Temporal trends in anticholinergic medication prescription in older people: repeated cross-sectional analysis of population prescribing data

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Abstract

Background: in older people, medications with anticholinergic (antimuscarinic) effects are associated with adverse clinical outcomes, the risk increasing with increasing anticholinergic exposure. Many anticholinergics are recognised as potentially inappropriate and efforts to reduce prescription have been ongoing. We examined temporal trends of anticholinergic prescription and exposure in older people.

Methods: anonymised data on all prescribed medication dispensed to people ≥65 years in Tayside, Scotland were obtained for the years 1995 (n = 67,608) and 2010 (n = 73,465). The Anticholinergic Risk Scale (ARS) was adapted (mARS) to include newer medications and medications identified in other scales as having moderate to strong anticholinergic activity. An individual’s mARS score was the sum of scores for individual medications. Differences in prescription of anticholinergic medications and mARS scores between 1995 and 2010 were examined.

Results: a significantly higher proportion of older people received any anticholinergic medication in 2010 compared with 1995 (23.7 versus 20.7%; P < 0.001). High anticholinergic exposure (mARS scores ≥3) was seen in 7.3% in 1995 and 9.9% in 2010 (P < 0.001). Prescription of individual anticholinergic medication was small—only three medications were prescribed to >2% of people. The risk of high anticholinergic exposure increased in those with polypharmacy, social deprivation, those living in care homes and women.

Conclusion: despite increasing evidence of adverse outcomes, the proportion of older people prescribed anticholinergic medications and the proportion with a high anticholinergic exposure has increased between 1995 and 2010. Prescription of individual drug is small so cumulative anticholinergic scores may help future efforts to reduce anticholinergic prescription in older people.

Keywords: anticholinergic medication, older people, prescription

Introduction

Medications with anticholinergic (antimuscarinic) effects have long been recognised as having clinically relevant adverse effects on older people including deteriorating cognitive function, delirium, poor physical function, falls, to institutionalisation and increased mortality [1–3]. Age-related changes in pharmacokinetics and pharmacodynamics likely contribute to the high incidence of adverse outcomes in older people. For example, the greater the propensity of anticholinergic medications to cross the blood–brain barrier, the greater the risk of central side effects [4]. Factors that are thought to increase the risk of anticholinergic side effects in older people include a reduction in M1 muscarinic receptors (the most abundant cholinergic receptor subtype in the central nervous system), an increase in...
blood–brain barrier permeability and the greater burden of multimorbidity [5].

Many older people are prescribed medication with anticholinergic effects with between 34 and 48% of older people regularly taking one [1, 2]. Many drugs have anticholinergic effects, and there is increasing interest in measuring total anticholinergic exposure rather than focussing on individual drugs. Greater anticholinergic exposure is associated with a greater risk of anticholinergic side effects [2, 6]. Concerns regarding the inappropriate use of anticholinergic medications in older people have been recognised and efforts to limit anticholinergic prescribing have been on-going for several decades [7, 8]. Newer drugs, with lower central nervous system penetration and less anticholinergic potential, have been developed in an effort to minimise potential adverse effects where anticholinergics are indicated [9]. It has additionally been advocated that all drugs with strong anticholinergic effects are used with caution and that, when necessary, alternative medication or non-drug therapies are used in this group [10].

The Beers Criteria and the more recent STOPP (Screening Tool of Older Persons potentially inappropriate Prescriptions) criteria have been used to limit the prescription of potentially inappropriate medication in older people [11–13]. Following the development of the Beers Criteria in 1997, reductions in prescribing of potentially inappropriate drugs in older people were demonstrated in the United States, but changes in prescription of individual anticholinergic drug varied from −41.5 to +55.0% [14]. Very little published data exist regarding changes in anticholinergic prescription in Europe, but potentially inappropriate prescribing remains common [15, 16]. Given the increasing evidence of risks of anticholinergic medication in older people, we aimed to determine changes in anticholinergic exposure in older people from 1995 to 2010 using a complete population dataset.

Methods

The study design is a repeated cross-sectional analysis of data for all prescriptions dispensed by community pharmacists to residents of the entire Tayside region of Scotland, UK. Data derived from routine National Health Service datasets were obtained from the University of Dundee Health Informatics Centre. Each prescription has a unique patient identifier allowing the creation of patient prescribing histories. Fully anonymised data were used, with Caldicott Guardian (regulatory) approval for access to this data, according to the Standard Operating Procedures for data management and data security. The East of Scotland Research Ethics Service has stated that under these circumstances, individual review and approval by Research Ethics Committee is not required.

Data were extracted for all medications dispensed in two 84 day periods before 31 March 1995 and 31 March 2010, for all Tayside residents aged ≥65 years registered with a Tayside General Practice. Additional patient demographic data were extracted: age, sex, socioeconomic status measured by the Scottish Index of Multiple Deprivation [SIMP] decile and place of residence. The Tayside population is well matched to the UK population in terms of age, sex and socioeconomic deprivation, although there are relatively few people from ethnic minorities.

The Anticholinergic Risk Scale (ARS) was developed by Rudolph et al. using 500 most prescribed medications. They ranked medication with anticholinergic potential on a scale of 0–3 (0, limited or none; 1, moderate; 2, strong; 3, very strong potential) based on information available on the dissociation constant for the muscarinic receptor and rates of anticholinergic adverse effects. An individual’s ARS score was the sum of the rankings for all prescribed medication [6].

We modified the ARS (henceforth referred to as mARS) to include newer medications with anticholinergic properties that are currently available in the United Kingdom. Table 1 gives the list of medications we included and their ranks (Supplementary data are available in Age and Ageing online, Appendix, Table S2). Medications with moderate to severe anticholinergic effects according to other scales (Anticholinergic Burden Scale and Anticholinergic Drug Scale) were added to our list. The Anticholinergic Burden Scale is an expert based on practical index that classifies the severity of a drug’s anticholinergic activity on cognition using a scale of 1 (mild), 2 (moderate) and 3 (severe) [17] and the Anticholinergic Drug Scale classifies drugs on a scale of 1–4 based on serum anticholinergic activity [18]. Unlike the Drug Burden Index score [19] which takes into account the dose of drug prescribed, we only ranked the drugs according to anticholinergic potential. Medications identified as having significant anticholinergic properties in the British National Formulary were also included and medications not available in the UK were excluded. The scoring of these additional drugs in the mARS were made using judgement based on available literature and expert knowledge. Following the original ARS, drugs with minimal anticholinergic effects were excluded [6].

Statistical analysis

Analysis was conducted using SPSS v17.0 statistical package. Percentages of people prescribed anticholinergic medication, and change in the proportion prescribed anticholinergic medications and mARS scores were examined between 1995 and 2010. Change over time in the proportion of people prescribed anticholinergic medication was assessed using $\chi^2$-tests, and confidence intervals of the difference in proportions between the 2 years were calculated using Wilson’s method. Logistic regression was used to predict the probability of an individual having a very high anticholinergic exposure (mARS score ≥3) in 2010 using age group, sex, number of medications, postcode derived deprivation score (deciles of the Scottish Index of Multiple Deprivation) and place of residence (own home versus residential care) as categorical variables.

Results

Characteristics of people included in the study are shown in Table 2. The number of people ≥65 years increased by
8.7% and the proportion of men rose 3.3% between 1995 and 2010. Polypharmacy significantly increased with almost 25% more people receiving five or more medications in 2010. A significantly greater proportion of older people were dispensed an anticholinergic drug in 2010 than 1995, and dispensing of multiple anticholinergics increased (Table 2). For those prescribed anticholinergic medications, the mean mARS increased from 2.19 in 1995 to 2.47 in 2010 (difference 0.28, 95% CI 0.25–0.31, $t = -18.8$, d.f. = 3144, $P < 0.001$).
Table 3. Change in mARS scores between 1995 and 2010

<table>
<thead>
<tr>
<th></th>
<th>mARS = 0%</th>
<th>Difference 2010–1995</th>
<th>mARS = 1–2%</th>
<th>Difference 2010–1995</th>
<th>mARS≥3%</th>
<th>Difference 2010–1995</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>1995 79.3</td>
<td>12.3</td>
<td>13.4</td>
<td>7.3</td>
<td>2.6</td>
<td><strong>2.3–2.9)</strong></td>
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<td></td>
<td>2010 76.3</td>
<td>–3.0 (–3.6 to –2.6)**</td>
<td>13.8</td>
<td>0.4 (–0.7)*</td>
<td>9.9</td>
<td><strong>2.4–3.4)</strong></td>
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<td>Age (years)</td>
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<tr>
<td>65–69</td>
<td>1995 82.5</td>
<td>12.1</td>
<td></td>
<td>5.4</td>
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<td></td>
<td>2010 80.8</td>
<td>–1.7 (–2.5 to –1.0)**</td>
<td>10.9</td>
<td>–1.2 (–1.6 to –0.8)**</td>
<td>8.3</td>
<td><strong>2.4–3.4)</strong></td>
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<tr>
<td>70–74</td>
<td>1995 80.1</td>
<td>13.7</td>
<td></td>
<td>6.3</td>
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<td></td>
<td>2010 77.6</td>
<td>–2.5 (–3.3 to –1.6)**</td>
<td>12.6</td>
<td>–1.1 (–1.8 to –0.4)*</td>
<td>9.8</td>
<td><strong>3.0–4.1)</strong></td>
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<td>75–79</td>
<td>1995 78.2</td>
<td>14.2</td>
<td></td>
<td>7.6</td>
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<td></td>
<td>2010 74.9</td>
<td>–3.3% (–4.4 to –2.3)**</td>
<td>14.6</td>
<td>0.4% (–0.4 to 1.2)</td>
<td>10.5</td>
<td><strong>2.3–3.6)</strong></td>
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<td>80–84</td>
<td>1995 76.1</td>
<td>14.5</td>
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<td>9.4</td>
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<td></td>
<td>2010 72.1</td>
<td>–4.0% (–5.2 to –2.8)**</td>
<td>16.8</td>
<td>2.4% (1.4–3.4)**</td>
<td>11.0</td>
<td><strong>1.8–2.5)</strong></td>
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<td>85–89</td>
<td>1995 73.9</td>
<td>14.6</td>
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<td>11.5</td>
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<td></td>
<td>2010 70.5</td>
<td>–4.3% (–5.8 to −2.7)**</td>
<td>17.6</td>
<td>3.0% (1.7–4.4)**</td>
<td>11.9</td>
<td><strong>0.8–1.6)</strong></td>
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<td>≥90</td>
<td>1995 74.6</td>
<td>12.6</td>
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<td>12.5</td>
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<tr>
<td></td>
<td>2010 71.3</td>
<td>–3.3% (–5.8 to −0.9)*</td>
<td>18.6</td>
<td>5.7% (3.7–7.6)**</td>
<td>10.2</td>
<td><strong>2.7–3.9)</strong></td>
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<tr>
<td>Female</td>
<td>1995 77.3</td>
<td>13.8</td>
<td></td>
<td>8.8</td>
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<tr>
<td></td>
<td>2010 73.4</td>
<td>–3.9% (–4.5 to −3.4)**</td>
<td>14.8</td>
<td>%0.5–1.5%**</td>
<td>11.8</td>
<td><strong>2.5–3.3)</strong></td>
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<tr>
<td>Male</td>
<td>1995 82.2</td>
<td>12.8</td>
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<td>5.0</td>
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<td></td>
<td>2010 80.1</td>
<td>–2.1% (–2.7 to −1.5)**</td>
<td>12.4</td>
<td>–0.4% (–1.0 to 0.1)</td>
<td>7.5</td>
<td><strong>2.1–2.9)</strong></td>
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<td>Medication no.</td>
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<tr>
<td>0–4</td>
<td>1995 88.5</td>
<td>8.3</td>
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<td>3.2</td>
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<tr>
<td></td>
<td>2010 90.9</td>
<td>2.5 (2.0–2.9)**</td>
<td>6.3</td>
<td>–2.1 (–2.4 to −1.7)**</td>
<td>2.8</td>
<td><strong>0.6–0.2)</strong></td>
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<tr>
<td>≥5</td>
<td>1995 58.3</td>
<td>25.0</td>
<td></td>
<td>16.6</td>
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</tr>
<tr>
<td></td>
<td>2010 63.8</td>
<td>5.5 (4.7–6.3)**</td>
<td>20.2</td>
<td>–4.8 (4.1–5.5)**</td>
<td>16.0</td>
<td>–0.7 (–1.3 to 0.0)</td>
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</table>

*P < 0.05.
**P < 0.001.

The proportion of older people with mARS ≥3 significantly increased from 7.3 to 9.9% and the absolute number of older people with mARS ≥3 increased 46% (7,185 in 2010 versus 4,930 in 1995). Almost half of older people with mARS ≥3 were prescribed more than one anticholinergic drug (43.2% in 1995 and 45.2% in 2010).

The proportion of people with mARS ≥3 increased in 2010 compared with 1995 in most age groups except in people ≥85 years (Table 3). Women were more likely to have mARS scores ≥3; men versus women was 5.0 versus 8.8% in 1995 and 7.5 versus 11.8% in 2010 (P < 0.001). The proportion of people receiving no medication with anticholinergic properties was higher in 2010 versus 1995 in both those receiving <5 or ≥5 medications. This should however be interpreted cautiously since many more people received ≥5 dispensed drugs in 2010 (39,709/73,465, 54.1%) compared with 1995 (20,649/67,608, 30.5%) (P < 0.001).

Multilevel regression analysis of factors associated with mARS ≥3 in 2010 was performed (Supplementary data are available in Age and Ageing online, Appendix, Table S1). The odds of having mARS ≥3 decreased with increasing age (OR 0.58 95% CI 0.50–0.68 in the over 90 age group versus the 65–69 year age group. The proportion of people with mARS ≥3 increased significantly with greater deprivation (7.1% in the most affluent decile versus 14.1% in the most deprived decile; OR 0.67 95% CI 0.58–0.78 in the most affluent). Risk of higher anticholinergic exposure increased significantly with greater total number of prescribed medications (P < 0.001). The proportion of people with mARS scores ≥3 was 2.8% in those receiving ≤4 medications increasing to 41.8% in those with ≥15 medications. The odds of having mARS scores ≥3 was much greater in people taking >15 medications compared with those taking 4 or less (OR 23.80 95% CI 21.41–26.46). People in care homes were more likely to receive a greater anticholinergic burden. 20.4% of those in care homes versus 9.5% of those living in their own home had mARS ≥3 (OR 1.71 95% CI 1.53–1.92). Overall the influence of age, sex, number of prescribed medications, social deprivation and place of residence on the chance of a person receiving medication with mARS ≥3 in 2010 was modest (Nagelkerke R² = 0.167, P < 0.001).

Table 1 shows changes in dispensing of individual drugs commonly prescribed in either/both 1995 and 2010. An individual’s risk of being prescribed any particular anticholinergic drug was small with only ranitidine in 1995 being dispensed to >5% of older people, and only three drugs being dispensed to >2% of older people in 2010 (amitriptyline, tio- tropium and ranitidine). There were significant changes in prescribing for several drugs. The sum of all medications with <250 prescriptions did not exceed 1.5% in any mARS category.

**Discussion**

The use of medication with anticholinergic properties in older people is high with almost a quarter receiving anticholinergic...
Temporal trends in anticholinergic medication prescription in older people

medications and almost a 10th having a high anticholinergic exposure. Despite continuing efforts to reduce inappropriate prescribing in older people, we have found that the proportion of people receiving any anticholinergic medication has increased in 2010 compared with 1995, and the proportion of older people with a very high anticholinergic exposure increased by a third from 7.3% in 1995 to 9.9% in 2010. As a result of demographic ageing, the increase in number of people prescribed anticholinergic drugs is greater. The increase in higher anticholinergic exposure (mARS ≥3) was seen across all ages and for both sexes. Polypharmacy increased between 1995 and 2010 with almost 55% of older people prescribed five or more medications. The risk of high anticholinergic exposure was greater in those with polypharmacy, social deprivation, those living in care homes and women.

Many drugs contributed to anticholinergic exposure in both 1995 and 2010, but the actual drugs implicated in both years differed significantly. However, the majority of anticholinergic drugs dispensed are not specifically identified as potentially inappropriate in the most recent Beers Criteria update [10], indicating that a focus only on selected drugs will not identify the majority of drugs contributing to total anticholinergic exposure.

Anticholinergic drugs are not necessarily inappropriate, but they do carry significant risk in older people. It is the frail older person with multimorbidity who is at the greatest risk of polypharmacy in general and a high anticholinergic exposure in particular. Although many drugs contribute to anticholinergic exposure, the majority are not specifically identified as problematic in existing inappropriate prescribing criteria like Beers [10]. Such criteria are useful for focussing attention on some of the most commonly prescribed drugs (for example, in 2010, amitriptyline alone accounted for 16.6% of all anticholinergic medications dispensed in this study, and for 25.2% of the total anticholinergic burden), but a cumulative-risk score like the mARS draws attention to total anticholinergic exposure in a more holistic way.

Comparing 1995 and 2010, the pattern of anticholinergic drugs prescribed has changed significantly, reflecting withdrawal of some drugs like thioridazine or introduction of new anticholinergic drugs for chronic obstructive airways disease or lower urinary tract symptoms (LUTS). For example, while the prescription of oxybutinin has seen no change, the number of prescriptions of newer drugs for LUTS is greater than that of oxybutynin alone in 2010. Urinary incontinence is a major problem in older people and anticholinergics can help reduce symptoms and improve quality of life. Around one-fourth of older people suffer from urge incontinence and the number of people prescribed anticholinergics is therefore likely to rise in the future [20].

Newer anticholinergic medications are more selective to the M3 cholinergic receptor which is present in the detrusor muscle, and are considered more efficient treatment options. Although more expensive, they are considered cost effective for urinary incontinence in younger people, but this may not be true in older people who are at a higher risk of side effects than people included in the clinical trials of these drugs [21]. Moreover, people with LUTS may in fact have a higher prevalence of co-morbidities including cardiovascular and neurological disorders that can increase harm from anticholinergic medications [22]. While single drugs may therefore improve the morbidity attached to a particular disease state like chronic obstructive airways disease or urinary incontinence, prescribing them without consideration of overall anticholinergic exposure carries unacknowledged risk. Therefore, when adding a drug such as tiotropium, it might be worth considering stopping other less effective anticholinergic medications in an effort to minimise anticholinergic exposure. Embedding mARS or other anticholinergic burden scores in electronic prescribing system would help focus clinicians’ attention on this, both at the point of prescribing new drugs and at medication review. Although the mARS may prove useful in clinical practice, available anticholinergic scores rank the drugs differently and their relative clinical impact is under debate.

A strength of this study is that it examines community dispensed drug use for an entire geographical population, but it does not include the indication for anticholinergic prescribing. We were also unable to examine the influence of other factors such as functional status, cognitive status and frailty which are likely to influence the prescription of anticholinergic medications. Data on over-the-counter medications with anticholinergic effects are not available. However, in the UK, there is no financial incentive for patients to buy medications over the counter as prescriptions are free to the over-65s. Any undercounting as a result of over-the-counter medications would in fact mean that this study underestimates anticholinergic exposure. Our findings are similar to previous studies in showing that anticholinergic prescribing is common, but few previous studies have examined change over time at population level.

Research is needed to better quantify both the benefits and harms of anticholinergic drugs in older people. In terms of benefits, most clinical trials exclude older people and those with multimorbidity, which often leaves clinicians uncertain about the effectiveness of drugs in this population [23, 24]. This particularly matters when drugs commonly cause adverse events. However, although polypharmacy and higher anticholinergic exposure are associated with incident frailty, the causality of this is not fully established, [2, 10, 25] and more research is needed to examine whether interventions to reduce anticholinergic exposure improve patient centred outcomes.

Conclusion

Despite growing understanding of anticholinergic adverse effects, a greater number of older people were prescribed anticholinergic drugs in 2010 than in 1995, and the rates of high anticholinergic exposure in people prescribed any anticholinergic also increased. Clinicians should regularly review the indications, benefits and risks of prescribing anticholinergics to older people, especially those with multimorbidity.
Evidence of increased risk of adverse outcomes in older people with anticholinergic medication use is accumulating. Efforts to reduce prescription of inappropriate medications have been ongoing for decades. Despite this prescription of anticholinergic medications and cumulative anticholinergic exposure has increased over 15 years. Prescription of individual medications was small so cumulative anticholinergic scores may be more useful in reducing prescription.

Key points

- Evidence of increased risk of adverse outcomes in older people with anticholinergic medication use is accumulating.
- Efforts to reduce prescription of inappropriate medications have been ongoing for decades.
- Despite this prescription of anticholinergic medications and cumulative anticholinergic exposure has increased over 15 years.
- Prescription of individual medications was small so cumulative anticholinergic scores may be more useful in reducing prescription.

Acknowledgements

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Conflicts of interest

No support was received from any organisation for the submitted work. A.M. has received research grants and honorariums from Pfizer, AstraZeneca, Servier, Sanofi Aventis and NAPP Pharmaceuticals, has been paid for developing and delivering educational presentations for the British Pain Society and the National Heart Foundation of Australia.

Supplementary data

Supplementary data mentioned in the text are available to subscribers in Age and Ageing online.

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Preparation to care for confused older patients in general hospitals: a study of UK health professionals

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Abstract

Background and Objective: in the UK, two-thirds of patients in general hospitals are older than 70, of whom half have dementia or delirium or both. Our objective was to explore doctors, nurses and allied health professionals’ perceptions of their preparation to care for confused older patients on general hospital wards.

Methods: using a quota sampling strategy across 11 medical, geriatric and orthopaedic wards in a British teaching hospital, we conducted 60 semi-structured interviews with doctors, nurses and allied healthcare professionals and analysed the data using the Consensual Qualitative Research approach.

Results: there was consensus among participants that education, induction and in-service training left them inadequately prepared and under-confident to care for confused older patients. Many doctors reported initial assessments of confused older patients as difficult. They admitted inadequate knowledge of mental health disorders, including the diagnostic features of delirium and dementia. Handling agitation and aggression were considered top priorities for training, particularly for nurses. Multidisciplinary team meetings were highly valued but were reported as too infrequent. Participants valued specialist input but reported difficulties gaining such support. Communication with confused patients was regarded as particularly challenging, both in terms of patients making their needs known, and staff conveying information to patients. Participants reported emotional and behavioural responses including frustration, stress, empathy, avoidance and low job satisfaction.

Conclusion: our findings indicate that a revision of training across healthcare professions in the UK is required, and that increased specialist support should be provided, so that the workforce is properly prepared to care for older patients with cognitive problems.

Keywords: dementia, delirium, workforce, education, general hospitals, older people