

# Anticholinergic Burden, Falls, and the Concept of Appropriate Polypharmacy in Indonesian Geriatric Clinics: A Multicentre Observational Study

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## ABSTRACT

**Background:** A high anticholinergic burden (ACB) scale score ( $\geq 3$ ) and polypharmacy have been viewed negatively due to possible adverse events. As Indonesian multicentre data in this field are lacking, this study aimed to provide regional data related to ACB, polypharmacy, and falls, and to analyse factors potentially linked to falls. **Methods:** Data from community-dwelling older adults aged  $\geq 60$  years were collected in 12 geriatric care centres through history taking and medical records. Bivariate and multivariate analyses were conducted to evaluate the association between covariates and falls. **Results:** Polypharmacy and high ACB (score  $\geq 3$ ) were observed in 43.9% and 1.8% of 626 older adults, respectively. The five most prescribed drug classes were calcium-channel blockers, angiotensin receptor blockers, statins, beta blockers, and proton pump inhibitors. The three most prescribed drugs with possible anticholinergic activity were furosemide, isosorbide dinitrate, and cetirizine. The prevalence of past-year falls was 16.8%. Falls were associated with age  $\geq 80$  years (odds ratio [OR] 2.44, 95% confidence interval [CI] 1.31-4.53), female sex (OR 2.08, 95% CI 1.30-3.31), transient ischaemic attack and cerebrovascular accident (OR 1.97, 95% CI 0.94-4.10), multimorbidity ( $\geq 3$  co-morbidities) (OR 1.80, 95% CI 1.07-3.03), depression (OR 1.79, 95% CI 1.00-3.23), and polypharmacy (OR 0.65, 95% CI 0.40-1.05). **Conclusion:** The prevalence of a high ACB score and falls were 1.8% and 16.8%, respectively.

*Approximately one in two older adults had polypharmacy. We observed a non-significant inverse relationship between polypharmacy and falls. This may possibly suggest appropriate polypharmacy and closer monitoring applied in geriatric settings, which requires further investigation.*

**Keywords:** polypharmacy; medical overuse; anticholinergic syndrome; geriatrics; accidental falls, aged

## INTRODUCTION

Approximately 30% of older adults aged  $\geq 65$  years fall every year. The fall rate appears to be even higher (50%) among people aged  $\geq 80$  years.<sup>1</sup> On the other hand, the rate of anticholinergic drug prescriptions for common diseases in older adults, including urinary incontinence, asthma, and dementia, are increasing.<sup>2</sup> Anticholinergic effects are commonly found in extensively used medications, including antiemetics, antihistamines, antidepressants, and antihypertensives.<sup>3</sup> The more types of drugs with anticholinergic effects consumed by an individual, the higher the cumulative effect; this is known as the anticholinergic burden.<sup>4</sup>

Polypharmacy and anticholinergic burden (ACB) have been viewed negatively because of their association with adverse events. Both ACB and polypharmacy may be linked to falls in the older population.<sup>5</sup> In addition, fall-related injuries are linked to significant disability, reduced mobility and independence, and increased mortality risk.<sup>6,7</sup>

However, Indonesian multicentre data in the field of polypharmacy and ACB, and their relationship with falls, are lacking. We initially hypothesised that anticholinergic burden and polypharmacy were independently associated with falls in older adults. Given the devastating effects of falls on the health and well-being of seniors, in the present study, we aimed to provide multicentre data related to ACB, polypharmacy, and falls, and to analyse factors that might be linked to falls in Indonesian community-dwelling older outpatients treated in geriatric care centres in Indonesia.

## METHODS

### Study Design and Subjects

We conducted this cross-sectional study by collecting data in geriatric care centres in secondary and tertiary hospitals in Indonesia,

namely Atma Jaya Private Hospital in North Jakarta, Cipto Mangunkusumo National General Hospital in Central Jakarta, Dr Hasan Sadikin General Hospital in Bandung, Dr Saiful Anwar General Hospital in Malang, Dr Kariadi General Hospital in Semarang, and Dr Moewardi General Hospital in Surakarta, Dr Soetomo General Hospital in Surabaya, Dr Wahidin Sudirohusodo General Hospital in Makassar, Dr Mohammad Hoesin General Hospital in Palembang, Siti Khadijah Islamic Hospital in Palembang, Haji Adam Malik General Hospital in Medan, and Dr Mohammad Djamil General Hospital in Padang. We collected data on older outpatients (aged  $\geq 60$  years) in the geriatric clinics, who were being taken care of by consultant geriatricians, as well as by physicians in geriatric medicine training or general internal medicine residency programmes. We collected data from April to October 2022. The minimum number of subjects to be recruited was 485, which was calculated using the formula for the sample size of the estimated proportion. The data sources were history taking, physical examination, and the medical record. We excluded patients with delirium and other acute illnesses, as well as those with incomplete data. Ethical approval was obtained from the Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia, with registration number KET-369/UN2.F1/ETIK/PPM.00.02/2020.

### Polypharmacy, Anticholinergic Burden, and Falls

We defined polypharmacy as the administration of five or more medications daily.<sup>8</sup> We classified drugs based on the ACB scale and other major drug groups, mentioned alphabetically as follows. (1) 5-alpha reductase inhibitor, (2) acarbose, (3) Angiotensin-converting enzyme inhibitors other than captopril, (4) acetaminophen, (5) allopurinol, (6) alpha agonist, (7) alpha blockers, (8) amiodarone, (9) amitriptyline, (10) antacid, (11) antiplatelet,

(12) angiotensin receptor blocker (ARB) or angiotensin receptor/neprilysin inhibitor (ARNi), (13) aripiprazole, (14) benzodiazepine, (15) beta blockers, (16) bicarbonate, (17) bisphosphonate, (18) brompheniramine maleate, (19) calcium channel blockers (CCB) other than nifedipine, (20) captopril, (21) carbamazepine, (22) cetirizine, (23) chlorpheniramine maleate, (24) chlorpromazine, (25) clozapine, (26) codeine, (27) colchicine, (28) cyproheptadine, (29) desloratadine, (30) digoxin, (31) dimenhydrinate, (32) diosmin hesperidin, (33) diphenhydramine, (34) domperidone, (35) dipeptidyl peptidase-4 inhibitor (DPP-4 inhibitor), (36) fentanyl, (37) fexofenadine, (38) furosemide, (39) gabapentin, (40) haloperidol, (41) hydrocortisone, (42) hydroxyurea, (43) hydroxyzine, (44) insulin, (45) isosorbide dinitrate (ISDN), (46) long-acting beta agonist (LABA) ± inhaled corticosteroid (ICS), (47) lactulose, (48) long-acting muscarinic antagonist (LAMA), (49) lenvatinib, (50) levocetirizine, (51) levodopa, (52) loperamide, (53) loratadine, (54) mesalazine, (55) metformin, (56) methotrexate, (57) metoclopramide, (58) metoprolol, (59) morphine, (60) mineralocorticoid receptor antagonist (MRA), (61) n-acetylcysteine (NAC), (62) nifedipine, (63) new oral anticoagulant (NOAC), (64) nonbenzodiazepine (Z-drugs), (65) non-steroidal antiinflammatory drug (NSAID), (66) olanzapine, (67) proton pump inhibitor (PPI), (68) prednisolone, (69) promethazine, (70) quetiapine, (71) ranitidine, (72) risperidone, (73) short-acting beta agonist (SABA), (74) short-acting muscarinic antagonist (SAMA), (75) sodium-glucose cotransporter 2 inhibitor (SGLT2i), (76) solifenacin, (77) selective serotonin reuptake inhibitor (SSRI), (78) statin, (79) sucralfate, (80) sulfonyleurea, (81) terfenadine, (82) theophylline, (83) thiazide, (84) thiazolidinedione, (85) trifluoperazine, (86) trihexyphenidyl, and (87) vitamin K antagonist (VKA). The aforementioned groups of drug were used to calculate the ACB score for each older outpatient. The data are shown with such grouping unless specifically stated otherwise, e.g. in the case of overall prevalences of CCB and ACE inhibitor administration. Falls were defined as a history of falls during the previous 12 months.

## Covariates

The covariates in this study consisted of (1) sex (determined according to the information from each person's identity card), (2) age group, classified into 60-79 years and ≥80 years, (3) living arrangement (whether the older adult lived alone or with a family member at the time of history taking), (4) history of transient ischaemic attack (TIA) and cerebrovascular accident, (5) history of diabetes mellitus, (6) chronic kidney disease, (7) heart failure, (8) depression, (9) polypharmacy,<sup>8</sup> (10) ACB score (classified into <3 and ≥3), (11) multimorbidity (the presence of three or more co-morbidities in an individual), (12) cognitive impairment, and (13) osteoarthritis. All covariates were dichotomous variables. Diseases in covariate numbers 4–8, and numbers 12-13 were diagnosed by an internal medicine resident or a geriatric medicine trainee, under the supervision of a consultant geriatrician(s). Falls were defined as a history of one or more falls during the previous 12 months.<sup>9</sup> We collected data regarding depression and cognitive impairment from a comprehensive geriatric assessment (CGA). The depression variable was determined based on the results of the five-item Geriatric Depression Scale (GDS-5) with a cut-off value of 2. We used a 10-point abbreviated mental test (AMT or AMT-10) and classified cognitive impairment with a cut-off value of 6.

## Statistical Analyses

We analysed the data using SPSS version 21 (IBM, Armonk, New York, USA). We provided descriptive data for polypharmacy, ACB scores, and falls. Due to the long list of descriptive results, we aimed to show the data of the 10 most frequently administered drugs in general and the 10 most frequently administered drugs with anticholinergic effects. The complete datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

To assess the association between falls, polypharmacy, high ACB score, and other covariates, we utilised the Chi-square test to perform bivariate analysis before multivariate analysis. Variables with p-value < 0.25 in the bivariate analysis were included in the multivariate analysis using the multiple logistic

regression method. We considered p-values <0.05 to indicate statistical significance.

## RESULTS

Polypharmacy and a high ACB (score  $\geq 3$ ) were observed in 43.9% and 1.8%, respectively, of the 626 older adults in this study (Table 1). Within the past year, 16.8% of the older adults reported a history of falls. A larger proportion of the study subjects were in the 60-79 years age group.

The 10 most frequently administered drugs in general are shown in Table 2. CCB, ARB $\pm$ ARNi, and statin drugs were among the most highly prescribed drugs. The 10 most frequently administered drugs with anticholinergic effects are shown in Table 3. Three most frequently

administered drugs with possible anticholinergic effects (ACB score = 1) were furosemide (8.5%), ISDN (7.7%), and cetirizine (4.5). The three most frequently administered drugs with definite anticholinergic effects (ACB score = 2-3) were trihexyphenidyl (0.8%), amitriptyline (0.7%), and chlorpheniramine maleate (0.2%) (Table 4).

Among our study population, 16.8% reported a history of past-year fall(s). Falls were associated with age  $\geq 80$  years (odds ratio [OR] 2.44, 95% confidence interval [CI] 1.31-4.53), female sex (OR 2.08, 95% CI 1.30-3.31), TIA and cerebrovascular accident (OR 1.97, 95% CI 0.94-4.10), multimorbidity ( $\geq 3$  co-morbidities) (OR 1.80, 95% CI 1.07-3.03), depression (OR 1.79, 95% CI 1.00-3.23), and polypharmacy (OR 0.65, 95% CI 0.40-1.05). (Table 5)

Table 1. Characteristics of subjects (n=626)

| Characteristics                         | Total (n=626)<br>N (%) | Past-year falls |              |
|---|------------------------|-----------------|--------------|
|   |                        | No<br>N (%)     | Yes<br>N (%) |
| <b>Sex</b>                              |                        |                 |              |
| Male                                    | 283 (45.2)             | 251 (88.7)      | 32 (11.3)    |
| Female                                  | 343 (54.8)             | 270 (78.7)      | 73 (21.3)    |
| <b>Age group</b>                        |                        |                 |              |
| 60-69 years                             | 315 (50.3)             | 273 (86.7)      | 42 (13.3)    |
| 70-79 years                             | 251 (40.1)             | 207 (82.4)      | 44 (17.6)    |
| 80 years and older                      | 60 (9.6)               | 41 (68.3)       | 19 (31.7)    |
| <b>Living arrangement</b>               |                        |                 |              |
| Living with family member(s)            | 587 (93.8)             | 489 (83.3)      | 98 (16.7)    |
| Living alone                            | 39 (6.2)               | 32 (82.1)       | 7 (17.9)     |
| <b>TIA and cerebrovascular accident</b> |                        |                 |              |
| No                                      | 581 (92.8)             | 489 (84.2)      | 92 (15.8)    |
| Yes                                     | 45 (7.2)               | 32 (71.1)       | 13 (28.9)    |
| <b>Diabetes mellitus</b>                |                        |                 |              |
| No                                      | 357 (57.0)             | 300 (84.0)      | 57 (16.0)    |
| Yes                                     | 269 (43.0)             | 221 (82.2)      | 48 (17.8)    |
| <b>Chronic kidney disease</b>           |                        |                 |              |
| No                                      | 570 (91.1)             | 472 (82.8)      | 98 (17.2)    |
| Yes                                     | 56 (8.9)               | 49 (87.5)       | 7 (12.5)     |
| <b>Heart failure</b>                    |                        |                 |              |
| No                                      | 471 (75.2)             | 395 (83.9)      | 76 (16.1)    |
| Yes                                     | 155 (24.8)             | 126 (81.3)      | 29 (18.7)    |
| <b>Depression</b>                       |                        |                 |              |
| No                                      | 554 (88.5)             | 469 (84.7)      | 85 (15.3)    |
| Yes                                     | 72 (11.5)              | 52 (72.2)       | 20 (27.8)    |
| <b>Polypharmacy</b>                     |                        |                 |              |
| No                                      | 351 (56.1)             | 285 (81.2)      | 66 (18.8)    |
| Yes                                     | 271 (43.9)             | 236 (87.1)      | 39 (12.9)    |
| <b>Anticholinergic burden</b>           |                        |                 |              |
| <3                                      | 615 (98.2)             | 512 (83.3)      | 103 (16.7)   |
| $\geq 3$ (high)                         | 11 (1.8)               | 9 (81.8)        | 2 (18.2)     |
| <b>Multimorbidity</b>                   |                        |                 |              |
| No                                      | 218 (34.8)             | 190 (87.2)      | 28 (12.8)    |
| Yes                                     | 408 (65.2)             | 331 (81.1)      | 77 (18.9)    |
| <b>Cognitive impairment</b>             |                        |                 |              |
| No                                      | 477 (76.2)             | 397 (83.2)      | 80 (16.8)    |
| Yes                                     | 149 (23.8)             | 124 (83.2)      | 25 (16.8)    |
| <b>Osteoarthritis</b>                   |                        |                 |              |
| No                                      | 530 (84.7)             | 439 (82.8)      | 91 (17.2)    |
| Yes                                     | 96 (15.3)              | 82 (85.4)       | 14 (14.6)    |

Note: TIA: Transient ischaemic attack; Multimorbidity: the presence of 3 or more co-morbidities in an individual.

**Table 2. The 10 most prescribed drug classes or types among Indonesian older adults**

| Rank | Drug class/type | n   | (%)    |
|------|-----------------|-----|--------|
| 1    | CCB             | 264 | (42.2) |
| 2    | ARB ±ARNi       | 251 | (40.1) |
| 3    | Statin          | 220 | (35.1) |
| 4    | Beta blockers   | 171 | (27.5) |
| 5    | PPI             | 155 | (24.8) |
| 6    | Antiplatelets   | 143 | (22.8) |
| 7    | Metformin       | 126 | (20.1) |
| 8    | Sulfonylurea    | 102 | (16.3) |
| 9    | Insulin         | 86  | (13.7) |
| 10   | Gabapentin      | 83  | (13.3) |

Note: ARB: Angiotensin receptor blocker; ARNi: angiotensin receptor neprilysin inhibitor; CCB: Calcium channel blocker; PPI: Proton pump inhibitor

**Table 3. The 10 most prescribed drugs with possible anticholinergic burden in Indonesian older adults**

| Rank | Drug type            | n  | (%)   |
|------|----------------------|----|-------|
| 1    | Furosemide           | 53 | (8.5) |
| 2    | Nitrate              | 48 | (7.7) |
| 3    | Cetirizine           | 28 | (4.5) |
| 4    | Theophylline         | 13 | (2.1) |
| 5    | Benzodiazepine       | 12 | (1.9) |
| 6    | Vitamin K antagonist | 11 | (1.8) |
| 7    | Prednisolone         | 9  | (1.4) |
| 8    | Ranitidine           | 7  | (1.1) |
| 9    | Digoxin              | 4  | (0.6) |
| 10   | Aripiprazole         | 3  | (0.5) |

**Table 4. The five most prescribed drugs with definite anticholinergic burden in Indonesian older adults**

| Rank | Drug type                | n | (%)   |
|------|--------------------------|---|-------|
| 1    | Trihexyphenidyl          | 5 | (0.8) |
| 2    | Amitriptyline            | 4 | (0.7) |
| 3    | Carbamazepine            | 1 | (0.2) |
| 4    | Chlorpheniramine maleate | 1 | (0.2) |
| 5    | Trifluoperazine          | 1 | (0.2) |

**Table 5. Results of bivariate and multivariate analyses to evaluate potential factors associated with falls**

|   | Crude Odds Ratio |           |         | Adjusted Odds Ratio |           |         |
|---|------------------|-----------|---------|---------------------|-----------|---------|
|   | OR               | 95% CI    | p-value | OR                  | 95% CI    | p-value |
| <b>Sex</b>                              |                  |           |         |                     |           |         |
| Male                                    | Ref              |           |         | Ref                 |           |         |
| Female                                  | 2.12             | 1.35-3.33 | 0.001   | 2.08                | 1.30-3.31 | 0.002   |
| <b>Age group</b>                        |                  |           |         |                     |           |         |
| 60-79 years                             | Ref              |           |         | Ref                 |           |         |
| 80 years and older                      | 2.59             | 1.43-4.67 | 0.001   | 2.44                | 1.31-4.53 | 0.005   |
| <b>Living arrangement</b>               |                  |           |         |                     |           |         |
| Living with family member(s)            | Ref              |           |         |                     |           |         |
| Living alone                            | 1.09             | 0.47-2.54 | 0.839   | N/A                 |           |         |
| <b>TIA and cerebrovascular accident</b> |                  |           |         |                     |           |         |
| No                                      | Ref              |           |         | Ref                 |           |         |
| Yes                                     | 2.16             | 1.09-4.27 | 0.024   | 1.97                | 0.94-4.10 | 0.072   |
| <b>Diabetes mellitus</b>                |                  |           |         |                     |           |         |

|                               |      |           |       |      |           |       |
|-------------------------------|------|-----------|-------|------|-----------|-------|
| No                            | Ref  |           |       |      |           |       |
| Yes                           | 1.14 | 0.75-1.74 | 0.534 | N/A  |           |       |
| <b>Chronic kidney disease</b> |      |           |       |      |           |       |
| No                            | Ref  |           |       |      |           |       |
| Yes                           | 0.69 | 0.30-1.56 | 0.457 | N/A  |           |       |
| <b>Heart failure</b>          |      |           |       |      |           |       |
| No                            | Ref  |           |       |      |           |       |
| Yes                           | 1.20 | 0.75-1.92 | 0.37  | N/A  |           |       |
| <b>Depression</b>             |      |           |       |      |           |       |
| No                            | Ref  |           |       | Ref  |           |       |
| Yes                           | 2.12 | 1.21-3.73 | 0.008 | 1.79 | 1.00-3.23 | 0.052 |
| <b>Polypharmacy</b>           |      |           |       |      |           |       |
| No                            | Ref  |           |       | Ref  |           |       |
| Yes                           | 0.71 | 0.46-1.10 | 0.125 | 0.65 | 0.40-1.05 | 0.079 |
| <b>Anticholinergic burden</b> |      |           |       |      |           |       |
| <3                            | Ref  |           |       |      |           |       |
| ≥3 (high)                     | 1.11 | 0.24-5.19 | 0.900 | N/A  |           |       |
| <b>Multimorbidity</b>         |      |           |       |      |           |       |
| No                            | Ref  |           |       | Ref  |           |       |
| Yes                           | 1.58 | 0.99-2.52 | 0.054 | 1.80 | 1.07-3.03 | 0.027 |
| <b>Cognitive impairment</b>   |      |           |       |      |           |       |
| No                            | Ref  |           |       |      |           |       |
| Yes                           | 1.00 | 0.61-1.64 | 0.998 | N/A  |           |       |
| <b>Osteoarthritis</b>         |      |           |       |      |           |       |
| No                            | Ref  |           |       |      |           |       |
| Yes                           | 0.82 | 0.45-1.52 | 0.533 | N/A  |           |       |

Note: OR: Odds ratio, CI: Confidence interval, Ref: reference, N/A: not applicable, TIA: Transient ischaemic attack; Multimorbidity: the presence of 3 or more co-morbidities in an individual

## DISCUSSION

### Prevalence of High Anticholinergic Burden, Polypharmacy, and Falls

Polypharmacy may not always be harmful, particularly when it is appropriate and clinically indicated. In this study, although approximately one out of two older adults had polypharmacy, geriatrician-led outpatient clinics in Indonesia managed to perform drug reconciliation to keep the anticholinergic burden low. Polypharmacy and a high ACB score ( $\geq 3$ ) were observed in 43.9% and 1.8% of older adults treated in geriatric care centres, respectively. Good practice of geriatric medicine may help promote active deprescribing for the patient's best outcome to avoid inappropriate polypharmacy. Inappropriate medication prescriptions led to significantly higher frequency of ambulatory care visits, emergency care visits, and hospitalisation.<sup>10</sup>

Inflamm-ageing in older adults is a sterile, chronic, low-grade inflammation that potentially contributes to the pathogenesis of age-related diseases.<sup>11</sup> A previous study reported that a

higher ACB score ( $\geq 4$ ) was associated with higher inflammatory markers, including serum C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-alpha), compared with cohorts with an ACB score of 0. Inflammation may be a mediator variable in the relationship between anticholinergic drugs and adverse outcomes.<sup>12</sup>

The prevalence of falls in the present study was 16.8%. Physicians in Indonesia commonly use scoring systems based on fall risk assessments, such as the Hendrich II Fall Risk Model.<sup>13</sup> Previously, scientists have also developed the Modification of Indonesian Fall Risk Assessment Tool (M-IFRAT).<sup>14</sup> However, common practice does not equal the best recommended practice. Regarding falls in hospitals and care homes, we believe that Indonesia should follow the best practice stated in the latest version of the World Falls Guidelines (WFG), which contains recommendations against using scored fall risk screening tools in hospitals for multifactorial fall risk assessments in older adults.<sup>15</sup>

### Factors Associated with Falls

We concluded that falls among community-dwelling older outpatients treated in geriatric care centres in Indonesia were associated with age  $\geq 80$  years, female sex, TIA and cerebrovascular accident, multimorbidity ( $\geq 3$  co-morbidities), depression, and polypharmacy.

We identified a significant relationship between falls and age  $\geq 80$  years. However, chronological age is not incorporated in the WFG algorithm for determining fall risk and severity.<sup>15</sup> Future assessment may consider the importance of chronological age to predict fall risk. We also found a statistically significant relationship between female sex and falls. Previous studies reported various findings in this regard. The present study results are similar to previously reported findings, which suggests that women have a higher likelihood of falls than men.<sup>16-19</sup> In contrast, our findings do not support the result of a study suggesting a higher risk of falls among men compared with women.<sup>20</sup>

TIA and cerebrovascular accident were associated with falls in the present older adult cohort. Previous data have suggested that falls are one of the most common complications after stroke, but it is less likely that falls lead to cerebrovascular events. The incidence of post-stroke falls has been reported to range between 7% in the first week and 73% in the first year after stroke.<sup>21</sup> This association may be due to impaired attention, muscle weakness, sensory impairment, visual abnormalities, and impaired spatial awareness.<sup>22</sup> Furthermore, falls occurring in community-dwelling patients after cerebrovascular accident also predict future falls.<sup>23</sup> Clinical practice potentially benefits mostly from inexpensive methods involving exercise because of its ease of administration and favourable fall prevention outcomes. A previous Cochrane review suggested low to very low-quality evidence supporting the use of exercise to reduce the rate of falls. Exercises such as balance training, ambulation training, perturbation/vibration-based training, and tai chi<sup>21</sup> can be delivered as a single intervention or a part of a multiple-intervention strategy.

In the present study, we found that multimorbidity was linked to falls among

Indonesian older adults. This finding was consistent with a multicentre study in Europe involving community-dwelling older adults in Switzerland, Austria, Germany, France, and Portugal, which suggested a higher rate of 3-year falls in older adults with the presence of three or more chronic diseases.<sup>24</sup> The number of chronic diseases has not yet been incorporated in the latest WFG algorithm for fall risk assessment.<sup>15</sup> This means that generally healthy and active older adults may be at higher risk of falls once they have multimorbidities; therefore, future guideline updates may need to consider this variable for fall risk assessment.

Falls were associated with depression in our study, possibly because of the bidirectional relationship between both problems.<sup>25</sup> Older adults with depression may have excessive fear of falling, associated with abnormalities in balance and gait. This association is mediated through motor, sensory, and cognitive pathways. Fear of falling is one of the three main initial questions in the opportunistic case-finding process endorsed in the WFG.<sup>15</sup> The latest NICE Guidelines state that psychological therapies should be considered as a first-line treatment for depression in adult populations. The recommended therapies include cognitive behavioural therapy (CBT), but in recent years, newer promising psychological treatments in recent years have also included mindfulness-based therapy and behavioural activation.<sup>26</sup> On the other hand, most people undergoing treatment are still prescribed antidepressants. However, the long-term prescription of antidepressants is concerning,<sup>27,28</sup> because both antidepressant usage and untreated depression contribute to an increased risk of falls.<sup>27</sup> Clinical decision tools, including the STOPPFalls antidepressant withdrawal algorithm, may potentially help doctors deprescribe these drugs rationally.<sup>27</sup>

We initially hypothesised that polypharmacy might be a risk factor for falls. Polypharmacy has been viewed negatively because of its association with safety risks, including adverse events and drug interactions.<sup>29</sup> However, we observed a potentially protective effect of polypharmacy in preventing falls. First, this may be due to appropriate polypharmacy

being applied to patients in geriatric clinics by consultant geriatricians, geriatric medicine fellows, and residents. Second, it may also be that certain drugs pose a higher fall risk than the number of medications.<sup>30</sup> It should be noted that the observed associations, including the inverse trend between polypharmacy and falls, should be interpreted cautiously due to the cross-sectional design and possible reverse causation. Confounding by indication may partly explain the observed inverse trend, as patients receiving multiple medications may also receive closer clinical monitoring and optimised management.

Unlike the interesting finding related to polypharmacy, we found no link between ACB and falls. A very low prevalence of high ACB in our cohort may have limited the statistical power to detect a significant association. In fact, a previous study suggested that the association between fall risk and lower levels of ACB remained inconsistent.<sup>30</sup>

#### **Role of Geriatrician-led Healthcare Services in Managing Polypharmacy and ACB**

The negative connotation of polypharmacy may not be relevant if the prescription of multiple medications is completely appropriate. Physicians can achieve appropriate polypharmacy by ensuring that patients obtain the most appropriate combination of drugs based on the best scientific evidence, and considering the clinical context of each patient.<sup>29</sup> Not only could we rely on geriatrician-led interventions, but also, deprescribing interventions could be delivered by a multidisciplinary team or pharmacist. Physicians can use validated tools for prescribing appropriateness, including STOPP/START<sup>31</sup> and PROMPT.<sup>32</sup> The use of such tools can help physicians assess both the over- and under-prescribing of drugs. The Scottish government published polypharmacy guidance for realistic prescribing in 2018, which emphasised a holistic patient-centred seven-step medication review. This process was not a linear one-off event, but rather, a cycle involving seven questions/steps for medication review. First, physicians should know what matters to the patient. Second, physicians should identify essential drug therapies. Before altering or stopping a drug, a physician may need to seek

advice from a specialist. Third, physicians should ask whether the patient is receiving unnecessary drug therapy. This step is achievable by checking for expired and valid indications and assessing risks and benefits. Fourth, physicians should clarify whether the therapeutic objectives are being achieved. Fifth, physicians should ask whether the patient is at risk of or experiences adverse drug reactions. Sixth, physicians should clarify whether the therapy is cost-effective. Seventh, physicians should know whether the patient is willing to take the drug as intended.

Regardless of the study result regarding ACB, in specific settings where geriatricians may not be able to train junior doctors in the field of polypharmacy, ACB may be built into a computerised clinical decision support system (CCDSS) designed to lower the rate of potentially inappropriate drug administration in older adults. This intervention has been proven to reduce the median ACB score from 1.3 at admission to 1.1 at discharge.<sup>33</sup>

#### **LIMITATIONS**

We are cognisant of the fact that cross-sectional studies may only identify the factors associated with falls, because causal relationships are less clear compared with the results of longitudinal studies. Thus, a future randomised clinical trial in this field may be necessary. To our knowledge, this is the first observational study to evaluate anticholinergic burden and polypharmacy in multiple geriatric clinics simultaneously. By involving various centres on different islands, our multicentre study may represent the real population more accurately. The multivariate analysis conducted in this multicentre study helped adjust for the variables appropriately. Another limitation of this study was the possible recall bias regarding the history of falls reported by each patient. In addition, as each study variable was dichotomised, we might have missed important findings of this study.

#### **CONCLUSION**

The prevalence of high ACB and falls were 1.8% and 16.8%, respectively. Nearly one in two Indonesian older adults in geriatric care centres had polypharmacy. We found that falls in

community-dwelling older outpatients treated in geriatric care centres in Indonesia were associated with age  $\geq 80$  years, TIA and cerebrovascular accident, multimorbidity ( $\geq 3$  co-morbidities), depression, and polypharmacy. We observed a non-significant inverse relationship between polypharmacy and falls. This may suggest the possibility of appropriate polypharmacy applied in Indonesian geriatric clinics, accompanied by closer monitoring, which requires further investigation.

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### CONFLICT OF INTEREST

The authors declare no conflict of interest.

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### AUTHORSHIP CONTRIBUTIONS

Conceptualization, SSe, MKA, R, NKS, KH, IF, ND, RI, IGPSA, SSu, AS, DAA, LD, NW, NR, RM, YMM, and FB; Data curation, Se, MKA, R, NKS, KH, IF, ND, RI, IGPSA, SSu, AS, DAA, LD, NW, NR, RM, YMM, and FB; Funding acquisition, -; Formal analysis, SSe, IF and MKA; Methodology, SSe, MKA, R, NKS, KH, IF, ND, RI, IGPSA, SSu, AS, DAA, LD, NW, NR, RM, YMM, and FB; Project administration, -; Supervision, SSe; Writing-original draft, SSe, MKA, R, NKS, KH, IF, ND, RI, IGPSA, SSu, AS, DAA, LD, NW, NR, RM, YMM, and FB; Writing-review & editing, SSe, MKA, R, NKS, KH, IF, ND, RI, IGPSA, SSu, AS, DAA, LD, NW, NR, RM, YMM, and FB.

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