

Abstract

Background

Adults with intellectual disability are prescribed high levels of medication, with polypharmacy and psychotropic polypharmacy common. However, reported rates vary between studies and there has been an over-reliance on obtaining data from convenience samples. The objective of this study was to determine the prevalence of medication use and polypharmacy in a population-level sample of adults with intellectual disabilities. Factors associated with polypharmacy and psychotropic polypharmacy are explored.

Methods

We used a total population sample of 217 adults with intellectual disabilities known to services in Jersey (sampling frame n=285). The Anatomical Therapeutic Chemical (ATC) classification system was used to categorise medications that participants were currently taking. We examined associations of polypharmacy and psychotropic polypharmacy with socioeconomic status, health and demographic variables using univariate and multivariate analysis.

Results

A total of 83.4% of participants were prescribed medication, with high doses common. 38.2% of participants were exposed to polypharmacy while 23% of participants were exposed to psychotropic polypharmacy. After controlling for demographic, health and socioeconomic characteristics, polypharmacy was significantly associated with older age, increased severity of intellectual disability, living in a residential setting and having increased co-morbidities. Psychotropic polypharmacy was associated with being male, being aged 50+ years and having had a psychiatric diagnosis over the life course. Being prescribed psychotropic drugs above the Defined Daily Dose (DDD) was not associated with having had a psychiatric diagnosis over the life course, suggesting the possibility of 'off label' prescribing.

Conclusions

Our results indicate that medication use, in high doses, alongside polypharmacy and psychotropic polypharmacy are highly prevalent in adults with intellectual disability. The exposure to multiple medications increases the risk of developing adverse drug events, drug-drug interactions and medication-related problems. Future population-level, prospective cohort studies should examine the prevalence of polypharmacy and psychotropic polypharmacy using standardised definitions and consider the potential impact of adverse drug events, drug-drug interactions and medication-related problems in this population.

Keywords: Polypharmacy, psychotropic polypharmacy, intellectual disability, socioeconomic status, health, medication

Accepted Version

Introduction

People with intellectual disability have considerably greater health needs than the general population (McMahon & Hatton, 2020; Kinnear *et al.* 2018; Hughes McCormack *et al.* 2018) and are more likely to die at an earlier age than their non-disabled peers (Glover *et al.* 2017; O'Leary *et al.* 2018). They are prescribed more medication than people without intellectual disabilities and polypharmacy is common in this population (Emerson *et al.* 2016; O' Dwyer *et al.* 2017; 2019; Hove *et al.* 2019). Although polypharmacy may be clinically indicated and considered appropriate (Masnoon *et al.* 2017), the concurrent use of many drugs increases the risk of an individual developing adverse effects and is related to poorer outcomes (O' Dwyer *et al.* 2018).

In recent years, the principal focus of medication research in people with intellectual disability has centred on psychotropic drug use (Gomes *et al.* 2019; Lunskey *et al.* 2018; Glover *et al.* 2015; Seehan *et al.* 2015; Bowring *et al.* 2017a; O' Dwyer *et al.* 2017). While it is important that the high use of psychotropic drugs in this population is addressed as a matter of urgency (Valdovinos *et al.* 2009; Matson and Mahon, 2010), it is also essential that overall prescribing patterns are examined. Medication use and polypharmacy, in particular, can serve as an important indicator of potential mortality as it represents the burden of disease that this population experiences (Hove *et al.* 2019). Studies of the prevalence of polypharmacy in people with an intellectual disability report rates varying from 11% to 60% (Stortz *et al.* 2014). There is also significant variation in the reported prevalence of psychotropic polypharmacy, with prevalence rates reported from 22% to 40% (O'Dwyer *et al.* 2017; Lunskey and Modi, 2018). This is consistent with the range of reported psychotropic prescribing

rates in the literature varying from 25% to 89% (Deb *et al.* 2015; Scheifes *et al.* 2016; Bowring *et al.* 2017). The high degree of reported variance in psychotropic prescribing rates and polypharmacy in general is a consequence of the heterogeneity of polypharmacy definitions (Masnoon *et al.* 2017), weak analytical approaches (Stortz *et al.* 2014) and convenience or clinic sampling being used in most studies (Stortz *et al.* 2014 Haider *et al.* 2014, Bowring *et al.* 2017a).

Another issue concerns the factors associated with polypharmacy and psychotropic polypharmacy. Recent evidence has identified gender is not associated with polypharmacy in adults with intellectual disability (Stolker *et al.* 2001; Haider *et al.* 2014; O'Dwyer *et al.* 2016), whereas institutional or residential living is associated with increased psychotropic medication use and medication use in general (Bowring *et al.* 2017a). Additionally, mental health or neurological conditions are reported to be strongly associated with polypharmacy (O'Dwyer *et al.* 2016). Findings are inconsistent on whether older age is associated with polypharmacy (O'Dwyer *et al.* 2016; Haider *et al.* 2014).

Despite the established evidence base in the general literature identifying that polypharmacy follows a societal gradient (Haider *et al.* 2009; Morin *et al.* 2018; Rawle *et al.* 2018; Assari and Bazargan, 2019) there is an absence lack of research in the intellectual disability arena focusing on socioeconomic issues, although Haider *et al.* (2014) identified that unemployment was strongly related to polypharmacy in a representative sample of adults with intellectual disability. The lack of such evidence may be a consequence of the low socioeconomic position that people with intellectual disability typically occupy within a societal gradient (Graham 2005;

Emerson and Hatton, 2009), resulting in inadequate heterogeneity of participants for meaningful analysis.

It is clear that there is a need for population-based sampling studies examining patterns and prevalence of polypharmacy and psychotropic polypharmacy using a standardised polypharmacy definition (Stortz *et al.* 2014). It is also important to identify factors associated with polypharmacy and psychotropic polypharmacy.

Therefore, this present study investigated the prevalence of medication use in a total administrative population of adults with intellectual disability in Jersey. More specifically, the aims of this study were:

- To determine the prevalence and patterns of polypharmacy and psychotropic polypharmacy in a total population sample of adults with intellectual disability.
- To examine the relationship between polypharmacy, psychotropic polypharmacy, socioeconomic status, health and demographic variables in a total population sample.

Methods

Study Design

Jersey Context

Jersey is a self-governing British Crown dependency with a population of just over 105,000 people (States of Jersey, 2019). All individuals with intellectual disability in Jersey have access to specialist intellectual disability services that operate peripatetically. People with complex, physical, behavioural or psychiatric needs are assigned a community nurse who coordinates the necessary specialist health and social care intellectual disability support. Most people with intellectual disability in

Jersey live with their family, in congregate care or in dispersed residential (<4 people) or independent homes in the community provided either by the Government or by a provider organisation.

Intellectual Disability Sample

At the time of data collection, 285 individuals were known to intellectual disability services in Jersey (i.e. these were adults [≥ 18 years] currently receiving, or adults at the time of data collection who had previously received support from intellectual disability services). A total administrative sample of 217 adults with intellectual disability in Jersey participated. This represented a 76% response rate. Eighty-five (39.2%) participants consented independently, while 132 (60.8%) participants were consented through proxy procedures. All information was collected by face-to-face interview with the person and/or a personal or nominated consultee (Department of Health, 2008). Medication data were collected directly from prescription charts, individual medication administration records or by examining any medication the person had in their possession.

Variables

Medication classification

Each participant or proxy representative was asked what medication they were prescribed, what dosage the medication was prescribed at, was it prescribed regularly, for a short course basis or on a PRN "*pro re nata*" basis. PRN medication was included if it had been prescribed in the previous 28-day prescribing cycle by a medical prescriber. Medication included oral, intramuscular, subcutaneous, sublingual, buccal, rectal, vaginal, ocular, otic, nasal, inhaled, nebulised, cutaneous (topical) and transdermal preparations. Each participant's medication record was

validated against their electronic health and social service record. All medicines were coded using the World Health Organisation (WHO) Anatomical Therapeutic Chemical (ATC) [WHO, nd] classification system. Neurological medicines were coded to pharmacological subgroup level (four elements), while all other medicines were coded to their main group level (one element) (Bowring *et al.* 2017). For psychotropic preparations, the Defined Daily Dosage (DDD) for each drug was computed. The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults (WHO, nd). Twenty percent of entries were cross-checked by the third author for accuracy and no errors were reported.

Polypharmacy

A recent review by Masnoon *et al.* (2017) identified 138 different definitions of polypharmacy. In the absence of a consensus, this study follows O'Dwyer *et al.* (2016) who define polypharmacy as the concurrent use of five or more drugs and excessive polypharmacy as ten or more drugs. Although this definition of polypharmacy relates to older people with intellectual disability, and older people's research more broadly, the concurrent use of five or more drugs has also been used in an Australian study for adults with intellectual disability (Haider *et al.* 2014) and a secondary analysis of longitudinal data in England (Emerson *et al.* 2016).

Psychotropic Polypharmacy

In a separate study, O'Dwyer *et al.* (2017) defines psychotropic polypharmacy as the concurrent use of two or more psychotropic agents in one individual (Mojtabai and Olfson 2010; Lake *et al.* 2012). Therefore, psychotropic polypharmacy was operationally defined as concurrent prescriptions for two or more psychotropic

agents from the following ATC classifications: N04A Anticholinergic Agents; N05A Antipsychotic drugs; N05B Anxiolytics; N05C Hypnotics & Sedatives; N06A Antidepressants; N06B Psychostimulants; N03A Antiepileptics as mood stabilisers.

Health

A continuous variable was developed using the ICD-10 (2015) English online version chapter headings I to XV (McMahon & Hatton, 2020) calculating the cumulative number of ICD-10 conditions a participant was reported to have (range 0-14). A binary measure (good vs poor) of self-rated (n=85) and proxy-rated health (n=82) was also used. This was adapted from the EQ-5D-5L health related quality of life questionnaire (EuroQol Research Foundation, 2009). Other binary variables such as epilepsy diagnosis, psychiatric diagnosis over the life course (diagnosed by a psychiatrist) and Down syndrome were also included.

Socioeconomic Status

Three objective indicators of socioeconomic status were used in this study; education, occupation and income. Due to the low variation in these three indicators for people with an intellectual disability, education was operationalised as 'formal education vs no formal education', income was classified as 'above or below £15,000 per annum (pa)' and occupation was defined as 'in employment vs unemployed'. For unadjusted comparisons, a socioeconomic status score (SES Score) was calculated. No formal education, income below £15,000pa and unemployment were scored at '1' per variable. Formal education, income above £15,000pa and being in employment was scored at '2' per variable. A score of 3

represented a low SES score and an SES score of ≥ 4 represented a higher SES score. Any SES variable with missing data was excluded from analysis.

Demographic characteristics

This study is part of a larger comparative study and all demographic variables were collected to mirror the general population 'Jersey Opinions and Lifestyle Survey' (States of Jersey, 2017). For residential status, a binary variable was created; residential care (full-time residential care for single occupancy [n=4], residential setting for multiple occupancy [n=100] and nursing home setting [n=3] [total residential care n=107]; [49.3%]) vs non-residential care (independent living [n=55] and family home [n=55] [total non-residential care n=110] [50.7%]).

Ethical Approval

Ethical approval was granted from The Faculty of Health and Medicine Research Ethics Committee at Lancaster University and by the Government of Jersey, Health and Community Services Ethics Committee in January and March 2017. The consent process and accompanying documentation was designed using guidance from the Mental Capacity Act (2005) and the Health Research Authority (<https://www.hra.nhs.uk/>). Further details of the consenting procedure for adults with an intellectual disability are outlined in McMahon, Bowring and Hatton (2019), Bowring et al. (2017a) and Bowring et al. (2017b).

Analysis

Data analysis was performed using the Statistical Package for the Social Sciences Version 25 (SPSS, Inc., Chicago, IL, USA). In the first stage of analysis simple frequency and descriptive statistics were undertaken to describe the total population

and categorise socio-demographic factors, health and the prevalence of polypharmacy and psychotropic polypharmacy. At the second stage of analysis a Pearson's χ^2 or Fishers Exact test of independence (or a Mann-Whitney U test or Kruskal–Wallis H test for continuous non-parametric variables or one-way ANOVA for continuous parametric variables) were used to determine any significant relationships between polypharmacy, psychotropic polypharmacy and/or DDD groupings. In the final stage of analysis, binary logistic regressions were undertaken to determine the unique contribution of demographic, health and socioeconomic characteristics on polypharmacy (no polypharmacy vs polypharmacy and excessive polypharmacy) and psychotropic polypharmacy (no psychotropic polypharmacy vs psychotropic polypharmacy). Statistically significant results of $p < 0.05$ are reported. There were no missing medication data. Apart from income where nine individuals refused to answer this question (4.1% of missing data) all other variables had less than 1% of missing data, which was randomly distributed.

Results

Personal Characteristics

Selected personal characteristics of participants are presented in Table 1. The mean age of participants was 44.5 years (SD=16.2, range=18–84 years). Just under half of the sample had a mild intellectual disability (n=108). In terms of overall intellectual disability population representation, the response rates across the different degrees of intellectual disability are broadly similar to other recent Jersey studies (Bowring *et al.* 2017 a,b) A substantial majority of participants were single (87.1%), unemployed

(76.4%) and, if employed, earning less than £15,000 per year (91.7%). The median (IQR) number of ICD-10 conditions was 3 (2,5.5).

+++ Insert Table 1 Here +++

Medication prevalence

Overall 83.4% (n=181) of participants were prescribed at least one medication (Mean=4.58 SD=4.42, range=0-21). The largest group of medications used were those coded to treat the nervous system (33.7% of drugs n=375), followed by those for the alimentary tract and metabolism (22.8% of drugs n=255) and those for the dermatological system (10.1% of drugs n=113). Table 2 outlines the ATC classification of all prescribed drugs by the number of people prescribed a particular class of medication.

+++ Insert Table 2 Here +++

Polypharmacy

In total, 38.2% (n=83) of participants were exposed to polypharmacy (≥ 5 medications) (Table 3) including 12.2% (n=33) who were exposed to excessive polypharmacy (≥ 10 medications).

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Psychotropic polypharmacy

Almost half 45.7% (n=97) of participants were prescribed one class of psychotropic drug, and a further 23% of participants (n=50) were exposed to psychotropic polypharmacy (range 2-6). Antipsychotics were the most frequently prescribed class of psychotropic drug in this study (25.3%, n=55). Six participants (2.8%) were prescribed two antipsychotic drugs.

Of the 55 people prescribed antipsychotic medication, 22.9% of these individuals (n=12.6) were prescribed a dosage above the DDD, whereas 77.1% of individuals (n=42.4) were prescribed antipsychotic medications below or equivalent to the DDD. Across the psychotropic drug classes, although drugs were generally more frequently prescribed below or equivalent to the DDD, prescribing above the DDD was relatively common. For example: N04A Anticholinergic Agents 73.2% vs 26.8%; N05B Anxiolytics 73.1% vs 26.9%; N05C Hypnotics & Sedatives 69.1% vs 30.9%; N06A Antidepressants 73.3% vs 26.7%; N03A Antiepileptics as mood stabilisers 83.7% vs 16.3%. Psychostimulants were equally prescribed above and below the DDD (50% vs 50%). For people prescribed psychotropic drugs, there was no association between the number of drugs prescribed above the DDD and gender (p=0.23), degree of intellectual disability (mild/moderate vs severe/ profound) (p=0.60), number of ICD-10 conditions (p=0.73) or having psychiatric disorder diagnosed over the life course (p=0.39). Nevertheless, people were more likely to be prescribed psychotropic drugs above the DDD if they were taking more drugs across all ATC categories (one-way ANOVA ($F(5,91) = 3.301, p = .009$) (see Figure 1.0 for a distribution of the DDD data) or from the Anticholinergic (p<0.001), Antipsychotic (p<0.001) or Anxiolytic (p<0.001) ATC classifications.

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Bivariate associations

No polypharmacy, polypharmacy and excessive polypharmacy

Bivariate associations between no polypharmacy, polypharmacy, excessive polypharmacy (all ATC classes of medication), psychotropic polypharmacy specifically, and the characteristics potentially associated with polypharmacy are presented in Table 4. Polypharmacy was associated with participants who were older (50+ years) ($p < 0.001$); lived in residential care ($p < 0.001$); had a more severe intellectual disability ($p < 0.001$); were unemployed ($p < 0.001$); had no formal qualifications ($p = 0.016$); had a lower SES score ($p < 0.001$); had an epilepsy diagnosis ($p = 0.040$); had a psychiatric diagnosis over their life course ($p = 0.005$); reported poorer self-rated health ($p < 0.004$) and had more ICD-10 conditions ($p < 0.001$). There was no significant association between polypharmacy and gender, marital status, income or Down syndrome.

Psychotropic polypharmacy

Psychotropic polypharmacy was associated with age; 50+ years ($p = 0.02$); unemployment ($p = 0.008$); lower SES score ($p < 0.037$); Down syndrome ($p = 0.007$); psychiatric diagnosis over the life course ($p < 0.001$) and more ICD-10 conditions ($p < 0.008$). There was no significant association between psychotropic polypharmacy

and gender, marital status, level of intellectual disability, residence, income, education, epilepsy, self or proxy rated health.

+++Insert Table 4 Here +++

Binary Logistic Regression

In the final stage of analysis two separate binary logistic regressions were undertaken. Polypharmacy and psychotropic polypharmacy were the dependent variables in each model respectively. Independent variables that were statistically significant and not mutually exclusive in bivariate analysis were entered into the models. Personal characteristics and circumstances such as age (50+ or below), gender (male or female), level of intellectual disability (mild/moderate or severe/profound), type of residence (residential care vs non-residential care), number of ICD-10 conditions (continuous variable), Down syndrome (yes or no), epilepsy diagnosis (yes or no), psychiatric disorder over the life course (yes or no), education (formal qualifications or no formal qualifications) and employment (employed or unemployed) were entered into each model.

Polypharmacy

The polypharmacy logistic regression model was statistically significant, $\chi^2(9) = 115.68, p < .0001$. It explained 59% (Nagelkerke R^2) of the variance in polypharmacy and correctly classified 82% of polypharmacy cases. Our results indicate (Table 5) that younger age (below 50 years) ([Odds ratio] OR: 0.11, 95% CI: 0.05-0.27), having a less severe intellectual disability (mild/moderate intellectual disability) (OR:

0.29, 95% CI: 0.11-0.79), not living in residential care (OR: 0.32, 95% CI: 0.13-0.80) and having fewer ICD-10 conditions (inverted OR: 0.63, 95% CI: 0.52-0.76) were associated with no polypharmacy exposure.

+++ Insert Table 5 Here +++

Psychotropic Polypharmacy

The psychotropic polypharmacy logistic regression model was statistically significant, $\chi^2(6) = 53.814$ $p < .0001$; it explained 34% (Nagelkerke R^2) of the variance in polypharmacy and correctly classified 80% of psychotropic polypharmacy cases. Our results indicate (Table 6) that younger age (50 years and younger) (OR: 0.44, 95% CI: 0.02-0.96), being female (inverted OR: 0.33, 95% CI: 0.15-0.74), and not being diagnosed with a psychiatric diagnosis over the life course (OR: 0.15, 95% CI: 0.07-0.31) were associated with no psychotropic polypharmacy.

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Discussion

This study provides population-based evidence about the polypharmacy of adults with intellectual disability living in Jersey. Our results indicate that 82% of adults with an intellectual disability were prescribed at least one medication (Mean=4.58 SD=4.42). Nearly 40% of adults with an intellectual disability were exposed to polypharmacy. Of these, just over 15% were exposed to excessive polypharmacy. Apart from neurological drugs, drugs for the alimentary tract and metabolism and

dermatological drugs were the most commonly prescribed. Psychotropic drug use was extensive with just under half of the participants prescribed at least one psychotropic drug (45.7%). Furthermore, people with intellectual disabilities were frequently prescribed psychotropic drugs above the recommended DDD.

These findings suggest that the prevalence of polypharmacy is lower than O' Dwyer *et al.*'s (2016) study (51.6%), but higher than three other studies which use the same definition for polypharmacy (≥ 5 medications) (Haider *et al.* (2014) [21%]; Cobigo *et al.* (2014) [21.5%]; Emerson *et al.* (2016) [8%]). This may partly be explained insofar as O' Dwyer *et al.*'s (2016) study focused on adults aged over 40 years while the Cobigo *et al.* (2013) study identified that polypharmacy was seven times higher in the 55–64 age group compared with those aged between 18 and 24 years old. In addition, Haider *et al.* (2014) had a low response rate of 14% whereas the Emerson *et al.* (2016) study was a secondary analysis of general population data and generally exclusive of adults with more severe intellectual disabilities and adults who live in residential or institutional settings. This, therefore, potentially underrepresents the true prevalence of polypharmacy in this population. Consequently, it is likely that; (1) data drawn from samples where participants are older are likely to report higher polypharmacy rates, and; (2) data drawn from general household sampling frames excluding the vast number of adults with more severe intellectual disabilities and adults who live in institutional settings are likely to report lower polypharmacy rates. It is also important to acknowledge that in an already compromised population, this population's response to multiple medications may vary; therefore, fewer than five medications may be an important consideration if potentially inappropriate prescribing practices exist (O'Dwyer *et al.* 2018; National Health Service [NHS], 2017).

Furthermore, across unadjusted comparisons, our results suggest significant relationships between polypharmacy and a number of factors such as socioeconomic factors (lower SES score/employment and education). Additionally, living in residential care, poorer self and proxy rated health, being aged 50 or over, increased morbidity including epilepsy and having a psychiatric diagnosis over the life course were also associated with polypharmacy. Being older, unemployed, having Down syndrome, an increased number of ICD-10 conditions and having a psychiatric diagnosis over the life course were all associated with psychotropic polypharmacy. Again, these unadjusted analyses are largely similar to recent findings (Haider *et al.* 2014; O' Dwyer *et al.* 2016; 2017; Bowring *et al.* 2017a).

Our results indicate the prevalence of psychotropic drug use is lower, but generally similar to those reported from other recent UK studies (e.g. Henderson *et al.* 2015, 49.1%; Sheehan *et al.* 2015, 49%) but higher than a recent Jersey-based study (Bowring *et al.* 2017, 37.7%). Of these drugs, antipsychotic agents were the most frequently prescribed drug with just over 25% of participants prescribed antipsychotic drugs. Conversely, Sheehan *et al.*'s (2015) review of primary care records identified that anxiolytics/hypnotics were the most frequently prescribed psychotropic drugs in their English study. Moreover, they identified that antidepressants were more frequently prescribed than antipsychotic drugs. The difference seen in our data may be accounted for insofar as; (1) our study categorises these classes of drugs (anxiolytics and hypnotics) independently following ATC guidance (WHO, nd); and, (2) our sample is more likely to include individuals known to services who may have more complex needs. Nevertheless, psychotropic polypharmacy was common, with

23% of participants prescribed two or more psychotropic medications. These findings are consistent with the existing evidence base that polypharmacy is common in this population and that psychotropic polypharmacy is highly prevalent (de Kuijper *et al.* 2010; Doan *et al.* 2013; Haider *et al.* 2014; Deb *et al.* 2015; Sheehan *et al.* 2015; O’Dwyer *et al.* 2016; Axmon *et al.* 2017).

For individuals prescribed psychotropic drugs we identified no demographic variables associated with being prescribed drugs above the DDD. Furthermore, our results indicate that people who are prescribed more drugs and drugs from the Anticholinergic, Antipsychotic and Anxiolytic ATC classifications in particular are more likely to be prescribed drugs that exceed the DDD. Given we found no significant relationship with a psychiatric diagnosis over the life course, it is theoretically possible that these classifications of drugs are prescribed in higher doses in response to other factors such as challenging behaviour. This ‘off label’ prescribing is a well-documented phenomenon with adults with intellectual disability (Gomes *et al.* 2019; Lunskey *et al.* 2018; Perry *et al.* 2018; Bowring *et al.* 2017a; Scheifes *et al.* 2016; Sheehan *et al.* 2015; Deb 2014; Doan *et al.* 2014).

In adjusted comparisons, our models have identified some differences in the factors associated with general polypharmacy and psychotropic polypharmacy. Firstly, being male was identified as an associated variable in the psychotropic polypharmacy model only. Bowring *et al.* (2017a) had similar findings in a population-level study and suggested that being male increased a person’s likelihood of being prescribed antipsychotic drugs. Nevertheless, Lunskey and Modi (2018) identified that women were more likely to be exposed to psychotropic polypharmacy in a recent Canadian

study. In this regard, gender had not been identified across any bivariate comparisons in this study, and to date, only certain studies have examined its association (Stolker *et al.* 2001; O'Dwyer *et al.* 2017), with mixed findings (Stortz *et al.* 2014).

Second, an increased number of ICD-10 conditions is associated with general polypharmacy, but not psychotropic polypharmacy; however, having a psychiatric diagnosis over the life course has been identified as a predictor of psychotropic polypharmacy only. Third, age (50+ years) is associated with increased polypharmacy and psychotropic polypharmacy. Fourth, having a more severe intellectual disability and living in a residential setting was associated with polypharmacy.

These findings highlight significant issues for individuals with intellectual disabilities. The use of a total population sampling methodology and a clearly defined polypharmacy definition with no missing medication data is a strength of this study; however, given the variance in prevalence rates across studies (e.g O' Dwyer *et al.*'s 2016; Haider *et al.* 2014; Cobigo *et al.* 2014; Emerson *et al.* 2016) there is a further need for prospective, population-based research covering the entire adult age profile and utilising a standardised definition.

This study also highlights that the prevalence of morbidity (e.g. increased number of ICD-10 conditions and psychiatric diagnosis over the life course) (Heslop *et al.* 2014; Hughes McCormack *et al.* 2017; Troller *et al.* 2017) is associated with general polypharmacy. The increasing longevity of people with an intellectual disability means that people with intellectual disability will be prescribed more medications as

they age. With this comes greater challenges as effective medications have the potential for producing desired and undesired effects (for example adverse drug events and drug-drug interactions). Although the significance of drug-drug interactions depends on many pharmacokinetic and pharmacodynamic factors, the risk of drug-drug interactions (Kohler *et al.* 2000; Palleria *et al.* 2013) and adverse drug reactions (Gnjidic *et al.* 2012) in this population presents a significant risk for people who are more likely to have increased health comorbidities and communication difficulties (Troller *et al.* 2016). In this context, drug-drug interactions may be very concerning for people with an intellectual disability and to date, this has been under examined (Joos *et al.* 2016).

Additionally, the level of intellectual disability was significant for general polypharmacy but not psychotropic polypharmacy after accounting for health and socioeconomic characteristics. This, again, is consistent with O'Dwyer *et al.* (2016) who found that individuals with a severe and profound intellectual disability were more likely to experience polypharmacy. However, in relation to psychotropic polypharmacy, other studies (Hurley *et al.* 2003; O'Dwyer *et al.* 2017) found no association between psychotropic polypharmacy and severity of intellectual disability. Adults with more severe intellectual disabilities are more likely to have a number of health issues (McMahon & Hatton, 2020), so the use of more medications is common, but psychiatric disorders do not impact adults with more severe intellectual disabilities more frequently (Axmon *et al.* 2018; Holden & Gitlesen, 2004). Consequently, this study suggests that of the people known to services with an intellectual disability, psychotropic polypharmacy is evenly distributed across individuals with mild/moderate and severe/profound intellectual disabilities.

Consistent with our finding, there is some evidence to suggest that people with intellectual disabilities who live in institutional settings are more likely to experience polypharmacy (O'Dwyer *et al.* 2016). It is important to consider that the severity of intellectual disability and type of residence may overlap, meaning that people with more complex needs may be more likely to live in residential settings and therefore it will be more probable that they will be taking more medications. Regarding psychotropic polypharmacy, Lunskey and Modi (2018) found this was more common in supervised group home settings while Lunskey *et al.* (2018) and Bowring *et al.* (2017a) identified that antipsychotics were prescribed to residents who lived in supervised residential settings. However, we found no association between residential setting and psychotropic polypharmacy in bivariate or multivariate analysis. Explanations for this dissimilarity may include the cumulative effects surrounding the increased awareness of the concerning use of psychotropic drugs in residential settings over the last number of years (Department of Health, 2012; Glover *et al.* 2015; Care Quality Commission, 2016; Bowring *et al.* 2017a); the development of clinical guidelines for the management and support of people with intellectual disability and challenging behaviour (NICE, 2015), or the more recent initiatives in the UK to stop inappropriate prescribing (e.g. STOMP, NHS, 2017).

Finally, in both adjusted models all socioeconomic factors became non-significant when health and personal characteristics were accounted for. The bivariate analysis identified that unemployment was associated with polypharmacy and psychotropic polypharmacy. As our study had only a small number of employed participants, it would be prudent to consider employment and polypharmacy in larger studies, as employment is associated with better wellbeing and mental health (Butterworth *et al.*

2011; Hergenrather *et al.* 2015; Robertson *et al.* 2019). It is also important to further examine if the presence of Down syndrome is associated with psychotropic polypharmacy in larger studies. Down syndrome became non-significant after adjusting for confounders; nonetheless, given Down syndromes prevalence (Loane *et al.* 2012), clinical complexity (Troller *et al.*, 2016; Carfi *et al.* 2020) and reported high use of psychotropic drugs in adult (Carfi *et al.* 2014; Carfi *et al.* 2020) and paediatric studies (Downes *et al.* 2015), further investigation is warranted.

There are several limitations to this study: (1) medication use reported in this study for individuals who lived independently without a MARs sheet or a prescription was based on participant or proxy self-report and through examining medication that the participant had in their possession. This increases the potential of information bias. While all medication was cross-checked with the individual's health and social care record, if this was not updated by health and social care staff then recently prescribed medication could be absent from our analysis; (2) we included all medication that had been prescribed in the preceding 28 days by a medical prescriber. There may be potentially medications prescribed that have not been taken by the participant and this could potentially inflate the prevalence of medication use; (3) these findings apply only to the administratively defined intellectual disability population in Jersey, while there may also be adults with intellectual disability not known to services who were not included; (4) there was a reliance on proxy respondents to answer some questions. To mitigate this, only objective indicators were used in the multivariate analysis; (5) the prescribing of psychotropic medication under or over the DDD reported in this study is only used to represent an estimate of psychotropic consumption, and it is not equivalent to the desired 'therapeutic effect' for the initial prescribing indication and (6) this sample is relatively small in comparison to other studies.

Implications for practice

It is important to understand the prevalence of polypharmacy and psychotropic polypharmacy as it generally represents the burden of ill-health in adults with intellectual disability experience and how health services respond. The varying evidence in the literature demonstrates a further need to focus on designing prospective studies that *examine* the prevalence and predictors of polypharmacy and psychotropic polypharmacy using standardised definitions. Nevertheless, there are more immediate modifiable factors that can be addressed such as undertaking medication reviews (Scheifes *et al.* 2016; Nabhanizadeh *et al.* 2019) and identifying medication combinations that potentially result in drug-drug interactions in adults who are exposed to polypharmacy. The interruption of prescribing cascades is an important and actionable opportunity to improve the health, wellbeing and quality of life of people with an intellectual disability (Rochon and Gurwith, 2017). This is particularly true for older adults with severe and profound intellectual disabilities who have a number of co-morbidities and who live in residential settings.

Conclusion

This study has identified that polypharmacy and psychotropic polypharmacy is common. Although the prescribing of multiple drugs can be clinically justified and appropriate, it presents significant risks as it increases the potential of adverse drug events and drug-drug interactions. There is an evident need for large, prospective based studies with a comparison group to fully ascertain the prevalence and predictive variables associated with polypharmacy and psychotropic polypharmacy using standardised definitions.

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Table 1: Selected Population Characteristics of the Total Population Sample

Characteristic	Total n=217 (%)	Men n=122 (56.2)	Women n=95 (43.8)
Age (years)			
Less than 35	79 (36.4)	54 (44.3)	25 (26.3)
35 - 49	53 (24.4)	29 (23.8)	24 (25.3)
50 - 64	58 (26.7)	24 (19.7)	34 (35.8)
Over 65	27 (12.4)	15 (12.3)	12 (12.6)
Marital Status			
In a relationship	20 (9.2)	9 (7.6)	11 (12.2)
Single	189 (87.1)	110 (92.4)	79 (87.8)
Level of Intellectual Disability			
Mild	108 (49.8)	64 (52.5)	44 (46.3)
Moderate	56 (25.8)	26 (21.3)	30 (31.6)
Severe	34 (15.7)	20 (16.4)	14 (14.7)
Profound	19 (8.8)	12 (9.8)	7 (7.4)
Socioeconomic Status			
Employed*	43 (23.6)	29 (29.0)	14 (17.1)
Unemployed	139 (76.4)	71 (71.0)	68 (82.9)
Earns over £15,000 pa	21 (10.1)	15 (12.5)	6 (6.8)
Earns under £15,000 pa	187 (89.9)	105 (87.5)	82 (93.2)
Formal qualifications	21 (9.8)	12 (9.9)	9 (9.6)
No formal qualifications	194 (90.2)	109 (90.1)	85 (90.4)
Health			
Number of ICD-10 Conditions	Median (IQR) 3 (2,5.5)	Median (IQR) 3 (1,5)	Median (IQR) 4 (2,6)

*People who are retired, in full time education or homemakers are excluded from analysis

Table 2: Anatomical Therapeutic Chemical (ATC) Classification of all Prescribed Drugs by Gender and Severity of Intellectual Disability

ATC Category	% of Total Men	% of Total Women	% of Total Mild/ Moderate Intellectual Disability	% of Total Severe/ Profound Intellectual Disability	Total Number Prescribed Drugs in ATC Class
	n (%)	n (%)	n (%)	n (%)	n (%)
Total	94	85	128	50	1117
N04A Anticholinergic agents	13 (7.2)	11 (6.1)	16 (8.8)	8 (4.4)	24 (2.1)
N05A Antipsychotic	44 (24.3)	17 (9.4)	41 (22.7)	20 (11.0)	61 (5.4)
N05B Anxiolytics	19 (10.5)	14 (7.7)	13 (7.2)	20 (11.0)	33 (2.9)
N05C Hypnotics and sedatives	8 (4.4)	2 (1.1)	9 (5.0)	1 (0.6)	10 (0.8)
N06A Antidepressants	22 (12.2)	24 (13.3)	40 (22.1)	6 (3.3)	46 (4.1)
N06B Psychostimulants	4 (2.2)	0	4 (2.2)	0	4 (0.36)
N03A Antiepileptics as mood stabilisers	5 (2.8)	5 (2.8)	4 (2.2)	6 (3.3)	10 (0.8)
N02A/B/C Analgesia	40 (22.1)	50 (27.6)	63 (34.8)	27 (14.9)	90 (8.9)
N03A Antiepileptics for nerve pain	3 (1.7)	3 (1.7)	6 (3.3)	0	6 (0.5)
N03A Antiepileptics for epilepsy	42 (23.2)	43 (23.8)	50 (27.6)	35 (19.3)	85 (7.6)
N04B Dopaminergic agents	1 (0.6)	0	1 (0.6)	0	1 (0.08)
N07B Drugs used in nicotine dependence	1 (0.6)	0	1 (0.6)	0	1 (0.08)
N - Other Neurologicals	0	4 (2.2)	4 (2.2)	0	4 (0.36)
A – Alimentary tract and metabolism	132 (72.9)	123 (68.0)	151 (83.4)	104 (57.5)	255 (22.8)
B – Blood and blood forming organs	19 (10.5)	14 (7.7)	24 (13.3)	9 (5.0)	33 (2.9)
C – Cardiovascular system	41 (22.7)	46 (25.4)	75 (41.4)	12 (6.6)	87 (7.7)
D – Dermatological	58 (32.0)	55 (30.4)	69 (38.1)	44 (24.3)	113 (10.1)
G – Genito-urinary system and sex hormones	12 (6.6)	24 (13.3)	29 (16.0)	7 (3.9)	36 (3.2)

H – Systemic hormonal preparations	11 (6.1)	15 (8.3)	17 (9.4)	9 (5.0)	26 (2.3)
J – Anti-infectives for systemic use	11 (6.1)	21 (11.6)	22 (12.2)	10 (5.5)	32 (2.8)
L – Antineoplastic and immunomodulating agents	2 (1.1)	0	2 (1.1)	0	2 (0.16)
M – Musculoskeletal system	19 (10.5)	20 (11.0)	25 (13.8)	14 (7.7)	39 (3.4)
P – Antiparasitic products, insecticides and repellents	2 (1.1)	2 (1.1)	2 (1.1)	2 (1.1)	4 (0.36)
R - Respiratory	45 (24.9)	36 (19.9)	65 (35.9)	16 (8.8)	81 (7.2)
S – Sensory organs	5 (2.8)	10 (5.5)	11 (6.1)	4 (2.2)	15 (1.3)
V – Various	10 (5.5)	9 (5.0)	5 (2.8)	14 (7.7)	19 (1.7)

Notes: percentages and totals are based on respondents

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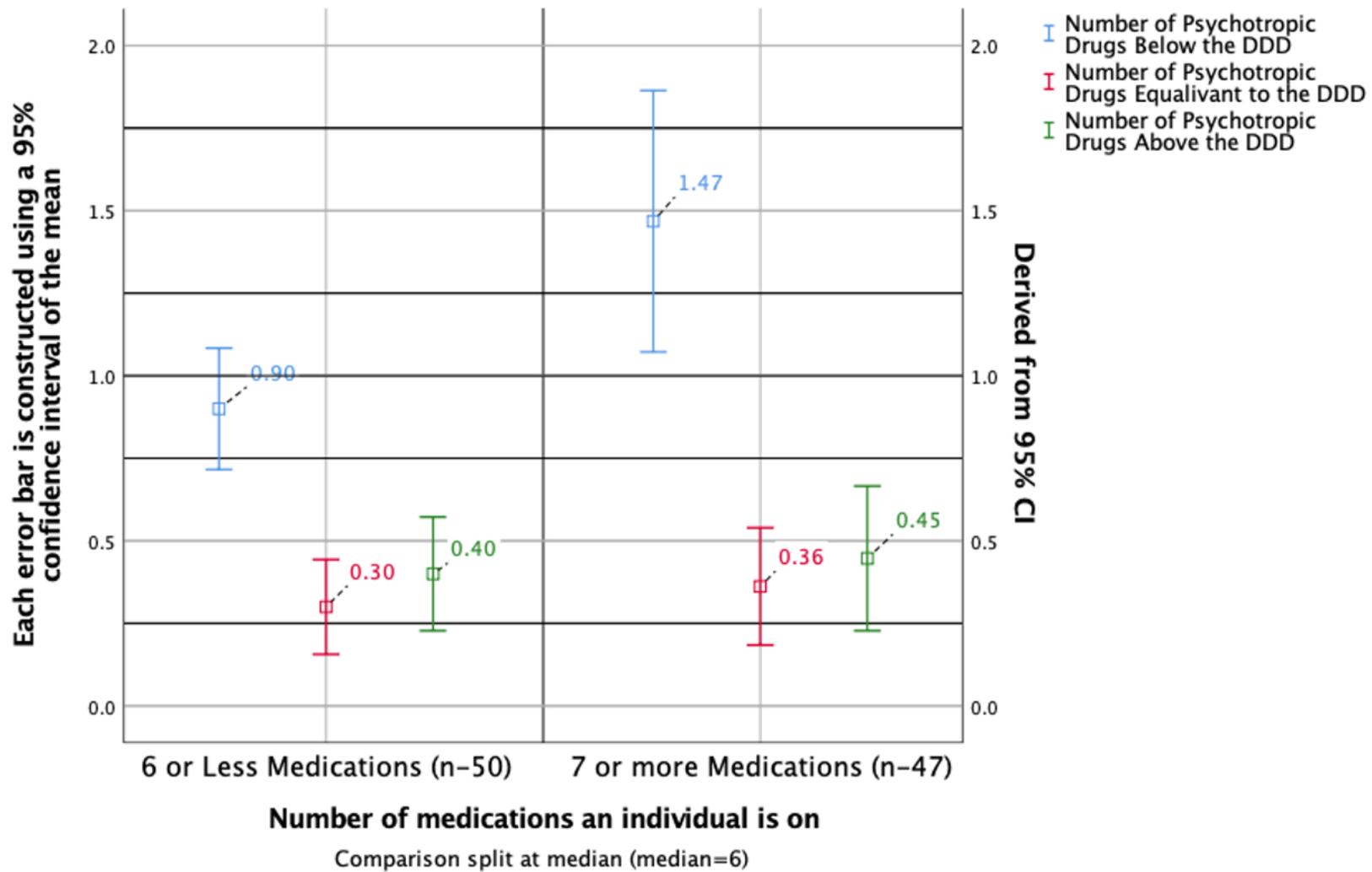
Table 3: Frequency of Prescribed Medications and Polypharmacy Classification

Number of Medications	Number of People	Polypharmacy Defined
0	39	No Polypharmacy
1	26	
2	23	
3	24	
4	22	
Total	134	61.8%
5	8	Polypharmacy
6	14	
7	13	
8	9	
9	6	
Total	50	23.0%
10	10	Excessive Polypharmacy
11	6	
12	5	
*13-21	12	
Total	33	

*Numbers below 5 are suppressed

Figure 1.0: Error line graph (95% CI) representing the mean number of drugs prescribed below, equivalent to and above the DDD by the total number of all ATC drugs (n-97)

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Employed*	43	37 (86.0)	5 (11.6)	1 (2.3)	$\chi^2 = 15.466$	40 (93.0)	3 (7.0)	$\chi^2(1)=7.801$
Unemployed	139	76 (54.7)	35 (25.2)	28 (20.1)	$p<0.001$	101 (72.7)	38 (27.3)	$p=0.008$
Income								
Earns under £15,000 pa	187	110 (58.8)	48 (25.7)	29 (15.5)	$\chi^2 = 5.333$	141 (75.4)	46 (24.6)	$\chi^2(1)=1.115$
Earns over £15,000 pa	21	17 (81.0)	1 (4.8)	3 (14.3)	$p=0.670$	18 (67.8)	3 (14.3)	$p=0.418$
Education								
No Formal qualifications	194	114 (58.8)	48 (24.7)	32 (16.5)	$\chi^2 = 7.831$	149 (76.8)	45 (23.2)	$\chi^2(1)=0.185$
Formal qualifications	21	19 (90.5)	1 (4.8)	1 (4.8)	$p=0.016$	17 (81.0)	4 (19.0)	$p=0.790$
SES Score								
Low SES Score	115	58 (50.4)	33 (28.7)	24 (20.9)	$\chi^2 = 21.906$	84 (73.0)	31 (27.0)	$\chi^2(1)=4.631$
Higher SES Score	62	53 (85.5)	5 (8.1)	4 (6.5)	$p<0.001$	54 (87.1)	8 (12.9)	$p=0.037$
Health								
Epilepsy	52	25 (48.1)	15 (28.8)	12 (23.1)	$\chi^2 = 6.307$	35 (67.3)	17 (32.7)	$\chi^2(1)=4.158$
No Epilepsy	162	108 (66.7)	34 (21.0)	20 (12.3)	$p=0.040$	131 (80.9)	31 (19.1)	$p=0.055$
Down Syndrome	29	16 (55.2)	11 (37.9)	2 (6.9)	$\chi^2 = 4.564$	28 (96.6)	1 (3.4)	$\chi^2(1)= 7.247$
No Down Syndrome	188	118 (62.8)	39 (20.7)	31 (16.5)	$p=0.086$	139 (73.9)	49 (26.1)	$p=0.007$
Psychiatric diagnosis over life course	73	36 (49.3)	18 (24.7)	19 (26.0)	$\chi^2 = 10.373$	38 (52.1)	35 (71.4)	$\chi^2(1)=37.890$
No Psychiatric diagnosis over life course	137	94 (68.6)	29 (21.2)	14 (10.2)	$p=0.005$	123 (89.8)	14 (10.2)	$p<0.001$
Poor Self-Rated Health	23	12 (52.2)	7 (30.4)	4 (17.4)	$\chi^2 = 10.510$	17 (73.9)	6 (26.1)	$\chi^2(1)=3.119$
Good Self-Rated Health	62	52 (83.9)	9 (14.5)	1 (1.6)	$p=0.004$	53 (85.5)	9 (14.5)	$p=0.085$
Poor Proxy-Rated Health	59	56 (94.9)	3 (5.1)	-	$p=1.0$	18 (78.3)	5 (21.7)	$\chi^2(1)= 1.292$
Good Proxy-Rated Health	23	22 (95.7)	1 (4.3)	-		52 (88.1)	7 (11.9)	$p=0.303$

Number of ICD-10 Conditions	217	2 (1,4)	4.5 (3,6)	7 (4.5,9)	$\chi^2(2) = 61.262$	3 (1,5)	4 (3,6)	$U = 3150.500$
(Median [IQR])					$p < 0.001$			$p = 0.008$

Notes: Bold text indicates statistically significant results

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Table 5: Strength of association (odds ratio with 95% confidence intervals) between personal and demographic characteristics and health and socioeconomic characteristics and polypharmacy

	B	Sig.	Exp(B)	95% C.I.	
				Lower	Upper
Age	-2.217	<.001***	.109	.045	.267
Gender	-.013	.975	.987	.432	2.256
Level of Intellectual Disability	-1.240	.016*	.289	.106	.794
Residence	-1.140	.015*	.320	.128	.802
ICD-10 Conditions	.467	<.001***	1.595	1.323	1.923
Epilepsy Diagnosis	.247	.604	1.280	.503	3.258
Psychiatric Diagnosis	-.633	.157	.531	.221	1.277
Education	-.603	.515	.547	.089	3.369
Employment	.133	.617	1.142	.679	1.920
Constant	.814	.509	2.257		

Notes: *** $p < 0.001$ ** $p < 0.01$ * $p < 0.05$;

ORs & 95% CIs rounded up to two decimal points in main text

Some ORs & 95% CIs inverted for ease of interpretation

Table 6: Strength of association (odds ratio with 95% confidence intervals) between personal and demographic characteristics and health and socioeconomic characteristics and psychotropic polypharmacy

	B	Sig.	Exp(B)	95% C.I.	
				Lower	Upper
Age	-.832	.040*	.435	.197	.962
Gender	1.118	.007**	3.060	1.364	6.868
ICD-10 Conditions	.049	.491	1.050	.914	1.206
Psychiatric Disorder	-1.940	<.001***	.144	.066	.312
Employment	.371	.151	1.450	.874	2.406
Down Syndrome	-1.561	.143	.210	.026	1.693
Constant	-1.037	.111	.354		

Notes: *** $p < 0.001$ ** $p < 0.01$ * $p < 0.05$;
 ORs & 95% CIs rounded up to two decimal points in main text
 Some ORs & 95% CIs inverted for ease of interpretation

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