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Deprescribing Anticholinergics in Primary Care Older Adults: Experience from Two Models and Impact on a Continuous Measure of Exposure

Running Title: Deprescribing Models in Primary Care

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ABSTRACT

BACKGROUND: Deprescribing interventions delivered through the electronic medical record have not significantly reduced the use of high-risk anticholinergics in prior trials. Pharmacists have been identified as ideal practitioners to conduct deprescribing, however little experience beyond collaborative consult models has been published.

OBJECTIVE: To evaluate the impact of two pilot pharmacist-based advanced practice models nested within primary care.

METHODS: Pilot studies of a collaborative clinic-based pharmacist deprescribing intervention and a telephone-based pharmacist deprescribing intervention were conducted. Patients receiving the clinic-based pharmacy model were aged 55 years and older and referred for deprescribing at a specialty clinic. Patients receiving the telephone-based pharmacy model were aged 65 years and older and called by a clinical pharmacist for deprescribing without referral. Deprescribing was defined as a discontinuation or dose reduction reported either in clinical records or through self-reporting.

RESULTS: The 18 patients receiving clinic-based deprescribing had a mean age of 68 years and 78% were female. Among 24 medications deemed eligible for deprescribing, 23 (96%) were deprescribed. The clinic-based deprescribing model resulted in a 93% reduction in median annualized total standardized dose (TSD), 56% lowered their annualized exposure below a cognitive risk threshold, and 4 (17%) of medications were represcribed within 6 months. The 24 patients receiving telephone-based deprescribing had a mean age of 73 years and 92% were female. Among 24 medications deemed eligible for deprescribing, 12 (50%) were deprescribed. There was

no change in the median annualized TSD, the annualized TSD was lowered below a cognitive risk threshold in 46%, and no medications were represcribed within 6 months. Few withdrawal symptoms or adverse events were reported in both groups.

CONCLUSIONS: Pharmacist-based deprescribing successfully reduced exposure to high-risk anticholinergics in primary care older adults, yet further work is needed to understand the impact on clinical outcomes.

Key words: deprescription, cholinergic antagonist, pharmaceutical services

Introduction

Anticholinergic medications are used by as many as 30% of primary care older adults in any given year, and as many as 60% when considering periods of up to 20 years in duration.[1-6] These medications have been consistently recognized by the American Geriatrics Society Beers Criteria™ as potentially inappropriate medications for older adults due to a higher risk of adverse events in older adults.[2,7,8] In addition to adverse effects of dry mouth, constipation, and urinary retention, anticholinergic medications have been associated with risks of cognitive impairment and dementia in multiple international studies.[1-5] Cognitive risks are considered cumulative, and thus may be conferred even from intermittent use over time. Additionally, quality measures have been developed by the Pharmacy Quality Alliance and incorporated by the Center for Medicare and Medicaid Services to report use of these high risk medications across populations.[9,10]

The cumulative nature of the adverse cognitive effects of anticholinergics reported in epidemiologic studies suggest a 30-50% increase in the risk of dementia among those using a minimum threshold of anticholinergics up to 20 years before the diagnosis of dementia.[1,3-5] The total standardized dose (TSD) has been used to quantify anticholinergic exposure in these epidemiologic studies, reporting the risk of dementia to be higher with a cumulative over 10-years TSD of 1095 and higher.[5] While no prospective, long-term randomized trial has yet shown the impact of a deprescribing intervention on either the TSD measure or cognition as an outcome, the TSD threshold

has potential as a clinical target to minimize the possible cognitive risks from anticholinergics.

In four prior studies, computerized decision support interventions were employed to reduce exposure to anticholinergic medications in hospitalized adults and primary care older adults.[11-14] These studies evaluating multicomponent interventions were not powered to identify differences in measures of deprescribing, however the consistent lack of change in medication exposure showed that these strategies were not successful in deprescribing anticholinergics or influencing clinical outcomes in either acute or outpatient care environments. While computerized decision support interventions have the advantage of scalability and reach, without clinical impact they may contribute to alert fatigue.

Human-intensive deprescribing interventions, in particular consultations conducted by pharmacists and/or physicians, are one approach to deprescribe medications.[15-17] Three studies employing pharmacist alone or pharmacist and physician collaborative consults to deprescribe anticholinergics in community-dwelling older adults have been reported.[17-19] Each of these studies followed a consult-based model in which recommendations to deprescribe were provided to a primary care or general practice physician, who was then responsible to implement the recommendations. Alternative approaches to deprescribing exist through collaborative practice agreements between pharmacists and physicians,

which may allow pharmacists prescriptive authority if agreed upon by both parties and allowed by state regulatory agencies. Such a role introduces the pharmacist as a deprescribing 'care coordinator', communicating with both patient and physicians and executing medication changes under verbal order directions from physicians. To our knowledge, pharmacist-based anticholinergic deprescribing interventions published to date have only followed consult-based models, introducing an opportunity to further explore alternative roles of pharmacists in deprescribing high-risk medications in older adults.

In an effort to aid two local health care institutions to reduce the prevalence of high-risk medications in compliance with clinical practice recommendations and quality standards, we developed and tested two pharmacist-based approaches for deprescribing in primary care. Our secondary goal was to describe the clinical impact of deprescribing interventions on various measures of deprescribing and cumulative use that may translate to cognitive risk thresholds.

Methods:

Study Design and Setting:

These pilot studies were conducted among patients receiving care within one of two large health systems in Indianapolis, Indiana. One location included a pharmacist and

physician collaborative drug therapy management program nested within the Eskenazi Health Healthy Aging Brain Center. Patients over the age of 55 years can be referred to this specialty clinic either by themselves or a provider with concerns about cognitive health, and referral to the pharmacist can be made to deprescribe medications with adverse cognitive effects, titrate antidepressants or dementia treatments, and to evaluate and support medication adherence. In this location, patients receive care through traditional face-to-face visits in a clinic setting with either the pharmacist alone or a multidisciplinary team including the pharmacist, a geriatrician with expertise in dementia care, a social worker, and a dementia care coordinator. In this setting, the pharmacist holds the authority to initiate, stop, and titrate medications under a collaborative practice agreement.

The second location, nested within primary care practices of Indiana University (IU) Health, included a pharmacist collaborating with primary care providers and communicating with patients through telephone-based visits. The pharmacist conducted visits by telephone and communicated with providers either through email or by telephone. In this setting, changes to medication orders could be performed either by the primary care provider or the pharmacist upon approval by the primary care provider.

Patients:

For the traditional clinic-based Eskenazi cohort, patients were included in the analysis if they were aged 55 years and older, receiving care in the Healthy Aging Brain Center, and

taking a medication eligible for deprescribing, defined as an anticholinergic with an Anticholinergic Cognitive Burden (ACB) score ≥ 2.[20] In the telephone-based cohort, patients were aged 65 years and older, receiving primary care from an IU Health physician, and using an anticholinergic medication for overactive bladder, which also holds an ACB score ≥ 2. Our health system partners chose to identify one class of high-risk medications to target for a pilot deprescribing trial, and collectively we chose anticholinergic overactive bladder medications due to the risks in older adults and availability of alternative therapies. These feasibility studies were conducted sequentially with a telephone-based intervention conducted from July 2017 to March 2018, and a clinic-based intervention conducted from September 2018 to June 2019. This work has been approved by the IU Institutional Review Board.

Intervention content and delivery:

At both sites, deprescribing of anticholinergics was conducted by the pharmacist through the following general steps: 1) Clarifying the indication for the anticholinergic, 2) Educating on potential risks of cognitive impairment in older adults, 3) Making a shared decision to deprescribe among patients, caregivers, and providers, 4) Identifying an appropriate alternative (not an anticholinergic or potentially inappropriate for older adults as defined by the American Geriatrics Society's Beers Criteria[7]) if desired, 5) Communicating the deprescribing plan with the appropriate provider(s), and 6) Monitoring and revising the plan as needed. The clinic-based pharmacist executed these steps within an approved collaborative practice agreement, which allowed medication

changes under the control of the pharmacist along with the prescription of alternatives as needed. The telephone-based pharmacist communicated steps of deprescribing with ordering providers and executed medication changes pursuant to the approval of the ordering provider. No templated language for education or motivational interviewing was employed, however study pharmacists were knowledgeable about common barriers to deprescribing, had experience titrating to alternative therapies, and had support of providers in the execution of the intervention.

Variables, Measures & Analysis:

From electronic medical records, demographic information was extracted including comorbidities and details about anticholinergic medications including name, strength, frequency, and indication. We reviewed clinical notes for results of deprescribing attempts, tolerability, and evidence of represcribing after six months. Attempted deprescribing was defined as evidence in the clinical note that a patient (or caregiver) agreed to and initiated a deprescribing attempt. Deprescribing was defined as a discontinuation or dose reduction reported either in clinical records or patient self-report.[21] Measures of deprescribing included proportion of medications deprescribed, proportion discontinued, relative change in continuous measures of anticholinergic exposure, and proportion of medications represcribed after six months. Represcribing up to six months following the last visit was determined by clinical notes or medication orders, regardless of whether the patient had follow-up visits with the pharmacist.

Cumulative measures of medication exposure have been previously used to characterize medications from multiple classes into a single measure.[3-6,22,23] A cumulative measure of anticholinergic exposure can be reported as an annualized TSD, calculated by multiplying the strength of medications, and standardizing strength against the minimum effective geriatric dose or the minimum effective daily dose,[24] and (in our report) extrapolating self-reported adherence to an annual duration. The TSD can be interpreted as the use of the lowest effective dose for a given period of time, often reported in number of days exposed. A study by Gray and colleagues identified a cumulative TSD of 1095 over a 10-year period was associated with a significantly increased risk of dementia.[5] Thus, extrapolating this 10-year measure to a one-year value (as a more immediate measure of exposure) suggests that the risk of dementia may be increased with merely 110 days (or more) of use of the minimum effective dose of a single anticholinergic in one year. The sum of all standardized doses for the ACB for 2 or 3 medications for each patient was aggregated to achieve a TSD. The annualized TSD is reported at each follow-up visit based on an active medication list or patient-reported medications six months after the last recorded visit with the pharmacist.

Adherence was determined from a hierarchy of sources: patient-reported adherence from pharmacist provider notes (preferred), refill history (if preferred method not available), and prescribed quantities (last resort). We assumed the adherence pattern was consistent over 365 days unless stated otherwise. Where frequency was vague or unreported, we

assumed once daily dosing for all medications so as not to over-inflate exposure through the use of minimum effective daily doses as a strength/dose standardization approach.

Represcribing was defined as any medical record evidence of restarting a deprescribed medication or resuming an original dose within six months of the last visit with the pharmacist. Indication and tolerability were also extracted from the electronic medical record.

We report descriptive statistics for demographic and clinical variables. No missing medication or demographic data was encountered. Means, medians, and associated measures of variability are reported for continuous variables and proportions for categorical variables. Because a variety of deprescribing outcomes have been reported in the existing literature, we present a comprehensive report of outcomes to encourage comparisons with other studies. We did not make comparisons between sites or over time as our sample size was not powered to detect meaningful differences, but rather to describe preliminary clinical experiences from two pharmacist-based approaches to deprescribing anticholinergics in primary care older adults.

Results:

Participant Characteristics:

Eighteen patients were included from the Eskenazi cohort receiving the clinic-based pharmacist intervention, , while 24 patients from the IU Health cohort received telephone-based pharmacist intervention. Table 1 reports demographic characteristics of all participants, with notable differences in the presence of cognitive impairment given the settings. In addition to a lower burden of cognitive impairment, patients receiving the telephone-based pharmacist intervention were generally older, more likely to be female, less racially diverse, and had a lower overall burden of comorbidities.

Among the 18 clinic-based patients, 35 anticholinergics with an ACB score ≥ 2 were identified, while 28 anticholinergics among 24 telephone-based patients were identified. Anticholinergics used by the clinic-based cohort were prescribed for a variety of indications, while those used by the telephone-based cohort were indicated exclusively for overactive bladder. Indications for anticholinergics used by the clinic-based cohort included overactive bladder (26%), pain (17%), nausea (11%), itching (8%), depression (8%), anxiety (6%), allergies (6%), and the following at a rate of 3% each: insomnia, tremors, cognition, irritable bowel, muscle spasm, and behaviors.

Measures of Anticholinergic Use:

Anticholinergics used by patients from both groups are reported in Table 2. The group receiving the clinic-based pharmacist intervention used 35 anticholinergic medications

with an ACB score of 2 or 3 at baseline, and the group receiving the telephone-based pharmacist intervention used 28 anticholinergics.

Deprescribing was deemed appropriate for 24 medications in both clinic-based and telephone-based groups (a total of 48 medications). Twenty-three medications were deprescribed (defined as a dose reduction OR discontinuation) in those receiving the clinic-based pharmacist intervention, while 12 medications were deprescribed in those receiving the telephone-based pharmacist intervention.

Table 3 reports deprescribing characteristics of both pharmacist-based deprescribing interventions. Among the 24 medications deemed appropriate for deprescribing, 96% were deprescribed in those receiving the clinic-based pharmacist intervention and 50% were deprescribed among those receiving the telephone-based intervention.

The population-based TSD was non-normally distributed, though we present both means and medians (along with respective measures of variability) for the purposes of comparisons with existing and future interventions. In those receiving the clinic-based pharmacist intervention, the median annualized TSD was reduced 93% (Figure 1) while the mean annualized TSD was reduced by 70% (Figure 2). In those receiving the telephone-based pharmacist intervention, the median annualized TSD was not reduced but the mean annualized TSD was reduced by 42%.

As noted previously, an increased risk of dementia has been associated with the use of anticholinergics at a TSD above 1095 over 10 years,[5] thus an extrapolated annualized threshold of cognitive risk is 110 TSD or less. At the time of the final visit, 56% of the clinic-based patients and 46% of the telephone-based patients achieved an annualized TSD below the theoretical cognitive risk threshold. There was little change in TSD six months after the last visit with the pharmacists.

The most common reasons documented for determining medications to be not appropriate for deprescribing were lost to follow-up, patient refused/nonadherent, and unsuccessful prior attempt to deprescribe. Among 4 medications deemed not appropriate for deprescribing in the telephone-based patients, all four fell out of the scope of the project as agreed upon by the partner institution, which was focused exclusively on medications used for overactive bladder symptoms.

Represcribing:

Four of 23 deprescribed medications were represcribed or restarted within six months of the last deprescribing visit among the group receiving the clinic-based pharmacist intervention (Table 2). Two medications for urinary incontinence were restarted by a urologist (symptom burden unknown), one medication was represcribed by a primary

care provider due to nightmares following dose reduction (paroxetine), and the fourth was represcribed by a dermatologist due to recurrence of symptoms (itching, managed with doxepin). In the telephone-based group, no deprescribed medications that were discontinued were represcribed following the last visit, however two medications for which the dose was reduced were increased due to symptom recurrence.

Discussion:

Both pharmacist-based deprescribing interventions successfully lowered the dose or discontinued high-risk anticholinergics in primary care older adults with durable reductions up to 6 months. With a discontinuation rate of 83% among medications attempted in the clinic-based population and 33% in the telephone-based population, our results provide feasibility of pharmacists deprescribing through collaborative practice models as a 'deprescribing coordinator'. Reductions in exposure experienced by the average patient could be described as a change from a medication such as amitriptyline 20 mg once daily for an entire year (two times the minimum effective geriatric dose of amitriptyline), to approximately 30 days of use in a given year, or 60 days at a reduced dose of 10 mg.

Pharmacists serve an important role in anticholinergic deprescribing interventions in primary care settings. A recent review by Nakham and colleagues identified that most interventions aiming to reduce anticholinergic burden in older adults included pharmacists either alone or as part of a team.[16] Two studies in this review describe pharmacists as a consultant, providing verbal recommendations to physicians who then execute recommendations at their discretion. While one study failed to show a significant reduction in the Drug Burden Index, a continuous measure of anticholinergic and sedative use,[19] a second showed a 56% reduction in the median score on the Drug Burden Index and a 15% reduction in the number of users of anticholinergic and sedative medications.[18] A third study by Moga and colleagues included a pharmacist as part of a clinical team providing care in an Alzheimer's Disease Center (similar to the clinic-based setting in this study) that also required primary care providers to execute recommendations. This trial reported a 36% reduction of the total Anticholinergic Drug Scale score.[17] Each of these consult-based models require primary care providers to execute the pharmacists' recommendations, which may limit the impact of the pharmacist on deprescribing rates and measures of high-risk medication use.[18,25]

In comparison, our clinic-based intervention resulted in a 93% reduction in the continuous measure of anticholinergic exposure (median annualized TSD; mean annualized TSD reduced by 70%) and discontinued 83% of the anticholinergics deemed appropriate for deprescribing. While the telephone-based group did not reduce the median annualized TSD, the mean annualized TSD was reduced by 42%, and 33% of

anticholinergics were discontinued. The advanced practice model used in these interventions, through which the pharmacist had authority to directly make medication changes, is perhaps the most appropriate explanation for differences between consult-based models reported in other studies. It should also be noted that patients receiving care from the clinic-based pharmacist intervention were receiving care in a specialty brain health clinic and were likely motivated to deprescribe anticholinergics to minimize risk factors for poor brain health, which may have inflated the deprescribing rates compared with other settings.

We also evaluated the sustainability of the deprescribing intervention by reporting represcribing rates within six months of the last visit with the deprescribing pharmacist. This measure has been poorly reported in related work, and recent evidence suggests represcribing may occur in up to 50% of deprescribing attempts up to 12 months.[26] While the clinic-based pharmacist intervention provided a list of medications for self-surveillance, neither approach in our studies executed post-deprescribing surveillance. Additional work is needed to both measure represcribing and better understand the sustainability of deprescribing.

Deprescribing trials are necessary to understand the impact of anticholinergics on important clinical outcomes, particularly long-term cognition.[27] While no randomized trial has yet discovered an improvement in cognition as a result of deprescribing

anticholinergics, sustained periods free of anticholinergic exposure will be extremely important when evaluating the impact on long-term cognition. Thus, represcribing rates and measures of anticholinergic exposure over time will be important to evaluate clinical outcomes. The annualized TSD, and its change over time, could be employed as a method to track exposure and ultimately a potential clinical target among users of anticholinergics. Two ongoing deprescribing trials will report valuable information on the ability of deprescribing interventions to influence continuous measures of exposure, as well as the clinical outcomes measured in response to deprescribing (ClinicalTrials.gov NCT04270474, NCT04121858).

Our findings have limitations worth noting. First, we used electronic medical records to report findings from a small feasibility study. While variables of medication use are readily available, other elements such as adverse events may be under-reported. Additionally, we utilized self-reported medication data from medical records to calculate cumulative measures, which may introduce recall and reporting bias that may have influenced our findings. Second, and as noted previously, it is unclear what measure and what level of anticholinergic reduction is required to influence clinical outcomes. Third, we report preliminary experiences from pilot trials, which include small sample sizes, and will need to be confirmed in other settings and with larger sample sizes. Lastly, although we report represcribing rates, we did not report incident prescriptions of narcotics, benzodiazepines, or other high-risk medications as an unintended consequence of deprescribing anticholinergics; this should be addressed in future deprescribing trials.

In summary, the impact of a deprescribing pharmacist with advanced practice capabilities may have a more significant impact on lowering the use of high-risk anticholinergics than pharmacists in consult-based models. Our findings support the development of deprescribing pharmacist interventions as an effective approach to reducing the use of anticholinergics, and the potential to apply these methods to any medications appropriate for a deprescribing attempt. Effective models of deprescribing are necessary to evaluate the impact on clinical outcomes resulting from deprescribing interventions.

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Table 1. Demographics and Baseline Characteristics of Both Study Cohorts

	Clinic-based deprescribing n=18	Telephone-based deprescribing n=24
Age		
Years, mean (SD)	67.8 (8.1)	72.8 (10.2)
Gender		
Female, N (%)	14 (78%)	22 (92%)
Race		
African American, N (%)	8 (44%)	1 (4%)
White, N (%)	10 (56%)	23 (96%)
Baseline Cognitive Diagnosis, N (%)		
Alzheimer's Disease or Related Dementia	3 (17%)	0 (0%)
Mild Cognitive Impairment	12 (67%)	1 (4%)
Normal Cognition	3 (17%)	23 (96%)
Comorbidities[†], N (%)		
Hypertension	18 (100%)	13 (54.1%)
Diabetes	10 (56%)	8 (33%)
Heart Disease[‡]	2 (11%)	11 (46%)
Stroke	4 (22%)	3 (12%)
Depression	16 (89%)	3 (12%)
Dyslipidemia[§]	15 (83%)	16 (67%)
Baseline Anticholinergic Use		
Total Number of ACh Drugs	63	32
Number of ACB Score 2+ Drugs	35	27
Number of ACh Drugs/Patient	3.5	1.1
Mean (SD) ACB Score	6.5	3.5
Annualized Mean (SD) TSD[¶]	829 (630)	502 (210)
Annualized Median (IQR) TSD[¶]	730 (779)	365 (365)
Number (%) of participants with ACh dose higher than MEGD	9 (50%)	8 (33%)

ACB = Anticholinergic Cognitive Burden; ACh = Anticholinergic; IQR = interquartile range; MEGD = Minimum effective geriatric dose; SD = standard deviation; TSD = Total standardized dose.

[†] Comorbidities were determined by diagnoses listed in medical records.

[‡] Defined as history of coronary artery disease, heart failure, or atrial fibrillation.

§ Determined by diagnosis or presence of statin in medication list.

¶ Example calculation of the TSD: Medication regimen = Paroxetine 20 mg once daily with a self-reported adherence of 85%.

Strength: Paroxetine 20 mg

Frequency: once daily

Adherence: 85% (taking 6 days/week or 312 days/year)

Minimum effective daily dose: 10 mg

(Total daily dose/Minimum effective daily dose)	x	(Adherence rate x 365)	=	TSD
(20 mg/10 mg)	x	(0.85 x 365)	=	624

Table 2. Anticholinergic-Specific Deprescribing Results

Clinic-based deprescribing (n=18)					
Drug	**Frequency**	**Deprescribing Initiated† (%)**	**Deprescribing Achieved‡**	**Discontinued**	**Re-prescribed§ (%)**
Amantadine	1	1 (100%)	1	0	0 (0%)
Amitriptyline	1	1 (100%)	1	1	0 (0%)
Benztropine	1	0 (0%)	0	0	0 (0%)
Cyclobenzaprine	3	2 (67%)	2	2	0 (0%)
Darifenacin	1	1 (100%)	1	1	0 (0%)
Dicyclomine	1	0 (0%)	0	0	0 (0%)
Diphenhydramine	2	1 (50%)	1	1	0 (0%)
Doxepin	1	1 (100%)	1	1	1 (100%)
Hydroxyzine	4	1 (25%)	1	1	0 (0%)
Imipramine	1	1 (100%)	1	1	0 (0%)
Meclizine	2	2 (100%)	2	2	0 (0%)
Methocarbamol	2	0 (0%)	0	0	0 (0%)
Nortriptyline	2	1 (50%)	1	1	0 (0%)
Olanzapine	1	1 (100%)	1	1	0 (0%)
Oxybutynin	5	5 (100%)	4	4	1 (25%)
Paroxetine	2	2 (100%)	2	1	1 (50%)
Promethazine	2	1 (50%)	1	0	0 (0%)
Solifenacin	2	2 (100%)	2	2	1 (50%)
Tropsium	1	1 (100%)	1	1	0 (0%)
Total	**35**	**24**	**23 (96%)**	**20 (83%)**	**4 (17%)**
Telephone-based deprescribing (n=24)					
Drug	**Frequency**	**Deprescribing Initiated† (%)**	**Deprescribing Achieved‡**	**Discontinued**	**Re-prescribed§ (%)**
Amitriptyline	1	0 (0%)	0	0	0 (0%)
Dicyclomine	1	0 (0%)	0	0	0 (0%)
Meclizine	1	0 (0%)	0	0	0 (0%)
Olanzapine	1	0 (0%)	0	0	0 (0%)
Oxybutynin	19	19 (100%)	11	8	2 (18%)
Tolterodine	5	5 (100%)	1	1	0 (0%)
Total	**28**	**24**	**12 (50%)**	**8 (33%)**	**2 (17%)**

† 'Deprescribing initiated' was defined as agreement between patient and pharmacist to deprescribe with taper schedule provided to patient.

‡ 'Deprescribing achieved' was defined as a dose reduction or discontinuation for any number of days.

§ Represcribed was defined as the restart of a discontinued medication, or return to original dose within six months of discontinuation or dose reduction.

Table 3. Summative Measures of Anticholinergic Deprescribing by Site

	Clinic-based deprescribing n=18	Telephone-based deprescribing n=24
Total Number of ACB 2/3 medications	35	28
Number of medications deemed appropriate for deprescribing	24	24
Number (%) of medications deprescribed[†]	23 (96%)	12 (50%)
Number (%) of deprescribed medications discontinued	20 (83%)	8 (33%)
Number (%) of deprescribed medications represcribed at 6 mo.	4 (17%)	0 (0%)
Annualized mean (SD) TSD at baseline	829 (630)	502 (210)
Relative reduction in mean annualized TSD from baseline to last visit	70%	42%
Annualized median (IQR) TSD at baseline	730 (778)	365 (365)
Relative reduction in median annualized TSD from baseline to last visit	93%	0%
Proportion with anticholinergic TSD below theoretical cognitive risk threshold[‡] **at baseline**	2 (11%)	0 (0%)
Proportion with anticholinergic TSD below theoretical cognitive risk threshold[‡] **at last visit**	10 (56%)	11 (46%)

ACB = Anticholinergic Cognitive Burden; IQR = interquartile range; SD = standard deviation; TSD = total standardized dose.

***** Deprescribing defined as dose reduction or discontinuation.

[‡] Risk threshold defined as annualized TSD of 110 or lower.

Figure Legends:

Figure 1. Median annualized TSD by group and time. TSD = total standardized dose.

Figure 2. Mean annualized TSD by group and time. TSD = total standardized dose.

Figure 1

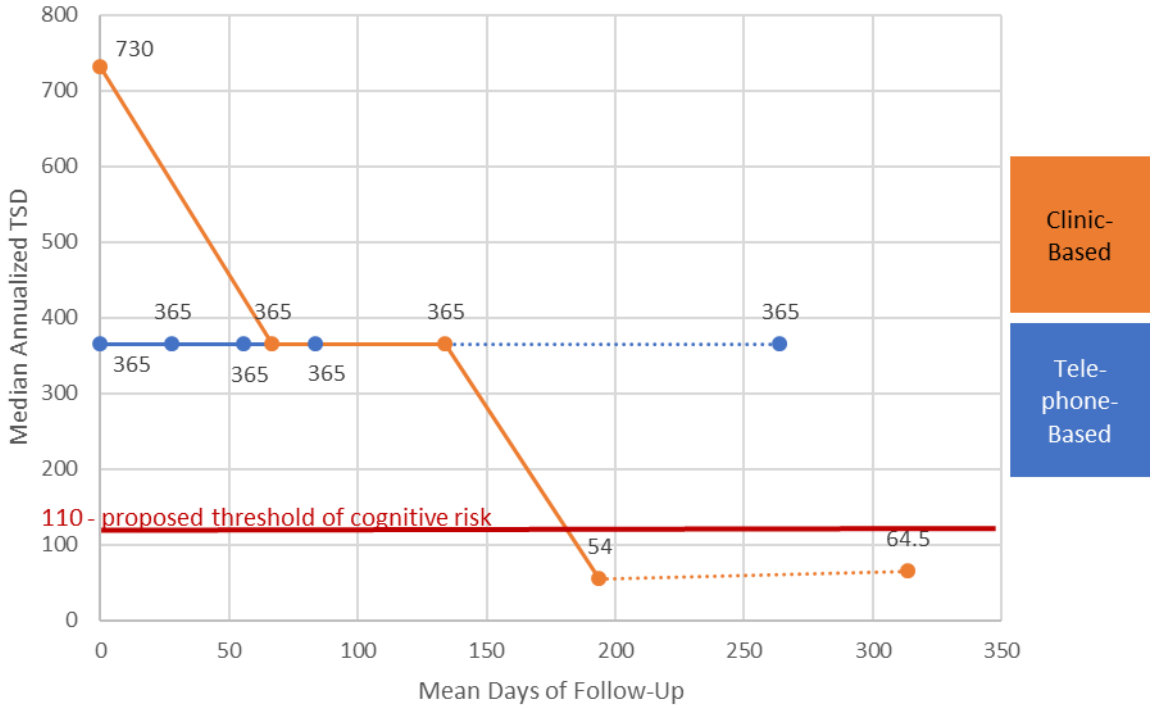

Figure 2: