Drug burden index, polypharmacy and patient health outcomes in cognitively intact older residents of aged care facilities in Malaysia

Abstract

Aim: To examine association of Drug Burden Index (DBI) and polypharmacy with patient health outcomes among cognitively intact older residents in aged care facilities.

Methods: A review of prescribed medications and related outcomes in a cross-sectional sample of older adults, aged 60 years and above, recruited from 11 aged care facilities in Peninsular Malaysia. Groningen Frailty Indicator (GFI) for frailty, Older People's Quality of Life-35 (OPQoL) for quality of life, Drug Burden Index (DBI) to quantify patients' exposure to anticholinergic and sedative medicines and Hospital Anxiety and Depression Scale (HADS) for mental health of the residents.

Results: More than two-third of a sampled population received at least one anticholinergic or sedative medication and more than one-quarter of them were exposed to polypharmacy. Exposure to DBI-associated medications in 3 in every 4 frail participants and was significantly correlated with frailty (r: +0.184, p=0.023). Frail population had significantly increased risk of polypharmacy (OR 6.07, 95% CI: 1.71–21.56, p=0.005). However, exposure to DBI-associated medications was not significantly associated with overall quality of life and activity of daily living measures.

Conclusion: Polypharmacy and anticholinergic and sedative burden were noticed in a substantial number of older adults in residential aged care and were associated with frailty. Investing in recruitment of pharmacists may benefit recognition of RACF quality of care as pharmacy services (including pharmacist) are virtually non-existent in Malaysian RACF.

Keywords: Aged care, drug burden, frailty, older people, polypharmacy

INTRODUCTION

In 2015, the older people constituted 12% (901 million) of the world population, and the total number of older persons is increasing by 3.26% annually.[1] In Malaysia, the older people account for 6% of the population (2016), and estimated to rise to 14.5% by 2040.[2] Because of age-related chronic diseases, the older people are likely to use regular long-term medications. Previous studies in the United States of America (USA) and Europe indicated a proportional increase in the number of medications used with age.[3,4] The use of 5 or more medications concurrently is common in residential aged care facilities (RACF).[5-8] Growing evidence suggests that polypharmacy in the older people is related to inappropriate medications.[9] The proportion of potentially inappropriate medications related to polypharmacy was three times higher in RACF.[10] Novaes et al., reported an "iatrogenic triad" of polypharmacy, inappropriate medications and drug-drug interactions in one in every three older people.[11]

The rising prevalence of medication inappropriateness in the older population is a major public health concern. For instance, the use of inappropriate medications is associated with poor physical functioning, that in the older people increases risks of falls, hip fracture and injuries. Nyborg et al., identified concomitant use of three or more psychotropic drugs, antihypertensives, and regular use of hypnotics as potentially inappropriate medications among Norwegian nursing home residents aged ≥70 years whereas Bor et al., identified that potentially inappropriate medications such as pantoprazole, trimetazidine and vinpoctine were significant risk factors for falls among Hungarian older people in nursing homes.[12,13] Juola et al., in Finland reported a stepwise association between use of multiple potentially harmful medications and poorer self-rated health, and poorer HRQoL.[14] However, one study in Malaysia depicted the prevalence of potentially inappropriate medications among RACF but observed non-significant changes in HRQoL.[15]

Commonly prescribed medications for older adults in hospitals and community pharmacies are anticholinergics and sedatives;[16,17] the number of anticholinergic prescriptions increased from 14,019 (20.6%) in 1995 to 17,448 (23.6%) in 2010.[18-19] Anticholinergic side effects resulting from inhibition of

muscarinic receptors include dry mouth, sleepiness, hallucinations, urinating problem, constipation and memory impairment.[15] A high anticholinergic and sedative burden is associated with poor functional outcomes,[20,21] and cognitive deficits.[20] In Australia, anticholinergic and sedative burden were associated with poorer physical function such as slow walking speed, slow narrow walking speed and poorer score on the Instrumental Activities of Daily Living (IADLs) scale; the association was stronger with sedative medications.[22]

Various implicit and explicit tools have been developed to identify potentially inappropriate prescribing and medication.[23-25] The Drug Burden Index (DBI) is used to estimate the exposure to anticholinergic and sedative medicines or burden.[26] Associations between DBI and patient health outcomes are still very limited particularly in residential aged care settings in developing countries.

The aim of this study is to identify exposure to drug burden index (DBI) associated medications and polypharmacy in older residents through a detailed medication review performed by the pharmacists. In addition, the study aimed to examine whether the DBI and polypharmacy were associated with frailty in older adults living in residential care in Malaysia.

METHODS

Study design, participants and setting

A cross-sectional sample of older population aged ≥ 60 years in residential aged care facilities (RACF) in mid-Western states of Peninsular Malaysia. In total, 11 RACF, run by not-for profit organisations, in Kuala Lumpur, Selangor, and Perak (Ipoh) were conveniently approached and selected. We assessed associations between DBI (i.e. exposure to anticholinergic and sedative medicines), exposure to polypharmacy and health outcomes (e.g. frailty) in RACF. Residents who met the criteria and had complete medical records were included in the study. Participants were able to take part if they had been permanent residents in the facility for six months or more, age ≥ 60 years, had at least 1 long-term medical condition, received at least 1 long-term medication, able to articulate and provided verbal or written consent to participate. An interviewer-administered comprehensive assessment form (CAF) was used to collect data and the interviews took approximately 30 minutes. The data

collection was completed in three months (July 2017 to September 2017). The form included information on demographic data (age, sex, race, marital status, education level, occupation history, number of children and siblings, physical activity level, and smoking, and alcohol status), QOL, mental health status, frailty status, and medication and medical history of the participants. In measuring covariates, patients' medical histories from the facilities were searched to determine if the participants had a clinical diagnosis of any long-term medical condition (including any cognitive related conditions, e.g. dementia). The data on co-morbid conditions were extracted from the medical records of the participants and documented as number of co-morbid conditions.

Assessment of patient health outcomes

Frailty was assessed using Groningen Frailty Indicator (GFI). The GFI, validated in institutional homes comprises fifteen dichotomous items with a score range from 0 (normal activity without restriction) to 15 (completely disabled).[27,28] The GFI instrument has been used and validated in Malaysia.[28] Participants with a score of ≥4 were considered frail.[27] The Katz ADL comprises six activities with each activity indicating independence or dependence. Total score range from 0 (full dependence) to 6 (full independence).[29] QoL was measured using the OPQOL questionnaire.[30] OPQOL comprises 35 items in 8 domains: life overall, health, social relationship, independence, home, psychological, financial and leisure. Each item had five-point Likert scales (1-5, higher scores indicating better QoL). Total OPQOL score range from 35 (worst possible) to 175 (best possible).[30,31] OPQOL is a multidimensional, population surveillance instrument, specifically designed for use with older populations.[30,31] Our reliability analysis found this instrument as reliable (Cronbach alpha: 0.70). Mental health status as a covariate was evaluated using the HADS.[11,32] HADS is a useful and valid instrument to screen anxiety and depression symptoms in older adults.[32] HADS consists of 14 items with each item rated on a four-point (0–3) Likert scale, providing a score range from 0 to 42, with a higher score indicating worse mental health status.[33]

Drug burden index and polypharmacy

Exposure to a DBI-associated medication was defined as exposure to an affected medication during the three months' period. DBI refers to anticholinergic and/or sedative medicines exposure. It was calculated with a validated formula of Drug Burden Index = D/ (D+ δ),[26] where D is the daily dose taken by the individual (derived from medical records), and δ is the minimum efficacious dose which was approved and registered by the Ministry of Health Malaysia (Formulari Ubat KKM (FUKKM, March 2016). The Malaysian product information and Monthly Index of Medical Specialities (MIMS Malaysia, paperback 2017) were used to identify medications with clinically significant anticholinergic and/or sedative effects. Complementary medications, health supplements and medications prescribed on a PRN basis (i.e. when required) were excluded.[34] For this study, polypharmacy is defined when participants are on ≥5 concurrent medications at a single time. Patients' medical records obtained from each participating RACF were searched to assess medicines use. The data collected included the name, dose, and dosing instructions of all the medications used three months prior to the start date of the study at each facility.

Statistical analysis

The data analysis was performed using Statistical Package for Social Sciences (SPSS version 24) ® with a significance level of 0.05. The collected data are presented as frequencies, percentages, means and standard deviations. Chi-square test was used to compare patient health outcomes and medication-related variables (e.g. frailty and polypharmacy; frailty and drug burden index). For assessing associations, Spearman correlation was used such as between drug burden index, medication appropriateness and patient health outcomes. The GFI, OPQOL, HADS depression and anxiety, and KATZ ADL scales were converted to binary variables. The KATZ ADL scores of 0 to 6 were reverse coded and categorised as dependence (score > 0) and independence (score = 0). Binary variables for total OPQOL score (35 to 175) were obtained using median split method.[35] A HADS score of 7 was used to categorise cases and non-cases of depression and anxiety.[36] It has been found that at a cut-off score

of 8+ (>7) for both subscales provide sensitivities and specificities of approximately 0.80.[32]

Univariate and multivariate logistic regression models were used to examine associations between (1) polypharmacy and GFI, OPQOL, HADS and KATZ ADL measures (binary variables) and (2) having a DBI>0 and GFI, OPQOL, HADS and KATZ ADL measures (binary variables). The potential confounders were identified based on their association with main variables and on the basis of a priori knowledge.[26,37] We determined variables necessary to control for confounding and that includes age, sex, marital status, co-morbidity, patient health outcomes, and medication-related variables.

RESULTS

Socio-demographic characteristics of the participants

The socio-demographic characteristics of study participants are presented in **Table 1**. During the data collection period, about 200 residents of aged care homes were screened. Of these, 151 met the inclusion criteria and participated in this study. A similar number of both genders (77 males, 51%) participated in this study. The mean age was 74.50 ± 8.40 and most participants were of Chinese ethnicity (n = 148, 98%). Half of the participants were single (n = 80, 53%) and had not received any formal education (n = 77, 51%). The average number of co-morbid conditions was 2.31 ± 1.19. **Figure 1** presents the pre-existing medication conditions at the time of study. Cardiovascular related conditions were the most common medical conditions associated with study participants. Only 6% of the participants had psychiatric conditions (e.g. schizophrenia or depression).

Patient health outcomes

Majority of the participants had some degree of dependence (78.8%) and were frail (68.2%), as shown in **Table 2**. The average quality of life score (total OPQOL score) was 109.9 ± 8.0 with the leisure domain recording the highest score (18.73 ± 1.3) and the financial domain with the lowest score (12.09 ± 1.3).

Medicines use of the participants

The average number of medications per participant was 3.54 ± 1.96 (**Table 2**). There were 41 participants (27.15%) who were taking more than 5 medications (polypharmacy). More than two-thirds (74.2%) of the study population received at least one anticholinergic or sedative medication included in the DBI. CVS medications were the most commonly used medications having anticholinergic properties.

The exposure to polypharmacy occurred in almost 35% of the frail population, which was significantly higher than non-frail participants (p = 0.001). No significant differences were observed for other groups (**Table 3**).

Drug Burden Index and patient health outcomes

Exposure to DBI-associated medications in 3 in every 4 frail participants. The DBI was significantly and positively correlated with GFI scores (r: +0.184, p = 0.023). Being exposed to DBI-associated medications was not significantly associated with total OPQOL scores as compared to not being exposed to a DBI. Among all OPQOL domains, only one (home) was significantly correlated with DBI (r: +0.189, p = 0.020), respectively.

In a multivariate logistic regression, frail participants had significantly increased odds of receiving 5 or more medications (OR 6.07, 95% CI: 1.71 – 21.56), as shown in **Table 4**. Frail participants and those with poor QOL had an increased risk of receiving DBI-associated medications, but their associations were not statistically significant.

DISCUSSION

The present study evaluates association of drug burden index and polypharmacy with patient health outcomes in older adults in RACF. Around two-third of participants were frail as measured by GFI scores. Drug burden as measured by DBI has an average score of 0.79 ± 0.63 and showed a correlation with frailty. Occurrence of polypharmacy was a feature of approximately a quarter of the participants. In this study, frailty was associated with higher exposure to polypharmacy (≥ 5 medications) in a population of older adults (≥ 60 years) in residential aged care in Malaysia.

There was a relatively high proportion of anticholinergic and sedative burden among residents (74.17%) and was significantly correlated with frailty as indicated by GFI. Many studies that have reported an association between drug burden and physical function in the older population have not included aged care home residents.[22,26,38,39] A five-year longitudinal study in the United States depicted that high DBI scores were associated with low functional outcomes measured using short physical performance battery, gait speed and grip strength;[26,38] a similar association was reported in other countries.[22,39] The predictive relationship between drug burden and frailty in this study was not strong possibly due to coefficient values and wide confidence intervals despite significant p-values; self-reported measures in this study may have also contributed to such results.

It is possible that more than half of the participants in this study are frail owing to their poor health status characterised by (mostly severe) disability, high degree of functional dependence, and medication inappropriateness, all of which are prevalent in residents of aged care facilities.[40] The older people residing in aged care facilities portray vulnerability within the ageing segment and their health needs are complex owing to multiple-comorbidities and aged-care changes in their pharmacokinetic and pharmacodynamics characteristics.[41,42] Frailty is also associated with deterioration in physical function and increased risk of falls, injury, fracture, hospital admission and mortality.[43–48] Although use of anticholinergic and sedative medications further impairs physical function,[16] there were no significant differences between drug burden and the frail and non-frail groups possibly due to the sample size and self-report measures of frailty.

Older people are often prescribed with inappropriate medications.[14,43,44] Although exposure to anticholinergic and sedative medications occurred in over three-quarter of a population of older adults in residential aged care, its association with lower or poorer quality of life was not statistically significant. In contrast, Harrison et al., (2018) found that exposure to DBI-associated medications was associated with lower QOL according to the EuroQol-5 Dimensions Questionnaire.[45] Medication inappropriateness identified by the Red-Yellow-Green List was also associated with reduced quality of life

measured using the EuroQol-5D (EQ-5D) and low functional status measured by the New Mobility Score.[46] Inappropriate medications potentially worsen health via noxious effects that may trigger a harmful prescribing cascade.[11]

Also, the risk of receiving five or more medications was six times higher for frail as compared to non-frail participants. A review showed a link between polypharmacy and poor physical functioning in which there was a significant difference in the polypharmacy and non-polypharmacy groups in terms of inappropriate medication use measured using STOPP.[47] A recent study conducted among community-dwelling older persons in Malaysia reported a high prevalence of polypharmacy among the older people and the main associated risk factor was inappropriate medications.[9] Other studies also reinforced medication inappropriateness as a risk factor of polypharmacy.[13,48] Around one in three older persons who take at least five medications is bound to experience an adverse drug reaction,[49] that lead to hospital presentations;[50] interestingly adverse drug reactions in at least one quarter of these older people are preventable by avoiding inappropriate medications.[50] Individuals taking ≥ 5 medications have higher risks of drug-drug interactions and drug-disease interactions compared to those taking fewer medications.

Potential role of pharmacists in aged care facilities

The current healthcare system in Malaysia has mandated laws to govern aged care facilities in Malaysia; Act 506 of the Care Centres Act 1993,[51] and Act 586,[52] of the Private Healthcare Facilities and Services Act 1998 govern the current welfare of older people in aged care facilities. Act 506 is implemented for the private sector, specifically the civil society and governs 244 care centres, old folks' homes, shelters, etc.[51] while Act 586 is implemented for the business-operated private sector and governs 21 nursing homes, 244 care centres, dual-key residences, retirement villages, etc.[52] More recently, the Private Aged Healthcare Facilities and Services Act 2017 was gazetted in 2018 under Act 802 but has not been mandated;[53] this act dictates the approval and licensing requirements to operate private aged care facilities and services.[53] The advent of these acts is expected to further strengthen the regulation of aged care facilities in Malaysia. However, the current acts do not mandate the presence

of pharmacists in RACF, and it might be worthwhile exploring their potential in improving patient safety of the aged care population.

Although the Pharmaceutical Services Division of the Ministry of Health Malaysia provides pharmaceutical care services such as Home Medication Reviews (HMR) and strategies to improve the Quality Use of Medicines to older patients residing in RACF and even their own homes, it is worth considering a mandatory approach for pharmacists to steer medication-optimisation strategies in RACF. Given that RACF in Malaysia are not deemed as healthcare facilities, residents are required to seek medical treatment at their own capacity in private or governmental healthcare facilities such as private clinics and hospitals, or government-subsidised health clinics and hospitals. This scenario may give rise to a long list of medications (and polypharmacy), in addition to duplication of medications. Although there are strategies in place to improve the welfare quality of life of residents in RACF in Malaysia, these services may be underutilised. It would be feasible to ensure community and hospital pharmacists conduct medication reviews on a part-time basis in RACF, as this has shown to improve the quality of medication use.[54] Since the HMR service has been established by the Ministry of Health, this strategy could be expanded to incorporate reviews for residents in RACF by implementing a schedule-based approach for government pharmacists to visit RACF on a weekly basis to provide medication review services. Pharmacists can take turns to perform these services on a rotation basis during office hours as a pilot programme so that financial reimbursements may not hinder the implementation of this service. Furthermore, appropriate training under the Continuous Professional Development scheme should be provided to pharmacists who will be providing the medication reviews to ensure optimal provision of care for the residents. It is recommended that the reviews be aided by tools such as medication review algorithms and medication-appropriateness quantifying tools.[55,56] Results from the pilot study will aid in further strengthening of this service. Such initiatives by pharmacists may ultimately improve the quality of life and reduce the incidence of frailty among the older people.

The strength of this study is grounded on its high reliability for all assessments. Despite robust methods, there are several limitations to the research. There

was a possibility of temporal and indication bias (decline in functioning may have preceded use of DBI-associated drugs). Although known cases were excluded, the presence of unknown cognitive issues in the study population may have influenced the study results. The use of an interviewer-administered questionnaire may have caused significant bias in the study outcomes. Participants were predominantly Chinese; therefore, the results cannot represent the entire older population in Malaysia. Recall bias may have been induced in self-reported measures. Selection bias may have been introduced into this study due to the study sites that represent aged care facilities in the urban area. The inclusion of different homes may have led to variation of results as prescribing patterns differ between clinicians. Although we observed a significant correlation between home domain of OPQOL and DBI, items in this domain may not be sensitive to people living in residential aged care homes.

In conclusion, the number of participants exposed to DBI-associated medications were more than double the number of those exposed to polypharmacy among older adults living in residential aged care facilities in Malaysia. However, exposure to DBI-associated medications was not significantly associated with overall quality of life measure. The anticholinergic and sedative burden, and polypharmacy were significantly associated with frailty. Prescribers should exercise caution when prescribing and medications must be reviewed periodically. Future longitudinal studies can evaluate impact of interventions such as periodic medication reviews on physical and cognitive function, and can determine cost-benefit relationships.

Conflict of interests' statement: The authors declare that they have no conflict of interests.

ETHICS STATEMENT

The ethics approval was obtained from the International Medical University Joint-Committee on Research and Ethics (Project ID: BPI-1-14-(09)2017). Also, permission from individual RACF management was obtained before data collection. The collected data was stored in a password-protected file accessible only to the researchers.

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Table 1: Socio-demographic characteristics of study participants (n=151)

Variables	n	%
Gender		
Male	77	50.99
Female	74	49.01
Age (Mean ± SD)	74.50 ± 8.40	
Age Group		
60 – 70	49	32.45
71 – 80	66	43.71
81 – 90	30	19.87
>90	6	3.97
Ethnicity		
Chinese	148	98.01
Indian	3	1.99
Marital Status		
Single	80	39.85
Married	50	37.59
Widowed	3	2.26
Education level		
None	77	53.47
Primary	59	40.97
Secondary	6	4.17
Tertiary	2	1.39
Number of co-morbid conditions, (Mean ± SD)	2.31 ± 1.19	

Table 2: Patient-reported outcomes (n= 151)

Variables	Value	Maximum	Minimum
Katz ADL, mean (SD)	1.00 (2.10)	6	0
Independence (score = 0), n (%)	32 (21.2)	-	-
Dependence (score > 0), n (%)	119 (78.80)	-	-
GFI Score, mean (SD)	4.60 (2.70)	13	0
Non-Frail (score < 4), n (%)	48 (31.80)	-	-
Frail (score ≥ 4), n (%)	103 (68.20)	-	-
HADS Score, mean (SD)	8.60 (5.20)	45	1
Anxiety Score, mean (SD)	4.00 (2.80)	11	0
No Anxiety (score 0-7), n (%)	132 (87.40)	-	-
Anxiety case (score > 7), n (%)	19 (12.60)	-	-
Depression Score, mean (SD)	4.90 (3.80)	36	0
No depression (score 0-7), n (%)	126 (83.4)	-	-
Depression case (score > 7), n (%)	24 (15.90)	-	-
OPQoL-35, mean (SD)	109.90 (8.0)	142	91
Good OPQOL (111-175), n (%)	72 (47.70)	-	-
Poor OPQOL (35-110), n (%)	79 (52.30)	-	-
Overall Life, mean (SD)	13.10 (1.50)	18	9
Health, mean (SD)	12.30 (1.20)	17	8
Social, mean (SD)	15.40 (1.20)	18	9
Independence, mean (SD)	12.60 (1.40)	15	9
Home, mean (SD)	15.20 (2.70)	20	9
Psychological, mean (SD)	13.80 (2.40)	20	8
Financial, mean (SD)	12.10 (1.30)	16	7
Leisure, mean (SD)	18.70 (1.30)	50	12
Medicine use & DBI			
Total number of medications, mean (SD)	3.54 (1.96)	9	1
Polypharmacy, n (%)	41 (27.15)		
DBI > 0 (n, %)	112 (74.17)		
DBI, mean (SD)	0.79 (0.63)	2	0
DBI, median (IQR)	0.67 (0.00 – 1.33)		

Note: KATZ ADL- Katz Index of Independence in Activities Daily Living; HADS- Hospital Anxiety and Depression Scale; OPQoL-35- Older People's Quality of Life-35; SD – Standard Deviation; IQR – Inter Quartile Range

Table 3: Frequencies and percentages of polypharmacy and DBI by patient-reported outcomes

Health Outcomes	Polypharmacy		Drug Burden Index (DBI)	
	No n (%)	**Yes** n (%)	**DBI = 0** n (%)	**DBI > 0** n (%)
GFI				
Non Frail (< 4)	**43 (28.48)***	**5 (3.31)**	16 (10.59)	32 (21.19)
Frail (≥ 4)	**67 (44.37)**	**36 (23.84)**	25 (16.56)	78 (51.66)
OPQOL-35				
Poor (35-110)	54 (35.76)	18 (11.92)	18 (11.92)	54 (35.76)
Good (111-175)	56 (37.10)	23 (15.23)	23 (15.23)	56 (37.09)
Overall Life, mean (SD)	13.16 (1.41)	13.05 (1.64)	13.20 (13.32)	13.11 (1.52)
Health, mean (SD)	12.33 (1.17)	12.24 (1.37)	12.48 (1.28)	12.24 (1.21)
Social, mean (SD)	15.34 (1.04)	15.49 (1.52)	15.28 (1.17)	15.41 (1.19)
Independence, mean (SD)	12.60 (1.38)	12.56 (1.55)	12.55 (1.45)	12.60 (1.42)
Home, mean (SD)	15.11 (2.73)	15.37 (2.59)	**14.40 (2.29)**	**15.46 (2.77)**
Psychological, mean (SD)	13.94 (2.47)	13.32 (2.15)	13.68 (2.79)	13.80 (2.25)
Financial, mean (SD)	12.07 (1.28)	12.12 (1.50)	11.83 (1.13)	12.18 (1.40)
Leisure, mean (SD)	18.83 (3.47)	18.46 (1.79)	19.25 (5.28)	18.54 (1.77)
Total OPQoL, mean (SD)	110.07 (7.96)	109.34 (8.31)	109.33 (9.23)	110.06 (7.60)
HADS – Depression				
No (≤ 7)	93 (61.59)	33 (21.85)	32 (21.19)	94 (62.25)
Yes (> 7)	17 (11.26)	7 (4.64)	9 (5.96)	15 (9.93)
HADS – Anxiety				
No (≤ 7)	97 (64.24)	35 (23.18)	35 (23.18)	97 (64.24)
Yes (> 7)	13 (8.61)	6 (3.97)	6 (3.97)	13 (8.61)
KATZ ADL				
Independence (= 0)	21 (13.91)	11 (26.80)	10 (6.62)	22 (14.57)
Dependence (> 0)	89 (58.94)	30 (19.87)	31 (20.53)	88 (58.28)

Note: * = p<0.05; Chi-Sq was used to obtain p-value; HADS = Hospital Anxiety and Depression Scale; KATZ ADL = Katz Index of Independence in Activities of Daily Living; OPQOL = Older People's Quality of Life; GFI = Groningen Frailty Indicator

Table 4: Unadjusted and adjusted Odds Ratios (95% CI) of reporting exposure to polypharmacy and DBI, by patient-reported outcomes

Health outcomes	**Polypharmacy** OR (95% CI), p-value	**Drug Burden Index (DBI) > 0** OR (95% CI), p-value
Unadjusted Models		
Frailty (GFI >4)	**4.62 (1.68-12.70), 0.001**	1.56 (0.74 – 3.30), 0.704
Poor QOL (OPQOL <110)	1.23 (0.59-2.53), 0.571	0.81 (0.39-1.67), 0.571
Depression (HADS >7)	1.28 (0.45-3.62), 0.643	0.78 (0.28-2.22), 0.643
Anxiety (HADS >7)	1.16 (0.44-3.05), 0.763	0.57 (0.23-1.42), 0.227
KATZ ADL (Dependence = 0)	0.64 (0.28-1.49), 0.303	1.29 (0.55-3.03), 0.558
Adjusted Models[a]		
Frail (GFI >4)	**6.07 (1.71-21.56), 0.005**	1.09 (0.39-3.04), 0.862
Poor QOL (OPQOL <110)	0.64 (0.26-1.59), 0.332	1.35 (0.49-3.68), 0.560
Depression (HADS >7)	1.01 (0.32-3.20), 0.990	0.39 (0.11-1.41), 0.152
Anxiety (HADS >7)	1.12 (0.29-4.30), 0.867	0.51 (0.11-2.37), 0.394
KATZ ADL (Dependence = 0)	1.37 (0.47-3.98), 0.567	1.60 (0.43-6.01), 0.487

OR = Odds Ratio; CI = Confidence Interval; QOL = Quality of Life;

Referents were non-frail, Good QOL, no depression, no anxiety, KATZ independence, no polypharmacy, DBI = 0

[a]Odds ratio adjusted for age, sex, marital status, co-morbid conditions, HADS-depression, HADS-anxiety, OPQOL, GFI, KATZ ADL, polypharmacy, DBI. Classification method used was logistic

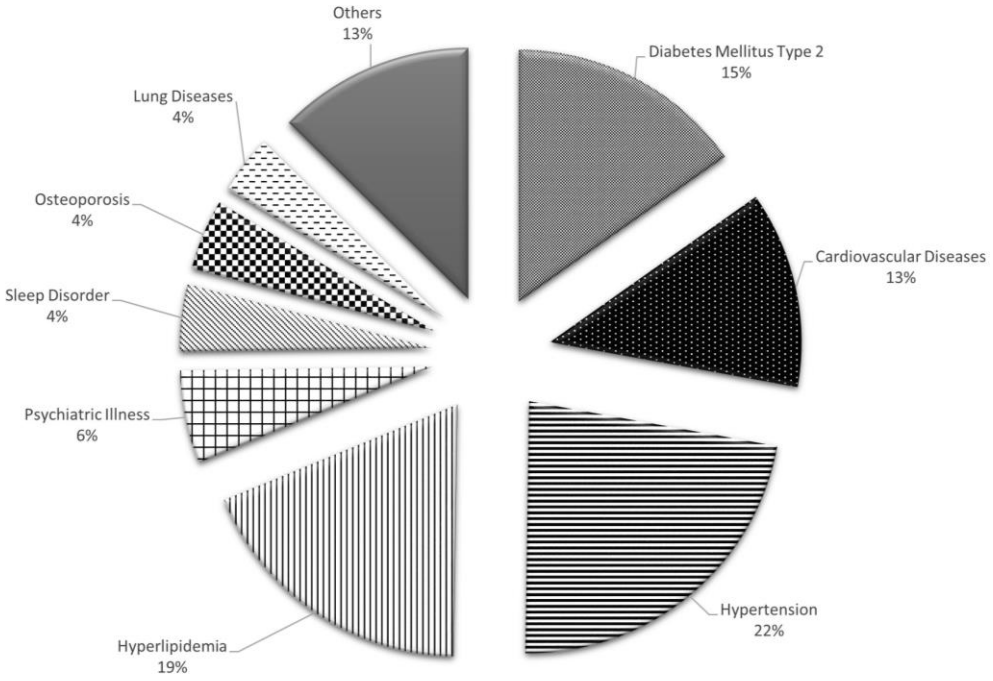

Figure 1: Pre-existing medication conditions at the time of data collection