

DISCHARGE PHARMACOTHERAPY PATTERNS AND MEDICATION BURDEN IN ISCHAEMIC STROKE PATIENTS WITH DOCUMENTED COGNITIVE DYSFUNCTION: A DESCRIPTIVE STUDY IN A ROMANIAN TERTIARY-CARE HOSPITAL

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Abstract

Discharge pharmacotherapy after acute ischaemic stroke (AIS) often involves multiple agents for secondary prevention and comorbidities, and medication burden may be clinically relevant in patients with cognitive impairment. This retrospective, cross-sectional, single-centre study characterised discharge pharmacological patterns and medication burden in patients with AIS and documented cognitive impairment hospitalised at a Romanian tertiary-care hospital during 2024 - 2025. Medicines were standardised to active substances using WHO ATC and national medicines nomenclature. Among 117 patients, 99.1%, 98.3%, 95.7%, and 95.7% received lipid-modifying, antithrombotic, cardiovascular, and antihypertensive therapies, respectively. Cognition-related active substances (N06BX and N06D) were prescribed to 52.1% of patients. The median active-substance count was 8 (IQR 6 - 10); 59.8% had polypharmacy and 28.2% had hyper-polypharmacy. Excluding cognition-related active substances reduced hyper-polypharmacy to 20.5%. No age-related differences were detected. Discharge treatment was characterised by extensive vascular and cardiovascular pharmacotherapy and substantial medication burden, to which cognition-related prescribing contributed without fully accounting for it.

Rezumat

Farmacoterapia la externare după accidentul vascular cerebral ischemic acut (AVC ischemic acut) implică adesea mai mulți agenți pentru prevenția secundară și pentru comorbidități. Povara medicamentoasă poate fi clinic relevantă la pacienții cu afectare cognitivă. Acest studiu retrospectiv, transversal, unicentric a caracterizat tiparele farmacologice la externare și povara medicamentoasă la pacienții cu AVC ischemic acut și afectare cognitivă documentată, internați într-un spital terțiar din România în perioada 2024 - 2025. Medicamentele au fost standardizate la nivel de substanță activă, utilizând clasificarea ATC a OMS și nomenclatorul național. Dintre cei 117 de pacienți, terapiile hipolipemizante, antitrombotice, cardiovasculare și antihipertensive au fost prescrise la 99,1%, 98,3%, 95,7% și 95,7%, respectiv. Substanțele active asociate cogniției (N06BX și N06D) au fost prescrise la 52,1% dintre pacienți. Numărul median de substanțe active a fost 8 (IQR 6 - 10); 59,8% au prezentat polimedicatie, iar 28,2% hiperpolimedicatie. Excluderea substanțelor asociate cogniției a redus hiperpolimedicatia la 20,5%. Nu au fost identificate diferențe legate de vârstă. Tratamentul la externare a fost caracterizat de o farmacoterapie vasculară și cardiovasculară extinsă și de o povară medicamentoasă substanțială, la care prescrierea asociată cogniției a contribuit fără a o explica în totalitate.

Keywords: acute ischaemic stroke, cognitive impairment, polypharmacy, medication burden, pharmacotherapy

Introduction

Pharmacotherapy at hospital discharge after acute ischaemic stroke (AIS) reflects both the requirements of secondary vascular prevention (1) and the patient's broader clinical status, with additional medications possibly needed for neurological, psychiatric, infectious, or other comorbid conditions (2-4). Antithrombotic, lipid-modifying, and antihypertensive therapies, along with diabetes and other cardiovascular conditions,

can coexist in the discharge regimen (2, 3). Consequently, patients may leave acute stroke care with multidrug regimens whose composition reflects both prevention of recurrent vascular events and the treatment of substantial multimorbidity that can be frequent among stroke patients (4-7). Contemporary secondary-prevention literature, including guidelines, supports sustained management of major modifiable vascular risk factors after ischaemic stroke (1, 3, 6), making

treatment with multiple drugs clinically expected in patients with several risk factors. Effective secondary prevention and treatment of cardiovascular and metabolic comorbidities are fundamental to reducing recurrent vascular risk (1, 3, 6-7), but the resulting regimen may impose substantial difficulty managing medications (3, 7, 12, 13).

Cognitive impairment (CI) is common after stroke and may affect independence and everyday functioning. Its course after the acute event is heterogeneous and may include improvement, persistence, or deterioration (7-10). Notably, acute cognitive performance may also be influenced by delirium, systemic illness and other potentially reversible factors (7-10). In this context, medication burden may be particularly relevant (7, 8), as the CI identified during the acute phase after stroke might be associated with poorer subsequent outcomes (9), and it may also affect adherence to pharmacological treatment, including therapies targeting vascular risk factors such as hypertension, atrial fibrillation, and dyslipidaemia. These vascular risk factors are also associated with an increased risk of cognitive impairment (7-11).

CI, neurological deficits, functional status, and multimorbidity may further affect the ability to manage treatment after discharge and increase reliance on family members or caregivers (4, 7-13). Evidence directly linking CI to medication non-adherence after stroke remains heterogeneous, although cognitively impaired stroke survivors may require greater assistance with medication administration (11-13). Medication self-management after stroke requires cognitive abilities such as understanding therapeutic instructions and remembering when and how medicines should be taken. Impairment in these abilities may compromise adherence, particularly in patients receiving complex regimens, while consistent use of preventive therapies remains important for reducing recurrent vascular risk (7, 13-17).

Given the high prevalence of post-stroke CI (18, 19) and its impact on quality of life (7), effective management remains a key clinical challenge. However, evidence supporting specific pharmacological interventions remains limited and heterogeneous, and the Quinn *et al.* guideline found insufficient evidence to recommend cholinesterase inhibitors, memantine, or nootropics for post-stroke cognitive impairment (20). In clinical practice, patients may receive heterogeneous medicinal products in the context of cognitive dysfunction alongside conventional secondary-prevention and comorbidity-related treatment (3, 4, 7, 20). To our knowledge, real-world data on discharge pharmacological patterns, medication burden, and cognition-related pharmacotherapy among patients with AIS and documented cognitive impairment remain limited, particularly in Romanian clinical settings. The present study aimed to characterise discharge pharmacological patterns and medication burden

in this population. Polypharmacy and hyper-polypharmacy, cognition-related medicinal products, and exploratory differences according to age were also evaluated. In addition to the primary active-substance count, medication burden was also described using medication-product counts as a complementary measure. The contribution of cognition-related agents to medication burden was assessed in a sensitivity analysis by excluding them from the active-substance count. The study was not designed to assess prescribing quality, guideline adherence, medication appropriateness, or causal relationships between medication exposure and clinical outcomes.

Materials and Methods

Study design and setting

This retrospective, cross-sectional, single-centre observational study used routinely collected real-world clinical data from the Cluj County Emergency Clinical Hospital, a tertiary-care hospital in Cluj-Napoca, Romania.

The study provides a description of pharmacotherapy at hospital discharge and does not assess longitudinal treatment changes or prescribing decisions over time. Patients admitted between 1 January 2024 and 31 December 2025 were considered for inclusion.

Study population and eligibility criteria

Patients were included if they met all of the following criteria: (1) age ≥ 18 years; (2) AIS recorded as the principal discharge diagnosis using the 10th revision of the International Classification of Diseases (ICD-10) (21) codes I63.3, I63.4, or I63.5, supported by the available clinical and/or neuroimaging documentation; (3) cognitive impairment present and recorded during the index hospitalisation as a secondary discharge diagnosis; (4) first eligible AIS hospitalisation for that patient during the study period; (5) survival to hospital discharge; and (6) available discharge medication documentation sufficient to determine the prescribed post-discharge therapeutic regimen.

Patients were excluded in the presence of any of the following: (1) a principal discharge diagnosis other than AIS as defined above; (2) documented cognitive impairment or dementia predating the index stroke; (3) in-hospital death; or (4) missing or incomplete discharge medication documentation that prevented ascertainment of the intended post-discharge pharmacological treatment.

The AIS codes I63.3, I63.4, and I63.5 were selected based on the cerebral infarction codes routinely used at the study centre. Stroke vascular territory was classified separately from clinical and neuroimaging documentation and was not inferred from the ICD-10 code.

Cognitive severity and the cognitive assessment methodology were outside the scope of the study.

The first eligible AIS hospitalisation was the first admission during the study period that met the study criteria. It did not require the index event to represent the patient's first-ever stroke. To reduce selection and classification variability, we included all eligible identified cases and standardised discharge medications using predefined active-substance and ATC-based classification rules. No formal sample-size calculation was performed.

Data collection and study variables

Eligible cases were identified by screening electronic discharge records in the electronic health record database of the Cluj County Emergency Clinical Hospital for the specified diagnoses, using the codes and presence of cognitive impairment. Demographic and clinical data were extracted. Additional variables included diagnostic and imaging findings, documented comorbidities, stroke-related complications, and discharge pharmacotherapy. Previous psychiatric history was recorded separately from anxiety- and depression-related diagnoses. Anxiety disorder, depressive disorder, and mixed anxiety-depressive disorder were treated as mutually exclusive diagnostic categories. Clinical and investigation findings were recorded when documented. No imputation of missing data was performed. Analyses were based on available documented information. Detailed characteristics of the study population are presented in the Results.

Assessment of discharge pharmacotherapy

The pharmacological assessment was based primarily on active substances included in the treatment plan at hospital discharge following the index AIS admission. Trade names were standardised to their active substances using the National Nomenclature of Medicinal Products for Human Use of the National Agency for Medicines and Medical Devices of Romania (ANMMDR) (22) and classified according to the World Health Organisation Anatomical Therapeutic Chemical (WHO ATC) classification system, using the WHO ATC/DDD Index 2026 (23). Pharmacological and therapeutic groups were defined primarily using the third and fourth ATC levels, as appropriate to the medication class under consideration. Medicinal products without a standard WHO ATC code, dietary supplements and vitamin preparations were excluded from the analysis.

Fixed-dose combination products were mapped to their constituent active substances for medication-burden calculations. In the pharmacological-pattern analysis, clinically relevant combination categories were additionally considered where appropriate. When the same active substance was present in more than one prescribed product for an individual patient, it was counted only once in the medication-burden calculation. Medication categories and subclasses were not mutually exclusive; individual patients could contribute to more than one pharmacological category.

Discharge pharmacological patterns

Pharmacological patterns were assessed across the major WHO ATC-based therapeutic domains and study-defined groupings, including antithrombotic therapy, lipid-modifying treatment, cardiovascular and anti-hypertensive therapy, drugs used in diabetes, neurological medications, psychotropic medications and cognition-related substances/medications. The study-defined groupings were used where a clinically meaningful treatment domain was not represented by a single WHO ATC subgroup. Pharmacological categories were defined primarily using the third and fourth ATC levels, as appropriate, and categories and subclasses were not necessarily mutually exclusive. Thus, patients could contribute to more than one related category. For example, statins were included within lipid-modifying therapy, while antihypertensive therapy overlapped with the cardiovascular grouping. The pharmacological-pattern analysis was intended to describe the main components of the discharge regimen rather than provide an exhaustive inventory of every prescribed medicinal product.

Exposure to each category was reported as the number and percentage of patients receiving at least one medicinal agent within that category, with each patient counted once within a category irrespective of the number of agents received for the pharmacological patterns. Relevant subclasses were reported separately where appropriate. Active-substance exposure was retained when substances were prescribed in combination products; thus, a statin contained in a combination product contributed to both the statin and the corresponding combination category.

Cognition-related medicinal products

Cognition-related pharmacotherapy was assessed as a study-defined clinical domain comprising selected medicinal products grouped based on their cognition-related indications described in the Romanian national medicines documentation (ANMMDR) and the WHO ATC classification, including substances classified under N06BX and N06D. This grouping was used descriptively within the clinically documented cognitive-impairment context and did not imply pharmacological equivalence, comparable efficacy, guideline endorsement, or medication appropriateness.

Medication burden and polypharmacy

Medication burden was assessed separately from pharmacological class exposure and was defined primarily as the number of distinct active medicinal substances prescribed for regular post-discharge use. Active substances contained in fixed-dose combination products were counted separately, whereas prescriptions containing the same active substance were counted once *per* patient.

Medication-product counts were also calculated as a complementary measure, with each fixed-dose combination counted as a single medication product. The

same criteria were applied to both the active-substance and medication-product counts.

All eligible medicinal agents were included in the medication-burden calculation irrespective of therapeutic class or whether their pharmacological class was reported separately in the pharmacological-pattern analysis. Regular ongoing treatments, including time-limited therapies forming part of the post-stroke treatment, such as dual antiplatelet therapy, were included. Regular ongoing treatments were defined as medications intended for use beyond 30 days after discharge. However, we excluded treatments prescribed only for the short-term management of an acute intercurrent condition, including courses of anti-infective therapy, short-course symptomatic treatments, and medications prescribed on an as-needed basis. Short-course treatment was defined as an intended duration of ≤ 30 days after discharge. Duration and as-needed status were determined from the discharge treatment instructions. Medication eligibility was independently reviewed by two investigators, with disagreements resolved by consensus.

Accordingly, the pharmacological-pattern analysis described the pharmacological exposures present in the discharge treatment plan, whereas the primary medication-burden analysis quantified the distinct active substances prescribed at discharge. The medication-product counts provided a complementary descriptive measure of burden.

For the medication-burden analysis, we classified patients by the number of active substances using commonly used thresholds: no polypharmacy (< 5), polypharmacy (5-9), or hyper-polypharmacy (≥ 10) (24). The same thresholds were applied to both the active-substance and medication-product counts.

Sensitivity analysis

The primary medication-burden calculation included cognition-related active substances when they met the predefined criteria. In the sensitivity analysis, we excluded these products from the active-substance count and reassessed medication burden, including the prevalence of polypharmacy and hyper-polypharmacy, using the same definitions as in the primary analysis. This analysis evaluated the contribution of cognition-related prescribing to medication burden. The same active-substance analysis was also performed within the age subgroups to assess whether subgroup findings were influenced by cognition-related prescribing. For the study population, medication-product burden was likewise described after excluding cognition-related medicinal products, using the same polypharmacy thresholds.

Exploratory subgroup analyses

Planned exploratory subgroup analyses were performed according to age (≥ 65 vs < 65 years) as mentioned above. The age threshold of 65 years was selected to distinguish older adults from younger patients. Analyses were restricted to medication-burden

outcomes and selected major pharmacological domains relevant to the study objectives.

Outcome measures

The primary outcome was the distribution of pharmacological categories and subclasses in the discharge treatment plan, as defined in Section 2.5 and presented in Section 3.2, including Figure 1.

Secondary outcomes included medication burden at discharge, the prevalence of polypharmacy and hyper-polypharmacy, as well as the number of cognition-related active substances prescribed *per patient*. Medication-product burden was reported as a complementary descriptive outcome.

Medication-burden outcomes and major pharmacological domains were explored in subgroup analyses according to age. In addition, a sensitivity analysis assessed the primary medication-burden after exclusion of cognition-related medicinal products, while medication-product burden was summarised descriptively after this exclusion for the study population.

Statistical analysis

Qualitative data were presented as counts and percentages. Quantitative data were presented as medians with first and third quartiles (Q1 - Q3). Associations between qualitative variables were assessed using Fisher's exact test or the chi-square test. Comparisons between two independent groups concerning quantitative variables were performed using the Wilcoxon rank-sum test. No inferential comparisons were performed for the complementary medication-product measure. All statistical tests used a significance level of 0.05 and two-tailed p-values. No multivariable adjustment was performed because the analyses were descriptive and exploratory. All statistical analyses were computed in R version 4.3.2 (25) (R Foundation for Statistical Computing, Vienna, Austria) and Microsoft Excel.

The analyses were primarily descriptive, with comparative analyses limited to subgroup analyses and a sensitivity analysis.

Ethical aspects

The Ethics Committee of the "Iuliu Hațieganu" University of Medicine and Pharmacy Cluj-Napoca, Romania, (approval no. 165/17 June 2026) and the Ethics Committee of the Cluj County Emergency Clinical Hospital (approval no. 18622/28 May 2026) reviewed and approved the study protocol. The study was conducted in accordance with applicable ethical and data-protection requirements, including the Declaration of Helsinki and GDPR.

Results and Discussion

Study population

A total of 117 patients met the eligibility criteria and were included in the analysis. The median age was 74 years (IQR 69 - 79), with 83.8% of patients aged ≥ 65 years. The observed age range was 41 - 96 years.

Women accounted for 54.7% of the cohort. Left carotid territory involvement was the most frequently documented vascular territory (41.9%), and 32.5% of patients had a history of previous ischaemic stroke. The cohort had a substantial vascular comorbidity burden. Hypertension was documented in 91.5% of patients, followed by dyslipidaemia in 54.7%, type 2 diabetes mellitus in 35.9%, atrial fibrillation in 23.1%,

and coronary artery disease in 22.2%. Heart failure was documented in 19.7%. Motor deficit was the most frequent neurological finding (60.7%), while dysarthria and hearing impairment were each documented in 19.7%. Table I presents additional demographic, clinical, comorbidity, complication, and neurological characteristics.

Table I

Demographic and clinical characteristics of the study population

Characteristic	n (%) or median (Q1 - Q3)
Demographic characteristics	
Age, years	74 (69 - 79)
Age $\geq$ 65 years	98 (83.8)
Female sex	64 (54.7)
Stroke characteristics	
Vascular territory	
↳ Right carotid	32 (27.4)
↳ Left carotid	49 (41.9)
↳ Multiple territories	3 (2.6)
↳ Vertebrobasilar	33 (28.2)
Medical history and documented comorbidities	
Previous ischaemic stroke	38 (32.5)
Previous psychiatric disorder	5 (4.3)
Hypertension	107 (91.5)
Dyslipidaemia	64 (54.7)
Type 2 diabetes mellitus	42 (35.9)
Atrial fibrillation	27 (23.1)
Coronary artery disease	26 (22.2)
Heart failure	23 (19.7)
Chronic kidney disease	15 (12.8)
Chronic respiratory disease	10 (8.6)
Hypothyroidism	16 (13.7)
Chronic liver disease	14 (12.0)
Anxiety disorder	14 (12.0)
Depressive disorder	9 (7.7)
Mixed anxiety-depressive disorder	19 (16.2)
Neurological deficits	
Aphasia, any	19 (16.2)
Dysarthria	23 (19.7)
Hearing impairment	23 (19.7)
Dysphagia	4 (3.4)
Motor deficit	71 (60.7)

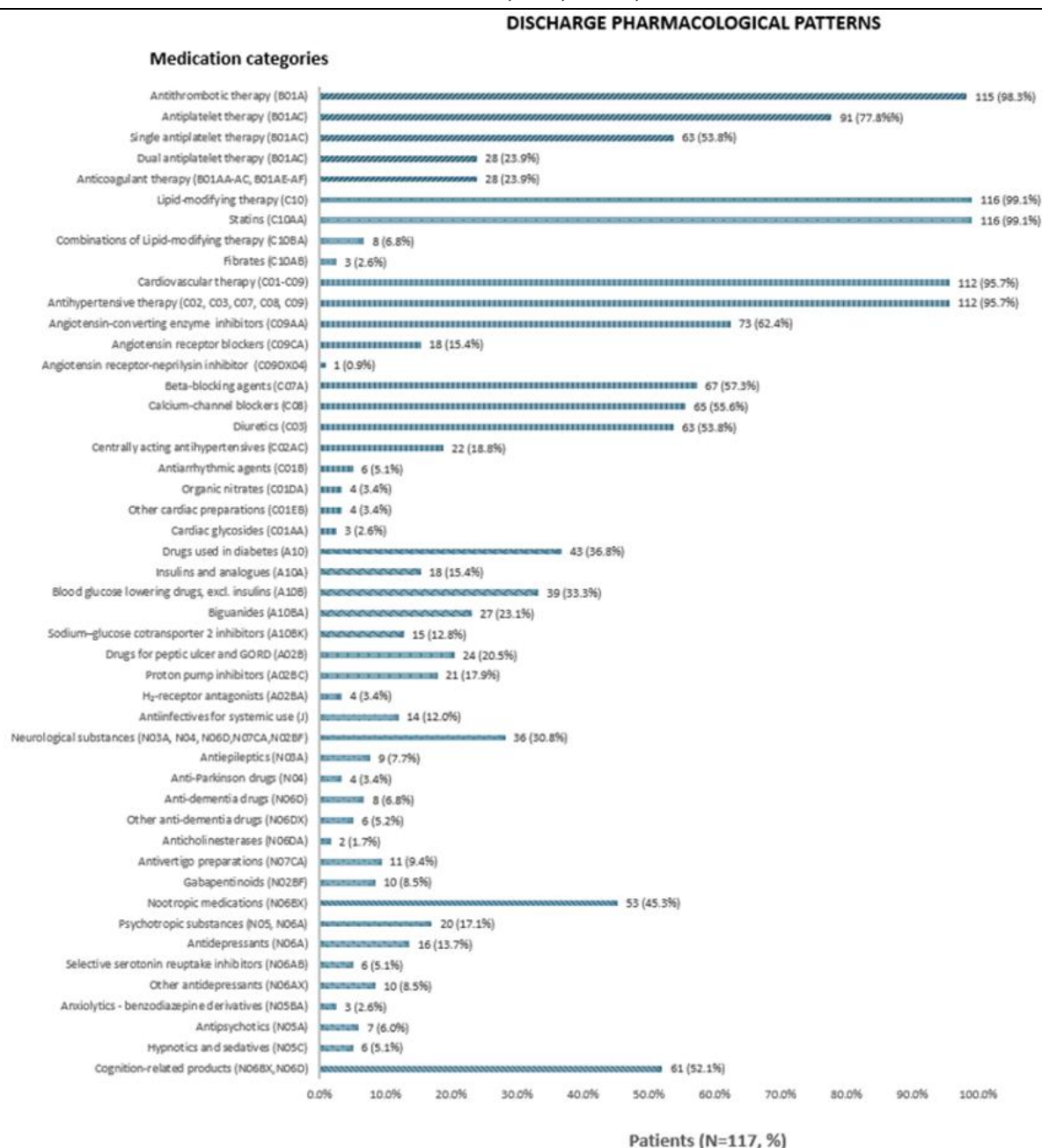
N = 117. Categorical variables are presented as n (%); age is presented as median (IQR)

Previous psychiatric history was recorded separately from anxiety- and depression-related diagnoses, which were mutually exclusive.

Discharge pharmacological patterns

Discharge pharmacotherapy was characterised by extensive use of therapies for vascular secondary prevention and cardiovascular risk management (Figure 1). Lipid-modifying therapy was prescribed to 99.1% of patients, with statin exposure present in all patients receiving lipid-modifying treatment, either as single-agent therapy or within combination products. Antithrombotic therapy was prescribed to 98.3% of patients. Cardiovascular therapy and antihypertensive therapy were prescribed to 95.7% of patients each,

with antihypertensive therapy being the predominant component of the cardiovascular group. Antiplatelet therapy was used in 77.8% of the cohort (91 patients), predominantly as single antiplatelet therapy (53.8%), whereas dual antiplatelet therapy and anticoagulant therapy were prescribed each to 23.9% of patients. Single and dual antiplatelet therapies were mutually exclusive. In addition, four (3.4%) patients received both single antiplatelet therapy and anticoagulation. Angiotensin-converting enzyme inhibitors, beta-blockers, calcium-channel blockers, and diuretics were the most frequently used cardiovascular classes, with each prescribed to more than half of the study population.

**Figure 1.**

Pharmacological treatment patterns at discharge

Horizontal bars represent the proportion of patients receiving each medication category at discharge; values are shown as n (%) WHO ATC codes are provided next to the categories. Categories were not mutually exclusive

Drugs used in diabetes were prescribed to approximately one-third of patients (36.8%). In contrast, drugs for peptic ulcer and gastro-oesophageal reflux disease (GORD) (20.5%) and systemic antiinfectives (12.0%) were less frequently prescribed. The neurological and psychotropic medications were prescribed to 30.8% and 17.1% of patients, respectively. The antivertigo medications and gabapentinoids were the most frequent neurological subclasses, while antidepressants predominated in the psychotropic medications group. Cognition-related medicinal products (substances) were prescribed to 61 patients (52.1%). Among these patients,

57 (93.4%) received one cognition-related medicinal product, and 4 (6.6%) received two. Nootropic medications (N06BX) were recorded in 53 patients (45.3%), whereas anti-dementia drugs (N06D) were prescribed to 8 patients (6.8%). Figure 1 shows the complete distribution of discharge pharmacological treatments and their corresponding WHO ATC classifications.

Medication burden and polypharmacy

Polypharmacy was highly prevalent at discharge. The median number of active substances at discharge was 8 (IQR 6 - 10; range 2 - 14). Of 117 patients, 103 (88.0%) received at least five active substances; 70

(59.8%) met the criteria for polypharmacy (5 - 9 substances), and 33 (28.2%) had hyper-polypharmacy (≥ 10 substances). Only 14 patients (12.0%) received fewer than five active substances.

When medication products, rather than active substances, were counted as a complementary measure, the median number of discharge medications was 7 (IQR 5 - 9). Overall, 19 patients (16.2%) received fewer than five medication products, 77 (65.8%) received 5 - 9, and 21 (18.0%) received ≥ 10 . After excluding cognition-related medicinal products from the product count across the entire cohort, the median was 7 (IQR 5 - 8), with 25 (21.4%), 80 (68.4%), and 12 (10.2%) receiving < 5 , 5 - 9, and ≥ 10 medication products, respectively.

Subgroup analyses

Exploratory subgroup analyses by age are summarised in Table II, Table III and Table IV; Table II shows demographic and clinical characteristics stratified by age to provide descriptive context for the subgroup findings. Table III describes medication-burden and cognition-related prescribing outcomes,

and Table IV describes major discharge pharmacological patterns.

Some demographic and clinical characteristics differed numerically between age groups, but these findings were descriptive and should be interpreted cautiously given the small number of patients aged < 65 years. No statistically significant age-related differences were observed across the major pharmacological domains assessed in Table IV.

Sensitivity analysis

The sensitivity analysis is summarised in Table III. In the sensitivity analysis, cognition-related medicinal products were excluded from the active-substance count. Under this definition, 18 patients (15.4%) received fewer than five medications, 75 (64.1%) had polypharmacy, and 24 (20.5%) had hyper-polypharmacy. The proportion of patients classified as having hyper-polypharmacy decreased from 28.2% in the primary analysis to 20.5% after excluding cognition-related active substances.

After excluding cognition-related active substances, polypharmacy distributions remained similar by age ($p = 0.696$).

Table II

Demographic and clinical characteristics according to age

Age ≥ 65 years:	≥ 65 years (n = 98)	< 65 years (n = 19)
Demographic characteristics		
Female sex, n (%)	53 (54.08)	11 (57.89)
Stroke characteristics (vascular territory), n (%)		
↳ Right carotid	28 (28.57)	4 (21.05)
↳ Left carotid	44 (44.9)	5 (26.32)
↳ Multiple territories	2 (2.04)	1 (5.26)
↳ Vertebrobasilar	24 (24.49)	9 (47.37)
Medical history and documented comorbidities		
Previous ischaemic stroke, n (%)	31 (31.63)	7 (36.84)
Previous psychiatric disorder, n (%)	4 (4.08)	1 (5.26)
Hypertension, n (%)	91 (92.86)	16 (84.21)
Atrial fibrillation, n (%)	27 (27.55)	0 (0)
Coronary artery disease, n (%)	25 (25.51)	1 (5.26)
Heart failure, n (%)	22 (22.45)	1 (5.26)
Dyslipidaemia, n (%)	55 (56.12)	9 (47.37)
Type 2 diabetes mellitus, n (%)	34 (34.69)	8 (42.11)
Chronic kidney disease, n (%)	12 (12.24)	3 (15.79)
Chronic respiratory disease, n (%)	7 (7.14)	3 (15.79)
Hypothyroidism, n (%)	15 (15.31)	1 (5.26)
Chronic liver disease, n (%)	11 (11.22)	3 (15.79)
Anxiety disorder, n (%)	11 (11.22)	3 (15.79)
Depressive disorder, n (%)	6 (6.12)	3 (15.79)
Mixed anxiety-depressive disorder, n (%)	13 (13.27)	6 (31.58)
Neurological deficits		
Dysarthria, n (%)	21 (21.43)	2 (10.53)
Hearing impairment, n (%)	22 (22.45)	1 (5.26)
Dysphagia, n (%)	4 (4.08)	0 (0)
Motor deficit, n (%)	61 (62.24)	10 (52.63)

N = 117. Categorical variables are presented as n (%). The categories were mutually exclusive. Medication burden and the major pharmacological patterns were broadly consistent across age groups, with no statistically significant differences observed in the assessed outcomes. The median number of distinct active substances was 8 in both groups (IQR 6 - 10 vs 5.5 - 9, respectively; $p = 0.515$), and the distribution of polypharmacy categories did not differ significantly ($p = 0.694$). Cognition-related medicinal products were prescribed with similar frequency in the two age groups (53.1% vs 47.4%, $p = 0.803$).

Table III

Key medication-burden and cognition-related prescribing outcomes in subgroup and sensitivity analyses

A. Subgroup analyses				
Outcome	Group 1	Group 2	Difference (95% CI)	P-value
Age	≥ 65 years (n = 98)	< 65 years (n = 19)		
Cognition-related medicinal products/substances (Yes), n (%)	52 (53.1)	9 (47.4)	(0.4695, 3.3603)	0.803
Number of cognition-related medicinal products, median (IQR)	1 (0 - 1)	0 (0 - 1)	—	0.551
Number of discharge active substances, median (IQR)	8 (6 - 10)	8 (5.5 - 9)	—	0.515
Polypharmacy distribution, n (%)*	11 (11.2)/58 (59.2)/29 (29.6)	3 (15.8)/12 (63.2)/4 (21.1)	—	0.694
B. Sensitivity analysis excluding cognition-related medicinal products				
Overall cohort (N = 117)				
Polypharmacy distribution, n (%)*	18 (15.4)/75 (64.1)/24 (20.5)	—	—	—
Age	≥ 65 years (n = 98)	< 65 years (n = 19)		
Number of discharge active substances excluding cognition-related products, median (IQR)	7 (5 - 9)	7 (5.5 - 8.5)	—	0.982
Polypharmacy distribution, n (%)*	14 (14.3)/63 (64.3)/21 (21.4)	4 (21.1)/12 (63.2)/3 (15.8)	—	0.696

Categorical data are presented as n (%) and continuous data as median (IQR). *Polypharmacy distributions are presented in the following order: no polypharmacy (< 5 substances)/polypharmacy (5 – 9 substances)/hyper-polypharmacy (≥ 10 substances). IQR, interquartile range. Cognition-related medicinal products were defined according to the study-specific classification

Table IV

Major discharge pharmacological patterns in exploratory subgroup analyses

Comparison according to age			
Pharmacological domain	≥ 65 years (n = 98), n (%)	< 65 years (n = 19), n (%)	P-value
Antithrombotic therapy (B01A)	96 (98.0)	19 (100.0)	1.000
Statins (C10AA)	97 (99.0)	19 (100.0)	1.000
Cardiovascular therapy (C01 - C09)	95 (96.9)	17 (89.5)	0.185
Drugs used in diabetes (A10)	35 (35.7)	8 (42.1)	0.597
Neurological medications (selected N groups)	30 (30.6)	6 (31.6)	0.934
Psychotropic medications (N05, N06A)	16 (16.3)	4 (21.1)	0.739

Categorical data are presented as n (%). P-values refer to between-group comparisons

Principal findings

This study provides a real-world description of the pharmacological environment at discharge in patients with AIS and documented cognitive impairment. Discharge treatment was dominated by pharmacological classes commonly used for secondary vascular prevention and cardiovascular risk management, with very high exposure to lipid-modifying, antithrombotic, cardiovascular, and antihypertensive therapies. At the same time, overall medication burden was substantial: patients received a median of eight active substances at discharge, 88.0% received at least five substances, 59.8% had polypharmacy, and 28.2% had hyper-polypharmacy. Cognition-related medicinal products were prescribed to 52.1% of the cohort, with most patients having received a single cognition-related product. The sensitivity analysis showed that excluding cognition-related active substances reduced the prevalence of hyper-polypharmacy from 28.2% to 20.5%. In contrast, only a small proportion of patients initially receiving at least five active substances were reclassified below the polypharmacy threshold.

Secondary prevention, multimorbidity and medication burden

The composition of discharge pharmacological treatment reflects the multidomain nature of secondary prevention after ischaemic stroke, in which antithrombotic treatment and management of blood pressure, lipids, diabetes, and other vascular risk factors are central components of care (1, 3). This interpretation is also supported by the substantial vascular comorbidity observed in the cohort, particularly hypertension, dyslipidaemia, type 2 diabetes mellitus, atrial fibrillation, coronary artery disease and heart failure. Numerical definitions of polypharmacy describe medication quantity. However, they do not necessarily indicate inappropriate prescribing, as the patient's overall clinical status should be considered (24). Polypharmacy is common in patients with multimorbidity (26-27). In stroke survivors of older age, multimorbidity is common. It can increase treatment complexity, while also being associated with less favourable functional and rehabilitation outcomes, including mortality, and the use of secondary-prevention therapy (4, 28-29). This is particularly relevant to the

present cohort, in which 83.8% of patients were aged ≥ 65 years. Medication count alone does not fully capture treatment burden, which also includes the healthcare tasks and practical demands of managing multiple conditions and treatments (30).

Moreover, many cardiovascular medication classes may be used for more than one clinical indication, including hypertension, coronary artery disease, and heart failure (31-33). The cardiovascular component of post-stroke pharmacotherapy may therefore reflect both secondary vascular prevention and the treatment of coexisting cardiovascular disease. The present study did not assess the specific indication or appropriateness of individual prescriptions.

Cognitive impairment and other post-stroke deficits may add to the practical challenges of medication self-management after discharge (11, 34). Regimen complexity represents an additional dimension of medication burden that is not captured by medication count alone (35). In older patients undergoing stroke rehabilitation, polypharmacy has been associated with poorer functional outcomes and a lower likelihood of home discharge (36). In a recent study by Beglinger *et al.* of older adults with multimorbidity and hyper-polypharmacy, 53.0% had low or medium medication adherence (37). The substantial medication burden observed in this cohort, together with the coexistence of multiple pharmacological domains, illustrates the multidimensional treatment demands that may confront cognitively impaired patients after discharge.

Cognitive impairment and medication-management implications

Stroke survivors must manage not only the pharmacological management of stroke, but also stroke-related sequelae and the demands of rehabilitation (4, 28-29). In this context, cognitive impairment and other post-stroke disabilities may complicate medication management and increase the need for assistance with treatment administration (7, 34-36). In the present cohort, neurological deficits were common, with motor impairment documented in more than half of the patients.

Cognitive impairment was identified from routine clinical documentation and diagnostic coding during the acute stroke admission, reflecting the real-world context in which discharge pharmacotherapy was prescribed. Accordingly, the study characterises pharmacological patterns in patients recognised as cognitively impaired during acute AIS rather than in a prospectively defined neuropsychological cohort. Cognitive status during the acute phase may be influenced by the stroke itself, delirium, mood and sleep disturbances, hepatic or renal dysfunction, medications, and pre-existing cerebral vulnerability. Subsequent trajectories may include improvement, persistence, or deterioration (7, 8). Acute-phase cognitive

impairment should therefore not necessarily be interpreted as a fixed long-term cognitive phenotype.

The pharmacological context may also matter because some central nervous system (CNS)-active medications can affect cognitive status, alertness, and functional performance in older adults. The AGS Beers Criteria identify several medications with anticholinergic or sedative properties, including certain hypnotics, as potentially inappropriate or requiring caution in older adults with cognitive impairment because of adverse CNS effects (38).

Furthermore, observational studies have associated long-term exposure to anticholinergic medications and benzodiazepines with poorer cognitive performance (39). These effects were not evaluated in the present study and are mentioned only as clinical context. Some relevant medication categories were infrequently represented in the cohort: hypnotics and sedatives were prescribed to 5.1% of patients, while antipsychotics were prescribed to 6.0% (Figure 1). Notably, anti-vertigo preparations were the most frequent neurological subclass (9.4%). Benzodiazepine derivatives were represented within the broader psychotropic categories but were not analysed separately (Figure 1). *Cognition-related prescribing, sensitivity and exploratory analyses*

Cognition-related medicinal products represented a substantial component of discharge pharmacotherapy, being prescribed to 52.1% of patients. These products were analysed as a heterogeneous study-defined grouping, reflecting their use in the documented prescribing context rather than pharmacological equivalence. Evidence supporting pharmacological treatment of post-stroke cognitive impairment remains limited (40). A recent European guideline found limited evidence regarding the clinical benefit of several cognition-directed therapies used in this setting (20). Accordingly, their frequency in our cohort should be interpreted primarily as a description of real-world prescribing practice rather than evidence of efficacy or guideline endorsement. The findings should also be interpreted within the Romanian tertiary-care context, where local diagnostic coding, discharge prescribing practices, and the national medicines nomenclature influenced how pharmacotherapy was documented and classified (22).

Excluding cognition-related medicinal products reduced hyper-polypharmacy from 28.2% to 20.5% and reclassified 9 of 33 patients with hyper-polypharmacy (27.3%) below the ≥ 10 -active-substance threshold. In contrast, only 4 of 103 patients receiving at least five active substances (3.9%) were reclassified below the polypharmacy threshold. Thus, cognition-related medicinal products had a greater influence on hyper-polypharmacy classification than on the overall prevalence of polypharmacy.

The exploratory age-stratified analyses showed similar medication burden, cognition-related prescribing,

and major pharmacological patterns in patients aged ≥ 65 and < 65 years. Although some clinical characteristics differed numerically between groups, these findings were descriptive and should be interpreted cautiously given the small number of younger patients. Substantial medication burden was observed in both age groups.

As prescribing determinants were not assessed, these differences should not be attributed to specific clinical or organisational factors and require confirmation in larger studies.

The substantial medication burden observed at discharge, together with documented cognitive impairment, may have practical implications for medication management during post-stroke care. This may be particularly relevant in older adults, who made up most of the cohort and align with the population addressed by the AGS Beers Criteria (38). In this population, polypharmacy may also increase the potential for adverse drug reactions and drug-drug interactions, adding to the complexity of medication management (41, 42). These findings reinforce the relevance of medication-management support during post-discharge stroke care (11, 34).

Strengths, limitations and future directions

Strengths include real-world assessment of discharge pharmacotherapy, medication standardisation using WHO ATC terminology, and a sensitivity analysis. Limitations include the retrospective, single-centre design (limited generalisability) and modest sample size. In-hospital deaths were excluded by design. Therefore, the findings apply only to patients who survived to hospital discharge. Individual prescriptions were not systematically linked to physician-documented indications; therefore, the study primarily describes prescribing patterns and medication burden rather than indication-specific prescribing. In the absence of a comparison group without cognitive impairment, no inference can be made regarding whether the overall medication burden was specifically attributable to cognitive impairment. Prescribing patterns may also reflect local clinical practice, while medication appropriateness, adherence, adverse effects, and subsequent outcomes were not evaluated. The findings are most applicable to patients managed in similar tertiary-care settings and should be generalised cautiously to other institutions or health-care systems with different diagnostic coding and prescribing practices.

Prospective multicentre studies incorporating standardised cognitive assessment, medication reconciliation, and longitudinal follow-up are needed to determine whether discharge medication burden, regimen complexity, and specific pharmacological exposures are associated with medication management, rehabilitation, cognitive trajectories, and functional recovery after AIS.

Conclusions

Patients with AIS and documented cognitive impairment were discharged with substantial multidrug regimens dominated by vascular and cardiovascular therapies. Cognition-related medicinal products contributed to medication burden but did not fully account for the high prevalence of polypharmacy and hyper-polypharmacy. The findings characterise medication burden and cognition-related prescribing in this population but do not establish CI-specific burden. These findings provide a real-world description of pharmacotherapy in a population in whom cognitive impairment and treatment complexity may make medication management particularly challenging and may inform further research on medication burden and medication management after stroke.

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Availability of data and materials

The data generated in the present study are included in the figures and/or tables of this article.

Ethics approval and consent to participate

The Ethics Committee of “Iuliu Hațieganu” University of Medicine and Pharmacy Cluj-Napoca approved the study protocol (approval no. 165/17 June 2026), and the Ethics Committee of the Cluj County Emergency Clinical Hospital approved it (approval no. 18622/28 May 2026). The study was conducted in accordance with the Declaration of Helsinki and applicable ethical and data-protection requirements. The requirement for informed consent was waived because the study was retrospective.

AI use disclosure

During the preparation of this manuscript, the authors used OpenAI's ChatGPT for editing assistance and language improvement, including improving spelling, grammar, word choice, readability, and clarity. The authors reviewed and revised all outputs from these tools and take full responsibility for the final content of the work.

Conflict of interest

The authors declare no conflict of interest.

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