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Anticholinergic medications in patients admitted with cognitive impairment or falls (AMiCI). The impact of hospital admission on anticholinergic cognitive medication burden. Results of a multicentre observational study

I. Weichert MRCP (UK)[1] | R. Romero-Ortuno PhD[2,3] | J. Tolonen PhD[4] | T. Soe MRCP, MRCP (Acute Medicine)[1] | C. Lebus MRCP, MRCP (Acute Medicine)[2] | S. Choudhury MRCP, MRCP (Acute Medicine)[5] | C. V. Nadarajah MRCP, MRCP (Acute Medicine)[5] | P. Nanayakkara MD, PhD, FRCP[6] | M. Orrù MD[7] | S. Di Somma MD, PhD[7] | on behalf the Global Research on Acute Conditions Team (GREAT)

[1]Department of Acute Medicine, The Ipswich Hospital NHS Trust, Ipswich, UK

[2]Department of Medicine for the Elderly, Cambridge University Hospitals NHS Trust, Addenbrooke's Hospital, Cambridge, UK

[3]Clinical Gerontology Unit, Department of Public Health and Primary Care, University of Cambridge, Cambridge, UK

[4]Department of Medicine and Rehabilitation, Helsinki University Hospitals, Helsinki, Finland

[5]Department of Acute Medicine, East and North Hertfordshire NHS Trust, Lister Hospital, Stevenage, UK

[6]Department of Acute Medicine, VU University Medical Center, Amsterdam, The Netherlands

[7]Department of Medical-Surgical Sciences and Translational Medicine, University La Sapienza, Rome, Italy

Correspondence
I. Weichert, Department of Acute Medicine, The Ipswich Hospital NHS Trust, Ipswich, UK.
Emails: immo.weichert.mail@gmail.com; immo.weichert@ipswichhospital.nhs.uk

Summary

What is known and objective: Drugs with anticholinergic properties increase the risk of falls, delirium, chronic cognitive impairment, and mortality and counteract procholinergic medications used in the treatment of dementia. Medication review and optimisation to reduce anticholinergic burden in patients at risk is recommended by specialist bodies. Little is known how effective this review is in patients who present acutely and how often drugs with anticholinergic properties are used temporarily during an admission. The aim of the study was to describe the changes in the anticholinergic cognitive burden (ACB) in patients admitted to hospital with a diagnosis of delirium, chronic cognitive impairment or falls and to look at the temporary use of anticholinergic medications during hospital stay.

Methods: This is a multi-centre observational study that was conducted in seven different hospitals in the UK, Finland, The Netherlands and Italy.

Results and discussion: 21.1% of patients had their ACB score reduced by a mean of 1.7%, 19.7% had their ACB increased by a mean of 1.6%, 22.8% of DAP naïve patients were discharged on anticholinergic medications. There was no change in the ACB scores in 59.2% of patients. 54.1% of patients on procholinergics were taking anticholinergics. Out of the 98 medications on the ACB scale, only 56 were seen. Medications with a low individual burden were accounting for 64.9% of the total burden. Anticholinergic drugs were used temporarily during the admission in 21.9% of all patients. A higher number of DAPs used temporarily during admission was associated with a higher risk of ACB score increase on discharge (OR = 1.82, 95% CI for OR: 1.36-2.45, $P < .001$).

What is new and conclusion: There was no reduction in anticholinergic cognitive burden during the acute admissions. This was the same for all diagnostic subgroups. The anticholinergic load was predominantly caused by medications with a low individual burden.

More than 1 in 5 patients not taking anticholinergics on admission were discharged on them and similar numbers saw temporary use of these medications during their admission. More than half of patients on cholinesterase-inhibitors were taking anticholinergics at the same time on admission, potentially directly counteracting their effects.

KEYWORDS
anticholinergic cognitive burden, anticholinergics, cholinesterase inhibitors, cognitive impairment, falls, medication review, medicines optimization

1 | WHAT IS KNOWN AND OBJECTIVE

The increasing age of the population is a success of individual and public health that unfortunately goes hand in hand with multimorbidity and polypharmacy. Of specific concern are prescription and over-the-counter medications that have anticholinergic activity. These include a wide variety of drugs including those for hypertension, cardiovascular and pulmonary disease. Over the last 25 years, there has been increasing evidence that cholinergic blockade in the central nervous system has been linked to adverse effects such as confusion, behavioural disturbances, reduced executive and motor functions, altered emotions[1-5] and increased risk of falls, delirium, chronic cognitive impairment and mortality.[6-9] An age-related increase in permeability of the blood-brain barrier is thought to contribute to this problem.[10] The use of multiple drugs with drugs with anticholinergic properties (DAPs) is thought to have an additive effect. The cumulative anticholinergic cognitive burden (ACB) of all therapies predicts more accurately the risk of adverse events.[11] Acetylcholinesterase inhibitors (AChE-I) are used in the treatment of mild-to-moderate Alzheimer's disease.[12] Up to 60% of patients with dementia are reported to receive at least one anticholinergic drug.[13,14] The combination of both pro- and anticholinergics can elicit an antagonistic response and further hasten cognitive decline.[15]

Review and optimization of medication are recommended by specialist representative bodies.[16] The widely used STOPP/START criteria for potentially inappropriate prescribing in older people were expanded in the latest version of 2014 to cover more drugs that have anticholinergic activity.[17] The 2015 revision of the Beer's criteria by the American Geriatric Society recommends avoiding anticholinergics in patients with chronic cognitive impairment and delirium.[18] The Silver Book by the British Geriatric Society defines standards for urgent and emergency care of frail older patients and advocates a medicines review at the time of crisis, with particular regard to sedative, psychotropic, hypotensive or anticholinergic medications.[19] Little is known about how effective the recommended review of DAPs is in patients at risk who present acutely and how often drugs with anticholinergic properties are used temporarily during an admission. We investigated the impact of hospital admission on the anticholinergic burden and the use of relevant medications in medical patients admitted with a diagnosis of delirium, chronic cognitive impairment or falls. As such, our main objective was to investigate the possible change of the ACB from admission to discharge and the temporary use of DAPs. The secondary goal was to identify differences in diagnostic and demographic subgroups including death and readmission.

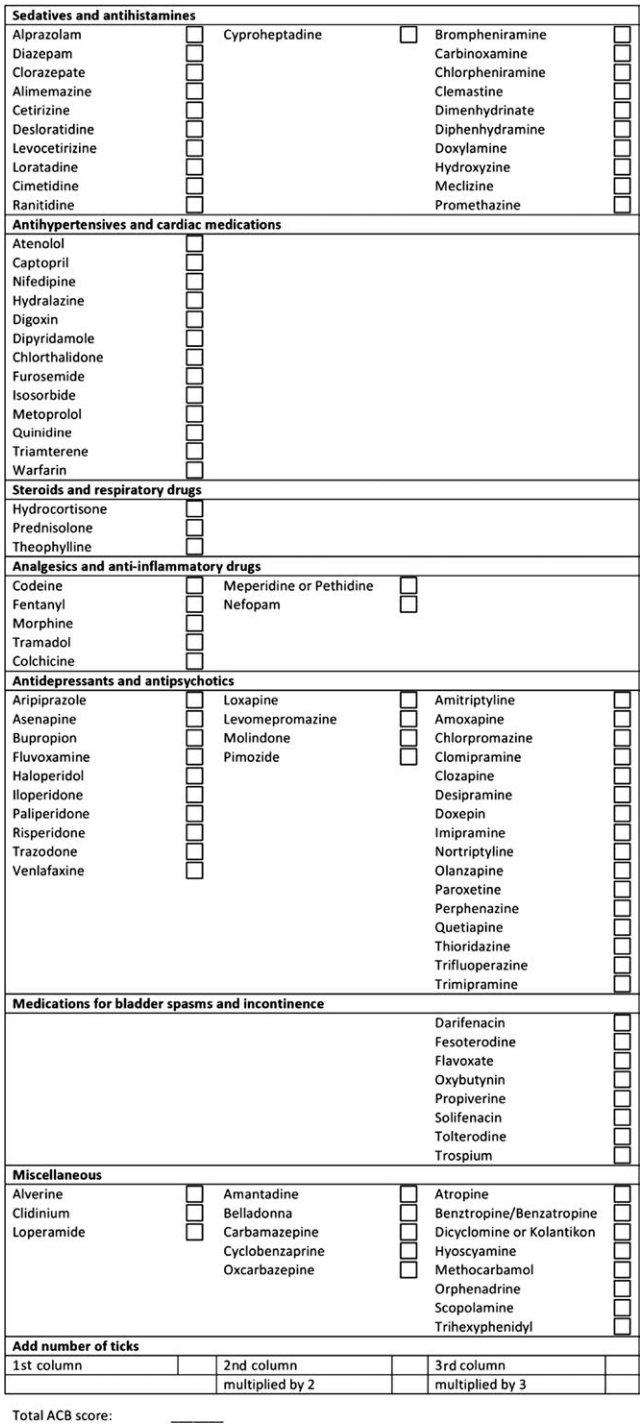
2 | METHODS

This multicentre observational study, which took place between October 2014 and March 2016, was conducted in 7 acute hospitals in the UK, Finland, the Netherlands and Italy as collaboration through the Global Research on Acute Conditions Team (GREAT Network, www.greatnetwork.org). None of the centres involved changed their approach to medication review or optimization in preparation for this study but continued throughout with their usual clinical current practice.

The project was screened in accordance with the recommendations of the UK Healthcare Quality Improvement Partnership and the NHS Health Research Authority and categorized as a service evaluation.[20,21] All centres registered the project with their local audit departments or obtained approval by their relevant institutional review boards.

Each centre selected patients prospectively over a period of at least 1 month. We included unscheduled emergency admissions under the medical teams (ie, acute medicine, general internal medicine and geriatric medicine) with a diagnosis of chronic cognitive impairment or dementia, acute confusional state or delirium, or falls. We recorded demographics, date of admission, diagnoses that led to inclusion in the study, use of AChE-Is, whether a new diagnosis of dementia had been made by discharge, the date of discharge or death, and whether patients were readmitted or died within 30 days after discharge. To record DAPs, we adapted the 2012 revision of the original ACB scale.[22] Medication names were translated to those in use in the participating centres and were grouped by indication and ACB. We added the opioid tramadol due to its central type-3 muscarinic receptor antagonism.[23] The relevant medications, as well as each patient's cumulative burden on admission and discharge and if used during the hospital stay, were recorded (Figure 1).

We compared demographic subgroups, diagnoses, length of stay (day 0 discharge, short stay of up to 3 days, stay up to 1 week and stay



Sedatives and antihistamines					
Alprazolam	☐	Cyproheptadine	☐	Brompheniramine	☐
Diazepam	☐			Carbinoxamine	☐
Clorazepate	☐			Chlorpheniramine	☐
Alimemazine	☐			Clemastine	☐
Cetirizine	☐			Dimenhydrinate	☐
Desloratidine	☐			Diphenhydramine	☐
Levocetirizine	☐			Doxylamine	☐
Loratadine	☐			Hydroxyzine	☐
Cimetidine	☐			Meclizine	☐
Ranitidine	☐			Promethazine	☐
Antihypertensives and cardiac medications					
Atenolol	☐				
Captopril	☐				
Nifedipine	☐				
Hydralazine	☐				
Digoxin	☐				
Dipyridamole	☐				
Chlorthalidone	☐				
Furosemide	☐				
Isosorbide	☐				
Metoprolol	☐				
Quinidine	☐				
Triamterene	☐				
Warfarin	☐				
Steroids and respiratory drugs					
Hydrocortisone	☐				
Prednisolone	☐				
Theophylline	☐				
Analgesics and anti-inflammatory drugs					
Codeine	☐	Meperidine or Pethidine	☐		
Fentanyl	☐	Nefopam	☐		
Morphine	☐				
Tramadol	☐				
Colchicine	☐				
Antidepressants and antipsychotics					
Aripiprazole	☐	Loxapine	☐	Amitriptyline	☐
Asenapine	☐	Levomepromazine	☐	Amoxapine	☐
Bupropion	☐	Molindone	☐	Chlorpromazine	☐
Fluvoxamine	☐	Pimozide	☐	Clomipramine	☐
Haloperidol	☐			Clozapine	☐
Iloperidone	☐			Desipramine	☐
Paliperidone	☐			Doxepin	☐
Risperidone	☐			Imipramine	☐
Trazodone	☐			Nortriptyline	☐
Venlafaxine	☐			Olanzapine	☐
				Paroxetine	☐
				Perphenazine	☐
				Quetiapine	☐
				Thioridazine	☐
				Trifluoperazine	☐
				Trimipramine	☐
Medications for bladder spasms and incontinence					
				Darifenacin	☐
				Fesoterodine	☐
				Flavoxate	☐
				Oxybutynin	☐
				Propiverine	☐
				Solifenacin	☐
				Tolterodine	☐
				Trospium	☐
Miscellaneous					
Alverine	☐	Amantadine	☐	Atropine	☐
Clidinium	☐	Belladonna	☐	Benztropine/Benzatropine	☐
Loperamide	☐	Carbamazepine	☐	Dicyclomine or Kolantikon	☐
		Cyclobenzaprine	☐	Hyoscyamine	☐
		Oxcarbazepine	☐	Methocarbamol	☐
				Orphenadrine	☐
				Scopolamine	☐
				Trihexyphenidyl	☐
Add number of ticks					
1st column		2nd column		3rd column	
		multiplied by 2		multiplied by 3	

Total ACB score: _____

FIGURE 1 Adapted Anticholinergic Burden Scale

longer than 1 week), outcomes including readmission and discharge to their own home. The Shapiro-Wilk test was used to test for normality, the Wilcoxon signed-rank test to compare the anticholinergic burden scores on admission and discharge, the 2 sample *t* test, Yates and Pearson's chi-square test to analyse subgroups. Multivariate binary logistic regression was conducted to identify possible baseline clinical, demographic and geographical confounders, including patients on and those not on DAPs, predicting an increase vs. decrease in ACB at discharge, as well as readmission and mortality. The point of statistical significance was set at $P < .05$. Statistical analysis was performed with RStudio version 1.0.143, apart from the multivariate binary logistic regression models, where IBM SPSS version 22.0 was used.

TABLE 1 Patient characteristics

Number of patients	549
Female (%)	58.3
Male (%)	41.7
Mean age (years)	79.6
Patients aged 65 years or older	89.8%
Admission diagnosis:	
Dementia (%)	27.0
Acute delirium (%)	34.8
Falls (%)	60.3
Dementia diagnosed during admission (%)	4.9
Patients on anticholinergics (%)	60.8
Patients on cholinesterase inhibitors (%)	6.7
Mean length of stay (days)	9.3
30-day readmission rate as % of all patients	15.7
As % of all patients that were discharged/survived	16.9
Mortality during index admission in %	7.7
Mortality within 30 days post-discharge in %	4.0

The data sets were complete for all but 5 patients (0.9%) where follow-up information was unavailable.

3 | RESULTS AND DISCUSSION

The baseline characteristics of the 549 patients included are summarized in Table 1. 60.8% of the patients were taking DAPs on admission. Mean ACB score was 2.1 (range 1-10, SD 1.5). 19.1% of all patients had an ACB of 3 or more (mean = 4, range 3-10, SD 1.3). There was no difference between ACB scores on admission compared to discharge or death ($P = .569$). There was no change in ACB scores in 59.2% of patients. 21.1% had their ACB score reduced by a mean of 1.7 (range 1-6, SD 1.1). 19.7% of patients had their ACB increased by a mean of 1.6 (range 1-5, SD 1.0). 22.8% of DAP-naïve patients were discharged on DAPs. No predictors of a decrease in the ACB scores were identified (Table 2a). Patients from the UK or Finland were less likely to have their ACB score increased. A higher number of DAPs used temporarily during admission was associated with a higher risk of ACB score increase on discharge (OR = 1.82, 95% CI for OR: 1.36-2.45, $P < .001$; Table 2b).

Of 98 medications on the ACB scale, 56 were observed in our patients. Figure 2 shows each drug on admission and discharge. The lighter shaded bars show the percentage of patients who had each drug discontinued or newly commenced by discharge. In Figure 3, the same medications are weighted by their anticholinergic burden to represent the percentage of each medication on the cumulative burden. Seven medications with the highest individual ACB of 3 were recorded on admission. These represent 13.8% of all recorded

TABLE 2 Multivariate binary logistic regression analysis. (a) Increase in ACB score. (b) Decrease in ACB score. (c) Inpatient mortality. (d) Readmission

	Odds ratio	95% CI for Odds ratio		*P* value
		Lower	Upper	
(a) Increase in ACB score				
Age	1.01	0.99	1.04	.224
Sex	0.94	0.55	1.59	.810
UK centre	0.05	0.01	0.36	.003
Finnish centre	0.04	0.01	0.27	.001
Dutch centre	0.14	0.02	1.11	.063
Italian centre	0.47	0.06	3.86	.481
From care home	0.97	0.47	1.98	.924
Chronic cognitive impairment or dementia	0.63	0.28	1.45	.281
Acute delirium or confusional state	0.98	0.44	2.20	.962
Falls	1.08	0.47	2.52	.852
Temporary used DAPs	1.82	1.36	2.45	<.001
(b) Decrease in ACB score				
Age	0.99	0.97	1.01	.372
Sex	1.01	0.62	1.63	.977
UK centre	1.30	0.27	6.37	.746
Finnish centre	0.35	0.07	1.71	.196
Dutch centre	0.78	0.12	5.02	.796
Italian centre	0.66	0.10	4.22	.663
From care home	1.26	0.67	2.38	.477
Chronic cognitive impairment or dementia	0.82	0.39	1.69	.583
Acute delirium or confusional state	0.61	0.29	1.25	.175
Falls	0.52	0.19	1.00	.053
Temporary used DAPs	1.13	0.83	1.52	.437
(c) Inpatient mortality				
Age	1.06	1.02	1.12	.010
Sex	1.15	0.52	2.53	.736
UK centre	0.57	0.19	1.74	.322
Finnish centre	0.04	0.01	0.26	.001
Dutch centre	0.45	0.07	2.74	.387
Italian centre	0.89	0.12	3.34	.435
From care home	2.54	1.10	5.86	.029
Chronic cognitive impairment or dementia	0.66	0.25	1.76	.408
Acute delirium or confusional state	1.48	0.56	3.93	.430
Falls	0.45	0.16	1.28	.135
Temporary used DAPs	2.20	1.45	3.35	<.001
(d) Readmission				
Age	1.01	0.99	1.03	.316
Sex	0.72	0.43	1.22	.221
UK centre	0.22	0.04	1.39	.107
Finnish centre	0.10	0.02	0.62	.013
Dutch centre	0.20	0.03	1.55	.122
Italian centre	0.45	0.05	3.79	.460
From care home	1.21	0.59	2.46	.599
Chronic cognitive impairment or dementia	0.44	0.18	1.05	.063
Acute delirium or confusional state	0.67	0.29	1.55	.352
Falls	0.64	0.27	1.51	.306
Temporary used DAPs	1.30	0.96	1.78	.095

CI, confidence interval.

drugs used or 31.9% of the anticholinergic burden. 6.0% of all patients were taking at least one of them. The anticholinergic load in our patients was predominantly caused by medications with a low individual burden which were accounting for 64.9% of the total burden (Table 3).

DAPs were used temporarily during the admission in 21.9% of all patients. Their mean ACB score was low at 0.4 (range 0-6, SD 0.9). We found 26 different medications, most frequently morphine, codeine, haloperidol, diazepam and furosemide (Table 4).

Tramadol, which we had added in our adaption of the ACB scale, was only seen in 2.7% of patients on admission and was used temporarily in 2.9%.

The results of our subgroup analysis are shown in Tables 5a-d.

Short stay patients (stay for a maximum of 3 days) were the only group that saw their ACB reduced ($P = .018$, Table 5d). This group had fewer patients on DAPs on discharge (48.4% vs 60.5%, $P = .022$), saw equal numbers of patients who had their anticholinergics reduced but fewer patients who had theirs increased (8.9% vs 22.8%, $P = .001$) compared to the patients who were not short stay.

Patients who could not return home but were discharged to sheltered accommodation, residential or nursing home, were older than the rest of the patients (82.0 vs 76.5 years, $P < .001$) but did not differ in ACB scores. They were the only subgroup which saw a significant increase in ACB by discharge ($P = .016$, Table 5d). More than double of these patients had their ACB increased (15.4 vs. 32.7%, $P < .001$), and they also saw a much higher temporary use of DAPs (in 34.6% vs 16.4% of patients, $P < .001$) with a higher burden of anticholinergics used temporarily (mean 0.7, SD 1.2 vs mean 0.2, SD 0.6, $P < .001$) compared to those who went back home.

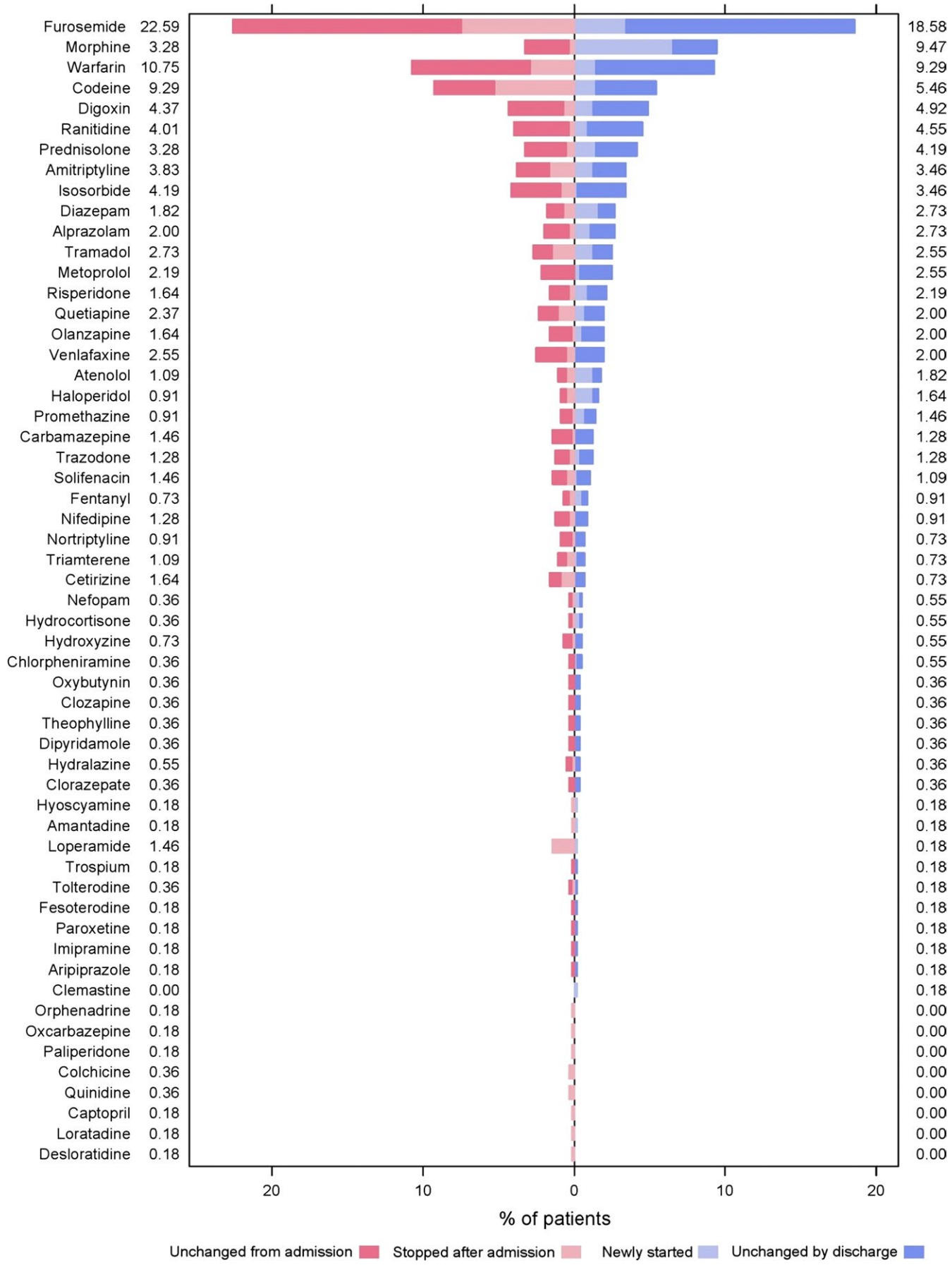


FIGURE 2 Medications with anticholinergic properties in all patients on admission and discharge

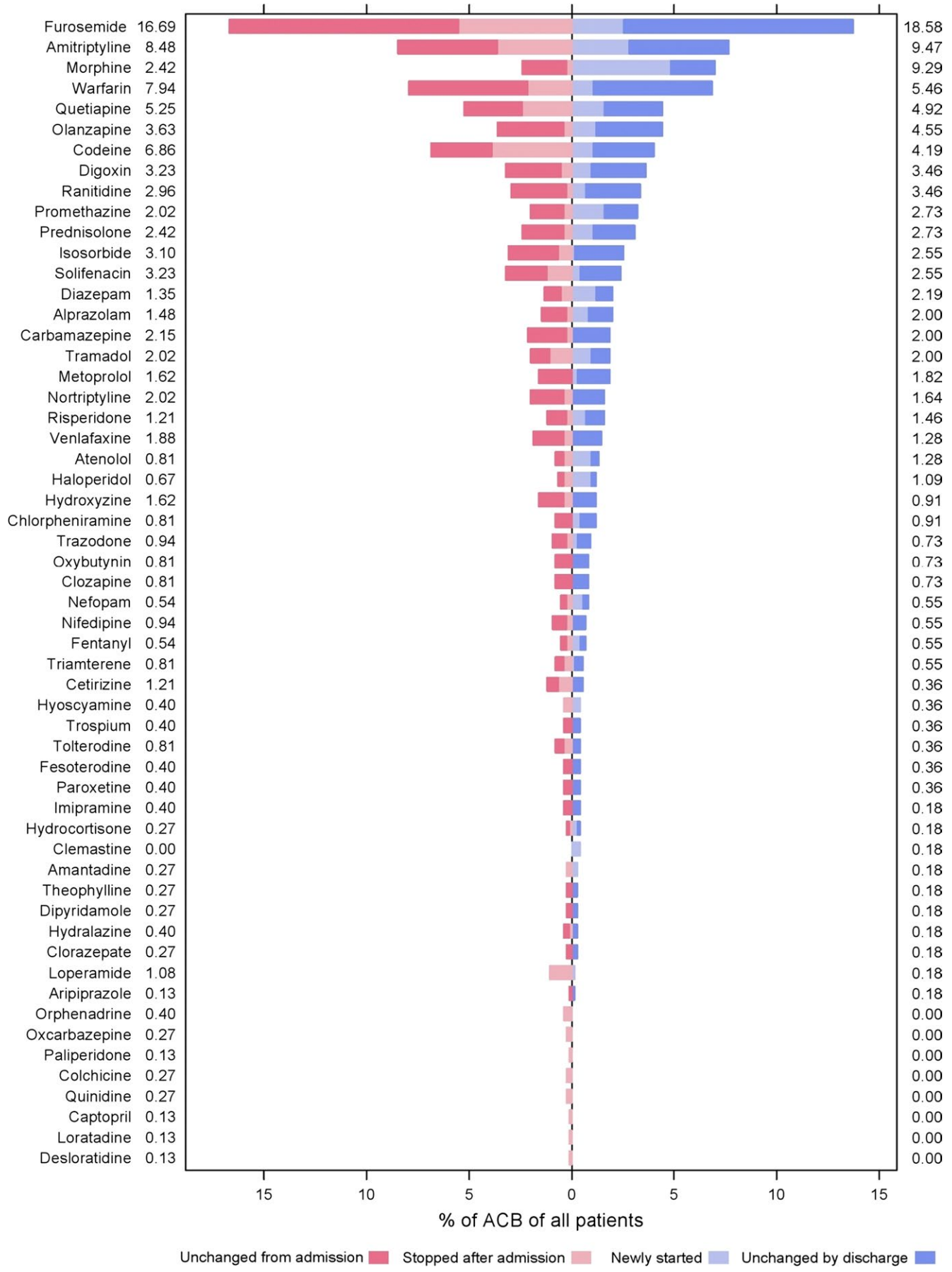


FIGURE 3 Medications with anticholinergic properties in all patients on admission and discharge, weighted by their individual anticholinergic burden

TABLE 3 Proportion of anticholinergic medications used in all patients on admission

	ACB = 1	ACB = 2	ACB = 3
% of DAPs	84.1	2.1	13.8
% of total ACB	64.9	3.2	31.9

TABLE 4 Temporarily used medications with anticholinergic properties

Medication	%
Morphine	28.3
Codeine	19.2
Haloperidol	15.0
Diazepam	14.2
Furosemide	14.2
Tramadol	13.3
Alprazolam	10.8
Warfarin	9.2
Hydrocortisone	6.7
Promethazine	4.2
Isosorbide	4.2
Risperidone	3.3
Digoxin	2.5
Metoprolol	2.5
Triamterene	2.5
Ranitidine	1.7
Fentanyl	1.7
Olanzapine	1.7
Carbamazepine	1.7
Chlorpheniramine	0.8
Atenolol	0.8
Prednisolone	0.8
Clozapine	0.8
Nortriptyline	0.8
Loperamide	0.8
Oxcarbazepine	0.8

Men in our study were younger than women (mean 77.7 vs. 81.0 years, $P = .003$) and were more likely to be prescribed temporary anticholinergic drugs (26.6% vs. 18.1%, $P = .022$, Table 5a) with a higher burden of anticholinergics used temporarily (mean 0.5, SD 1.1 vs mean 0.3, SD 0.7 $P = .004$).

Patients who died during index admission as well as those who were readmitted or died within the 30-day follow-up period did not differ from the rest of the patients in ACB on admission or discharge/death (Table 5d). Those who died had a smaller proportion of patients on DAPs at death. Our data do not allow us to differentiate between expected and unexpected deaths, though it is likely that this reduction in number of patients may be due to the deliberate stopping of medications in those who were not able to take them anymore or who had been commenced on an end of life care pathway.

Prescribing behaviour in all diagnostic subgroups of dementia, delirium or falls, as well as in those with newly diagnosed dementia, was similar with no statistically significant change in ACB scores or number of patients on anticholinergic drugs, as well as with regard to the temporary use of drugs with anticholinergic properties (Table 5b). Figure 4 shows the distributions of anticholinergic burden in each of the diagnostic groups on admission and discharge.

AChE-I (Table 5b) was found on admission in 18.2% of patients with a diagnosis of chronic cognitive impairment (or in 6.7% of all patients). Of these patients on procholinergics, 54.1% were also taking DAPs. This subgroup did not differ from the rest with regard to the number of patients on DAPs, ACB scores or the number of naïve patients newly started on DAPs (Table 5c). Table 6 lists DAPs found on admission in patients on AChE-Is. Temporary DAPs were prescribed less in this group compared to patients not on procholinergics on admission (13.5% vs 22.5% of patients, P, .001). This combination of antagonistic drugs makes little sense but is unfortunately frequently encountered.[14,24] Some of the side effects of dementia drugs, such as urinary frequency, incontinence, diarrhoea or insomnia, may be misinterpreted as new comorbidities or manifestations of frailty in patients with cognitive impairment.[25] The resulting prescribing of anticholinergics will offset their efficiency and may hasten cognitive decline.

The use of drugs with the highest anticholinergic burden was low amongst our patients, and the anticholinergic load was caused predominantly by drugs with lesser activity. Adverse drug events are the result of the anticholinergic load of multiple medications rather than of a single drug.[26] Combined anticholinergic use increases hospitalizations and mortality in older people[27] and hastens cognitive decline. For one point in the ACB, a decline in the Mini-mental State Examination[28] (MMSE) score of 0.33 over 2 years has been suggested.[7] Furthermore, an increase in the cumulative ACB by one has been linked with a 26% increase in mortality.[29]

More than one-third of medications included in the ACB scale were not in use in our patients. This reflects the availability of these medications within the countries that took part in our study. In a globalized world with access to non-formulary drugs when travelling abroad or by purchasing them online via regulated or rogue pharmacies, we do not suggest the use of a shortened ACB scale.

Temporary medications were used in more than 1 in 5 patients. This was the same in all diagnostic subgroups including patients with an acute delirium, potentially worsening their confusion. It may be difficult to fully avoid these but non-pharmacological approaches to prevent or treat delirium including addressing the environment in which patients are cared for may reduce their need.[30]

Our study is not without limitations. Our aim was to analyse the impact of an acute admission on the anticholinergic burden. We did not record comorbidities and did not identify terminally ill patients or those with end-stage dementia. Overall, rates for readmission and mortality were nevertheless similar to those in patients described in large cohort studies looking at outcomes of elderly patients admitted.[31] All participating centres were acute hospitals

TABLE 5 (a) Gender, (b) diagnoses, (c) patients on cholinesterase inhibitors (AChE-I) and (d) other subgroups

	All	Female	Male	
(a)				
% of all patients	100.0	58.3	41.7	
Gender (%)				
Female	58.3	100.0	0.0	$P < .001$
Male	41.7	0.0	100.0	
Age				
Mean	79.6	81.0	77.7	$P = .003$
SD	13.1	13.5	12.3	
Patients on AChE-I on admission (%)	6.7	5.3	8.3	$P = .223$
Patients on DAPs on admission (%)	60.8	58.1	64.6	$P = .147$
ACB Score on admission				
Range	0-10	0-8	0-10	$P = .558$
Mean	1.3	1.3	1.4	
SD	1.6	1.6	1.6	
Patients on DAPs on discharge (%)	57.7	55.6	60.3	$P = .319$
ACB score on discharge				
Range	0-10	0-8	0-10	$P = .603$
Mean	1.3	1.3	1.3	
SD	1.6	1.6	1.6	
Patients on temporary DAPs (%)	21.9	18.1	26.6	$P = .022$
ACB score temp.DAPs				
Range	0-6	0-3	0-6	
Mean	0.4	0.3	0.5	
SD	0.9	0.7	1.1	$P = .004$
Patients who had ACB reduced (%)	21.1	21.3	21.0	$P = 1.000$
Patients who had ACB increased (%)	19.7	19.4	19.7	$P = 1.000$
Patients with no change in ACB (%)	59.2	59.4	59.4	$P = 1.000$
DAP naïve started on DAPs (%)	22.8	20.9	24.7	$P = 1.000$
ACB on admission vs discharge $P =$	0.569	0.760	0.512	

	All	Dementia		Delirium		Falls		New dementia	
(b)									
% off all patients	100.0	27.0		34.8		60.3		4.9	
Gender (%)									
Female	58.3	60.8	$P = .563$	56.5	$P = .563$	60.1	$P = .380$	59.3	$P = 1.000$
Male	41.7	39.2		43.5		39.9		40.7	
Age									
Mean	79.6	83.7	$P < .001$	79.3	$P = .606$	79.5	$P = .819$	88.2	$P < .001$
SD	13.1	7.1		12.1		14.0		5.2	
Patients on AChE-I on admission (%)	6.7	17.6	$P < .001$	5.2	$P = .396$	5.7	$P = .329$	3.7	$P = 1.000$
Patients on DAPs on admission: (%)	60.8	66.9	$P = .096$	64.4	$P = .274$	57.1	$P = .026$	63.0	$P = .826$

(Continues)

TABLE 5 (Continued)

	All	Dementia		Delirium		Falls		New dementia	
ACB Score on admission									
Range	0-10	0-7	*P* = .144	0-7	*P* = .318	0-10	*P* = .134	0-6	*P* = .598
Mean	1.3	1.5		1.5		1.3		1.5	
SD	1.6	1.7		1.6		1.6		1.8	
Patients on DAPs on discharge (%)	57.7	58.1	*P* = .993	59.7	*P* = .603	56.8	*P* = .643	59.3	*P* = 1.000
ACB score on discharge									
Range	0-10	0-7	*P* = .452	0-7	*P* = .277	0-10	*P* = .346	0-8	*P* = .959
Mean	1.3	1.4		1.4		1.3		1.3	
SD	1.6	1.8		1.7		1.6		1.8	
Patients on temporary DAPs (%)	21.9	17.6		23.6		20.8		11.1	
ACB score temp.DAPs									
Range	0-6	0-4	*P* = .072	0-6	*P* = .186	0-5	*P* = .137	0-5	*P* = .433
Mean	0.4	0.3		0.4		0.3		0.3	
SD	0.9	0.7		1.0		0.7		1.0	
Patients who had ACB reduced (%)	21.1	27.0	*P* = .053	23.6	*P* = .406	17.5	*P* = .015	25.9	*P* = .506
Patients who had ACB increased (%)	19.7	18.9	*P* = .882	23.6	*P* = .118	17.8	*P* = .218	18.5	*P* = 1.000
Patients with no change in ACB (%)	59.2	54.1	*P* = .164	52.9	*P* = .041	64.7	*P* = .002	55.6	*P* = .684
DAP naïve started on DAPs (%)	22.8	28.6	*P* = .922	26.5	*P* = .887	20.4	*P* = 1.000	20.0	*P* = 1.000
ACB on admission vs discharge *P*=	0.569	0.320		0.760		0.995		0.661	

	All	AChE-I on admission	
(c)			
% of all patients	100.0	6.7	
Gender (%)			
Female	58.3	48.6	*P* = .290
Male	41.7	51.4	
Age			
Mean	79.6	83.4	*P* = .001
SD	13.1	6.0	
Patients on AChE-I on admission (%)	6.7	100.0	
Patients on DAPs on admission: (%)	60.8	54.1	*P* = .483
ACB Score on admission			
Range	0-10	0-6	*P* = .933
Mean	1.3	1.3	
SD	1.6	1.6	
Patients on DAPs on discharge (%)	57.7	54.1	*P* = .766
ACB score on discharge			
Range	0-10	0-6	*P* = .809
Mean	1.3	1.2	
SD	1.6	1.6	

(Continues)

TABLE 5 (Continued)

	All	AChE-I on admission	
Patients on temporary DAPs (%)	21.9	13.5	
ACB score temp.DAPs			
Range	0-6	0-1	$P < .001$
Mean	0.4	0.1	
SD	0.9	0.3	
Patients who had ACB reduced (%)	21.1	13.5	$P = .334$
Patients who had ACB increased (%)	19.7	13.5	$P = .446$
Patients with no change in ACB (%)	59.2	73.0	$P = .111$
DAP naïve started on DAPs (%)	22.8	23.5	$P = .906$
ACB on admission vs discharge $P=$	0.569	0.755	

	All	Died during admission		Short stay (3 d max)		Unable to return home		30 d readmission	
(d)									
% of all patients	100.0	7.7		22.6		18.9		15.7	
Gender (%)									
Female	58.3	57.1		59.7		63.5		53.5	
Male	41.7	42.9	$P = .965$	40.3	$P = .800$	36.5	$P = .228$	46.5	$P = .291$
Age									
Mean	79.6	84.4		78.2		82.0		79.7	
SD	13.1	9.0	$P = .001$	13.4	$P = .194$	9.0	$P < .001$	11.9	$P = .713$
Patients on AChE-I on admission (%)	6.7	2.4	$P = .394$	7.3	$P = .954$	2.9	$P = .230$	7.0	$P = 1.000$
Patients on DAPs on admission: (%)	60.8	73.8	$P = .104$	57.3	$P = .410$	61.5	$P = .532$	68.6	$P = .079$
ACB Score on admission									
Range	0-10	0-5		0-10		0-6		0-7	
Mean	1.3	1.6		1.3		1.3		1.5	
SD	1.6	1.5	$P = .309$	1.8	$P = .728$	1.4	$P = .777$	1.5	$P = .188$
Patients on DAPs on discharge* (%)	57.7	59.5	$P = .916$	48.4	$P = .022$	66.3	$P = .029$	62.8	$P = .339$
ACB score on discharge*									
Range	0-10	0-7		0-10		0-8		0-8	
Mean	1.3	1.3		1.1		1.6		1.5	
SD	1.6	1.6	$P = .898$	1.7	$P = .074$	1.8	$P = .025$	1.9	$P = .166$
Patients on temporary DAPs (%)	21.9	38.1	$P = .013$	18.5	$P = .373$	34.6	$P < .001$	27.9	$P = .059$
ACB score temp.DAPs									
Range	0-6	0-5		0-3		0-6		0-6	
Mean	0.4	0.8		0.3		0.7		0.4	
SD	0.9	1.4	$P = .030$	0.6	$P = .056$	1.2	$P < .001$	0.9	$P = .220$
Patients who had ACB reduced (%)	21.1	35.7	$P = .027$	21.0	$P = 1.000$	13.5	$P = .172$	20.9	$P = .872$

(Continues)

TABLE 5 (Continued)

	All	Died during admission		Short stay (3 d max)		Unable to return home		30 d readmission	
Patients who had ACB increased (%)	19.7	23.8	*P* = .594	8.9	*P* = .001	32.7	*P* < .001	18.6	*P* = 1.000
Patients with no change in ACB (%)	59.2	40.5	*P* = .015	70.2	*P* = .007	53.8	*P* = .073	60.5	*P* = .982
DAP naïve started on DAPs (%)	22.8	27.3	*P* = .922	15.1	*P* = .358	32.5	*P* = .100	18.5	*P* = .360
ACB on admission vs discharge *P* =	.569	.382		.018		.016		.944	

*or at death if the patient died during the index admission

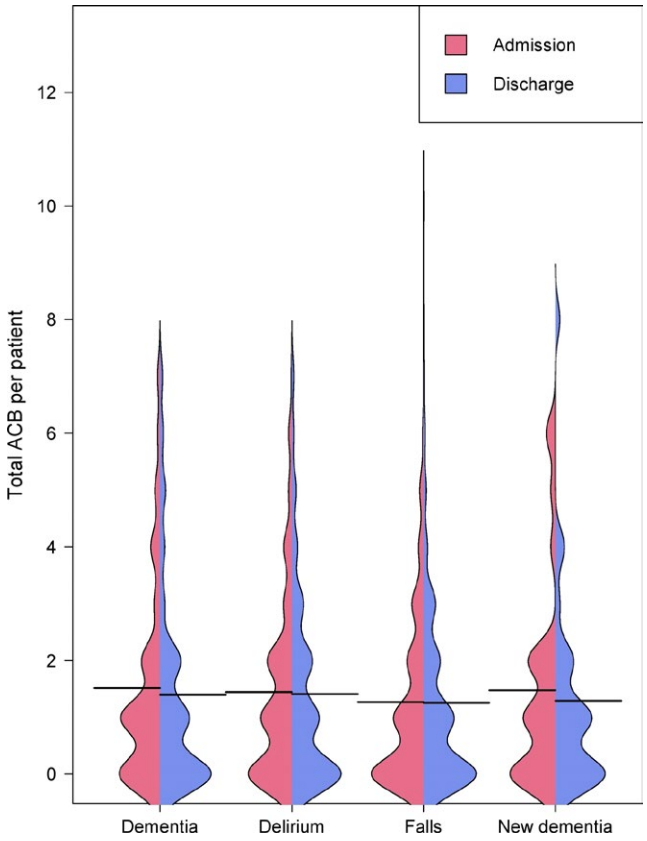


FIGURE 4 Distribution of anticholinergic burden on admission and discharge by diagnosis

TABLE 6 Medications with anticholinergic properties used in patients on procholinergic drugs on admission

Medication	%
Furosemide	16.1
Alprazolam	9.7
Quetiapine	9.7
Isosorbide	6.5
Risperidone	6.5
Trazodone	6.5
Olanzapine	6.5
Ranitidine	3.2
Quinidine	3.2
Warfarin	3.2
Codeine	3.2
Fentanyl	3.2
Morphine	3.2
Aripiprazole	3.2
Venlafaxine	3.2
Amitriptyline	3.2
Clozapine	3.2
Nortriptyline	3.2
Oxybutynin	3.2

either at regional or at teaching hospital level. We did not look into potential differences of the organization of medication management in these facilities. The clinicians involved in the project were also—at least in part—the same clinicians looking after the patients included in our study. These factors may have potentially also accounted for the regional differences highlighted by the regression analysis, that is that for patients recruited in UK or Finnish centres, the probability for an increase in ACB score was lower. Studies comparing the organization of medicines review and optimization in different healthcare systems will be necessary to investigate this in future.

Our results mirror community-based studies that have shown that there is considerable scope for improvement of prescribing practices in older people.[14] Theoretical models have shown that a reduction in anticholinergic burden can be achieved in 59% of patients that score at least one point on the ACB scale and that a reduction from a score of 3 or above to 2 is possible in 85% of the cases.[32] Various approaches to tackle anticholinergic burden have been suggested. For many indications of DAPs, there exist alternatives that allow reducing the anticholinergic load. This can include drugs with lesser or no anticholinergic activity or non-pharmacological approaches.[33] The provision of guidelines and education alone do not seem to be sufficient to ensure best medicines review and optimization in older people. Random control trials have shown an improvement in the quality of prescribing and deprescribing via the use of multidisciplinary teams, geriatric case conferences, medication review by pharmacists and the use of information technology to support medication decisions.[34]

4 | WHAT IS NEW AND CONCLUSION

To our knowledge, this is the first multicentre study to investigate the effect of an acute admission on the ACB. There was no reduction in cumulative scores in our patients who presented as unscheduled emergency admissions with a history of falls, acute delirium or dementia. Similar numbers of patients had their ACB reduced or increased. The same medications, whilst stopped in some patients, were started in others. More than one in 5 patients who were not taking anticholinergics when admitted were prescribed them by discharge. This prescribing pattern was the same for all diagnostic subgroups. Short-stay patients had their ACB burden reduced by discharge. In contrast, patients who were not able to be discharged back to their home were the only subgroup identified which saw a significant increase in ACB from admission to discharge. Despite more than 25 years of evidence and national as well as international recommendations, much more needs to be done to improve medication management in these patients. "Imperative drugging – the ordering of medicine in any and every malady is no longer regarded as the chief function of the doctor" but "one of the first duties of the physician is to educate the masses not to take medicines."[35,36] These quotes by Sir William Osler are even more valid today, nearly a century after his death. To substantiate them will require a joint effort from both primary and secondary care, through more education, more focused involvement from pharmacists and multidisciplinary teams, both in the community and in hospitals, and also by raising awareness in patients, their caregivers and support groups alike.

5 | ROLE OF THE FUNDING SOURCE AND CONFLICT OF INTERESTS

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ORCID

I. Weichert http://orcid.org/0000-0002-6071-8650

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