



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

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WHAT IS KNOWN

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 emotions¹⁻⁵ 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 optimisation 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

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2 crisis, with particular regard to sedative, psychotropic, hypotensive or anticholinergic
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4 medications.¹⁹
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9 10 OBJECTIVE

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15 Little is known about how effective the recommended review of DAPs is in patients at risk
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17 who present acutely and how often drugs with anticholinergic properties are used temporarily
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19 during an admission. We investigated the impact of hospital admission on the anticholinergic
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21 burden and the use of relevant medications in medical patients admitted with a diagnosis of
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23 delirium, chronic cognitive impairment, or falls. As such, our main objective was to
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25 investigate the possible change of the ACB from admission to discharge and the temporary
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27 use of DAPs. The secondary goal was to identify differences in diagnostic and demographic
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29 subgroups including death and readmission.
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56 The project was screened in accordance with the recommendations of the UK Healthcare
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58 Quality Improvement Partnership and the NHS Health Research Authority and categorised as
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1 a service evaluation.^{20,21} All centres registered the project with their local audit departments
2 or obtained approval by their relevant institutional review boards.
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6 Each centre selected patients prospectively over a period of at least one month. We included
7 unscheduled emergency admissions under the medical teams (i.e. acute medicine, general
8 internal medicine, and geriatric medicine) with a diagnosis of chronic cognitive impairment
9 or dementia, acute confusional state or delirium, or falls. We recorded demographics, date of
10 admission, diagnoses that led to inclusion in the study, use of AChE-Is, whether a new
11 diagnosis of dementia had been made by discharge, the date of discharge or death, and if
12 patients were readmitted or died within 30 days after discharge. To record DAPs we adapted
13 the 2012 revision of the original ACB scale.²² Medication names were translated to those in
14 use in the participating centres and were grouped by indication and ACB. We added the
15 opioid Tramadol due to its central type-3 muscarinic receptor antagonism.²³ The relevant
16 medications, as well as each patient's cumulative burden on admission and discharge and if
17 used during the hospital stay, were recorded (Figure 1).
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34 We compared demographic subgroups, diagnoses, length of stay (day 0 discharge, short stay
35 of up to 3 days, stay up to 1 week and stay longer than one week), outcomes including
36 readmission and discharge to their own home. The Shapiro-Wilk test was used to test for
37 normality, the Wilcoxon signed-rank test to compare the anticholinergic burden scores on
38 admission and discharge, the two sample t-test, Yates and Pearson's chi-square test to analyse
39 subgroups. Multivariate binary logistic regression was conducted to identify possible baseline
40 clinical, demographic and geographical confounders, including patients on and those not on
41 DAPs, predicting an increase vs. decrease in ACB at discharge, as well as readmission and
42 mortality. The point of statistical significance was set at $p < 0.05$. Statistical analysis was
43 performed with RStudio version 1.0.143, apart from the multivariate binary logistic
44 regression models, where IBM SPSS version 22.0 was used.
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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 ($p=0.569$).

There was no change in ACB scores in 59.2% of patients. 21.1% of 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, $p<0.001$ -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. 17 medications with the highest individual ACB of 3 were recorded on admission. These represent 13.8% of all recorded 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.

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4 Tramadol, which we had added in our adaption of the ACB scale, was only seen in 2.7% of
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6 patients on admission and was used temporarily in 2.9%.
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11 The results of our subgroup analysis are shown in tables 5 a – d.
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16 Shot stay patients (stay for a maximum of three days) were the only group that saw their
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18 ACB reduced ($p= 0.018$, table 5d). This group had fewer patients on DAPs on discharge
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20 (48.4% vs 60.5%, $p= 0.022$), saw equal numbers of patients who had their anticholinergics
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22 reduced but fewer patients who had theirs increased (8.9% vs 22.8%, $p= 0.001$) compared to
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24 the patients who were not short stay.
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27 Patients who could not return home but were discharged to sheltered accommodation,
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29 residential or nursing home, were older than the rest of the patients (82.0 vs 76.5 years, $p<$
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31 0.001) but did not differ in ACB scores. They were the only subgroup which saw a significant
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33 increase in ACB by discharge ($p = 0.016$ – table 5d). More than double of these patients had
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35 their ACB increased (15.4 vs. 32.7%, $p < 0.001$) and they also saw a much higher temporary
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37 use of DAPs (in 34.6% vs 16.4% of patients, $p< 0.001$) with a higher burden of
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39 anticholinergics used temporarily (mean 0.73, SD 1.24 vs mean 0.22, SD 0.55, $p< 0.001$)
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41 compared to those who went back home.
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46 Men in our study were younger than women (mean 77.7 vs. 81.0 years, $p=0.003$) and were
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48 more likely to be prescribed temporary anticholinergic drugs (26.6% vs. 18.1%, $p=0.022$,
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50 table 5a) with a higher burden of anticholinergics used temporarily (mean 0.50, SD 1.1 vs
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52 mean 0.3, SD 0.7 $p= 0.004$).
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55 Patients who died during index admission as well as those who were readmitted or died
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57 within the 30 day follow up period did not differ from the rest of the patients in ACB on
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59 admission or discharge/death (table 5 d). Those who died had a smaller proportion of patients
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2 on DAPs at death. Our data do not allow us to differentiate between expected and unexpected
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4 deaths; though it is likely that this reduction in number of patients may be due to the
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6 deliberate stopping of medications in those who were not able to take them anymore or who
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8 had been commenced on an end of life care pathway.
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11 Prescribing behaviour in all diagnostic subgroups of dementia, delirium or falls, as well as in
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13 those with newly diagnosed dementia, was similar with no statistically significant change in
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15 ACB scores or number of patients on anticholinergic drugs, as well as with regards to the
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17 temporary use of drugs with anticholinergic properties (table 5 b). Figure 4 shows the
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19 distributions of anticholinergic burden in each of the diagnostic groups on admission and
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21 discharge.
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27 AChE-I (table 5b) were found on admission in 18.2% of patients with a diagnosis of chronic
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29 cognitive impairment (or in 6.7% of all patients). Of these patients on procholinerics, 54.1%
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31 were also taking DAPs. This subgroup did not differ from the rest with regards to the number
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33 of patients on DAPs, ACB scores, or the number of naïve patients newly started on DAPs
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35 (table 5c). Table 6 lists DAPs found on admission in patients on AChE-Is. Temporary DAPs
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37 were prescribed less in this group compared to patients not on procholinerics on admission
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39 (13.5% vs 22.5% of patients, p , 0.001). This combination of antagonistic drugs makes little
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41 sense but is unfortunately frequently encountered.^{14,24} Some of the side effects of dementia
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43 drugs, such as urinary frequency, incontinence, diarrhoea, or insomnia may be misinterpreted
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45 as new comorbidities or manifestations of frailty in patients with cognitive impairment.²⁵
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48 The resulting prescribing of anticholinergics will offset their efficiency and may hasten
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50 cognitive decline.
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57 The use of drugs with the highest anticholinergic burden was low amongst our patients and
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59 the anticholinergic load was caused predominantly by drugs with lesser activity. Adverse
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2 drug events are the result of the anticholinergic load of multiple medications rather than of a
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4 single drug.²⁶ Combined anticholinergic use increases hospitalizations and mortality in older
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6 people²⁷ and hastens cognitive decline. For one point in the ACB, a decline in the Mini-
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8 mental State Examination²⁸ (MMSE) score of 0.33 over 2 years has been suggested.⁷
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10 Furthermore, an increase in the cumulative ACB by one has been linked with a 26% increase
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12 in mortality.²⁹
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18 More than one-third of medications included in the ACB scale were not in use in our patients.
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20 This reflects the availability of these medications within the countries that took part in our
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22 study. In a globalised world with access to non-formulary drugs when travelling abroad or by
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24 purchasing them online via regulated or rogue pharmacies, we do not suggest the use of a
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26 shortened ACB scale.
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32 Temporary medications were used in more than 1 in 5 patients. This was the same in all
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34 diagnostic subgroups including patients with an acute delirium, potentially worsening their
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36 confusion. It may be difficult to fully avoid these but non-pharmacological approaches to
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38 prevent or treat delirium including addressing the environment in which patients are cared for
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40 may reduce their need.³⁰
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46 Our study is not without limitations. Our aim was to analyse the impact of an acute admission
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48 on the anticholinergic burden. We did not record comorbidities and did not identify
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50 terminally ill patients or those with end-stage dementia. Overall, rates for readmission and
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52 mortality were nevertheless similar to those in patients described in large cohort studies
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54 looking at outcomes of elderly patients admitted.³¹ All participating centres were acute
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56 hospitals either at regional or teaching hospital level. We did not look into potential
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58 differences of the organisation of medication management in these facilities. The clinicians
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2 involved in the project were also – at least in part – the same clinicians looking after the
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4 patients included in our study. These factors may have potentially also accounted for the
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6 regional differences highlighted by the regression analysis i.e. that for patients recruited in
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8 UK or Finnish centres the probability for an increase in ACB score was lower. Studies
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10 comparing the organisation of medicines review and optimisation in different health care
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12 systems will be necessary to investigate this in future.
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18 Our results mirror community-based studies that have shown that there is considerable scope
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20 for improvement of prescribing practices in older people.¹⁴ Theoretical models have shown
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22 that a reduction in anticholinergic burden can be achieved in 59% of patients that score at
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24 least one point on the ACB scale and that a reduction from a score of 3 or above to 2 is
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26 possible in 85% of the cases.³² Various approaches to tackle anticholinergic burden have
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28 been suggested. For many indications of DAPs there exist alternatives that allow reducing the
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30 anticholinergic load. This can include drugs with lesser or no anticholinergic activity or non-
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32 pharmacological approaches.³³ The provision of guidelines and education alone do not seem
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34 to be sufficient ensure best medicines review and optimisation in older people. Random
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36 control trials have shown an improvement in the quality of prescribing and deprescribing via
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38 the use of multidisciplinary teams, geriatric case conferences, medication review by
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40 pharmacists and the use of information technology to support medication decisions.³⁴
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48 WHAT IS NEW AND CONCLUSION

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

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References:

1. Feinberg M. The Problems of Anticholinergic Adverse Effects in Older Patients. *Drugs Aging*. 1993;3(4):335-348. doi:10.2165/00002512-199303040-00004.
2. Han L, Agostini J V, Allore HG. Cumulative anticholinergic exposure is associated with poor memory and executive function in older men. *J Am Geriatr Soc*. 2008;56(12):2203-2210. doi:10.1111/j.1532-5415.2008.02009.x.
3. Cao Y-J, Mager DE, Simonsick EM, et al. Physical and cognitive performance and burden of anticholinergics, sedatives, and ACE inhibitors in older women. *Clin Pharmacol Ther*. 2008;83(3):422-429. doi:10.1038/sj.clpt.6100303.
4. Cancelli I, Beltrame M, Gigli GL, Valente M. Drugs with anticholinergic properties: cognitive and neuropsychiatric side-effects in elderly patients. *Neurol Sci*. 2009;30(2):87-92. doi:10.1007/s10072-009-0033-y.
5. Rovner BW, David A, Lucas-Blaustein MJ, Conklin B, Filipp L, Tune L. Self-care capacity and anticholinergic drug levels in nursing home patients. *Am J Psychiatry*. 1988;145(1):107-109. doi:10.1176/ajp.145.1.107.
6. Campbell N, Boustani M, Limbil T, et al. The cognitive impact of anticholinergics: a clinical review. *Clin Interv Aging*. 2009;4:225-233. doi:10.2147/CIA.S5358.
7. Fox C, Richardson K, Maidment ID, et al. Anticholinergic medication use and cognitive impairment in the older population: The medical research council cognitive function and ageing study. *J Am Geriatr Soc*. 2011;59(8):1477-1483. doi:10.1111/j.1532-5415.2011.03491.x.
8. Ruxton K, Woodman RJ, Mangoni A a. Drugs with anticholinergic effects and cognitive impairment, falls and all-cause mortality in older adults: A systematic review and meta-analysis. *Br J Clin Pharmacol*. 2015;(May 2016):1-12. doi:10.1111/bcp.12617.
9. Tune LE, Bylsma FW. Benzodiazepine-induced and anticholinergic-induced delirium

- 1
2 in the elderly. *Int Psychogeriatr*. 1991;3(2):397-408.
3
4 <http://www.ncbi.nlm.nih.gov/pubmed/1687445>. Accessed May 1, 2016.
5
6
7 10. Zeevi N, Pachter J, McCullough LD, Wolfson L, Kuchel GA. The blood-brain barrier:
8 Geriatric relevance of a critical brain-body interface. *J Am Geriatr Soc*.
9 2010;58(9):1749-1757. doi:10.1111/j.1532-5415.2010.03011.x.
10
11
12
13 11. Kay GG, Abou-Donia MB, Messer WS, Murphy DG, Tsao JW, Ouslander JG.
14 Antimuscarinic drugs for overactive bladder and their potential effects on cognitive
15 function in older patients. *J Am Geriatr Soc*. 2005;53(12):2195-2201.
16 doi:10.1111/j.1532-5415.2005.00537.x.
17
18
19
20
21
22 12. Van De Glind EMM, Van Enst WA, Van Munster BC, et al. Pharmacological
23 treatment of dementia: A scoping review of systematic reviews. *Dement Geriatr Cogn*
24 *Disord*. 2013;36(3-4):211-228. doi:10.1159/000353892.
25
26
27
28
29 13. West T, Pruchnicki MC, Porter K, Emptage R. Evaluation of anticholinergic burden of
30 medications in older adults. *J Am Pharm Assoc (2003)*. 2013;53(5):496-504.
31 doi:10.1331/JAPhA.2013.12138.
32
33
34
35
36 14. Mate KE, Kerr KP, Pond D, et al. Impact of Multiple Low-Level Anticholinergic
37 Medications on Anticholinergic Load of Community-Dwelling Elderly With and
38 Without Dementia. *Drugs and Aging*. 2015;(May 2016). doi:10.1007/s40266-014-
39 0230-0.
40
41
42
43
44
45 15. Lu C, Tune LE. Chronic exposure to anticholinergic medications adversely affects the
46 course of Alzheimer disease. *Am J Geriatr Psychiatry*. 2003;11:458-461.
47
48
49
50 16. Kaufmann CP, Tremp R, Hersberger KE, Lampert ML. Inappropriate prescribing: A
51 systematic overview of published assessment tools. *Eur J Clin Pharmacol*.
52 2014;70(1):1-11. doi:10.1007/s00228-013-1575-8.
53
54
55
56
57 17. O'Mahony D, O'Sullivan D, Byrne S, O'Connor MN, Ryan C, Gallagher P.
58 STOPP/START criteria for potentially inappropriate prescribing in older people:
59
60

- 1
2 Version 2. *Age Ageing*. 2015;44(2):213-218. doi:10.1093/ageing/afu145.
3
- 4 18. By the American Geriatrics Society 2015 Beers Criteria Update Expert Panel.
5
6 American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate
7
8 Medication Use in Older Adults. *J Am Geriatr Soc*. 2015;63(11):2227-2246.
9
10 doi:10.1111/jgs.13702.
11
12
- 13 19. Cooke M, Oliver D, Burns A. *Quality Care for Older People With Urgent &*
14
15 *Emergency Care Needs*. British Geriatric Society; 2012.
16
17 http://www.bgs.org.uk/campaigns/silverb/silver_book_complete.pdf. Accessed May 1,
18
19 2016.
20
21
- 22 20. Brain J, Schofield J, Gerrish K, et al. A Guide for Clinical Audit, Research and Service
23
24 Review. *Res Serv Rev*. 2011:1-29. [http://www.hqip.org.uk/resources/hqip-guide-for-](http://www.hqip.org.uk/resources/hqip-guide-for-clinical-audit-research-and-service-review/)
25
26 [clinical-audit-research-and-service-review/](http://www.hqip.org.uk/resources/hqip-guide-for-clinical-audit-research-and-service-review/).
27
28
- 29 21. NHS Health Research Authority. Is my study research? [http://www.hra-](http://www.hra-decisiontools.org.uk/research/)
30
31 [decisiontools.org.uk/research/](http://www.hra-decisiontools.org.uk/research/). Accessed December 3, 2014.
32
33
- 34 22. Aging Brain Care. ACB Scale - 2012 revision.
35
36 http://www.agingbraincare.org/uploads/products/ACB_scale_-_legal_size.pdf.
37
38 Published 2012. Accessed May 2, 2016.
39
40
- 41 23. Shiga Y, Minami K, Shiraishi M, et al. The inhibitory effects of tramadol on
42
43 muscarinic receptor-induced responses in *Xenopus* oocytes expressing cloned M(3)
44
45 receptors. *Anesth Analg*. 2002;95(5):1269-73, table of contents.
46
47 <http://www.ncbi.nlm.nih.gov/pubmed/12401609>. Accessed May 2, 2016.
48
49
- 50 24. Carnahan RM, Lund BC, Perry PJ, Chrischilles EA. The concurrent use of
51
52 anticholinergics and cholinesterase inhibitors: Rare event or common practice? *J Am*
53
54 *Geriatr Soc*. 2004;52(12):2082-2087. doi:10.1111/j.1532-5415.2004.52563.x.
55
56
- 57 25. Gill SS, Mamdani M, Naglie G, et al. A Prescribing Cascade Involving Cholinesterase
58
59 Inhibitors and Anticholinergic Drugs. *Arch Intern Med*. 2005;165(7):808-813.
60

- 1
2 doi:10.1001/archinte.165.7.808.
3
4
5 26. Tune LE. Anticholinergic effects of medication in elderly patients. In: *Journal of*
6
7 *Clinical Psychiatry*. Vol 62. ; 2001:11-14.
8
9 27. Gnjidic D, Hilmer SN, Hartikainen S, et al. Impact of High Risk Drug Use on
10
11 Hospitalization and Mortality in Older People with and without Alzheimer's Disease:
12
13 A National Population Cohort Study. *PLoS One*. 2014;9(1):e83224.
14
15 doi:10.1371/journal.pone.0083224.
16
17 28. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for
18
19 grading the cognitive state of patients for the clinician. *J Psychiatr Res*.
20
21 1975;12(3):189-198. doi:10.1016/0022-3956(75)90026-6.
22
23 29. Cai X, Campbell N, Khan B, Callahan C, Boustani M. Long-term anticholinergic use
24
25 and the aging brain. *Alzheimer's Dement*. 2013. doi:10.1016/j.jalz.2012.02.005.
26
27 30. NICE. *Delirium: Prevention , Diagnosis and Management (CG103)*.; 2010.
28
29 31. Walsh B, Roberts HC, Nicholls PG. Features and outcomes of unplanned hospital
30
31 admissions of older people due to ill-defined (R-coded) conditions: retrospective
32
33 analysis of hospital admissions data in England. *BMC Geriatr*. 2011;11(1):62.
34
35 doi:10.1186/1471-2318-11-62.
36
37 32. He Z, Ball PA. Can medication management review reduce anticholinergic burden
38
39 (ACB) in the elderly? Encouraging results from a theoretical model. *Int*
40
41 *Psychogeriatrics C Int Psychogeriatr Assoc*. 2013;25(9):1425-1431.
42
43 doi:10.1017/S1041610213000872.
44
45 33. Hanlon JT, Semla TP, Schmader KE, Samuel MJ. Alternative Medications for
46
47 Medications in the Use of High-Risk Medications in the Elderly and Potentially
48
49 Harmful Drug-Disease Interactions in the Elderly Quality Measures. *J Am Geriatr Soc*.
50
51 2015;63(12):e8-e18. doi:10.1111/jgs.13807.
52
53 34. Topinková E, Baeyens JP, Michel JP, Lang PO. Evidence-based strategies for the
54
55
56
57
58
59
60

- 1
2 optimization of pharmacotherapy in older people. *Drugs and Aging*. 2012;29(6):477-
3
4 494. doi:10.2165/11632400-000000000-00000.
5
6 35. Osler W. *Aequanimitas and Other Addresses*. Second Edi. P. Blakiston's Son & Co.;
7
8 1910.
9
10 36. Osler W, Bean RB, Bean WB. *Sir William Osler: Aphorisms from His Bedside*
11
12 *Teachings and Writings*. New York: H. Schuman; 1950.
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
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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 datasets were complete for all but five patients (0.9 %) where follow-up information was unavailable.

Table 2: Multivariate binary logistic regression analysis

a) Increase in ACB score

	Odds	95% C.I.* for		P value
	Ratio	Odds Ratio		
		Lower	Upper	
Age	1.01	0.99	1.04	0.224
Sex	0.94	0.55	1.59	0.810
UK centre	0.05	0.01	0.36	0.003
Finnish centre	0.04	0.01	0.27	0.001
Dutch centre	0.14	0.02	1.11	0.063
Italian centre	0.47	0.06	3.86	0.481
From care home	0.97	0.47	1.98	0.924
Chronic cognitive impairment or dementia	0.63	0.28	1.45	0.281
Acute delirium or confusional state	0.98	0.44	2.20	0.962
Falls	1.08	0.47	2.52	0.852
Temporary used DAPs	1.82	1.36	2.45	<0.001

*Confidence interval

b) Decrease in ACB Score

	Odds	95% C.I. for Odds		P value
	Ratio	Ratio		
		Lower	Upper	
Age	0.99	0.97	1.01	0.372
Sex	1.01	0.62	1.63	0.977
UK centre	1.30	0.27	6.37	0.746
Finnish centre	0.35	0.07	1.71	0.196
Dutch centre	0.78	0.12	5.02	0.796
Italian centre	0.66	0.10	4.22	0.663
From care home	1.26	0.67	2.38	0.477
Chronic cognitive impairment or dementia	0.82	0.39	1.69	0.583
Acute delirium or confusional state	0.61	0.29	1.25	0.175
Falls	0.52	0.19	1.00	0.053
Temporary used DAPs	1.13	0.83	1.52	0.437

c) Inpatient mortality

	Odds	95% C.I. for Odds		P value
	Ratio	Ratio		
		Lower	Upper	
Age	1.06	1.02	1.12	0.010
Sex	1.15	0.52	2.53	0.736
UK centre	0.57	0.19	1.74	0.322
Finnish centre	0.04	0.01	0.26	0.001
Dutch centre	0.45	0.07	2.74	0.387
Italian centre	0.89	0.12	3.34	0.435
From care home	2.54	1.10	5.86	0.029
Chronic cognitive impairment or dementia	0.66	0.25	1.76	0.408
Acute delirium or confusional state	1.48	0.56	3.93	0.430
Falls	0.45	0.16	1.28	0.135
Temporary used DAPs	2.20	1.45	3.35	<0.001

2d) Readmission

	Odds	95% C.I. for Odds		P value
	Ratio	Ratio		
		Lower	Upper	
Age	1.01	0.99	1.03	0.316
Sex	0.72	0.43	1.22	0.221
UK centre	0.22	0.04	1.39	0.107
Finnish centre	0.10	0.02	0.62	0.013
Dutch centre	0.20	0.03	1.55	0.122
Italian centre	0.45	0.05	3.79	0.460
From care home	1.21	0.59	2.46	0.599
Chronic cognitive impairment or dementia	0.44	0.18	1.05	0.063
Acute delirium or confusional state	0.67	0.29	1.55	0.352
Falls	0.64	0.27	1.51	0.306
Temporary used DAPs	1.30	0.96	1.78	0.095

Table 3: Proportion of anticholinergic medications used in all patients on admission

	ACB = 1	ACB = 2	ACB = 3
% of DAPs	84.12	2.09	13.79
% of total ACB	64.87	3.23	31.90

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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

Table 5 a) Gender

		All	Female	Male	
1					
2	% of all patients	100.0	58.3	41.7	
3					
4	Gender (%) Female	58.3	100.0	0.0	
5	Male	41.7	0.0	100.0	p < 0.001
6	Age Mean	79.6	81.0	77.7	
7	SD	13.1	13.5	12.3	p = 0.003
8					
9	Patients on AChE-I on admission (%)	6.7	5.3	8.3	p = 0.223
10	Patients on DAPs on admission: (%)	60.8	58.1	64.6	p = 0.147
11					
12	ACB Score on admission Range	0 - 10	0 - 8	0 - 10	
13	Mean	1.3	1.3	1.4	
14	SD	1.6	1.6	1.6	p = 0.558
15					
16	Patients on DAPs on discharge (%)	57.7	55.6	60.3	p = 0.319
17	ACB score on discharge Range	0 - 10	0 - 8	0 - 10	
18	Mean	1.3	1.3	1.3	
19	SD	1.6	1.6	1.6	p = 0.603
20					
21	Patients on temporary DAPs (%)	21.9	18.1	26.6	
22	ACB score temp.DAPs Range	0 - 6	0 - 3	0 - 6	
23	Mean	0.4	0.3	0.5	
24	SD	0.9	0.7	1.1	p = 0.004
25					
26	Patients who had ACB reduced (%)	21.1	21.3	21.0	p = 1.000
27	Patients who had ACB increased (%)	19.7	19.4	19.7	p = 1.000
28	Patients with no change in ACB (%)	59.2	59.4	59.4	p = 1.000
29	DAP naïve started on DAPs (%)	22.8	20.9	24.7	p = 1.000
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31	ACB on admission vs discharge p =	0.569	0.760	0.512	
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Table 5c) Patients on cholinesterase inhibitors (AChE-I)

	All	AChE-I on admission	
1			
2			
3	% of all patients	100.0	6.7
4	Gender (%)		
5	Female	57.1	48.6
6	Male	42.9	51.4
7			p= 0.290
8	Age		
9	Mean	84.4	83.4
10	SD	9.0	6.0
11			p= 0.001
12	Patients on AChE-I on admission (%)	6.7	100.0
13	Patients on DAPs on admission: (%)	60.8	54.1
14			p= 0.483
15	ACB Score on admission		
16	Range	0 - 10	0 – 6
17	Mean	1.3	1.3
18	SD	1.6	1.6
19			p= 0.933
20	Patients on DAPs on discharge (%)	57.7	54.1
21			p= 0.766
22	ACB score on discharge		
23	Range	0 - 10	0 – 6
24	Mean	1.3	1.2
25	SD	1.6	1.6
26			p= 0.809
27	Patients on temporary DAPs (%)	21.9	13.5
28	ACB score temp.DAPs		
29	Range	0 - 6	0 – 1
30	Mean	0.4	0.1
31	SD	0.9	0.3
32			p<0.001
33	Patients who had ACB reduced (%)	21.1	13.5
34			p= 0.334
35	Patients who had ACB increased (%)	19.7	13.5
36			p= 0.446
37	Patients with no change in ACB (%)	59.2	73.0
38			p= 0.111
39	DAP naïve started on DAPs (%)	22.8	23.5
40			p= 0.906
41	ACB on admission vs discharge p=	0.569	0.755
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Table 5d) Other subgroups

	All	Died during admission	Short stay (3 days max)	Unable to return home	30 day readmission				
% of all patients	100.0	7.7	22.6	18.9	7.7				
Gender (%) Female	57.1	59.7	63.5	57.1	59.7				
Male	42.9	p= 0.965	40.3	p= 0.800	36.5	p= 0.228	42.9	p= 0.965	40.3
Age Mean	84.4	78.2	82.0	84.4	78.2				
SD	9.0	p= 0.001	13.4	p= 0.194	9.0	p <0.001	9.0	p= 0.001	13.4
Patients on AChE-I on admission (%)	6.7	2.4	p= 0.394	7.3	p= 0.954	2.9	6.7	2.4	p= 0.394
Patients on DAPs on admission: (%)	60.8	73.8	p= 0.104	57.3	p=0.410	61.5	60.8	73.8	p= 0.104
ACB Score on admission Range	0 – 10	0 – 5		0 – 10		0 - 6	0 – 10	0 – 5	
Mean	1.3	1.6		1.3		1.3	1.3	1.6	
SD	1.6	1.5	p= 0.309	1.8	p= 0.728	1.4	1.6	1.5	p= 0.309
Patients on DAPs on discharge (%)	57.7	59.5	p= 0.916	48.4	p=0.022	66.3	57.7	59.5	p= 0.916
ACB score on discharge Range	0 – 10	0 – 7		0 – 10		0 - 8	0 – 10	0 – 7	
Mean	1.3	1.3		1.1		1.6	1.3	1.3	
SD	1.6	1.6	p= 0.898	1.7	p= 0.074	1.8	1.6	1.6	p= 0.898
Patients on temporary DAPs (%)	21.9	38.1		18.5	p= 0.373	34.6	21.9	38.1	
ACB score temp.DAPs Range	0 - 6	0 – 5		0 – 3		0 - 6	0 - 6	0 – 5	
Mean	0.4	0.8		0.3		0.7	0.4	0.8	
SD	0.9	1.4	p= 0.030	0.6	p= 0.056	1.2	0.9	1.4	p= 0.030
Patients who had ACB reduced (%)	21.1	35.7	p= 0.027	21.0	p= 1.000	13.5	21.1	35.7	p= 0.027
Patients who had ACB increased (%)	19.7	23.8	p= 0.594	8.9	p= 0.001	32.7	19.7	23.8	p= 0.594
Patients with no change in ACB (%)	59.2	40.5	p= 0.015	70.2	p= 0.007	53.8	59.2	40.5	p= 0.015
DAP naïve started on DAPs (%)	22.8	27.3	p= 0.922	15.1	p= 0.358	32.5	22.8	27.3	p= 0.922
ACB on admission vs discharge p=	0.569	0.382		0.018		0.016	0.569	0.382	

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

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Figure 1: Adapted Anticholinergic Burden Scale

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

Total ACB score: _____

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

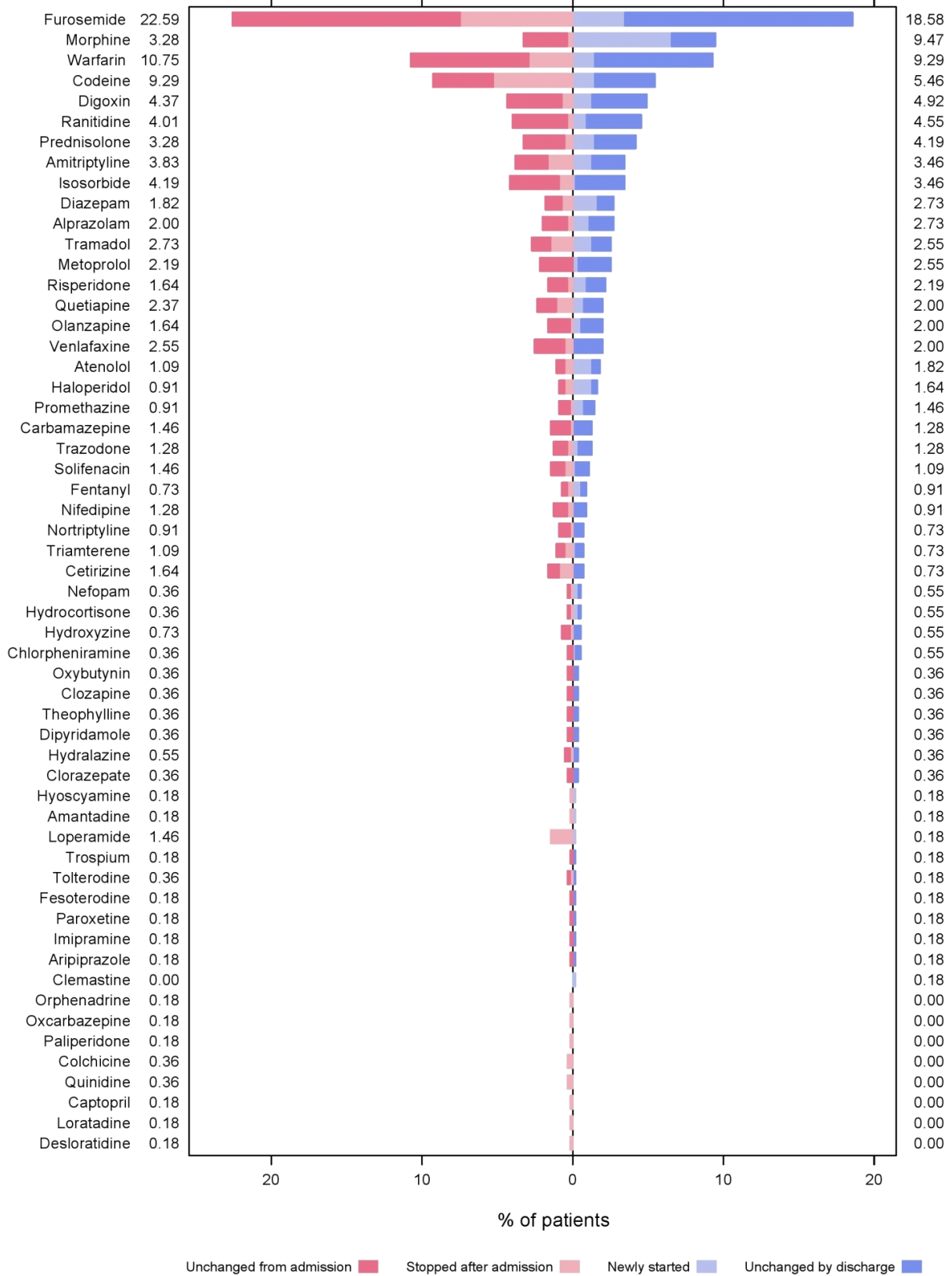


Figure 3: Medications with anticholinergic properties in all patients on admission and discharge, weighted by their individual anticholinergic burden

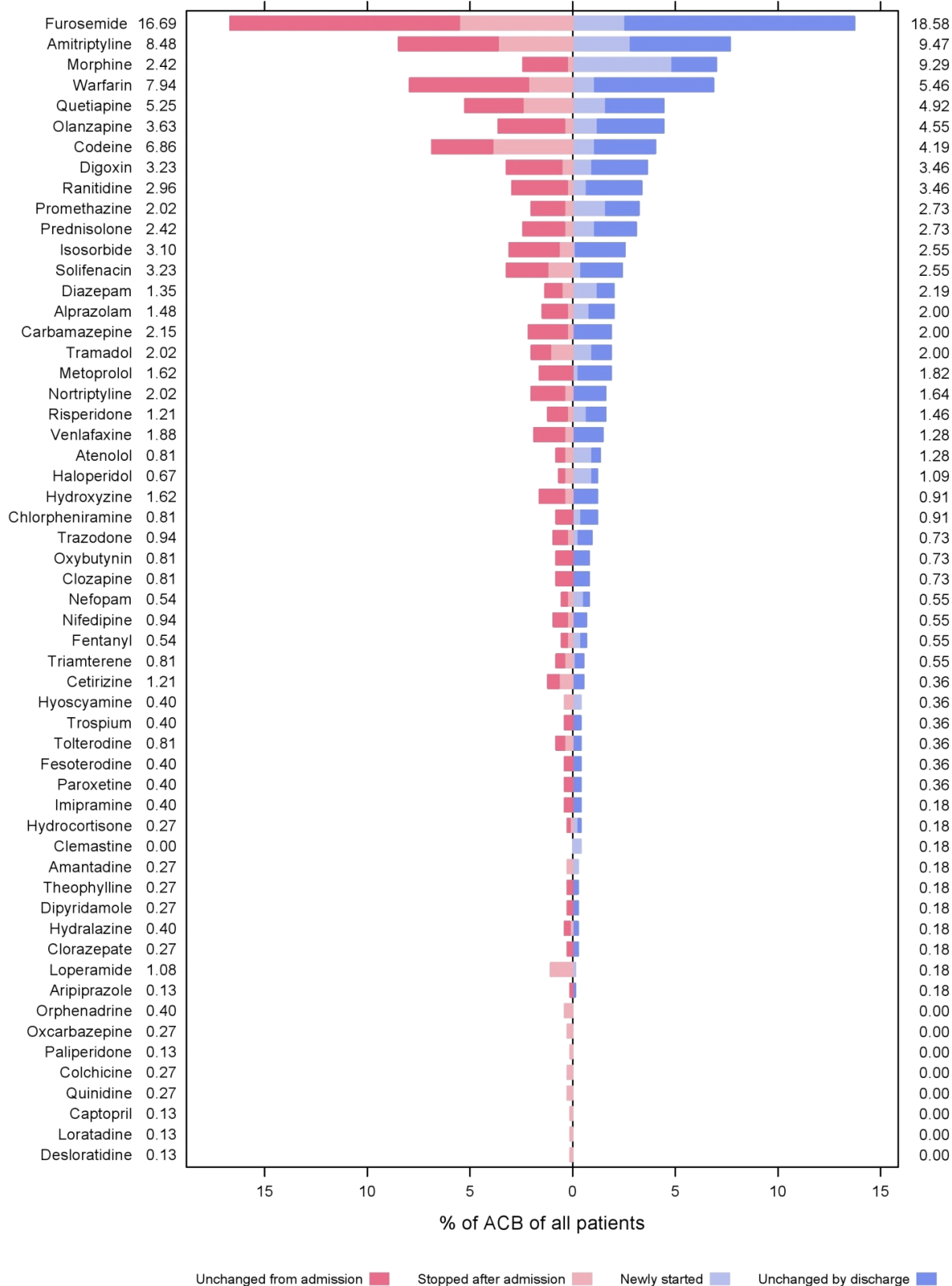
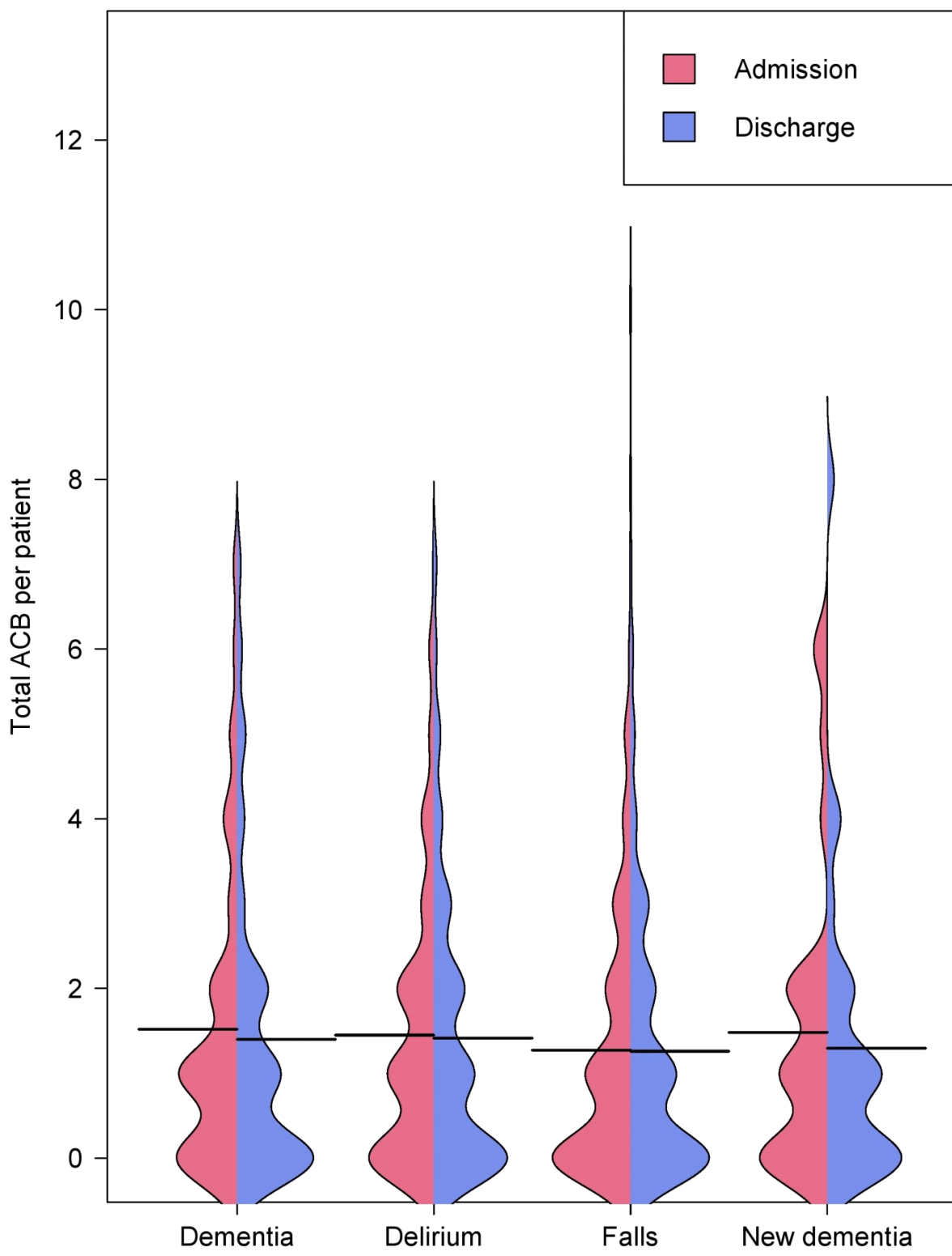


Figure 4: Distribution of anticholinergic burden on admission and discharge by diagnosis



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