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Analysis of high potency anticholinergic prescribing in Scottish nursing home patients

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Analysis of High Potency Anticholinergic Prescribing in Scottish Nursing Home Patients

CAPSTONE PROJECT PAPER

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Abstract:

Purpose:

The aim of this study was to compare the use of two or more high-potency anticholinergic (HPA) medications between patients 65 years and older in nursing homes and in the greater community using prescribing data.

Methods:

This secondary data analysis of the NHS Scotland PIS databased used prescription data from a nationally representative patient-level database. Patients were included were ≥65 years old, received ≥2HPA prescriptions from 2011Q2-2012Q1(11/12), 2016Q1-2017Q2(16/17), 2018Q2-2017Q1(18/19). The principle endpoint of this study was to assess for a change in patient's relative risk of receiving ≥2HPA prescriptions.

Results:

29,301 patients were identified. From 11/12 to 16/17 all community ≥65 years of age, and nursing home patients 65-74, 75-84 showed a relative risk reduction. 16/17 to 18/19, community patients 65-74 years and ≥85 no significant change in relative risk and 75-84 showed a relative risk increase. 16/17 to 18/19 nursing home patients 65-74 relative risk reduction and 75-84 no significant change. 16/17 to 18/19 nursing home patients aged ≥85 experienced a relative risk increase.

Conclusion:

Nursing home patients ≥85 years in 2018/2019 showed an increase in relative risk from patients in 2016/17, this group may still be at risk for the high anticholinergic burden.

Acronyms and Abbreviations:

Q1'2011 – Q2'2012 (11/12)

Q1'2016 – Q2'2017 (16/17)

Q1'2018 – Q2'2019 (18/19)

American Geriatric Society (AGS)

British National Formulary (BNF)

Community Health Index (CHI)

High Potency Anticholinergic (HPA)

Information Services Division (ISD)

Modified Anticholinergic Risk Scale (mARS)

National Health System (NHS)

National Institute for Health and Care Excellence (NICE)

National Therapeutic Indicators (NTI)

Prescription Information System (PIS)

Unique Patient Identifier (UPI)

Introduction:

Medications with anticholinergic properties antagonize the neurotransmitter acetylcholine by competitively binding to the muscarinic and nicotinic receptors (Nishtala et al., 2016). Anticholinergic receptors are proliferative throughout the body and play an essential role in cognitive processing and movement (Svoboda et al., 2017). This mechanism of action is utilized directly in the treatment of Parkinson's Disease, schizophrenia, incontinence, and Alzheimer's disease (Svoboda et al., 2017). However, other medications such as antidepressants, antipsychotics, and antihistamines have anticholinergic properties outside of the direct mechanism of action. In this case, the anticholinergic effect of these medications manifests as anticholinergic side effects. Table 1 identifies the most common anticholinergic side effect and their subsequent consequences.

Medications with a strong antagonism of the muscarinic receptors have more significant anticholinergic side effects (Mulsant et al., 2003). Additionally, using several anticholinergic medications concurrently increases the significance of side effects through cumulative exposure (Mulsant et al., 2003). Researchers quantify this effect by analyzing the serum anticholinergic activity (Mulsant et al., 2003). For clinical purposes, anticholinergic risk scales (ARS) identify patients at risk of side effects through quantifying the anticholinergic burden. The NHS Scotland polypharmacy guidelines utilize the modified Anticholinergic Risk Scale (mARS) to categorize medications available in the United Kingdom on a scale of 0-3 of anticholinergic potential (PrescQIPP, 2016). A

score of 0 indicates limited or none, 1- moderate, 2- strong, and 3- very strong anticholinergic potential (PrescQIPP, 2016).

Side Effect	Consequences
Peripheral	
Decreased Sweating	Thermoregulatory impairment leading to hypothermia
Decreased Salivation	Dental decay, periodontal disease, ulceration of gums, difficulty chewing and swallowing, respiratory infections, denture misfit, mucosal damage
Urinary Hesitancy	Urinary retention, urinary tract infection, bladder distention
Decreased Gastrointestinal Motility	Constipation, decreased gastric emptying, fecal impaction
Dilation of Pupils	Photophobia, precipitation of acute narrow angle glaucoma, dizziness, vision disturbances
Increased Heart Rate	Angina, myocardial infarction, conduction disturbances
Central	
Impaired Concentration, Confusion, Attention Deficient, Memory Impairment	Exacerbation of cognitive impairment

Table 1: Anticholinergic Side Effects (Mintzer & Burns, 2000; Libermann, 2004)

Anticholinergic side effects can be devastating in older adults and result in decreased quality of life. As shown in Table 1, side effects can be both central and peripheral. Several studies described this phenomenon in elderly individuals (Liberman, 2004; Flacker, 1998; Tune, 2001; Feinberg, 1993). This disproportionate effect in the elderly community arises not only from the nature of the side effects but several other reasons. Older individuals are more likely to have chronic conditions such as angina, diabetes mellitus, constipation, glaucoma, urinary dysfunction, sleep disturbances, and dementia that may be exacerbated by a high anticholinergic burden (Feinberg, 1993). Aging results in changes in pharmacokinetics and pharmacodynamics, such a 30%

decrease in hepatic clearance and 50% decrease in renal clearance (Koltz, 2009). These changes may result in increased sensitivity to medications.

Of particular concern in the geriatric community is the potential for a high anticholinergic burden to worsen delirium and amply cognitive decline. Ancelin et al., in a study of individuals aged 60 years and older without baseline dementia, found that older individuals with a high anticholinergic burden had deficits in cognition (2006). Britt & Gregory, in their 2016 systematic review, found similar findings demonstrating that the use of anticholinergic medications is associated with adverse cognitive effects in cognitively healthy individuals, and more so in individuals with preexisting cognitive impairment (2016). Finally, the most common cause of drug-induced delirium is highly anticholinergic medications (Tune, 2001).

Elderly patients residing in nursing homes are another subsection of the geriatric population at particularly high risk for an increased anticholinergic burden. In comparison to older patients living in the community, nursing home patients are more likely to have more comorbid conditions and decreased functional status. The 1983 study by Blazer et al., compared Tennessee Medicaid recipients aged 65 years and older living in the community and nursing homes. Among nursing home patients, 59% received at least one drug with anticholinergic properties. In comparison, 23% of community patients received at least one drug with anticholinergic properties (Blazer, 1983). More concerning, 10-17% of nursing home patients received three or more anticholinergic medications (Blazer, 1983). Of note, this study was conducted in 1983 before widespread attention was brought

to this cause by the medical community. Therefore, these results may be an overestimation in today's standards. Similarly, a 2016 study of Veterans aged 65 years and older residing in nursing homes found among residents with dementia or cognitive impairment 50.7% took medications that could exacerbate cognitive impairment, with the most common medicines antipsychotics at 35.4% (Aspinall et al. 2015). Many antipsychotics and antidepressant drugs have a high anticholinergic burden, yet in a study of 3,000 nursing home patients, 43% used at least one psychotropic agent (Spore et al., 1993). Therefore, the literature suggests that nursing home patients are acutely vulnerable to receiving a high anticholinergic burden.

In the United States, the American Geriatric Society (AGS) produces the AGS Beers Criteria to identify medications that are potentially inappropriate for use in older individuals. The 2019 Beers Criteria identifies highly anticholinergic medications such as first-generation antihistamines, antispasmodics, skeletal muscle relaxants as potentially inappropriate medications for use in older individuals (American Geriatrics Society, 2019). The guidelines recommend avoiding the use of multiple anticholinergic agents due to the risk of cognitive decline (American Geriatrics Society, 2019). Additionally, it is recommended to avoid the use of highly anticholinergic medications in patients with dementia or at risk of developing dementia due to the potential of inducing or worsening dementia (American Geriatrics Society, 2019). However, use of the Beers Criteria is limited to mediations currently available on the US market. In the United Kingdom, several sources provide recommendations around the use of anticholinergic medications. The Scottish Government published the 2018 Polypharmacy Guidance, Realistic Prescribing

outlining strategies to mitigate the potentially harmful effects of polypharmacy in older individuals. This guideline recommends reducing the anticholinergic burden in patients through avoiding or deprescribing highly anticholinergic medications and avoiding the combination of multiple anticholinergic medications (Scottish Government Polypharmacy Model of Care Group, 2018). In England, the National Institute for Health and Care Excellence (NICE) 2018 guidelines on dementia states that highly anticholinergic medications may cause cognitive impairment (2018). NICE guidance on dementia diagnosis recommends to identify cognitive decline due to anticholinergic medications and to minimize the anticholinergic burden (2018). Further research is needed to determine if reducing the anticholinergic burden in those with dementia improve cognitive outcomes compared to usual care (NICE, 2018).

Within Scotland, the National Health System (NHS) utilizes National Therapeutic Indicators (NTI) to produce further guidance on the use of anticholinergic medications in elderly individuals. To develop NTIs, the Information Services Division (IDS) Scotland uses the Prescription Information System (PIS). This database consists of prescription data from all 5.3 million individuals utilizing the NHS Scotland System (IDS Scotland). The Health Boards/Health and Social Care Partnerships then use NITs to direct prescribing actions throughout Scotland (Information Services Division Scotland). The 2018 NTI looked at preventing falls, fracture, and delirium through analyzing "the number of people aged ≥75 years dispensed >10 items of strong or very strong anticholinergics (mARS 2&3) per annum as a percentage of all people ≥75 years" (NHS Scotland, 2018). This analysis showed that the prescribing of strong anticholinergics to older individuals had decreased

slightly over the last three years (NHS Scotland, 2018). This NTI observed trends within the NHS prescribing boards, or regions, but did not further stratify the data by age or residency status to explore if a difference exists among patients residing in the community or nursing homes.

The purpose of this analysis is to further the work of NHS Scotland's 2018 NTI regarding the use of anticholinergic medications in elderly individuals. The objective is to compare the use of two or more high-potency anticholinergic (HPA) medications among patients 65 years and older in nursing homes and the greater community using prescribing data. Stratification of anticholinergic prescribing by age and residency status allows for a closer examination of the data and the potential to identify which Scottish patients may benefit from further review of anticholinergic medication use. The endpoint of this study is to assess for a change in a patient's relative risk of receiving more than 2 HPA prescriptions from 2011 to 2019.

Methods:

Dataset:

Data for this study was obtained from the PIS dataset. This comprehensive prescription claims dataset includes all community prescriptions dispensed and claimed for reimbursement by the 5.3 million Scottish citizens who currently use the NHS Scotland. Excluded from this dataset are prescriptions dispensed in hospitals. Within the PIS dataset is information on prescriber, dispenser, patient, organizational structure, and drug information. This dataset is maintained by the ISD.

Notable elements include unique patient identifier (UPI) and community health index (CHI) capture. UPI is a unique number assigned to patients to link prescription events and therefore quantify the number of patients receiving a particular medication in a de-identified manner. CHI capture rate is a surrogate measure to guarantee that each prescription captured is valid, and therefore assess the completeness of the PIS database. As of 2016, the CHI capture rate was almost 100%, indicating the dataset is an accurate representation of community prescribing within NHS Scotland.

Population Estimates:

Control data of patients not receiving ≥2HPA prescriptions were obtained through population estimates. The Scottish government does not keep an annual nursing home patient census. To estimate the total number of patients living in nursing homes the PIS database was queried to find the number of patients aged ≥65, residing in nursing homes, and receiving at least one prescription. This data was further stratified by 10-year age bands. The number of patients not receiving ≥2HPA prescriptions residing in the community was obtained through National Records of Scotland mid-year population estimates of 2011, 2016, and 2018. This data was pre-stratified into 5-year age bands (2020). Finally, the number of patients not receiving ≥2HPA prescriptions in nursing homes was subtracted to arrive at the final number of community patients.

Definition of High-Potency Anticholinergic Medications:

Medications were defined as HPA based on the mutual inclusion in the 2018 NTI "Falls, fractures, and delirium" and mARS class 3. Inclusion of mARS class 3 medications

ensures this study examined only those medications with the highest potential to cause anticholinergic side effects. A comprehensive list of medication is included in the appendix. The identified medications were sorted into the corresponding British National Formulary (BNF) paragraphs. The British National Formulary is a publication which categorizes all available formulary medications into a coded hierarchy. The paragraph indicates the medication's class. This step prevented inaccurate counts resulting from patients switching from drugs within the same class.

Sampling and Analytical Strategy:

Using SAP Business Objects BI Platform 4.2 the PIS database was processed by building quires to extract specific data. The first query applied the following filters to build the core group of patients: (1) over 65 years of age (2) valid CHI capture (3) prescriber located within one of the 14 Scottish Health Boards (4) captured within the calendar year/quarters Q2 2011-Q1 2012 (11/12), Q2 2016-Q1 2017 (16/17), Q2 2018-Q1 2019 (18/19) (5) HPA BNF paragraph. To create the two groups of interest, "nursing home residency" and "community residency", the core group was stratified by nursing home residency. Next, utilizing UPI's each group was quired to quantify how many patients received ≥2HPA prescriptions. Finally, each group was separated into the following 10-year age bands: 65-74, 75-85, and over 85.

To visualize a change in number of patients receiving ≥2HPA prescriptions, the rate of patient's receiving ≥2HPA prescriptions per 1000 patients was calculated for each 10 year age band within the specified residency status using Microsoft Excel 16.35. To assess if a statistically significant change in patient's relative risk of receiving ≥2 HPA

prescriptions occurred the risk ratio and relative risk reduction from 11/12 to 16/17 and 16/17 to 18/19 was calculated. Open Epi was used for all statistical comparisons (Dean, Sullivan, Soe, 2013)

Results:

During the specified time, 29,301 patients aged ≥65 were identified to receive ≥2 HPA prescriptions. Of 9,303 patients identified in 18/19, 7% resided in nursing homes (Table 2). Among total nursing home patients identified to receive ≥2HPA prescriptions in 18/19, 15% were aged 65-74, 23% were 75-84, and 62% were over 85 years old (Table 2). Among total community patients identified to receive ≥2HPA medications in 18/19, 42% were 65-74, 23% were 75-84, and 23% were over 85 years old (Table 2). These patterns are reflected in 11/12 and 16/1,7 as shown in Table 2.

	65-74	75-84	85+
Q2 2011 – Q1 2012			
Nursing Home (n=574)	89 (15%)	130 (23%)	355 (62%)
Community(n= 10656)	4460 (42%)	3774 (35%)	2422 (23%)
Q2 2016 – Q1 2017			
Nursing Home (n=560)	103 (18%)	172 (30%)	285 (51%)
Community (n=8208)	4583 (56%)	2827 (34%)	798 (10%)
Q2 2018 – Q1 2019			
Nursing Home (n=588)	95 (16%)	178 (30%)	315 (54%)
Community (n=8715)	4753 (55%)	3061 (35%)	901 (10%)

Table 2: Number of patients receiving ≥2HPA prescriptions and percentage of patients receiving ≥2HPA prescriptions stratified by age band and residency status (n=29,301)

	Q2'11-Q1'12	Q2'16-Q1'17	Q1'18-Q2-19
Nursing Home 65-74	38.1	26.3	19.2
Community 65-74	9.4	8.4	8.4
Nursing Home 75-84	18.5	14.3	12.7
Community 75-84	13	9.4	9.6
Nursing Home 85+	10.9	11.3	15.6
Community 85+	53.6	1.6	8.7

Table 3: Rate of ≥2 HPA prescriptions per 1000 residents of nursing homes or community, respectively, stratified by age band.

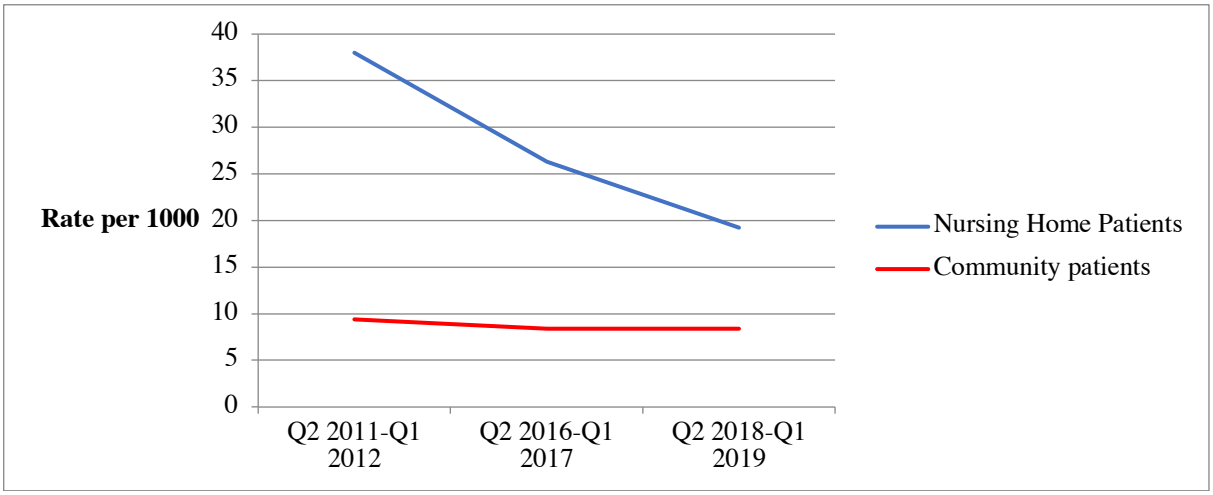

Figure 1: Rate of patients aged 65-74 receiving ≥2 HPA prescriptions stratified by residency

	11/12 to 16/17		16/17 to 18/19	
	Relative Risk (RR)	Relative Risk Change (RRR)	Relative Risk (RR)	Relative Risk Change (RRR)
Nursing homes	0.69 (0.52, 0.91) p=0.0050	31% reduction	0.74 (0.60, 0.97) p=0.015	26% reduction
Community	0.89 (0.85, 0.93) p <0.000001	11% reduction	1.01 (0.97, 1.05) p=0.29	NS

Table 4: Relative risk ratio and relative risk reduction for patients aged 65-74 stratified by residency status
NS= Indicates not statistically significant results

Looking at patients aged 65-74, the rate of nursing home patients receiving ≥2 HPA prescriptions was 38.1 per 1000 patients in 11/12, 26.3 per 1000 in 16/17, and 19.2 per 1000 in 18/19 (Table 3, Figure 1). Among those residing in the community, the rate of patients receiving ≥2 HPA prescriptions was 9.4 per 1000 in 11/12, 8.4 per 1000 in 16/17, 8.4 per 1000 in 18/19 (Table 3, Figure 1). This corresponds to nursing home patients in 16/17 had 31% less risk of receiving ≥2 HPA prescriptions compared to patients in 11/12 (Table 4). Then, nursing home patients in 18/19 had 26% less risk of receiving ≥2 HPA prescriptions compared to patients in 16/17 (Table 4). Community patients in 16/17 had 11% less risk of being prescribed ≥2 HPA medications compared to patients in 11/12, and community patients in 18/19 had a non-statistically significant change in relative risk (Table 4).

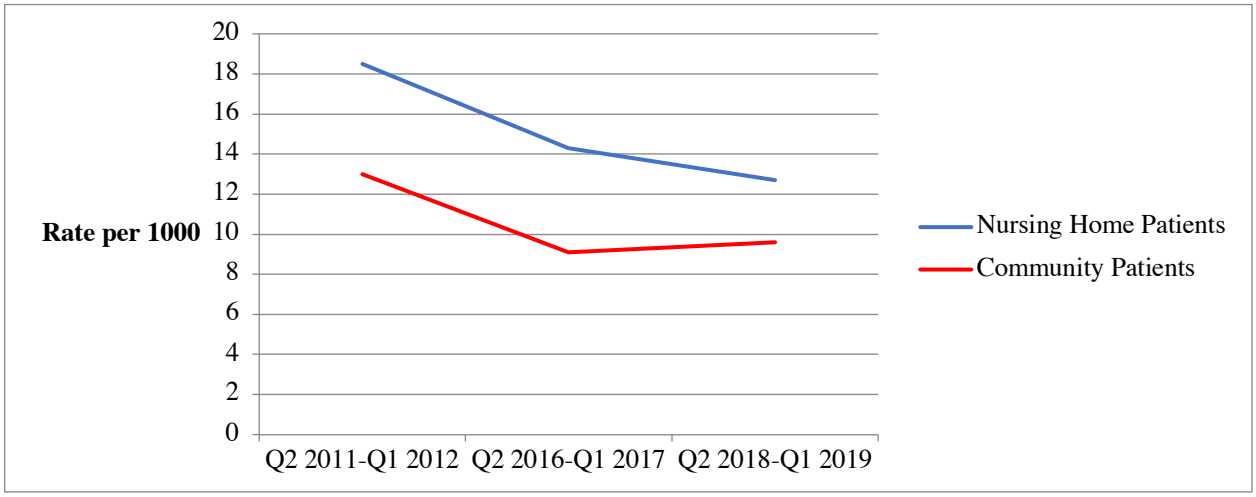

Figure 2: Rate of patients aged 74-84 receiving ≥2 HPA prescriptions stratified by residency

	11/12 to 16/17		16/17 to 18/19	
	Relative Risk (RR)	Relative Risk Change (RRR)	Relative Risk (RR)	Relative Risk Change (RRR)
Nursing Homes	0.77 (0.62, 0.97) p=0.013	23% reduction	0.89 (0.72, 1.10) p=0.14	NS
Community	0.71 (0.68, 0.75) p <0.01	29% reduction	1.06 (1.01, 1.12) p=0.01	6.2% increase

Table 5: Relative risk ratio and relative risk reduction for patients aged 75-84 stratified by residency status
NS= Indicates not statistically significant results

In patients aged 75-84, the rate of nursing patients receiving ≥2HPA prescriptions per 1000 patients was 18.5 per 1000 in 11/12, 14.3 per 1000 in 16/17, and 12.7 per 1000 in 18/19 (Table 3, Figure 2). For community patients, the rate of patients receiving ≥2 HPA prescriptions was 13 per 1000 patients in 11/12, 9.4 per 1000 in 16/17, and 9.6 per 1000 in 18/19 (Table 3, Figure 2). Comparing these values to the change in relative risk, nursing home patients aged 75-84 in 16/17 had 23% less risk of being prescribed ≥2 HPA medications compared to patients in 11/12 (Table 5). The change in relative risk for nursing home patients in 16/17 to 18/19 was statistically insignificant. Further, community patients aged 75-84 in 16/17 had 29% less of being prescribed ≥2 HPA medications risk compared to patients in 11/12 (Table 5), and community patients in 18/19 had 6.2% more risk of being prescribed ≥2 HPA medications than those in 16/17.

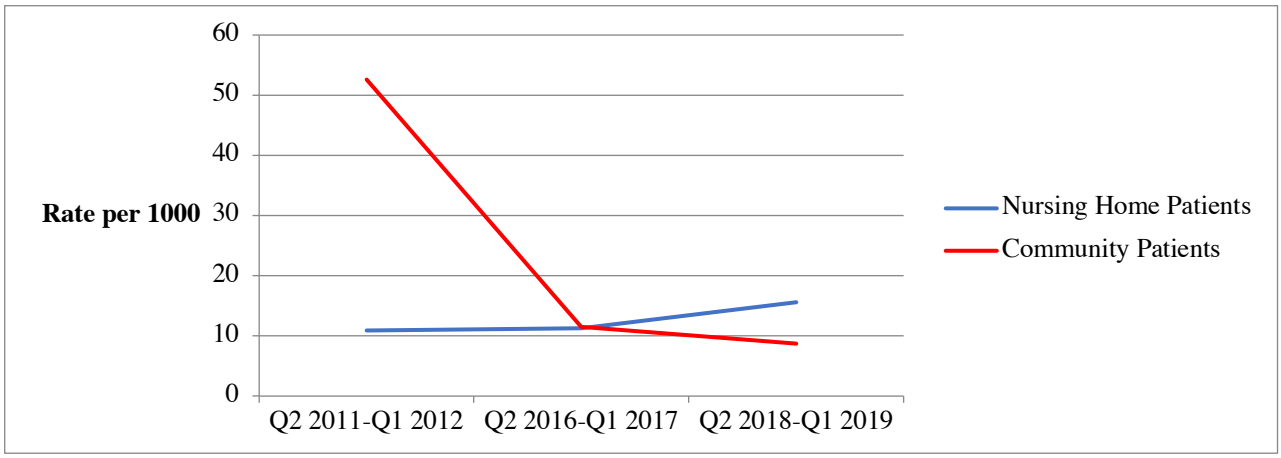

Figure 3: Rate of patients aged 85 and older receiving ≥2 HPA prescriptions stratified by residency

	11/12 to 16/17		16/17 to 18/19	
	Relative Risk (RR)	Relative Risk Change (RRR)	Relative Risk (RR)	Relative Risk Change (RRR)
Nursing Homes	0.98 (0.84, 1.15) p=0.41	NS	1.37 (1.17, 1.60) p <0.01	37% increase
Community	0.27 (0.25, 0.30) p<0.01	72% reduction	1.02 (0.93, 1.13) p=0.33	NS

Table 6: Relative risk ratio and relative risk reduction for patients aged 85 years and older stratified by residency status
NS= Indicates not statistically significant results

Among community patients aged ≥85, the rate of nursing home patients receiving ≥2 HPA prescriptions was 10.9 per 1000 in 11/12, 11.3 per 1000 in 16/17, and 15.6 per 1000 in 18/19 (Table 3, Figure 3). The rate of community patients receiving ≥2HPA prescriptions was 53.6 per 1000 in 11/12, 1.6 per 1000 in 16/17, and 8.7 per 1000 in 18/19 (Table 3, Figure 3). Further, from 11/12 to 16/17 nursing home patients over 85 years old had a statistically insignificant change in risk of receiving ≥2HPA prescriptions (Table 6). Nursing home patients in 18/19 had a 37% more risk of being prescribed ≥2HPA medications than those in 16/17 (Table 6). Community patients over 85 years old in 16/17 had 72% less risk of receiving ≥2HPA prescriptions than those in 11/12, and from 16/17

to 18/19 patients had a statistically insignificant change in the risk of being prescribed ≥2HPA medications (Table 6).

Discussion:

When looking at the number of patients identified as receiving ≥2HPA prescriptions, the percentage of nursing home patients is consistently smaller than those in the community. One would expect this trend, considering regardless of HPA use, more patients reside in the community versus nursing homes. However, it is of particular interest to note the contrasting trends in age band and residency status. Across all three time periods, the majority of nursing home patients receiving ≥2HPA prescriptions were over 85 years old. In comparison, the majority of community patients receiving ≥2HPA prescriptions were 65-74 years old. Again, this trend is expected; older patients are frailer with more complex conditions and, therefore, more likely to take several medications. Further, many of the HPA medications identified are antispasmodics or antipsychotics, utilized commonly in the older population for symptomatic control. Based on these assumptions, one would expect to see the rate of HPA medication use increase with age.

To begin discussing trends from 11/12 to 16/17, nursing home patients aged 65-84 and community patients aged ≥65 experienced a decrease in the rate of receiving ≥2HPA prescriptions. For these patients, the reduction in rates corresponds to a significant relative risk reduction. Meaning nursing home patients 65-84 and community patients ≥65 in 16/17 had less risk of receiving ≥2HPA prescriptions compared to the patients in 11/12. In continuation of this trend, nursing home patients aged 65-74 in 18/19 experienced a further

decline in rates and significant relative risk reduction compared to patients in 16/17. Relative risk reductions and a decrease in rates coincide with the implementation of NHS advice (2015-2017) to decrease the number of HPA medications prescribed to older adults. Therefore, the decline seen may suggest the beneficial effects of the NHS initiatives. In contrast, nursing home patients aged ≥85 from 11/12 to 16/17 showed a non-statistically significant change in relative risk and a small reduction in rates.

Next, from 16/17 to 18/19, one can see three different trends. First, in continuation of the trend seen above, nursing home patients aged 65-74 had a further decline in rates and relative risk reduction. Second, nursing home patients aged 75-84, community patients aged 65-74 and ≥85 years showed a non-statistically significant change in relative risk. This non-statistically significant change in relative risk suggests a plateau in the NHS efforts to decrease HPA prescribing among older adults. Meaning, the initial NHS advice reached its maximum effect, and all patients able deprescribed from HPA medications. Third, community patients 75-84 in 18/19 showed more risk of receiving ≥2HPA medications compared to patients in 16/17. The small relative risk increase in this population is concerning but mitigated by the fact that in previous years, 11/12 to 16/17, this same population showed a relative risk reduction. This small increase in rates suggests that this group needs further NHS guidance to maintain the reduction in relative risk seen in earlier years.

Finally, nursing home patients aged ≥85 in 18/19 showed increased rates and significantly more risk of receiving ≥2HPA prescriptions compared to patients in 16/17.

These results are concerning for several reasons. First, older patients are more vulnerable to experiencing polypharmacy and adverse drug events. Second, nursing home patients are frailer with more comorbidities, making them a subset of the population with the potential to experience the most harm from using multiple HPA and the most benefit from the NHS prescribing advice. Most likely, the increase in anticholinergic burden is due to HPA medications used for symptomatic control, such as antipsychotics for delirium and antispasmodics for urinary incontinence. Therefore, deprescribing may not be possible, explaining the lack of relative risk reduction in this population. Moving forward, nursing home patients over 85 years old may benefit from additional medication reviews to determine if HPA medicines prescribed are inappropriate. As well, it may also be that the older nursing home population was not appropriately targeted by the NHS prescribing advice, with younger patients benefiting more. Finally, the NHS may need to implement a more specific effort aimed at older nursing home patients.

Limitations:

As a review of a prescription claims database, this study has several limitations. First, this study could not identify the indications, dosages, or quantity prescribed with the HPA prescriptions. The presumed anticholinergic burden varies based on duration, dosage, or frequency of HPA medication use. These omissions limit the ability of this analysis to separate which medications were given as needed, potentially having a smaller effect of anticholinergic burden, versus more significant chronic therapies. Second, this dataset was unable to link the prescription of HPA medications to adverse patient outcomes. So, while this study inferred based on previous biological and clinical

studies that an increase in anticholinergic burden lead to an increase in side effects, this analysis was unable to demonstrate this phenomenon. Finally, nursing home and community patients are different in that nursing home patients are more likely to have complex comorbid conditions causing an increase in the number of prescriptions. One must consider this fundamental difference when drawing conclusions from this analysis.

Further Directions:

Building off the NHS NTI, this analysis demonstrated which patient populations benefited most and the least from the NHS prescribing advice on anticholinergics. With this study as a baseline, there are future pathways to determine how to improve NHS guidance on HPA prescribing. To aid in determining why the NHS prescribing advice was ineffective in nursing home patients aged 85 and older, further analysis could break this data down by individual HPA medications. This stratification may identify which medications are driving the increase in risk. Additionally, stratifying both community and nursing home patients by other factors such as gender, NHS health board, and HPA medication class may provide insight into which patients remain on HPA medications despite the NHS prescribing advice. Finally, this study analyzed only those patients with the highest anticholinergic burden. Further analysis could expand on this data by looking at patients with any degree of anticholinergic burden risk.

Conclusion:

From 2015 to 2017, Scottish NHS recommended against prescribing HPA to elderly patients, and deprescribe unnecessary HPA medications. This analysis shows the majority of elderly patients in Q2'2016-Q1'2017 residing in nursing homes and the community experienced less risk of receiving ≥2HPA prescriptions in comparison to patients Q2'2011-Q1'2012. Then from Q2'2016-Q1'2017 to Q2'2018-Q1'2019 the relative risk reduction plateaued. These trends suggest the beneficial effect of the NHS prescribing advice. Nursing home patients aged 85 and older in Q2'2018-Q1'2019 showed more risk of receiving ≥2HPA prescriptions in comparison to patients in Q2'2016-Q1'2017, suggesting that patients aged ≥85 in nursing homes are at risk for a higher anticholinergic burden, did not benefit from the NHS prescribing advice, and should be targeted for further action.

Appendix 1.

1. Amitriptyline
2. Amitriptyline HCl with perphenazine
3. Atropine sulfate
4. Benztropine mesylate
5. Chlorphenamines maleate
6. Clemastine
7. Clomipramine HCl
8. Clozapine
9. Cyproheptadine HCl
10. Darifenacin
11. Desipramine HCl
12. Doxepin
13. Epinephrine, Atropine, and papaverine
14. Flavoxate HCl
15. Fluphenazine Deaconate
16. Fluphenazine Enanthate
17. Fluphenazine HCl
18. Hydroxyzine Embonate
19. Imipramine HCl
20. Levomepromazine
21. Morphine with Atropine
22. Nortriptyline
23. Nortriptyline with Fluphenazine
24. Orphenadrine Citrate
25. Oxybutynin HCl
26. Phenylpropanolamine with Clementine
27. Procyclidine HCl
28. Promethazine HCl
29. Promethazine Teoclate
30. Thioridazine
31. Tizanidine HCl
32. Tolterodine

Citations:

1. Dean, A. G., Sullivan, K. M., Soe, M. M. (2013, April 6) *Open Source Epidemiological Statistic for Public Health,* Version 3.01. Retrieved from www.OpenEpi.com
2. National Records of Scotland (2020). *Mid-Year Population Estimates*. Retrieved from: nrscotland.gov.uk
3. Charlesworth, C. J. et al. (2015). Polypharmacy among adults aged 65 years and older in the United States: 1988-2010. *Journal of Gerontology Series: Biomedical Sciences and Medical Services*. 70(8), 989-995. DOI: 10.1093/Gerona/glv013
4. Nishtala, S. P., Salahudeen, M. S., Hilmer S. N. (2016). Anticholinergics: Theoretical and clinical overview, expert opinion on drug safety. *Expert Opinion on Drug Safety*. 15(6), 753-768. DOI: 10.1517/14740338.2016.1165664
5. Svoboda, J., Popelikova, A., & Stucklik, A. (2017) Drug interfering with muscarinic acetylcholine receptors and their effects on place navigation. *Frontiers in Psychiatry*, 8(215). DOI: 10.3389/fpsyt.2017.00215
6. American Geriatrics Society. (2019). American Geriatrics Society 2019 updated AGS Beers criteria for potentially inappropriate medication use in older adults. *American Journal of the American Geriatrics Society,* 00, 1-21. DOI: 10.1111/jgs.15767.
7. Scottish Government Polypharmacy Model of Care Group. (2018). Polypharmacy guidance, realistic prescribing 3rd edition. Scottish Government. Retrieved from therapeutics.scot.nhs.uk
8. National Institute for Health and Care Excellence. (2018). *Dementia: assess management and support for people living with dementia*. (NICE Guideline CG42). Available at: https://www.nice.org.uk/guidance/ng97
9. Qato, D. M., Alexander, G. C., Conti, R. M., Johnson, M., Schumm, P., Lindau S. T. (2008). Use of prescriptions and over-the-counter medications and dietary supplements among older adults in the United States. *Journal of the American Medical Association*, 300(24), 2867-2878. DOI: 1o.1001/jama.2008/892.
10. Koltz, U. (2009). Pharmacokinetic and drug metabolism in the elderly. *Drug Metabolism Review*, 41(2), 67-76. DOI: 10.1080/03602530902722679.
11. Mintzer, J., & Burns, A. (2000). Anticholinergic side effects of drugs in elderly people. Journal of the Royal Society of Medicine, 93, 457-4562. DOI: 10.1177/014107680009300903
12. Liberman III, J. A., (2004). Managing anticholinergic side effects. *Primary Care Companion to the Journal of Clinical Psychiatry,* 6(suppl 2), 20-23.
13. Flacker, J. M., Cummings, V., Mach, J. R., Bettin, K., Kiely, Dan., Wei, J. (1998). The association of serum anticholinergic activity with delirium in elderly medical patients. *American Journal of Geriatric Psychiatry,* 6(1), 31-41. DOI: https://doi.org/10/1097/00019442-199802000-00005
14. Tune, L. E. (2001). Anticholinergic effects of medications in elderly patients. *Journal of Clinical Psychiatry,* 62(suppl 21),
15. Feinberg, M. (1993). The problems of anticholinergic adverse effects in older patients. *Drugs & Aging*, 3, 335-348. DOI: https://doi.org/10/2165/00002512-199303040-00004

16. Britt, D. M., Day, G. S. (2016). Over-prescribed medications underappreciated risks: a review of the cognitive effects of anticholinergic medications in older adults. *Science of Medicine*, 111(3), 207-214.
17. Ancelin, M. L., Artero, S., Portet, F., Dupuy, A. M., Touchon, J., Ritchie, K. (2006). Non-degenerative mild cognitive impairment in elderly people and use of anticholinergic drugs: longitudinal cohort study. *The British Medical Journal,* 332(7539), 455-9. DOI: 10.1136/bmj.38740.439664.DE.
18. National Health Service Scotland. (2018). National Therapeutic Indicators 2018 [report]. Edinburgh, Scotland. Information Services Division.
19. *Information Services Division Scotland*. (n.d.). Information Services Division Scotland. Retrieved February 25, 2020, from idsascotland.org
20. Blazer II, D. G. (1983). The risk of anticholinergic toxicity in the elderly: A study of prescribing practices in two populations. *Journal of Gerontology,* 38(1), 31-35. DOI: 10.1093/geronj/38.1.31
21. Aspinall, S. L., et al. (2015. Epidemiology of drug-disease interactions in older veteran nursing home residents. *Journal of American Geriatric Society*. 63(1), 77-84. DOI: 10.1111/jgs.13197
22. Spore, D., Mor, V., Larrat, E. P., Hiris, J., Hawes, C. (1993). Regulatory environment and psychotropic use in board-and-care facilities: Results of a 10-state study. *Journal of Gerontology,* 51A(3), M131-M141. DOI: 10.1093/Gerona/51a.3.m131.
23. Mulsant, B. H., Pollock, B. G., Kirshner, M. (2003) Serum anticholinergic activity in a community-based sample of older adults. *Archives of General Psychiatry*, 60, 198-203. DOI: 10.1001/archpsyc.60.2.198
24. Anticholinergic Drugs. (November 2016). PrescQIPP Community Interest Company. Retrieved February 2020, from prescqipp.info
25. Alvares-Madrazo, S., McTaggart, S., Nangle, C., Nicholson, E., Bennie, M. (2016). Data resource profile: the Scottish national prescribing information system (PIS). *International Journal of Epidemiology*, 45(3), 714-715f. DOI: 10.1093/ije/dyq060.