Journal of the
American Geriatrics Society

CLINICAL INVESTIGATION

Exploring Antipsychotic Initiation Among Persons Living With Dementia in a Comprehensive Dementia Care Program

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Received: 13 March 2025 | **Revised:** 13 May 2025 | **Accepted:** 16 May 2025

Funding: The time for D.R.L. was provided through fellowship support from the Health Resources and Services Administration (HRSA) as part of the National Research Services Award T32 Primary Care Research Fellowship at UCLA (T32HP19001). G.S.K. was funded by the Medical Student Training in Aging Research Program and the National Institute on Aging (T35AG026736).

Keywords: antipsychotic medications | comprehensive dementia care | neuropsychiatric behavioral symptoms | psychotropic medications | survival analysis

ABSTRACT

Background: Antipsychotic medications (APMs) are frequently prescribed for persons living with dementia despite limited benefits and increased risks. This study examined patient characteristics of those prescribed APMs, indications for initiation, and survival outcomes.

Methods: This retrospective cohort study of community-dwelling patients enrolled in a comprehensive dementia care program (2012–2014) focused on 190 patients not on an APM at baseline, with survival analyses including 200 additional patients on an APM at program entry. Patients were followed for 2 years for APM initiation and until January 2024 for mortality. Baseline measures included patient and caregiver demographics, Mini-Mental State Exam (MMSE), Functional Activities Questionnaire (FAQ), Modified Caregiver Strain Index (MCSI), caregiver Patient Health Questionnaire-9 (PHQ-9), and Neuropsychiatric Inventory Questionnaire (NPI-Q). Indications for APM initiation were abstracted from electronic health records. Logistic regression models examined associations between baseline characteristics and APM initiation. Survival was assessed using Kaplan–Meier estimates and Cox proportional hazards models.

Results: Among 190 patients (mean [SD] age, 81.2 [8.4] years; 60% female, and 80% Alzheimer's or dementia not otherwise specified) who were not on APMs at program enrollment, 65 (34%) initiated and 125 (66%) did not initiate an APM. NPI-Q severity (AOR 1.10, 95% CI 1.04–1.16) and NPI-Q distress (AOR 1.06, 95% CI 1.02–1.10) were associated with APM initiation. Agitation and psychotic symptoms were the most common indications, with quetiapine being the most frequently prescribed APM. Median survival was 37.8 months (IQR 19.3–63.2) for patients on an APM at baseline, 63.1 months (IQR 28.4–86.8) for patients initiating an APM, and 68.9 months (IQR 50–97.9) for patients not initiating an APM ($p < 0.001$).

Preliminary findings were presented in part at the May 5, 2023 American Geriatrics Society Annual Meeting; Long Beach, California.

Conclusions: APM initiation was common despite enrollment in a comprehensive dementia care program that prioritizes non-pharmacologic strategies. Survival differences underscore the need for risk–benefit discussions of APMs and goals of care discussions with caregivers.

1 | Introduction

There are currently more than 6.9 million Americans living with Alzheimer's disease and related dementias, with the prevalence of this disease expected to rise to about 13 million by 2050 [1]. Dementia is a progressive disease characterized by functional impairment and worsening cognition. Among the many symptoms associated with dementia, neuropsychiatric behavioral symptoms such as aggression, agitation, mood disorders, and hallucinations are common, particularly, as the disease advances [2]. These symptoms often impact the quality of life for patients, caregivers, and families [3].

Despite multiple studies showing limited clinical benefit and increased harms (e.g., cardiovascular and cerebral events, falls, and memory decline) associated with treating behavioral symptoms with antipsychotic medications (APMs) [4, 5], they continue to be commonly prescribed off-label [6]. The prevalence of APM use varies based on the setting but is estimated to range from 11% to 29% in community-dwelling persons living with dementia [7–12]. Additionally, older adults with dementia receiving home health care are twice as likely to be prescribed an APM compared to their counterparts without dementia [7].

In 2016, the American Psychiatric Association released guidelines focusing on the proper use of APMs including documentation of indications, development of a treatment plan, ongoing monitoring of symptoms and treatment response, and careful consideration of type and method of APM administration [13]. However, it is not clear how and whether these guidelines are being utilized in clinical practice, particularly, among primary care providers and within comprehensive dementia care programs.

Comprehensive dementia care is a holistic and interdisciplinary approach to dementia care. Many components of comprehensive dementia care programs, including comprehensive assessments, care plan development, ongoing monitoring, and care coordination, facilitate an environment to better understand APM prescribing practices to improve appropriate use [14–16]. These dementia care programs often focus on optimizing non-pharmacologic strategies to manage neuropsychiatric behavioral symptoms first. This is typically achieved by providing caregiver education and support, which may involve teaching caregivers to describe and investigate behavioral symptoms and their triggers, create and implement strategies for managing these symptoms, and evaluate the effectiveness of these strategies–an approach known as DICE [17]. Despite the potential for comprehensive dementia care programs to reduce and mitigate use of APMs for behavioral disturbances, little is known about APM use in this patient population.

This study used data from patients of a health system-based comprehensive dementia care program [18] to explore factors associated with APM initiation, indications for initiating, and survival based on whether patients were prescribed an APM during the study period or were on an APM at entry into the program. Findings from this study can inform process improvement strategies, including targeted deprescribing initiatives and enhanced training programs for healthcare providers, ultimately promoting safer and more effective dementia care.

2 | Methods

2.1 | Study Design and Study Sample

This retrospective observational cohort study included patients from the UCLA Alzheimer's and Dementia Care (ADC) program [18], a health system-based comprehensive dementia care program that employs nurse practitioners serving as dementia care specialists (DCSs) who comanage and support patients living with dementia and their caregivers. These DCSs are trained in performing comprehensive assessments, developing care plans that optimize non-pharmacologic approaches to manage neuropsychiatric behavioral disturbances, providing caregiver support and care coordination, and facilitating advanced care planning. The patients evaluated in this study were part of the original cohort of participants enrolled in the ADC program from 2012 to 2014 as part of the Centers for Medicare and Medicaid Services (CMS) Innovations Challenge Award [18]. Patients eligible for this program were community-dwelling, had a diagnosis of dementia, a designated caregiver, and a physician who would partner with the program. The primary analysis was limited to 190 patients who stayed in the ADC program for 2 years (evaluation period of the original cohort) and were not on an antipsychotic at enrollment (Figure 1). Additional analyses used for survival compared the 190 patients in the primary analysis to patients on an APM at baseline ($n = 200$). The UCLA Institutional Review Board (IRB) approved this study.

2.2 | Measures

Patient demographic characteristics were collected at baseline and included age, gender, education level, marital status, race and ethnicity, and dementia type. Cognitive performance was measured by the Mini-Mental Status Examination score (MMSE, range from 0 to 30 with ≤ 18 indicating moderate to severe dementia) [19]. Functional status was measured by the Functional Activities Questionnaire (FAQ) score (range from 0 to 10, with ≥ 9 indicating functional impairment) [20]. Behavioral symptoms were measured by the Neuropsychiatric Inventory Questionnaire (NPI-Q) Severity score (range from 0 to 36, with higher scores indicating more severity) [21]. These variables were obtained from the DCS notes, including initial evaluation and annual follow-up visit notes.

Caregivers were self-identified individuals who provided supervision and assistance with daily activities. Caregiver

Summary

- Key points
  - Antipsychotic use among persons living with dementia in a health system-based comprehensive dementia care program is common, with agitation and psychosis being the most frequent indications for use.
  - Worse patient behavioral symptoms and subsequent caregiver distress are associated with antipsychotic initiation.
  - Antipsychotic use is associated with survival time, with the shortest survival among patients using an antipsychotic for a longer duration of time.
- Why does this paper matter?
  - Comprehensive dementia care programs can provide the environment to potentially mitigate and deprescribe harmful medications. However, even within a comprehensive dementia care program, antipsychotic medications are commonly prescribed in response to neuropsychiatric symptoms, and their use may be a marker for shorter survival. These findings highlight the importance of regularly assessing the need for these medications, optimizing risks and benefits, and engaging in ongoing goals-of-care discussions.

characteristics were also collected from the DCS notes at baseline and included gender, relationship to the participant, living with the patient, caregiver distress related to neuropsychiatric behavioral symptoms (NPI-Q distress score, range 0–60, with higher numbers indicating more distress) [21], caregiver depressive symptoms using the Patient Health Questionnaire-9 (PHQ-9, range 0–27, with ≥10 indicating moderate to severe depression) [22], and caregiver strain using the Modified Caregiver Strain Index (MCSI, range 0–26, with ≥13 indicating high strain) [23].

Electronic health record notes from primary care physicians and DCSs were reviewed to obtain narrative information about indications for starting an APM. Training sessions were performed with chart abstractors (D.R.L., D.B.R., G.S.-K., and B.Y.) and entered in Research Electronic Data Capture (REDCap, Version 12.4.19) [24, 25] from June 2022 to November 2022. Practice guidelines [13] were used to create categories and codes for APM indications: (1) agitation, such as physical and verbal aggression; (2) psychotic symptoms, such as hallucinations and delusions; (3) mood issues, such as anxiety and depression; (4) sleep disturbance and insomnia; (5) sexual disinhibition; (6) oppositional behavior; (7) wandering; (8) risk of harm to self or others; (9) severe intractable distress; (10) patient's living situation being at risk; and (11) no indication.

The type of APM started and whether the use of other concurrent psychotropic medications, including antidepressants, benzodiazepines, and other hypnotics and antiepileptics, was also collected from the electronic health record. The complete list of medications considered in this analysis is included in Table S1. Additionally, whether the patient was still on the APM at the time of death, disenrollment from the program, or at medical record abstraction was also obtained.

Death was defined as all-cause mortality. Death dates were obtained from the UCLA electronic health record and could have occurred anytime from a participant's enrollment in the ADC program through January 31, 2024, when the death date data were collected.

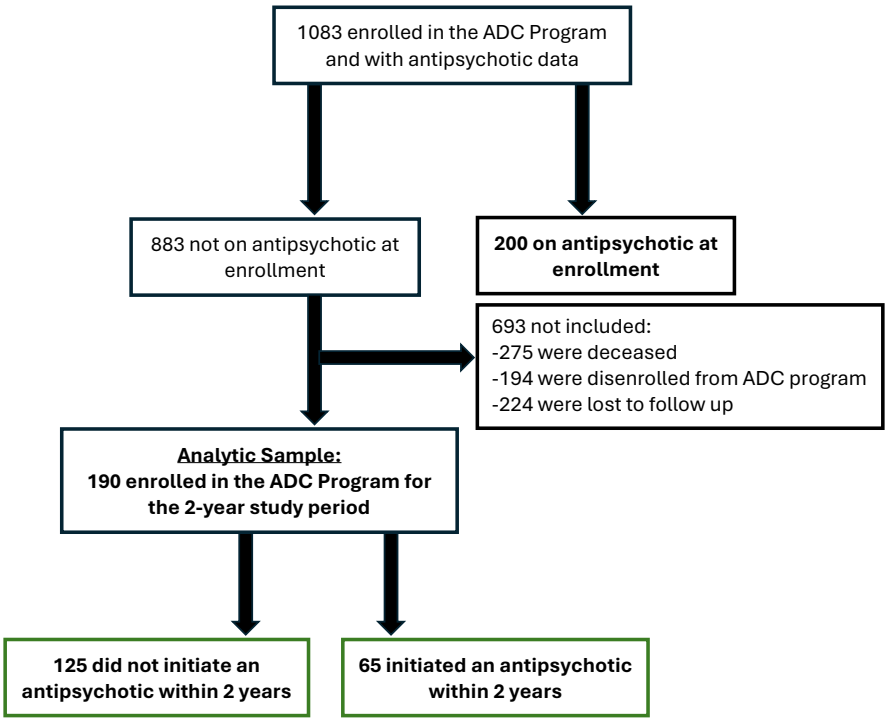

FIGURE 1 | Flow diagram of included patients. Figure depicts the selection of the analytic sample, outlining the inclusion of 190 patients in the primary analysis and 200 patients on an antipsychotic medication (APM) at baseline.

2.3 | Quantitative Analysis

Descriptive statistics were used to summarize patient and caregiver demographic and clinical variables. To compare these variables between groups—those who initiated an APM within 2 years of entry into the program and those who did not—continuous variables were compared using the Wilcoxon rank-sum test and categorical variables were compared using Fischer's exact test. We evaluated the association between initiating an APM versus not initiating an APM as the outcome, with MMSE (≤ 18 vs. > 18 [ref]), FAQ (≥ 9 vs. < 9 [ref]), caregiver PHQ-9 (≥ 10 vs. < 10 [ref]), MCSI (≥ 13 vs. < 13 [ref]), NPI-Q severity caregiver (continuous variable), and NPI-Q distress (continuous variable) as predictors. A series of multivariable logistic regressions was conducted for each predictor. Models were adjusted for prespecified confounders and patient characteristics, including patient age (in years), patient gender (female vs. male), dementia type (Alzheimer's: yes vs. no), and whether the caregiver lives with the patient (yes vs. no). The multivariable logistic regression results were summarized using adjusted odds ratios (aOR), their 95% confidence intervals (CIs) and *p*-values.

Survival analysis was performed evaluating the association between APM use (not initiating an APM within 2 years vs. initiating an APM within 2 years) and time to death. Kaplan–Meier estimates were used to construct survival curves, and the log-rank test was used to compare survival distributions across groups. To provide additional insight into the effects of APMs on survival, we also included survival analyses comparing these groups to patients on an APM at baseline. Multivariable Cox proportional hazards models were used to estimate hazard ratios (HRs) for time to death comparing patients initiating an APM within 2 years to patients who did not initiate an APM, adjusting for baseline measures of patient age (years), gender (female vs. male), dementia type (Alzheimer's: yes vs. no), FAQ score, MMSE, and NPI-Q severity scores. All tests were two-sided with the statistical significance level set at $p < 0.05$. Statistical analyses were performed using Stata/SE version 18 (StataCorp, College Station, TX 77845) and R statistical software (v4.1.3).

2.4 | Qualitative Analysis

The research team approached analyzing the narrative indications for starting an APM in three steps. First, chart abstractors categorized indications by reading the narrative text, with about 18% of charts being double abstracted. Disagreements on how to determine indications were discussed among chart abstractors, and a codebook with consensus rules was created. Of note, more than one indication could be chosen for each text. Second, these narrative texts were then independently reviewed by two coders (D.R.L. and G.S.K.) to determine representative exemplary quotes. The two coders discussed differences in choosing the list of quotes. Lastly, all representative quotes were then evaluated by five members of the research team (D.R.L., G.S.-K., B.Y., K.S., and D.B.R.). The chosen quotes were agreed upon by all authors.

3 | Results

3.1 | Baseline Patient and Caregiver Characteristics

There were 190 patients included in the primary analyses of this study (Table 1) with a mean age of 81.2 years (SD 8.4); 60% were female, 42% had college graduate degrees or higher, 51% were married, and 78% had Alzheimer's dementia or Dementia not otherwise specified (NOS). Over 2 years, 65 patients were initiated on an APM (34%), while 125 patients did not initiate an APM (66%). In bivariate analyses, patients who were initiated on an APM had worse NPI-Q severity and distress scores (both $p < 0.001$). Patient age, gender, race and ethnicity, education level, marital status, dementia type, cognitive scores, functional status scores, caregiver gender, caregiver relationship, living situation, caregiver PHQ-9, and MCSI scores were not significantly different between the two groups. The additional 200 patients already on an APM at baseline, who were included in the survival analysis, were more likely to have lower educational attainment, poorer cognitive function, greater functional impairment, and more severe behavioral symptoms (Table S2).

3.2 | Characteristics Associated With Initiating an Antipsychotic

After adjusting for patient and caregiver characteristics, more patient behavioral symptoms (NPI-Q severity score AOR 1.10, 95% CI 1.04–1.16) and greater caregiver distress in response to behavioral symptoms (NPI-Q distress AOR 1.06, 95% CI 1.02–1.10) were associated with APM initiation (Table 2). MMSE scores, patient FAQ scores, caregiver PHQ-9, and MCSI did not differ significantly between groups.

3.3 | Indications for Initiating and Choice of Antipsychotic Medications

A list of representative quotes used to categorize indications for initiating an APM is presented in Table 3. Agitation was the most frequent indication (62%), followed by psychotic symptoms (38%), insomnia or sleep disturbances (14%), risk of harm to self or others (12%), anxiety, depression, or mood disturbance (6%), wandering (5%), oppositional behavioral (5%), and other measures have failed (2%). More than one indication was selected 49% of the time. "Other reasons" was also common (25%). Sexual disinhibition, severe intractable distress, and the patient's living situation being at risk were not reported as reasons for initiating an APM in this cohort.

Among the 65 patients started on an APM, quetiapine was prescribed most frequently (65%), followed by risperidone (20%), olanzapine (12%), and haloperidol (3%). About half of the patients received two or more different APMs (38% received two and 11% received three) during the follow-up period. Concurrent APM and other psychotropic medication use was common; 71% were on antidepressants, 63% were on benzo-hypnotics, and 37% were on antiepileptics (Table S3). Additionally, 74% of the

TABLE 1 | Baseline characteristics of patients and caregivers.

	Overall, $n = 190$	No APM initiation, $n = 125$	APM initiation, $n = 65$	p
Patient characteristics				
Age in years, mean (SD)	81.2 (8.4)	80.9 (8.1)	81.8 (8.9)	0.49
Female (%)	114 (60%)	74 (59.2%)	40 (61.5%)	0.88
Race and ethnicity				0.49
Hispanic	17 (9.3%)	10 (8.5%)	7 (10.8%)	
Non-Hispanic Black	13 (7.1%)	10 (8.5%)	3 (4.6%)	
Non-Hispanic White	138 (75.8%)	86 (73.5%)	52 (80.0%)	
Other[a]	14 (7.7%)	11 (9.4%)	3 (4.6%)	
Education, *n* (%)				0.20
Less than HS grad	20 (10.6%)	10 (8.1%)	10 (15.4%)	
HS grad and some college	89 (47.3%)	57 (46.3%)	32 (49.2%)	
College grad and higher	79 (42.0%)	56 (45.5%)	23 (35.4%)	
Married, *n* (%)	95 (50.5%)	60 (48.8%)	35 (53.8%)	0.54
Dementia type, *n* (%)				0.13
Alzheimer's	74 (43.3%)	56 (48.7%)	18 (32.1%)	
Vascular	7 (4.1%)	5 (4.3%)	2 (3.6%)	
Lewy body	7 (4.1%)	2 (1.7%)	5 (8.9%)	
Frontotemporal	4 (2.3%)	3 (2.6%)	1 (1.8%)	
Dementia NOS	59 (34.5%)	35 (30.4%)	24 (42.9%)	
Parkinson's	1 (0.6%)	1 (0.9%)	0 (0.0%)	
Mixed	19 (11.1%)	13 (11.3%)	6 (10.7%)	
MMSE ≤ 18, *n* (%)	74 (45.1%)	45 (41.3%)	29 (52.7%)	0.19
FAQ Score ≥ 9, *n* (%)	164 (89.1%)	104 (86.0%)	60 (95.2%)	0.079
NPI-Q severity, median (IQR)	9 (5–14)	8 (4–13)	12 (7–18)	< 0.001
Caregiver characteristics				
Female (%)	131 (68.9%)	85 (68.0%)	46 (70.8%)	0.74
Relationship				0.91
Spouse/partner	83 (43.7%)	53 (42.4%)	30 (46.2%)	
Child	89 (46.8%)	60 (48.0%)	29 (44.6%)	
Other[b]	18 (9.5%)	12 (9.6%)	6 (9.2%)	
Lives with patient (%)	120 (64.2%)	77 (61.6%)	43 (69.4%)	0.33
PHQ-9 ≥ 10, *n* (%)	25 (13.6%)	14 (11.5%)	11 (17.7%)	0.26
MCSI ≥ 13, *n* (%)	83 (45.1%)	49 (40.5%)	34 (54.0%)	0.088
NPI-Q distress, median (IQR)	11 (5–17)	9 (4–16)	13 (8–26)	< 0.001

Abbreviations: APM = antipsychotic medication; NOS = not otherwise specified.
[a]Other = Other race and ethnicity category refers to non-Hispanic Asian, non-Hispanic Pacific Islander, and non-Hispanic American Indian or Alaskan Native.
[b]Other relationships include friend, hired caregiver, and other family member.

TABLE 2 | Association of baseline characteristics with antipsychotic initiation.

Characteristics[a]	APM initiation, aOR (95% CI)	*p*
Patient NPI-Q severity score	1.10 (1.04–1.16)	0.001
Patient MMSE (≤18 vs. >18)	1.59 (0.79–3.17)	0.19
Patient FAQ Score (≥9 vs. <9)	3.65 (0.84–15.79)	0.084
Caregiver NPI-Q Distress Score	1.06 (1.02–1.10)	0.002
Caregiver PHQ-9 Score (≥10 vs. <10)	1.26 (0.46–3.42)	0.65
Caregiver MCSI Score (≥13 vs. <13)	1.41 (0.70–2.84)	0.33

Abbreviations: aOR = adjusted odds ratio; APM = antipsychotic medication; CI = confidence interval; NOS = not otherwise specified.
[a]Each model was adjusted for patient characteristics, including age (years), gender (female vs. male), and type of dementia (Alzheimer's: yes vs. no), as well as the caregiver's living situation with the patient (yes vs. no). Firth's penalized likelihood approach was applied to reduce small-sample bias in logistic regression estimates.

patients remained on an APM at the time of death, disenrollment, or medical record abstraction.

3.4 | Survival Analysis

The median survival was 63.1 months (IQR 28.4–86.8) for patients initiated on an APM and 68.9 months (IQR 50.0–97.9) for patients who did not initiate an APM ($p = 0.048$). Analyses comparing these two groups to patients on an APM at baseline showed the shortest survival for patients on an APM at baseline (median survival 37.8 months, IQR 19.3–63.2) (Figure 2, $p < 0.001$). In adjusted models, patients who were on an APM at baseline had a significantly higher mortality risk compared to those who initiated an APM (HR 1.56, 95% CI 1.06–2.32, $p = 0.026$) and those who did not initiate an APM (HR 2.19, 95% CI 1.52–3.17, $p < 0.001$). In contrast, the mortality risk did not differ significantly between patients who initiated an APM and those who did not initiate an APM (HR 1.40, 95% CI 0.89–2.19, $p = 0.14$) (Table S4).

4 | Discussion

In this health system-based comprehensive dementia care program, the initiation of APMs within 2 years of program enrollment was high, despite the program emphasizing behavioral methods first [18, 26]. Patients who experienced more severe behavioral symptoms and accompanying caregiver distress were more likely to initiate an APM, and the indications were most often due to agitation and psychotic symptoms. Median survival time was shortest for individuals who were on an antipsychotic at baseline and longest for those who were not started on an antipsychotic.

The high use of APMs, particularly, at baseline and relative to community-dwelling older adults in other studies [7, 10], may reflect that patients with more challenging psychosocial factors and symptoms were both referred to and retained in this comprehensive dementia care program. Patient behavioral and psychological symptoms (NPI-Q scores) were the main predictors for starting an antipsychotic medication, similar to other studies [7, 27]. This study expands the literature by identifying the specific contexts in which APMs are likely prescribed within comprehensive dementia care programs, shedding light on the drivers and indications for their use. Understanding these factors is, particularly, important, as randomized controlled trials comparing comprehensive dementia care programs to usual care have demonstrated improved patient and caregiver outcomes without significant differences in APM use at 12 and 18 months [28, 29]. Our study findings suggest that comprehensive dementia care programs may have opportunities to further reduce APM reliance.

Characterizing reasons for APM prescribing and developing strategies to reduce their use is becoming increasingly important, especially as they are part of dementia quality measures and new payment reform [30]. In particular, the Guiding an Improved Dementia Experience (GUIDE) Model, which is an alternative payment model introduced by the Centers for Medicare and Medicaid Services (CMS) in 2023 [31] to support the provision of comprehensive dementia care, includes a negative payment adjustment for the use of high-risk medications such as antipsychotics. This type of policy reform incentivizes comprehensive dementia care programs to incorporate validated tools such as the DICE method [17], Goal Attainment Scaling targeting high-risk medications [32, 33], and other innovative approaches, such as leveraging the electronic health record [34]. Although a minority of healthcare organizations will participate in the GUIDE model, future reforms to Medicare Advantage and other payment plans may broaden access to comprehensive dementia care. These reforms could also strengthen efforts to monitor and reduce high-risk medication use while further integrating deprescribing and behavioral management strategies.

The survival analysis in this study showed a significant difference in all-cause mortality between groups. This exploratory analysis found that patients on an APM at baseline had the shortest survival time, followed by patients who initiated an APM within 2 years. The differences in survival could reflect longer exposure to APMs, especially since this study found about three fourths of patients who initiated an APM, which are known to increase the risk of death [35, 36] and other adverse effects [2, 37, 38] remained on these medications at the time of death, disenrollment, or medical record abstraction. The use of these medications could also serve as a marker for disease progression, indicating to providers that broader goals of care conversations with patients and family members are needed. This objective indicator may be, particularly, important for primary care providers as they provide the majority of dementia care in

TABLE 3 | Indications and frequency for initiating an antipsychotic medication.

Indications	Frequency ($n = 65$)	Representative quotes
Agitation (physical or verbal aggression)	40 (62%)	"She paces, talks to herself in the mirror, and sometimes spits at us." "She escalates quickly, yelling abusive remarks like 'I never want to see you again!'"
Psychotic symptoms (hallucinations, delusions)	25 (38%)	"She sat in the car thinking she was going somewhere." "She believes her computer was hacked and she is being watched through cameras." "She argues with herself in the mirror and sees unexplained lines on the floor."
Insomnia, sleep disturbances	9 (14%)	"She wakes up at night, becomes more confused the next day." "Patient wanders the house from 1:30–3:30 AM and sleeps in different locations."
Risk of harm to self or others	8 (12%)	"She chased people out of the house, ran into traffic, and wielded a knife." "She attempted to exit through a window." "She jumped on her daughter's back and tried to scratch her."
Anxiety, depression, mood disturbances	4 (6%)	"After her sister's passing, she paced the hallways non-stop, wanting to visit her sister."
Wandering	3 (5%)	"Frequent wandering outside led to a mechanical fall." "The patient walked outside and yelled for the neighbor's help in the middle of the night, and the police were called."
Oppositional behavior	3 (5%)	"She refuses care, including bathing and diaper changes." "She resisted dressing and leaving the house for medical appointments."
No indication documented	6 (9%)	"PCP started without documentation."
Other measures have failed	1 (2%)	"The staff thinks that music and dance make her more excited/agitated."
Other reasons	16 (25%)	"Nursing home staff tied patient down to his chair for his protection given history of falls. Per family, the nursing home no longer desires to take care of the patient."

the United States, about half of whom do not feel comfortable managing dementia [39]. This could be a point for involving palliative care services for planning next steps [40], referral to a comprehensive dementia care program that has expertise with advanced care planning and neuropsychiatric behavioral management, or initiating these conversations by educating patients and caregivers about the disease trajectory and using a structured framework to document goals of care across the dementia continuum (e.g., patient preferences during mild, moderate, and severe stages) [41]. Future studies could examine whether APM initiation plays a mediating role in key dementia-related outcomes.

This study has several strengths, including using mixed methods to gain a deeper understanding of APM initiation for patients enrolled in a comprehensive dementia care program and robust characterization of patients and caregivers. There are several limitations to this study. First, this evaluation was conducted at a single academic medical center within a comprehensive dementia care program, which may limit the generalizability of findings to patients receiving usual dementia care. Second, while DCSs documented the clinical context surrounding APM initiation in detail, this study did not assess APM deprescribing practices or duration of use. Future studies could provide valuable insights into these prescribing practices and the concurrent use of additional psychotropic and opioid medications. Additionally, the analysis was restricted to patients who remained in the program for at least 2 years and had available APM data. As a result, patients who withdrew due to death, loss to follow-up, or disenrollment (e.g., because of hospice enrollment) were not included in the main analyses, which may have led to an underestimation of APM use, as psychotropic medication use tends to increase at the end of life [42]. Lastly, this study did not collect data on the duration of antipsychotic exposure; however, future longitudinal studies could help clarify potential associations with mortality.

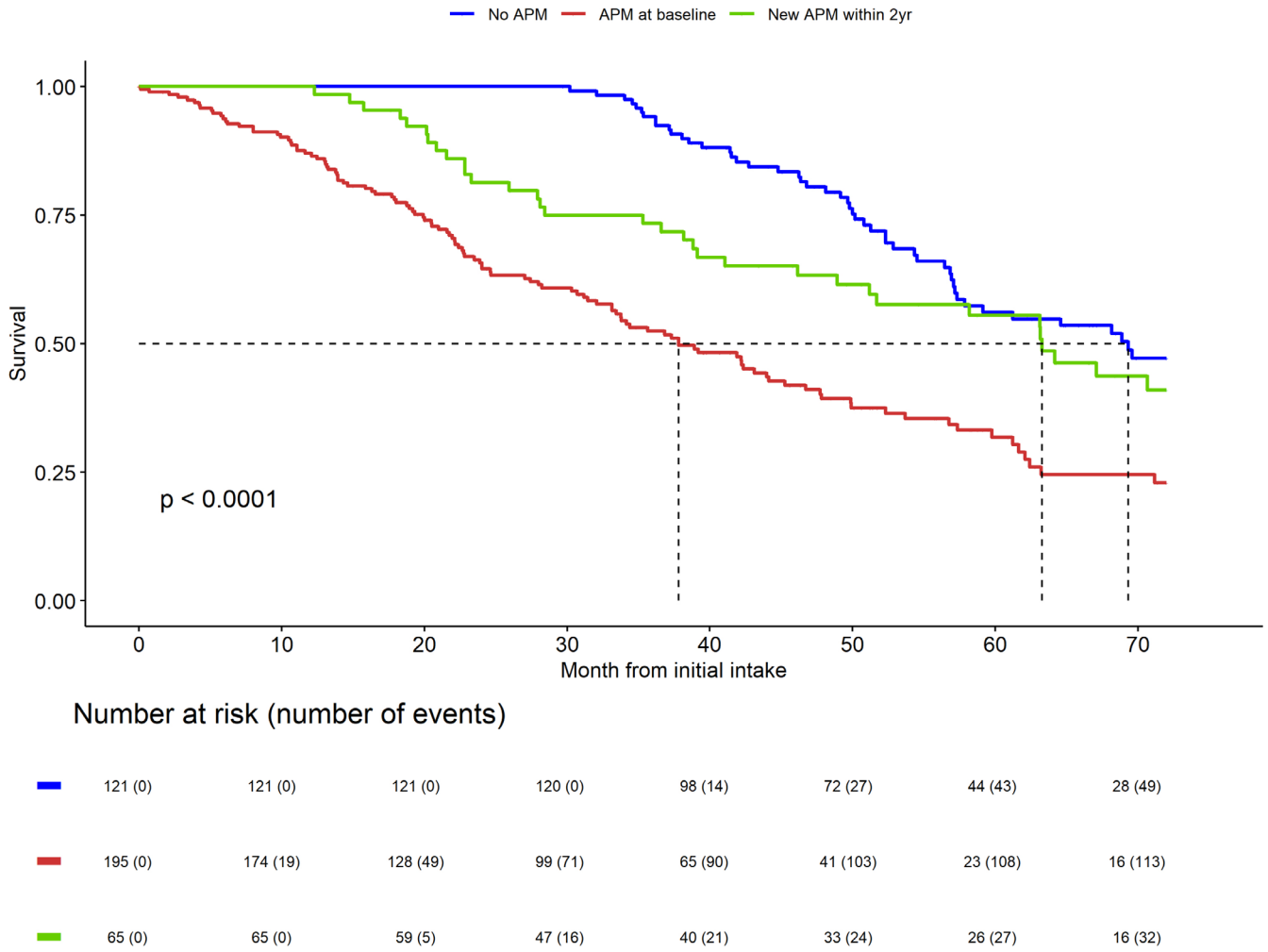

FIGURE 2 | Comparison of median time to death between patients on an antipsychotic medication (APM) at baseline, APM initiation, and no APM initiation. Figure shows Kaplan–Meier survival curves comparing survival among patients on an APM at baseline (red), those who initiated an APM within 2 years (green), and those with no APM use during study period (blue). The dashed lines indicate the median time to death in months for each group. A log-rank test was used to compare survival distributions between groups ($p < 0.001$). The risk table below the figure displays the number of patients at risk and the number of events (deaths) at each time point.

5 | Conclusions

This study highlights the high initiation of APMs among persons living with dementia, even though patients were enrolled in a comprehensive dementia care program that prioritizes non-pharmacologic symptom management. Neuropsychiatric symptoms were the primary driver for initiating an APM, with agitation and psychosis being the main indications. The differences in survival underscore the importance of discussing the potential adverse risks of APMs, while also considering that their use may be a prognostic marker and stimulus for additional goals of care conversations and advanced care planning. As more effort is being placed on the dissemination and implementation of comprehensive dementia care programs, future improvement efforts should prioritize ways to monitor and deprescribe APMs.

Author Contributions

Concept and Design: David R. Lee, Grace Sassana-Khadka, Tahmineh Romero, Katherine Sy Serrano, and David B. Reuben. Acquisition of subjects and/or data, analysis, and interpretation of data: David R. Lee, Grace Sassana-Khadka, Tahmineh Romero, Betsy Yang, Katherine Sy Serrano, Andrea Centeno, and David B. Reuben. Manuscript preparation: David R. Lee, Grace Sassana-Khadka, Tahmineh Romero, Betsy Yang, and David B. Reuben. Critical revision of the manuscript: David R. Lee, Grace Sassana-Khadka, Tahmineh Romero, Betsy Yang, Katherine Sy Serrano, Andrea Centeno, and David B. Reuben. Statistical analysis: David R. Lee and Tahmineh Romero. Administrative, technical, or material support: David R. Lee, Tahmineh Romero, Katherine Sy Serrano, Andrea Centeno, and David B. Reuben. D.R.L. had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. All authors reviewed and approved the final version of this manuscript.

Acknowledgments

The authors express their gratitude to the work provided by the UCLA ADC Program's dementia care specialists and administrative staff.

Conflicts of Interest

The authors declare no conflicts of interest.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.