psychotropic classes in order to get a complete picture of psychotropic prescribing. We found that atypical antipsychotics and SSRI antidepressants were the most frequently prescribed antipsychotic and antidepressant subclasses. We also examined psychotropic polypharmacy and found that a fifth of participants exhibiting challenging behaviours but who did not report a mental health

disorder were exposed to inter-class psychotropic polypharmacy. Unsurprisingly, we found that over 8 in 10 participants reporting a mental health disorder reported that they received psychiatric treatment, but just over a quarter reported receiving psychological treatment in the form of counselling or behavioural support.

The huge psychiatric burden experienced by people with both epilepsy and intellectual disability is increasingly coming to light, with greater regulation of services by the Health Information and Quality Authority (HIQA) in Ireland and international spotlight focused on institutional settings and deinstitutionalisation policies. The drive to encourage greater research in people with epilepsy and intellectual disability, and the ever increasing focus on psychotropic prescribing in this population group, further underscores the opportune nature of the research in this thesis and provides a baseline level of knowledge of the topics discussed.

8.1.1 Highlights of thesis (linked to objectives)

1. Epilepsy prevalence was found to be 35.8%, at the higher end of ranges reported in previous literature, despite the study conducted across all residential type settings (a).
2. Epilepsy prevalence was strongly associated with living in a residential/campus setting and having a severe/profound intellectual disability (a).
3. Four in ten participants reported at least one seizure in the last year, despite 88.8% of participants with epilepsy reporting use of regular AEDs (a, b).

4. Over a quarter of participants with epilepsy were found to have an AED load ≥2 (PDD/DDD), with 40.8% of participants reporting taking AED monotherapy, 48% AED polytherapy and 11.2% no AED therapy (b).
5. Over three in ten participants with epilepsy were prescribed one psychotropic medication with the potential to lower the seizure threshold whilst over one in five were prescribed two or more (c).
6. Over three quarters (76%) of participants taking two or more psychotropic medications with the potential to lower the seizure threshold reported no seizures in the last year (c).
7. Participants with seizure data classified as taking at least one moderate/high risk medication for lowering the seizure threshold were significantly less likely to experience a seizure compared to participants taking no potential seizure threshold-lowering medication (c).
8. Almost two thirds of participants with epilepsy who take a regular AED were found to exhibit challenging behaviour, with aggressive/destructive behaviours and stereotyped behaviours significantly more likely in participants living in residential/campus settings, after adjusting for confounders (d).
9. Over half of participants exhibiting challenging behaviours reported taking AED polytherapy (d).
10. The highest median AED load was found in participants exhibiting aggressive/destructive behaviour, with the lowest median AED load found in participants exhibiting stereotyped behaviour (d).

11. Participants with a severe/profound intellectual disability exhibiting SIB and aggressive/destructive behaviour had significantly higher median AED loads compared to participants not exhibiting these behaviours (d).
12. Half of the participants in Wave 3 of this study (n=513) reported a mental health disorder with a greater prevalence found in residential/campus settings (e).
13. Antipsychotics were found to be the most commonly reported psychotropic class in participants reporting a mental health disorder (71.2%), with anxiolytics (24.2%) and hypnotics and sedatives (14.2%) prescribed less frequently (e).
14. Six in ten participants in this study (n=513) reported taking psychotropic medication, with 35.3% exposed to inter-class psychotropic polypharmacy (e).
15. A fifth of participants exhibiting challenging behaviour but who did not report a mental health disorder were exposed to inter-class psychotropic polypharmacy (e).
16. Living in a residential/campus setting, reporting a mental health disorder and exhibiting challenging behaviour were found to be significantly associated with exposure to inter-class psychotropic polypharmacy, adjusting for confounders (e).
17. Participants with a moderate or severe/profound level of intellectual disability were found to be significantly less likely to be exposed to inter-class psychotropic polypharmacy (e).

8.1.2 Epilepsy prevalence

Our study found a prevalence of epilepsy of 35.8% in a representative group of older adults with an intellectual disability living in both community and residential/campus settings. Our epilepsy prevalence lies at the higher end of the range of estimates reported in studies (14-44%) [1, 2], and is an increase from Wave 1 of this study where a prevalence of 30.7%

was reported [3]. The prevalence of epilepsy was found to be significantly associated ($p<0.001$) with place of residence with most people reporting having epilepsy living in residential/campus settings. In contrast, Mc Grother et al. (2006) did not find a significantly higher prevalence of epilepsy in those living in residential care [4]. Our findings also showed that the prevalence of epilepsy was significantly associated with level of intellectual disability ($p<0.001$). This echoes findings of Robertson et al. (2015) who also found the prevalence of epilepsy to be related to level of intellectual disability [5]. Gender and age were not found to be associated with epilepsy prevalence in this study. Our findings revealed a higher prevalence of epilepsy in females, contrasting with studies in the general population where a higher prevalence is found in males [4]. Similar to Branford et al. (1998), we found that the prevalence of epilepsy decreased in older age groups [6], perhaps related to increased mortality in people with epilepsy and intellectual disability [7].

In this study, a high prevalence of psychiatric/emotional disorders were found in participants with epilepsy (57.7%), consistent with findings in other studies of people with epilepsy and intellectual disability [8, 9]. Our results show that higher levels of mood (37.8% vs 30.1%) and anxiety disorders (34.2% vs 31.3%) but lower levels of psychotic disorders (7.1% vs 8.5%) were found in participants reporting a diagnosis of epilepsy compared to those without epilepsy. Our findings also highlight the considerable physical comorbidity associated with a diagnosis of epilepsy, with a significantly greater prevalence of dementia, dementia and/or Alzheimer's disease and constipation in people with epilepsy. Similar results can be found in other studies of people with intellectual disability and epilepsy [2, 10, 11].

We found high levels of antiepileptic drug (AED) use in people with epilepsy with almost half of participants taking AED polytherapy, underlining the drug resistant nature of epilepsy in people with intellectual disability. The mood stabilising AEDs were predominantly prescribed, repeating findings from O'Dwyer et al. (2018) in Wave 1 of this IDS-TILDA cohort [3]. Regards other co-prescribed psychotropic drugs, a lower prevalence of antipsychotics (39.3% vs 47.7%), antidepressants (30.6% vs 35.2%) and lithium (2.6% vs 3.1%) and a higher prevalence of anxiolytics (17.3% vs 13.6%), hypnotics & sedatives (11.2% vs 8.2%), drugs for dementia (5.6% vs 1.1%) (p=0.002) and anticholinergic drugs (13.8% vs 12.5%) were found in participants reporting an epilepsy diagnosis.

8.1.3 Antiepileptic drug use

Our results highlight the high antiepileptic medication burden faced by people with epilepsy and intellectual disability. Over a quarter of participants were found to have a total AED load ≥2. Seven participants in this study took five AEDs with the highest AED load (PDD/DD) found to be 8.33, high considering the average maintenance dose would be an AED load of 1. Lammers et al. (1995) found that all participants with an AED load >4 had neurological adverse effects [12]. A higher prevalence (non-significant) of polytherapy and having an AED load <2 was found in females, with an equal prevalence of AED load ≥2 in both males and females. When examining numerical AED load, a significantly higher median AED load was found in community group homes (1.27) compared to independent/family settings (0.50).

Almost half of participants were found to take AED polytherapy with four in ten taking AED monotherapy. The highest prevalence of polytherapy was found in residential/campus settings (57.4%) which also accounted for the setting with the greatest

prevalence of participants with an AED load ≥2. O'Dwyer et al. (2018) also found a higher prevalence of polytherapy (61.2%) in residential settings in Wave 1 of this cohort [3]. Our findings also revealed that taking AED polytherapy and having an AED load ≥2 was significantly associated with participants reporting that epilepsy limits their ability to do household chores, work, social activities, sports activities, and going out alone.

Mood stabilising AEDs (valproic acid, carbamazepine, and lamotrigine) were the most commonly prescribed AEDs in this study, although they are first line AEDs for many seizure types. O'Dwyer et al. (2018) also found mood stabilising AEDs to be the most popular in Wave 1 of this longitudinal study [3]. Levetiracetam was the most commonly prescribed AED outside of the mood stabilising AEDs. The benzodiazepine AEDs, clobazam and clonazepam, were also commonly prescribed. Benzodiazepines are commonly used in people with intellectual disability as both a regular AED and as rescue medicine [13]. They can be an effective add-on therapy in refractory epilepsy [13]. Tolerance is a problem with benzodiazepines. In addition, due to psychiatric issues with mood and anxiety in this population, people with intellectual disability can already suffer a high burden of benzodiazepine load [13].

8.1.4 Risk of antiepileptic drug overtreatment

Our findings highlight the challenge of drug resistant epilepsy in people with intellectual disability. Polytherapy and high dosages are often employed in a bid to treat seizures in this population, despite evidence showing that this may be of little benefit, and create complications of overtreatment [14]. Over half of participants who reported taking AED polytherapy and seven in ten participants with an AED load ≥2 still reported at least one seizure in the last year, highlighting the drug resistant nature of epilepsy in people with

intellectual disability. It is believed that only a minority of people with drug resistant epilepsy benefit from high dosages, thus the majority are unnecessarily exposed to adverse effects with little therapeutic gain [14].

8.1.5 Rescue medications

Our findings reveal that buccal midazolam was the preferred medication for acute seizure control in people with epilepsy and intellectual disability in Wave 3 of this study. Over two thirds of participants exposed to AED polytherapy reported prescription of buccal midazolam compared to just under half of participants exposed to AED monotherapy. We also found that a higher AED load (≥2) was associated with prescription of buccal midazolam. Rectal diazepam was not prescribed in Wave 3 in contrast to Wave 1 of this longitudinal study [3]. Evidence from randomised controlled trials has shown better efficacy in seizure control when using buccal midazolam compared to rectal diazepam [15]. Furthermore, in Wave 1 of this study, buccal midazolam was an unlicensed medicine in Ireland and not available on community drug schemes which further explains the preference for rectal diazepam in the opening Wave of this longitudinal study [3].

8.1.6 Review of epilepsy

A significantly greater proportion of participants with an AED load ≥2 reported attending an epilepsy clinic or specialist (83.0%), compared to those with an AED load <2 (43.6%). Our findings show that of participants reporting no AED therapy, less than one in ten reported getting their epilepsy reviewed by a neurologist. A greater number of participants exposed to AED polytherapy (44.7%) reported getting their epilepsy reviewed by a neurologist compared to 26.3% of participants exposed to AED monotherapy. Over half of

participants with an AED load ≥2 had their epilepsy reviewed by a neurologist compared to a quarter of participants with an AED load <2. These results highlight the need for neurologists and specialist neurology teams to review complex seizures and AED regimens.

8.1.7 Visiting A&E in the last year with epilepsy

Our findings show that one in ten participants with a diagnosis of epilepsy reported visiting A&E in the last year due to epilepsy. Convulsions are the main reason for avoidable hospitalisation in people with intellectual disability and are said to account for 40% of all emergency hospital admissions [13]. Only participants who reported taking regular AED therapy were found to have visited A&E in the last year, with a similar proportion reporting AED monotherapy (10.0%) and AED polytherapy (11.6%). However, with regards to categorised AED load, a greater proportion of participants with a higher AED load ≥2 (16.0%) reported visiting A&E compared to participants with a lower AED load <2 (7.4%). A higher median AED load was found for participants visiting A&E in the last year with epilepsy (1.870) compared to a median AED load of 1.000 for participants not visiting A&E with epilepsy, illustrating the greater AED burden of those attending A&E for treatment, indicative of more complex morbidity.

8.1.8 Receiving education to manage epilepsy

Our findings reveal that three quarters of participants reporting a diagnosis of epilepsy reported that they did not receive education to manage their epilepsy. Only a fifth of participants reporting no AED therapy reported receiving education, with a third of participants who reported taking AED polytherapy stating same. A higher proportion of participants (36%) with an AED load ≥2 reported receiving education to manage their

epilepsy compared to 19.5% of participants with an AED load <2. While prescribers may perceive that the person with intellectual is incapable of understanding factors related to their epilepsy, more accessible educational materials are needed to address this problem. This is especially prudent in light of deinstitutionalisation policies where greater numbers of people are living independently and in community settings in order to ensure that they are able to safely manage their epilepsy.

8.1.9 Seizure frequency

Our findings show that 40.5% of participants reporting a diagnosis of epilepsy reported at least one seizure in the last year. High rates of refractory epilepsy have been reported in this population group [6, 16]. A Swedish study by Forsgren et al. (1990) found only 32% of epilepsy participants were seizure free in the previous year, while a UK study by Branford et al. (1998) found almost three quarters of participants continued to suffer seizures despite AED treatment [6, 16]. Of participants reporting no AED therapy, 81% reported having no seizure in the last year. A significantly higher proportion of participants exposed to AED polytherapy reported at least one seizure in the last year (57.6%), compared to 26% of participants exposed to AED monotherapy. Unsurprisingly, over seven in ten participants with an AED load $\geq$2 reported experiencing at least one seizure in the last year. Participants reporting that epilepsy limits their ability to undertake certain everyday tasks was also significantly associated with a higher seizure frequency and taking AED polytherapy. A significantly higher proportion of participants reporting at least one seizure in the last year (56.3%) reported having a prescription for emergency buccal midazolam compared with 43.7% of participants reporting no seizures in the last year.

8.1.10 Seizure types

Our findings highlight the high prevalence of generalised seizure types (54.6%) in people with intellectual disability and the difficulties in identifying focal seizures. Tonic-clonic seizures (42.3%) were the most common seizure type reported with low numbers of participants' reporting simple partial (<5) and complex partial seizures (<5). Correctly identifying seizure type in people with intellectual disability is very challenging [17]. Shepherd et al. (1989) in a study of school children, found a greater prevalence of generalised tonic-clonic and myoclonic seizures and a decrease in partial seizures with increasing disability [18, 19]. This was attributed to a lack of satisfactory investigation in people with intellectual disability as few people had undertaken electrophysiological tests [18, 19]. While we do not have any information on the medical tests undertaken by the participants in this study, it is very likely that lack of proper investigation also contributed to the disparity in focal seizure reporting. Due to small numbers of participants reporting focal seizures and large numbers of participants reporting unknown seizure types, we were unable to do any meaningful analysis specifically on focal seizures and this is one of the limitations of this study. For the purposes of analysis, unknown seizures and focal seizures were combined into a new category of other seizures. We found that experiencing generalised seizures were reported by a significantly greater proportion of participants exposed to AED polytherapy (70.2%) and those having an AED load $\geq$2 (79.6%).

8.1.11 Psychiatric comorbidity in people with epilepsy

Our findings identified a high prevalence of a psychiatric/emotional disorder (57.7%) in people with epilepsy and intellectual disability. Psychopathology is common both in people with epilepsy and in people with intellectual disability [20], with a bidirectional relationship

believed to exist between epilepsy and psychiatric disorders [21, 22]. Of participants reporting a diagnosis of epilepsy, 7.1% reported a psychotic disorder, 37.8% a mood disorder and 34.2% an anxiety disorder. A greater proportion of participants exposed to AED polytherapy reported a diagnosis of psychotic and anxiety disorders, while a greater proportion of participants exposed to AED monotherapy reported a mood disorder. Mental health disorders were reported by a greater proportion of participants having an AED load <2.

8.1.12 Prevalence of psychotropic medication in people with epilepsy

Psychotropic medication was widely reported by people with epilepsy and intellectual disability. Of participants reporting an epilepsy diagnosis, 39.3% were prescribed antipsychotics, 30.6% antidepressants and 17.3% anxiolytics. In contrast, of those not reporting an epilepsy diagnosis, 47.7% were prescribed antipsychotics, 35.2% antidepressants and 13.6% anxiolytics. A significantly higher prevalence of the antipsychotic haloperidol (p=0.006) was found in those not reporting a diagnosis of epilepsy (6.8%) compared to those reporting a diagnosis pf epilepsy (1.5%). A study examining quetiapine, olanzapine and haloperidol in healthy subjects found EEG abnormalities were found to occur significantly more often in people taking haloperidol and olanzapine [23]. A significantly higher prevalence of the antidepressants escitalopram (p=0.028), mirtazapine (p=0.023) and trazodone (p=0.012) were found in those reporting a diagnosis of epilepsy compared to those not reporting a diagnosis of epilepsy. SSRI antidepressants are believed to be safe for use in people with epilepsy [24].

8.1.13 Psychotropic medication with the potential to lower the seizure threshold

Our findings reveal that over three in ten participants with epilepsy were prescribed one psychotropic medication with the potential to lower the seizure threshold while over one in five were prescribed two or more. Participants taking at least one medication classified as moderate/high risk for lowering the seizure threshold were significantly less likely to experience a seizure compared to participants taking no medication of this class after adjusting for confounders. Studies have shown that for the majority of psychotropic drugs prescribed appropriately within the therapeutic dose range, seizure incidence is reported to be <0.5% when other risk factors are excluded [25]. We also found that psychotropic polypharmacy was prevalent in this cohort with one in five participants taking two or more psychotropic medications with the potential to lower the seizure threshold. However, 76% of these reported no seizures in the last year indicating no cumulative increased seizure risk. Chlorpromazine was the most frequently co-prescribed high risk psychotropic medicine in our study but 91.7% of participants taking chlorpromazine reported no seizure in the last year. Few drugs classified as high risk were prescribed to participants with epilepsy and recommended doses were used, an indication of the caution of prescribers.

8.1.14 Adverse behavioural effects of antiepileptic drug therapy

Research has shown that AEDs have the propensity to provoke either positive or negative behavioural side effects in people with intellectual disability [26]. Our findings show that over half of participants exhibiting challenging behaviours reported taking AED polytherapy. However, we did not find a significant association between AED use (monotherapy or polytherapy) and exhibiting challenging behaviours. This is in contrast to studies in people with epilepsy and intellectual disability who found an association

between challenging behaviours and AED polytherapy [27, 28]. However, a meta-analysis of studies examining this association did not find a definite association between the rate of challenging behaviours and polytherapy with AED medications [29].

The highest median AED load (PDD/DDD) was found in participants exhibiting aggressive/destructive behaviour, with the lowest median AED load found in participants exhibiting stereotyped behaviour. The binary logistic regression analysis also showed that a higher AED load was associated with exhibiting aggressive/destructive behaviour after adjusting for age, level of intellectual disability and type of residence. Of interest, participants with a severe/profound intellectual disability exhibiting SIB and aggressive/destructive behaviour had significantly higher median AED loads compared to participants not exhibiting these behaviours. Mood stabilising AEDs were found to be prescribed to nine in ten participants exhibiting challenging behaviours in this study although they are first line for many seizure types.

The association between AED load and some behaviours may occur as the presence of behaviours prompts a response, and one response is to prescribe. This may explain the high levels of mood stabilising AEDs in this population group and high AED loads in participants exhibiting certain behaviours. However, we can only report associations between AED load and challenging behaviours in this cross-sectional study, thus, our findings lead us to question whether the presence of challenging behaviours in people with epilepsy and intellectual disability leads to greater prescribing of AEDs for their mood stabilising properties, thus contributing to higher AED loads; or if the dosages of AED medication required to treat refractory seizures produces high AED loads, leading to greater levels of challenging behaviours. This question will need to be answered in higher powered, prospective, controlled studies of people with epilepsy and intellectual disability.

8.1.15 Mental health in people with an intellectual disability

Our findings highlight the substantial burden of mental health disorders in people with an intellectual disability, with 50.7% of all participants with available data in Wave 3 of this study reporting a mental health disorder. Over half of participants reporting a mental health disorder were found to live in residential/campus settings. Almost three quarters of participants reporting a mental health disorder and having behavioural data (BPI-S) were found to exhibit challenging behaviours. Of participants reporting a mental health disorder, 38.8% exhibited SIB, 50.5% exhibited aggressive/destructive behaviour and 61.7% exhibited stereotyped behaviour. However, 38.1% of participants who exhibited challenging behaviours did not report a mental health disorder. We found that over eight in ten participants reporting a mental health disorder reported receiving psychiatric treatment with the majority receiving psychiatric treatment from a psychiatrist. Just over a quarter of participants reported receiving psychological treatment.

Identifying mental health problems in the intellectual disability population requires great skill as many people with an intellectual disability are incapable of identifying or indeed reporting psychiatric symptoms and rely on others to do so on their behalf [30]. Reid (1972) found schizophrenia difficult to identify in people with an intellectual disability due to communication deficits making diagnosing psychoses and hallucinations problematic [31].

Mood disorders are also challenging to identify in people with severe intellectual disabilities and may result in a deficiency in their care through under-treatment [32]. Our findings show that participants reporting a mental health disorder with a moderate and severe/profound intellectual disability were significantly less likely to report prescription of antidepressants. Whether this is due to difficulties in identification of specific mental

health disorders or reluctance to prescribe antidepressants, the increased life expectancy of people with intellectual disability demands better screening for mental health disorders in people with more severe intellectual disability and greater access to suitable treatment. Clinicians also need to be mindful of diagnostic overshadowing when considering mental health disorders. Hassiotis et al. (2012) [33] found that considerable mental health challenges faced by participants were often unidentified and untreated. Mason et al. (2004) examined diagnostic overshadowing bias and found a reduced likelihood of considering a schizophrenic diagnosis and drug and alcohol problems, in addition to reduced consideration of psychiatric admission or use of medication in people with intellectual disability [34].

8.1.16 Psychotropic pharmacotherapy for mental health and behavioural disorders

Our findings reveal high levels of psychotropic medication prescribing, with 45.0% of participants in this study with available mental health data reporting being prescribed antipsychotics, 33.3% antidepressants, 15.8% anxiolytics and 9.9% hypnotics & sedatives. Antipsychotics were the predominant psychotropic class amongst participants reporting mental health disorders, with a higher prevalence of atypical antipsychotics. Atypical antipsychotic prescribing has surpassed that of typical antipsychotics in recent decades due to a reduction in adverse effects and the mood stabilising properties of atypical antipsychotics [35, 36]. Hypnotics & sedatives were infrequently prescribed, with z drugs the most popular subclass of this type of medication. Olanzapine (15.4%), risperidone (14.2%) and quetiapine (5.5%) were the most frequently prescribed atypical antipsychotics, with chlorpromazine (6.4%) and haloperidol (4.3%) the most frequently prescribed typical antipsychotics. The popularity of these antipsychotics is mirrored in a UK cross-sectional

study of people with intellectual disability (n=2319) from 39 clinical services which also found these five antipsychotics as the most popular in their sample [37].

8.1.17 Off-label prescribing of medication to treat challenging behaviours

Our findings show high levels of psychotropic prescribing, particularly atypical antipsychotics (22.4%) in participants exhibiting challenging behaviours without reporting a mental health diagnosis. Studies in people with intellectual disability have shown that low dose atypical antipsychotics with anxiolytic properties are frequently employed to treat underlying anxiety associated with behavioural issues [38]. SSRI antidepressants are also used off-label for treating behavioural problems [39]. This off-label prescribing of psychotropics is commonly encountered in this population group [39] to treat challenging behaviour, with conflicting results [40-42]. Atypical antipsychotics are not without adverse effects thus greater evidence of efficacy and safety is required for prolonged periods of use [43, 44].

8.1.18 Psychotropic polypharmacy

High levels of inter-class psychotropic polypharmacy were found in this study (35.3%), with 8.8% of participants reporting intra-class antipsychotic polypharmacy. McMahon et al. (2020) in a cross-sectional total population UK study of 217 people with intellectual disability aged 18 years and older, found a lower psychotropic polypharmacy prevalence of 23% in their study [45]. In our study, over half of participants reporting a mental health disorder and a fifth of participants exhibiting challenging behaviour with no mental health diagnosis reported were exposed to inter-class psychotropic polypharmacy. The binary logistic regression showed that participants with a moderate or severe/profound level of

intellectual disability were significantly less likely to report inter-class psychotropic polypharmacy. In contrast, participants living in a residential/campus setting, reporting a mental health disorder and exhibiting challenging behaviour were significantly more likely to report inter-class psychotropic polypharmacy. O'Dwyer et al. (2017) [46], Lunsky et al. (2018) [47] and McMahon et al. (2020) [45] also found that living in a residential/campus setting to be significantly associated with exposure to inter-class psychotropic polypharmacy. Undoubtedly, a higher prevalence of psychotropic medication is reported in institutional settings compared with community based settings [48]. Moreover, participants reporting a diagnosis of epilepsy were found to be less likely to report inter-class psychotropic polypharmacy although no significant association was found. This may be due to concerns regarding the effects of potential seizure threshold-lowering medications in people with a diagnosis of epilepsy.

8.1.19 Prevalence of psychotropic medication and type of residence

High levels of psychotropic medication were found in residential/campus settings in this study echoing results from previous studies in this population [48, 49]. De-prescribing psychotropic medication in people with intellectual disability is difficult due to the risks of exacerbating any underlying condition and prompting adverse effects [50, 51]. Nøttestad & Linaker (2003) found that levels of psychotropic medication remained the same both pre- and post-movement to community settings highlighting the challenge of reducing psychotropic medication in this population [48].

8.2 Limitations

The principal limitations and challenges of these studies included:

8.2.1 Cross-sectional study design

The observational cross-sectional study design is an important limitation of this study. This type of study design allows us to examine factors in a given population at a given point in time [52]. There is a lack of a causal effect relationship in these studies as information is not available regarding whether the factor of interest precedes or follows the effect [52]. This was a limitation with regards to whether psychotropic medication led to seizures or whether AEDs contributed to behavioural adverse effects. We were only able to describe associations and not causation in the data. In our multivariate analysis, any probable bias was removed where possible by adjusting for confounders. Nevertheless, residual confounding factors may remain. There is also the risk that potential risk factors contributing to seizure or behavioural outcomes were under-represented in this study population.

8.2.2 Sample population

Ageing of participants between Waves 1 and 3 had a negative impact on the sample representativeness by the third Wave leading to under-representation of people aged <50 years, with mild intellectual disability and who live in independent/family settings. A sample refreshment was undertaken in Wave 4 to address these disparities. In addition, our sample is drawn from the National Intellectual Disability Database of Ireland (NIDD), a database that collates information on people that use or are entitled to avail of services. Thus, people not registered in this database are not included in this research. The latest NIDD report detailing findings to the end of December 2017 found a lower prevalence rate

for people with a mild intellectual disability (1.92 per 1,000), compared to people with a moderate, severe or profound intellectual disability (3.49 per 1,000) [53]. This is a major problem in intellectual disability research, as the use of 'convenience samples' [54] often fails to include people not availing of services, but intellectually disabled none the less. Emerson refers to this group of people as the 'hidden majority' [54]. As outlined in *Chapter 1*, a number of factors can contribute to this phenomenon including a) general reduction in health/disability supervision following completion of education in health and welfare agencies; b) specialised health and welfare support rationing to adults with disabilities; c) stigma of intellectual disability resulting in reluctance to self-identify as having intellectual disability or to use services; d) less impact of intellectual deficiencies with intellectual disability in non-educational settings [54].

8.2.3 Missing data

Missing data in Wave 3, particularly in relation to medication and behavioural data was a limitation of this thesis, affecting all of the studies to some degree. Medication data were collected in the PIQ and 60 participants were missing this data in Wave 3 as previously outlined. PIQs not returned, a lack of awareness from field researchers regarding sections of the PIQ not completed, and time constraints are some of the likely factors contributing to this. As a result of this missing medication data, we had to exclude 19 people with a diagnosis of epilepsy from our study, affecting the power of the study, as small numbers in some subgroups limited the range of possible statistical tests that could be undertaken. From Wave 4 onwards, medication data is being sought from the PCRS that holds the medication data of public community drug schemes in Ireland. It is hoped that this will both complement and further enhance the reliability of the medication data. Behavioural data

were missing for 97 of the total number of participants with medication data (n=549) in this study, including 32 people with an epilepsy diagnosis in *Chapter 6*. Lack of availability of suitable proxies to complete the Behaviour Problems Inventory Short form (BPI-S) is a possible explanation. Guidelines stated that the proxy needed to know the participant well, for a minimum of 6 months. Level of engagement from both participants and carers/proxies lies at the centre of the success of this study. Time constraints of carers/proxies and a lack of understanding or interest in the study may also be contributory factors. Awareness of these issues has been taken into consideration by the study management with shorter questionnaires in Wave 4, reducing the need for follow up or additional interviews. While multiple visits were made to some participants in Wave 3, the goal for future Waves is to complete the interview in one sitting to reduce the burden on both the participant and proxy. For people with severe mental health difficulties, multiple visits may still be needed so flexibility in the study protocol will continue to be needed to ensure inclusivity.

8.2.4 Patient/proxy reported data

IDS-TILDA is designed as a self-report study [55, 56]. While the information obtained from this type of study is very useful, particularly in relation to medication adherence; barriers to use; identification of adverse effects; beliefs regarding health and medication use; information on consumption of prescription and over-the-counter (OTC) medications/ herbal drugs; and other information not necessarily ascertained by medical and dispensing records, it is not without having its difficulties. Recall bias, misinformation, misinterpretation and non-response are just some of the difficulties that can be encountered [57-60], and may account for some of the missing data in this study. Much of

the medication and clinical data would have been confirmed by a proxy in this study. However, limitations of this would be under-reporting as a result of a lack of knowledge (proxy effect) and over-reporting of issues the proxy deems most relevant (saliency principle) [60]. A further limitation of patient/proxy reported data is lack of confirmation of a Doctor's diagnosis from clinical records and accurate timelines of when a diagnosis was made and when treatment was initiated.

8.2.5 Lack of reporting of focal seizures

The self-reporting of an epilepsy diagnosis and seizure type is a significant limitation of this study, together with a lack of access to clinical records. We found low numbers of participants reporting focal seizures, likely due to difficulties in identifying this seizure type in people with intellectual disability. High levels of challenging behaviour may also have made seizure identification difficult. Many participants reported unknown seizure types, a limitation of self-report studies in epilepsy. For the purposes of analysis, focal and unknown seizure types were grouped together into a new variable titled 'other seizure types'.

8.2.6 Literature review

This thesis utilised a focused literature review style instead of undertaking a systematic review. A systematic review uses more robust methods using PRISMA (Preferred Reporting Items for Systematic reviews and Meta Analyses) guidelines [61], predefined search terms and detailed protocols. Lack of a systematic review in this thesis may have resulted in relevant literature being missed, affecting the interpretation of our results. However, a comprehensive focused literature review was undertaken searching PubMed, Science Direct, Embase, Scopus, Web of Science, CINAHL, Google Scholar and numerous Journals

in the fields of epilepsy and intellectual disability. A grey literature search was also undertaken.

8.3 Recommendations & implications for practice

8.3.1 Multidisciplinary medication reviews

This study highlights the significant psychiatric and behavioural comorbidity associated with a diagnosis of intellectual disability and epilepsy and the clinical complexity associated with prescribing psychotropic medication. This complexity is undoubtedly magnified by the policy of deinstitutionalisation, whereby increasing numbers of prescribers in primary care will be expected to manage the extensive multimorbidity and polypharmacy in this population group. This will necessitate the occurrence of regular multidisciplinary medication reviews, involving all healthcare providers involved in the care of people with intellectual disability to ensure appropriate treatment is commenced with a careful balancing of the need for treatment against the risks of adverse effects.

Carers and families can also play a key role in these medication reviews to optimise treatment, and they are central to the successful execution of deinstitutionalisation policies. The STOMP initiative in the UK found that a lack of influence on the prescribing process was also felt by family carers, professional carers', and other advocates who deemed it the responsibility of others [62]. A multi-stakeholder qualitative study in the UK by Sheehan et al. (2019) examining psychotropic medication use and decision making for adults with intellectual disability found that both family and paid carers were happy to have a role in decision-making where their voice was heard and genuinely sought [63]. Anecdotal evidence of carers of changes in mood and behaviour of people following adjustments of medication regimens, sedative and cognitive effects of certain psychotropic

medications, seizure frequency changes following the addition of antidepressants or antipsychotics, assists prescribers by helping to plug the information gap where individuals with intellectual disability are unable to provide this information. Thus the expertise of carers is a crucial element to ensuring optimum outcomes from treatment, and helping to keep people with an intellectual disability free from avoidable harm.

Recently in Ireland (March 2020), the HSE (health service) established the National Clinical Programme for People with Disability (NCPPD) following Ireland's ratification of the United Nations Convention on the Rights of Persons with Disability (UNCRPD), which supports a social and human rights-based service provision model [64]. The NCPPD places the service user, their family, community and representative organisations at the centre of the programme with an influence on decision making [64]. This affords healthcare professionals and multidisciplinary teams an opportunity to adopt and foster an inclusive non-paternalistic model of healthcare for people with intellectual disability, with greater choice of healthcare interventions and increased availability of counselling and behavioural support for challenging behaviours to reduce reliance on psychotropic medication. For people with epilepsy, the National Clinical Care Programme for Epilepsy (NCPE) also offers a holistic model of integrated person-centred care through assessment, monitoring the impact of care, and coordinating care to enhance a patient's journey [65]. This thesis has highlighted the importance of building greater capacity in epilepsy outreach clinics as part of the NCPE and the provision of specialist neurology and psychiatric services to ensure people with complex care needs achieve the highest standards of care and quality of life.

8.3.2 Pharmacist input in pharmacotherapy decisions

Owing to the huge reliance on pharmaceutical care for people with an intellectual disability, pharmacists as the experts in medication have the potential to play a central role in their care by optimising treatment outcomes. A narrative review by O'Dwyer et al. (2015) [66] examining pharmacists medicine related interventions found that pharmacists exerted positive influences on the care of people with an intellectual disability by promoting patient safety, and by enhancing the quality and appropriateness of medication use [66]. However, this review also highlights the lack of research in this area [66], which the authors attribute to lack of education and experience in providing pharmaceutical care to people with intellectual disability, little opportunity for collaboration with general practice and a deficiency in documenting and publishing practice experiences. Available evidence suggests pharmacists are skilled in identifying and resolving drug therapy problems in collaboration with other health care professionals [66-70]. Pharmacists have the ability to take a leading role in multidisciplinary medication reviews in both residential/campus settings and increasingly in community settings with advancement of deinstitutionalisation. They have expertise in providing medication advice, highlighting risks and benefits, de-prescribing where necessary, advising on suitable polytherapy schedules and consolidating prescribing from different specialities to ensure opportunities for medication related harm are minimal.

8.3.3 Treatment using psychotropic medications with a risk of seizure worsening - considerations and implications

Our findings suggest psychotropic medication, in therapeutic dosages, recommended to be avoided or used with caution in people with epilepsy did not provoke increased seizure

frequency in this intellectual disability cohort. Some psychotropic medication are found to be associated with increased seizure risk, for example the antipsychotic clozapine [71], antidepressants clomipramine, amoxapine, maprotiline, bupropion [72, 73], and high dose amitriptyline [74]. However, most psychotropic drugs prescribed appropriately within the therapeutic dose range results in reported seizure incidence <0.5% when other risk factors are excluded [25]. Other factors contributing to increased seizure risk in people with epilepsy and intellectual disability need to be identified. While prescribers are correct to be cautious, it is important that each medication's risk of lowering the seizure threshold is appropriately assessed on a case-by-case basis and that generic warnings on whole classes of psychotropic medication do not prevent appropriate therapy being considered. Greater evidence of seizure risk related to psychotropics in people with intellectual disability is needed so that medication information to inform prescribing is updated, to reflect current available evidence, thus ensuring information is not clouded by outdated a priori assumptions.

8.3.4 Understanding the relationship between antiepileptic drugs, antiepileptic drug load and challenging behaviour in people with epilepsy and intellectual disability

Our findings suggest that challenging behaviours are a considerable problem for people with epilepsy and intellectual disability. Almost two-thirds of participants with epilepsy, taking a regular AED and available information were found to exhibit challenging behaviours with an increased prevalence among those with greater severity of intellectual disability. We found that higher median AED loads (PDD/DDD) were associated with exhibiting both SIB and aggressive/destructive behaviour amongst specific subgroups when comparing demographic and clinical characteristics. Nonetheless, due to the many

possible contributory factors and the cross-sectional study design, we are unable to determine if the presence of challenging behaviours in people with epilepsy and intellectual disability leads to greater prescribing of AEDs for their mood stabilising properties, thus contributing to higher AED loads; or if the dosages of AED medication required to treat refractory seizures produces high AED loads, leading to greater levels of challenging behaviours. Future, larger, higher powered studies in people with epilepsy and intellectual disability should examine the relationship between AED load (PDD/DDD) and challenging behaviours, and determine if high AED load does contribute to behavioural problems in this population group and assess possible risk factors.

8.3.5 Measuring antiepileptic drug load using the PDD/DDD ratio

The extensive use of antiepileptic drugs in people with epilepsy and intellectual disability necessitates an accurate measure of AED load, particularly in relation to the risk of overtreatment and adverse behavioural effects. The PDD/DDD ratio [75] has disadvantages, but it is another strategy of analysing use of AEDs and a simple, easy to calculate measure of antiepileptic drug load. For research purposes, while not taking into consideration individual renal or hepatic function, it allows comparison of individual AED regimens with international standardised DDD values. It may be useful as a tool for pharmacists and doctors to assess the burden of AEDs taken by a patient and identify those at risk of overtreatment and adverse effects. The categories employed by Lammers et al. (1995) (≤ 2 and >2) may indicate to prescribers the AED load thresholds where greater prevalence of adverse neurological effects are possible and initiate monitoring for adverse effects. This ratio may also be useful to guide appropriate dosage in clinical practice and is a more effective measure of AED load than a monotherapy/polytherapy classification.

8.3.6 Better identification of seizure types

It is very difficult to diagnose epilepsy in people with intellectual disability. It has been estimated that a quarter of individuals with a diagnosis of both intellectual disability and epilepsy referred to a specialist centre were misdiagnosed [76, 77]. Many differential diagnoses can mimic a seizure including syncope, vascular, psychiatric, behavioural, metabolic, movement, sleep disorders and drug related effects [77]. If incorrectly diagnosed, people may receive the wrong treatment, unnecessary treatment or no treatment at all [78]. Small numbers of focal seizures were reported in this study, likely due to lack of identification.

EEG and other investigations may be difficult to undertake in people with intellectual disability, particularly in people with severe/profound intellectual disability who may exhibit stereotyped behaviour. These factors together with communication difficulties can hamper accurate seizure identification. Carers must be educated about epilepsy, types of seizures, the importance of reporting any concerns or events and how to accurately describe what they witness.

8.3.7 Improved strategies for dealing with drug-resistant epilepsy

Drug resistant epilepsy is one of the greatest challenges for people with a dual diagnosis of epilepsy and intellectual disability, with its aetiology poorly understood. Despite high levels of AED use, significant numbers of people continue to report seizures. In this study, 57.6% of participants taking AED polytherapy and 70.4% of participants with an AED load $\geq$2 reported at least one seizure in the last year. Studies have shown that maximum doses and AED polytherapy may be of limited benefit while creating complications of overtreatment [14]. It is believed that only a minority of people benefit from these kinds of regimens,

leading to unnecessary exposure to overtreatment and adverse effects with minimal benefit [14]. A greater focus must be placed on drug development of AEDs that act on epileptogenesis and the underlying pathology of epilepsy and associated syndromes, instead of merely targeting seizure occurrence. Greater attention needs be focused on the possible bi-directional relationship between mental illness like depression and epilepsy [22], and an increased awareness by prescribers of the necessity to adequately treat both conditions. Neurobiological factors common to drug resistant epilepsy, disease severity, and psychiatric comorbidity need to be fully examined [79].

8.3.8 Standardisation of diagnostic criteria and terminology of mental health disorders

The multiplicity of definitions of mental health disorders and diagnostic criteria employed in studies has led to a wide range (7-97%) [80] of prevalence rates of mental health disorders being reported [30], leading to significant difficulties in conducting meaningful comparison. Undoubtedly, the study setting has a major impact on prevalence rates, but there is a need for standardisation of what constitutes a mental illness and validated diagnostic criteria in this population. Diagnostic criteria from the WHO or DSM were designed for use in the general population, and sensitivity may be lacking in people with intellectual disability. Criteria that allows mental illness to be readily identifiable in all levels of intellectual disability is warranted to enable growth of an evidence base that can inform mental health policy in this population group and ensure that all individuals with mental illness can avail of appropriate treatment and are not prejudiced by diagnostic overshadowing.

8.3.9 Awareness of appropriate therapy for mental health disorders and challenging behaviour

This thesis has highlighted the high levels of psychotropic prescribing among people reporting mental health conditions and exhibiting challenging behaviours. Antipsychotics were the leading psychotropic class among participants in this study (45%), a finding similar to other studies of people with intellectual disability [46, 81-83]. A high prevalence of psychotropic prescribing, often off-label [39] is found in people with intellectual disability, with long durations of treatment and extensive polypharmacy, contributing to the risk of over-medication, particularly in institutional settings. Initiatives like STOMP (stopping over medication of people with a learning disability, autism or both with psychotropic medication) [84] in the UK and the WHO's third Global Patient Safety Challenge 'medication without harm' [85] have sought to improve prescribing and reduce avoidable medication related harm.

While greater reliance on atypical antipsychotics, with their improved side effect profile has been reported [37, 39, 40] , use of low dose atypical antipsychotics to treat challenging behaviours [38] needs greater investigation to assess efficacy and determine if any adverse effects arise from long term exposure. Under-treatment is also a cause of concern in this population group, particularly in people with severe/profound intellectual disability. Difficulties in accurately identifying mood disorders in people with more severe intellectual disability [86] may lead to under-treatment [32]. We found that participants with a moderate and severe/profound intellectual disability were significantly less likely to report prescription of antidepressants compared to participants with less severe levels of intellectual disability, highlighting the need for tools to accurately identify mood disorders

in people with the most severe intellectual disability to aid selection of appropriate pharmacotherapy.

8.3.10 More research in people with epilepsy and intellectual disability

Little research is published in the field of epilepsy and intellectual disability, despite reports of a high prevalence of epilepsy in people with intellectual disability [2]. This has resulted in a paucity of comparable studies on this topic. Shankar et al. (2018) have highlighted this issue by exposing a lack of published research and conference presentations on epilepsy and intellectual disability [87]. They found only 5% of published research in epilepsy related to intellectual disability [87]. Regarding major intellectual disability conferences, only 1.4% of research presentations concerned people with both epilepsy and intellectual disability [87]. More studies are needed to examine this topic to create an evidence base regarding the burden of antiepileptics in people with epilepsy and intellectual disability, use of psychotropics in this group, their impact on seizure control, and adverse behavioural side effects of antiepileptic drug therapy.

More research should also be undertaken concerning use of the AED load (PDD/DDD) ratio to better understand comorbidity in people with a dual diagnosis of epilepsy and intellectual disability, particularly with regards to challenging behaviours, cognitive and bone health. The research in this thesis has highlighted the significant AED polypharmacy and high AED load burden (PDD/DDD) experienced by people with epilepsy and intellectual disability, with a considerable proportion of participants still experiencing seizures (40.5%) in this study. Thus prescribers should put greater focus on minimising AED load where possible, and utilise tools such as the AED PDD/DDD ratio to assess overall AED load burden to avoid unnecessary complications of overtreatment.

Much anecdotal evidence exists of carers and family of people with epilepsy reporting an association between use of AEDs and challenging behaviours [88]. Challenging behaviours are widely recognised as a major factor contributing to family carer stress [89, 90], often prompting placement in residential care [90]. A mixed methods research design study including qualitative interviews of carers and family of people with epilepsy and intellectual disability could explore the patient and carer experience in relation to AEDs and challenging behaviours, in a bid to better understand this relationship and its impact on people with intellectual disability. In addition, a randomised, controlled, complex intervention study [91] could be designed in this population group to evaluate the incidence of challenging behaviours with regards to AED load, and whether challenging behaviours respond to AED treatment.

8.4 Future research recommendations

Each Wave of medication data in this study seeks to improve on the last, with Wave 4 data incorporating linked data from the PCRS medication claims database to collect GMS and DPS data which should hopefully improve the quality of the data obtained. Future Waves of this study will also seek to obtain LTI data. This should also reduce the reliance on medication data obtained from the kardex/medication record (missing data in Wave 3) in the PIQ. In addition, as further Waves of data are collected, meaningful longitudinal analysis can be undertaken to give a better understanding of the ageing process and the impact of medication and comorbidity on people with both epilepsy and intellectual disability. Due to incomplete medication dosage data in Wave 1 of this study, this thesis was not able to accurately examine data between Wave 1 and Wave 3 demanding further waves to be completed first.

We found a lack of an association between psychotropic medication with the potential to lower the seizure threshold and seizure frequency. However, this study was not randomised to match the activities of psychotropic medications or AEDs in relation to seizures with controls. In addition, due to the observational cross-sectional study design, we can only describe associations between seizure frequency and demographic and clinical factors. Future studies examining this issue should be prospective in nature, and controlled to allow potential contributory factors of increased seizure frequency to be identified.

The behavioural impact of AEDs should also be examined more fully in higher powered studies to fully understand this association and to allow potential risk factors to be fully examined. While we found an association between a higher median AED load and exhibiting aggressive/destructive behaviour and SIB in various subgroups, the nature of the study design limits our interpretation of these results as we can only describe associations between AED load, challenging behaviour and demographic and clinical factors. Future studies should be undertaken in a larger cohort, prospective in design and controlled to address these limitations.

We found extensive psychotropic prescribing in our study investigating psychotropic pharmacotherapy in older adults with an intellectual disability (*Chapter 7*). While we can examine associations between demographic and clinical characteristics, this study is limited by lack of information regarding the motivation for prescribing the psychotropic – we can analyse the dosage data and speculate about the drug indication, but we do not have information to determine whether the particular psychotropic, for example antipsychotic, was prescribed for mental health disorders or to treat challenging behaviours. Future work should address this limitation.

There is minimal data available in intellectual disability research regarding the long term safety of prolonged use of low dose atypical antipsychotics for treating challenging behaviours, thus collecting accurate adverse effect data, specific to vascular or other known complications in a longitudinal study like IDS-TILDA would be very useful. However, it is worth noting that accurate self-reporting of side effects is difficult in people with an intellectual disability. The most recent Wave of data collected in IDS-TILDA, Wave 4 (2019/2020) also includes data arising from a 'Health-fair' where various objective measures of health (for example blood pressure, blood glucose, cholesterol, hemoglobin, c-reactive protein, TSH, follicle hair sample, urea breath test, oral health assessment and nutrition intake assessment, feet assessment) were obtained from consenting participants. Perhaps this data will allow more accurate examination of adverse effects of medication but due to Covid-19, this Health-fair was unable to be completed by all willing participants in Wave 4. Future Waves of data intend to build on these additional health assessments which will afford greater information regarding the health characteristics of participants in this study and better opportunities to address these unanswered questions.

8.5 Pathway to impact

This thesis has provided a detailed evidence base for people ageing with epilepsy and intellectual disability in Ireland, thus allowing future comparison with the ageing of the general population, a fundamental goal of the IDS-TILDA study. Two studies have been published to date, examining the impact of potential seizure threshold-lowering psychotropic medication on seizure frequency and the behavioural effects of antiepileptic drugs. Further work has been recommended in both these areas, so to inform and engage other researchers in this field, presentations at international conferences including

IASSIDD and ILAE are planned. The usefulness of the AED load ratio (PDD/DDD) was explored in detail, and found to have a potential use as a practical measure of drug burden in this population, therefore, a publication is planned exploring the results obtained from this study (*Chapter 4*) to inform both health professionals and researchers in this field. In addition, a further publication is intended to address psychotropic pharmacotherapy in people with intellectual disability in the context of psychiatric and behavioural comorbidity (*Chapter 7*). Presentation of these results at international conferences and research seminars will be used to encourage discussion and research collaboration.

A dissemination goal of this research would be to make it accessible to the general public and people with intellectual disability to encourage greater public and patient involvement in epilepsy research, and to foster increased research activities and publications. This would be achieved through engaging and sharing this research with intellectual disability advocates, disability groups and societies, including Epilepsy Ireland. A qualitative element was missing in this research, so getting the voice of the individual with epilepsy and intellectual disability in this manner would help obtain a complete understanding of the impact of these results and direct future dissemination goals, research priorities and strategies.

8.6 Conclusion

Living with an intellectual disability in Ireland is at a watershed moment. Ireland is undergoing the policy of deinstitutionalisation and moving people out of institutional settings and into community settings. This has created challenges, as providers of care in the community familiarise themselves with the comorbidities and polytherapy challenges of caring for people with an intellectual disability. Where in the past, people with an

intellectual disability were excluded from research, the current trend of PPI (public and patient involvement in research) and inclusion in research activities has shone a light on the morbidity, polypharmacy and environmental difficulties faced by people with intellectual disability. The psychiatric burden is extensive, encompassing mental health disorders, behavioural disturbances, and widespread psychotropic pharmacotherapy prescribing. Understanding the pharmaceutical care complexities, both adverse effects and appropriateness of treatment, is a necessary step in ensuring a good quality of life for people with an intellectual disability. Multidisciplinary medication reviews encompassing pharmacist, medical, and social care professional input should be undertaken regularly to ensure that optimum therapy is prescribed and adjustments made where necessary. This is particularly important in people with epilepsy and other neurological illnesses where medication regimens are complicated and the psychiatric burden is high, as highlighted in this thesis. These people are at high risk of overtreatment so tools designed to detect high medication burdens are needed to prevent unnecessary adverse effects. Ultimately, a balance must be struck between necessary treatment and ensuring the person with intellectual disability and epilepsy can enjoy the quality of life they are entitled to.

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Appendices

Appendix 1 IDS-TILDA study ethical approval

THE UNIVERSITY OF DUBLIN
TRINITY COLLEGE

SCHOOL OF MEDICINE
FACULTY OF HEALTH SCIENCES

Trinity College, Dublin 2, Ireland
Tel: +353 1 896 1476
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Professor Dermot Kelleher, MD, FRCPI, FRCP, F Med Sci
Head of School of Medicine
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School Administrator
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Prof. Mary McCarron
School of Nursing and Midwifery,
Trinity College Dublin,
24 D'Olier Street, Dublin 2

10th July, 2008

Study Title: An Intellectual Disability Supplement to the Irish Longituddinal Study on Ageing (TILDA)

Dear Prof. McCarron,

Further to the meeting of the Faculty of Health Sciences Research Ethics Committee on 27th May 2008, I am pleased to inform you that the above project has been approved without further audit.

Yours sincerely,

Dr. Orla Sheils
Chairperson
Faculty of Health Sciences Ethics Committee

Appendix 2 Medication data collection form in the PIQ

144. MEDICATIONS

We would like to record all medications that you take on a regular basis, take every day or every week. This will include prescription and non-prescription medications, over –the-counter medicines, vitamins and herbal and alternative medicines.

PLEASE WRITE DOWN ALL MEDICATIONS/TABLETS YOU TAKE AND HOW OFTEN YOU TAKE THEM, PLEASE USE ONE LINE PER MEDICATION

Don't know what medication I take, record by proxy ☐ [1] PLEASE COMPLETE MEDICATION FORM

Don't take any medication [1] GO TO QUESTION 145

Name of Medication	Dosage Strength	Frequency	Route	Date First Prescribed
Examples of medication completion form :				
Epilim Chrono	200mgs	Twice a day (BD)	Orally(PO)	Sept 2009
One touch ultra test strip(blood glucose)	1 strip	Before meals	-	June 2010
Neo-cytamen Injection(hydroxycobalamin)	1000micrograms	Monthly	IM	Nov 2010
Xalatan eye drops	2 drops (left eye)	Nocte (At night)	Instill	June 2010
Emulsifying Ointment		PRN	Topically	Jan 2009
Vegepa (Omega fishoil)		2 daily	PO	June 2005
Ensure Plus		1 daily	PO	Oct 2007

TRINITY COLLEGE DUBLIN | THE UNIVERSITY OF DUBLIN
COLÁISTE NA TRÍONÓIDE

Name of Medication	Dosage Strength	Frequency	Route	Date Prescribed
1				
2				
3				
4				
5				
6				
7				
8				
9				
10				
11				
12				
13				
14				
15				
16				
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Appendix 3 IDS-TILDA Data Protection Policy

IDS-TILDA DEPARTMENTAL DATA PROTECTION MANAGEMENT POLICY

Appendix 3 IDS-TILDA Data Protection Policy (*Continued*)

Purpose of the Policy

The purpose of this policy is to assist members of IDS-TILDA to fulfil their responsibilities with respect to the collection, storage and retention of data and records associated with, and arising from, their research activities.

This policy establishes uniform data management standards and identifies the shared responsibilities for assuring that IDS-TILDA has integrity and that it efficiently and effectively serves the needs of the department.

This policy will cover the day to day access requirements of IDS-TILDA paper data, electronic data and the equipment that gives access to the data.

Objectives of the Policy

Raise awareness that data constitute an important resource and that the value of data as a department resource is increased through its widespread and appropriate use while its value is diminished through misuse, misinterpretation, or unnecessary restriction to its access.

Help ensure that data comply with all relevant legislation such as the Data Protection Act and the Freedom of Information Act;

Raise awareness of data access v. privacy issues and formalise procedures for access management.

Improve ease of access. Assure that data is easily located, easily accessed once located, and that people have enough information about the data to understand what they have found.

Facilitate database integration.

Reduce the redundancy of the data by defining an official record of reference.

Appendix 3 IDS-TILDA Data Protection Policy (*Continued*)

Data Classification

All data to be collected, processed and stored in IDS-TILDA should be identified and classified using the college data classification table below or similar.

Data Classification	Information	Description	Examples	Handling
Non Confidential	Public	Such data is available to anyone to see, and is often made available to public via the college website,	Publications, Articles, Presentations	Access to this data is not usually restricted.
	University Internal	Such data is generally available to all staff and students in College	Publications, Articles, Presentations	Access is usually restricted to members of College Staff
Confidential	Restricted	Personal data. This data is only made available to authorised members of IDS-TILDA	Participants Name, address, telephone numbers,	Access is restricted to IDS-TILDA members only
	Critical	Sensitive personal data.	Information relating to the mental & physical health of individuals	Access to such data is tightly controlled

Data sets related to individual study participants.

Where data sets are collected relating to individuals you may also want to label data sets with regard to whether the data is.

Personal data means any information about a living individual who can be identified from that information and other information which is in, or likely to come into, the data controller's possession.

Anonymised data is data prepared from personal data but from which the person cannot be readily identified by the recipient of the information.

Coded data is identifiable personal data in which the details that could identify someone are concealed in a code, but which can readily be decoded by those using the personal data. Such coded data is not anonymised data.

Linked data is typically used when it may be necessary to refer back to the original recodes for further information, or for verification. Unlinked data usually ensures confidentiality but prevents follow-up, verification or feedback.

With both linked and unlinked anonymised data it is sometimes possible to deduce an individual's identity through combinations of information. The most important identifiers are:

- Unusual disease or treatment;
- Partial address, geocode or similar;
- Details of health professionals responsible for care;
- Specific/unusual occupation or place of work;
- Combinations of details such as birth date, place of birth etc.

Data Handling Procedures

Once data has been classified, appropriate handling procedures should be agreed on and documented.

#	Data Type	Handling Procedures
1	Critical Data	• Is authorised for use by the Data Manager, Project director only. • May not be removed from premises • Must be encrypted at all times • Must never be transported on insecure USB media
2	Restricted Data	• Is authorised for use by the Data Manager, Project Director & research staff • Must be encrypted at all times • May not be removed from premises
3	Coded Data	• Is authorised for use by Data Manager, Project Director & research staff • Must be encrypted at all times
4	Participant Contact Records	• Is authorised for use by the Participant's signed consent form. • Must be encrypted when stored & transferred • Can be transmitted by Email but only if fully encrypted
5	Public Data	• No requirement for encryption • Approved for public distribution

Appendix 3 IDS-TILDA Data Protection Policy (*Continued*)

Daily Data Management

It is the responsibility of all members of IDS-TILDA to adhere to the following office policy.

- All members of IDS-TILDA are issued with their individual secure login and password.
- Each member is responsible for their login and password and should never give this out for other people to use.
- All members have access to an encrypted laptop or desktop.
- The laptops are in a secured press in office 1. It is the responsibility of each member of staff to ensure they leave the laptop back in the press when they are finished. The press is to be locked and the key put back in the designated area.
- The Muse has five hot desks which have five encrypted desktops for members of IDS-TILDA to use. IDS-TILDA has a secure and dedicated link for accessing the required data.
-

Responsibilities

Project Director

- Responsible for ensuring project compliance with all relevant legislation
- Responsible for Data Management Policy content
- Responsible for ensuring compliance with data management policy

Data Manager

- Responsible for backup and recovery of all project data
- Responsible for promoting ongoing awareness of data management policy among project staff
- Responsible for ensuring the integrity of dataset

Researchers

- Responsible for compliance with Data Management Policy

Appendix 3 IDS-TILDA Data Protection Policy (*Continued*)

Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin

An Intellectual Disability Supplement to The Irish Longitudinal Study on Ageing

Intellectual Disability Supplement to the Irish Longitudinal Study on Ageing (IDS-TILDA)

Interdisciplinary Post Graduate Training Opportunities

Research Student information and Agreement Protocol

Intellectual Disability Supplement to TILDA,
The University of Dublin, Trinity College,
School of Nursing & Midwifery, 24 D'Olier Street,
Dublin 2,
Ireland

Telephone: (01) 8963186 / (01) 896 3187
Fax: (01) 8963001

Email: idstilda@tcd.ie

Developed	Date	Review Date
Prof. Mary McCarron, Prof. Philip McCallion, Eilish Burke	2013	
Reviewed		
Eilish Burke, MaryAnn O'Donovan, Prof Philip McCallion, Prof Mary McCarron		13.5.2016

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Appendix 3 IDS-TILDA Data Protection Policy (*Continued*)

Introduction

The Intellectual Disability Supplement to The Irish Longitudinal Study on Ageing (IDS-TILDA) is a longitudinal study of the ageing of a random and representative sample of over 700 people with intellectual disability aged 40 and over is now entering its third wave of data collection. There are opportunities to analyze the data and there may be opportunities to access data from the main TILDA project to use in comparative studies. The first and second waves of data have already supported the theses of several PhD, MSc. and MD students. Applications are currently being considered for PhD theses that may utilize either waves of data further.

Definitions of terms

Students: Refers to full/part-time PhD, MSc, MD, interns or students on placement. Herein after referred to as student.

Investigators: Refers to the principal investigator and co-principal investigator of the IDS-TILDA study; Prof Mary McCarron and Prof Philip McCallion.

Core IDS-TILD team: Please refer to governance structure of the IDS-TILDA project in

Critical Considerations

There are several critical considerations:

1. The investigators (PIs) and the core IDS-TILDA team have already identified and are continuing to identify a number of research questions that the research team itself will be addressing. Understandably pursuit of these questions will not be appropriate for a PhD or MD thesis. In addition, as the investigators agree to additional specific PhD, MSc. and MD theses this will further narrow the scope of available research questions. It is therefore important that the unique questions for a particular PhD, MSc. or MD thesis be defined and approved by the PIs/Project Manager early in any process. No work using IDS-TILDA data may proceed without this approval.
2. With reference to interns and/or students on placement it is essential that agreement of area for investigation is obtained prior to commencement of placement.
3. All Students must attain placement deliverables within the specific time and to the appropriate standard as designated by the project manager/supervisor and the principle investigators.
4. Consistent with funder goals for student training and with the investigators' own commitment to postgraduate education, participation in IDS-TILDA by students is designed to offer **research experience** as well as access to data. There will be an expectation that students will participate in trainings, data collection where appropriate (dependent on stage of project and status of student) and data analyses and any other work within the IDS-TILDA team necessary to work within the research team advancing the entire project

Appendix 3 IDS-TILDA Data Protection Policy (*Continued*)

5. For students completing a thesis using IDS-TILDA data and for achievement of advanced academic qualification, the IDS-TILDA investigators will be members of the thesis committee, preferably with the PI as the main supervisor, to ensure that all data protections and data sharing understandings are fully respected.
6. For students accessing IDS-TILDA data from another university outside Trinity College the investigators will be part of their supervisory team.
7. IDS-TILDA is a critical study whose data is already informing public policy debates and decision-making. As such the timely delivery of data is of critical concern and requires that expectations be agreed with students about timelines for completion of any agreed publications and theses.
8. Publication of findings from IDS-TILDA data must comply with Data Use Policy of the Intellectual Disability Supplement of The Irish Longitudinal Study on Ageing (see accompanying protocol).
9. Confidentially and data management protocols must be complied with at all times including restrictions on use of data outside of IDS-TILDA offices and password protected computers.

Rationale

It is precisely because the IDS-TILDA dataset offers a unique and exciting opportunity for multiple interdisciplinary students to experience being part of a national and international research team and to develop theses that are on the cutting edge of research knowledge of the ageing of people with ID that guidelines for their participation are necessary.

Expectations and Opportunities

To address the outlined considerations and to enrich the students training and placement experience there are a number of expectations and opportunities with regards the initial proposal, training, and timely publication

The Proposal

Applicants are encouraged to propose unique research questions allied to the main IDS-TILDA study and or they may be invited to undertake a structured PhD on an investigator- identified topic:

- Students should review the IDS-TILDA report to see the range of data available to begin the process of identifying research questions and considering if there is sufficient data to help answer those questions.
- Students will have the opportunity of undertaking an internship under the guidance of the PIs and direct supervision of a designated team member to help them better understand the data and develop their own unique research question. The type and duration of the internship will be worked out on an individual basis with each potential student.
- The internship will be guided by the key performance indicators specific for each student.

- Students beginning during the period between waves of data collection may have an opportunity to suggest additional protocol questions but this will not be possible at other times and any additions agreed will be limited so as not to overburden participants. Investigators decisions will be final.
- Often students may wish to add qualitative components to the protocol. These too are possible but the over-riding concern for the investigators will be the level of burden on participants and the need to preserve the sample for future waves of data collection. Investigators decisions will be final.
- A proposal in a format agreed with the investigators must be presented to the investigators who will then consider it for approval. It is likely that a face-to-face meeting will be required and students should expect that some changes to the proposal will be necessary before approval.
- In order to ensure that each students' work and the research studies being undertaken by the research team are unique, students may only access and use data that the investigators have agreed is necessary to answer the research question and study objectives identified in the proposal.
- For all students only the agreed data may be accessed as per the IDS-TILDA data protection protocol.
- As part of the proposal approval process, the student and the investigators will agree a time frame for the completion of the various components of the thesis including trainings and data collection and the student will commit to adhering to this agreed schedule. All placement students will adhere to their agreed key performance indicators and timeline as agreed on commencement of placement.
- It is recognized that there may be unforeseen circumstances influencing completion of aspects for the thesis/ placement work and it is the responsibility of the students to keep the supervisory team informed of concerns and to work with the team to agree on plans to address any such issues.
- Should issues arise a review process will be agreed upon to address the issues that have arisen. Regardless of who is the main thesis supervisor, the IDS-TILDA PI will be the final arbitrator of whether sufficient progress is being made to permit continued access to and use of IDS-TILDA data.
- It is understood that data collected as part of IDS-TILDA, even where used for a thesis becomes part of the IDS-TILDA dataset.

PhD/MD, MSc, Intern or MSc. Placement Training

IDS-TILDA offers opportunities for PhD/MD /MSc /Intern /Placements level research training likely to support the development of students for a future research career. Students whether they are F/T or P/T will commit to:

- Attendance at the full training programme or formal induction with the IDS-TILDA team offered to all field workers/and all students in the administration of the IDS-TILDA protocol and research process.
- Collection of data on 40-60 study participants under the supervision of the research team. --Where possible and /or appropriate students will be assigned

subjects to reflect their research interests, for example family carer's, or geographical regions where specific research questions are likely to be better captured.
- Participation in developing materials responsive to ethical approval requirements by various sites
- Participation in the preparation of materials to be forward to study participants and study sites, for example assist in photocopying of materials and preparation for postage in line with the 'Keeping in Touch' Strategy of the IDS-TILDA project.
- Adherence to the highest ethical principles and the meeting of requirements for confidentially, storage of data, accessing data, consent and maintenance of data integrity.
- Preparation, cleaning and entry of data.
- Assisting with analysis of data.
- Development of publications in a timely manner.
- Appropriate acknowledgment to participants and funders in all publications.

In furtherance of their preparation students will also:

- Schedule regular supervisory meetings as agreed with the supervisory team and keep record of all meetings.
- Attend PhD monthly meetings and master classes where applicable.
- Access grant writing, statistical and other training opportunities in College.
- Submit work for review on a schedule agreed with the supervisory committee.
- Submit all poster/ oral presentations, journal articles and any other publications to PIs for review prior to submission.

Timely Publication

To ensure that project needs as well as student needs are met:

1. Students must commit and adhere to the overall goals and targets of the main project as set out by the PI and project manager and research team.
2. Students must complete work on their own research question within a timeframe negotiated with their supervisory team. There will be an expectation that student transfers to PhD status will be timely and the thesis will be completed within 3-4 years. The PI cannot guarantee beyond the four year timeframe that others may not be permitted to pursue a similar question.
3. The PhD/MD/MSc student will have the opportunity to be first author on all publications resulting from the thesis with the understanding that the PIs and project staff (as determined by the PI) will be co-authors.
4. Should it not be possible for the PhD/MD/MSc student to submit articles from the thesis within one year of a successful viva/completion of the thesis in the case of MSc, the investigators may assign the first authorship to someone else with the PhD/MD/MSc student as a co-author.

Appendix 3 IDS-TILDA Data Protection Policy (*Continued*)

5. In the case of student intern/placement the publication must be at an appropriate standard judged by the IDS-TIILDA supervisor/PI, be delivered within the agreed timeframe relative to the number of week's placement and at minimum first draft level.

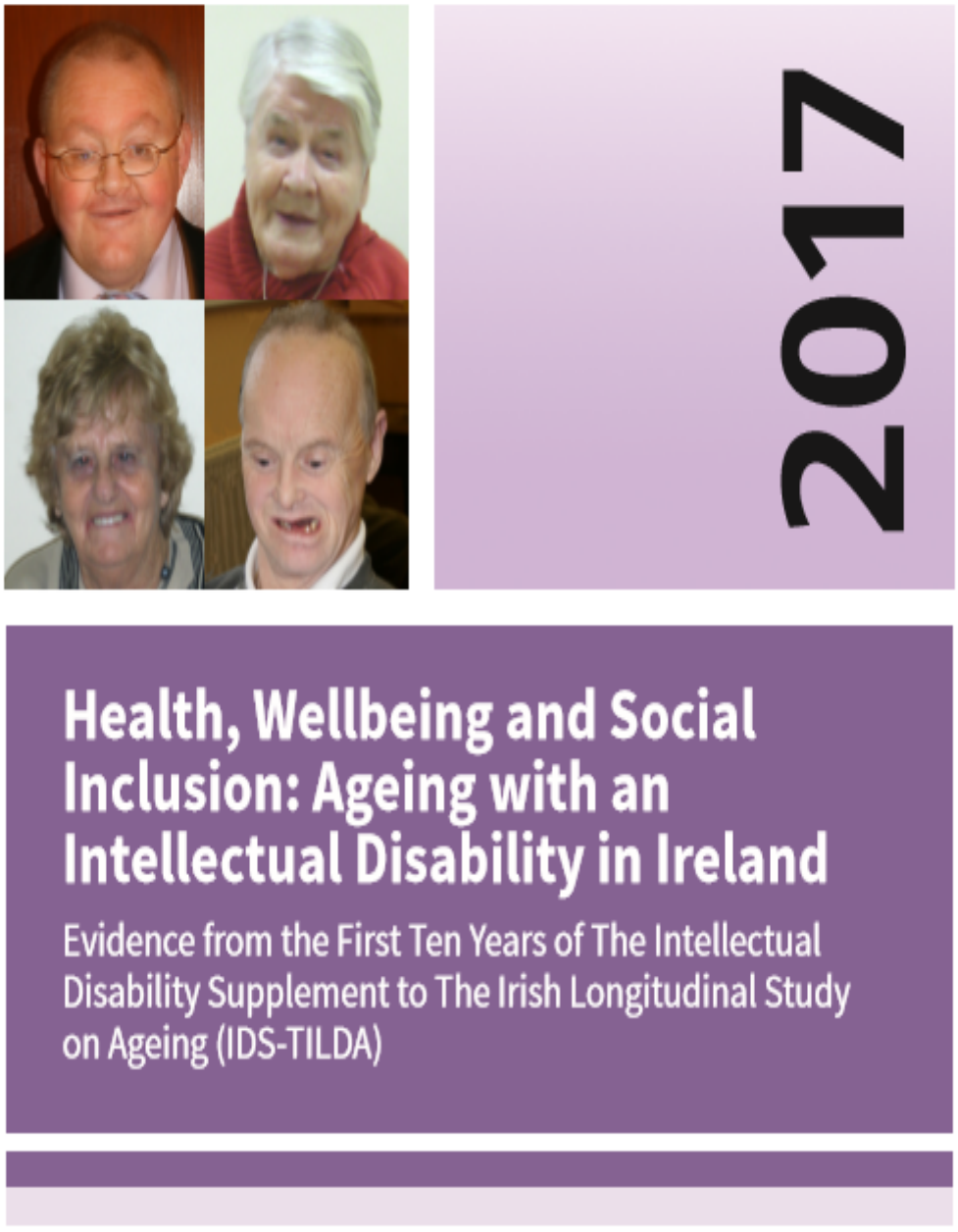
Agreement

I _____ have read the above principles document and have had the opportunity to discuss the contents with PI/Project Manager/IDS-TILDA Supervisor, and have all my questions satisfactory answered. I understand the commitments inherent within the document and I agree to fulfil and adhere to these.

_____	_____	_____
Student Signature	Principal Investigator	IDS-TILDA Supervisor
Date _____	Date_____	Date_____

Copy to be retained by Research student and copy to be retained by the IDS-TILDA office

Appendix 4 Wave 3 Report cover



Appendix 5 Example of letter of invitation to consent to interview

Trinity College Dublin
The University of Dublin

Intellectual Disability Supplement to TILDA
The University of Dublin, Trinity College
School of Nursing & Midwifery, 2 Clare Street, Dublin 2
Tel: + 353 1 896 3186/3187
Fax: + 353 1 896 3001 Email: idstilda@tcd.ie

The Intellectual Disability Supplement to The Irish Longitudinal Study on Ageing (IDS-TILDA)

Dear Participant,

Thank you for being part of the IDS-TILDA study for the past 10 years. Your support and help with our study is very important.

It has been 3 years since we last came out to speak to you. We will call out to speak to you again soon. We would like you to continue being part of the IDS-TILDA study.

You can continue to take part in this study in one of three ways:

- Independently,
- With someone to support you, or
- Another person can answer questions for you.

We want everyone to take part in the study. We need to talk to many people with an intellectual disability so we know what their lives are like as they grow older.

A researcher will phone you soon to arrange a time to call out to speak to you. A nurse will also contact you to arrange a health assessment.

For more information please read the information booklet or get someone to support you to read it. Further information can be found in the IDS-TILDA Data Statement on our website: https://www.idstilda.tcd.ie/

If you have any questions, please phone us on 01 – 896 3187.

Yours sincerely,

Prof. Mary McCarron
Professor Mary McCarron
Principal Investigator
IDS-TILDA

Appendix 6 Example of information booklet cover provided in Wave 3

£

Trinity College Dublin
The University of Dublin

An Intellectual Disability Supplement to The Irish Longitudinal Study on Ageing

Intellectual Disability Supplement to The Irish Longitudinal Study on Ageing (IDS-TILDA)

WAVE 3
INFORMATION BOOKLET

This study is being carried out by Trinity College Dublin

Appendix 7 Example of consent form in Wave 3

CONSENT FORM

IDS-TILDA PARTICIPANT Wave 3

Please read the information below and sign this consent form if you wish to take part in this third wave of the study.

I agree with the following statement

I have gone through the information about this study ☐

I know who to contact if I have any other questions. ☐

Any questions that I might have had were answered. ☐

Appendix 8 Variables used in thesis

Chapter	Carried over from Wave 1	Pre-Interview Questionnaire (PIQ)	Computer Assisted Personal Interview (CAPI)	Variables created (using variables collected in PIQ/CAPI)
Chapter 3 and Chapter 4	**Demographic characteristics** - Level of intellectual disability - Cause of intellectual disability	**Medication data** - Medication name - ATC code - Strength - Frequency - Route of administration - Date prescribed	**Demographic characteristics** - Gender - Age range - Type of residence **Do you suffer from the following type of seizure?** - Tonic-clonic - Tonic - Atonic - Clonic - Myoclonic - Absence - Simple partial - Complex partial - Other - Unclear - Don't know **Since your last interview, has a doctor ever diagnosed you with the following conditions?** - Dementia only - Alzheimer's Disease only - Parkinson's Disease - TIA - Stroke - Heart Attack - Abnormal Heart Rhythm - High Blood Pressure - High Cholesterol - Congestive heart failure	**Type of therapy** - Monotherapy - Polytherapy - No AED therapy **Number of AEDs prescribed** - 0 - 1 - 2 - 3 - 4 - 5 **Categorised number of AEDs prescribed** - No AEDs - 1-2 - 3-4 - 5-9 **Categorised type of seizures** - Generalised Seizures - Other Seizures **Exhibit challenging behaviour** - Yes/No **Type of challenging behaviour** - Self-injurious behaviour - Aggressive/destructive behaviour - Stereotyped behaviour

Appendix 8 Variables used in thesis (*Continued*)

Chapter	Carried over from Wave 1	Pre-Interview Questionnaire (PIQ)	Computer Assisted Personal Interview (CAPI)	Variables created (using other variables collected in PIQ/CAPI)
Chapter 3 and Chapter 4			- Heart murmur - Angina - Diabetes - Varicose ulcers - Arthritis - Osteoporosis - Thyroid disease - Asthma - Chronic lung disease - Constipation - Gastro reflux - Stomach ulcer - Coeliac - Irritable bowel syndrome - Chronic liver damage - Multiple sclerosis - Cerebral palsy - Scoliosis - Muscular dystrophy - Spina bifida - Cancer - Psychiatric emotional disorder **Since your last interview, has a doctor ever diagnosed you with the following emotional/ psychiatric disorders?** - Schizophrenia - Hallucinations - Psychosis - Anxiety - PTSD - Depression - Emotional problems	**Category of emotional/psychiatric disorder** - Psychotic disorder - Mood disorder - Anxiety disorder **Other CNS medicines** - Antipsychotics - Antidepressants - Anxiolytics - Hypnotics & sedatives - Lithium - Anti-cholinergic - Drugs for dementia **Seizure frequency** - None in the last year - At least one in the last year

Appendix 8 Variables used in thesis (*Continued*)

Chapter	Carried over from Wave 1	Pre-Interview Questionnaire (PIQ)	Computer Assisted Personal Interview (CAPI)	Variables created (using variables collected in PIQ/CAPI)
Chapter 3 and Chapter 4			- Mood swings - Manic depression - Something else - Unclear - Don't know **How often have you had a seizure?** - Daily - Weekly (not daily) - More than once month (not weekly) - Less than once/month **Do you keep a record of your seizures?** Yes/No **Are any of the following medications prescribed for you?** - Buccal Midazolam - Clobazam - Lorazepam - **When did you get your epilepsy reviewed?** Month/Year **Who reviewed your epilepsy?** - GP - Neurologist - Psychiatrist - Clinical Nurse Specialist - Other - Don't know	

Appendix 8 Variables used in thesis (*Continued*)

Chapter	Carried over from Wave 1	Pre-Interview Questionnaire (PIQ)	Computer Assisted Personal Interview (CAPI)	Variables created (using other variables collected in PIQ/CAPI)
Chapter 3 and Chapter 4			**Attend epilepsy clinic or specialist?** - Yes/No **Have you ever visited A&E in the last year with epilepsy?** - Yes/No **Have you ever received education on how to manage epilepsy?** - Yes/No **Does epilepsy limit your ability to do?** - Household chores - Work - Social activities - Sports activities - Driving - Going out alone - Other - Don't know None of the above	
Chapter 5	**Demographic characteristics** - Same as Chapter 3/4	**Medication data** - Same as Chapter 3/4	**Demographic characteristics** - Same as Chapter 3/4	**Type of therapy** Per Chapter 3/4 **Categorised type of seizures** Per Chapter 3/4 **Categorised total number of potential seizure threshold-lowering drugs** - 0 / 1/ 2+

Appendix 8 Variables used in thesis (*Continued*)

Chapter	Carried over from Wave 1	Pre-Interview Questionnaire (PIQ)	Computer Assisted Personal Interview (CAPI)	Variables created (using other variables collected in PIQ/CAPI)
Chapter 5				**Categorised potential seizure threshold-lowering medication risk Maudsley 2018** - Low risk - Moderate risk/high risk - No seizure threshold-lowering medication **Category of emotional/psychiatric disorder** Per Chapter 3/4 **Other CNS medicines** Per Chapter 3/4
Chapter 6	**Demographic characteristics** Same as Chapter 3/4	**Medication data** Same as Chapter 3/4 **Challenging behaviour** *Frequency & severity scale (self-injurious/ aggressive/destructive behaviour):* - Self-biting - Head hitting - Body hitting - Self-scratching - Pica - Objects in nose - Hair pulling - Teeth grinding	**Demographic characteristics** - Same as Chapter 3/4	**Type of therapy** Per Chapter 3/4 **Categorised type of seizures** Per Chapter 3/4 **Exhibit challenging behaviour** Per Chapter 3/4 **Type of challenging behaviour** Per Chapter 3/4 **Category of emotional/psychiatric disorder** Per Chapter 3/4

Appendix 8 Variables used in thesis (*Continued*)

Chapter	Carried over from Wave 1	Pre-Interview Questionnaire (PIQ)	Computer Assisted Personal Interview (CAPI)	Variables created (using other variables collected in PIQ/CAPI)
Chapter 6		- Hitting others - Kicking others - Pushing others - Biting others - Grabbing & pulling others - Scratching others - Pinching others - Verbally abusive with others - Destroying things - bullying *Frequency scale (stereotyped behaviour):* - Rocking & repetitive body movements - Sniffing objects/own body - waving & shaking arms - Manipulating - Repetitive hand and/or finger movements - Yelling & screaming - Pacing, jumping, bouncing, running - Rubbing self - Gazing at hands or objects		**Other CNS medicines** Per Chapter 3/4 **AED load** PDD/DDD (participants with epilepsy)

Appendix 8 Variables used in thesis *(Continued)*

Chapter	Carried over from Wave 1	Pre-Interview Questionnaire (PIQ)	Computer Assisted Personal Interview (CAPI)	Variables created (using other variables collected in PIQ/CAPI)
Chapter 7	**Demographic characteristics** Same as Chapter 3/4	**Medication data** Same as Chapter 3/4	**Demographic characteristics** - Same as Chapter 3/4 **Since your last interview, has a doctor ever diagnosed you with the following conditions?** Per Chapter 3/4 **Since your last interview, has a doctor ever diagnosed you with epilepsy?** Yes/No **Since your last interview, has a doctor ever diagnosed you with the following emotional/ psychiatric disorders?** Per Chapter 3/4 **Since your last interview, did you get psychiatric treatment?** Yes/No **Who gives you psychiatric treatment?** - Psychiatrist - GP - Other **Since your last interview, did you get psychological treatment?** Yes/No **Who gives you psychological treatment?** - Psychologist - Counsellor	**Type of therapy** Per Chapter 3/4 **Category of emotional/psychiatric disorder** Per Chapter 3/4 **Have categorised emotional/ psychiatric/mental health disorder?** - Yes/No **Other CNS medicines** Per Chapter 3/4 **Psychotropic drug groups** - Atypical antipsychotics - Typical antipsychotics - SSRI - SNRI - TCA - Other (trazodone/ agomelatine/mirtazapine) - Mood stabilising AED (Valproic acid/ Lamotrigine/ Carbamazepine) - Mood stabilising AED (no epilepsy diagnosis) - Anxiolytic benzodiazepines

Appendix 8 Variables used in thesis (*Continued*)

Chapter	Carried over from Wave 1	Pre-Interview Questionnaire (PIQ)	Computer Assisted Personal Interview (CAPI)	Variables created (using other variables collected in PIQ/CAPI)
Chapter 7			- CNS - Other	- Other anxiolytics (Hydroxyzine/ Buspirone) - Z drugs - Prolonged acting hypnotic benzodiazepines - Short acting hypnotic benzodiazepines - Any psychotropic medication (for mental health indication) - Antipsychotics and antidepressants - Antipsychotics and anxiolytics - Antidepressants and anxiolytics - Mood stabilising AED (no epilepsy diagnosis and antipsychotic - Antipsychotic and lithium - Antipsychotic and hypnotic and sedative - Antidepressant and hypnotic and sedative - Anxiolytic and hypnotic and sedative

Appendix 9 Communication during CAPI interview

Communication style	Total n=436 n (%)	Epilepsy diagnosis n=147 n (%)	No diagnosis of epilepsy n=289 n (%)	P value
Words				**<0.001***
Yes	343 (78.7)	101 (68.7)	242 (83.7)	
No	93 (21.3)	46 (31.3)	47 (16.3)	
Signs				0.775
Yes	41 (9.4)	13 (8.8)	28 (9.7)	
No	395 (90.6)	134 (91.2)	261 (90.3)	
Vocalisations				0.380
Yes	65 (14.9)	25 (17.0)	40 (13.8)	
No	371 (85.1)	122 (83.0)	249 (86.2)	
Eye expressions				0.868
Yes	70 (16.1)	23 (15.6)	47 (16.3)	
No	366 (83.9)	124 (84.4)	242 (83.7)	
Facial expressions				0.144
Yes	109 (25.0)	43 (29.3)	66 (22.8)	
No	327 (75.0)	104 (70.7)	223 (77.2)	
Bodily movements				**0.027***
Yes	48 (11.0)	23 (15.6)	25 (8.7)	
No	388 (89.0)	124 (84.4)	264 (91.3)	
Gestures				0.358
Yes	66 (15.1)	19 (12.9)	47 (16.3)	
No	370 (84.9)	128 (87.1)	242 (83.7)	

n=436 participants with communication data. P value: Chi Square. **Statistically significant results marked in bold and with an asterisk***.

Appendix 10 Side effects of all medication (Wave 3)

"Do you experience any side effects from taking any of your medications?"

	Total **n=226** **n (%)**	**Epilepsy diagnosis** **n=61** **n (%)**	**No epilepsy diagnosis** **n=165** **n (%)**	**P value**
Yes	18 (8.0)	4 (6.6)	14 (8.5)	0.786
No	208 (92.0)	57 (93.4)	151 (91.5)	

n=226 participants who answered this question. P value: Fisher's Exact Test 2-sided.

"Which tablet and what side effect?" – participant text answers given:

- Antidepressant side effects.
- Clopixol (zuclopenthixol) caused weight gain and low blood pressure.
- Constipation.
- Drowsiness.
- Dry mouth.
- Difficult to know which medication causes the side effects.
- Hot flushes.
- Thirsty and sleepy sometimes from haloperidol.
- Tablets make participant sleepy.
- Shaky hand- don't know what tablet.
- Sometimes gets drowsy.
- Had stomach problems from medication in the past, from depot inj.
- Tiredness.
- Toilet trips.
- Unclear.
- Weight gain- risperidone.
- Xarelto (rivaroxaban) – some nose bleeds which required hospitalisation.

Appendix 11 Median tests/descriptive statistics for demographic and clinical characteristics and AED load (n=190)

Variable	n	Median AED load (95%CI)	Median Statistic	Median p value	Variance	Min	Max	IQR	Skewness (Std Error)	Kurtosis (Std Error)
Gender	190	1.00 (0.80-1.27)	0.835	0.443 [y]						
Male	80	1.17 (0.67-1.67)			2.382	0.00	6.0	2.32	0.959 (0.269)	0.009 (0.532)
Female	110	0.98 (0.70-1.27)			2.938	0.00	8.33	1.42	1.800 (0.230)	2.953 (0.457)
Age	190	1.00 (0.80-1.27)	2.681	0.262						
<50 years	20	1.23 (0.60-1.93)			4.589	0.00	8.33	1.53	1.924 (0.512)	3.724 (0.992)
50-64 years	126	1.00 (0.80-1.42)			2.704	0.00	6.58	2.18	1.141 (0.216)	0.425 (0.428)
65+ years	44	0.82 (0.67-1.20)								
Place of residence	190	1.00 (0.80-1.27)	6.669	**0.036***						
Independent/family	20	0.50 (0.30-0.80)			1.096	0.00	4.01	1.10	1.816 (0.512)	3.307 (0.992)
Community group home	55	1.27 (0.90-2.04)			2.913	0.00	6.58	2.13	1.266 (0.322)	1.128 (0.634)
Residential	115	1.00 (0.67-1.33)			2.759	0.00	8.33	1.60	1.556 (0.226)	2.182 (0.447)
Level of intellectual disability	182	1.00 (0.80-1.30)	0.889	0.641						
Mild	29	0.83 (0.40-1.40)			1.683	0.00	5.25	1.68	1.423 (0.434)	1.795 (0.845)
Moderate	77	1.00 (0.67-1.78)			2.521	0.00	6.58	2.17	1.127 (0.274)	0.753 (0.541)
Severe/profound	76	1.12 (0.70-1.35)			2.928	0.00	8.33	1.18	1.831 (0.276)	3.195 (0.545)
Cause of intellectual disability	186	1.00 (0.80-1.27)	9.191	**0.010***						
Down Syndrome	28	0.71 (0.40-1.00)			0.463	0.00	2.58	0.85	0.940 (0.441)	0.398 (0.858)
Other aetiology	49	1.57 (1.00-2.13)			2.873	0.00	6.50	2.13	1.019 (0.340)	0.339 (0.668)
Cause unknown	109	0.87 (0.67-1.27)			2.938	0.00	8.33	2.02	1.583 (0.231)	2.257 (0.459)

Appendix 11 Median tests/descriptive statistics for demographic and clinical characteristics and AED load (n=190) (*Continued*)

Variable	n	Median AED load (95%CI)	Median Statistic	Median p value	Variance	Min	Max	IQR	Skewness (Std Error)	Kurtosis (Std Error)
Attend epilepsy clinic or specialist	186	1.00 (0.80-1.30)	4.502	**0.048*** [y]						
Yes	102	1.30 (0.90-2.27)			3.486	0.00	8.33	2.52	1.079 (0.239)	0.497 (0.474)
No	84	0.75 (0.60-1.07)			1.123	0.00	5.34	1.11	1.910 (0.263)	4.675 (0.520)
Who reviewed epilepsy- GP	186	1.00 (0.80-1.30)	0.220	0.752 [y]						
Yes	68	0.98 (0.67-1.27)			1.430	0.00	5.34	1.24	1.317 (0.291)	1.280 (0.574)
No	118	1.00 (0.75-1.50)			3.404	0.00	8.33	2.04	1.317 (0.223)	1.087 (0.442)
Who reviewed epilepsy- Psychiatrist	186	1.00 (0.80-1.30)	0.074	0.913 [y]						
Yes	54	0.93 (0.67-1.42)			1.635	0.00	4.96	1.27	1.429 (0.325)	1.558 (0.639)
No	132	1.00 (0.80-1.30)			3.137	0.00	8.33	2.15	1.389 (0.211)	1.446 (0.419)
Who reviewed epilepsy- Neurologist	186	1.00 (0.80-1.30)	5.194	**0.034*** [y]						
Yes	64	1.67 (1.00-2.58)			3.887	0.00	8.33	2.93	1.031 (0.299)	0.383 (0.590)
No	122	0.80 (0.67-1.11)			1.770	0.00	6.33	1.29	1.601 (0.219)	2.305 (0.435)
Who reviewed epilepsy- CNS	186	1.00 (0.80-1.30)	0.433	0.940 [y]						
Yes	3	2.92 (0.93-4.64)			3.447	0.93	4.64	-	-0.218 (1.225)	-
No	183	1.00 (0.80-1.30)			2.700	0.00	8.33	1.77	1.515 (0.180)	2.009 (0.357)
Who reviewed epilepsy- other	186	1.00 (0.80-1.30)	0.127	0.922 [y]						
Yes	5	0.80 (0.00-6.33)			7.977	0.00	6.33	5.18	0.762 (0.913)	-2.095 (2.000)
No	181	1.00 (0.80-1.30)			2.596	0.00	8.33	1.80	1.503 (0.181)	2.076 (0.359)

Appendix 11 Median tests/descriptive statistics for demographic and clinical characteristics and AED load (n=190) (*Continued*)

Variable	n	Median AED load (95%CI)	Median Statistic	Median p value	Variance	Min	Max	IQR	Skewness (Std Error)	Kurtosis (Std Error)
Who reviewed epilepsy-don't know	186	1.00 (0.80-1.30)	4.235	0.075 [y]						
Yes	14	0.26 (0.00-1.07)			0.610	0.00	2.67	0.87	1.849 (0.597)	3.432 (1.154)
No	172	1.06 (0.87-1.34)			2.790	0.00	8.33	1.92	1.420 (0.185)	1.629 (0.368)
Psychotic disorder	190	1.00 (0.80-1.27)	0.618	0.626						
Yes	12	1.19 (0.60-2.50)			1.635	0.00	4.64	1.67	1.484 (0.637)	2.522 (1.232)
No	178	1.00 (0.80-1.27)			2.770	0.00	8.33	1.79	1.490 (0.182)	1.875 (0.362)
Mood disorder	190	1.00 (0.80-1.27)	0.240	0.734						
Yes	71	0.93 (0.67-1.34)			2.510	0.00	8.33	1.23	1.983 (0.285)	4.565 (0.563)
No	119	1.00 (0.80-1.35)			2.806	0.00	6.58	2.27	1.269 (0.222)	0.919 (0.440)
Anxiety disorder	190	1.00 (0.80-1.27)	0.458	0.600						
Yes	65	1.07 (0.80-1.53)			2.657	0.00	8.33	1.70	1.732 (0.297)	3.707 (0.586)
No	125	0.93 (0.67-1.27)			2.730	0.00	6.58	1.96	1.401 (0.217)	1.234 (0.430)
Take antidepressants	190	1.00 (0.80-1.27)	0.919	0.423 [y]						
Yes	59	1.18 (0.80-1.60)			3.124	0.00	8.33	1.53	1.759 (0.311)	3.121 (0.613)
No	131	0.93 (0.67-1.23)			2.511	0.00	6.58	2.03	1.338 (0.212)	1.129 (0.420)
Take antipsychotics	190	1.00 (0.80-1.27)	1.044	0.383 [y]						
Yes	73	1.11 (0.80-1.42)			1.844	0.00	5.25	1.20	1.409 (0.281)	1.354 (0.555)
No	117	0.90 (0.67-1.33)			3.227	0.00	8.33	2.19	1.447 (0.224)	1.652 (0.444)
Take anxiolytics	190	1.00 (0.80-1.27)	2.807	0.138 [y]						
Yes	33	1.30 (0.80-1.76)			1.506	0.00	4.45	1.93	0.739 (0.409)	-0.398 (0.798)
No	157	0.93 (0.67-1.23)			2.951	0.00	8.33	1.82	1.529 (0.194)	1.855 (0.385)

Appendix 11 Median tests/descriptive statistics for demographic and clinical characteristics and AED load (n=190) (*Continued*)

Variable	n	Median AED load (95%CI)	Median Statistic	Median p value	Variance	Min	Max	IQR	Skewness (Std Error)	Kurtosis (Std Error)
Take hypnotic & sedatives (excl midazolam incl melatonin)	190	1.00 (0.80-1.27)	2.641	0.162 [y]						
Yes	22	1.43 (0.67-3.17)			4.418	0.00	8.33	2.57	1.598 (0.491)	2.379 (0.953)
No	168	0.93 (0.70-1.18)			2.442	0.00	6.58	1.85	1.401 (0.187)	1.350 (0.373)
Take drugs for Dementia	190	1.00 (0.80-1.27)	0.011	0.690 [y]						
Yes	4	1.29 (0.00-2.67)			1.803	0.00	2.67	2.48	0.032 (1.014)	-5.229 (2.619)
No	186	1.00 (0.80-1.27)			2.718	0.00	8.33	1.79	1.502 (0.178)	1.916 (0.355)
Take Anti-cholinergic (N04A)	190	1.00 (0.80-1.27)	0.522	0.627 [y]						
Yes	20	1.34 (0.90-2.73)			2.759	0.00	6.33	2.24	1.366 (0.512)	1.311 (0.992)
No	170	0.98 (0.67-1.23)			2.687	0.00	8.33	1.88	1.536 (0.186)	2.124 (0.370)
Seizure type categorised	190	1.00 (0.80-1.27)	11.591	**0.001***						
Generalised seizures	102	1.59 (1.00-2.25)			3.365	0.00	8.33	2.62	1.018 (0.239)	0.444 (0.474)
Other seizures	88	0.67 (0.60-0.90)			1.243	0.00	6.58	1.02	2.394 (0.257)	7.746 (0.508)
Categorised number of seizure types	190	1.00 (0.80-1.27)	20.731	**<0.001***						
1	73	1.00 (0.67-1.67)			2.258	0.00	5.34	1.95	1.063 (0.281)	0.115 (0.555)
2+	32	3.20 (1.50-4.10)			4.191	0.40	8.33	2.99	0.662 (0.414)	-0.166 (0.809)
Unknown number	85	0.67 (0.53-0.93)			1.252	0.00	6.58	1.05	2.498 (0.261)	8.347 (0.517)
Challenging behaviours	156	1.00 (0.80-1.33)	0.129	0.847 [y]						
Yes	100	0.98 (0.67-1.42)			2.730	0.00	8.33	1.90	1.588 (0.241)	2.602 (0.478)
No	56	1.06 (0.75-1.40)			2.990	0.00	6.58	2.02	1.406 (0.319)	1.374 (0.628)

Appendix 11 Median tests/descriptive statistics for demographic and clinical characteristics and AED load (n=190) (*Continued*)

Variable	n	Median AED load (95%CI)	Median Statistic	Median p value	Variance	Min	Max	IQR	Skewness (Std Error)	Kurtosis (Std Error)
Exhibit SIB	157	1.00 (0.80-1.33)	0.093	0.889 [y]						
Yes	58	1.04 (0.70-1.53)			2.485	0.00	8.33	1.43	2.136 (0.314)	5.951 (0.618)
No	99	1.00 (0.67-1.33)			3.025	0.00	6.58	2.27	1.224 (0.243)	0.621 (0.481)
Exhibit aggressive/ destructive behaviour	151	1.00 (0.80-1.34)	0.694	0.505 [y]						
Yes	61	1.17 (0.67-1.60)			3.490	0.00	8.33	2.20	1.404 (0.306)	1.701 (0.604)
No	90	0.94 (0.67-1.33)			2.444	0.00	6.58	1.80	1.527 (0.254)	2.000 (0.503)
Exhibit stereotyped behaviour	156	1.00 (0.80-1.33)	1.242	0.340 [y]						
Yes	79	0.93 (0.67-1.35)			2.448	0.00	8.33	1.34	1.844 (0.271)	4.142 (0.535)
No	77	1.11 (0.80-1.40)			3.164	0.00	6.58	2.12	1.298 (0.274)	0.931 (0.541)

[y] Yates Continuity Correction. ** unable to compute due to lack of power

- Information not available. **Statistically significant results marked in bold and with as asterisk*.**

Note:
Psychotic Disorder encompasses psychosis, hallucinations and schizophrenia.
Mood Disorder encompasses depression, manic depression, mood swings and emotional problems.
Anxiety Disorder encompasses anxiety.
Seizure type categorized is based on 2017 ILAE classification of seizures.

Appendix 12 Median tests/descriptive statistics of AEDs and AED load (n=190)

Variable	n	Median AED load (95% CI)	Median Statistic	df	Median p value	Variance	Min	Max	IQR	Skewness (Std Error)	Kurtosis (Std Error)
Carbamazepine	190	1.00 (0.80-1.27)	6.323	1	**0.018*[y]**						
Yes	65	1.47 (0.90-1.80)				1.926	0.10	5.25	2.04	0.948 (0.297)	-0.087 (0.586)
No	125	0.83 (0.67-1.00)				3.077	0.00	8.33	1.63	1.705 (0.217)	2.495 (0.430)
Valproic acid	190	1.00 (0.80-1.27)	8.785	1	**0.005*[y]**						
Yes	74	1.41 (1.00-1.93)				2.614	0.13	6.56	2.47	1.036 (0.279)	0.220 (0.552)
No	116	0.73 (0.60-1.00)				2.581	0.00	8.33	1.34	1.964 (0.225)	4.078 (0.446)
Lamotrigine	190	1.00 (0.80-1.27)	28.673	1	**<0.001*[y]**						
Yes	59	1.67 (1.33-2.53)				2.856	0.33	8.33	2.23	1.222 (0.311)	1.466 (0.613)
No	131	0.67 (0.60-0.93)				2.311	0.00	6.58	1.27	1.836 (0.212)	3.057 (0.420)
Levetiracetam	190	1.00 (0.80-1.27)	25.185	1	**<0.001*[y]**						
Yes	45	3.13 (2.00-4.10)				4.252	0.17	8.33	3.43	0.356 (0.354)	-0.626 (0.695)
No	145	0.80 (0.67-0.93)				1.169	0.00	5.34	1.10	1.577 (0.201)	2.508 (0.400)
Phenytoin	190	1.00 (0.80-1.27)	7.695	1	**0.014*[y]**						
Yes	10	3.03 (1.59-4.10)				2.356	1.00	6.58	1.60	1.162 (0.687)	2.502 (1.334)
No	180	0.93 (0.70-1.17)				2.593	0.00	8.33	1.52	1.616 (0.181)	2.365 (0.360)
Eslicarbazepine	190	1.00 (0.80-1.27)	2.246	1	0.431[y]						
Yes	2	5.56 (4.62-6.50)				1.767	4.62	6.50	-	-	-
No	188	1.00 (0.80-1.23)				2.541	0.00	8.33	1.74	1.537 (0.177)	2.204 (0.353)
Zonisamide	190	1.00 (0.80-1.27)	10.497	1	**0.004*[y]**						
Yes	9	4.92 (4.11-6.56)				1.480	3.23	6.58	2.21	-0.207 (0.717)	-1.385 (1.400)
No	181	0.93 (0.70-1.17)				2.086	0.00	8.33	1.48	1.677 (0.181)	3.275 (0.359)

Appendix 12 Median tests/descriptive statistics of AEDs and AED load (n=190) (*Continued*)

Variable	n	Median AED load (95% CI)	Median Statistic	df	Median p value	Variance	Min	Max	IQR	Skewness (Std Error)	Kurtosis (Std Error)
Pregabalin	190	1.00 (0.80-1.27)	2.193	1	0.304 [y]						
Yes	5	2.04 (0.57-8.33)				9.667	0.57	8.33	5.36	1.193 (0.913)	0.748 (2.000)
No	185	1.00 (0.80-1.23)				2.460	0.00	6.58	1.77	1.387 (0.179)	1.286 (0.355)
Lacosamide	190	1.00 (0.80-1.27)	5.706	1	0.053 [y]						
Yes	5	4.01 (2.67-5.34)				1.255	2.67	5.34	2.17	-0.124 (0.913)	-1.918 (2.000)
No	185	0.95 (0.75-1.20)				2.564	0.00	8.33	1.57	1.630 (0.179)	2.540 (0.355)
Topiramate	190	1.00 (0.80-1.27)	6.884	1	**0.027*** [y]						
Yes	6	4.23 (2.00-6.56)				2.752	2.00	6.56	2.93	0.177 (0.845)	-0.633 (1.741)
No	184	0.94 (0.75-1.18)				2.489	0.00	8.33	1.60	1.613 (0.179)	2.524 (0.356)
Rufinamide	190	1.00 (0.80-1.27)	2.246	1	0.431 [y]						
Yes	2	4.26 (3.62)				0.819	3.62	4.90	-	-	-
No	188	1.00 (0.80-1.23)				2.639	0.00	8.33	1.74	1.556 (0.177)	2.194 (0.353)
Primidone	190	1.00 (0.80-1.27)	2.246	1	0.431 [y]						
Yes	2	3.32 (2.53-4.10)				1.232	2.53	4.10	1.57	-	-
No	188	1.00 (0.80-1.23)				2.681	0.00	8.33	1.74	1.536 (0.177)	2.066 (0.353)
Phenobarbital	190	1.00 (0.80-1.27)	7.766	1	**0.012*** [y]						
Yes	13	2.36 (1.30-4.96)				3.373	0.80	6.56	3.38	0.664 (0.616)	-0.608 (1.191)
No	177	0.93 (0.67-1.17)				2.512	0.00	8.33	1.57	1.630 (0.183)	2.572 (0.363)
Clobazam	190	1.00 (0.80-1.27)	26.233	1	**<0.001*** [y]						
Yes	21	3.60 (2.60-4.92)				3.062	1.33	8.33	2.39	0.838 (0.501)	0.676 (0.972)
No	169	0.80 (0.67-1.00)									

Appendix 12 Median tests/descriptive statistics of AEDs and AED load (n=190) (*Continued*)

Variable	n	Median AED load (95% CI)	Median Statistic	df	Median p value	Variance	Min	Max	IQR	Skewness (Std Error)	Kurtosis (Std Error)
Clonazepam	190	1.00 (0.80-1.27)	5.558	1	**0.041*** [y]						
Yes	11	1.76 (0.93-5.25)				5.941	0.25	8.33	3.19	1.329 (0.661)	1.362 (1.279)
No	179	0.93 (0.70-1.20)				2.433	0.00	6.58	1.77	1.416 (0.182)	1.421 (0.361)

[y] Yates Continuity Correction. ** unable to compute due to lack of power. - Information not available. Due to low numbers of participants prescribed some AEDs (<5), gabapentin and perampanel were removed from table. **Statistically significant results marked in bold and with as asterisk*.**

Appendix 13 Median tests/descriptive statistics of potential seizure threshold-lowering psychotropic drugs and AED load (n=190)

Variable	n	Median AED load (95% CI)	Median Statistic	df	Median p value	Variance	Min	Max	IQR	Skewness (Std Error)	Kurtosis (Std Error)
Chlorpromazine	190	1.00 (0.80-1.27)	1.012	1	0.479[y]						
Yes	12	0.67 (0.53-1.66)				0.793	0.00	2.73	1.07	1.061 (0.637)	0.111 (1.232)
No	178	1.00 (0.80-1.30)				2.802	0.00	8.33	1.86	1.451 (0.182)	1.721 (0.362)
Haloperidol	190	1.00 (0.80-1.27)	0.241	1	0.927[y]						
Yes	3	0.90 (0.00-1.87)				0.875	0.00	1.87	-	0.112 (1.225)	-
No	187	1.00 (0.80-1.30)				2.717	0.00	8.33	1.83	1.486 (0.178)	1.877 (0.354)
Zuclopenthixol	190	1.00 (0.80-1.27)	0.241	1	0.927[y]						
Yes	3	0.60 (0.00-1.30)				0.423	0.00	1.30	-	0.230 (1.225)	-
No	187	1.00 (0.80-1.30)				2.714	0.00	8.33	1.83	1.480 (0.178)	1.870 (0.354)
Olanzapine	190	1.00 (0.80-1.27)	1.785	1	0.259[y]						
Yes	27	1.33 (0.67-2.04)				2.368	0.00	5.25	1.46	1.183 (0.448)	0.397 (0.872)
No	163	0.93 (0.70-1.23)				2.754	0.00	8.33	1.96	1.557 (0.190)	2.192 (0.378)
Quetiapine	190	1.00 (0.80-1.27)	0.254	1	0.871[y]						
Yes	9	1.33 (0.58-2.68)				1.862	0.33	4.64	1.45	1.773 (0.717)	3.157 (1.400)
No	181	1.00 (0.80-1.27)				2.742	0.00	8.33	1.82	1.492 (0.181)	1.913 (0.359)
Lithium	190	1.00 (0.80-1.27)	5.706	1	0.053[y]						
Yes	5	2.13 (1.66-8.33)				7.831	1.66	8.33	3.65	2.145 (0.913)	4.666 (2.000)
No	185	0.95 (0.75-1.20)				2.507	0.00	6.58	1.77	1.380 (0.179)	1.193 (0.355)
Risperidone	190	1.00 (0.80-1.27)	0.002	1	0.860[y]						
Yes	23	0.93 (0.67-1.59)				1.313	0.00	4.80	1.07	1.592 (0.481)	3.091 (0.935)
No	167	1.00 (0.80-1.33)				2.870	0.00	8.33	1.97	1.443 (0.188)	1.674 (0.374)
Aripiprazole	190	1.00 (0.80-1.27)	0.329	1	0.905[y]						
Yes	5	2.13 (0.00-2.73)				1.315	0.00	2.73	2.12	-0.864 (0.913)	-0.931 (2.000)
No	185	1.00 (0.80-1.27)				2.735	0.00	8.33	1.76	1.508 (0.179)	1.911 (0.355)

Appendix 13 Median tests/descriptive statistics of potential seizure threshold-lowering psychotropic drugs and AED load (n=190) (*Continued*)

Variable	n	Median AED load (95% CI)	Median Statistic	df	Median p value	Variance	Min	Max	IQR	Skewness (Std Error)	Kurtosis (Std Error)
Citalopram	190	1.00 (0.80-1.27)	1.251	1	0.540 [y]						
Yes	4	4.63 (0.00-4.96)				5.654	0.00	4.96	3.81	-1.953 (1.014)	3.835 (2.619)
No	186	1.00 (0.80-1.23)				2.574	0.00	8.33	1.73	1.598 (0.178)	2.434 (0.355)
Escitalopram	190	1.00 (0.80-1.27)	1.571	1	0.315 [y]						
Yes	18	0.87 (0.57-1.73)				2.543	0.00	6.56	1.29	2.331 (0.536)	6.332 (1.038)
No	172	1.00 (0.80-1.33)				2.714	0.00	8.33	1.88	1.443 (0.185)	1.761 (0.368)
Venlafaxine	190	1.00 (0.80-1.27)	0.767	1	0.607 [y]						
Yes	8	1.60 (0.00-5.34)				2.810	0.00	5.34	2.04	1.443 (0.752)	2.626 (1.481)
No	182	0.98 (0.80-1.23)				2.699	0.00	8.33	1.79	1.514 (0.180)	2.002 (0.358)
Paroxetine	190	1.00 (0.80-1.27)	0.241	1	0.927 [y]						
Yes	3	0.67 (0.60-1.42)				0.207	0.60	1.42	-	1.686 (1.225)	-
No	187	1.00 (0.80-1.30)				2.724	0.00	8.33	1.83	1.476 (0.178)	1.855 (0.354)
Fluoxetine	190	1.00 (0.80-1.27)	0.926	1	0.585 [y]						
Yes	6	1.30 (0.00-4.37)				2.420	0.00	4.37	2.50	1.012 (0.845)	0.751 (1.741)
No	184	1.00 (0.80-1.23)				2.712	0.00	8.33	1.76	1.516 (0.179)	1.989 (0.356)
Mirtazapine	190	1.00 (0.80-1.27)	0.241	1	0.857 [y]						
Yes	11	1.07 (0.40-2.00)				0.770	0.00	3.13	1.03	0.982 (0.661)	1.246 (1.279)
No	179	1.00 (0.80-1.30)				2.802	0.00	8.33	1.90	1.457 (0.182)	1.734 (0.361)
Sertraline	190	1.00 (0.80-1.27)	0.112	1	0.905 [y]						
Yes	5	1.00 (0.25-2.67)				0.881	0.25	2.67	1.53	1.408 (0.913)	2.297 (2.000)
No	185	1.00 (0.80-1.30)				2.738	0.00	8.33	1.80	1.479 (0.179)	1.848 (0.355)

Appendix 13 Median tests/descriptive statistics of potential seizure threshold-lowering psychotropic drugs and AED load (n=190) (*Continued*)

Variable	n	Median AED load (95% CI)	Median Statistic	df	Median p value	Variance	Min	Max	IQR	Skewness (Std Error)	Kurtosis (Std Error)
Trazodone	190	1.00 (0.80-1.27)	1.688	1	0.361 [y]						
Yes	7	1.80 (0.00-5.25)				2.858	0.00	5.25	1.72	1.446 (0.794)	2.995 (1.587)
No	183	1.00 (0.80-1.23)				2.697	0.00	8.33	1.83	1.514 (0.180)	2.001 (0.357)

[y] Yates Continuity Correction. ** unable to compute due to lack of power. -Information not available. Due to low numbers of participants prescribed some potential seizure threshold lowering psychotropic drugs (<5), flupenthixol, promazine, trifluoperazine, trimipramine and duloxetine were removed from table. **Statistically significant results marked in bold and with as asterisk*.**

Appendix 14 Median tests/descriptive statistics of epilepsy limiting activities and AED load (n=190)

Variable	n	Median AED load (95%CI)	Median Statistic	df	Median p value	Variance	Min	Max	IQR	Skewness (Std Error)	Kurtosis (Std Error)
Household chores	190	1.00 (0.80-1.27)	8.914	1	**0.007*** [y]						
Yes	14	3.29 (1.23-6.33)				4.347	0.60	6.58	3.76	0.292 (0.597)	-1.178 (1.154)
No	176	0.93 (0.67-1.17)				2.293	0.00	8.33	1.57	1.642 (0.183)	2.807 (0.364)
Work	190	1.00 (0.80-1.27)	8.914	1	**0.007*** [y]						
Yes	14	3.04 (1.23-6.50)				5.538	0.60	8.33	4.07	0.668 (0.597)	-0.429 (1.154)
No	176	0.92 (0.67-1.17)				2.165	0.00	6.56	1.57	1.434 (0.183)	1.467 (0.364)
Social activities	190	1.00 (0.80-1.27)	9.547	1	**0.004*** [y]						
Yes	20	2.55 (1.23-4.62)				5.910	0.00	8.33	3.77	0.604 (0.512)	-0.663 (0.992)
No	170	0.92 (0.67-1.16)				2.026	0.00	6.56	1.50	1.410 (0.186)	1.408 (0.370)
Sports activities	190	1.00 (0.80-1.27)	10.082	1	**0.004*** [y]						
Yes	12	4.20 (2.43-6.50)				5.025	0.60	8.33	3.53	0.171 (0.637)	-0.236 (1.232)
No	178	0.93 (0.70-1.17)				2.076	0.00	6.56	1.50	1.480 (0.182)	1.737 (0.362)
Driving	190	1.00 (0.80-1.27)	5.558	1	**0.041*** [y]						
Yes	11	3.40 (1.00-6.50)				3.979	0.67	6.58	2.78	0.495 (0.661)	-0.464 (1.279)
No	179	0.93 (0.70-1.18)				2.452	0.00	8.33	1.53	1.612 (0.182)	2.505 (0.361)
Going out alone	190	1.00 (0.80-1.27)	15.495	1	**<0.001*** [y]						
Yes	25	3.17 (1.73-4.44)				4.655	0.60	8.33	3.48	0.576 (0.464)	-0.493 (0.902)
No	165	0.83 (0.67-1.00)				1.862	0.00	6.56	1.39	1.507 (0.189)	1.814 (0.376)
Other	190	1.00 (0.80-1.27)	0.329	1	0.905 [y]						
Yes	5	2.80 (0.95-6.58)				5.558	0.95	6.58	4.37	0.790 (0.913)	-0.318 (2.000)
No	185	1.00 (0.75-1.27)				2.582	0.00	8.33	1.74	1.528 (0.179)	2.120 (0.355)

Appendix 14 Median/descriptive statistics of epilepsy limiting activities and AED load (n=190) (*Continued*)

Variable	n	Median AED load (95%CI)	Median Statistic	df	Median p value	Variance	Min	Max	IQR	Skewness (Std Error)	Kurtosis (Std Error)
None of the above	190	1.00 (0.80-1.27)	13.628	1	**<0.001*** [y]						
Yes	147	0.80 (0.67-1.00)				1.755	0.00	6.56	1.26	1.702 (0.200)	2.699 (0.397)
No	43	2.58 (1.35-3.60)				4.215	0.00	8.33	3.10	0.717 (0.361)	-0.065 (0.709)

[y] Yates Continuity Correction. ** unable to compute due to lack of power. -Information not available. **Statistically significant results marked in bold and with as asterisk*.**

Appendix 15 Mann Whitney U analysis for AEDs and AED load (n=190)

Variable	n	Median AED load (95%CI)	Mann Whitney U	P value	Mean rank	Z value	Approximate r value: z/√N	Cohen effect
Carbamazepine	190	1.00 (0.80-1.27)	3144.500	**0.011***		-2.556	0.2	Small effect
Yes	65	1.47 (0.90-1.80)			109.62			
No	125	0.83 (0.67-1.00)			88.16			
Valproic Acid	190	1.00 (0.80-1.27)	2877.500	**<0.001***		-3.831	0.3	Medium effect
Yes	74	1.41 (1.00-1.93)			114.61			
No	116	0.73 (0.60-1.00)			83.31			
Lamotrigine	190	1.00 (0.80-1.27)	2048.500	**<0.001***		-5.184	0.4	Medium effect
Yes	59	1.67 (1.33-2.53)			126.28			
No	131	0.67 (0.60-0.93)			81.64			
Levetiracetam	190	1.00 (0.80-1.27)	1217.500	<0.001**		-6.353	0.5	Large effect
Yes	45	3.13 (2.00-4.10)			140.94			
No	145	0.80 (0.67-0.93)			81.40			
Phenytoin	190	1.00 (0.80-1.27)	348.000	**0.001***		-3.265	0.2	Small effect
Yes	10	3.03 (1.59-4.10)			150.70			
No	180	0.93 (0.70-1.17)			92.43			
Eslicarbazepine	190	1.00 (0.80-1.27)	16.000	**0.009***		-2.226	0.2	Small effect
Yes	2	5.56 (4.62-6.50)			181.50			
No	188	1.00 (0.80-1.23)			94.59			
Zonisamide	190	1.00 (0.80-1.27)	66.000	**<0.001***		-4.654	0.3	Medium effect
Yes	9	4.92 (4.11-6.56)			178.67			
No	181	0.93 (0.70-1.17)			91.36			

Appendix 15 Mann Whitney U analysis for AEDs and AED load (n=190) (*Continued*)

Variable	n	Median AED load (95%CI)	Mann Whitney U	P value	Mean rank	Z value	Approximate r value: z/√N	Cohen effect
Lacosamide	190	1.00 (0.80-1.27)	92.000	**0.002***		-3.057	0.2	Small effect
Yes	5	4.01 (2.67-5.34)			169.60			
No	185	0.95 (0.75-1.20)			93.50			
Topiramate	190	1.00 (0.80-1.27)	123.500	**0.001***		-3.236	0.2	Small effect
Yes	6	4.23 (2.00-6.56)			166.92			
No	184	0.94 (0.75-1.18)			93.17			
Rufinamide	190	1.00 (0.80-1.27)	34.000	**0.036***		-1.993	0.1	Small effect
Yes	2	4.26 (3.62)			172.50			
No	188	1.00 (0.80-1.23)			94.68			
Primidone	190	1.00 (0.80-1.27)	62.000	0.114		-1.631	0.1	Small effect
Yes	2	3.32 (2.53-4.10)			158.50			
No	188	1.00 (0.80-1.23)			94.83			
Phenobarbital	190	1.00 (0.80-1.27)	523.000	**0.001***		-3.283	0.2	Small effect
Yes	13	2.36 (1.30-4.96)			143.77			
No	177	0.93 (0.67-1.17)			91.95			
Pregabalin	190	1.00 (0.80-1.27)	256.000	0.088		-1.704	0.1	Small effect
Yes	5	2.04 (0.57-8.33)			136.80			
No	185	1.00 (0.80-1.23)			94.38			
Clobazam	190	1.00 (0.80-1.27)	382.500	**<0.001***		-5.864	0.4	Medium effect
Yes	21	3.60 (2.60-4.92)			161.79			
No	169	0.80 (0.67-1.00)			87.26			

Appendix 15 Mann Whitney U analysis for AEDs and AED load (n=190) (*Continued*)

Variable	n	Median AED load (95%CI)	Mann Whitney U	P value	Mean rank	Z value	Approximate r value: z/√N	Cohen effect
Clonazepam	190	1.00 (0.80-1.27)	603.500	**0.031***		-2.155	0.2	Small effect
Yes	11	3.60 (2.60-4.92)			130.14			
No	179	0.80 (0.67-1.00)			93.37			

** Does not Satisfy assumption of equal distributions so caution with p value as fails assumption of non-parametric tests- see Levine table 18 in appendices. Cohen (1988) criteria for r: 0.1= small effect, 0.3= medium effect, 0.5=large effect, 0.7=very large effect. Due to low numbers of participants prescribed some AEDs (<5), gabapentin, perampanel were removed from table. S**tatistically significant results marked in bold & with an asterisk*.**

Appendix 16 Median test/descriptive statistics for miscellaneous variables and AED load (n=190)

Variable	n	Median AED load (95% CI)	Median Statistic	df	Median p value	Variance	Min	Max	IQR	Skewness (Std Error)	Kurtosis (Std Error)
Type of therapy	168	1.19 (0.95-1.47)	117.265	1	**<0.001*** [y]						
Monotherapy	78	0.67 (0.60-0.67)				0.092	0.10	1.67	0.41	0.664 (0.272)	0.667 (0.538)
Polytherapy	90	2.47 (1.93-2.92)				2.702	0.57	8.33	2.45	0.965 (0.254)	0.532 (0.503)
Seizure frequency	184	1.00 (0.80-1.30)	20.930	1	**<0.001***						
None in last Year	110	0.67 (0.60-0.90)				1.031	0.00	4.96	0.94	1.698 (0.230)	3.082 (0.457)
At least one in last Year	74	2.13 (1.50-2.92)				3.893	0.00	8.33	3.07	0.738 (0.279)	-0.189 (0.552)
Categorized number of AED's	168	1.19 (0.95-1.47)	69.641	2	**<0.001***						
1-2 AED	116	0.80 (0.67-0.93)				0.390	0.10	3.62	0.76	1.553 (0.225)	3.223 (0.446)
3-4 AED	45	3.23 (2.68-3.96)				1.919	1.18	6.58	2.02	0.572 (0.354)	-0.298 (0.695)
5-9 AED	7	5.07 (4.01-8.33)				2.378	4.01	8.33	2.46	1.267 (0.794)	1.185 (1.587)
Attend epilepsy clinic or specialist	186	1.00 (0.80-1.30)	4.502	1	**0.048*** [y]						
Yes	102	1.30 (0.90-2.27)				3.486	0.00	8.33	2.52	1.079 (0.239)	0.497 (0.474)
No	84	0.75 (0.60-1.07)				1.123	0.00	5.34	1.11	1.910 (0.263)	4.675 (0.520)
Visited A&E with epilepsy	171	1.00 (0.80-1.33)	0.799	1	0.523						
Yes	17	1.87 (0.67-2.92)				2.819	0.33	6.00	2.66	0.927 (0.550)	0.354 (1.063)
No	154	1.00 (0.75-1.30)				2.750	0.00	8.33	1.76	1.580 (0.195)	2.276 (0.389)
Had education to manage Epilepsy?	173	1.00 (0.80-1.30)	3.271	1	0.103						
Yes	42	1.60 (1.00-2.43)				2.915	0.00	6.58	2.49	0.899 (0.365)	0.222 (0.717)
No	131	0.90 (0.67-1.18)				2.442	0.00	8.33	1.40	1.803 (0.212)	3.468.420)

[y] Yates Continuity Correction. ** unable to compute due to lack of power. - Information not available. **Statistically significant results marked in bold and with as asterisk*.**

Appendix 17 Levine test for homogeneity of variance – demographic and clinical factors

Variable + AED Load	Levine Statistic (Based on median & with adjusted df)	Df1	Df2	P value	Satisfy assumption of equal distributions
Gender	0.293	1	174.461	0.589	Yes
Age	1.986	2	172.011	0.140	Yes
Place of residence	1.564	2	180.913	0.212	Yes
Level of intellectual disability	0.640	2	170.601	0.529	Yes
Cause of intellectual disability	3.539	2	156.732	**0.031**	**No**
Who reviewed epilepsy - GP	5.952	1	159.261	**0.016**	**No**
Who reviewed epilepsy - psychiatrist	3.006	1	171.357	0.085	Yes
Who reviewed epilepsy - neurologist	12.520	1	174.728	**0.001**	**No**
Who reviewed epilepsy - CNS	0.011	1	183.788	0.917	Yes
Who reviewed epilepsy - other	2.391	1	161.740	0.124	Yes
Who reviewed epilepsy - don't Know	3.648	1	176.409	0.058	Yes
Do you suffer - psychotic disorder	0.583	1	185.310	0.446	Yes
Do you suffer - mood disorder	1.081	1	188.000	0.300	Yes
Do you suffer - anxiety disorder	0.043	1	187.629	0.835	Yes
Other psychotropic class - antidepressants	0.038	1	185.889	0.845	Yes
Other psychotropic class - antipsychotics	2.841	1	172.268	0.094	Yes
Other psychotropic class - anxiolytics	0.870	1	173.910	0.352	Yes
Other psychotropic class - hypnotics & Sedatives excluding midazolam including melatonin	1.150	1	177.782	0.285	Yes
Other psychotropic class - drugs for dementia	<0.001	1	185.163	0.986	Yes
Other psychotropic class - anti-cholinergic	<0.001	1	188.000	0.993	Yes
Seizure type categorised	20.851	1	173.532	**<0.001**	**No**
Categorised number of seizure types	9.727	2	177.751	**<0.001**	**No**
Challenging behaviours	0.090	1	153.671	0.764	Yes
Exhibit SIB	1.299	1	154.805	0.256	Yes
Exhibit Aggressive/destructive behaviour	1.212	1	146.350	0.273	Yes
Exhibit Stereotyped behaviour	1.142	1	152.688	0.287	Yes

If the p value is significant, then the null hypothesis is rejected which means the assumption of equal distributions between the two groups is not satisfied. Therefore, cannot interpret the p value from the Mann Whitney U test. **Statistically significant results marked in bold and with an asterisk***.

Appendix 18 Levine test for potential seizure threshold-lowering psychotropic drugs, AEDs & limiting activities

Variable + AED load	Levine statistic (based on median & with adjusted df)	Df1	Df2	P value	Satisfy assumption of equal distributions
Potential seizure threshold-lowering chlorpromazine	2.041	1	182.515	0.155	Yes
Potential seizure threshold-lowering trifluoperazine	-	-	-	-	-
Potential seizure threshold-lowering haloperidol	0.508	1	186.619	0.477	Yes
Potential seizure threshold-lowering zuclopenthixol	0.929	1	186.317	0.336	Yes
Potential seizure threshold-lowering olanzapine	0.035	1	185.911	0.851	Yes
Potential seizure threshold-lowering quetiapine	0.438	1	186.731	0.509	Yes
Potential seizure threshold-lowering lithium	0.315	1	155.439	0.575	Yes
Potential seizure threshold-lowering risperidone	2.123	1	180.889	0.147	Yes
Potential seizure threshold-lowering aripiprazole	0.280	1	186.519	0.597	Yes
Potential seizure threshold-lowering promazine	-	-	-	-	-
Potential seizure threshold-lowering citalopram	0.102	1	177.989	0.750	Yes
Potential seizure threshold-lowering escitalopram	0.567	1	187.882	0.452	Yes
Potential seizure threshold-lowering venlafaxine	0.021	1	187.781	0.886	Yes
Potential seizure threshold-lowering paroxetine	1.389	1	186.377	0.240	Yes
Potential seizure threshold-lowering fluoxetine	0.047	1	187.768	0.829	Yes
Potential seizure threshold-lowering mirtazapine	1.669	1	181.069	0.198	Yes
Potential seizure threshold-lowering sertraline	0.889	1	185.734	0.347	Yes
Potential seizure threshold-lowering trimipramine	-	-	-	-	-
Potential seizure threshold-lowering trazodone	0.027	1	187.925	0.870	Yes
Potential seizure threshold-lowering duloxetine	-	-	-	-	-

Appendix 18 Levine test for potential seizure threshold-lowering psychotropic drugs, AEDs & limiting activities (*Continued*)

Variable + AED load	Levine statistic (based on median & with adjusted df)	Df1	Df2	P value	Satisfy assumption of equal distributions
AED - carbamazepine	0.163	1	166.126	0.687	Yes
AED - valproic acid	1.287	1	184.346	0.258	Yes
AED - lamotrigine	2.252	1	187.739	0.135	Yes
AED - levetiracetam	39.118	1	174.441	**<0.001***	**No**
AED - phenytoin	0.021	1	187.027	0.886	Yes
AED - eslicarbazepine	0.042	1	187.000	0.839	Yes
AED - zonisamide	0.001	1	184.157	0.981	Yes
AED - pregabalin	3.161	1	158.108	0.077	Yes
AED - lacosamide	0.167	1	185.390	0.684	Yes
AED - gabapentin	-	-	-	--	-
AED - topiramate	0.139	1	186.603	0.710	Yes
AED - rufinamide	0.292	1	187.000	0.590	Yes
AED - primidone	0.152	1	187.000	0.697	Yes
AED - phenobarbital	0.769	1	187.992	0.382	Yes
Limiting Activities - household chores	3.676	1	187.812	0.057	Yes
Limiting Activities - work	6.087	1	184.638	**0.015***	**No**
Limiting Activities - social activities	12.180	1	180.040	**0.001***	**No**
Limiting Activities - sports activities	3.952	1	186.025	**0.048***	**No**
Limiting Activities - driving	1.240	1	187.915	0.267	Yes
Limiting Activities - going out alone	10.684	1	186.371	**0.001***	**No**
Limiting Activities - other	1.128	1	187.918	0.289	Yes
Limiting Activities - none of the above	15.443	1	186.211	**<0.001**	**No**
Limiting Activities - don't know	-	-	-	-	-

If the p value is significant, then the null hypothesis is rejected which means the assumption of equal distributions between the two groups is not satisfied. Therefore, cannot interpret the p value from the Mann Whitney U test. **Statistically significant results marked in bold and with an asterisk***. - unable to calculate due to low numbers.

Appendix 19 Levine statistic for miscellaneous variables

Variable + AED drug load	Levine statistic (based on median & with adjusted df)	Df1	Df2	P value	Satisfy assumptions of equal distributions
Type of therapy - mono/polytherapy	75.715	1	94.259	**<0.001***	**No**
Seizure frequency - none in the last year/at least one in the last year	39.236	1	160.062	**<0.001***	**No**
Categorised number of AED	19.712	2	108.584	**<0.001***	**No**
Attend epilepsy clinic or specialist	18.085	1	150.901	**<0.001***	**No**
Visited A&E with epilepsy	0.202	1	166.564	0.654	Yes
Had education to manage epilepsy	1.946	1	168.346	0.165	Yes

If the p value is significant, then the null hypothesis is rejected which means the assumption of equal distributions between the two groups is not satisfied. Therefore, cannot interpret the p value from the Mann Whitney U test. **Statistically significant results marked in bold and with an asterisk***.

Appendix 20 Binary logistic regression of factors associated with seizure frequency (n=182) (Model 2 for Chapter 5)

Characteristic	Odds ratio (95% CI)	P value
Gender		
Male	1 (reference)	
Female	1.793 (0.850-3.781)	0.125
Age		
<50 years	1 (reference)	
50-64 years	0.958 (0.278-3.300)	0.946
65+ years	0.546 (0.133-2.248)	0.402
Level of intellectual disability		
Mild	1 (reference)	
Moderate	1.115 (0.369-3.372)	0.847
Severe/profound	0.990 (0.317-3.092)	0.987
Type of AED therapy		
No AED therapy/ monotherapy	1 (reference)	
Polytherapy	**5.391 (2.489-11.674)**	**<0.001***
Type of residence		
Independent/community group home	1 (reference)	
Residential	**2.973 (1.265-6.985)**	**0.012***
Categorized number of potential seizure threshold-lowering medications		
No seizure threshold-lowering medications	1 (reference)	
1	0.809 (0.345-1.900)	0.627
2+	**0.190 (0.067-0.538)**	**0.002***
Types of seizures		
Other seizures	1 (reference)	
Generalised seizures	**4.745 (2.215-10.167)**	**<0.001***

Reference category: seizure frequency- none in the last year
Cox & Snell R2 = 0.291 Nagelkerke R^2 = 0.394
Reference groups- male, age <50 years, mild ID, no AED therapy/monotherapy, independent/family/community group home, taking no seizure threshold-lowering medicines and other seizures
Statistically significant results marked in bold and with an asterisk*
Model Chi Square= 62.582, df=10, **p=<0.001.** Correctly classified 77.5% of cases.

Appendix 21 Statistical parameters of drug dosages for individual AEDs

Drug	Median Dose (mg)	Max Dose (mg)	Min Dose (mg)	Average Dose (mg)
Valproic acid (n=78)	1200	3000	200	1332.1
Lamotrigine (n=61)	250	700	25	281.1
Carbamazepine (n=68)	600	1600	100	670.5
Levetiracetam (n=47)	2000	3500	250	1883.7
Phenytoin (n=4)	300	450	250	327.5
Clobazam (n=23)	20	40	5	18.7
Eslicarbazepine (n=2)	1600	2000	1200	1600
Zonisamide (n=9)	400	600	100	352.8
Pregabalin (n=5)	75	525	50	154.2
Clonazepam (n=11)	2	10	0.75	3.5
Lacosamide (n=5)	250	400	200	266.7
Topiramate (n=6)	175	400	100	205
Phenobarbital (n=13)	90	165	30	50
Rufinamide (n=2)	2000	3200	800	2000
Primidone (n=3)	250	250	250	250

Due to low numbers of participants prescribed some AEDs (<5), gabapentin, perampanel were removed from table.

Appendix 22 Bivariate analysis of psychotropic subgroups with regards to gender of participants (n=549)

Prescription of	Total n=549 n (%)	Male n= 236 n (%)	Female n=313 n (%)	P value
Any antipsychotic	245 (44.6)	115 (48.7)	130 (41.5)	0.093
Typical antipsychotics	78 (14.2)	40 (17.0)	38 (12.1)	0.110
Atypical antipsychotics	191 (34.8)	91 (38.6)	100 (32.0)	0.107
Any antidepressant	184 (33.5)	61 (25.9)	123 (39.3)	**0.001***
SSRI	128 (23.3)	42 (17.8)	86 (27.5)	0.008
SNRI	21 (3.8)	8 (3.4)	13 (4.2)	0.644
TCA	15 (2.7)	3 (1.3)	12 (3.8)	0.068
Other (mirtazapine, trazodone, agomelatine)	28 (5.1)	9 (3.8)	19 (6.1)	0.234
Mood stabilising AED	212 (38.6)	88 (37.3)	124 (39.6)	0.579
Mood stabilising AED (no epilepsy diagnosis)	56 (10.2)	23 (9.8)	33 (10.5)	0.750
Lithium	16 (2.9)	5 (2.1)	11 (3.5)	0.336
Any anxiolytics	83 (15.1)	41 (17.4)	42 (13.4)	0.200
Anxiolytic benzodiazepine	80 (14.6)	41 (17.4)	39 (12.5)	0.106
Drugs for dementia	15 (2.7)	5 (2.1)	10 (3.2)	0.444
Anti-cholinergic N04A	71 (12.9)	35 (14.8)	36 (11.5)	0.250
Any hypnotics & sedatives	51 (9.3)	17 (7.2)	34 (10.9)	0.144
Z drugs	30 (5.5)	8 (3.4)	22 (7.0)	0.063
Prolonged acting hypnotic benzodiazepines	10 (1.8)	5 (2.1)	5 (1.6)	0.752 [a]

p=Chi Square test, [a] Fisher Exact test (2 sided). P value: for Chi Square Test after applying Bonferroni Correction α=0.05/18= 0.0028 thus p<0.0028 for significance. Due to low numbers of participants reporting some psychotropic subclasses (<5), 'other anxiolytic' category (hydroxyzine/buspirone) was removed from table. The category short acting hypnotic benzodiazepines (n=5) was removed from table due to low numbers in the male subgroup. **Statistically significant results marked in bold and with an asterisk***

Appendix 23 Bivariate analysis of psychotropic subgroups with regards to type of residence (n=549)

Prescription of	Total n=549 n (%)	Independent/ with family n=78 n (%)	Community group home n=223 n (%)	Residential/ campus setting n=248 n (%)	P value
Any antipsychotic	245 (44.6)	14 (18.0)	93 (41.7)	138 (55.7)	**<0.001***
Typical antipsychotics	78 (14.2)	7 (9.0)	24 (10.8)	47 (19.0)	**0.014***
Atypical antipsychotics	191 (34.8)	10 (12.8)	77 (34.5)	104 (41.9)	**<0.001***
Any antidepressant	184 (33.5)	15 (19.2)	74 (33.2)	95 (38.3)	**0.008***
SSRI	128 (23.3)	13 (16.6)	50 (22.4)	65 (26.2)	0.203
TCA	15 (2.7)	0 (0)	7 (3.1)	8 (3.2)	-
Other (mirtazapine, trazodone, agomelatine)	28 (5.1)	2 (2.6)	7 (3.1)	19 (7.7)	-
Mood stabilising AED	212 (38.6)	19 (24.4)	69 (30.9)	124 (50.0)	**<0.001***
Mood stabilising AED (no epilepsy diagnosis)	56 (10.2)	4 (5.1)	18 (8.1)	34 (13.7)	**0.037***
Lithium	16 (2.9)	3 (3.9)	5 (2.2)	8 (3.2)	-
Any anxiolytics	83 (15.1)	4 (5.1)	30 (13.5)	49 (19.8)	**0.005***
Anxiolytic benzodiazepines	80 (14.6)	4 (5.1)	28 (12.6)	48 (19.4)	**0.004***
Drugs for dementia	15 (2.7)	0 (0)	7 (3.1)	8 (3.2)	-
Anti-cholinergic N04A	71 (12.9)	4 (5.1)	22 (9.9)	45 (18.1)	**0.002***
Any Hypnotics & sedatives	51 (9.3)	2 (2.6)	20 (9.0)	29 (11.7)	0.052

p=Chi Square test, [a] Fisher's Exact test (2 sided). **–** denotes unable to calculate p value due to small numbers in subgroups. Due to low numbers of participants reporting some psychotropic subclasses (<5), 'other anxiolytic' category (hydroxyzine/buspirone) was removed from table. The categories SNRI (n=21), Z drugs (n=30) and prolonged acting hypnotic benzodiazepines (n=10) were removed from table due to low numbers in the independent/family subgroup. The category short acting hypnotic benzodiazepines was removed from table due to low numbers in residential/campus setting subgroup. **Statistically significant results marked in bold and with an asterisk***

Appendix 24 Bivariate analysis of psychotropic subgroups with regards to age of participants (n=549)

Prescription of	Total n=549 n (%)	Age <50 years n=64 n (%)	Age 50-64 years n=346 n (%)	Age 65+ years n=139 n (%)	P value
Any antipsychotic	245 (44.6)	29 (45.3)	146 (42.2)	70 (50.4)	0.261
Typical antipsychotics	78 (14.2)	7 (10.9)	47 (13.6)	24 (17.3)	0.419
Atypical antipsychotics	191 (34.8)	27 (42.2)	114 (33.0)	50 (36.0)	0.342
Any antidepressant	184 (33.5)	26 (40.6)	107 (30.9)	51 (36.7)	0.210
SSRI	128 (23.3)	16 (25.0)	78 (22.5)	34 (24.5)	0.853
SNRI	21 (3.8)	2 (3.1)	13 (3.8)	6 (4.3)	-
TCA	15 (2.7)	4 (6.3)	5 (1.4)	6 (4.3)	-
Other (mirtazapine, trazodone, agomelatine)	28 (5.1)	4 (6.3)	17 (4.9)	7 (5.0)	-
Mood stabilising AED	212 (38.6)	21 (32.8)	140 (40.5)	51 (36.7)	0.444
Mood stabilising AED (no epilepsy diagnosis)	56 (10.2)	5 (7.8)	35 (10.1)	16 (11.5)	0.719
Lithium	16 (2.9)	3 (4.7)'	8 (2.3)	5 (3.6)	-
Any anxiolytics	83 (15.1)	10 (15.6)	49 (14.2)	24 (17.3)	0.684
Anxiolytic benzodiazepines	80 (14.6)	10 (15.6)	48 (13.9)	22 (15.8)	0.832
Anti-cholinergic N04A	71 (12.9)	9 (14.1)	45 (13.0)	17 (12.2)	0.935
Any hypnotics & sedatives	51 (9.3)	6 (9.4)	30 (8.7)	15 (10.8)	0.767
Z drugs	30 (5.5)	3 (4.7)	17 (4.9)	10 (7.2)	-
Prolonged acting hypnotic benzodiazepines	10 (1.8)	3 (4.7)	5 (1.5)	2 (1.4)	-

p=Chi Square test, [a] Fisher's Exact test (2 sided). - Unable to calculate p value due to small numbers in subgroups. Due to low numbers of participants reporting some psychotropic subclasses (<5), 'other anxiolytic' category (hydroxyzine/buspirone) was removed from table. The categories drugs for dementia (n=15) and short acting hypnotic benzodiazepines (n=5) were also removed from table due to low numbers in subgroups age <50 years and age 65+ years respectively. **Statistically significant results marked in bold and with an asterisk*.**

Appendix 25 Bivariate analysis of psychotropic subgroups with regards to level of intellectual disability (n=507)

Prescription of	Total n=507 n (%)	Mild n=122 n (%)	Moderate n=231 n (%)	Severe/profound n=154 n (%)	P value Chi Square
Any antipsychotic	232	51 (41.8)	102 (44.2)	79 (51.3)	0.233
Typical antipsychotics	75	16 (13.1)	27 (11.7)	32 (20.8)	0.040
Atypical antipsychotics	180	38 (31.1)	85 (36.8)	57 (37.0)	0.514
Any antidepressant	172	48 (39.3)	83 (35.9)	41 (26.6)	0.059
SSRI	116	34 (27.9)	56 (24.2)	26 (16.9)	0.078
SNRI	21	5 (4.1)	12 (5.2)	4 (2.6)	0.456
TCA	15	5 (4.1)	7 (3.0)	3 (1.9)	-
Other (mirtazapine, trazodone, agomelatine)	28	7 (5.7)	13 (5.6)	8 (5.2)	0.977
Mood stabilising AED	201	38 (31.1)	83 (35.9)	80 (51.9)	0.001*
Mood stabilising AED (no epilepsy diagnosis)	53	12 (9.8)	29 (12.6)	12 (7.8)	0.319
Lithium	16	3 (2.5)	4 (1.7)	9 (5.8)	-
Any anxiolytics	76	12 (9.8)	39 (16.9)	25 (16.2)	0.185
Anxiolytic benzodiazepines	73	12 (9.8)	36 (15.6)	25 (16.2)	0.253
Drugs for dementia	14	3 (2.5)	9 (3.9)	2 (1.3)	-
Anti-cholinergic N04A	69	11 (9.0)	26 (11.3)	32 (20.8)	0.007
Any hypnotics & sedatives	47	4 (3.3)	23 (10.0)	20 (13.0)	0.020
Prolonged acting hypnotic benzodiazepines	10	2 (1.6)	4 (1.7)	4 (2.6)	-

p=Chi Square test, [a] Fisher's Exact test (2 sided) - Unable to calculate p value due to small numbers in subgroups. Due to low numbers of participants reporting some psychotropic subclasses (<5), 'other anxiolytic' category (hydroxyzine/buspirone) was removed from table. Z drugs (n=26) and short acting hypnotic benzodiazepines (n=5) were also removed due to low numbers in the mild intellectual disability category. **Statistically significant results marked in bold and with an asterisk*.**

Appendix 26 DDD - Defined Daily Doses used in AED load analysis [92]

Antiepileptic Drug (AED)	DDD used
Carbamazepine	1000mg
Valproic acid	1500mg
Lamotrigine	300mg
Levetiracetam	1500mg
Phenytoin	300mg
Clobazam	20mg
Eslicarbazepine	800mg
Zonisamide	200mg
Pregabalin	300mg
Clonazepam	8mg
Lacosamide	300mg
Gabapentin	1800mg
Topiramate	300mg
Phenobarbital	100mg
Rufinamide	1400mg
Perampanel	8mg
Primidone	1250mg

Appendix 27 Abstract for Chapter 5 (Published Paper)

Background:

This study explored antiepileptic drug use, frequency of seizures, and the effect of psychotropic drugs with the potential to lower the seizure threshold in persons diagnosed with epilepsy and intellectual disability.

Method:

Data for this study were drawn from Wave 3 of the Intellectual Disability Supplement to the Irish Longitudinal Study on Ageing (IDS-TILDA). Psychotropic drugs were categorised for potential seizure threshold-lowering risk (low, moderate, high). Binary logistic regression was performed to identify factors associated with seizure frequency.

Results:

Epilepsy prevalence was 35.8% (n=196), of which 57.7% reported a mental health condition. Participants with seizure data classified as taking at least one moderate/high risk medication, were significantly less likely to experience a seizure compared to participants taking no potential seizure threshold-lowering medication.

Conclusions:

Psychotropic drugs recommended to be avoided or used with caution did not provoke increased seizure frequency in this cohort.

Appendix 28 Abstract for Chapter 6 (Published Paper)

Background:

Antiepileptic drugs (AEDs) may affect mood and behaviour in people with epilepsy and intellectual disability. A high AED load, derived from AED polytherapy and/or high doses of AEDs, has been suggested to be a risk factor for behavioural side effects.

Methods:

Data were drawn from Wave 3 of the Intellectual Disability Supplement to the Irish Longitudinal Study on Ageing (IDS-TILDA). The Behaviour Problems Inventory Short Form (BPI-S) was used to assess challenging behaviours. AED load was calculated and median AED loads obtained. Non-parametric tests and binary logistic regression were performed to determine the relationship between AED load and challenging behaviours.

Results:

Of participants with a reported diagnosis of epilepsy who were taking a regular AED and had completed BPI-S (n=142), 62.7% (n=89) exhibited challenging behaviours. Challenging behaviour was found to be more prevalent in those with more severe levels of intellectual disability ($p<0.001$). Aggressive/destructive behaviour and stereotyped behaviour were significantly more likely in participants living in residential/campus settings. For participants with a severe/profound intellectual disability, a significantly higher median AED load was found for participants exhibiting aggressive/destructive behaviour and self-injurious behaviour (SIB) compared to participants not exhibiting these behaviours,

indicating a high AED load may contribute to some behavioural problems in this population group.

Conclusions:

However, many factors can influence behavioural outcomes, creating difficulties in determining those that are associated and the nature of the association. Careful monitoring of AED load, together with increased vigilance for breakthrough behavioural issues is essential for dealing with these complex cases. Larger studies are needed to account for the potential confounding factors.

Appendix 29 Supplementary Table S 5.1 – Psychotropic drugs having the potential to lower the seizure threshold (adapted from the Maudsley Prescribing Guidelines 13th Edition 2018 [93])

Antipsychotics	Risk	ATC code	Maudsley Prescribing Guidelines 2018 [93]
Chlorpromazine Promazine	High Risk	N05AA01 N05AA03	AVOID- Best avoided in people with epilepsy [94]. Doses of chlorpromazine above 1G/day have a 9% incidence of seizures.
Zuclopentixol (Depot Antipsychotics)	High Risk	N05AF05	AVOID- the kinetics of depots are complex and seizure may be delayed. Difficult to withdraw drug.
Flupentixol (Depot Antipsychotics)	High Risk	N05AF01	AVOID- the kinetics of depots are complex and seizure may be delayed. Difficult to withdraw drug.
Olanzapine	Moderate Risk	N05AH03	Care Required- Associated with seizures in randomised controlled trials [72]. Olanzapine is associated with EEG abnormalities [23]. Overall risk of lowering the seizure threshold is expected to be low [95]. Olanzapine has been recommended by some for people with epilepsy [96].
Quetiapine	Moderate Risk	N05AH04	Care Required- Associated with seizures in randomised controlled trials [72].
Risperidone	Low Risk	N05AX08	Low risk of lowering the seizure threshold [95]. Incidence of seizures similar to placebo in randomised controlled trials [72]. Evidence of safety in a case series of adolescents with epilepsy [97]. Recommended in people with epilepsy [96].
Aripiprazole	Low Risk	N05AX12	Rarely lowers seizure threshold [95]. Incidence of seizures similar to placebo in randomised controlled trials [72].
Haloperidol	Low Risk	N05AD01	Low risk of lowering the seizure threshold [95].
Trifluoperazine	Low Risk	N05AB06	Low risk of lowering the seizure threshold [95].
Mood Stabiliser			
Lithium	Moderate Risk	N05AN01	Care Required- Low risk of seizures [98]. Anticonvulsant in animal models [98]. Limited data shows increases or decreases in seizure frequency in people with epilepsy [98].

Appendix 29 Supplementary Table S 5.1 – Psychotropic drugs having the potential to lower the seizure threshold (adapted from the Maudsley Prescribing Guidelines 13th Edition 2018 [93]) (*Continued*)

Antidepressants	Risk	ATC code	Maudsley Prescribing Guidelines 2018 [93]
TCAs (Tri-cyclic Antidepressants) Trimipramine	High Risk	 N06AA06	AVOID- Most TCAs are epileptogenic, in particular at higher doses- chiefly clomipramine and amitriptyline [72-74]. Doxepin possible lower risk from one small study in people with epilepsy [98].
Trazodone	Moderate Risk	N06AX05	Care Required- Some risk of seizures suggested in limited data [73, 98].
Venlafaxine	Moderate Risk	N06AX16	Care Required- Effective in people with epilepsy [99], recommended [24] but evidence mixed regarding seizure risk [98].
Duloxetine	Probably Low Risk (analysis-low risk)	N06AX21	Use with caution- Limited data. Has been recommended in people with epilepsy [24, 99]. Risk of seizure probably negligible [98].
Mirtazapine	Low Risk	N06AX11	Recommended in people with epilepsy [24, 96]. Not known to be proconvulsant [72].
SSRI (Selective Serotonin Reuptake Inhibitors) Escitalopram Citalopram Sertraline Fluoxetine Paroxetine	Low Risk	 N06AB10 N06AB04 N06AB06 N06AB03 N06AB05	Recommended in people with epilepsy [24, 100]. SSRIs may be anticonvulsant [101] at therapeutic doses and pro-convulsant in overdose [94]. Preferred SSRI with lowest risk of interaction with AEDs include citalopram/ escitalopram followed by sertraline [24, 96, 100, 102]. Escitalopram preferred over citalopram as lower risk of seizures in overdose [98]. Despite low risk of seizures (e.g. Fluoxetine) [98], drug interactions with AEDs should be considered [24, 100].

Appendix 30 Supplementary Table S 5.2 - Maximum prescribed daily dose of potential seizure threshold- lowering psychotropic medication in participants with epilepsy in Wave 3 (n=196)

Psychotropic drug	Maximum prescribed daily dose
Antipsychotics	
Chlorpromazine (n=12)	500mg
Promazine (n<5)	150mg
Olanzapine (n=29)	20mg
Quetiapine (n=9)	600mg
Risperidone (n=25)	5mg
Aripiprazole (n=5)	25mg
Haloperidol (n<5)	10mg
Trifluoperazine (n<5)	8mg
Mood stabiliser	
Lithium (n=5)	800mg
Antidepressants	
Trimipramine (n<5)	50mg
Trazodone (n=7)	150mg
Venlafaxine (n=8)	150mg
Duloxetine (n<5)	30mg
Mirtazapine (n=11)	45mg
Escitalopram (n=19)	20mg
Citalopram (n<5)	60mg
Sertraline (n=5)	175mg
Fluoxetine (n=6)	30mg
Paroxetine (n<5)	50mg
Depot antipsychotics	***Max dose prescribed (not given daily)***
Zuclopenthixol (n<5)	400mg IM q10/7
Flupentixol (n<5)	40mg IM q14/7

Appendix 31 Supplementary Table S 6.1 - Categories of challenging behaviours [103] and AED load

Behaviour category (n) Total	Type of behaviour (n) Exhibit	Median AED load (95%CI) Exhibit behaviour	Median AED load (95%CI) Do not exhibit behaviour
Self-Injurious behaviour (SIB)			
(n=130)	Self- biting (n=10)	1.48 (0.67-2.00)	1.33 (1.00-1.76)
(n=130)	Head hitting (n=12)	1.46 (0.80-2.80)	1.32 (1.00-1.73)
(n=132)	Body hitting (n=9)	1.00 (0.53-1.60)	1.33 (1.00-1.73)
(n=131)	Self-scratching (n=35)	1.35 (1.00-1.66)	1.30 (0.87-1.87)
(n=131)	Pica (n<5)	5.0 (1.66-8.33)	1.33 (1.00-1.60)
(n=130)	Objects in nose (n=0)	-	1.33 (1.00-1.60)
(n=128)	Hair pulling (n<5)	1.66	1.33 (1.00-1.67)
(n=124)	Teeth grinding (n=6)	2.01 (0.60-6.33)	1.30 (0.93-1.60)
Aggressive/destructive behaviour			
(n=130)	Hitting others (n=27)	1.50 (1.00-3.17)	1.17 (0.900-1.570)
(n=130)	Kicking others (n=10)	3.26 (0.80-5.25)	1.29 (0.93-1.50)
(n=130)	Pushing others (n=21)	1.66 (1.00-3.34)	1.17 (0.87-1.47)
(n=129)	Biting others (n<5)	0.76 (0.10-1.42)	1.33 (1.00-1.66)
(n=129)	Grabbing & pulling others (n=15)	1.50 (0.67-4.44)	1.29 (0.93-1.60)
(n=130)	Scratching others (n<5)	1.35 (1.000-3.170)	1.33 (0.95-1.66)
(n=129)	Pinching others (n=5)	1.35 (0.100-3.620)	1.33 (1.00-1.67)
(n=127)	Verbally abusive with others (n=26)	1.54 (1.00-2.92)	1.17 (0.87-1.53)
(n=128)	Destroying things (e.g. rips clothes, throws chairs, smashes tables) (n=10)	1.04 (0.67-2.00)	1.32 (0.95-1.66)
(n=129)	Bullying (being mean or cruel e.g. grabbing toys or food from others) (n=8)	0.95 (0.33-5.25)	1.33 (1.00-1.57)

Appendix 31 Supplementary Table S 6.1 - Categories of challenging behaviours [103] and AED load *(Continued*)

Behaviour category (n) Total	Type of behaviour (n) Exhibit	Median AED load (95%CI) Exhibit behaviour	Median AED load (95%CI) Do not exhibit behaviour
Stereotyped behaviour			
(n=130)	Rocking & repetitive body movements (n=30)	0.83 (0.60-1.50)	1.334 (1.00-1.87)
(n=129)	Sniffing objects, own body (n<5)	1.06 (0.53- 1.66)	1.33 (1.00-1.67)
(n=127)	Waving & shaking arms (n=15)	1.35 (0.60-1.87)	1.33 (1.00-1.67)
(n=128)	Manipulating (e.g. twirling, spinning) (n<5)	0.53 (0.33-0.60)	1.33 (1.00-1.66)
(n=130)	Repetitive hand and/or finger (n=16)	0.90 (0.60-1.87)	1.33 (1.00-1.67)
(n=131)	Yelling & screaming (n=39)	1.35 (0.90-1.87)	1.23 (0.95-1.67)
(n=130)	Pacing, jumping, bouncing, running (n=10)	0.74 (0.33-4.64)	1.33 (1.00-1.67)
(n=130)	Rubbing self (n=16)	0.67 (0.60-2.68)	1.35 (1.07-1.67)
(n=128)	Gazing at hands or objects (n=16)	0.98 (0.53- 2.68)	1.34 (1.07-1.73)
(n=128)	Bizarre movements/ postures (n=6)	1.36 (0.33-3.34)	1.33 (1.00-1.67)
(n=129)	Clapping hands (n=11)	1.47 (0.53-3.27)	1.32 (1.00-1.73)
(n=129)	Grimacing (n=17)	1.00 (0.67-1.60)	1.33 (1.00-1.67)

(n) Total = AED load data and completed BPI-S. <5 denotes fewer than 5 participants to protect anonymity.

Appendix 32 Supplementary Table S 6.2 - Bivariate analysis of demographic characteristics of participants with a reported epilepsy diagnosis (n=196) and participants without a reported epilepsy diagnosis (n=352) (Adapted from Monaghan et al. (2021) [104])

Characteristic	All participants with medicine data n=548 n (%)	With epilepsy n=196 n (%)	Without epilepsy n=352 n (%)	P value
Gender				0.665
Male	236 (43.1)	82 (41.8)	154 (43.8)	
Female	312 (56.9)	114 (58.2)	198 (56.2)	
Age				0.475
<50 years	64 (11.7)	21 (10.7)	43 (12.2)	
50-64 years	345 (63.0)	130 (66.3)	215 (61.1)	
65+ years	139 (25.3)	45 (23.0)	94 (26.7)	
Level of intellectual disability	(n=506)	(n=187)	(n=319)	**<0.001***
Mild	121 (23.9)	31 (16.6)	90 (28.2)	
Moderate	231 (45.7)	77 (41.2)	154 (48.3)	
Severe/profound	154 (30.4)	79 (42.2)	75 (23.5)	
Place of residence				**<0.001***
Independent	78 (14.2)	20 (10.2)	58 (16.5)	
Community group home	222 (40.5)	60 (30.6)	162 (46.0)	
Residential/campus	248 (45.3)	116 (59.2)	132 (37.5)	
Type of therapy				**<0.001***
AED monotherapy	135 (24.6)	80 (40.8)	55 (15.6)	
AED polytherapy	109 (19.9)	94 (48.0)	15 (4.3)	
No AED therapy	304 (55.5)	22 (11.2)	282 (80.1)	
Exhibiting any challenging behaviours	(n=451)	(n=161)	(n=290)	0.331
Yes	275 (61.0)	103 (64.0)	172 (59.3)	
No	176 (39.0)	58 (36.0)	118 (40.7)	
Exhibiting categorised behaviours	(n=451)	(n=161)	(n=290)	
SIB	143 (31.7)	59 (36.7))	84 (29.0)	0.113
Aggressive/destructive behaviour	164 (36.4)	64 (39.8)	100 (34.5)	0.217
Stereotyped behaviour	209 (46.3)	82 (50.9)	127 (43.8)	0.154

n=196: Participants with report of a diagnosis of epilepsy. n=352: Participants with no report of a diagnosis of epilepsy. n= 548: All participants with medication data and confirmed epilepsy status. n=1 individuals with medication data excluded from analysis as no confirmed epilepsy status. P value: Chi Square

Statistically significant results marked in bold and with an asterisk*

Appendix 33 Supplementary Table S 6.3 - Bivariate analysis of AEDs among those with a reported epilepsy diagnosis, taking a regular AED and exhibiting SIB (n=141), aggressive/destructive behaviour (n=137) and stereotyped behaviour (n=141)

Characteristic	Total SIB n=141	Exhibit SIB n=52	P value	Total aggressive/ destructive behaviour n=137	Exhibit aggressive/ destructive behaviour n=54	P value	Total stereotyped behaviour n=141	Exhibit stereotyped behaviour n=71	P value
Antiepileptic drugs									
Older generation									
Valproic acid	65 (46.1)	24 (46.2)	0.992	65 (47.4)	28 (51.9)	0.405	65 (46.1)	36 (50.7)	0.269
Phenytoin	8 (5.7)	1 (1.9)	0.258 [a]	8 (5.8)	2 (3.7)	0.479 [a]	8 (5.7)	1 (1.4)	**0.033 [a]**
Carbamazepine	58 (41.1)	17 (32.7)	0.119	55 (40.1)	19 (35.2)	0.339	58 (41.1)	27 (38.0)	0.450
Primidone	<5	<5	1.000 [a]	<5	<5	1.000 [a]	<5	0 (0)	0.245 [a]
Phenobarbital	10 (7.1)	3 (5.8)	0.745 [a]	10 (7.3)	3 (5.6)	0.740 [a]	10 (7.1)	2 (2.8)	0.055 [a]
Clobazam	18 (12.8)	2 (3.8)	0.015	17 (12.4)	8 (14.8)	0.491	17 (12.1)	6 (8.5)	0.185
Clonazepam	10 (7.1)	3 (5.8)	0.745 [a]	9 (6.6)	4 (7.4)	0.739 [a]	10 (7.1)	6 (8.5)	0.745 [a]
Newer generation									
Lamotrigine	47 (33.3)	18 (34.6)	0.805	44 (32.1)	19 (35.2)	0.535	46 (32.6)	23 (32.4)	0.953
Gabapentin	<5	<5	0.369 [a]	<5	0 (0)	1.000 [a]	<5	<5	1.000 [a]
Topiramate	6 (4.3)	2 (3.8)	1.000 [a]	6 (4.4)	2 (3.7)	1.000 [a]	6 (4.3)	3 (4.2)	1.000 [a]
Levetiracetam	38 (27.0)	12 (23.1)	0.428	38 (27.7)	16 (29.6)	0.690	38 (27.0)	18 (25.4)	0.667
Zonisamide	7 (5.0)	1 (1.9)	0.261 [a]	7 (5.1)	2 (3.7)	0.704 [a]	7 (5.0)	0 (0)	**0.006 [a]**
Pregabalin	<5	<5	0.626 [a]	<5	<5	0.647 [a]	<5	<5	1.000 [a]
Rufinamide	<5	<5	0.134 [a]	<5	<5	0.154 [a]	<5	<5	0.496 [a]
Eslicarbazepine	<5	0 (0)	0.531 [a]	<5	0 (0)	0.519 [a]	<5	0 (0)	0.245 [a]
Lacosamide	<5	<5	1.000 [a]	<5	<5	0.562 [a]	<5	<5	0.620 [a]
Perampanel	<5	<5	0.369 [a]	<5	0 (0)	1.000 [a]	<5	<5	1.000 [a]

P value: Chi Square, [a] Fisher Exact Test (2 sided). P value: for Chi Square Test and applying Bonferroni Correction α=0.05/17= 0.0029 thus p<0.0029 for significance. <5 denotes fewer than 5 participants to protect anonymity. **Statistically significant results marked in bold and with an asterisk***

Appendix 34 Supplementary Table S 6.4 - Bivariate analysis of type of behaviour among those with reported epilepsy diagnosis and those without an epilepsy diagnosis

Type of behaviour (n=completed BPI-S)	Total n (%)	With epilepsy n (%)	Without epilepsy n (%)	P value
Self-biting (n=433)	32 (7.4)	12 (37.5)	20 (62.5)	0.835
Head hitting (n=433)	35 (8.1)	14 (40.0)	21 (60.0)	0.588
Body hitting (n=435)	37 (8.5)	12 (32.4)	25 (67.6)	0.607
Self-scratching (n=436)	79 (18.1)	37 (46.8)	42 (53.2)	0.023
Pica (n=437)	11 (2.5)	3 (27.3)	8 (72.7)	0.753[a]
Objects in nose (n=434)	<5	0 (0)	<5	0.556[a]
Hair pulling (n=433)	8 (1.8)	1 (12.5)	7 (87.5)	0.269[a]
Teeth grinding (n=415)	25 (6.0)	7 (28.0)	18 (72.0)	0.409
Hitting others (n=428)	83 (19.4)	36 (43.4)	47 (56.6)	0.118
Kicking others (n=427)	25 (5.9)	12 (48.0)	13 (52.0)	0.191
Pushing others (n=430)	61 (14.2)	27 (44.3)	34 (55.7)	0.137
Biting others (n=429)	6 (1.4)	2 (33.3)	4 (66.7)	1.000[a]
Grabbing & pulling others (n=431)	42 (9.7)	20 (47.6)	22 (52.4)	0.084
Scratching others (n=427)	9 (2.1)	4 (44.4)	5 (55.6)	0.727[a]
Pinching others (n=428)	21 (4.9)	7 (33.3)	14 (66.7)	0.830
Verbally abusive with others (n=426)	91 (21.4)	32 (35.2)	59 (64.8)	0.992
Destroying things (n=430)	41 (9.5)	16 (39.0)	25 (61.0)	0.582
Bullying (n=429)	29 (6.8)	10 (34.5)	19 (65.5)	0.933
Rocking & repetitive body movements (n=435)	84 (19.3)	35 (41.7)	49 (58.3)	0.181
Sniffing objects (n=432)	16 (3.7)	5 (31.3)	11 (68.8)	0.708
Waving & shaking arms (n=432)	58 (13.4)	18 (31.0)	40 (69.0)	0.501
Manipulating (n=430)	18 (4.2)	4 (22.2)	14 (77.8)	0.242
Repetitive hand/finger (n=432)	47 (10.9)	17 (36.2)	30 (63.8)	0.909
Yelling & screaming (n=439)	113 (25.7)	45 (39.8)	68 (60.2)	0.269
Pacing (n=431)	50 (11.6)	13 (26.0)	37 (74.0)	0.135
Rubbing self (n=436)	53 (12.2)	20 (37.7)	33 (62.3)	0.695

Appendix 34 Supplementary Table S 6.4 - Bivariate analysis of type of behaviour among those with reported epilepsy diagnosis and those without an epilepsy diagnosis (*Continued*)

Type of behaviour (n=completed BPI-S)	Total n (%)	With epilepsy n (%)	Without epilepsy n (%)	P value
Gazing (n=431)	45 (10.4)	19 (42.2)	26 (57.8)	0.286
Bizarre movements (n=431)	21 (4.9)	6 (28.6)	15 (71.4)	0.524
Clapping hands (n=432)	42 (9.7)	13 (31.0)	29 (69.0)	0.524
Grimacing (n=433)	60 (13.9)	23 (38.3)	37 (61.7)	0.629

P value: Chi Square, [a] Fisher Exact Test (2 sided). P value: for Chi Square Test and applying Bonferroni correction α=0.05/30= 0.0017 thus p<0.0017 for significance. <5 denotes fewer than 5 participants to protect anonymity.
Statistically significant results marked in bold and with an asterisk*

Appendix 35 Supplementary Table S 6.5 - Mann Whitney U Test - AED load, demographic & clinical characteristics associated with SIB (n=136)

SELF-INJURIOUS BEHAVIOUR							
Variable	**n**	**Median AED load (95% CI)**	**IQR**	**Mann Whitney U**	**P value**	**Mean rank**	**Z value**
Gender							
Male	60	1.37 (0.75-2.00)		350.000	0.433		-0.785
Exhibit	20	1.67 (0.93-2.68)	1.98			33.00	
Do not exhibit	40	1.05 (0.67-2.30)	2.56			29.25	
Female	76	1.30 (1.00-1.60)		761.000	0.502		0.672
Exhibit	31	1.07 (0.70-1.57)	1.00			36.45	
Do not exhibit	45	1.33 (1.00-2.25)	2.26			39.91	
Age							
<50 years	15	1.67 (0.67-3.62)		23.500	0.613		-0.521
Exhibit	7	1.80 (0.60-8.33)	2.95			8.64	
Do not exhibit	8	1.37 (0.53-6.00)	2.69			7.44	
50-64 years	91	1.33 (1.00-1.87)		956.000	0.921		0.100
Exhibit	32	1.38 (0.67-2.00)	1.90			45.63	
Do not exhibit	59	1.30 (0.80-2.30)	2.53			46.20	
65+ years	30	0.97 (0.67-1.35)		92.500	0.518		-0.657
Exhibit	12	1.09 (0.70-1.50)	0.71			16.79	
Do not exhibit	18	0.84 (0.60-1.87)	1.42			14.64	
Type of residence							
Independent/family/ community group home	51	1.35 (0.90-2.27)		250.000	0.948		0.065
Exhibit	13	1.60 (0.67-2.58)	1.88			25.77	
Do not exhibit	38	1.29 (0.80-2.43)	2.36			26.08	
Residential/campus	85	1.30 (0.93-1.57)		846.500	0.681		-0.411
Exhibit	38	1.25 (0.93-1.67)	1.60			44.22	
Do not exhibit	47	1.30 (0.67-1.87)	2.55			42.01	
Level of intellectual disability							
Mild	20	1.24 (0.67-2.60)		24.000	0.516		0.756
Exhibit	2	0.95 (0.90-1.00)	-			7.50	
Do not exhibit	18	1.35 (0.67-2.67)	2.20			10.83	
Moderate	54	1.43 (0.87-2.25)		388.000	0.240		1.176
Exhibit	18	0.85 (0.67-2.58)	1.95			23.94	
Do not exhibit	36	1.82 (1.00-2.73)	2.30			29.28	
Severe/ profound	55	1.30 (0.80-1.57)		255.500	**0.048***		-1.978
Exhibit	31	1.42 (1.00-1.67)	1.60			31.76	
Do not exhibit	24	0.71 (0.53-1.47)	1.26			23.15	
Type of seizures							
Generalised seizures	76	1.84 (1.27-2.73)		686.000	0.693		0.394
Exhibit	26	1.64 (0.67-2.80)	2.62			37.12	
Do not exhibit	50	2.09 (1.18-3.13)	3.10			39.22	
Other seizures	60	0.97 (0.67-1.33)		345.500	0.167		-1.380
Exhibit	25	1.07 (0.80-1.53)	0.93			34.18	
Do not exhibit	35	0.80 (0.60-1.30)	1.07			27.87	

Appendix 35 Supplementary Table S 6.5 - Mann Whitney U Test - AED load, demographic & clinical characteristics associated with SIB (n=136) *(Continued)*

SELF - INJURIOUS BEHAVIOUR							
Variable	**n**	**Median AED load (95% CI)**	**IQR**	**Mann Whitney U**	**P value**	**Mean rank**	**Z value**
Type of therapy							
Monotherapy	59	0.67 (0.60-0.67)		249.000	**0.007***		-2.718
Exhibit	25	0.67 (0.60-0.93)	0.40			37.04	
Do not exhibit	34	0.57 (0.40-0.67)	0.36			24.82	
Polytherapy	77	2.53 (1.87-3.00)		680.000	0.855		0.183
Exhibit	26	2.33 (1.60-3.27)	1.80			38.35	
Do not exhibit	51	2.60 (1.87-3.17)	2.67			39.33	
Seizure frequency							
None in the last year	76	0.92 (0.67-1.18)		575.000	0.137		-1.488
Exhibit	35	1.00 (0.67-1.42)	0.99			42.57	
Do not exhibit	41	0.80 (0.57-1.18)	0.87			35.02	
At least one in the last year	57	2.58 (1.67-3.40)		290.500	0.657		-0.444
Exhibit	15	2.58 (1.50-4.17)	2.67			30.63	
Do not exhibit	42	2.55 (1.73-3.60)	3.44			28.42	
Comorbid mental health disorder							
Have psychotic disorder	10	1.19 (0.60-2.68)		9.000	0.610		-0.640
Exhibit	4	1.37 (0.70-2.68)	1.63			6.25	
Do not exhibit	6	1.09 (0.33-4.64)	1.63			5.00	
Have mood disorder	47	1.30 (0.800-1.53)		304.000	0.551		0.596
Exhibit	24	1.00 (0.67-1.53)	0.91			22.83	
Do not exhibit	23	1.34 (0.60-2.43)	2.57			25.22	
Have anxiety disorder	47	1.33 (0.93-1.73)		279.500	0.941		0.075
Exhibit	24	1.20 (0.80-1.80)	1.32			23.85	
Do not exhibit	23	1.33 (0.60-2.43)	2.32			24.15	
Take antipsychotics							
Yes	54	1.24 (0.93-1.53)		415.500	0.372		0.892
Exhibit	28	1.00 (0.70-1.57)	1.00			25.66	
Do not exhibit	26	1.32 (0.87-2.43)	2.00			29.48	
No	82	1.35 (0.80-2.00)		581.500	0.316		-1.002
Exhibit	23	1.60 (0.95-2.80)	2.67			45.72	
Do not exhibit	59	1.17 (0.67-2.25)	2.60			39.86	
Take antidepressants							
Yes	45	1.42 (1.00-1.80)		257.500	0.648		0.457
Exhibit	17	1.42 (0.80-1.80)	1.23			21.85	
Do not exhibit	28	1.41 (1.00-2.25)	2.28			23.70	
No	91	1.17 (0.80-1.67)		905.500	0.602		-0.521
Exhibit	34	1.34 (0.70-2.00)	1.95			47.87	
Do not exhibit	57	1.00 (0.67-2.27)	2.50			44.89	

IQR- Interquartile Range. **Statistically significant results marked in bold and with an asterisk ***

Appendix 36 Supplementary Table S 6.6 - Mann Whitney U Test - AED load, demographic & clinical characteristics associated with aggressive/destructive behaviour (n=132)

AGGRESSIVE/DESTRUCTIVE BEHAVIOUR							
Variable	**n**	**Median AED load (95% CI)**	**IQR**	**Mann Whitney U**	**P value**	**Mean rank**	**Z value**
Gender							
Male	58	1.37 (0.75-1.87)		325.500	0.172		-1.367
Exhibit	25	1.47 (0.93-2.80)	2.38			32.98	
Do not exhibit	33	0.87 (0.60-2.30)	2.18			26.86	
Female	74	1.30 (1.00-1.57)		531.500	0.295		-1.048
Exhibit	26	1.43 (0.90-2.67)	2.64			41.06	
Do not exhibit	48	1.22 (0.80-1.67)	1.60			35.57	
Age							
<50 years	14	1.74 (0.67-4.01)		13.000	0.181		-1.422
Exhibit	6	2.88 (0.60-8.33)	5.33			9.33	
Do not exhibit	8	1.47 (0.53-4.01)	1.23			6.13	
50-64 years	88	1.32 (1.00-1.73)		756.500	0.193		-1.302
Exhibit	33	1.53 (1.00-2.92)	2.80			49.08	
Do not exhibit	55	1.11 (0.80-1.87)	2.10			41.75	
65+ years	30	0.97 (0.67-1.35)		89.000	0.439		-0.805
Exhibit	12	1.18 (0.67-1.87)	1.05			17.08	
Do not exhibit	18	0.84 (0.60-1.76)	1.34			14.44	
Type of residence							
Independent/family/ community group home	50	1.38 (0.90-2.30)		257.500	0.502		0.671
Exhibit	12	1.26 (0.67-2.53)	1.64			23.04	
Do not exhibit	38	1.54 (0.80-2.58)	2.36			26.28	
Residential/campus	82	1.24 (0.87-1.53)		553.000	0.008 **		-2.652
Exhibit	39	1.50 (1.00-2.92)	2.80			48.82	
Do not exhibit	43	0.87 (0.60-1.33)	1.20			34.86	
Level of intellectual disability							
Mild	20	1.24 (0.67-2.60)		40.500	0.904		-0.124
Exhibit	6	1.09 (0.33-5.25)	2.56			10.75	
Do not exhibit	14	1.35 (0.33-3.13)	2.15			10.39	
Moderate	53	1.33 (0.80-2.27)		349.500	0.720		0.358
Exhibit	20	1.27 (0.67-2.92)	2.49			26.03	
Do not exhibit	33	1.33 (0.87-2.43)	1.96			27.59	
Severe/profound	52	1.32 (0.80-1.57)		157.500	**0.001***		-3.278
Exhibit	24	1.55 (1.33-3.34)	2.42			33.94	
Do not exhibit	28	0.64 (0.53-1.30)	1.01			20.13	
Types of seizures							
Generalised seizures	72	1.90 (1.33-2.73)		436.500	**0.047***		-1.990
Exhibit	27	2.73 (1.35-4.44)	3.80			42.83	
Do not exhibit	45	1.67 (0.95-2.43)	2.55			32.70	
Other seizures	60	0.92 (0.67-1.30)		382.000	0.450		-0.755
Exhibit	24	1.04 (0.60-1.47)	0.92			32.58	
Do not exhibit	36	0.78 (0.60-1.30)	0.95			29.11	

Appendix 36 Supplementary Table S 6.6 - Mann Whitney U Test - AED load, demographic & clinical characteristics associated with aggressive/destructive behaviour (n=132) *(Continued)*

AGGRESSIVE/DESTRUCTIVE BEHAVIOUR							
Variable	**n**	**Median AED load (95% CI)**	**IQR**	**Mann Whitney U**	**P value**	**Mean rank**	**Z value**
Type of therapy							
Monotherapy	58	0.67 (0.53-0.67)		305.000	0.174		-1.359
Exhibit	21	0.67 (0.60-0.93)	0.40			33.48	
Do not exhibit	37	0.60 (0.40-0.67)	0.38			27.24	
Polytherapy	74	2.56 (1.87-3.00)		524.500	0.136		-1.492
Exhibit	30	2.77 (1.87-3.62)	2.95			42.02	
Do not exhibit	44	2.29 (1.73-3.00)	2.19			34.42	
Seizure frequency							
None in the last year	74	0.92 (0.67-1.17)		537.500	0.177		-1.351
Exhibit	30	1.04 (0.67-1.42)	0.89			41.58	
Do not exhibit	44	0.69 (0.60-1.11)	1.00			34.72	
At least one in the last year	55	2.58 (1.67-3.60)		186.500	**0.006***		-2.753
Exhibit	19	3.62 (2.67-5.07)	2.40			36.18	
Do not exhibit	36	1.75 (1.17-2.73)	2.67			23.68	
Comorbid mental health disorder							
Have psychotic disorder	10	1.19 (0.60-2.68)	1.12	18.000	0.257		1.279
Exhibit	4	0.84 (0.33-1.66)	2.34			4.00	
Do not exhibit	6	1.32 (0.70-4.64)				6.50	
Have mood disorder	44	1.32 (0.87-1.53)		197.500	0.343		-0.948
Exhibit	25	1.35 (1.00-1.66)	1.14			24.10	
Do not exhibit	19	0.87 (0.60-1.76)	1.16			20.39	
Have anxiety disorder	44	1.34 (1.00-1.76)		194.500	0.269		-1.105
Exhibit	23	1.50 (1.00-2.92)	2.67			24.54	
Do not exhibit	21	1.33 (0.60-1.80)	1.27			20.26	
Take antipsychotics							
Yes	52	1.30 (0.93-1.57)		325.000	0.875		-0.157
Exhibit	29	1.07 (0.80-1.87)	1.73			26.79	
Do not exhibit	23	1.30 (0.75-1.73)	1.10			26.13	
No	80	1.34 (0.80-2.00)		449.000	**0.042***		-2.038
Exhibit	22	2.27 (1.17-3.62)	2.66			49.09	
Do not exhibit	58	1.00 (0.67-1.76)	2.11			37.24	
Take antidepressants							
Yes	43	1.42 (1.00-1.80)		281.000	0.195		1.297
Exhibit	24	1.25 (0.67-1.87)	1.45			19.79	
Do not exhibit	19	1.73 (1.00-3.13)	2.13			24.79	
No	89	1.17 (0.80-1.67)		523.000	**0.005***		-2.804
Exhibit	27	2.00 (1.00-3.60)	2.62			56.63	
Do not exhibit	62	0.84 (0.67-1.40)	1.80			39.94	

** Does not satisfy assumption of homogeneity of variance necessitating caution in interpreting the Mann Whitney U test. IQR- Interquartile Range. **Statistically significant results marked in bold and with an asterisk ***

Appendix 37 Supplementary Table S 6.7 - Mann Whitney U Test – AED load, demographic & clinical characteristics associated with stereotyped behaviour (n=136)

STEREOTYPED BEHAVIOUR							
Variable	**n**	**Median AED load (95% CI)**	**IQR**	**Mann Whitney U**	**P value**	**Mean rank**	**Z value**
Gender							
Male	59	1.33 (0.75-1.87)		466.500	0.473		0.718
Exhibit	35	1.18 (0.67-1.80)	2.08			28.67	
Do not exhibit	24	1.57 (0.67-3.13)	2.64			31.94	
Female	77	1.27 (0.95-1.53)		785.000	0.543		0.608
Exhibit	33	1.00 (0.67-1.60)	1.39			37.21	
Do not exhibit	44	1.29 (1.00-1.76)	1.93			40.34	
Age							
<50 years	15	1.67 (0.67-3.62)		29.500	0.594		0.552
Exhibit	10	1.64 (0.60-3.62)	1.85			7.55	
Do not exhibit	5	1.67 (0.67-6.00)	4.04			8.90	
50-64 years	91	1.30 (0.93-1.67)		1130.000	0.451		0.754
Exhibit	45	1.00 (0.67-1.66)	2.24			43.89	
Do not exhibit	46	1.32 (1.00-2.58)	2.24			48.07	
65+ years	30	0.97 (0.67-1.35)		114.500	0.869		0.168
Exhibit	13	1.00 (0.53-1.87)	1.09			15.19	
Do not exhibit	17	0.90 (0.67-1.76)	1.43			15.74	
Type of residence							
Independent/family/ community group home	51	1.35 (0.90-2.270)		329.000	0.319		0.996
Exhibit	16	1.08 (0.60-2.80)	1.96			22.94	
Do not exhibit	35	1.40 (1.00-2.53)	1.93			27.40	
Residential/campus	85	1.17 (0.87-1.50)		870.500	0.910		0.113
Exhibit	52	1.09 (0.70-1.57)	1.50			42.76	
Do not Exhibit	33	1.17 (0.75-2.25)	2.39			43.38	
Level of intellectual disability							
Mild	20	1.24 (0.67-2.60)		25.500	1.000		<0.001
Exhibit	3	1.00 (0.33-5.25)	-			10.50	
Do not exhibit	17	1.30 (0.67-2.60)	1.97			10.50	
Moderate	53	1.33 (0.80-2.27)		355.000	0.900		0.125
Exhibit	24	1.70 (0.67-2.80)	2.28			26.71	
Do not exhibit	29	1.33 (0.80-2.58)	2.09			27.24	
Severe/ Profound	56	1.18 (0.80-1.47)		340.500	0.979		-0.026
Exhibit	38	1.26 (0.67-1.57)	1.10			28.54	
Do not exhibit	18	1.12 (0.60-2.53)	2.47			28.42	
Types of seizures							
Generalised seizures	76	1.78 (1.18-2.67)		858.000	0.151		1.437
Exhibit	40	1.43 (0.80-2.00)	2.53			35.05	
Do not exhibit	36	2.37 (1.30-3.23)	2.77			42.33	
Other seizures	60	0.92 (0.67-1.30)		442.000	0.929		-0.089
Exhibit	28	0.97 (0.60-1.47)	0.96			30.71	
Do not exhibit	32	0.89 (0.67-1.30)	0.79			30.31	

Appendix 37 Supplementary Table S 6.7 - Mann Whitney U Test - AED load, demographic & clinical characteristics associated with stereotyped behaviour (n=136) *(Continued)*

STEREOTYPED BEHAVIOUR							
Variable	**n**	**Median AED load (95% CI)**	**IQR**	**Mann Whitney U**	**P value**	**Mean rank**	**Z value**
Type of therapy							
Monotherapy	61	0.67 (0.60-0.67)		478.000	0.816		0.233
Exhibit	33	0.60 (0.53-0.67)	0.28			30.52	
Do not exhibit	28	0.67 (0.40-0.80)	0.48			31.57	
Polytherapy	75	2.53 (1.87-3.00)		736.500	0.698		0.388
Exhibit	35	2.00 (1.60-3.17)	2.12			36.96	
Do not exhibit	40	2.59 (1.76-3.23)	2.61			38.91	
Seizure frequency							
None in the last year	77	0.90 (0.67-1.17)		672.000	0.578		-0.557
Exhibit	44	0.93 (0.67-1.35)	1.04			40.23	
Do not exhibit	33	0.87 (0.67-1.17)	0.79			37.36	
At least one in the last year	56	2.51 (1.67-3.34)		404.000	0.683		0.408
Exhibit	23	1.93 (0.95-4.17)	3.54			27.43	
Do not exhibit	33	2.58 (1.67-3.60)	2.76			29.24	
Co - morbid mental health condition							
Have psychotic disorder	10	1.19 (0.60-2.68)		12.000	1.000		<0.001
Exhibit	6	1.18 (0.33-4.64)	2.64			5.50	
Do not exhibit	4	1.19 (0.87-1.34)	0.41			5.50	
Have mood disorder	46	1.19 (0.70-1.53)		202.000	0.474		-0.715
Exhibit	31	1.33 (0.67-1.66)	1.20			24.48	
Do not exhibit	15	1.07 (0.53-1.76)	1.23			21.47	
Have anxiety disorder	47	1.33 (0.93-1.73)		287.000	0.478		0.709
Exhibit	30	1.09 (0.70-1.66)	1.33			22.93	
Do not exhibit	17	1.34 (0.87-2.53)	1.89			25.88	
Take antipsychotics							
Yes	54	1.24 (0.93-1.53)		350.000	0.633		0.477
Exhibit	36	1.09 (0.67-1.66)	1.18			26.78	
Do not exhibit	18	1.30 (0.87-2.43)	1.64			28.94	
No	82	1.30 (0.80-1.93)		881.500	0.438		0.775
Exhibit	32	1.15 (0.60-2.00)	2.40			38.95	
Do not exhibit	50	1.30 (0.80-2.53)	2.58			43.13	
Take antidepressants							
Yes	44	1.38 (1.00-1.76)		236.000	0.925		-0.094
Exhibit	20	1.50 (0.93-1.87)	1.33			22.70	
Do not exhibit	24	1.30 (0.80-2.67)	2.31			22.33	
No	92	1.06 (0.80-1.50)		1184.000	0.317		1.001
Exhibit	48	0.94 (0.67-1.57)	1.95			43.83	
Do not exhibit	44	1.25 (0.80-2.43)	2.20			49.41	

IQR- Interquartile Range. **Statistically significant results marked in bold and with an asterisk ***

Appendix 38 Supplementary Table S 6.8 - Behavioural definitions used in study

Behaviour type	Definition in Pre-interview Questionnaire (PIQ)
Self-injurious behaviour	Self-injurious behaviour (SIB) causes damage to the person's own body; i.e., damage has either already occurred, or is expected.
Aggressive/destructive behaviour	Aggressive or destructive behaviours are deliberate overt attacks directed towards other individuals or property.
Stereotyped behaviour	Stereotyped behaviours look unusual, strange or inappropriate to the average person. They are voluntary acts that occur repeatedly in the same way over and over again, and they are characteristic for that person. However, they do not cause physical damage.

Appendix 39 Supplementary Table S 7.1 Bivariate analysis of antidepressant subgroups with regards to participants reporting psychotic, mood and/or anxiety disorders (n=513)

Antidepressant	Total n=513 n (%)	Have mental health disorder n=260 n (%)	P value	Have psychotic disorder n=44 n (%)	P value	Have mood disorder n=180 n (%)	P value	Have anxiety disorder n=177 n (%)	P value
SSRI	119 (23.2)	92 (35.4)	**<0.001** [a]	13 (29.6)	0.297 [a]	65	**<0.001*** [a]	64 (36.2)	**<0.001*** [a]
Citalopram	16 (3.1)	13 (5.0)	0.013 [a]	2 (4.6)	0.639	9 (5.0)	0.072 [a]	8 (4.5)	0.185 [a]
Escitalopram	35 (6.8)	23 (8.8)	0.065 [a]	<5	-	12 (6.7)	0.918 [a]	15 (8.5)	0.281 [a]
Paroxetine	17 (3.3)	13 (5.0)	0.031 [a]	3 (6.8)	0.172	7 (3.9)	0.593 [a]	8 (4.5)	0.268 [a]
Fluoxetine	23 (4.5)	21 (8.1)	**<0.001*** [a]	4 (9.1)	0.125	18 (10.0)	**<0.001*** [a]	16 (9.0)	**<0.001*** [a]
Sertraline	28 (5.5)	22 (8.5)	0.002 [a]	3 (6.8)	0.724	19 (10.6)	**<0.001*** [a]	17 (9.6)	0.003 [a]
SNRI	19 (3.7)	17 (6.5)	**0.001*** [a]	6 (13.6)	0.003	15 (8.3)	**<0.001*** [a]	11 (6.2)	0.029 [a]
Venlafaxine	15 (2.9)	13 (5.0)	0.005 [a]	5 (11.4)	0.006	12 (6.7)	**<0.001*** [a]	8 (4.5)	0.119 [a]
Other	27 (5.3)	20 (7.7)	0.012* [a]	5 (11.4)	0.071	13 (7.2)	0.144	11 (6.2)	0.484 [a]
Mirtazapine	17 (3.3)	13 (5.0)	0.031 [a]	2 (4.6)	0.649	8 (4.4)	0.293 [a]	6 (3.4)	0.944 [a]
Trazodone	9 (1.8)	7 (2.7)	0.176	3 (6.8)	0.034	5 (2.8)	0.289	5 (2.8)	0.287
TCA	13 (2.5)	7 (2.7)	0.817 [a]	3 (6.8	0.092	6 (3.3)	0.393	5 (2.8)	0.773

P= Fisher Exact test (2 sided) [a] Chi Square test. P value: for Chi Square Test after applying Bonferroni Correction α=0.05/13= 0.004 thus p<0.004 for significance. <5 denotes fewer than 5 participants. Due to low numbers of participants reporting some psychotropic subclasses (<5), the categories duloxetine, agomelatine, clomipramine, trimipramine, lofepramine, doxepin, dosulepin and amitriptyline were removed from table. - denotes unable to calculate p value due to small numbers in subgroups. **Statistically significant results marked in bold and with an asterisk*.**

Appendix 40 Supplementary Table S 7.2 Bivariate analysis of antipsychotic subgroups with regards to participants reporting psychotic, mood and/or anxiety disorder (n=513)

Antipsychotic	Total n=513 n (%)	Have mental health disorder n=260 n (%)	P value	Have psychotic disorder n=44 n (%)	P value	Have mood disorder n=180 n (%)	P value	Have anxiety disorder n=177 n (%)	P value
Typical antipsychotic	70 (13.6)	55 (21.2)	**<0.001*** [a]	18 (40.9)	**<0.001*** [a]	37 (20.6)	**0.001 *** [a]	40 (22.6)	**<0.001*** [a]
Chlorpromazine	33 (6.4)	24 (9.2)	**0.009*** [a]	5 (11.4)	0.189	13 (7.2)	0.592 [a]	17 (9.6)	**0.034*** [a]
Haloperidol	22 (4.3)	19 (7.3)	**0.001*** [a]	8 (18.2)	**0.001***	15 (8.3)	**0.001*** [a]	15 (8.5)	**0.001*** [a]
Zuclopenthixol	14 (2.7)	11 (4.2)	**0.034*** [a]	7 (15.9)	**<0.001***	8 (4.4)	0.093	7 (4.0)	0.257
Atypical antipsychotics	184 (35.9)	148 (56.9)	**<0.001*** [a]	32 (72.7)	**<0.001*** [a]	102 (56.7)	**<0.001*** [a]	108 (61.0)	**<0.001*** [a]
Olanzapine	79 (15.4)	63 (24.2)	**<0.001*** [a]	16 (36.4)	**<0.001*** [a]	40 (22.2)	**0.002*** [a]	44 (24.9)	**<0.001*** [a]
Risperidone	73 (14.2)	59 (22.7)	**<0.001*** [a]	10 (22.7)	0.092 [a]	43 (23.9)	**<0.001*** [a]	43 (24.3)	**<0.001*** [a]
Quetiapine	28 (5.5)	23 (8.8)	**0.001** [a]	5 (11.4)	0.081	16 (8.9)	**0.012*** [a]	15 (8.5)	**0.029 *** [a]
Aripiprazole	15 (2.9)	13 (5.0)	**0.005*** [a]	2 (4.6)	0.374	13 (7.2)	**<0.001***	11 (6.2)	**0.001***

p= Fisher Exact test (2 sided) [a] Chi Square test. Due to low numbers of participants reporting some psychotropic subclasses (<5), the categories fluphenazine, flupenthixol, trifluoperazine, promazine, benperidol, sulpride, ziprasidone and amisulpride were removed from table. **Statistically significant results marked in bold and with an asterisk*.**

Appendix 41 Supplementary Table S 7.3 Bivariate analysis of lithium, anxiolytic and hypnotic & sedative subgroups with regards to participants reporting psychotic, mood and/or anxiety disorders (n=513)

	Total **n=513** **n (%)**	**Have mental health disorder** **n=260** **n (%)**	**P value**	**Have psychotic disorder** **n=44** **n (%)**	**P value**	**Have mood disorder** **n=180** **n (%)**	**P value**	**Have anxiety disorder** **n=177** **n (%)**	**P value**
Lithium	14 (2.7)	13 (5.0)	**0.001*** [a]	3 (6.8)	0.110	11 (6.1)	**0.001**	10 (5.6)	**0.007**
Anxiolytic benzodiazepines	78 (15.2)	61 (23.5)	**<0.001*** [a]	11 (25.0)	0.058 [a]	38 (21.1)	**0.006*** [a]	45 (25.4)	**<0.001*** [a]
Diazepam	38 (7.4)	32 (12.3)	**<0.001*** [a]	5 (11.4)	0.359	20 (11.1)	**0.019 *** [a]	24 (13.6)	**<0.001*** [a]
Alprazolam	17 (3.3)	12 (4.6)	0.095 [a]	3 (6.8)	0.172	8 (4.4)	0.293 [a]	11 (6.2)	**0.008*** [a]
Lorazepam	21 (4.1)	17 (6.5)	**0.005*** [a]	3 (6.8)	0.412	9 (5.0)	0.446 [a]	10 (5.6)	0.197 [a]
Hypnotics & sedatives	51 (9.9)	37 (14.2)	0.001* [a]	7 (15.9)	0.184	29 (16.1)	0.001* [a]	28 (15.8)	0.001* [a]
Z drugs	30 (5.8)	21 (8.1)	**0.029*** [a]	3 (6.8)	0.735	16 (8.8)	**0.031 *** [a]	15 (8.5)	0.066 [a]
Zolpidem	12 (2.3)	8 (3.1)	0.262 [a]	3 (6.8)	0.075	7 (3.8)	0.123	6 (3.4)	0.356
Zopiclone	18 (3.5)	13 (5.0)	0.063 [a]	0 (0)	-	9 (5.0)	0.177 [a]	9 (5.1)	0.159 [a]

Appendix 41 Supplementary Table S 7.3 Bivariate analysis of anxiolytic and hypnotic & sedative subgroups with regards to participants reporting psychotic, mood and/or anxiety disorders (n=513) (*Continued*)

	Total **n=513** **n (%)**	**Have mental health disorder** **n=260** **n (%)**	**P value**	**Have psychotic disorder** **n=44** **n (%)**	**P value**	**Have mood disorder** **n=180** **n (%)**	**P value**	**Have anxiety disorder** **n=177** **n (%)**	**P value**
Prolonged acting hypnotic	10 (1.9)	8 (3.1)	0.106	<5	-	5 (2.7)	0.332	8 (4.5)	**0.004***
Flurazepam	9 (1.8)	7 (2.7)	0.176	<5	-	5 (2.7)	0.289	7 (4.0)	**0.010***
Short acting hypnotic	5 (1.0)	4 (1.5)	0.373	<5	-	4 (2.2)	0.054	4 (2.3)	0.050
Melatonin	9 (1.8)	7 (2.7)	0.176	3 (6.8)	**0.034***	7 (3.8)	**0.011***	<5	0.174

p= Fisher Exact test (2 sided) [a] Chi Square test. <5 denotes fewer than 5 participants. Due to low numbers of participants reporting some psychotropic subclasses (<5), the categories chlordiazepoxide, bromazepam, prazepam, hydroxyzine, buspirone, nitrazepam, temazepam, lormetazepam and triazolam and other anxiolytics were removed from table. **Statistically significant results marked in bold and with an asterisk*. Anxiolytics PRN included where prescribed.**

Appendix 42 Supplementary Table S 7.4 Bivariate analysis of psychotropic subgroups with regards to the gender of participants who report a mental health disorder (n=260)

Prescription of	Total n=260 n (%)	Male n= 112 n (%)	Female n=148 n (%)	P value
Any psychotropic	233 (89.6)	101 (90.2)	132 (89.2)	0.796
Psychotropic polypharmacy (Range 2-5)	147 (56.5)	64 (57.1)	83 (56.1)	0.864
Any antipsychotic	185 (71.2)	87 (77.7)	98 (66.2)	0.043
Typical antipsychotics	55 (21.2)	27 (24.1)	28 (18.9)	0.310
Atypical antipsychotics	148 (56.9)	71 (63.4)	77 (52.0)	0.067
Any antidepressant	131 (50.4)	50 (44.6)	81 (54.7)	0.107
SSRI	92 (35.4)	34 (30.4)	58 (39.2)	0.140
SNRI	17 (6.5)	7 (6.3)	10 (6.8)	0.870
TCA	7 (2.7)	2 (1.8)	5 (3.4)	0.702
Other (mirtazapine, trazodone, agomelatine)	20 (7.7)	8 (7.1)	12 (8.1)	0.772
Mood stabilising AED	123 (47.3)	57 (50.9)	66 (44.6)	0.314
Mood stabilising AED (no epilepsy diagnosis)	38 (14.6)	17 (15.2)	21 (14.2)	0.823
Lithium	13 (5.0)	5 (4.5)	8 (5.4)	0.730
Any anxiolytics	63 (24.2)	32 (28.6)	31 (20.9)	0.155
Anxiolytic benzodiazepine	61 (23.5)	32 (28.6)	29 (19.6)	0.091
Drugs for dementia	7 (2.7)	2 (1.8)	5 (3.4)	0.702
Anti-cholinergic N04A	61 (23.5)	31 (27.7)	30 (20.3)	0.163
Any hypnotics & sedatives	37 (14.2)	13 (11.6)	24 (16.2)	0.292
Z drugs	21 (8.1)	6 (5.4)	15 (10.1)	0.161
Prolonged acting hypnotic benzodiazepines	8 (3.1)	4 (3.6)	4 (2.7)	0.729[a]

p=Chi Square test [a] Fisher Exact test (2 sided). P value: for Chi Square Test after applying Bonferroni Correction α=0.05/18= 0.0028 thus p<0.0028 for significance. Due to low numbers of participants reporting some psychotropic subclasses (<5), 'other anxiolytic' category (hydroxyzine/buspirone) was removed from table. The category short acting hypnotic benzodiazepines (n=4) was removed from table due to low numbers in male subgroup. **Statistically significant results marked in bold and with an asterisk.**

Appendix 43 Supplementary Table S 7.5 Bivariate analysis of psychotropic subgroups with regards to the type of residence of participants who report a mental health disorder (n=260)

Prescription of	Total n=260 n (%)	Independent/ with family n=17 n (%)	Community group home n=95 n (%)	Residential/ campus setting n=148 n (%)	P value
Any psychotropic	233 (89.6)	15 (88.2)	89 (93.7)	129 (87.2)	-
Psychotropic polypharmacy (Range 2-5)	147 (56.5)	10 (58.8)	51 (53.7)	86 (58.1)	0.779
Any antipsychotic	185 (71.2)	11 (64.7)	65 (68.4)	109 (73.6)	-
Typical antipsychotics	55 (21.2)	6 (35.3)	13 (13.7)	36 (24.3)	-
Atypical antipsychotics	148 (56.9)	8 (47.1)	58 (61.1)	82 (55.4)	0.478
Any antidepressant	131 (50.4)	10 (58.8)	49 (51.6)	72 (48.6)	0.699
SSRI	92 (35.4)	8 (47.1)	33 (34.7)	51 (34.5)	0.581
TCA	7 (2.7)	0 (0)	4 (4.2)	3 (2.0)	-
Mood stabilising AED	123 (47.3)	8 (47.1)	33 (34.7)	82 (55.4)	0.007
Mood stabilising AED (no epilepsy diagnosis)	38 (14.6)	4 (23.5)	11 (11.6)	23 (15.5)	-
Lithium	13 (5.0)	3 (17.6)	4 (4.2)	6 (4.1)	-
Any anxiolytics	63 (24.2)	2 (11.8)	19 (20.0)	42 (28.4)	-
Anxiolytic benzodiazepines	61 (23.5)	2 (11.8)	17 (17.9)	42 (28.4)	-
Drugs for dementia	7 (2.7)	0 (0)	5 (5.3)	2 (1.4)	-
Anti-cholinergic N04A	61 (23.5)	4 (23.5)	17 (17.9)	40 (27.0)	-
Any Hypnotics & sedatives	37 (14.2)	2 (11.8)	15 (15.8)	20 (13.5)	-

p=Chi Square test [a] Fisher Exact test (2 sided). **–** denotes unable to calculate p value due to small numbers in subgroups. Due to low numbers of participants reporting some psychotropic subclasses (<5), 'other anxiolytic' category (hydroxyzine/buspirone) and short acting hypnotic benzodiazepines category were removed from table. The categories SNRI (n=17), other antidepressants (n=20) Z drugs (n=21) and prolonged acting hypnotic benzodiazepines (n=8) were removed from table due to low numbers in independent/family subgroup. **Statistically significant results marked in bold and with an asterisk.**

Appendix 44 Supplementary Table S 7.6 Bivariate analysis of psychotropic subgroups with regards to the age of participants who report a mental health disorder (n=260)

Prescription of	Total n=260 n (%)	Age <50 years n=30 n (%)	Age 50-64 years n=156 n (%)	Age 65+ years n=74 n (%)	P value
Any psychotropic	233 (89.6)	27 (90.0)	140 (89.7)	66 (89.2)	-
Psychotropic polypharmacy (Range 2-5)	147 (56.5)	18 (60.0)	90 (57.7)	39 (52.7)	0.714
Any antipsychotic	185 (71.2)	21 (70.0)	111 (71.2)	53 (71.6)	0.986
Typical antipsychotics	55 (21.2)	5 (16.7)	33 (21.2)	17 (23.0)	0.775
Atypical antipsychotics	148 (56.9)	20 (66.7)	91 (58.3)	37 (50.0)	0.255
Any antidepressant	131 (50.4)	16 (53.3)	83 (53.2)	32 (43.2)	0.348
SSRI	92 (35.4)	10 (33.3)	60 (38.5)	22 (29.7)	0.420
Other (mirtazapine, trazodone, agomelatine)	20 (7.7)	2 (6.7)	13 (8.3)	5 (6.8)	-
Mood stabilising AED	123 (47.3)	11 (36.7)	80 (51.3)	32 (43.2)	0.242
Mood stabilising AED (no epilepsy diagnosis)	38 (14.6)	3 (10.0)	23 (14.7)	12 (16.2)	-
Lithium	13 (5.0)	3 (10.0)	6 (3.8)	4 (5.4)	-
Any anxiolytics	63 (24.2)	6 (20.0)	39 (25.0)	18 (24.3)	0.842
Anxiolytic benzodiazepines	61 (23.5)	6 (20.0)	38 (24.4)	17 (23.0)	0.869
Drugs for dementia	7 (2.7)	0 (0)	5 (3.2)	2 (2.7)	-
Anti-cholinergic N04A	61 (23.5)	4 (13.3)	42 (26.9)	15 (20.3)	0.204
Any hypnotics & sedatives	37 (14.2)	2 (6.7)	21 (13.5)	14 (28.9)	-
Z drugs	21 (8.1)	0 (0)	12 (7.7)	9 (12.2)	-
Prolonged acting hypnotic benzodiazepines	8 (3.1)	2 (6.7)	4 (2.6)	2 (2.7)	-

p=Chi Square test. [a] Fisher Exact test (2 sided). - Unable to calculate p value due to small numbers in subgroups. Due to low numbers of participants reporting some psychotropic subclasses (<5), 'other anxiolytic' category (hydroxyzine/buspirone) was removed from table. The category SNRI (N=17) was also removed from table due to low numbers in subgroups age <50 years. The categories TCA and short acting hypnotic benzodiazepines (n=5) were also removed due to low numbers in the age 65+ years subgroup. **Statistically significant results marked in bold and with an asterisk.**

Appendix 45 Supplementary Table S 7.7 Bivariate analysis of psychotropic subgroups with regards to the level of intellectual disability of participants who report a mental health disorder (n=244)

Prescription of	Total n=244 n (%)	Mild n=45 n (%)	Moderate n=109 n (%)	Severe/profound n=90 n (%)	P value
Any psychotropic	220 (90.2)	42 (93.3)	98 (89.9)	80 (88.9)	-
Psychotropic polypharmacy (Range 2-5)	137 (56.1)	27 (60.0)	65 (59.6)	45 (50.0)	0.334
Any antipsychotic	175 (71.7)	32 (71.1)	79 (72.5)	64 (71.1)	0.973
Typical antipsychotics	52 (21.3)	9 (20.0)	22 (20.2)	21 (23.3)	0.840
Atypical antipsychotics	140 (57.4)	25 (55.6)	65 (59.6)	50 (55.6)	0.815
Any antidepressant	126 (51.6)	30 (66.7)	61 (56.0)	35 (38.9)	**0.005***
SSRI	87 (35.7)	20 (44.4)	44 (40.4)	23 (25.6)	**0.037***
SNRI	17 (7.0)	5 (11.1)	8 (7.3)	4 (4.4)	-
Other (mirtazapine, trazodone, agomelatine)	20 (8.2)	5 (11.1)	7 (6.4)	8 (8.9)	-
Mood stabilising AED	117 (48.0)	16 (35.6)	50 (45.9)	51 (56.7)	0.058
Mood stabilising AED (no epilepsy diagnosis)	35 (14.3)	7 (15.6)	17 (15.6)	11 (12.2)	0.770
Any anxiolytics	59 (24.2)	6 (13.3)	33 (30.3)	20 (22.2)	0.071
Anxiolytic benzodiazepines	57 (23.4)	6 (13.3)	31 (28.4)	20 (22.2)	0.125
Anti-cholinergic N04A	59 (24.2)	10 (22.2)	25 (22.9)	24 (26.7)	0.783
Any hypnotics & sedatives	34 (13.9)	3 (6.7)	17 (15.6)	14 (15.6)	0.297
Prolonged acting hypnotic benzodiazepines	8 (3.3)	2 (4.4)	3 (2.8)	3 (3.3)	-

p=Chi Square test [a] Fisher Exact test (2 sided - Unable to calculate p value due to small numbers in subgroups. Due to low numbers of participants reporting some psychotropic subclasses (<5), 'other anxiolytic' category (hydroxyzine/buspirone) and short acting hypnotic benzodiazepines were removed from table. Lithium (n=13), Z drugs (n=18) and drugs for dementia (n=7) were also removed due to low numbers in the mild intellectual disability category. TCA (n=7) was removed due to low numbers in the severe/profound intellectual disability category. **Statistically significant results marked in bold and with an asterisk.**

Appendix 46 Supplementary Table S 7.8 Binary logistic regression of demographic and clinical factors associated with reporting a mental health disorder (A)

	Reporting mental health disorder (n=386)	
Characteristic	Odds Ratio (95%CI)	P Value
Gender		0.754
Male	1 (Reference)	
Female	0.925 (0.569-1.505)	
Age		
<50 years	1 (Reference)	
50-64 years	0.994 (0.469-2.105)	0.988
65+ years	1.660 (0.710-3.883)	0.243
Level of intellectual disability		
Mild	1 (Reference)	
Moderate	1.654 (0.846-3.235)	0.141
Severe/profound	2.165 (1.006-4.658)	**0.048***
Type of residence		
Family/independent	1 (Reference)	
Community group home	1.579 (0.664-3.756)	0.302
Residential/campus	2.041 (0.831-5.011)	0.120
Take psychotropic polypharmacy		**<0.001***
No	1 (Reference)	
Yes	8.794 (5.071-15.250)	
Exhibit challenging behaviour		
No	1 (Reference)	
Yes	2.047 (1.202-3.485)	**0.008***
Have epilepsy diagnosis		
No	1 (Reference)	
Yes	1.253 (0.749-2.095)	0.390

Reference groups- male gender, <50 years, mild intellectual disability, independent/family residence, no psychotropic polypharmacy, no challenging behaviour, no epilepsy diagnosis.

Statistically significant results marked in bold and with an asterisk*.

Reference category: Did not report a mental health disorder.

Cox & Snell R^2 0.275 Nagelkerke R^2 0.366

Appendix 47 Supplementary Table S 7.9 Binary logistic regression of demographic and clinical factors associated with reporting a mental health disorder (B)

	Reporting mental health disorder (n=386)	
Characteristic	Odds Ratio (95%CI)	P Value
Gender		0.744
Male	1 (Reference)	
Female	0.914 (0.534-1.565)	
Age		
<50 years	1 (Reference)	
50-64 years	1.227 (0.554-2.715)	0.614
65+ years	1.769 (0.721-4.344)	0.213
Level of intellectual disability		
Mild	1 (Reference)	
Moderate	2.327 (1.133-4.781)	**0.021***
Severe/profound	2.552 (1.128-5.774)	**0.025***
Type of residence		
Family/independent	1 (Reference)	
Community group home	0.987 (0.375-2.599)	0.979
Residential/campus	1.437 (0.529-3.905)	0.477
Categorised number of psychotropic drugs		
0	1 (Reference)	
1 (mono)	10.128 (5.207-19.701)	**<0.001***
2+ (poly)	28.623 (14.306-57.268)	**<0.001***
Exhibit challenging behaviour		0.178
No	1 (Reference)	
Yes	1.502 (0.831-2.713)	
Have epilepsy diagnosis		0.442
No	1 (Reference)	
Yes	1.248 (0.709-2.195)	

Reference groups- male gender, <50 years, mild intellectual disability, independent/family residence, no psychotropic medication, no challenging behaviour, no epilepsy diagnosis.

Statistically significant results marked in bold and with an asterisk*.

Reference category: Did report mental health disorder.

Cox & Snell R^2 0.369 Nagelkerke R^2 0.492

Appendix 48 Supplementary Table S 7.10 – Categories of challenging behaviours

Behaviour category	Type of behaviour
Self-Injurious Behaviour (SIB)	
	Self- Biting
	Head Hitting
	Body Hitting
	Self-Scratching
	Pica
	Objects in Nose
	Hair Pulling
	Teeth Grinding
Aggressive/destructive behaviour	
	Hitting Others
	Kicking Others
	Pushing Others
	Biting Others
	Grabbing & Pulling Others
	Scratching Others
	Pinching Others
	Verbally Abusive with Others
	Destroying Things (e.g. rips clothes, throws chairs, smashes tables)
	Bullying (being mean or cruel e.g. grabbing toys or food from others)
Stereotyped behaviour	
	Rocking & Repetitive Body Movements
	Sniffing Objects, Own Body
	Waving & Shaking Arms
	Manipulating (e.g. twirling, spinning)
	Repetitive Hand and/or Finger
	Yelling & Screaming
	Pacing, Jumping, Bouncing, Running
	Rubbing Self
	Gazing at Hands or Objects
	Bizarre Movements/Postures
	Clapping Hands
	Grimacing

Appendix 49 Supplementary Table S 7.11 List of psychotropic drugs prescribed in Wave 3 of study

Psychotropic class	Psychotropic subclass	Drug name
Antipsychotics	Typical antipsychotics	Chlorpromazine
		Fluphenazine
		Trifluoperazine
		Haloperidol
		Zuclopenthixol
		Flupenthixol
		Promazine
		Beniperidol
	Atypical antipsychotics	Olanzapine
		Quetiapine
		Sulpride
		Amisulpride
		Risperidone
		Aripiprazole
		Ziprasidone
Antidepressants	SSRI	Citalopram
		Escitalopram
		Paroxetine
		Fluoxetine
		Sertraline
	SNRI	Duloxetine
		Venlafaxine
	Other	Mirtazapine
		Trazodone
		Agomelatine
	TCA	Clomipramine
		Lofepramine
		Trimipramine
		Doxepin
		Dosulepin
		Amitriptyline
Anxiolytics	Anxiolytic benzodiazepines	Diazepam
		Chlordiazepoxide
		Bromazepam
		Prazepam
		Alprazolam
		Lorazepam
	Other	Hydroxyzine
		Buspirone
Mood stabilising agent		Lithium

Appendix 49 Supplementary Table S 7.11 List of psychotropic drugs prescribed in study (*Continued*)

Psychotropic class	Psychotropic subclass	Drug name
Antiepileptics		Valproic Acid
		Lamotrigine
		Carbamazepine
		Levetiracetam
		Phenobarbital
		Primidone
		Phenytoin
		Rufinamide
		Eslicarbazepine
		Topiramate
		Gabapentin
		Zonisamide
		Pregabalin
		Lacosamide
		Perampanel
		Clobazam
		Clonazepam
Hypnotics & sedatives	Z Drug hypnotics	Zolpidem
		Zopiclone
	Prolonged acting hypnotics	Nitrazepam
		Flurazepam
	Short acting hypnotics	Lormetazepam
		Triazolam
		Temazepam
	Other	Melatonin
Drugs for dementia		Memantine
		Donepezil
Anti-cholinergic (NO4A)		Biperiden
		Procyclidine
		Benzatropine

Appendix 50 Supplementary Table S 7.12 Median prescribed psychotropic dosages in Wave 3 (n=549)

Psychotropic class	Total n=549 n (%)	Median prescribed daily dosage PO (mg) + range if applicable. Depot max dosage prescribed where given IM (mg). (All dosages regular not PRN medication)
Antipsychotics		
Chlorpromazine	35 (6.4)	150mg PO (50-950mg)
Fluphenazine	3 (0.6)	Depot max 100mg q 2/52
Trifluoperazine	4 (0.7)	6mg PO (1-14mg)
Haloperidol	27 (4.9)	4.5mg PO (1-40mg)
Zuclopenthixol	14 (2.6)	26mg PO (10-100mg), DEPOT max 550mg q 1/52
Olanzapine	83 (15.2)	10mg PO (2.5-20mg) (n=4 missing dosage)
Quetiapine	28 (5.1)	150mg PO (25-800mg)
Risperidone	77 (14.1)	2mg PO (0.125-20mg), DEPOT max 25mg q 2/52 (n=2 missing dosage)
Aripiprazole	15 (2.7)	15mg PO (2.5-30mg)
Flupenthixol	4 (0.7)	DEPOT max 400mg q 21/7
Antidepressants		
Citalopram	17 (3.1)	20mg PO (10-60mg) (n=1 missing dosage)
Escitalopram	36 (6.6)	10mg PO (2.5-20mg)
Paroxetine	18 (3.3)	40mg PO (20-60mg)
Fluoxetine	25 (4.6)	20mg PO (10-60mg)
Sertraline	32 (5.8)	100mg PO (25-300mg)
Duloxetine	4 (0.7)	30mg PO (30-120mg) (n=1 missing dosage)
Mirtazapine	18 (3.3)	30mg PO (15-45mg)
Venlafaxine	17 (3.1)	112.5mg PO (37.5-225mg)
Trimipramine	6 (1.1)	75mg PO (25-100mg)
Clomipramine	3 (0.6)	75mg PO (75-100mg)
Lofepramine	2 (0.4)	140mg PO (n=1 missing dosage)
Amitriptyline	3 (0.6)	50mg PO (25-200mg)
Trazodone	9 (1.6)	150mg PO (50-300mg)
Antiepileptics		
Valproic acid	108 (19.7)	1200mg PO (200-3000mg) (n=3 missing dosage)
Lamotrigine	71 (13.0)	200mg PO (25-700mg)
Carbamazepine	93 (17.0)	600mg PO (100-1800mg) (n=1 missing dosage)
Levetiracetam	48 (8.8)	2000mg PO (250-3500mg) (n=2 missing dosage)
Phenobarbital	14 (2.6)	90mg PO (30-165mg)
Primidone	4 (0.7)	250mg PO (n=2 missing dosage)
Phenytoin	11 (2.0)	300mg PO (250-500mg)
Rufinamide	2 (0.4)	2000mg PO (800-3200mg)
Eslicarbazepine	2 (0.4)	1600mg PO (1200-2000mg)
Topiramate	6 (1.1)	187.5mg PO (100-400mg)
Zonisamide	9 (1.6)	400mg PO (100-600mg)

Appendix 50 Supplementary Table S 7.12 Median prescribed psychotropic dosages in Wave 3 (n=549) (*Continued*)

Psychotropic class	Total n=549 n (%)	Median prescribed daily dosage PO (mg) + range if applicable. Depot max dosage prescribed where given IM (mg). (All dosages regular not PRN medication)
Antiepileptics (*Continued*)		
Pregabalin	17 (3.1)	175mg PO (50-525mg)
Lacosamide	6 (1.1)	200mg PO (200-400mg)
Clobazam	23 (4.2)	20mg PO (5-40mg)
Clonazepam	20 (3.6)	1.5mg PO (0.25-10mg) (n=1 missing dosage)
Mood stabilising agents		
Lithium	16 (2.9)	600mg PO (400-2080mg)
Anxiolytics		
Diazepam	39 (7.1)	5mg PO (2-30mg) (n=30 regular medication)
Chlordiazepoxide	2 (0.4)	20mg PO
Bromazepam	2 (0.4)	2.25mg PO (1.5-3mg)
Alprazolam	18 (3.3)	0.625mg PO (0.25-2.5mg) (n=12 regular medication)
Lorazepam	21 (3.8)	1mg (0.5-1.5mg) (n=5 regular medication)
Hydroxyzine	2 (0.4)	25mg PO
Buspirone	2 (0.2)	12.5mg PO (10-15mg)
Hypnotics & sedatives		
Zolpidem	12 (2.2)	8.75mg PO (5-10mg)
Flurazepam	9 (1.6)	15mg PO (15-30mg) (n=7 regular medications, n=1 missing)
Temazepam	3 (0.6)	10mg PO (n=1 regular medication)
Zopiclone	18 (3.3)	7.5mg PO (3.75-7.5mg) (n=16 regular medication)
Melatonin	9 (1.6)	3mg PO (2-7.5mg) (n=8 regular medication)
Drugs for dementia		
Memantine	9 (1.6)	15mg PO (5-25mg)
Donepezil	7 (1.3)	10mg PO (5-10mg)
Anti-cholinergic (N04A)		
Biperiden	53 (9.7)	2mg PO (1-6mg)
Procyclidine	18 (3.3)	5mg PO (2.5-30mg)
Benzatropine	2 (0.4)	28mg PO (24-32mg)

Due to low numbers of participants being prescribed some psychotropic medication (<5), fluphenazine, trifluoperazine, sulpiride, amisulpride, flupenthixol, benperidol, promazine, ziprasidone, duloxetine, clomipramine, lofepramine, agomelatine, doxepin, dosulepin, amitriptyline, primidone, rufinamide, eslicarbazepine, gabapentin, perampanel, chlordiazepoxide, bromazepam, prazepam, hydroxyzine, buspirone, nitrazepam, temazepam, lormetazepam, triazolam and benzatropine were removed from table. Topiramate (n=6) (median 187.5mg PO (100-400mg) and zonisamide (n=9) (median 400mg PO (100-600mg) were also removed from table due to low numbers in the 'have categorised mental health disorder' category.