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ORIGINAL RESEARCH

Differentiation Between Early and Severe Stages of Dementia in Claims Data Based on Diagnosis, Prescription, and Utilization Patterns

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ABSTRACT

Introduction: Claims data typically lack clinical parameters such as dementia severity, limiting insights into disease progression and related healthcare utilization and costs. Although diagnoses, prescriptions, and utilization patterns may serve as proxies, their validity is unclear. This study aimed to identify and validate these parameters to distinguish early from severe dementia stages.

Methods: Baseline data from 737 patients with dementia were analyzed. Dementia severity was assessed using the Mini-Mental State Examination and classified as early (≥ 27), mild (20–26), and moderate to severe (0–19). Healthcare utilization was recorded via structured interviews. Diagnoses, long-term care levels, and prescribed medications were extracted from physicians' files. Ordinal logistic regression evaluated associations between predictors and severity, with average marginal effects (AME) quantifying impact. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were computed for key predictors.

Results: Among the sample (56% female patients, mean age 80), 18% were in the early stages, 43% mild, and 39% moderate to severe. Antipsychotic prescriptions (odds ratio (OR) 3.40, 95% confidence interval (CI) 1.94–5.95), antidementia drugs (OR 2.31, 95% CI 1.56–3.40), and higher long-term care levels (OR 5.59, 95% CI 2.23–13.99 for level ≥ 4) were associated with advanced severity. AME analysis revealed that antipsychotic use reduced early-stage probability by 14% and increased severe-stage probability by 21%. Similarly, antidementia drugs lowered early-stage probability by 9% and raised severe-stage probability by 13%. Increasing care levels were associated with a 2–16% decline in early-stage probability and a 3–34% rise in severe-stage probability. The combined model showed high specificity (99.6%) and PPV (84.6%) for severe dementia, but sensitivity and NPV for early stage were low.

Conclusion: Antidementia drugs, antipsychotics, and long-term care level serve as robust predictors of moderate to severe dementia, whereas early-stage detection remains challenging.

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Future studies should validate these markers and explore additional predictors to improve early detection in claims data.

Keywords: Alzheimer's disease; Antidementia drug treatment; Antipsychotics; Claims data; Dementia; Dementia severity; Healthcare utilization; Real-world data; Real-world evidence

Key Summary Points

Why carry out this study?

Real-world data, like claims data, typically lack clinical parameters such as dementia severity, reducing their utility in healthcare decision-making for evaluating the cost-effectiveness of innovative therapies, e.g., disease-modifying drugs for Alzheimer's disease.

This study aimed to identify and validate predictors (documented diagnoses, prescriptions, healthcare utilization patterns) commonly available in German claims records to differentiate early-stage from moderate-to-severe dementia.

What was learned from the study?

The analysis revealed that antipsychotic use, guideline-based antidementia drug prescriptions, and higher long-term care levels are strongly associated with moderate-to-severe dementia, achieving high specificity and positive predictive value.

Despite the strong performance for advanced dementia, the model demonstrated lower sensitivity in detecting early-stage dementia, indicating that many early cases may remain unclassified.

These findings underscore the potential of integrating routine claims data for dementia severity classification while highlighting the need for additional markers and refined algorithms to enhance early detection and guide efficient resource allocation.

INTRODUCTION

Routinely collected real-world data from health insurers complement evidence from randomized controlled trials and are becoming increasingly important, particularly for regulatory decision-making [1–4]. Although administrative claims data has proven valuable in identifying disease cases using diagnostic codes, a critical limitation is the lack of clinical parameters that enable a more detailed look into the disease severity. This limitation reduces the utility of claims data in understanding healthcare service utilization costs in the progression of different diseases in vulnerable populations, such as dementia.

This is especially important if interventions aim to start as early as possible and claims data could be used to reveal the impact of such interventions in different disease stages. Without the prospect of a cure, dementia care needs to ensure the best possible individualized treatment and care as early as possible to delay the progression of cognitive decline, increase or maintain health-related quality of life, and enable individuals to live as long as possible in the community. Hence, the therapeutic goal is to relieve the burden on patients, caregivers, and the healthcare system [5]. Several disease-modifying drug treatments that target dementia at onset or even before symptoms occur, such as lecanemab or donanemab, are currently in development or already recommended for approval by responsible regulatory authorities [6, 7].

However, successfully implementing these treatments and care strategies requires a precise understanding of the affected populations and their needs at different stages of dementia [8–10]. Therefore, to ensure the efficient allocation of limited resources and to assess the cost-effectiveness of innovative therapies, it is essential to identify the target population, analyze their healthcare utilization patterns, and evaluate the impact of dementia severity on health economic outcomes. Currently, this is not possible on the basis of claims data because of the missing information on disease severity, and so far, no claims-based algorithm to measure dementia severity exists [11–13].

Recent studies have addressed this gap by developing models using proxy measures (e.g., claims-based frailty index) or machine learning approaches to estimate dementia severity [14–17]. However, these approaches are often accompanied by a lack of generalizability due to a focus on specific healthcare settings and are confounded by undercoding or underdiagnosing of early-stage dementia [18–20]. Healthcare utilization and prescription patterns can indirectly indicate disease severity and treatment adjustments over time [21, 22]. However, the low treatment rates of people living with dementia (PwD) with antidementia drugs pose an additional challenge [23, 24]. A more precise and comprehensive classification of dementia severity in claims data may be achieved by integrating broader prescribing patterns, e.g., antipsychotic use alongside diagnostic codes and documented prodromal features, risk factors, and comorbidities [17, 25, 26]. However, so far, such approaches have not been systematically validated.

Given these challenges and opportunities, this primary data-based study aims to (1) identify predictors of dementia severity using documented diagnoses according to the 10th edition of the International Classification of Diseases and Related Health Problems (ICD-10), prescription, and healthcare utilization patterns commonly available in German claims records and (2) validate their ability to distinguish early from advanced dementia stages to provide novel insights into the potential of real-world data for assessing dementia severity and supporting regulatory and clinical decision-making.

METHODS

Study Design and Recruitment

This cross-sectional analysis utilized merged baseline data from three independent trials: DelpHi-MV (ClinicalTrials.gov identifier NCT01401582), InDePendent (ClinicalTrials.gov identifier NCT04741932), and DCM:IMPact (German Clinical Trials Register Reference No. DRKS00025074). These trials' detailed designs and methodologies have been published previously [27–29].

In total, 1218 community-dwelling PwD had been recruited through general practitioner (GP) practices, physician networks, or daycare centers by qualified study nurses. Participants were eligible for inclusion if they met the following criteria: a DemTect [30] score < 9 or a listed clinical dementia diagnosis, age ≥ 70 years, and residing at home. Written informed consent had been obtained from all participants, and the trials were approved by the Ethical Committee of the Chamber of Physicians of Mecklenburg-Western Pomerania (registry numbers BB 20/11 for DelpHi-MV, BB01/2019 for DCM:IMPact, and BB144/20 for InDePendent). This has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Seven hundred thirty-seven participants (61%) with complete baseline data on cognitive impairment, diagnoses, prescriptions and healthcare utilization were considered for the current analysis.

Data Assessment

Sociodemographic and Clinical Characteristics

Study nurses conducted comprehensive, standardized, computer-assisted face-to-face interviews at the participants' homes, in which the following variables were assessed: age, sex, cognitive impairment according to the Mini-Mental State Examination (MMSE) [31], and the care level assigned by the long-term care insurance for the amount of care and support a patient receives owing to their functional impairment in daily activities—not the underlying disease severity [27–29]. The care level ranges from 1 to 5, with 1 indicating some problems and 5 indicating extreme problems and determining entitlement to formal care services or financial reimbursement for informal caregiving. In addition, the diagnoses according to the ICD-10 classification and prescribed medication listed in the medical record of the treating physician were collected.

Dementia Severity

Cognitive impairment was assessed using the MMSE and categorized into four severity groups based on the national S3 dementia guideline, representing the highest methodological quality for evidence-based recommendations: no indication of dementia (MMSE ≥ 27), mild dementia (MMSE 20–26), moderate dementia (MMSE 10–19), and severe dementia (MMSE ≤ 9) [32]. Additionally, patients without a listed clinical dementia diagnosis were screened using the DemTect procedure, whereby a score < 9 indicates dementia. The DemTect is considered more sensitive and suitable for detecting early stages of dementia compared to the MMSE [33]. Consequently, participants with an MMSE ≥ 27 and Demtect < 9 were classified as having early-stage dementia due to the initial screening result. As a result of the small group size, patients with moderate or severe dementia were combined into one group for the analyses.

Healthcare Utilization

Healthcare resource use was also assessed within the baseline interviews using the standardized FIMA questionnaire tailored to elderly individuals considering the specifications and all settings in the German healthcare system [34]. Detailed information about the frequencies of the utilization of the following medical care services was recorded: physician consultation (GP, specialists), therapies (e.g., occupational, physical, and speech therapy), and hospital contacts. Prescribed medications were extracted from medication lists provided by the treating physicians. To improve the validity and precision of the data, study nurses interviewed caregivers, participants, and professional care staff wherever possible.

Selection of Pattern to Differentiate Dementia Severity Stages

Pre- and post-diagnostic factors were included to cover all stages of dementia severity and mitigate potential selection bias. Pre-diagnostic patterns to identify the early stages were chosen on the basis of Teipel et al. [35], which comprised diagnostic codes for comorbidities, risk, and prodromal factors. Patterns reflecting the post-diagnostic treatment and care of more severe stages were mainly derived from the most recent German S-3 dementia guideline [32]. Finally, the potential factors to differentiate dementia severity stages were checked for availability in both the claims data and the used dataset. Variables with fewer than ten observations were excluded to ensure explanatory power and heterogeneity.

Statistical Analyses

The sociodemographic and clinical characteristics of study participants and health resource utilization were presented using descriptive statistics. One-way analysis of variance (ANOVA) (continuous variables) and chi-square tests (categorical variable, > 2 conditions) were employed to assess group differences across dementia severity stages. Ordered logistic regression models, adjusting for age, sex, and the respective original trial, were used to explore associations between predictors and dementia severity, with odds ratios (ORs) reported. Average marginal effects (AME) were calculated to estimate how predictors influenced the probabilities of specific severity stages. The Bonferroni correction was applied to correct for multiple comparisons ($\alpha_{corrected} = 0.001$).

Additionally, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were computed for selected statistically significant predictors, individually and in combination, to assess their ability to differentiate and exclude overlapping severity stages. Depending on the direction of the observed associations, it was assumed that sensitivity and PPV might increase while specificity and NPV might decrease with increasing severity or vice versa.

All statistical analyses were conducted with STATA/IC software, version 18 [36].

RESULTS

Sample Characteristics

The 737 participants (mean age 80.3 years; 56% female patients) were categorized into

early-stage (18%), mild (43%), and moderate/severe dementia (39%), according to the MMSE. Patients with early-stage dementia were significantly younger (early-stage 79 years vs. mild 80 years vs. moderate/severe 81 years; $p=0.032$) and less likely to have a listed clinical dementia diagnosis (38.9% vs. 22.2% vs. 16.8%; $p\leq0.001$, respectively). Table 1 summarizes the sample characteristics.

Associations Between Diagnosis and Treatment Patterns and Dementia Severity

After the Bonferroni correction was applied, ordinal logistic regression analysis revealed the following statistically significant associations: antipsychotic use (OR 3.40, 95% confidence interval (CI) 1.94–5.95, $p\leq0.001$) and antidementia drug prescriptions according to guidelines (OR 2.31, 95% CI 1.56–3.40, $p\leq0.001$) were strong predictors of moderate to severe dementia. Additionally, care levels demonstrated a stepwise relationship with increasing dementia severity, from care level 2 (OR 2.04, 95% CI 1.33–3.12, $p\leq0.001$) to care level 4 or higher (OR 5.59, 95% CI 2.23–13.99, $p\leq0.001$). Conversely, fewer medications (OR 0.90, 95% CI 0.86–0.95, $p\leq0.001$) were associated with milder dementia stages. Other variables, including unspecified and specified dementia diagnoses, cancer, and therapies, were no longer significant after Bonferroni correction. Table 2 shows the results of the ordinal logistic regression analysis. Additionally, Supplementary Table 1 reports the unadjusted frequencies and group differences of comorbidities and healthcare utilization between different stages.

The AME analysis revealed that antipsychotic prescriptions decreased the probability of being classified as early-stage dementia according to the MMSE by 14% while increasing the probability of being classified as having moderate/severe dementia by 21%. Similarly, antidementia drug treatments reduced the probability of early-stage dementia classification by 10% and increased the probability of moderate/severe dementia by 14%. Depending on the care level, probabilities of early-stage classification decrease by 2–16%, and moderate/severe classification probabilities increase by 3–33%. Other factors, including age, sex, comorbidities, and health service utilization, did not significantly predict the classification of dementia severity. Table 3 presents the AME for the respective severity stages.

Performance Metrics for Dementia Severity Classification: Sensitivity, Specificity, NPV, and PPV

The analysis revealed clear patterns of predictors (antidementia drugs, antipsychotics, and care level) to discriminate dementia severity. For antidementia drugs, sensitivity increased from 15.3% in early-stage dementia to 34.3% in moderate-to-severe dementia, and specificity rose from 72.0% to 79.6%. NPV was highest in the early stage (79.7%) but decreased to 65.6% in the severe stages. PPV showed a notable rise from 10.5% to 51.6%, indicating a stronger association with severe dementia. For antipsychotics, sensitivity was lowest in the early stages (3.8%) but increased to 17.8% in severe cases, while specificity improved from 87.3% to 93.1%. Early-stage NPV was high (80.8%) but declined to 64.1% for severe stages. PPV showed a marked improvement from 6.1% to 62.2%, emphasizing its utility in identifying severe dementia. For care level, sensitivity rose substantially from 11.5% in the early stages to 40.2% in severe dementia, with a slight increase in specificity from 70.6% to 82.7%. NPV declined from 78.7% to 68.6%, while PPV increased significantly from 7.8% to 59.6%, underscoring its strength as a predictor of severe dementia. All predictors combined achieved the highest specificity of up to 99.6% and PPV of up to 84.6% for moderate-to-severe dementia, demonstrating excellent discriminatory power. Table 4 summarizes diagnostic performance.

DISCUSSION

This study provides novel insights into the potential of routinely collected real-world data for classifying dementia severity on the basis of diagnostic codes, prescribing patterns, and healthcare utilization. Our findings suggest

Table 1 Sample characteristics

	Total sample		Early-stage dementia MMSE ≥ 27		Mild dementia MMSE 20–26		Moderate to severe dementia MMSE 0–19		*p* value
	n **= 737**	**95% CI**	***n*** **= 131 (17.8%)**	**95% CI**	***n*** **= 320 (43.4%)**	**95% CI**	***n*** **= 286 (38.8%)**	**95% CI**	
Demographics									
Age, mean (SD)	80.3 (5.9)	79.8–80.7	79.1 (5.7)	78.2–80.1	80.3 (5.2)	79.7–80.8	80.8 (6.5)	80.0–81.5	**0.032**[b]
Sex (female patients), *n* (%)	413 (56.0)	0.52–0.59	64 (48.8)	0.40–0.57	185 (57.8)	0.52–0.63	164 (57.3)	0.51–0.62	0.187[c]
Clinical characteristics									
Listed clinical dementia diagnosis, *n* (%)									
No diagnosis, *n* (%)	170 (23.0)	0.20–0.26	51 (38.9)	0.30–0.47	71 (22.19)	0.17–0.27	48 (16.7)	0.12–0.21	**≤ 0.001**[c]
Unspecified dementia diagnosis, *n* (%)	328 (44.5)	0.40–0.481	51 (38.9)	0.30–0.47	142 (44.38)	0.39–0.49	135 (47.20)	0.39–0.49	
Specified dementia diagnosis, *n* (%)	239 (32.4)	0.29–0.35	29 (22.14)	0.15–0.30	107 (33.44)	0.28–0.38	103 (36.01)	0.30–0.41	
Alzheimer's disease, *n* (%)	110 (14.9)	0.12–0.17	11 (8.40)	0.04–0.14	47 (14.69)	0.11–0.19	52 (18.18)	0.14–0.23	**0.033**[c]
Other dementia disease, *n* (%)	129 (17.5)	0.14–0.20	18 (13.74)	0.08–0.20	60 (18.75)	0.14–0.23	51 (17.83)	0.13–0.22	0.438[c]
Number of diagnoses, mean (SD)	12.3 (8.2)	11.7–12.8	13.1 (7.8)	11.7–14.4	12.7 (7.5)	11.9–13.5	11.4 (9.0)	10.3–12.4	0.070[b]
Number of medications, mean (SD)	7.5 (3.7)	7.2–7.8	7.9 (3.2)	7.4–8.5	7.7 (4.0)	7.3–8.2	7.1 (3.4)	6.7–7.5	**0.034**[b]

Table 1 continued

	Total sample		Early-stage dementia MMSE ≥ 27		Mild dementia MMSE 20–26		Moderate to severe dementia MMSE 0–19		*p* value
	n = 737	95% CI	*n* = 131 (17.8%)	95% CI	*n* = 320 (43.4%)	95% CI	*n* = 286 (38.8%)	95% CI	
Care level[a]									
No care level, *n* (%)	281 (38.1)	0.34–0.41	75 (57.2)	0.48–0.65	157 (49.0)	0.43–0.54	49 (17.1)	0.13–0.21	**≤ 0.001**[c]
1, *n* (%)	38 (5.1)	0.03–0.07	5 (3.8)	0.01–0.08	13 (4.0)	0.02–0.06	20 (6.9)	0.04–0.10	
2, *n* (%)	225 (30.5)	0.27–0.33	36 (27.4)	0.20–0.35	87 (27.1)	0.22–0.32	102 (35.6)	0.30–0.41	
3, *n* (%)	142 (19.2)	0.16–0.22	13 9.9)	0.05–0.16	54 (16.8)	0.13–0.21	75 (26.2)	0.21–0.31	
4 or higher, *n* (%)	51 (6.9)	0.05–0.08	2 (1.5)	0.01–0.05	9 (2.8)	0.01–0.05	40 (13.9)	0.10–0.18	

p values in bold indicate $p < 0.05$

CI confidence interval, *MMSE* Mini-Mental State Examination (range 0–30, higher score indicates better cognitive function), *SD* standard deviation

[a]The care level assigned by the long-term care insurance indicates the amount of care and support a patient receives owing to their functional impairment, ranging from 1 to 5, with 1 indicating some problems and 5 indicating extreme problems

[b]Differences in means: one-way ANOVA

[c]Differences in proportions: chi-square tests

that the combination of antidementia drug prescriptions, antipsychotic use, and assigned care levels serves as a strong predictor of moderate to severe dementia, demonstrating high specificity and PPV. Conversely, early-stage dementia classification showed lower sensitivity, highlighting challenges in identifying individuals at an earlier disease stage on the basis of real-world data.

The predictive performance of our model varied across dementia severity stages. For moderate to severe dementia, specificity and PPV were particularly high when combining antidementia drugs, antipsychotic use, and care level (specificity 99.6%, PPV 84.6%). This indicates that these variables reliably identify individuals with severe dementia and produce few misclassifications among those with less severe dementia, making them valuable markers for classifying dementia severity in claims data. Additionally, the increase in PPV across stages, particularly for antipsychotic use (from 6.1% in early-stage to 62.2% in severe dementia), aligns with clinical practice, where these medications are more frequently prescribed with behavioral and psychological symptoms progress [37–39]. This is also underlined by the AME analysis, demonstrating antipsychotic prescriptions reduced early-stage probability by 14% and increased severe-stage classification by 21%, reinforcing their strong association with advanced disease.

Consistently, early-stage dementia classification showed lower sensitivity and PPV, particularly for antidementia drug use (sensitivity 15.3%, PPV 10.5%). This suggests that many individuals in the early stages could remain undetected, possibly because of a lack of dementia-specific pharmacological treatment, which could be considered as a result of underdiagnosis. The AME analysis further supports this, showing that antidementia drug treatment reduced the probability of being classified as early-stage dementia by 9% while increasing the probability of moderate to severe dementia classification by 14%. Previous studies indicated that only 39% of people who screened positive

Table 2 Associations between diagnosis and treatment patterns and dementia severity

N = 737	Severity stages of dementia according to MMSE[a]			
	OR	**SE**	**95% CI**	***p* value**
Demographics				
Age[c]	1.01	0.01	0.98–1.04	0.349
Sex (ref. male)[c]	1.14	0.19	0.81–1.60	0.424
Clinical characteristics				
Number of diagnoses[c]	0.99	0.01	0.96–1.02	0.619
Listed clinical dementia diagnosis[c]				
Unspecified dementia (ref. no diagnosis)	1.72	0.35	1.16–2.57	0.007
Specified dementia (ref. no diagnosis)	1.75	0.39	1.11–2.73	0.014
Comorbidities[d]				
Abnormalities of gait (ref. no diagnosis)	0.82	0.22	0.48–1.41	0.495
Tremor (ref. no diagnosis)	1.87	1.17	0.54–6.41	0.318
Extremity injury (ref. no diagnosis)	0.84	0.40	0.32–2.17	0.719
Anxiety (ref. no diagnosis)	0.83	0.51	0.24–2.81	0.768
Cognitive impairment (ref. no diagnosis)	1.34	0.97	0.32–5.53	0.679
Depression (ref. no diagnosis)	1.16	0.26	0.74–1.81	0.515
Memory impairment (ref. no diagnosis)	0.66	0.21	0.34–1.26	0.213
Visual impairment (ref. no diagnosis)	1.04	0.47	0.43–2.53	0.924
Hearing impairment (ref. no diagnosis)	0.81	0.20	0.50–1.33	0.422
Other sensory disorders (ref. no diagnosis)	0.66	0.79	0.06–6.99	0.734
Insomnia (ref. no diagnosis)	0.81	0.51	0.23–2.78	0.734
Other sleeping disorder (ref. no diagnosis)	1.02	0.57	0.34–3.07	0.964
Sleep apnea (ref. no diagnosis)	0.41	0.24	0.12–1.34	0.143
Constipation (ref. no diagnosis)	0.52	0.30	0.16–1.61	0.261
Dizziness (ref. no diagnosis)	0.75	0.22	0.42–1.34	0.347
Obesity (ref. no diagnosis)	1.43	0.38	0.84–2.42	0.178
Alcohol abuse (ref. no diagnosis)	0.72	0.41	0.23–2.25	0.573
Nicotine abuse (ref. no diagnosis)	0.66	0.45	0.17–2.54	0.557
Atrial fibrillation (ref. no diagnosis)	0.72	0.15	0.47–1.08	0.121
Carotid artery stenosis (ref. no diagnosis)	0.71	0.27	0.33–1.51	0.385
Cerebrovascular disease (ref. no diagnosis)	0.92	0.18	0.62–1.37	0.709
Type 2 diabetes mellitus (ref. no diagnosis)	1.09	0.18	0.78–1.53	0.588
Hypercholesterolemia (ref. no diagnosis)	0.71	0.19	0.41–1.22	0.217
Hypertension (ref. no diagnosis)	1.14	0.21	0.78–1.66	0.477
Ischemic heart disease (ref. no diagnosis)	1.36	0.24	0.96–1.94	0.083

Table 2 continued

N = 737	Severity stages of dementia according to MMSE[a]			
	OR	**SE**	**95% CI**	***p* value**
Gastritis (ref. no diagnosis)	1.49	0.43	0.84–2.64	0.172
Reflux disease (ref. no diagnosis)	0.73	0.19	0.43–1.24	0.253
Stomach ulcer (ref. no diagnosis)	1.95	1.25	0.55–6.91	0.297
Epilepsy (ref. no diagnosis)	4.71	2.70	1.53–14.50	0.007
Parkinsons disease (ref. no diagnosis)	1.31	0.50	0.61–2.78	0.477
Cancer (ref. no diagnosis)	1.61	0.36	1.03–2.50	0.034
Osteoarthritis (ref. no diagnosis)	0.95	0.17	0.66–1.37	0.823
Other rheumatoid arthritis (ref. no diagnosis)	0.76	0.38	0.28–2.05	0.594
Senility (ref. no diagnosis)	1.72	0.60	0.86–3.42	0.121
Unspecific pain (ref. no diagnosis)	0.97	0.26	0.57–1.64	0.930
Healthcare utilization				
Number of medications[d]	0.90	0.02	0.86–0.95	**≤ 0.001**
PIM (ref. no use)[d]	0.87	0.19	0.56–1.33	0.533
Antipsychotics (ref. no use)[c]	3.40	0.97	1.94–5.95	**≤ 0.001**
Sedative and hypnotics (ref. no use)[c]	1.14	0.46	0.51–2.55	0.742
Antidepressants (ref. no use)[c]	1.17	0.27	0.74–1.87	0.484
Antidementia drug treatment (ref. no use)[c]	2.31	0.45	1.56–3.40	**≤ 0.001**
Number GP contacts[d]	0.99	0.01	0.97–1.02	0.744
Specialist contacts (ref. no use)[c]	0.72	0.13	0.49–1.05	0.095
Number hospital contacts[c]	0.99	0.01	0.97–1.00	0.373
Therapies contacts (ref. no use)[c]	0.69	0.11	0.50–0.96	0.031
Nursing contacts (ref. no use)[c]	0.89	0.16	0.61–1.29	0.541
Care level[b,c]				
1 (ref. no assignment)	1.22	0.51	0.54–2.77	0.620
2 (ref. no assignment)	2.04	0.44	1.33–3.12	**≤ 0.001**
3 (ref. no assignment)	2.19	0.62	1.25–3.82	0.006
4 or higher (ref. no assignment)	5.59	2.61	2.23–13.99	**≤ 0.001**

p values in bold indicate $p \leq 0.001$

CI confidence interval, GP general practitioner, *MMSE* Mini-Mental State Examination (range 0–30, higher score indicates better cognitive function), *OR* odds ratio, *PIM* potentially inappropriate medication, *SE* standard error

[a]Ordinal scaled variable with 1 indicating early-stage, 2 mild, and 3 moderate to severe dementia

[b]The care level assigned by the long-term care insurance indicates the amount of care and support a patient receives owing to their functional impairment, ranging from 1 to 5, with 1 indicating some problems and 5 indicating extreme problems

[c]Assumption based on literature: factor/variable is associated with higher severity

[d]Assumption based on literature: factor/variable is associated with lower severity

Table 3 Average marginal effects of diagnosis and treatment patterns on dementia severity stages

N = 737	Early-stage dementia (17.8%)			Mild dementia (43.4%)			Moderate to severe dementia (38.8%)		
	AME	95% CI	*p* value	AME	95% CI	*p* value	AME	95% CI	*p* value
Demographics									
Age[b]	± 0.00	− 0.01 to 0.01	0.349	± 0.00	− 0.01 to 0.01	0.350	± 0.00	− 0.00 to 0.01	0.348
Sex (ref. male)[b]	− 0.01	− 0.05 to 0.02	0.424	− 0.01	− 0.02 to 0.01	0.426	0.02	− 0.03 to 0.08	0.423
Clinical characteristics									
Number of diagnoses[b]	± 0.00	− 0.01 to 0.01	0.619	± 0.00	− 0.01 to 0.01	0.619	± 0.00	− 0.01 to 0.01	0.619
Listed clinical dementia diagnosis[b]									
Unspecified dementia (ref. no diagnosis)	− 0.07	− 0.12 to − 0.01	0.010	− 0.02	− 0.04 to − 0.01	0.007	0.09	0.02 to 0.16	0.006
Specified dementia (ref. no diagnosis)	− 0.07	− 0.13 to − 0.01	0.016	− 0.02	− 0.04 to − 0.01	0.026	0.09	0.02 to 0.17	0.014
Comorbidities[c]									
Abnormalities of gait (ref. no diagnosis)	0.02	− 0.04 to 0.08	0.495	0.01	− 0.02 to 0.04	0.498	− 0.03	− 0.12 to 0.06	0.495
Tremor (ref. no diagnosis)	− 0.07	− 0.22 to 0.07	0.318	− 0.03	− 0.10 to 0.03	0.317	0.11	− 0.10 to 0.33	0.316
Extremity injury (ref. no diagnosis)	0.02	− 0.09 to 0.13	0.719	0.01	− 0.04 to 0.06	0.719	− 0.03	− 0.20 to 0.13	0.719
Anxiety (ref. no diagnosis)	0.02	− 0.12 to 0.17	0.768	0.01	− 0.05 to 0.07	0.768	− 0.03	− 0.24 to 0.18	0.768
Cognitive impairment (ref. no diagnosis)	− 0.03	− 0.20 to 0.13	0.679	− 0.01	− 0.09 to 0.06	0.679	0.05	− 0.19 to 0.30	0.679
Depression (ref. no diagnosis)	− 0.01	− 0.07 to 0.03	0.515	− 0.01	− 0.03 to 0.01	0.514	0.02	− 0.05 to 0.10	0.514
Memory impairment (ref. no diagnosis)	0.05	− 0.02 to 0.12	0.212	0.02	− 0.01 to 0.06	0.221	− 0.07	− 0.18 to 0.04	0.212

Table 3 continued

N = 737	Early-stage dementia (17.8%)			Mild dementia (43.4%)			Moderate to severe dementia (38.8%)		
	AME	95% CI	*p* value	AME	95% CI	*p* value	AME	95% CI	*p* value
Visual impairment (ref. no diagnosis)	− 0.01	− 0.11 to 0.10	0.924	± 0.00	− 0.05 to 0.04	0.924	0.01	− 0.15 to 0.16	0.924
Hearing impairment (ref. no diagnosis)	0.02	− 0.03 to 0.08	0.421	0.01	− 0.01 to 0.03	0.424	− 0.03	− 0.12 to 0.05	0.421
Other sensory disorders (ref. no diagnosis)	0.04	− 0.23 to 0.33	0.734	± 0.00	− 0.11 to 0.15	0.734	− 0.07	− 0.49 to 0.34	0.734
Insomnia (ref. no diagnosis)	0.02	− 0.12 to 0.17	0.734	0.01	− 0.05 to 0.08	0.734	− 0.03	− 0.25 to 0.18	0.734
Other sleeping disorder (ref. no diagnosis)	± 0.00	− 0.13 to 0.13	0.964	± 0.00	− 0.06 to 0.06	0.964	± 0.00	− 0.19 to 0.20	0.964
Sleep apnea (ref. no diagnosis)	0.10	− 0.03 to 0.24	0.143	0.04	− 0.01 to 0.11	0.150	− 0.15	− 0.36 to 0.05	0.142
Constipation (ref. no diagnosis)	0.07	− 0.05 to 0.21	0.261	0.03	− 0.02 to 0.10	0.268	− 0.11	− 0.31 to 0.08	0.261
Dizziness (ref. no diagnosis)	0.03	− 0.03 to 0.10	0.347	0.01	− 0.01 to 0.04	0.348	− 0.04	− 0.15 to 0.05	0.346
Obesity (ref. no diagnosis)	− 0.04	− 0.10 to 0.01	0.178	− 0.02	− 0.05 to 0.01	0.184	0.06	− 0.02 to 0.15	0.177
Alcohol abuse (ref. no diagnosis)	0.03	− 0.09 to 0.17	0.573	0.01	− 0.04 to 0.08	0.573	− 0.05	− 0.26 to 0.14	0.573
Nicotine abuse (ref. no diagnosis)	0.04	− 0.11 to 0.21	0.557	0.02	− 0.05 to 0.09	0.557	− 0.07	− 0.30 to 0.16	0.556
Atrial fibrillation (ref. no diagnosis)	0.03	− 0.01 to 0.08	0.121	0.01	− 0.01 to 0.04	0.126	− 0.05	− 0.13 to 0.01	0.119

Table 3 continued

N = 737	Early-stage dementia (17.8%)			Mild dementia (43.4%)			Moderate to severe dementia (38.8%)		
	AME	95% CI	*p* value	AME	95% CI	*p* value	AME	95% CI	*p* value
Carotid artery stenosis (ref. no diagnosis)	0.04	− 0.05 to 0.13	0.385	0.01	− 0.02 to 0.06	0.388	− 0.05	− 0.19 to 0.07	0.384
Cerebrovascular disease (ref. no diagnosis)	0.01	− 0.03 to 0.05	0.710	± 0.00	− 0.01 to 0.02	0.709	− 0.01	− 0.08 to 0.05	0.709
Type 2 diabetes mellitus (ref. no diagnosis)	− 0.01	− 0.05 to 0.02	0.588	− 0.01	− 0.02 to 0.01	0.589	0.01	− 0.04 to 0.07	0.588
Hypercholesterolemia (ref. no diagnosis)	0.04	− 0.02 to 0.10	0.217	0.01	− 0.01 to 0.04	0.219	− 0.06	− 0.15 to 0.03	0.215
Hypertension (ref. no diagnosis)	− 0.01	− 0.06 to 0.02	0.477	− 0.01	− 0.02 to 0.01	0.480	0.02	− 0.04 to 0.09	0.477
Ischemic heart disease (ref. no diagnosis)	− 0.03	− 0.08 to 0.01	0.082	− 0.01	− 0.03 to 0.01	0.089	0.05	− 0.01 to 0.11	0.081
Gastritis (ref. no diagnosis)	− 0.04	− 0.11 to 0.02	0.171	− 0.02	− 0.05 to 0.01	0.178	0.07	− 0.03 to 0.17	0.171
Reflux disease (ref. no diagnosis)	0.03	− 0.02 to 0.10	0.254	0.01	− 0.01 to 0.04	0.256	− 0.05	− 0.14 to 0.03	0.252
Stomach ulcer (ref. no diagnosis)	− 0.08	− 0.23 to 0.07	0.298	− 0.03	− 0.10 to 0.03	0.301	0.11	− 0.10 to 0.34	0.297
Epilepsy (ref. no diagnosis)	− 0.18	− 0.32 to − 0.05	0.007	− 0.08	− 0.15 to − 0.02	0.009	0.27	0.07 to 0.47	0.006
Parkinsons disease (ref. no diagnosis)	− 0.03	− 0.12 to 0.05	0.477	− 0.01	− 0.05 to 0.02	0.479	0.04	− 0.08 to 0.18	0.477
Cancer (ref. no diagnosis)	− 0.05	− 0.11 to − 0.01	0.034	− 0.02	− 0.05 to − 0.01	0.040	0.08	0.01 to 0.16	0.033
Osteoarthritis (ref. no diagnosis)	± 0.00	− 0.03 to 0.04	0.823	± 0.00	− 0.01 to 0.02	0.823	− 0.01	− 0.07 to 0.05	0.823

Table 3 continued

N = 737	Early-stage dementia (17.8%)			Mild dementia (43.4%)			Moderate to severe dementia (38.8%)		
	AME	95% CI	*p* value	AME	95% CI	*p* value	AME	95% CI	*p* value
Other rheumatoid arthritis (ref. no diagnosis)	0.03	− 0.08 to 0.15	0.594	0.01	− 0.04 to 0.07	0.595	− 0.04	− 0.22 to 0.12	0.594
Senility (ref. no diagnosis)	− 0.06	− 0.14 to 0.01	0.121	− 0.03	− 0.07 to 0.01	0.129	0.09	− 0.02 to 0.21	0.120
Unspecific pain (ref. no diagnosis)	± 0.00	− 0.06 to 0.06	0.930	± 0.00	− 0.02 to 0.03	0.930	± 0.00	− 0.09 to 0.08	0.930
Healthcare utilization									
Number of medications[b]	0.01	0.01 to 0.01	**≤ 0.001**	0.01	0.002 to 0.01	**≤ 0.001**	− 0.01	− 0.02 to − 0.01	**≤ 0.001**
PIM (ref. no use)[c]	0.01	− 0.03 to 0.06	0.533	0.01	− 0.01 to 0.03	0.535	− 0.02	− 0.10 to 0.05	0.533
Antipsychotics (ref. no use)[b]	− 0.14	− 0.21 to − 0.08	**≤ 0.001**	− 0.06	− 0.10 to − 0.03	**≤ 0.001**	0.21	0.12 to 0.31	**≤ 0.001**
Sedative and hypnotics (ref. no use)[b]	− 0.01	− 0.11 to 0.08	0.742	− 0.01	− 0.05 to 0.03	0.742	0.02	− 0.11 to 0.16	0.742
Antidepressants (ref. no use)[b]	− 0.02	− 0.07 to 0.03	0.484	− 0.01	− 0.03 to 0.01	0.485	0.02	− 0.05 to 0.11	0.484
Antidementia drug treatment (ref. no use)[b]	− 0.10	− 0.14 to − 0.05	**≤ 0.001**	− 0.04	− 0.07 to − 0.02	**≤ 0.001**	0.14	0.08 to 0.21	**≤ 0.001**
Number GP contacts[c]	± 0.00	− 0.01 to 0.01	0.744	± 0.00	− 0.01 to 0.01	0.744	± 0.00	− 0.01 to 0.01	0.744
Specialist contacts (ref. no use)[b]	0.03	− 0.01 to 0.08	0.105	0.01	− 0.01 to 0.03	0.061	− 0.05	− 0.12 to 0.01	0.088
Number hospital contacts[b]	± 0.00	− 0.01 to 0.01	0.372	± 0.00	− 0.01 to 0.01	0.379	± 0.00	− 0.01 to 0.01	0.373

Table 3 continued

N = 737	Early-stage dementia (17.8%)			Mild dementia (43.4%)			Moderate to severe dementia (38.8%)		
	AME	95% CI	*p* value	AME	95% CI	*p* value	AME	95% CI	*p* value
Therapies contacts (ref. no use)[b]	0.04	0.00 to 0.08	0.030	0.02	0.00 to 0.04	0.047	− 0.06	− 0.12 to − 0.01	0.033
Nursing contacts (ref. no use)[b]	0.01	− 0.03 to 0.06	0.545	0.01	− 0.01 to 0.02	0.522	− 0.02	− 0.08 to 0.04	0.538
Care level[a,b]									
1 (ref. no assignment)	− 0.02	− 0.14 to 0.08	0.610	− 0.01	− 0.04 to 0.02	0.692	0.03	− 0.11 to 0.18	0.628
2 (ref. no assignment)	− 0.09	− 0.14 to − 0.03	**≤ 0.001**	− 0.04	− 0.07 to − 0.01	**0.005**	0.13	0.05 to 0.21	**≤ 0.001**
3 (ref. no assignment)	− 0.09	− 0.16 to − 0.03	0.004	− 0.05	− 0.09 to − 0.01	0.033	0.14	0.03 to 0.25	0.008
4 or higher (ref. no assignment)	− 0.16	− 0.23 to − 0.10	**≤ 0.001**	− 0.17	− 0.29 to − 0.04	**0.007**	0.33	0.15 to 0.51	**≤ 0.001**

p values in bold indicate $p \leq 0.001$

AME average marginal effects, *CI* confidence interval, *GP* general practitioner, *PIM* potentially inappropriate medication

[a]The care level assigned by the long-term care insurance indicates the amount of care and support a patient receives owing to their functional impairment, ranging from 1 to 5, with 1 indicating some problems and 5 indicating extreme problems

[b]Assumption based on literature: factor/variable is associated with higher severity

[c]Assumption based on literature: factor/variable is associated with lower severity

for dementia received a formal diagnosis, leading to only 30% of patients being treated with adequate antidementia drugs [18, 24, 40]. In particular, the coded prevalence of mild cognitive impairment corresponded to less than 10% of its actual prevalence [41]. Current variables available in German claims data could be insufficient to classify early stages adequately. For this purpose, further research is needed—including advanced machine learning approaches applied to additional markers that also consider risk factors that occur years before dementia onset—to improve early-stage detection, predict transitions between dementia stages, and uncover latent trajectory patterns. Even though these approaches may appear promising, they also depend on improved coding adherence for claims data [14–17]. Therefore, incentives are needed to improve physicians' coding practices, enabling access to optimal treatment and care and strengthening the quality of real-world data as a basis for decision-making.

The role of care levels as a severity marker was also evident, with PPV rising from 7.8% in early-stage to 59.6% in severe dementia. This stepwise increase highlights the utility of long-term care assignments in stratifying disease severity and corresponds to previous research demonstrating increased nursing care needs across different severity stages due to functional impairment [42–44]. The AME analysis confirmed that higher care levels significantly decreased

Table 4 Diagnostic performance metrics for dementia severity classification

N = 737	Early-stage dementia (17.8%)				Mild dementia (43.4%)				Moderate to severe dementia (38.8%)			
	Sensitivity (%)	Specificity (%)	NPV (%)	PPV (%)	Sensitivity (%)	Specificity (%)	NPV (%)	PPV (%)	Sensitivity (%)	Specificity (%)	NPV (%)	PPV (%)
Antidementia drug only	15.3	72.0	79.7	10.5	22.5	71.7	54.7	37.9	34.3	79.6	65.6	51.6
Antipsychotic use only	3.8	87.3	80.8	6.1	8.1	86.6	55.1	31.7	17.8	93.1	64.1	62.2
Antidementia drug and antipsychotic use	2.3	95.4	81.9	9.7	1.3	93.5	55.2	12.9	8.4	98.5	62.9	77.4
Care level only[a]	11.5	70.6	78.7	7.8	19.7	68.8	52.8	32.6	40.2	82.7	68.6	59.6
Antidementia drug and care level[a]	3.1	91.4	81.4	7.1	4.1	89.7	54.9	23.2	13.6	96.2	63.7	69.6
Antipsychotic use and care level[a]	0.8	94.6	81.5	2.9	2.2	93.5	55.5	20.6	9.1	98.2	63.0	76.5

Table 4 continued

N = 737	Early-stage dementia (17.8%)				Mild dementia (43.4%)				Moderate to severe dementia (38.8%)			
	Sensitivity (%)	Specificity (%)	NPV (%)	PPV (%)	Sensitivity (%)	Specificity (%)	NPV (%)	PPV (%)	Sensitivity (%)	Specificity (%)	NPV (%)	PPV (%)
Antidementia drug and antipsychotic use and care level[a]	0.8	98.0	82.0	7.7	0.3	97.1	55.9	7.7	3.9	99.6	62.0	84.6

NPV negative predictive value indicates the probability that an individual with a negative result does not belongs to the assigned severity category, *PPV* positive predictive value indicates the probability that an individual with a positive result truly belongs to the assigned severity category

[a]The care level assigned by the long-term care insurance indicates the amount of care and support a patient receives owing to their functional impairment, ranging from 1 to 5, with 1 indicating some problems and 5 indicating extreme problems

early-stage classification probability (e.g., care level 4+, – 16%) while substantially increasing moderate to severe classification probabilities (+34%). These findings underscore the need to integrate care levels as a crucial predictor into prospective claims-based severity algorithms.

While our study identified strong predictors of dementia severity, several variables lost significance after applying the Bonferroni correction. Notably, diagnoses such as cancer were initially associated with dementia severity. However, they did not remain significant after correction of the *p* value, suggesting that cancer may co-occur with dementia, but the role as an independent predictor of severity is limited within the dataset used. The literature reveals contrasting evidence, including studies reporting an inverse association between cancer and dementia, indicating PwD may be less likely to be diagnosed with cancer and vice versa. At the same time, other findings suggest a positive association and highlight disparities in cancer care among patients with dementia [45, 46]. Thus, further research is needed.

Additionally, statistically significant unadjusted group differences occur for depression and diabetes. However, the recorded diagnoses increase from the early stages, peak in the mild stage, and decline again in the moderate to severe stages. The dementia progression could accompany decreased healthcare utilization and related diseases underdiagnoses. This tendency is in line with previous research. Eisele et al. [47] pointed out that the utilization of ambulatory medical care services increased in the year before and in the year after the incidence of dementia. Building upon this, Michalowsky et al. [40] demonstrated an association between dementia progression and reduced healthcare utilization. In the present analyses, the respective coefficients of healthcare utilization variables such as GP contacts, specialist visits, and therapies underscore these negative trends with dementia severity, even if these were not statistically significant. Nevertheless, prospective claims data analyses should examine this hypothesis to clarify the role of comorbidities in predicting dementia severity.

Overall, the findings have significant implications for both research and clinical practice.

Classifying dementia severity using real-world data can facilitate epidemiological surveillance, guide healthcare resource allocation, and support health economic evaluations. However, several limitations should be acknowledged. The sample used does not represent the German population, particularly regarding PwD. While it is assumed that up to two-thirds of patients are affected by Alzheimer's disease, the present sample covers only 46% of Alzheimer's cases in patients with a dementia-type specific diagnosis. However, 45% of the sample has an unspecific diagnosis, reflecting the clinical and coding practice of treating physicians [18]. A further limitation is the heterogeneity in diagnostic and prescribing practices across physicians, which may introduce variability unrelated to underlying dementia progression and could confound our identified associations. The role of antidementia drugs may be overestimated since memantine is officially recommended for later stages while acetylcholinesterase inhibitors target early disease [32]. In real-world practice, however, memantine is often used off-label in milder stages, especially when acetylcholinesterase inhibitors cause side effects or drug interactions [48]. Additionally, given known overuse and adverse events [49], antipsychotic prescriptions may reflect prescribing practices rather than underlying disease progression, and thus represent a potential confounder in our analysis. Moreover, the lower sensitivity for early-stage dementia suggests that claims-based approaches may miss a significant proportion of individuals in the initial disease phases. However, the present data does not include all the variables that a complete claims dataset contains, such as data for specific outpatient services or laboratory tests. Therefore, future studies should explore additional markers, such as cognitive screening data or healthcare service utilization patterns in longitudinal data, to improve early-stage detection and classification. As a result of data minimization, congruence between administrative claims and patient-reported data could not be assessed, as no individual variables were captured in both sources. Additionally, while specificity and PPV were high for severe dementia, these findings must be validated in external datasets to confirm their robustness and to examine the generalizability of these findings across diverse populations.

CONCLUSION

This study demonstrates that prescription patterns and care levels could be valuable indicators for distinguishing between early and advanced dementia stages in real-world data. While their combined specificity and PPV for moderate to severe dementia were high, particularly the sensitivity for early-stage classification remains a challenge. Moreover, accurate identification of dementia in administrative data is hampered by inadequate coding practices and underdiagnosis, with 23% of dementia cases not recorded and specific etiologies missing in 68% of records. Future efforts should aim to refine early detection models, explore complementary data sources to improve dementia severity stratification, and facilitate targeted access to necessary dementia treatments.

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Data Availability. The data used in the analysis is available upon request from the authors, in compliance with ethical and data protection regulations.

Declarations

Conflict of Interest. Moritz Platen, Maresa Buchholz, Anika Rädke, Eva Gläser, Audrey Iskandar, Neeltje van den Berg, Wolfgang Hoffmann and Bernhard Michalowsky have nothing to disclose.

Ethical Approval. This analysis utilized merged baseline data from three independent trials that were approved by the Ethical Committee of the Chamber of Physicians of Mecklenburg-Western Pomerania (registry numbers BB 20/11 for DelpHi-MV, BB01/2019 for DCM:IMPact, and BB144/20 for InDePendent) and have been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Written informed consent was obtained from all study participants.

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