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Effect of Collaborative Dementia Care on Potentially Inappropriate Medication Use: Outcomes from the Care Ecosystem Randomized Clinical Trial

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Abstract

Introduction—Potentially inappropriate medications (PIMs) cause adverse events and death. We evaluate the Care Ecosystem collaborative dementia care program on medication use among community-dwelling persons living with dementia (PLWD).

Methods—Secondary analysis of a randomized clinical trial comparing Care Ecosystem to usual care on changes in PIMs, over 12 months between March 2015 and May 2020. Secondary outcomes included change in number of medications, clinically relevant PIMs and anti-dementia medications.

Results: Of 804 PLWD, N=490 had complete medication data. Care Ecosystem resulted in significantly fewer PIMs compared to usual care (−0.35; 95% CI, −0.49 to −0.20; P <.0001). Number needed to prevent an increase in 1 PIM was 3. Total medications, PIMs for dementia or cognitive impairment, CNS-active PIMs, anticholinergics, benzodiazepines and opioids were also fewer. Anti-dementia medication regimens were modified more frequently.

Conclusion: The Care Ecosystem medication review intervention embedded in collaborative dementia care optimized medication use among PLWD.

Trial Registration: ClinicalTrials.gov identifier: NCT02213458

Keywords

dementia; potentially inappropriate medications; polypharmacy; anti-dementia medications; medication review; pharmacist

1 INTRODUCTION

Potentially inappropriate medication (PIM) use and polypharmacy are highly prevalent (14–74%) and dangerous among persons living with dementia (PLWD), leading to worsening cognition, adverse drug events, and death.[1–8] While safe and effective medication use is a goal for all patients, PLWD routinely require more attention and closer monitoring given complex comorbid conditions, behavioral and psychological symptoms of dementia (BPSD), and evolving symptoms with disease progression.[9] However, dementia care and medication prescribing is frequently suboptimal because it is reactive, crisis-oriented, fragmented, and focused on deficits and losses.[10] Consistent medication oversight is often lacking, while safer medication alternatives and non-drug treatments are not reliably trialed. As a result, PIMs use and polypharmacy contribute to substantial medical, psychological, and financial challenges for PLWD, their caregivers, and the healthcare system.[11–13]

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Efficacy and safety of medications can be affected by comorbidities, age-related physiologic changes involving drug pharmacokinetics and pharmacodynamics, and communication challenges between providers, PLWD, and caregivers.[13] Proactive medication management requires collaboration and continuity. Pharmacist-led medication reviews with recommendations sent directly to prescribing providers have been shown to reduce medication-related problems, inappropriate prescribing, and facilitate deprescribing efforts.[14–19] Medication recommendations include minimizing or avoiding the use of anticholinergics,[6, 8, 20, 21] antipsychotics,[1, 8, 22] sedatives,[8, 20, 22] and other central nervous system (CNS)-active drugs,[8, 22] all of which can worsen cognition, increase fall-related injuries, and increase risk of mortality in PLWD.[22, 23] More research on the impact of PIMs and polypharmacy on clinical and patient important outcomes as well as successful interventions to optimize medications for PLWD are needed.[13]

The Care Ecosystem is a collaborative dementia care program that improved quality of life, reduced emergency department use among PLWD and improved caregiver well-being in a randomized clinical trial[24] and is among the most effective dementia care interventions.[25] A unique feature of the Care Ecosystem is a medication review intervention that aims to monitor and reduce inappropriate or problematic medications, enhance PLWD, caregiver, and healthcare provider knowledge about the patient's medications, and provide strategies to optimize medication outcomes. We report for the first time the effectiveness of the Care Ecosystem medication review intervention aimed at reducing PIMs and polypharmacy among PLWD.

2 METHODS

2.1 Study Design

Secondary analysis of a multicenter, single-blind, randomized clinical trial (RCT) comparing a telephone-based collaborative dementia care program, the Care Ecosystem (CE), with usual care (UC) delivered over 12 months for community-dwelling PLWD-caregiver dyads. Design, protocol, and primary outcomes of the Care Ecosystem clinical trial have been published.[24] Enrollment occurred between March 20, 2015 and May 16, 2019, with a last follow-up date of May 16, 2020. All study procedures and consent materials were approved by the Institutional Review Boards at the University of California, San Francisco and University of Nebraska Medical Center. Dyads, including PLWD, or their legally authorized representative, and caregivers provided written informed consent prior to participating in the trial.

2.2 Study Participants

Eight hundred and four PLWD-caregiver dyads were enrolled in the Care Ecosystem trial, where 780 were initially randomized and 24 additional participants were randomized in an extension of the trial (Supplement Table 1). All participants were randomized (2:1) to receive the Care Ecosystem medication review intervention or usual care over 12 months. To be eligible, participants had to be 45 years or older; have a diagnosis of dementia; reside in California, Nebraska, or Iowa; speak English, Spanish, or Cantonese; have Medicare or Medicaid insurance; and have a primary caregiver. Demographic, medication, and survey

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data was collected prospectively by telephone in the participant's preferred language (English, Spanish, or Cantonese). We excluded participants with missing medication lists (no medical record medication list was available within 6 months of baseline or 12-month follow up dates) and participants who were enrolled in hospice, died, withdrew, or no longer met eligibility criteria.

2.3 Medication Data Sources

Comprehensive medication data were obtained from retrospective chart review of routinely collected medical records. We collected data on the total number of medications listed in the medical record, including prescription and over-the-counter medications, dietary supplements and herbal products, that were scheduled or taken as needed. We collected baseline and follow-up (12-month) medication lists for participants with complete data sets. Medication lists were collected close to participants' baseline dates (mean difference 22.1 days +/− 32.9 days) and follow-up dates (mean difference 28.6 days ± 34.6 days), and the mean time between baseline and follow-up medication lists was 12 months (mean = 12.4 +/− 1.8 months). There were no differences in the timing or method of medication list ascertainment by treatment group.

2.4 Intervention

The Care Ecosystem medication review intervention was delivered by telephone over 12 months by an interprofessional care team that included unlicensed care team navigators (CTNs) with training in dementia as the primary point of contact, and licensed dementia specialists (pharmacist, advanced practice nurse, and social worker) who provided supervision and direct consultation to the dyad as needed.

The medication review intervention was protocol-guided and supported by a cloud-based database with integrated software from mHealthCoach© and Salesforce© that was customized to support patient management and current medication information. The care team assisted with proactive medication monitoring by tracking and reducing inappropriate or problematic medication use; optimizing anti-dementia medications; enhancing participant, caregiver, and prescribing provider knowledge about the PLWD's medications; and recommending strategies to optimize medication therapy with prescribing providers (Figure 2 and Figure 3).[24, 26]

After randomization to the Care Ecosystem, dyads were assigned a CTN who obtained a comprehensive medication history during initial care planning and recorded it in the study database. A pharmacist or trained clinician then reviewed the participant's active medications within the database, including prescription and over-the-counter medications, dietary supplements, and herbal products. On average, CTNs followed up monthly to screen for medication changes, questions, side effects, adverse drug events, lack of efficacy, and other medication-related problems. When a PLWD experienced major care transitions, such as a hospitalization, rehabilitation stay, or long-term care placement, CTNs repeated a full comprehensive medication review.

The care team discussed medication use, medical history and relevant vitals and labs with the dyad and reviewed medical records when available. Personalized medication

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care plans were collaboratively developed by the care team and included a current list of medications and dosing calendar along with drug education handouts and the pharmacist's counseling and recommendations. Drug education handouts included general information on medication adherence, safety and costs, an overview of anti-dementia medications, and medications to avoid that can worsen memory or cognition. Counseling consisted of medication use instructions, monitoring parameters for safety and efficacy of medications, and addressing adherence issues or costs. Recommendations included strategies to optimize medication therapy, such as stopping or starting medications, adjusting doses, or substituting unnecessary, potentially inappropriate, or high-risk medications for safer alternatives or non-pharmacological strategies. Medication care plans were sent by the CTNs directly to the dyad and to the PLWD's primary care provider or other prescribing providers. The dyad was encouraged to review the personalized medication care plan with their providers. Medication reviews and care plans were completed following enrollment (months 0–3) and again when there were medication changes during transitions of care, or if the dyad reported changes or had questions about their medications. The care team did not prescribe nor deprescribe medications for PLWDs or document in the medical record.

Participants in usual care were sent quarterly newsletters with general dementia-related articles, and received contact information for national caregiver, Alzheimer's, and aging associations. For the duration of the clinical trial, all participants continued to receive health care and services from their usual healthcare providers.

2.5 Potentially Inappropriate Medications

PIMs were defined by the American Geriatrics Society 2019 Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults,[23] an explicit tool for identifying medications where risks may outweigh benefits for adults aged 65 and over. We included 33 participants < 65 years because adverse effects and risks with PIMs are concerning among persons with dementia regardless of age (e.g., anticholinergics, benzodiazepines, antipsychotics, opioids).

PIMs were coded according to the 2020 edition of American Hospital Formulary Service Drug Information (AHFS DI®) Essentials™ therapeutic class. (A full list of PIMs drug classes is included in Supplement Table 2). We also evaluated PIMs for dementia or cognitive impairment, and CNS-active drugs to be avoided in persons with dementia, delirium, or a history of falls and fractures according to the 2019 Beers Criteria.[23] Due to an increased risk of cognitive decline, medications with anticholinergic properties were identified using the Anticholinergic Cognitive Burden (ACB) Scale.[27] The ACB Scale produced a summative score for medications with no (score of 0), possible (score of 1), and definite (score of 2 or 3) anticholinergic effects. The ACB score for each participant was computed by summing these values for each recorded medication. Some medications belonged to more than one of these categories.

Outcome Assessments—The primary outcome was the change in the number of PIMs obtained from medical records, and evaluated from baseline to follow-up. Prespecified secondary outcomes included change in the total number of medications, PIMs to be

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avoided in dementia or cognitive impairment[23], CNS-active drugs to be avoided in persons with dementia, delirium, or a history of falls and fractures[23], summative ACB Scale score[27] and number of prescriptions for antipsychotics, benzodiazepines, and opioids. We also included a binary indicator of whether or not a participant's use of anti-dementia medications changed from baseline (i.e., started, stopped or changed treatment with an acetylcholinesterase inhibitor, donepezil, galantamine, rivastigmine and/or NMDA receptor antagonist, memantine).

Statistical Analysis—Descriptive statistics were used to summarize participant demographics, clinical characteristics, and medication exposures at baseline. Participants were analyzed by the group to which they had been randomized after excluding participants according to criteria above (complete case analysis, N=490). To determine if the complete case analysis sample differed from the total RCT population (N=804) at baseline in demographic (age, gender, race, ethnicity, region of residence, educational level, baseline dementia stage, number of comorbidities) and outcome variables (number of medications and PIMs), we conducted a chi-square goodness-of-fit test. Variables with continuous data were dichotomized at the mean, median, or none versus one or more. There were no significant differences between any demographic or outcome variables (all $p>0.05$). In order to examine whether the missing data for medications followed a pattern based on covariates or intervention groups, an analysis using Little's MCAR test was applied.[28] The P value from this analysis, including all covariates, was not significant ($P = 0.211$) including all covariates for medications, demographics, and clinical data. Sensitivity analyses including separate groups of covariates all had higher P values than the overall MCAR test. This indicates that we can conclude no patterns existed and the missing data are missing completely at random.

Analysis of covariance (ANCOVA) was used to evaluate change from baseline to follow up in the mean number of PIMs prescriptions between groups for our primary and secondary outcomes. Baseline values of the medication outcome variable were included as a covariate in all analyses.[29, 30] We also adjusted for age, gender, region of residence, baseline dementia stage[31], and total number of comorbidities (Table 1). Comorbidities were defined by the Charlson Comorbidity Index[32] along with depression, hypercholesterolemia, hypertension, vascular disease, history of pneumonia, or other self-reported comorbidity.[33, 34] All P values were 2-sided. The primary analysis test of significance was conducted with a threshold of .05. P values for secondary medication outcomes analyses were unadjusted for multiple comparisons. We examined the distribution of the variables and, as a sensitivity analysis, transformed non-normally distributed variables (participant age in years squared and baseline dementia stage square rooted). There were no differences between the models with untransformed and transformed variables. Untransformed results are reported. To evaluate anti-dementia medication use, adjusted odds ratios were calculated using the proportion of participants in each group who changed their use of anti-dementia medications at follow-up. Appropriate medication adjustments can include starting or adding anti-dementia medications if indicated or stopping because of side effects/lack of benefit. Statistical analyses were carried out using STATA V.14 (StatCorp, College Station, TX, USA).

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3. RESULTS

3.1 Study Participants

Among 804 PLWD enrolled in the Care Ecosystem trial, 527 were randomized to receive Care Ecosystem and 277 were randomized to receive usual care (Figure 1). A total of 490 participants (304 [58%] CE; 186 [67%] UC) had medical record medication lists available for analysis at baseline and follow-up (average 12 months). Reasons for exclusion included missing medication lists (153 [29%] CE participants; 64 [23%] UC participants) or hospice medication lists (2 [0.4%] CE; 4 [1%] UC). Of participants who had baseline medication lists available, participants who died (47 [10%] CE; 20 [8%] UC), withdrew (14 [3%] CE; 2 [0.8%] UC), and no longer met eligibility criteria (7 [1%] CE; 1 [0.4%] UC) were also excluded.

More women were in CE vs UC (176 [57.9%] CE; 90 [48.4%] UC). All other baseline demographics, clinical characteristics, and medication exposures were similar between treatment groups (Table 1). The mean (SD) age of participants at baseline was 77.1 (9.1) years; 266 (54%) were women; 49 (10%) self-identified as being of Hispanic, Latinx, or Spanish origin; and 287 (59%) PLWD-caregiver dyads resided in California. At baseline, 66% of participants were prescribed one or more PIMs with a mean (SD) of 1.5 (1.6) PIMs, 10.4 (5.2) medications, and 1.5 (1.8) ACB Scale score.

Outcome Assessments—After adjusting for age, gender, region of residence, dementia stage, comorbidities, and baseline value of the medication outcome variable, the Care Ecosystem intervention resulted in significantly fewer PIMs prescriptions compared to UC (−0.35 PIMs; 95% confidence interval [CI], −0.49 to −0.20; P <.0001) after 12 months (Table 2). The number needed to treat to prevent an increase in one PIM was 3.[35] Similarly, the total number of medications increased significantly less in the Care Ecosystem (−0.53; 95% CI, −0.92 to −0.14; P = .008) when compared with usual care (Table 2). The percentage of PLWD in the Care Ecosystem taking 10 or more medications increased by 2% (from 52% to 54%), compared to a 5% increase (from 49% to 54%) in the usual care group.

All secondary PIMs-related medication outcomes significantly increased more in usual care than Care Ecosystem after 12 months. Care Ecosystem participants received fewer PIMs for dementia or cognitive impairment (−0.14; 95% CI, −0.23 to −0.05; P = .002) and CNS-active PIMs (−0.28; 95% CI, −0.42 to −0.14; P <.0001) than usual care participants at the end of the 12-month period (Table 2). ACB Scale score significantly increased more by 0.20 points in usual care than Care Ecosystem 95% CI, −0.39 to −0.01; P =.035) after 12 months. Additionally, compared to usual care, we found significant decreases in the number of prescriptions for benzodiazepines (−0.05; 95% CI, −0.09 to −0.01; P =.008) and opioids (−0.09; 95% CI, −0.14 to −0.03; P =.002) but not antipsychotics (−0.03; 95% CI, −0.08 to 0.00; P =.126), although a reduction was observed (Table 2). Table 3 summarizes the most common changes in PIMs for dementia or cognitive impairment between baseline and follow-up. The number of participants and the total number of PIMs for dementia or cognitive impairment decreased in the Care Ecosystem compared to increases in usual care.

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After 12 months, changes in prescriptions for anti-dementia medications were more likely to occur in the Care Ecosystem (26.3%) compared to usual care (16.7%) (adjusted odds ratio 1.82; 95% CI, 1.14 to 2.92; P=−.012). Changes included starting a new anti-dementia medication if they were not prescribed one at baseline, addition of an anti-dementia medication if previously taking one at baseline, or stopping an anti-dementia medication from baseline. Changes occurred more frequently in the Care Ecosystem for acetylcholinesterase inhibitors, memantine or both (Supplement Table 3).

4. DISCUSSION

In this 12-month trial of the Care Ecosystem, the medication review intervention embedded in a collaborative dementia care program significantly reduced the number of PIMs among community-dwelling PLWD compared to participants receiving usual care, with a number needed to treat to prevent an increase in one PIM of 3.

High rates of PIMs (66%) and polypharmacy (89%) were common in our study population, consistent with other studies.[1–7, 22] This demonstrates the need for proactive medication management and monitoring to reduce PIMs and medication burden in this vulnerable population. As expected, the total number of medications and PIMs drug classes increased over time. Yet, for those receiving Care Ecosystem medication reviews, rates of total medications and PIMs use increased significantly less compared to usual care for all PIMs drug classes we evaluated, except for antipsychotics for which we found a trend. Although the Care Ecosystem emphasizes non-pharmacological treatment for behavioral and psychological symptoms of dementia, the lack of significance for antipsychotics may reflect the difficulty in managing these symptoms. It is critical that PIMs be avoided in PLWD due to adverse effects on cognition and increased risk of falls and fractures. The Care Ecosystem medication review intervention effectively prevented an increase in the use of CNS-active and anticholinergic medications, and decreased benzodiazepines and opioids among PLWD.

While reducing or minimizing PIMs and polypharmacy are important, along with non-pharmacological interventions to help manage BPSD, prescribing anti-dementia medications may also help improve cognition and management of agitation, aggression, psychosis, depression, anxiety, delusions, and apathy.[36] A recent study examining rates of anti-dementia medications prescribed through pharmacies in Japan found the use of acetylcholinesterase inhibitors, memantine, and particularly their combination was associated with a reduction in the use of psychotropic PIMs.[37] In this trial, the Care Ecosystem medication review intervention was more likely to start, add or stop anti-dementia medications compared to usual care. Actively managing anti-dementia medications to ensure their effectiveness and safety is crucial to improving quality of life and managing BPSD in PLWD.[38]

Randomized trials of other interventions have encountered challenges in deprescribing PIMs[39] or demonstrated efficacy in improving medication use among PLWD. Moga et al implemented a patient-centered, pharmacist-physician team medication therapy management program in an Alzheimer’s clinic which decreased use of inappropriate anticholinergic medications.[14] Among nursing home patients with dementia in the Netherlands, van der

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Speck et al implemented a structured medication review every 6 months by pharmacists, physicians, and nurses, which improved the appropriateness of psychotropic medications for neuropsychiatric symptoms.[16] Both of these interventions targeted the discontinuation of specific medication classes (i.e., anticholinergics or psychotropics). In Germany, a home-based, nurse-led dementia care management program improved the use of anti-dementia medications, but had no effect on PIMs.[40] In contrast to prior trials, the Care Ecosystem demonstrated a broader impact by reducing multiple PIMs drug classes and optimizing anti-dementia medications, along with improving PLWD quality of life, health care use, and caregiver well-being.[24]

We believe that being embedded in a longitudinal, comprehensive dementia care program synergistically contributed to the success of our Care Ecosystem medication intervention, and may make it appealing to health systems leaders and other stakeholders who are looking to improve not only medication management but also overall dementia care. In the Care Ecosystem model, CTNs build rapport and establish ongoing relationships with dyads. Their care calls incorporate structured medication reviews and regular screening for safety or behavior concerns and medication changes. CTNs organize and clarify medications for PLWD who often have multiple prescribing providers. The care team develops a holistic view of the dyad's health and social situation by working with dyads and providers on selecting, personalizing, and monitoring responses to pharmacological and non-pharmacological treatments. The Care Ecosystem medication review intervention provides education, expert recommendations, proactive medication monitoring, and non-pharmacological strategies to optimize dementia care. While the medication interviews were conducted by the unlicensed CTNs, medication changes and problems were always reviewed by our dementia specialists and discussed with the dyad and their providers as appropriate. The Care Ecosystem model has proven to be cost efficient[41] and among the most effective dementia care interventions with previously reported effects on patient quality of life, emergency room visit use, and caregiver well-being.[24, 25] Our study identifies another major benefit of this care model: its broad impact on medication optimization and safety through synergism between our medications reviews and collaborative dementia care.

Limitations

Our study has several limitations. First, we chose to evaluate the number of medications over 12 months using medical record medication lists. Medical record medication lists can be outdated, incomplete, or not fully accurate, and laboratory results, diagnosis codes or indications, and previously-tried medications may not be entered systematically.[42–44] We minimized bias in outcomes by standardizing our medical record data collection and review protocols for the intervention and control groups. Also, we were not able to evaluate the appropriateness of the medication regimen, the lowest effective dose, or as needed medication use. This may cause an under- or over-identification of PIMs that are clinically justifiable, such as the use of antipsychotics as second-line therapy after non-pharmacological and first-line pharmacological therapies have failed. Second, PLWD in our study continued to receive routine care from their primary providers. Medication adjustments were ultimately made at the discretion of these providers, which may differ from efficacy, safety, and cost-savings recommendations made by the Care Ecosystem team.

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Furthermore, this study only includes community-dwelling PLWD who identify a caregiver, and may not generalize to other dementia populations.

Conclusion

Telephone-based collaborative dementia care delivered by CTNs and dementia specialists over 12 months significantly reduced the number of PIMs among community-dwelling PLWD compared to usual care. In the Care Ecosystem medication review intervention, unlicensed CTNs periodically queried caregivers for medication lists and concerns, incorporated interprofessional teamwork with pharmacists, nurses, and social workers, and developed and kept up-to-date medication plans that were integrated into the PLWD's overall dementia care. This personalized medication plan was communicated with dyads and prescribing clinicians along with care plans that addressed the PLWD's medical needs, challenging behavioral symptoms, caregiver needs, complex legal and financial circumstances, and safety concerns. Given the potential for adverse cognitive effects and medication-related problems in this population, there is a growing need for proactive medication management to optimize medications and reduce PIMs for community-dwelling PLWD with the aid of their caregivers. This study provides promising insight into a PIMs reduction strategy and medication optimization intervention for this vulnerable patient population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data Sharing Statement:

See Supplement 3.

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Research in Context

Systematic review:

The authors reviewed published literature on interventions to reduce potentially inappropriate medications (PIMs) among persons living with dementia (PLWD). Specific medication classes of anticholinergics or psychotropics have decreased in some studies and one study improved the use of anti-dementia medications but had no effect on PIMs.

Interpretation:

Our collaborative dementia care medication review intervention significantly reduced multiple PIMs drug classes and modified anti-dementia medication regimens more frequently among community-dwelling PLWD after 12 months compared to usual care. In addition to improving PLWD quality of life, health care use, and caregiver well-being, the Care Ecosystem collaborative dementia care program with medication review has the potential to optimize medication use.

Future directions:

The Care Ecosystem collaborative dementia care program with medication review is being implemented at various healthcare systems. Its impact on medication use in PLWD across multiple sites will be evaluated.

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Highlights

- Compared to usual care, the Care Ecosystem medication review intervention prevented increases in potentially inappropriate medications (PIMs).
- Use of anticholinergics, benzodiazepines and opioids were significantly reduced, with a trend for antipsychotics.
- Anti-dementia medications were adjusted more frequently.
- The Care Ecosystem medication review intervention embedded in collaborative dementia care optimized medication use.

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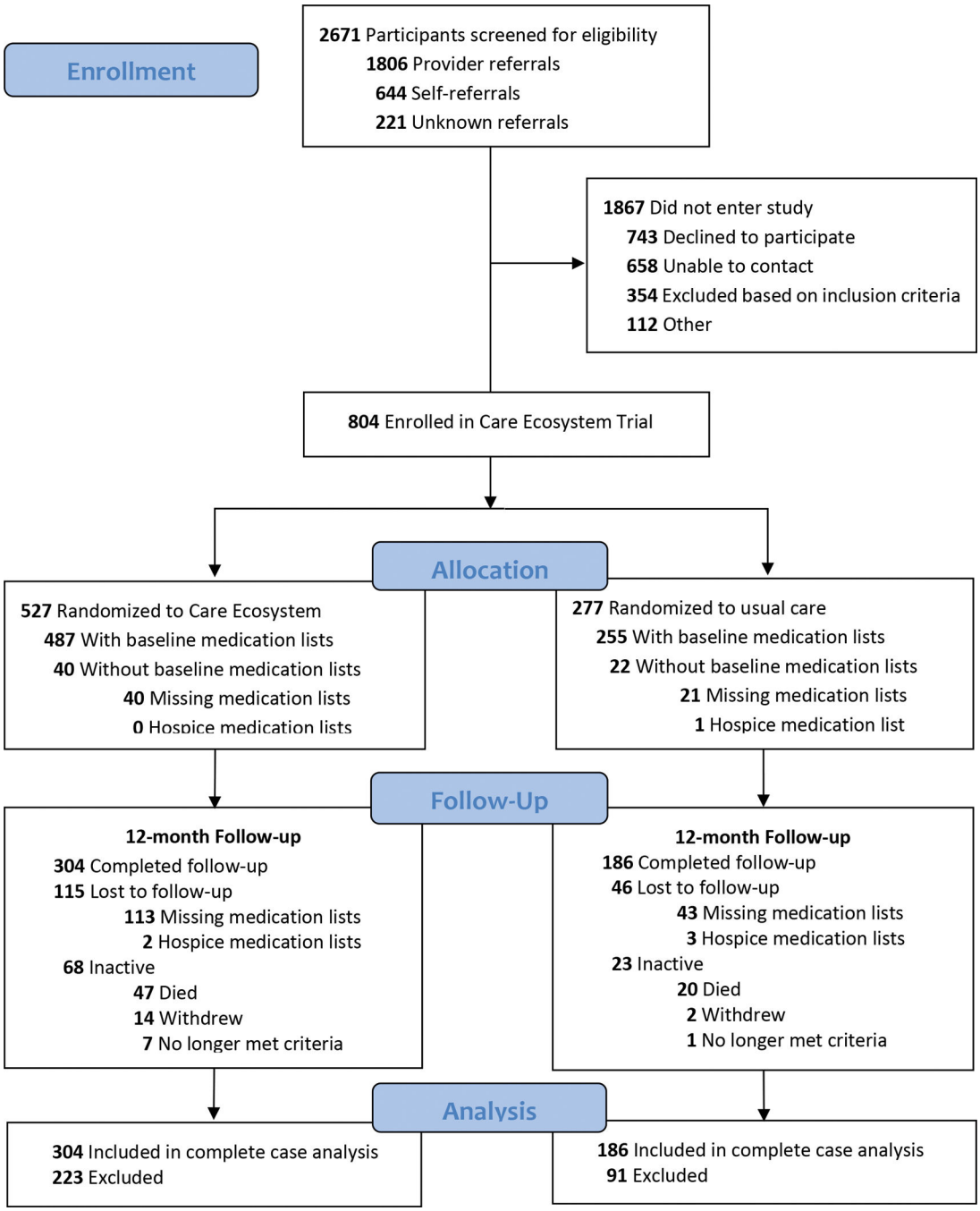

Figure 1.
CONSORT Flow Diagram

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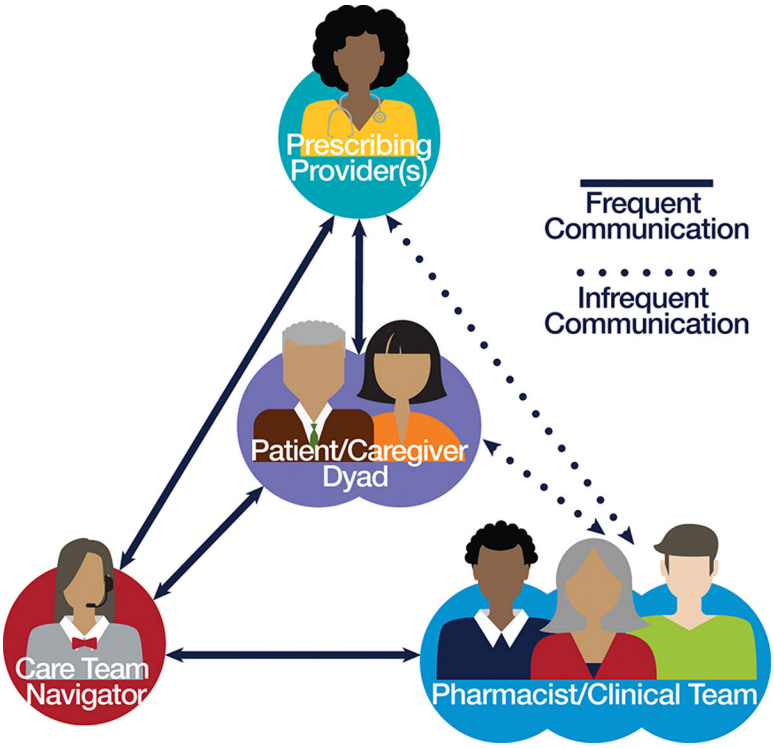

Figure 2.
The Care Ecosystem Medication Review Intervention and Monitoring Process

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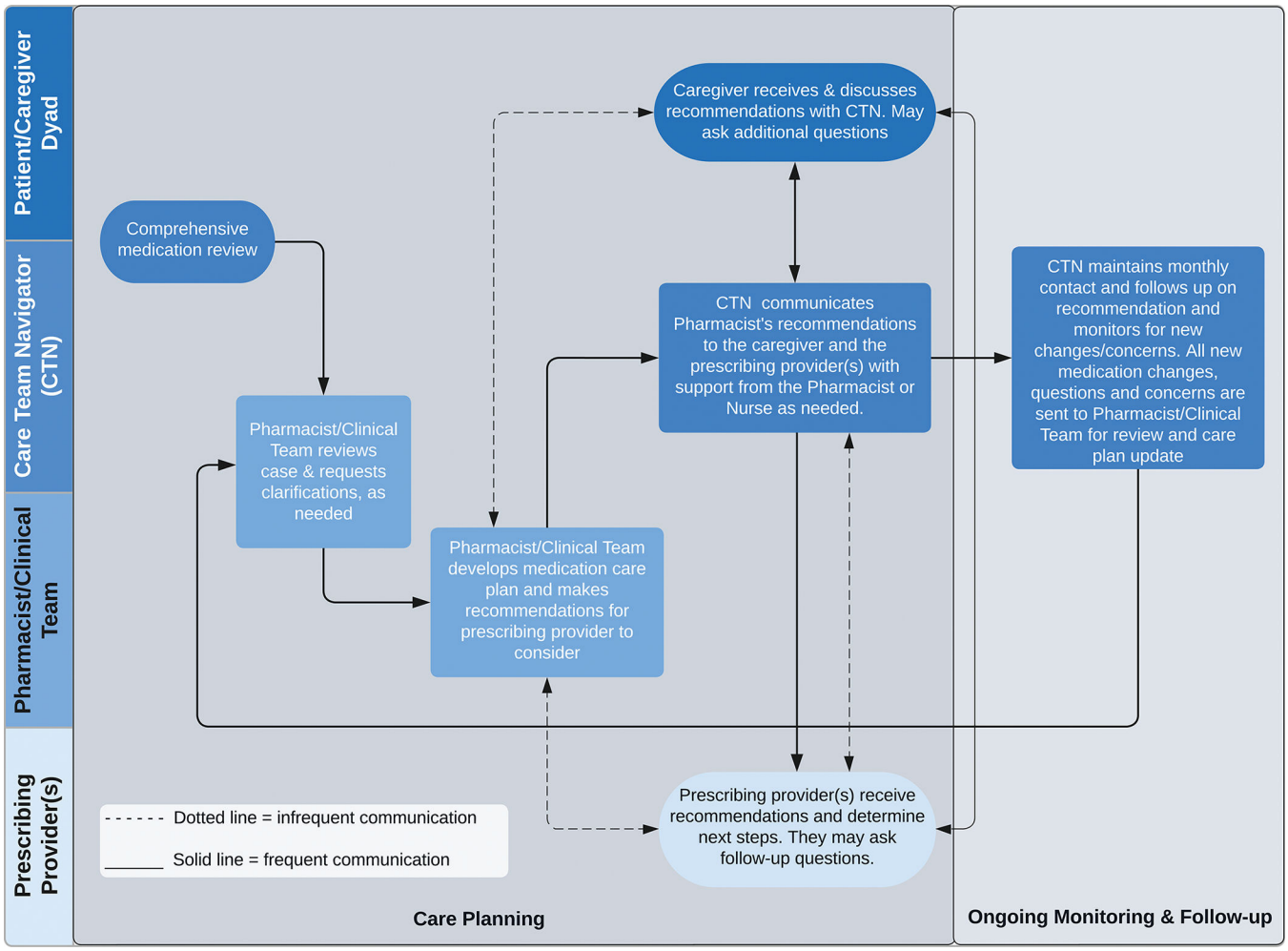

Figure 3.
Flowchart of the Care Ecosystem Medication Review Intervention and Monitoring Process

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Table 1.

Baseline participant demographics, clinical characteristics, and medication exposures of persons living with dementia

Characteristic[a]	Care Ecosystem	Usual Care
Persons living with dementia	**N = 304**	**N = 186**
Age, years, mean (SD)	77.4 (8.6)	76.5 (9.8)
Female	176 (57.9)	90 (48.4)
Race		
White	243 (79.9)	161 (86.6)
African American	15 (4.9)	5 (2.7)
Asian	21 (6.9)	10 (5.4)
Other or mixed	4 (1.3)	1 (0.5)
Not reported	21 (6.9)	9 (4.8)
Ethnicity		
Not Hispanic or Latinx	272 (89.4)	167 (89.8)
Hispanic or Latinx	30 (9.9)	19 (10.2)
Not reported	2 (0.7)	0
Preferred Language		
English	282 (92.8)	180 (96.8)
Spanish	14 (4.6)	4 (2.2)
Cantonese	8 (2.6)	2 (1.0)
Region of Residence		
California	181 (59.5)	106 (57.0)
Nebraska/Iowa	123 (40.5)	80 (43.0)
Educational Level		
College graduate or higher	156 (51.3)	105 (56.4)
Some college	61 (20.1)	34 (18.3)
High school graduate	59 (19.4)	40 (21.5)
Less than high school	28 (9.2)	7 (3.8)
Dementia Stage[b]		
Mild	182 (59.9)	110 (59.1)
Moderate	93 (30.6)	55 (29.6)
Advanced	29 (9.5)	21 (11.3)
Number of comorbidities[c], mean (SD)	2.8 (1.90)	2.6 (1.8)
Medication exposures		
Number of medications[d], mean (SD)	10.4 (5.2)	10.3 (5.0)
≥5 medications	271 (89)	167 (90)
≥10 medications	158 (52)	92 (49)

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Characteristic[a]	Care Ecosystem	Usual Care
Persons living with dementia	**N = 304**	**N = 186**
Number of potentially inappropriate medications[d], mean (SD)	1.5 (1.6)	1.4 (1.5)
PIMs for dementia or cognitive impairment[e], mean (SD)	0.4 (0.8)	0.4 (0.7)
CNS-active PIMs[e], mean (SD)	1.4 (1.4)	1.3 (1.3)
Anticholinergic Cognitive Burden Scale score[f], mean (SD)	1.6 (2.0)	1.4 (1.6)
0	114 (37.5)	71 (38.2)
1	75 (24.7)	47 (25.3)
≥ 2	115 (37.8)	68 (36.5)
Antipsychotics[e], mean (SD)	0.2 (0.4)	0.2 (0.4)
Benzodiazepines[e], mean (SD)	0.1 (0.3)	0.1 (0.3)
Opioids[e], mean (SD)	0.2 (0.5)	0.2 (0.4)

[a]Unless otherwise indicated, data are the number (percentage) of study participants in the specified category.

[b]Dementia stage was based on the Quick Dementia Rating Scale using cut points that have been validated to correspond to Clinical Dementia Rating Scale scores of 1 or less for mild, 2 for moderate, and 3 for advanced or severe.[31]

[c]Self-reported comorbidities were summarized by participant across 16 medical comorbidities.

[d]Total number of medications includes prescription and over-the-counter medications, dietary supplements and herbal products, that are scheduled or taken as needed.

[e]Potentially inappropriate medications (PIMs) were defined using American Geriatrics Society 2019 Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. CNS-active PIMs include PIMs for persons with dementia or cognitive impairment, delirium, or history of falls or fractures were also defined by the 2019 Beers Criteria and include antipsychotics, benzodiazepines and opioids.[23]

[f]Medications with anticholinergic properties were defined using the Anticholinergic Cognitive Burden (ACB) Scale.[27] ACB scores were summarized by participant for each anticholinergic medication prescribed.

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Table 2.

Treatment effects for primary and secondary medication outcome measures[a]

	Mean (SD)					
	Care Ecosystem N = 304		Usual Care N = 186		Difference between means (95% CI)[b]	
	Baseline	Follow-up	Baseline	Follow-up		*P*
Primary Medication Outcome						
Number of PIMs[c]	1.49 (1.59)	1.43 (1.51)	1.42 (1.48)	1.72 (1.69)	−0.35 (−0.49 to −0.20)	<.0001
Secondary Medication Outcomes						
Number of medications	10.43 (5.23)	10.68 (5.38)	10.28 (5.01)	11.03 (5.42)	−0.53 (−0.92 to −0.14)	.008
PIMs for dementia or cognitive impairment[c]	0.44 (0.76)	0.45 (0.78)	0.39 (0.74)	0.56 (1.04)	−0.14 (−0.23 to −0.05)	.002
CNS-active PIMs[c]	1.40 (1.42)	1.41 (1.36)	1.33 (1.28)	1.63 (1.61)	−0.28 (−0.42 to −0.14)	<.0001
ACB Scale score[d]	1.62 (1.98)	1.64 (1.99)	1.40 (1.56)	1.69 (1.97)	−0.20 (−0.39 to −0.01)	.035
Antipsychotics[c]	0.15 (0.37)	0.17 (0.40)	0.15 (0.40)	0.21 (0.47)	−0.03 (−0.08 to 0.00)	.126
Benzodiazepines[c]	0.13 (0.33)	0.12 (0.34)	0.11 (0.34)	0.16 (0.43)	−0.05 (−0.09 to −0.01)	.008
Opioids[c]	0.20 (0.50)	0.18 (0.49)	0.16 (0.44)	0.23 (0.52)	−0.09 (−0.14 to −0.03)	.002

Abbreviations: PIMs, potentially inappropriate medications; CNS, central nervous system; ACB Scale, Anticholinergic Cognitive Burden Scale

[a]Differences in medication outcomes at follow-up between groups using analysis of covariance. Covariates were baseline values of the medication outcome variable, age, gender, region of residence, dementia stage, and number of comorbidities.

[b]Difference in medication outcomes means between groups using analysis of covariance. A negative value indicates that the outcome was reduced in the Care Ecosystem group when compared with the Usual Care group.

[c]PIMs were defined using American Geriatrics Society 2019 Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. CNS-active PIMs include PIMs for persons with dementia or cognitive impairment, delirium, or history of falls or fractures were also defined by the 2019 Beers Criteria and include antipsychotics, benzodiazepines and opioids.[23]

[d]Medications with anticholinergic properties were defined using the Anticholinergic Cognitive Burden (ACB) Scale.[27] ACB scores were summarized by participant for each anticholinergic medication prescribed.

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Table 3.

Most common changes of PIMs for dementia or cognitive impairment between baseline and follow-up[a]

	N (%)					
	Care Ecosystem N = 304			Usual Care N = 186		
	Baseline	Follow-Up	Δ[b]	Baseline	Follow-Up	Δ[b]
Persons with any PIM	202 (66.4)	201 (66.1)	−1	122 (65.6)	135 (72.6)	+13
Number of PIMs	453	436	−17	265	320	+55
Drug Class and Generic Medication Name						
PIMs for dementia or cognitive impairment [c]						
Definite Anticholinergics[d]	62 (20.4)	64 (21.1)	+2	31 (16.7)	42 (22.6)	+11
Quetiapine	27 (8.9)	31 (10.2)	+4	12 (6.5)	21 (11.3)	+9
Diphenoxylate/Atropine	0	1 (0.3)	+1	0	3 (1.6)	+3
Diphenhydramine	8 (2.6)	6 (2.0)	−2	2 (1.1)	0	−2
Solifenacin	7 (2.3)	5 (1.6)	−2	0	2 (1.1)	+2
Paroxetine	5 (1.6)	3 (1.0)	−2	2 (1.1)	4 (2.2)	+2
Tolterodine	2 (0.7)	2 (0.7)	0	2 (1.1)	0	−2
Benzodiazepines	38 (12.5)	36 (11.8)	−2	18 (9.7)	26 (14.0)	+8
Lorazepam	17 (5.6)	17 (5.6)	0	10 (5.4)	19 (10.2)	+9
Clonazepam	6 (2.0)	6 (2.0)	0	6 (3.2)	7 (3.8)	+1
Alprazolam	9 (3.0)	7 (2.3)	−2	3 (1.6)	2 (1.1)	−1
Temazepam	3 (1.0)	3 (1.0)	0	1 (0.5)	2 (1.1)	+1
Nonbenzodiazepine, benzodiazepine receptor agonist hypnotics ("Z-Drugs")	5 (1.6)	4 (1.3)	−1	1 (0.5)	2 (1.1)	+1
Zolpidem	4 (1.3)	3 (1.0)	−1	1 (0.5)	2 (1.1)	+1
Antipsychotics	45 (14.8)	50 (16.4)	+5	24 (12.9)	35 (18.8)	+11
Quetiapine	27 (8.9)	31 (10.2)	+4	12 (6.5)	21 (11.3)	+9
Risperidone	10 (3.3)	12 (3.9)	+2	5 (2.7)	5 (2.7)	0
Haloperidol	0	2 (0.7)	+2	2 (1.1)	5 (2.7)	+3
Olanzapine	4 (1.3)	3 (1.0)	−1	1 (0.5)	1 (0.5)	0
Aripiprazole	3 (1.0)	2 (0.7)	−1	4 (2.2)	3 (1.6)	−1

Abbreviations: PIMs, potentially inappropriate medications

[a] For each drug class, PIMs with the greatest increases or decreases between baseline and follow-up are listed. This list is not inclusive of all PIMs that changed.

[b] Change in number of study participants between baseline and follow-up.

[c] PIMs were defined using American Geriatrics Society 2019 Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults.[23]

[d] Medications with Anticholinergic Cognitive Burden (ACB) Scale scores of 2 or higher, indicating clinical anticholinergic effect or may cause delirium.[27]

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