Title

Psychotropic medication usage in sporadic versus genetic behavioral-variant frontotemporal dementia.

Journal

Alzheimers and Dementia, 21(2)

Authors

Vargas-Gonzalez, Juan-Camilo

Dimal, Nico

Cortez, Kasey

et al.

Publication Date

2025-02-01

DOI

10.1002/alz.14448

Peer reviewed

Received: 23 May 2024 | Revised: 20 September 2024 | Accepted: 23 September 2024

DOI: 10.1002/alz.14448

Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

RESEARCH ARTICLE

Psychotropic medication usage in sporadic versus genetic behavioral-variant frontotemporal dementia

Juan-Camilo Vargas-Gonzalez[1,2] | Nico Dimal[1,2] | Kasey Cortez[2] | Hilary Heuer[3] | Leah K. Forsberg[4] | Brian S. Appleby[5] | Sami Barmada[6] | Andrea Bozoki[7] | David Clark[8] | Yann Cobigo[3] | R. Ryan Darby[9] | Bradford C. Dickerson[10] | Kimiko Domoto-Reilly[11] | Douglas R. Galasko[12] | Daniel H. Geschwind[13] | Nupur Ghoshal[14] | Neill R. Graff-Radford[15] | Ian M. Grant[16] | David Irwin[17] | Ging-Yuek Robin Hsiung[18] | Lawrence S. Honig[19] | Kejal Kantarci[4] | Gabriel C. Léger[12] | Irene Litvan[12] | Ian R. Mackenzie[18] | Joseph C. Masdeu[20] | Mario F. Mendez[13] | Chiadi U. Onyike[21] | Belen Pascual[20] | Peter Pressman[22] | Eliana Marisa Ramos[13] | Erik D. Roberson[23] | Emily Rogalski[24] | Brad F. Boeve[4] | Adam L. Boxer[3] | Howie J. Rosen[3] | Maria Carmela Tartaglia[1,2,25] | ALLFTD Consortium Investigators

Correspondence
Juan-Camilo Vargas-González, Cognitive and Behavioural Neurology, Division of Neurology, University of Toronto, Toronto Western Hospital, 399 Bathurst St. FW-4-128, Toronto, ON M5T 2S6, Canada.
Email: juancamilo.vargasgonzalez@mail.utoronto.ca

Funding information
National Institute on Aging, Grant/Award Numbers: U01AG045390, U01AG016976; National Institute of Neurological Disorders and Stroke, Grant/Award Number: U54NS092089

Abstract

INTRODUCTION: Psychotropic medication (PM) use in behavioral-variant frontotemporal dementia (bvFTD) is higher than in other dementias. However, no information exists on whether PM use differs between sporadic and genetic bvFTD.

METHODS: We analyzed data from sporadic and genetic bvFTD participants with PM prescriptions in the Advancing Research and Treatment in Frontotemporal Lobar Degeneration/Longitudinal Evaluation of Familial Frontotemporal Dementia Subjects study. We estimated ordinal odds ratio (OOR) of having more PM comparing sporadic and genetic bvFTD. Finally, we explored the neuropsychiatric symptom (NPS) combinations using classification and regression trees (CART).

RESULTS: We included 263 with sporadic and 193 with genetic bvFTD. The OOR for sporadic bvFTD to be on PM was 1.75 (95% confidence interval: 1.21 to 2.53) for the fully adjusted model. CART revealed the most common NPS combination was apathy + personality changes in 18% of participants.

DISCUSSION: Participants with sporadic bvFTD were twice as likely to be on PM compared to genetic bvFTD. The reason for increased PM usage in sporadic bvFTD participants should be further investigated.

KEYWORDS
behavioral symptoms, frontotemporal dementia, frontotemporal lobar degeneration, medication usage, psychotropic drugs

Highlights

- We report on patients with behavioral variant frontotemporal dementia (bvFTD).
- We evaluated the psychotropic medication (PM) prescription at baseline in the cohort.
- Patients with sporadic bvFTD had more prescriptions for PM than genetic patients.
- The frequency of symptoms combination was different in sporadic and genetic bvFTD.

1 | BACKGROUND

Neuropsychiatric symptoms (NPS; such as depression, anxiety, apathy, psychosis, and disinhibition) are common in neurodegenerative diseases. Their high frequency and increased severity are associated with higher patient distress, increased mortality risk, and higher institutionalization rates.[1] Psychotropic medications (PMs) are frequently used as symptomatic treatments for NPS in dementia. Behavioral-variant frontotemporal dementia (bvFTD) is a progressive condition characterized by multiple neuropsychiatric and behavioral symptoms.[2] The high frequency of NPS is associated with higher PM usage by patients with bvFTD compared to other syndromes, such as dementia due to Alzheimer's disease (AD).[3] Importantly, higher use of PMs in patients with dementia is associated with a higher risk of death, including antipsychotics alone[4] and antidepressants or benzodiazepines when patients are already on antipsychotics.[5]

Previous research has demonstrated that sporadic and genetic bvFTD are associated with multiple NPS.[6] Whether there is a higher frequency of NPS in sporadic or genetic bvFTD is unknown as conflicting results were reported with a study in this cohort showing greater NPS in sporadic bvFTD[7] while another study found higher frequency and intensity of NPS in genetic bvFTD.[8] There is limited information about whether this differential behavioral burden translates into differential PM usage when comparing sporadic and genetic bvFTD and if differential usage is associated with different behavioral symptom profiles. We aimed to evaluate whether PM usage differs between sporadic and genetic bvFTD after controlling for symptom burden, using data from a North American multicenter study.

2 | METHODS

We included 456 patients participating in the Advancing Research and Treatment in Frontotemporal Lobar Degeneration (ARTFL)/Longitudinal Evaluation of Familial Frontotemporal Dementia Subjects (LEFFTDS) Longitudinal Frontotemporal Lobar Degeneration (ALLFTD) study, a collaborative multicenter study that includes data from 26 sites across North America for participants diagnosed with a frontotemporal lobar degeneration spectrum disorder. ALLFTD resulted from the merger of ARTFL and LEFFTDS consortia. ALLFTD participants undergo a comprehensive assessment, including a clinical interview, physical and neurological examination, standardized neuropsychological testing, functional evaluation, and biospecimen collection. All participants in ALLFTD had their genetic status evaluated.

For this study, we included the cross-sectional baseline information of participants diagnosed with bvFTD for whom the genetic status has been established and with data on PM usage. We classified a participant as having genetic bvFTD if, during the genetic testing,[9] a known pathogenic or likely pathogenic mutation was found; all other participants with known genetic status and without known pathologic mutations were classified as sporadic.

For the present analysis, we included data on the Clinical Dementia Rating (CDR) Plus behavior and language modules from the National Alzheimer's Coordinating Center (NACC) Behavior and Language Domains (CDR-plus-NACC-FTLD),[10] and we obtained the Global (0 = none, 0.5 = questionable/very mild, 1 = mild, 2 = moderate, 3 = severe) score and the sum of the boxes using the scoring rules developed by the ARTFL/LEFFTDS consortium[11–13] that use information across eight domains: memory, orientation, judgement and problem solving, community affairs, home and hobbies, personal care, behavior, and language. We included behavioral information from two sources collected in ALLFTD; first the informant-based Neuropsychiatric Inventory Questionnaire (NPI-Q) score; second, the NACC Uniform Data Set (UDS) clinician judgment of symptoms behavioral component, which is a clinician rating based on information from patient and caregiver, clinical history, and medical records, as well neurological assessment to judge if the individual symptoms are present or not. The clinician judgment of symptoms assesses the presence or absence of the most common symptoms of bvFTD. Also, we included information on the age of onset (in years), education (in years), and Geriatric Depression Scale (GDS) score.

The medication prescription was collected using the NACC A4 form, and for this analysis, we included all the PMs collected in the

form, which include citalopram, duloxetine, escitalopram, fluoxetine, gabapentin, mirtazapine, paroxetine, quetiapine, sertraline, venlafaxine, bupropion, alprazolam, clonazepam, lorazepam, and trazodone. The included medications were those that were collected in the standardized NACC A4 used in ALLFTD; the NACC A4 standardized data form only includes one antipsychotic and that is quetiapine. We did not include cholinesterase inhibitors because they are mainly prescribed to treat memory-related symptoms in AD. The NACC A4 form does not record information regarding who prescribed the medication.

2.1 | Statistical analysis

This is a cross-sectional analysis of participants with sporadic and genetic bvFTD from ALLFTD. Univariate comparisons of demographic and clinical variables between sporadic and genetic bvFTD were performed. We then modeled PM usage as the outcome as an ordinal variable using the following levels: 0 PM, 1 PM, 2 PM, and ≥ 3 PM. We performed proportional odds logistic models[14] using MASS package version 7.3.6 and used the ordinal odds ratio (OOR) for the interpretation. The first model evaluated the association of the dichotomous genetic status on the categorical count of PMs without adjusting for other factors. In the second model, we assessed the association of the dichotomous genetic status on the categorical count of PM adjusting for the global CDR-plus-NACC-FTLD category. Finally, in the third model, we evaluated the association of the genetic status on the number of PMs used after controlling for CDR-plus-NACC-FTLD global score, sex, NPI-Q score, and GDS score. We constructed a directed acyclic graph (DAG), created with DAGitty,[15] to select the confounders to be included in the fully adjusted model. In Figure S1 in supporting information we present the DAG figure before and after selecting the minimally sufficient adjusting set of covariables. Furthermore, in Figure S2 in supporting information we present a simpler DAG in which we included NPI-Q as the only measure of behavior, and the CDR as the only measure of function. In this less complex model, the covariables include CDR-plus-NACC-FTLD global score, sex, and NPI-Q.

Also, In the Supplementary File in supporting information, we present the results from two exploratory analyses in which we explored fully adjusted models. In the first, we restricted to PMs that were likely used as antidepressants (bupropion, citalopram, duloxetine, escitalopram, fluoxetine, mirtazapine, paroxetine, sertraline, and venlafaxine), and in the second to PMs that were likely used for agitation/sedation (alprazolam, clonazepam, gabapentin, lorazepam, mirtazapine, quetiapine, and trazodone). Additionally, we present the results of the fully adjusted models stratified by sex to explore possible differences between females and males. Finally, we present the exploratory model with a reduced set of covariables obtained using the DAG model in Figure S2.

Finally, we performed an exploratory analysis using a classification and regression tree (CART) analysis to evaluate the NPS and behavioral combinations present in the cohort to explore explanations for the differences in PM usage. In short, CART is a technique that resorts to data recursive partitioning to obtain the combinations of the characteristics in the participant group. Every partition group is mutually exclusive and exhaustive, meaning all participants will be allocated to a group and only one group.[16] In the CART analysis, we obtained the combinations of NPS and behavioral symptoms in the participants and the number of participants in the genetic and sporadic categories on every combination. For the CART analysis, we used the report from the NACC UDS clinician judgment on behavioral symptoms presence of agitation, anxiety, apathy, depressed mood, disinhibition, hallucinations/delusions, irritability, personality changes (from NACC UDS: "the subject exhibits bizarre behavior or behavior uncharacteristic of the subject, such as unusual collecting, suspiciousness, unusual dress, or dietary changes," and/or "subject fails to take others' feelings into account") and rapid eye movement sleep behavior disorder. In the hallucinations/delusions category, we included participants with visual and auditory hallucinations and delusional beliefs.

We did not make any prediction with the CART model. We performed the analysis using R version 4.3.1.

RESEARCH IN CONTEST

1. **Systematic review**: We reviewed the literature using traditional databases including PubMed, Medline, and Embase. The information regarding differences in psychotropic medication (PM) usage between genetic and sporadic behavioral variant frontotemporal dementia (bvFTD) is scarce, but we reference relevant information in dementia that can illuminate our research.
2. **Interpretation**: Sporadic bvFTD patients are taking more PMs than patients with genetic bvFTD. We hypothesize that the differences result from varying combinations of behavioral symptoms observed between sporadic and genetic bvFTD groups.
3. **Future directions**: Future research should delve deeper into the factors associated with the increased likelihood of PM use in sporadic bvFTD, considering that some PMs carry health risks and could have implications for outcome and quality of life. Moreover, these studies should investigate neuropsychiatric symptoms more thoroughly to identify patterns that lead to increased PM usage.

3 | RESULTS

Our sample consisted of 456 participants, with 263 sporadic and 193 genetic bvFTD. See Table 1 for results and comparisons. Sporadic participants were older at disease onset with a mean age of 58.7 ± 8.9 years compared to genetic participants at 53.2 ± 9.6 years; also, there were fewer female participants in the sporadic group than in the genetic. The genetic group comprised: 100 participants (51.8%) with *C9orf72* repeat expansion, 60 participants (31.1%) with

TABLE 1 Demographic and clinical description of sporadic and genetic bvFTD.

	Sporadic (*N* = 263)	Genetic (*N* = 193)	*p* value
Sex female, *n* (%)	89 (33.8%)	92 (47.7%)	0.003
Age of onset, mean (SD), years	58.7 (8.9)	53.2 (9.6)	<0.001
Education, mean (SD), years	16.2 (2.5)	15.4 (2.4)	<0.001
Hand dominance, *n* (%)			0.157
Left	31 (11.8%)	14 (7.3%)	
Right	227 (86.6%)	172 (89.6%)	
Ambidextrous	4 (1.5%)	6 (3.1%)	
CDR-plus-NACC-FTLD global, *n* (%)			0.228
0.5	20 (7.6%)	14 (7.3%)	
1	112 (42.6%)	69 (35.8%)	
2	120 (45.6%)	104 (53.9%)	
3	11 (4.2%)	6 (3.1%)	
CDR-plus-NACC-FTLD sum of boxes, mean (SD)	8.2 (3.8)	8.4 (4.0)	0.669
Patient level of independence, *n* (%)			0.168
Able to live independently	59 (23.0%)	56 (29.3%)	
Requires some assistance with complex activities	108 (42.2%)	78 (40.8%)	
Requires some assistance with basic activities	65 (25.4%)	38 (19.9%)	
Completely dependent	24 (9.4%)	19 (9.9%)	
NPI-Q, mean (SD)	11.8 (7.0)	10.0 (6.5)	0.005
GDS, mean (SD)	3.3 (3.4)	2.6 (2.9)	0.020
FAQ, mean (SD)	18.0 (8.3)	17.4 (8.3)	0.560
Predominant domain that was first recognized as changed, *n* (%)			0.279
Cognition	51 (19.5%)	33 (18.1%)	
Behavior	207 (79.3%)	143 (78.6%)	
Motor	3 (1.1%)	6 (3.3%)	
MoCA total score, mean (SD)	19.9 (10.9)	19.6 (9.7)	0.742
NACC UDS clinician judgment of behavioral symptoms, *n* (%)			
Apathy	224 (85.2%)	144 (74.6%)	0.005
Depressed mood	60 (22.8%)	29 (15.0%)	0.038
Visual hallucinations	11 (4.2%)	10 (5.2%)	0.615
Auditory hallucinations	4 (1.5%)	9 (4.7%)	0.046
Delusional beliefs	31 (11.8%)	32 (16.6%)	0.143
Disinhibition	217 (82.5%)	155 (80.3%)	0.550
Irritability	172 (65.4%)	99 (51.3%)	0.002
Agitation	106 (40.3%)	55 (28.5%)	0.009
Personality changes	240 (91.3%)	178 (92.2%)	0.710
REM sleep behavior disorder	16 (6.1%)	1 (0.5%)	0.002
Anxiety	71 (27.0%)	37 (19.2%)	0.052
Psychotropic medication prescriptions, *n* (%)			<0.001
0	85 (32.3%)	100 (51.8%)	
1	103 (39.2%)	58 (30.1%)	
2	64 (24.3%)	27 (14.0%)	
≥ 3	11 (4.2%)	8 (4.1%)	

(Continues)

TABLE 1 (Continued)

	Sporadic (*N* = 263)	Genetic (*N* = 193)	*p* value
Psychotropic medications, *n* (%)			
Citalopram	23 (8.7%)	7 (3.6%)	0.029
Escitalopram	41 (15.6%)	20 (10.4%)	0.105
Fluoxetine	9 (3.4%)	6 (3.1%)	0.853
Paroxetine	3 (1.1%)	8 (4.1%)	0.039
Sertraline	50 (19.0%)	17 (8.8%)	0.002
Duloxetine	7 (2.7%)	10 (5.2%)	0.161
Mirtazapine	9 (3.4%)	10 (5.2%)	0.353
Venlafaxine	8 (3.0%)	3 (1.6%)	0.306
Bupropion	13 (4.9%)	7 (3.6%)	0.498
Alprazolam	9 (3.4%)	4 (2.1%)	0.392
Clonazepam	10 (3.8%)	8 (4.1%)	0.853
Lorazepam	6 (2.3%)	2 (1.0%)	0.317
Trazodone	40 (15.2%)	15 (7.8%)	0.016
Quetiapine	28 (10.6%)	18 (9.3%)	0.644
Gabapentin	11 (4.2%)	5 (2.6%)	0.361
Gait disturbance, *n* (%)			0.001
Normal	175 (66.8%)	153 (80.1%)	
Slight alteration	57 (21.8%)	29 (15.2%)	
Walks with difficulty but require no assistance	17 (6.5%)	6 (3.1%)	
Severe disturbance	12 (4.6%)	3 (1.6%)	
Type of gait disturbances in participants with gait abnormalities, *n* (%)			0.232
Hemiparetic	1 (1.2%)	1 (3.3%)	
Lower motor neuron	3 (3.6%)	0 (0.0%)	
Ataxic gait	2 (2.4%)	1 (3.3%)	
Parkinsonian	37 (44.0%)	20 (66.7%)	
Apractic	8 (9.5%)	0 (0.0%)	
Antalgic	9 (10.7%)	3 (10.0%)	
Other	24 (28.6%)	5 (16.7%)	
Frequent falls, *n* (%)	46 (17.5%)	16 (8.3%)	0.005
Presenting tremor, *n* (%)	35 (13.3%)	24 (12.4%)	0.784
Presenting clinically significant slowness, *n* (%)	71 (27.0%)	35 (18.1%)	0.027
UPDRS total score, mean (SD)	4.4 (7.9)	3.1 (6.6)	0.066
PSPRS score, mean (SD)	7.8 (7.2)	6.2 (7.5)	0.034
Signs consistent with ALS/PLS diagnosis in supplemental UPDRS, *n* (%)	12 (4.6%)	9 (4.7%)	0.947

Note: CDR-plus-NACC-FTLD: Clinical Dementia Rating plus behavior and language modules from the NACC behavior and language domains.
Abbreviations: ALS/PLS, amyotrophic lateral sclerosis/primary lateral sclerosis; bvFTD, behavioral-variant frontotemporal dementia; CDR, Clinical Dementia Rating; FAQ, Functional Activities Questionnaire; GDS, Geriatric Depression Scale; MoCA, Montreal Cognitive Assessment; NACC, National Alzheimer's Coordinating Center; NPI-Q, Neuropsychiatric Inventory Questionnaire; PSPRS, progressive supranuclear palsy rating scale; REM, rapid eye movement; SD, standard deviation; UDS, Uniform Data Set; UPDRS, unified Parkinson's disease rating scale.

microtubule-associated protein tau gene (*MAPT*) mutations, 24 participants (12.4%) with progranulin gene (*GRN*) mutations, and 9 participants (4.7%) with other mutations. Of all patients included, 131 (28.7%) knew their genetic status at baseline. Comparing non-behavioral symptoms, sporadic patients have higher prevalence of gait abnormalities (33.2% vs. 19.9%; *p* value 0.001), higher prevalence of frequent falls (17.5% vs. 8.3; *p* value 0.005), and higher prevalence of bradykinesia (27.0% vs. 18.1%; *p* value 0.027) compared to genetic participants.

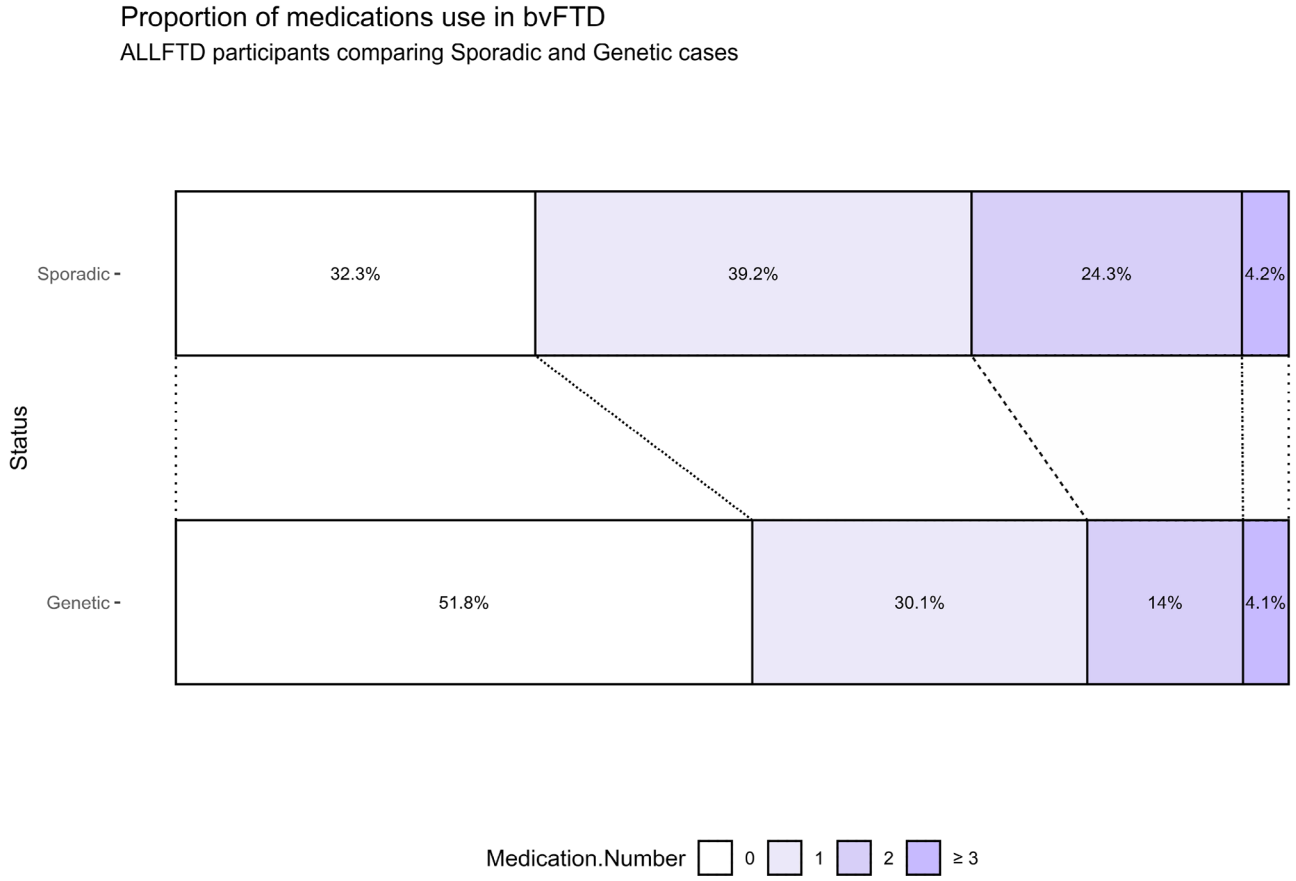

FIGURE 1 Proportion of PM usage in sporadic and genetic participants bvFTD. ALLFTD, Advancing Research and Treatment in Frontotemporal Lobar Degeneration/Longitudinal Evaluation of Familial Frontotemporal Dementia Subjects; bvFTD, behavioral-variant frontotemporal dementia; PM, psychotropic medication.

We found that the NPI-Q and GDS scores were higher in the sporadic compared to genetic bvFTD group. Also, agitation, apathy, depressed mood, and irritability were more common in sporadic participants while auditory hallucinations were more common in genetic participants.

The PM usage in sporadic bvFTD was higher than in genetic bvFTD. Figure 1 shows the proportion of PM usage in both groups. The CDR-plus-NACC-FTLD global distribution was similar in both groups. See Tables S1–S4 in supporting information for stratified descriptions by each CDR-plus-NACC-FTLD global stage.

In the first model, we found an unadjusted OOR of 2.05 (95% confidence interval [CI]: 1.45 to 2.93) for the risk of being on more PMs in the sporadic bvFTD participants compared to genetic participants. In the second model, adjusting by CDR-plus-NACC-FTLD, we found an adjusted OOR (aOOR) of 2.13 (95% CI: 1.50 to 3.05) for greater PM usage at baseline in participants with sporadic bvFTD compared to genetic participants. Participants with higher CDR-plus-NACC-FTLD global had a higher risk of more PM usage with an aOOR of 2.21 (95% CI: 1.05 to 4.67). Finally, in the third fully adjusted model, we found an aOOR of 1.78 (95% CI: 1.23 to 2.58) for sporadic participants of using more PMs than the genetic participants. Also, in this model, NPI-Q with an aOOR of 1.09 (95% CI: 1.06 to 1.12) and GDS with an aOOR of 1.11 (95% CI: 1.05 to 1.18) were associated with increased PM. Table 2 presents the results of the three models. The exploratory analysis restricted to PMs likely used as antidepressants showed an aOOR of 1.62 (95% CI: 1.10 to 2.40) for increased PM usage in sporadic patients, while the exploratory analysis restricted to PMs likely used for agitation/sedation resulted in an aOOR of 1.50 (95% CI: 0.97 to 2.35) for increased PM usage in sporadic patients. Both models are presented in Tables S5 and S6 in supporting information. The exploratory stratified analysis by sex showed that males with sporadic bvFTD had a higher risk of having more PM prescriptions compared to genetic ones with an aOOR of 2.14 (95% CI: 1.31 to 3.51), while females with sporadic origin had an aOOR of 1.30 (95% CI: 0.74 to 2.28) of having more PM prescriptions compared to genetic bvFTD females; the full results for the models are presented in Table S7 in supporting information. Finally, Table S8 in supporting information presents the results exploring the use of a reduced model; in this model, the results of the effect of sporadic origin are consistent with the full model, with an aOOR of 1.85 (95% CI: 1.28 to 2.66).

Using the NACC UDS clinician judgment for behavioral symptoms, we found 19 NPS combinations in the CART analysis, as shown in Figure 2; also, in Table 3, we present all the combinations of NPS, their frequencies, and the distribution between sporadic and genetic within

TABLE 2 Proportional odds logistic models comparing the baseline PM usage between sporadic and genetic bvFTD.

Variable	OOR	95% CI lower	95% CI upper	*p* value
Model 1				
Sporadic disease	*2.05*	*1.45*	*2.93*	*<0.001*
Model 2				
Sporadic disease	*2.13*	*1.5*	*3.05*	*<0.001*
CDR-plus-NACC-FTLD global				
Linear	2.21	1.05	4.67	0.038
Quadratic	1.81	1.01	3.24	0.046
Cubic	0.96	0.7	1.4	0.934
Model 3				
Sporadic disease	*1.75*	*1.21*	*2.53*	*0.002*
CDR-plus-NACC-FTLD global				
Linear	1.62	0.76	3.47	0.212
Quadratic	2.33	1.28	4.24	0.005
Cubic	0.99	0.7	1.41	0.963
Female sex	0.92	0.64	1.32	0.649
NPI-Q	1.09	1.06	1.12	<0.001
GDS	1.11	1.05	1.18	<0.001

Note: CDR plus NACC FTLD: Clinical Dementia Rating plus behavior and language modules from the NACC behavior and language domains.
Abbreviations: bvFTD, behavioral-variant frontotemporal dementia; CDR, Clinical Dementia Rating; CI, confidence interval; GDS, Geriatric Depression Scale; NCC, National Alzheimer's Coordinating Center; NPI-Q, neuropsychiatric inventory questionnaire; OOR, ordinal odds ratio; PM, psychotropic medication.

every combination. The most common combinations were apathy + personality changes in 18% of the participants, apathy + irritability in 15.4%, agitation + apathy + disinhibition + irritability in 9.4%, agitation + apathy + depressive mood + irritability in 6.8%, agitation + anxiety + apathy + irritability in 5.7%, hallucination/delusions alone in 5.5%, and disinhibition + irritability in 5.3%.

4 | DISCUSSION

Our study found that participants with sporadic bvFTD are more likely to be on PMs than participants with genetic bvFTD disease at baseline evaluation. A previous publication on the same cohort of ALLFTD participants showed that sporadic participants have a higher burden of NPS, mainly irritability and depression.[7] Consequently, we expected that the increased likelihood of more PM would disappear after adjusting for NPI and GDS. However, our adjusted results showed that sporadic bvFTD participants are almost twice as likely to be on a PM compared to genetic bvFTD; our exploratory analyses results were in the same direction when we analyzed only prescriptions likely for mood disorders and prescriptions likely for agitation/sedation.

Previous research has shown that the number of PMs is higher in frontotemporal dementia than in dementia due to AD, even though NPS are similar in both groups.[3] Our findings show that this elevated PM usage is also present within the bvFTD participants and varies according to their genetic status. However, the reason for this increase in PM usage in sporadic participants remains unclear, and we do not know if it translates into an increased risk of death in bvFTD sporadic patients, as previous research has shown for increased PM usage in dementia.[4,5]

Some studies have reported mixed results when comparing the prevalence of NPS between sporadic and genetic patients in bvFTD. An FTD study (bvFTD: 75.9%), from southern Italy reported that patients with sporadic disease have a higher prevalence of disinhibition (66% vs. 36%; $P = 0.02$), but no differences in depression or irritability;[17] this was in keeping with our previous finding that sporadic bvFTD participants have higher NPI-Q scores than genetic cases. In contrast, another Italian cohort (bvFTD: 66.8%) found no differences between sporadic and genetic participants in frequency of NPS, measured by the Frontal Behavioral Inventory B (5.8 ± 5.9 vs. 6.0 ± 5.2; $P = 0.63$).[8] These two Italian cohorts comprised mostly bvFTD but included other FTD syndromes. Considering all these findings, we posit that the likelihood of being on more PMs is not exclusively linked to individual symptoms.

We also investigated symptom combinations as it was evident that the prevalence of these symptom combinations varies between the two groups, and certain PM needs might stem from these different symptom combinations. Interestingly, CART analysis demonstrated that even symptoms with comparable proportions in both groups manifest in distinct combinations for sporadic and genetic participants. This variance could influence distinct patterns in PM needs—some symptom combinations may be treated with the same medication, while others necessitate multiple PMs. This aspect warrants deeper exploration in subsequent research endeavors.

Also, bvFTD symptoms may differ in the early phases. For example, in a large cohort of genetic patients from Europe and Canada, *GRN* mutations were associated with early memory complaints, *MAPT* variants were associated with disinhibition, and *C9orf72* patients did not have a specific pattern;[18] however, additional information from the UK has shown that *C9orf72* expansion carriers have a higher frequency of psychotic symptoms even early on in their disease course.[19] In contrast, there is no published specific pattern for sporadic patients with bvFTD. We hypothesize that there could be a differential PM usage pattern during the early phases in sporadic and genetic bvFTD. Clinical research of this early phase is an active area, and there are recent standardized proposed criteria to explore prodromal bvFTD disease[20] that will allow us to further examine disease presentation in all the different groups.

Our study is the first to show that PM usage differs between sporadic and genetic bvFTD cases. However, it is difficult to know whether this is only due to higher symptomatology in sporadic bvFTD or psychosocial aspects that may be impacting the medication usage. One hypothesis is that there may be greater tolerance of symptoms in familial cases, whereas sporadic bvFTD patients and families may be more likely to report and seek treatments to alleviate psychiatric symptoms.

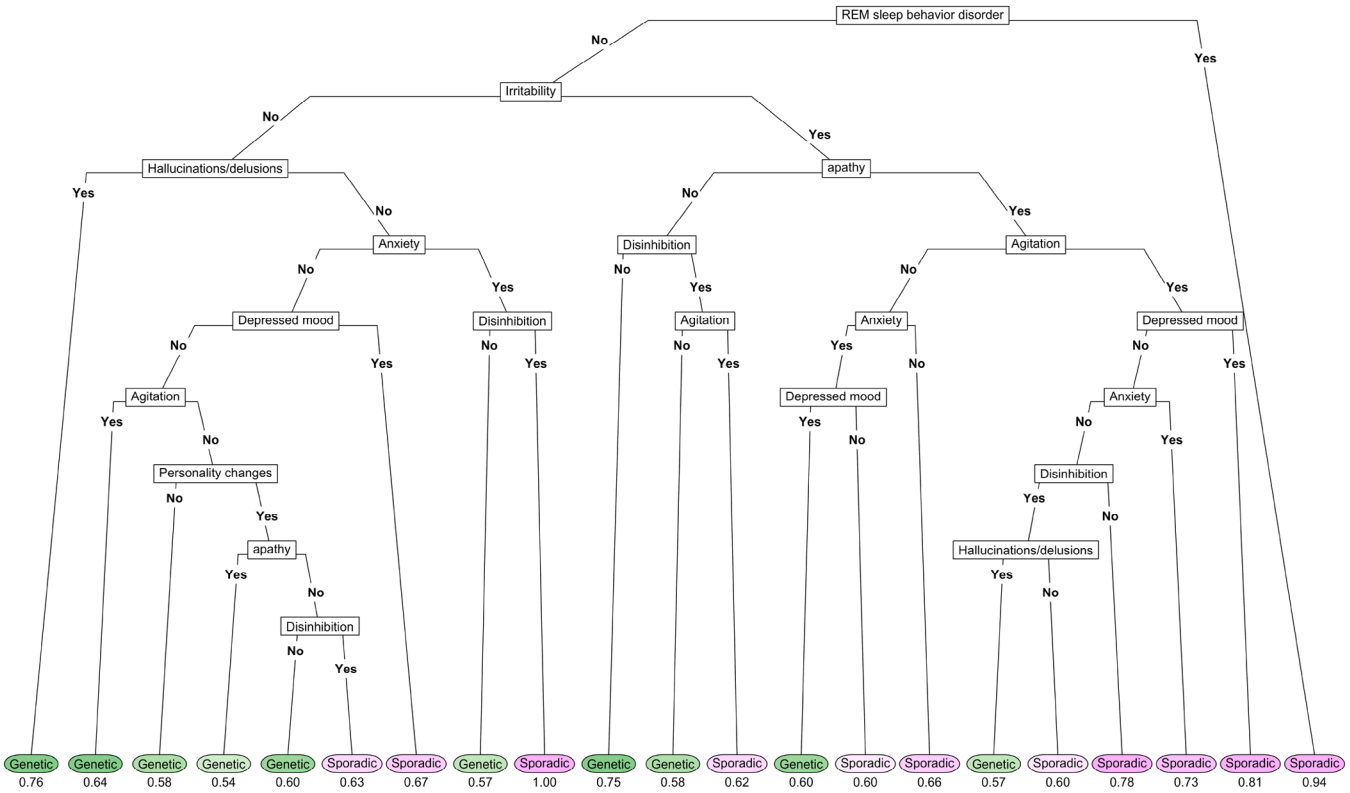

FIGURE 2 CART model showing the clinician judgment of behavioral symptoms combinations according to their sporadic or genetic status in participants with bvFTD in ALLFTD participants. In the CART figure, every one of the nodes in white is distributed between those participants with and without the characteristic. The last nodes in purple color are assigned to symptom combinations with a higher proportion in the sporadic participants while the green color is assigned to combinations with a higher proportion in the genetic cases. The number under the node is the proportion of all the participants with that specific combination of symptoms that are in the sporadic or genetic group. ALLFTD, Advancing Research and Treatment in Frontotemporal Lobar Degeneration/Longitudinal Evaluation of Familial Frontotemporal Dementia Subjects; bvFTD, behavioral-variant frontotemporal dementia; CART, classification and regression tree; REM, rapid eye movement.

Supporting this hypothesis, a survey from the state of Washington showed that having a family history of dementia is associated with a belief that interventions are not helpful and a decreased intention to seek active management.[21]

There may be some dimensions related to using a PM that we are not capturing in our analysis. We do not have information on the order of symptom onset, which can modify the number of PM prescriptions. Also, we do not have information regarding whether our bvFTD participants were initially diagnosed with a psychiatric disorder. For example, results from Colombia showed that 71.4% of the patients with bvFTD were initially diagnosed with a psychiatric disorder.[22] Also, the authors found differences in the diagnosed disorders by sex. Women had a diagnosis of depression in 26.3% and bipolar disorder in 26.3% of the cases; in contrast, men had a diagnosis of anxiety in 33.3% of the cases. This initial psychiatric diagnosis can lead to an increase in PM prescription and can modify the type and number of PM usage by the participants by the time they were recruited into ALLFTD. Additionally, a recent case–control study has reported that a family history of primary psychiatric disease is higher in sporadic bvFTD,[23] but not in AD or healthy controls, which could explain why some sporadic bvFTD patients are initially diagnosed and treated as a primary psychiatric disorder before arriving to the bvFTD diagnosis. Finally, an interesting finding from our exploratory analysis stratified by sex was that in the fully adjusted model males with sporadic bvFTD had an increased aOOR of 2.14 (95% CI: 1.31 to 3.51) of having more PM, while sporadic females only had a non-significant aOOR of 1.30 (95% CI: 0.74 to 2.28) of having more PM prescriptions compared to genetic bvFTD. Moreover, the sex distribution in the genetic group is fairly equally distributed while in the sporadic bvFTD group there is a preponderance of males (66.2%). This discrepancy likely warrants further investigation.

We believe our study has the following strengths. First, we have a large patient cohort, and most participants were unaware of their genetic status at baseline, which diminished the risk of information bias related to knowing genetic status. Second, based on previous research, we selected our confounding adjustment set with a DAG, an approximation that improves our confidence in the results. We used a logistic regression model that used the ordinal nature of the outcome measure without the necessity of transforming the outcome or using approximations that do not fit the data structure. Also, our results were robust in the different exploratory analyses.

However, we acknowledge some weaknesses in our study. We do not have the order of symptom onset, nor a full set of psychiatric assessments. We do not know the proportion of bvFTD participants initially diagnosed with a psychiatric condition. We also have no

TABLE 3 NPS combinations from NACC UDS clinician judgment in ALLFTD cohort according to genetic or sporadic bvFTD.

Symptoms combination*	Percentage of total patients, *n* (%)	Sporadic, *n* (%)	Genetic, *n* (%)
Hallucination/delusions**	25 (5.5 %)	6 (24%)	19 (76%)
Irritability	8 (1.8 %)	2 (25%)	6 (75%)
Agitation	11 (2.4 %)	4 (36.3%)	7 (63.7%)
Personality changes	5 (1.1 %)	2 (40%)	3 (60%)
Anxiety + apathy + depressed mood + irritability	10 (2.2 %)	4 (40%)	6 (60%)
Disinhibition + irritability	24 (5.3 %)	10 (41.7%)	14 (58.3%)
Anxiety	7 (1.5 %)	3 (43.9%)	4 (57.1 %)
Agitation + apathy + disinhibition + hallucination/delusions** + Irritability	7 (1.5 %)	3 (43.9%)	4 (57.1 %)
Apathy + personality changes	82 (18 %)	38 (46.3%)	44 (53.7%)
Anxiety + apathy + irritability	15 (3.3 %)	9 (60%)	6 (40%)
Agitation + apathy + disinhibition + irritability	43 (9.4 %)	26 (60.5%)	17 (39.5%)
Agitation + disinhibition + irritability	16 (3.5 %)	10 (62.5%)	6 (37.5%)
Disinhibition + personality changes	19 (4.2 %)	12 (63.2%)	7 (36.8%)
Apathy + irritability	70 (15.4 %)	46 (66%)	24 (34%)
Depressed mood	9 (2 %)	6 (66.7%)	3 (33.3%)
Agitation + anxiety + apathy + irritability	26 (5.7 %)	19 (73.1%)	7 (26.9%)
Agitation + apathy + irritability	9 (2 %)	7 (77.8%)	2 (22.2%)
Agitation + apathy + depressed mood + irritability	31 (6.8 %)	25 (80.7%)	6 (19.3%)
REM sleep behavioral disorder	17 (3.7 %)	16 (94.1%)	1 (5.9%)
Anxiety + disinhibition	10 (2.2 %)	10 (100%)	0 (0%)

Abbreviations: ALLFTD, Advancing Research and Treatment in Frontotemporal Lobar Degeneration/Longitudinal Evaluation of Familial Frontotemporal Dementia Subjects; bvFTD, behavioral-variant frontotemporal dementia; CART, classification and regression trees; NACC-UDS, National Alzheimer's Coordinating Center Uniform Data Set; NPSs, neuropsychiatric symptoms; REM, rapid eye movement.
*A total of 12 (2.6 %) of the participants did not have NPSs, including five sporadic and seven genetic cases.
**For the CART analysis, we combined all hallucinations and delusions in a single category.

information on the diagnostic route that sporadic and genetic patients followed and if they are patients of a specialized center or only participants in the study. Participants that consulted more health-care providers before a bvFTD diagnosis may have a higher likelihood of being prescribed additional PMs. Furthermore, we do not have information about the initial reason for the PM usage or who prescribed the medications, and so some of those medications may have been initially prescribed for a different diagnosis. Also, some molecules may have been selected to address more than one NPS or relieve non-NPS symptoms. Also, regarding antipsychotics we only have the information regarding quetiapine use; we acknowledge that some participants might be using other commonly prescribed antipsychotics such as olanzapine and risperidone, and we might not be fully including the patients presenting more agitation.

Furthermore, we did not analyze individually the most relevant genetic mutations as we did not have the sample size on the individual genetic groups to obtain reliable results. Previous recommendations suggest that a CART analysis should have at least 100 participants.

In summary, our findings indicate that sporadic bvFTD is associated with a higher likelihood of using more PM, and this increased risk remains significant even after adjusting for factors such as NPS and depression scales. Also, we found that the frequency of the NPS and behavioral combinations is different between sporadic and genetic cases. Subsequent studies should evaluate further the factors associated with the increased likelihood of PM use in sporadic bvFTD as some PMs carry health risks and could have implications for outcome and quality of life. Additionally, studies should address the chronology of PM usage as NPS evolve over time, which may modify PM prescription. Identification of patterns that lead to increased PM usage may result in more rational prescribing practices across sporadic and genetic bvFTD.

AFFILIATIONS

[1]Division of Neurology, University of Toronto, Toronto, Ontario, Canada

[2]Memory Clinic, University Health Network, Toronto, Ontario, Canada

[3]Memory and Aging Center, Department of Neurology, Weill Institute for Neurosciences, University of California San Francisco, San Francisco, California, USA

[4]Department of Neurology, Mayo Clinic, Rochester, Minnesota, USA

[5]Department of Neurology, Case Western Reserve University, Beachwood, Ohio, USA

[6]University of Michigan, Ann Arbor, Michigan, USA

[7]Department of Neurology, University of North Carolina, Chapel Hill, North Carolina, USA

[8]Indiana University, Indianapolis, Indiana, USA

[9]Vanderbilt University, Nashville, Tennessee, USA

[10]Department of Neurology, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts, USA

[11]Department of Neurology, University of Washington, Seattle, Washington, USA

[12]University of California San Diego, San Diego, California, USA

[13]Department of Neurology, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, California, USA

[14]Memory Diagnostic Center, Department of Neurology, Washington University School of Medicine in St. Louis, St. Louis, Missouri, USA

[15]Mayo Clinic, Jacksonville, Florida, USA

[16]Department of Psychiatry and Behavioral Sciences, Mesulam Center for Cognitive Neurology and Alzheimer's Disease, Northwestern Feinberg School of Medicine, Chicago, Illinois, USA

[17]Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA

[18]University of British Columbia, Vancouver, British Columbia, Canada

[19]Neurology Department and Taub Institute, Columbia University Irving Medical Center, New York, New York, USA

[20]Nantz National Alzheimer Center, Houston Methodist, Houston, Texas, USA

[21]Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

[22]University of Colorado Denver, Denver, Colorado, USA

[23]Department of Neurology, University of Alabama at Birmingham, Birmingham, Alabama, USA

[24]Healthy Aging & Alzheimer's Research Care (HAARC) Center, Department of Neurology, University of Chicago, Chicago, Illinois, USA

[25]Tanz Centre for Research in Neurodegenerative Diseases, University of Toronto, Toronto, Ontario, Canada

ACKNOWLEDGMENTS

We extend our appreciation to the clinicians and coordinators at all ARTFL/LEFFTDS centers, and particularly to our patients and their families for their participation in this research. B. C. Dickerson is a consultant for Acadia, Alector, Arkuda, Biogen, Denali, Eisai, Genentech, Lilly, Merck, Novartis, Takeda, and Wave Lifesciences; receives royalties from Cambridge University Press, Elsevier, and Oxford University Press; and receives grant funding from the NIA>, the National Institute of Neurological Disorders and Stroke, the National Institute of Mental Health, and the Bluefield Foundation. K. Domoto-Reilly receives research support from the NIH and serves as an investigator for a clinical trial sponsored by Lawson Health Research Institute. N. Ghoshal has participated or is currently participating in clinical trials of anti-dementia drugs sponsored by Bristol Myers Squibb, Eli Lilly/Avid Radiopharmaceuticals, Janssen Immunotherapy, Novartis, Pfizer, Wyeth, SNIFF (The Study of Nasal Insulin to Fight Forgetfulness), and the A4 (The Anti-Amyloid Treatment in Asymptomatic Alzheimer's Disease) trial. She receives research support from the Tau Consortium and the Association for Frontotemporal Dementia and is funded by the NIH. N. R. Graff-Radford receives royalties from UpToDate and has participated in multicenter therapy studies sponsored by Biogen, TauRx, and Lilly. He receives research support from the NIH. D. Irwin receives support from the NIH, BrightFocus Foundation, and Penn Institute on Aging. G.-Y. R. Hsiung has served as an investigator for clinical trials sponsored by AstraZeneca, Eli Lilly, and Roche/Genentech. He receives research support from the Canadian Institutes of Health Research and the Alzheimer Society of British Columbia. E. D. L. S. Honig receives research funding from Abbvie, Acumen, Alector, Biogen, BMS, Eisai, Genentech/Roche, Janssen/J&J, Transposon, UCB, Vaccinex, and consulting fees from Biogen, Cortexyme, Eisai, Medscape, and Prevail/Lilly. K. Kantarci served on the data safety monitoring board for Takeda Global Research & Development Center and the data monitoring boards of Pfizer and Janssen Alzheimer Immunotherapy and received research support from Avid Radiopharmaceuticals, Eli Lilly, the Alzheimer's Drug Discovery Foundation, and the NIH. I. Litvan is supported by the NIH grants: 2R01AG038791-06A, U01NS100610, U01NS80818, R25NS098999; U19 AG063911-1 and 1R21NS114764-01A1; the Michael J. Fox Foundation, Parkinson Foundation, Lewy Body Association, CurePSP, Roche, Abbvie, Biogen, Centogene, EIP-Pharma, Biohaven Pharmaceuticals, Novartis, Brain Neurotherapy Bio, and United Biopharma SRL—UCB. She is a scientific advisor for the Amydis and Rossy Center for Progressive Supranuclear Palsy at the University of Toronto. She receives her salary from the University of California, San Diego and as chief dditor of *Frontiers in Neurology*. M. F. Mendez receives research support from the NIH. C. U. Onyike receives research funding from the NIH, Lawton Health Research Institute, National Ataxia Foundation, Alector, and Transposon. He is also supported by the Robert and Nancy Hall Brain Research Fund, the Jane Tanger Black Fund for Young-Onset Dementias, and a gift from Joseph Trovato. He is a consultant with Alector Inc., Acadia Pharmaceuticals, and Reata Pharmaceuticals. E. M. Ramos receives research support from the NIH. E. D. Roberson has received research support from the NIH, the Bluefield Project to Cure Frontotemporal Dementia, the Alzheimer's Association, the Alzheimer's Drug Discovery Foundation, the BrightFocus Foundation, and Alector; has served as a consultant for AGTC and on a data monitoring committee for Lilly; and owns intellectual property related to tau and progranulin. B. F. Boeve has served as an investigator for clinical trials sponsored by Alector, Biogen, Transposon, and Cognition Therapeutics. He serves on the scientific advisory board of the Tau Consortium, which is funded by the Rainwater Charitable Foundation. He receives research support from NIH. R. R. Darby receives research funding from the NIH and the Bluefield Project to Cure Frontotemporal Dementia. A. L. Boxer receives research support from the NIH, the Tau Research Consortium, the Association for Frontotemporal Degeneration, the Bluefield Project to Cure Frontotemporal Dementia, Corticobasal Degeneration Solutions, the Alzheimer's Drug Discovery Foundation, and the Alzheimer's Association. He has served as a consultant for Aeovian, AGTC, Alector, Arkuda, Arvinas, Boehringer Ingelheim, Denali, GSK, Life Edit, Humana, Oligomerix, Oscotec, Roche, TrueBinding, Wave, and Merck, and received research support from Biogen, Eisai, and Regeneron. H. J. Rosen has received research support from Biogen Pharmaceuticals; has consulting agreements with Wave Neuroscience, Ionis Pharmaceuticals, Eisai Pharmaceuticals, and Genentech; and receives research support from NIH and the state

of California. M. C. Tartaglia has served as an investigator for clinical trials sponsored by Biogen, Avanex, Green Valley, Roche/Genentech, Bristol Myers Squibb, Eli Lilly/Avid Radiopharmaceuticals, and Janssen. She receives research support from the Canadian Institutes of Health Research. This work is supported by the NIH grants: U01AG045390, U54NS092089, and U01AG016976.

CONFLICT OF INTEREST STATEMENT

J.-C. Vargas-González reports no disclosures relevant to the manuscript. N.-P. Dimas reports no disclosures relevant to the manuscript. K. Cortes reports no disclosures relevant to the manuscript. H. Heuer reports no disclosures relevant to the manuscript. L. K. Forsberg receives research support from the NIH. B. S. Appleby receives research support from the Centers for Disease Control and Prevention, the National Institutes of Health (NIH). S. Barmada reports no disclosures relevant to the manuscript. A. Bozoki reports no disclosures relevant to the manuscript. D. Clark reports no disclosures relevant to the manuscript. Y. Cobigo reports no disclosures relevant to the manuscript. R. R. Darby reports no disclosures relevant to the manuscript. D. R. Galasko reports no disclosures relevant to the manuscript. D. H. Geschwind reports no disclosures relevant to the manuscript. I. M. Grant reports no disclosures relevant to the manuscript. D. G. C. Léger reports no disclosures relevant to the manuscript. I. R. Mackenzie reports no disclosures relevant to the manuscript. J. C. Masdeu reports no disclosures relevant to the manuscript. B. Pascual reports no disclosures relevant to the manuscript. P. Pressman reports no disclosures relevant to the manuscript. E. Rogalski reports no disclosures relevant to the manuscript. Author disclosures are available in the supporting information.

CONSENT STATEMENT

All human participants in ARTFL/LEFFTDS study provided informed consent before joining the study.

ORCID

Juan-Camilo Vargas-Gonzalez https://orcid.org/0000-0002-1719-2200

REFERENCES

1. Tannenbaum R, Boltz M, Ilyas A, et al. Hospital practices and clinical outcomes associated with behavioral symptoms in persons with dementia. *J Hosp Med*. 2022;17:702-709. doi:10.1002/jhm.12921
2. Rascovsky K, Hodges JR, Knopman D, et al. Sensitivity of revised diagnostic criteria for the behavioural variant of frontotemporal dementia. *Brain J Neurol*. 2011;134:2456-2477. doi:10.1093/brain/awr179
3. Tartaglia MC, Hu B, Mehta K, et al. Demographic and neuropsychiatric factors associated with off-label medication use in frontotemporal dementia and Alzheimer's disease. *Alzheimer Dis Assoc Disord*. 2014;28:182-189. doi:10.1097/WAD.0b013e3182a7159d
4. Jennum P, Baandrup L, Ibsen R, Kjellberg J. Increased all-cause mortality with use of psychotropic medication in dementia patients and controls: a population-based register study. *Eur Neuropsychopharmacol*. 2015;25:1906-1913. doi:10.1016/j.euroneuro.2015.08.014
5. Nørgaard A, Jensen-Dahm C, Gasse C, Wimberley T, Hansen ES, Waldemar G. Association of benzodiazepines and antidepressants with 180-day mortality among patients with dementia receiving antipsychotic pharmacotherapy: A nationwide registry-based study. *J Clin Psychiatry*. 2020;81:19m12828. doi:10.4088/JCP.19m12828
6. Benussi A, Premi E, Gazzina S, et al. Progression of behavioral disturbances and neuropsychiatric symptoms in patients with genetic frontotemporal dementia. *JAMA Netw Open*. 2021;4:e2030194. doi:10.1001/jamanetworkopen.2020.30194
7. Heuer HW, Wang P, Rascovsky K, et al. Comparison of sporadic and familial behavioral variant frontotemporal dementia (FTD) in a North American cohort. *Alzheimers Dement*. 2020;16:60-70. doi:10.1002/alz.12046
8. Benussi A, Libri I, Premi E, et al. Differences and similarities between familial and sporadic frontotemporal dementia: an Italian single-center cohort study. *Alzheimers Dement Transl Res Clin Interv*. 2022;8:e12326. doi:10.1002/trc2.12326
9. Ramos EM, Dokuru DR, Van Berlo V, et al. Genetic screening of a large series of North American sporadic and familial frontotemporal dementia cases. *Alzheimers Dement*. 2020;16:118-130. doi:10.1002/alz.12011
10. Miyagawa T, Brushaber D, Syrjanen J, et al. Utility of the global CDR® plus NACC FTLD rating and development of scoring rules: data from the ARTFL/LEFFTDS consortium. *Alzheimers Dement*. 2020;16:106-117. doi:10.1002/alz.12033
11. Morris JC. The clinical dementia rating (CDR): current version and scoring rules. *Neurology*. 1993;43:2412-2414. doi:10.1212/wnl.43.11.2412-a
12. Knopman DS, Kramer JH, Boeve BF, et al. Development of methodology for conducting clinical trials in frontotemporal lobar degeneration. *Brain*. 2008;131:2957-2968. doi:10.1093/brain/awn234
13. Knopman DS, Weintraub S, Pankratz VS. Language and behavior domains enhance the value of the clinical dementia rating scale. *Alzheimers Dement*. 2011;7:293-299. doi:10.1016/j.jalz.2010.12.006
14. French B, Shotwell MS. Regression models for ordinal outcomes. *JAMA*. 2022;328:772-773. doi:10.1001/jama.2022.12104
15. Textor J, van der Zander B, Gilthorpe MS, Liśkiewicz M, Ellison GT. Robust causal inference using directed acyclic graphs: the R package 'dagitty'. *Int J Epidemiol*. 2016;45:1887-1894. doi:10.1093/ije/dyw341
16. Lemon SC, Roy J, Clark MA, Friedmann PD, Rakowski W. Classification and regression tree analysis in public health: methodological review and comparison with logistic regression. *Ann Behav Med*. 2003;26:172-181. doi:10.1207/S15324796ABM2603_02
17. Capozzo R, Sassi C, Hammer MB, et al. Clinical and genetic analyses of familial and sporadic frontotemporal dementia patients in Southern Italy. *Alzheimers Dement*. 2017;13:858-869. doi:10.1016/j.jalz.2017.01.011
18. Tavares TP, Mitchell DGV, Coleman KK, et al. Early symptoms in symptomatic and preclinical genetic frontotemporal lobar degeneration. *J Neurol Neurosurg Psychiatry*. 2020;91:975-984. doi:10.1136/jnnp-2020-322987
19. Snowden JS, Rollinson S, Thompson JC, et al. Distinct clinical and pathological characteristics of frontotemporal dementia associated with C9ORF72 mutations. *Brain*. 2012;135:693-708. doi:10.1093/brain/awr355
20. Barker MS, Gottesman RT, Manoochehri M, et al. Proposed research criteria for prodromal behavioural variant frontotemporal dementia. *Brain J Neurol*. 2022;145:1079-1097. doi:10.1093/brain/awab365
21. Lee W, Gray SL, Zaslavsky O, Barthold D, Marcum ZA. Association between having a family member with dementia and perceptions of

dementia preventability. *Aging Ment Health*. 2022;26:270-276. doi:10.1080/13607863.2020.1839866

22. Zapata-Restrepo L, Rivas J, Miranda C, et al. The psychiatric misdiagnosis of behavioral variant frontotemporal dementia in a Colombian sample. *Front Neurol*. 2021;12:729381. doi:10.3389/fneur.2021.729381
23. Icho S, Korten N, Reus L, et al. Relationship between sporadic behavioral variant frontotemporal dementia and primary psychiatric disorders: a study in families. *J Clin Psychiatry*. 2022;83:43658. doi:10.4088/JCP.21m13932

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Vargas-Gonzalez J-C, Dimal N, Cortez K, et al.; ALLFTD Consortium Investigators. Psychotropic medication usage in sporadic versus genetic behavioral-variant frontotemporal dementia. *Alzheimer's Dement*. 2025;21:e14448. https://doi.org/10.1002/alz.14448