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ORIGINAL RESEARCH ARTICLE

Associations Between Low-Value Medication in Dementia and Healthcare Costs

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Abstract

Background Low-value medications (Lvm) provide little or no benefit to patients, may be harmful, and waste healthcare resources and costs. Although evidence from the literature indicates that Lvm is highly prevalent in dementia, evidence about the financial consequences of Lvm in dementia is limited. This study analyzed the association between receiving Lvm and healthcare costs from a public payers' perspective.

Methods This analysis is based on data of 516 community-dwelling people living with dementia (PwD). Fourteen Lvm were extracted from dementia-specific guidelines, the German equivalent of the Choosing Wisely campaign, and the PRISCUS list. Healthcare utilization was retrospectively assessed via face-to-face interviews with caregivers and monetarized by standardized unit costs. Associations between Lvm and healthcare costs were analyzed using multiple linear regression models.

Results Every third patient ($n = 159$, 31%) received Lvm. Low-value antiphlogistics, analgesics, anti-dementia drugs, sedatives and hypnotics, and antidepressants alone accounted for 77% of prescribed Lvm. PwD who received Lvm were significantly less cognitively impaired than those not receiving Lvm. Receiving Lvm was associated with higher medical care costs ($b = 2959$ €; 95% CI 1136–4783; $p = 0.001$), particularly due to higher hospitalization ($b = 1911$ €; 95% CI 376–3443; $p = 0.015$) and medication costs ($b = 905$ €; 95% CI 454–1357; $p < 0.001$).

Conclusion Lvm were prevalent, more likely occurring in the early stages of dementia, and cause financial harm for payers due to higher direct medical care costs. Further research is required to derive measures to prevent cost-driving Lvm in primary care, that is, implementing deprescribing interventions and moving health expenditures towards higher value resource use.

Key Points

Low-value medications are highly prevalent in dementia care and could lead to higher costs for public payers.

Low-value medications occur in the early stages of dementia (i.e., at the beginning of the disease).

Implementing deprescribing interventions could improve outcomes for patients while saving resources.

1 Introduction

Rapidly increasing healthcare expenditures are challenging health systems worldwide. Due to high healthcare costs, debates have risen about unnecessary expenditure and whether spending focus should move toward higher-value resource use [1]. Shrank et al. [2] estimated the total annual cost of waste to be between US$760 billion to US$935 billion in the US, representing 25% of the total US healthcare spending. Up to US$101.2 billion could be traced back to overtreatment and low-value care, defined as care unlikely to

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benefit patients regarding potential harms, costs, or available alternatives [2–4].

Low-value care or overtreatment are related terms classified under the overarching category of overuse [5]. Evidence to date has been derived primarily from administrative and routinely collected data and focused mainly on the prevalence of low-value medical tests and procedures. In contrast, prescribed low-value medications (Lvm) were underrepresented in recent research [6, 7]. Further, current publications emphasize evidence gaps in the factors promoting overuse (provider vs patient-centered) and for downstream harmful effects (physical, psychological, economic), especially financial harms [8, 9]. In addition, only 15% of low-value care recommendations report economic value at all, representing a significant evidence gap in decision support for physicians and other stakeholders in healthcare [10].

Chronic age-associated diseases such as dementia still represent one of the highest societal and economic burdens on healthcare systems in an aging population worldwide. While there are 57 million people living with dementia (PwD) worldwide, a recent forecast estimates this figure will reach 153 million in < 30 years [11]. Without a prospect of cure, dementia care aims to ensure the best possible individualized care. However, only 39% of people who screened positive for dementia received a formal diagnosis [12], only 30% of PwD are treated with adequate anti-dementia drugs [13, 14], and only 36% were provided with non-drug therapies following the pertinent guidelines [15].

Moreover, a preceding study revealed that at least 31% of the PwD received low-value care, particularly Lvm associated with reduced quality of life and increased hospitalization [16]. In addition, 93% of PwD were affected by at least one drug-related problem and associated additional costs, suggesting that Lvm could also amplify adverse downstream effects for both PwD and payers [17]. Previous studies show the likelihood for PwD and aged individuals receiving low-value prescriptions increases with age, degree of comorbidity, and higher deficits in their daily living [7, 18]. While medication costs in PwD likewise increase with comorbidity and functional impairment, severely cognitively impaired patients are more likely treated with less high-priced drugs, suggesting inadequate medication and poor resource use [19].

However, as long as financial resources are wasted on low-value care, they will not be available to address the unmet needs of current and future PwD, underlining the ethical, economic, and political challenges associated with low-value care [3]. Despite the projected prevalence of dementia and the associated economic and societal impacts, there is insufficient evidence to date on the harms and costs associated with low-value medications in dementia care. Therefore, the objective of this analysis was to analyze the association between receiving Lvm and direct medical care costs from a payers' perspective in community-dwelling PwD.

2 Materials and Methods

2.1 Design of the DelpHi-MV Trial, Setting, and Participant Flow

This cross-sectional analysis is based on baseline data of the cluster-randomized, controlled interventional trial DelpHi-MV (Dementia: life- and person-centered Help in Mecklenburg-Western Pomerania) [20]. Initially, 125 general practitioners (GPs) screened 6838 patients in their practices for dementia using the short interview-based DemTect screening procedure [21]. A total of 1166 (17%) patients met the eligibility criteria (DemTect < 9, aged ≥ 70 years, living at home), were informed about the study by their GP, and were asked to provide written informed consent as approved by the Ethical Committee of the Chamber of Physicians of Mecklenburg-Western Pomerania (registry number BB 20/11). Informed consent was provided by a total of 634 eligible patients (54%). The enrolment and thus the data collection at baseline began on 1 January 2012 and ended on 31 December 2014 [20, 22]. The baseline assessment was completed for 516 PwD, constituting the basis for the presenting analysis. The comprehensive design and participant flow have been described in more detail elsewhere [22].

2.2 Sociodemographic and Clinical Characteristics

Sociodemographic data (age, sex, living situation) and the following clinical variables covering the 12 preceding months were assessed at baseline through a comprehensive, standardized, computer-assisted interview carried out by dementia-specific qualified nurses: cognitive impairment according to the Mini-Mental State Examination (MMSE) [23], comorbidity according to the number of ICD-10 (International Statistical Classification of Diseases and Related Health Problems, 10th revision) diagnoses listed in the GP files [24], depression symptoms according to the Geriatric Depression Scale (GDS) [25], and deficits in daily living activities according to the Bayer Activities of Daily Living Scale (B-ADL) [26].

Furthermore, comorbidities were assessed using a score based on the Charlson comorbidity index (CCI) [27], which considered the following diseases: myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, rheumatic disease, peptic ulcer disease, mild liver disease, diabetes without chronic complication, diabetes with chronic complication, hemiplegia or paraplegia, renal disease, any

malignancy, including lymphoma and leukemia, except malignant neoplasm of skin, moderate or severe liver disease, metastatic solid tumor, and AIDS/HIV [27].

2.3 Healthcare Resource Utilization

The utilization of healthcare resources was also assessed within the baseline interview [20]. The questionnaires captured detailed information about the frequencies of the utilization of the following medical care services: physician consultation (GP, specialists), medication, aids, other outpatient treatments (e.g., occupational, physical and speech therapy), and in-hospital care (acute and planned in-hospital treatment). Besides the number of hospital admissions, the days per stay were also recorded. To improve the validity and precision of the data, study nurses interviewed caregivers, participants, and professional care staff wherever possible.

2.4 Low-Value Medication Measurement

The following three sources were used as references to elicit Lvm in dementia: (i) the German "S3 Guideline: Dementia" published by the German Association for Psychiatry, Psychotherapy and Psychosomatics and the German Society for Neuroscience [28], which lists selected medications that are ineffective and should be avoided; (ii) the PRISCUS list [29], including a total of 83 substances from 18 drug classes that are potentially inadequate for elderly individuals; and (iii) defined harmful recommendations of the German counterpart of the international "Choosing Wisely" campaign [30]. Two reviewers and, in the case of deviations, a third reviewer selected the Lvm-related recommendations according to the following criteria: (i) relevance, (ii) targeted audience, (iii) differentiation criteria for inappropriateness, as well as (iv) evaluability in the data set used for the present analysis [31]. A total of 51 Lvm recommendations were identified. Due to overlap or duplication, recommendations were broken down into individual components and grouped into measurable treatments according to the suggestions of previous studies [6, 31]. In conclusion, 14 measurable active substance classes, including 40 active substances identified as Lvm treatments, provided the basis for this analysis. All Lvm used are demonstrated in Table 1, including active substances, data requirements, and counts. The comprehensive selection process of the respective treatments has been described in more detail elsewhere [32].

2.5 Cost Analysis

A bottom-up prevalence-based cost-of-illness design was used to calculate the average healthcare costs per person living with dementia for a retrospective period of 12 months [33]. In this analysis, healthcare costs comprise the direct costs for medical care services from the payers' perspective. Average medical care costs per patient were calculated using the captured healthcare resource utilization added by their respective published standardized unit costs [34]. When current unit costs were not available, they were extrapolated to 2020 using the average annual inflation rate (for 2016: 0.5%, 2017: 1.5%, 2018: 1.8%, 2019: 1.5%, 2020: 0.5%) [35]. Costs were calculated in Euros (€). Formal and informal care and indirect costs, such as lost productivity, were not considered in this analysis. Detailed information on the monetary valuation of the respective services is summarized in Table 2.

2.6 Statistical Analysis

Study participants' sociodemographic and clinical characteristics, health resource utilization, and healthcare costs were presented using descriptive statistics. The statistical significance of group differences (receiving no Lvm vs at least one Lvm) was determined using *t* tests and Fisher exact tests. Multiple linear regression models were performed to assess the associations between Lvm and healthcare costs. The dependent variables were total medical care costs from the payers' perspective and the following subcategories: costs for physician treatments (GP and specialists), inpatient treatments, medications, medical aids, and outpatient treatments, resulting in a total of six different models. Lvm (dichotomous: receiving no Lvm vs at least one Lvm) was used as an independent variable. Models were furthermore adjusted for the following sociodemographic and clinical factors: age, sex, cognition (MMSE), functional impairment (B-ADL), depression (GDS), as well as patients' diagnoses (dichotomous: yes/no for each) according to the CCI and number of diagnoses (number of ICD-10 diagnoses) to consider the context in which treatments were prescribed and to minimize confounding. Since patients were recruited in different clusters (i.e., GP practices), patient outcomes, treatment, and care could be stochastically dependent on the GP practice. Therefore, we used random effects to adjust for the effects of the clusters in each of our regression models. Due to the highly skewed distribution of medical care costs, standard errors and confidence intervals were determined using nonparametric bootstrapping (2000 replications) [36]. All statistical analyses were performed in STATA/IC 16 [37].

Table 1 14 Low-value medication (Lvm) treatments: active substances included, data requirements, and counts

Lvm by active substance class	Active substance (further condition)	Data requirements[a]	PwD receiving Lvm, *n* (%)
Low-value antiphlogistics/analgesics	Dexketoprofen	ATC (M01AE17)	59 (30.41)
	Etoricoxib	ATC (M01AH05)	
	Indometacin	ATC (M02AA23, M01AB01)	
	Meloxicam	ATC (M01AC06)	
	Naproxen	ATC (M01AE02)	
	Diclofenac	ATC (M01AB05, M02AA15)	
Low-value antidementia drug treatments	Memantine (does not comply with the guidelines for mild dementia)	ATC (N06DX01) MMSE (≥20)	37 (19.07)
	Naftidrofuryl	ATC (C04AX21)	
	Piracetam	ATC (N06BX03)	
	Dihydroergotoxine	ATC (N06DX07)	
Low-value sedatives/hypnotics	Chloral hydrate	ATC (N05CC01)	28 (14.43)
	Chlordiazepoxide	ATC (N05BA02)	
	Clobazam	ATC (N05BA09)	
	Diazepam	ATC (N05BA01)	
	Zopiclone	ATC (N05CF01)	
	Diphenhydramine	ATC (N05CM20)	
	Doxylamine	ATC (N05CM21)	
	Medazepam	ATC (N05BA03)	
	Nitrazepam	ATC (N05CD02)	
	Zolpidem	ATC (N05CF02)	
Low-value antidepressants	Amitriptyline	ATC (N06AA09)	25 (12.89)
	Amitriptyline oxide	ATC (N06AA25)	
	Doxepin	ATC (N06AA12)	
	Trimipramine	ATC (N06AA06)	
Low-value antihypertensives	Clonidine	ATC (S01EA04, C02AC01)	16 (8.25)
	Doxazosin	ATC (C02CA04)	
	Methyldopa	ATC (C02AB01)	
Low-value spasmolytics	Solifenacin	ATC (G04BD08)	10 (5.15)
	Tolterodine	ATC (G04BD07)	
Low-value antipsychotics	Levomepromazine	ATC (N05AA02)	7 (3.6)
	Olanzapine	ATC (N05AH03)	
	Haloperidol	ATC (N05AD01)	
	Quetiapine (does not comply with the guidelines for agitation and aggression)	ATC (N05AH04) NPI[b] (≥ 1)	
Low-value antiarrhythmics	Acetyldigoxin	ATC (C01AA02)	4 (2.06)
	Flecainide	ATC (C01BC04)	
	Sotalol	ATC (C07AA07)	
Low-value muscle relaxants	Baclofen	ATC (M03BX01)	4 (2.06)
	Tetrazepam	ATC (M03BX07)	
Low-value antiemetics	Dimenhydrinate	ATC (A04AB02)	2 (1.03)
Low-value ergotamine	Dihydroergocryptine	ATC (N04BC03)	1 (0.52)
Low-value vitamin E		ATC (A11HA03)	1 (0.52)

ATC Anatomical Therapeutic Chemical, *Lvm* low-value medications, *MMSE* Mini-Mental State Examination, range 0–30, higher score indicates better cognitive function, *NPI* Neuropsychiatric Inventory, score ≥ 5 indicates clinically relevant symptoms, *PwD* people with dementia

[a]Beyond demographic data (e.g., age)

[b]Score for agitation and aggression

Table 2 Methods and used unit costs for monetary valuation of medical care services (based on Michalowsky et al. [53])

Cost categories	Services	Units	Unit costs[a]	Unit cost and source for monetary valuation
Outpatient physician treatment	GP or specialists	Visits	21.16 €–82.38 €, depending on specialization	Cost per visit [34]
Inpatient treatment	In-hospital treatment and rehabilitation	Days	598.97 € and 123.07 €, respectively	Average per diem cost for in-hospital treatment in Mecklenburg-Western Pomerania and for specialization of rehabilitation [34]
Medications	Regularly prescribed drugs (Rx-drugs)	Quantity	Market prices, 256.12 €[b]	Pharmaceutical Index of the Scientific Institute of the AOK [54]
Medical aids	Aids such as tub-lifts, tub-seats, walking sticks, walkers, and others	Quantity	Market prices, 170.61 €[b]	Market prices [34]
Other outpatient treatment	Occupational therapy, speech therapy, physiotherapy, and others	Visits	27.62 €	Cost per contact and reimbursement schedules of statutory health insurance [55]

AOK Allgemeine Ortskrankenkasse, *GP* general practitioner

[a]Inflation included

[b]When drugs, aids or services were unknown, or market prices were not available

3 Results

3.1 Sociodemographic and Clinical Characteristics

Study participants were primarily female (60%), on average 80 (SD 5.5) years old, and mildly cognitively (MMSE mean score 22.2, SD 5.4) and functionally impaired (B-ADL mean score 3.7, SD 2.6). PwD who received Lvm ($n=159$) were slightly younger (79 vs 80 y, $p=0.073$), were less cognitively impaired (23.0 vs 21.7, $p=0.013$), took on average more drugs (9 vs 7, $p<0.001$), and were more depressed (3.5 vs 3.0, $p=0.032$), according to the GDS, compared with PwD who received no Lvm treatments ($n=357$). There were no significant differences for any of the other variables. The sample characteristics are presented in Table 3.

3.2 Healthcare Resource Utilization and Costs

PwD who received at least one Lvm had higher utilization of medical treatments. Significant differences were observed in the prevalence (32 vs 23%, $p=0.045$) and frequency (1.2 vs 0.6, $p=0.037$) of specialist consultations. Moreover, PwD with Lvm had more inpatient treatments (39 vs 26%, $p=0.007$), especially acute (28 vs 19%, $p=0.019$) and planned (14 vs 7%, $p=0.019$) in-hospital treatments, and they stayed longer in hospitals (6 vs 3 days, $p=0.009$) than PwD without Lvm. They also received significantly more anti-dementia drugs (37 vs 26%, $p=0.020$) and used other outpatient treatments more often (68 vs 59%, $p=0.039$). All results on the percentage and frequency of healthcare resource utilization are depicted in Table 4.

Total cost for medication was valued at 181,153 € for the total sample, of which Lvm accounts for 29,983 € (17%) and the remaining medications for 151,170 € (83%). Payers' expenditures for PwD receiving Lvm were significantly higher than those for PwD who did not receive any Lvm (8514 € vs 5539 €, $p<0.001$). This trend was also evident for specialists' costs (382 € vs 305 €, $p=0.035$), cost for inpatient treatments (4501 € vs 2380 €, $p=0.003$), in particular, cost for acute in-hospital treatments (2996 € vs 1749 €, $p=0.031$), and also medication costs (2450 € vs 1538 €, $p<0.001$). Cost differences between Lvm recipients and Lvm non-recipients are presented in Table 5.

3.3 Association Between Low-Value Medication Treatment and Healthcare Costs

PwD who received Lvm had significantly higher medical treatment costs ($b=2959$ €; 95% CI 1136–4783; $p=0.001$) due to significantly higher costs for inpatient treatments ($b=1911$ €; 95% CI 376–3443; $p=0.015$) and medications ($b=905$ €; 95% CI 454–1357; $p<0.001$). In contrast, there were no significant associations between receiving Lvm and costs for outpatient physician treatments, medical aids, and other outpatient treatments. The latter model was no longer significant.

Regarding sociodemographic and clinical co-variables, age was associated with less direct medical care costs. In contrast, functional and cognitive impairment was

Table 3 Sociodemographic and clinical characteristics of the total sample and subsample

Characteristic	Total sample $n=516$	PwD receiving Lvm		p value[a]
		Yes $n=159$	No $n=357$	
Age, years				
Mean (SD)	80.0 (5.5)	79.3 (5.5)	80.3 (5.5)	0.073[b]
Range	70–100	70–96	70–100	
Sex, *n* (%)				
Female	307 (59.5)	104 (65.4)	203 (56.9)	0.080[c]
MMSE				
Mean (SD)	22.2 (5.4)	23.0 (4.4)	21.7 (5.7)	**0.013**[b]
Range	3–30	8–30	3–30	
Severity of dementia, *n* (%)				
No hint for dementia, MMSE score > 26	108 (22.7)	33 (21.0)	75 (23.5)	
Mild dementia, MMSE score 20–26	239 (50.2)	94 (59.9)	145 (45.5)	
Moderate dementia, MMSE score 10–19	107 (22.5)	27 (17.2)	80 (25.1)	
Severe dementia, MMSE score < 10	22 (4.6)	3 (1.9)	19 (6.0)	
Living situation, *n* (%)				
Alone	260 (50.9)	84 (52.8)	176 (50.0)	0.568[c]
Number of ICD-10 diagnoses				
Mean (SD)	13.2 (7.8)	13.7 (7.3)	12.9 (8.0)	0.318[b]
Range	1–58	3–36	1–58	
Formally diagnosed with dementia, *n* (%)				
Yes	366 (71.1)	110 (69.6)	256 (71.7)	0.674[c]
Charlson Score				
Mean (SD)	3.3 (2.3)	3.3 (2.1)	3.4 (2.3)	0.632[b]
Range	0–15	0–15	0–13	
Number of drugs taken				
Mean (SD)	7.3 (3.6)	8.8 (4.1)	6.7 (3.1)	**< 0.001**[b]
Range	0–26	1–26	0–18	
B-ADL				
Mean (SD)	3.7 (2.6)	3.5 (2.3)	3.7 (2.7)	0.357[b]
Range	1–10	1–10	1–10	
GDS				
Mean (SD)	3.2 (2.5)	3.5 (2.8)	3.0 (2.3)	**0.032**[b]
Range	0–14	0–14	0–13	

Values in bold indicate $p < 0.05$

B-ADL Bayer–Activities of Daily Living Scale, range 0–10, lower score indicates better performance, *GDS* Geriatric Depression Scale, sum score 0–15, score ≥ 6 indicates depression, *ICD* International Statistical Classification of Diseases and Related Health Problems, *Lvm* low-value medications, *MMSE* Mini-Mental State Examination, range 0–30, higher score indicates better cognitive function, *PwD* people with dementia, *SD* standard deviation

[a]Referring to PwD who received no Lvm vs. at least one Lvm

[b]Differences in means: *t* test two-tailed

[c]Differences in proportions: Fisher's exact tests

associated with higher medical care costs. Additionally, comorbidities such as chronic pulmonary, rheumatic disease and moderate or severe liver disease and diabetes with chronic complications were also associated with increased medical treatment costs. Table 6 summarizes the associations between healthcare costs and Lvm treatments.

Table 4 Percentage and frequency of healthcare resource utilization

Medical treatments	Total sample $n=516$	PwD receiving Lvm		p value[a]
		Yes $n=159$	No $n=357$	
Percentage of utilization, *n* (%)				
Outpatient physician treatment	516 (100.0)	159 (100.0)	357 (100.0)	
GP	516 (100.0)	159 (100.0)	357 (100.0)	
Specialists	128 (25.5)	48 (31.6)	80 (22.8)	**0.045**[b]
Inpatient treatment	153 (30.2)	61 (38.6)	92 (26.4)	**0.007**[b]
Acute in-hospital treatment	109 (21.8)	44 (28.4)	65 (18.8)	**0.019**[b]
Planned in-hospital treatment	47 (9.4)	22 (14.3)	25 (7.2)	**0.019**[b]
Rehabilitation	31 (6.1)	12 (7.6)	19 (5.5)	0.424[b]
Medications	484 (98.4)	158 (99.4)	326 (97.9)	0.447[b]
Anti-dementia drugs	144 (29.5)	58 (36.5)	86 (26.1)	**0.020**[b]
Medical aids	499 (98.6)	151 (97.4)	348 (99.2)	0.209[b]
Other outpatient treatment	315 (61.6)	108 (68.4)	207 (58.6)	**0.039**[b]
Frequency of utilization, mean (SD)				
Number of GP contacts	7.00 (6.4)	6.9 (5.3)	7.1 (6.8)	0.745[c]
Number of specialist contacts	0.8 (2.9)	1.2 (4.5)	0.6 (1.6)	**0.037**[c]
Days stayed in-hospital per year	4.0 (9.6)	5.7 (11.2)	3.3 (8.6)	**0.009**[c]
Number of medical aids	4.7 (2.7)	5.0 (2.8)	4.6 (2.7)	0.138[c]
Number of other outpatient treatment visits	11.2 (35.7)	10.8 (17.0)	11.3 (41.4)	0.881[c]

Values in bold indicate $p < 0.05$

GP General practitioner, *Lvm* low-value medications, *PwD* people living with dementia *SD* standard deviation

[a]Referring to PwD who received no Lvm vs at least one Lvm

[b]Differences in proportions: Fisher's exact tests

[c]Differences in means: *t* test two-tailed

Table 5 Healthcare costs [€] among people living with dementia treated with low-value medications

Item	Total sample $n = 516$ Mean (SD)	PwD receiving Lvm		p Value[a]
		Yes, $n = 159$ Mean (SD)	No, $n = 357$ Mean (SD)	
Medical treatments	6501 (7899)	8514 (9260)	5539 (6973)	**< 0.001**[b]
Outpatient physician treatment	499 (424)	549 (472)	477 (400)	0.074[b]
GP	170 (155)	167 (128)	171 (165)	0.745[b]
Specialists	329 (384)	382 (451)	305 (347)	**0.035**[b]
Inpatient treatment	2994 (6883)	4501 (8349)	2380 (6018)	**0.003**[b]
Acute in-hospital treatment	2136 (5952)	2996 (6875)	1749 (5455)	**0.031**[b]
Planned in-hospital treatment	759 (3492)	1101 (4049)	607 (3209)	0.144[b]
Rehabilitation	175 (769)	254 (918)	140 (690)	0.128[b]
Medications	1833 (1919)	2450 (2372)	1538 (1581)	**<0.001**[b]
Medical aids	933 (1071)	933 (984)	932 (1108)	0.992[b]
Other outpatient treatment	130 (772)	120 (509)	134 (864)	0.844[b]

Values in bold indicate $p < 0.05$

GP General practitioner, *Lvm* low-value medications, PwD people with dementia, *SD* standard deviation

[a]Referring to PwD who received no Lvm vs at least one Lvm

[b]Differences in proportions: Fisher's exact tests

[c]Differences in means: *t* test two-tailed

Table 6 Multivariable associations between PwD who received Lvm and direct medical care costs

	Medical care costs	Outpatient physician treatment	Inpatient treatment	Medications	Medical aids	Other outpatient treatment
PwD who received Lvm *b* (SE) [95% CI]	2959 (930)** [1136–4783]	63 (46) [−27 to 153]	1911 (782)* [376–3443]	905 (231)*** [454–1357]	−10 (99) [−205 to 183]	31 (44) [−56 to 118]
R^2 overall	0.22***	0.08***	0.16***	0.18***	0.16***	0.10‡
N	427	449	436	448	444	449

Linear mixed models with random effects for general practitioner

The models used were adjusted for sociodemographic and clinical variables: age, sex, cognition (MMSE), functional impairment (B-ADL), depression (GDS), and comorbidities (CCI)

b observed coefficient, *B-ADL* Bayer–Activities of Daily Living Scale, *CCI* Charlson comorbidity index, *CI* confidence interval, *GDS* Geriatric Depression Scale, *Lvm* low-value medications, *MMSE* Mini-Mental State Examination, *PwD* people with dementia, *SE* standard error

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$

‡*p*-value not significant

4 Discussion

Derived from patterns of healthcare resource utilization by community-dwelling PwD, this analysis adds evidence about promoting factors and the downstream financial consequences of low-value dementia medical care, demonstrating that Lvm represents a noticeable part of total medication costs (17%) associated with increased healthcare costs from the public payers' perspective. Higher medical treatment costs underline this finding, primarily due to higher inpatient treatment and medication costs. Additionally, PwD receiving Lvm were more frequently treated by physician specialists and outpatient therapies, more often hospitalized, and took a higher number of drugs, particularly anti-dementia drugs. In addition, the results revealed that younger and, to all appearances, early-stage and thus healthier PwD are more likely to receive Lvm.

Assuming healthcare costs would increase because of Lvm, it is uncertain whether this is due to individual patient-related or systemic provider-centric factors. Several studies have already examined the patient-related factors that increase the likelihood of receiving Lvm, reporting higher age, degree of comorbidity, and higher deficits in activities of daily living [7, 18]. The findings of our descriptive analysis of primary data are not in line with these results. Our sample showed no significant differences in age, comorbidity, or functional impairment between PwD with and without Lvm.

In contrast, those who received Lvm were significantly less cognitively impaired but more depressive than PwD not receiving Lvm treatments. While an elevated depression score is potentially suggestive of mental comorbidities, better cognitive function indicates healthier patients. However, Michalowsky et al. [19] demonstrated that increasing cognitive impairment is associated with fewer drugs, meaning that PwD who are less cognitively impaired receive more medication. Our results show that PwD receiving Lvm took more drugs (9 vs 7) than PwD without Lvm treatments. A higher number of drugs could promote drug-related problems that could cause harm to both the patient and the healthcare system, for example due to increasing hospitalization [38, 39]. Based on our findings, especially in the early stages of dementia, there is a risk for Lvm, which clinicians should consider as early as possible on the patient journey.

Regarding the increasing inpatient treatment costs, Wohlgemuth et al. [17] revealed an association between higher inpatient costs and inappropriate drug choice, which is significantly linked to Lvm treatments. Also, a recent analysis showed an increased likelihood of hospitalization for PwD who received Lvm, underscoring this tendency [32]. These findings are consistent with the present study, demonstrating the higher use of acute (28 vs 19%) and planned (14 vs 7%) in-hospital treatments in PwD receiving Lvm compared with PwD without Lvm treatments.

Recently published studies examined the downstream effects of low-value care procedures in hospitals. They revealed that patients who received low-value care were associated with higher Medicare costs and longer lengths of stay [40, 41], which is in line with the results of our analysis, demonstrating that PwD who received Lvm treatments were more frequently hospitalized (39 vs 26%) and stayed longer in hospitals (6 vs 3 days). The higher utilization of in-hospital services resulted in higher inpatient treatment costs (4501 € vs 2380 €) compared with PwD without Lvm treatments. Hospitalization is a crucial cost-driver and is connected to Lvm in dementia. Further research is needed to generate evidence about the causality between both factors

and identify strategies to avoid cost-intensive unnecessary hospitalizations.

According to outpatient physician treatments, specialists have a crucial role in dementia care since they increasingly provide differential diagnostic and post-diagnostic support by prescribing anti-dementia drug treatment [42]. The present analysis shows that the consultation prevalence of specialists (32 vs 23%) and prescription prevalence of anti-dementia drugs (37 vs 26%) were higher for PwD receiving Lvm than for PwD without Lvm treatments. Despite their crucial role regarding post-diagnostic dementia care, outpatient physicians could likewise promote Lvm. A previous survey of GPs showed that although 57% of the GPs have seen negative consequences, 67% regularly provided low-value care because they want to offer interventions instead of watchful waiting to meet their patients' expectations [43]. Further studies reported cognitive biases, comprising an overestimation of benefits and an underestimation of harms from both patient and physician perspectives [44–46]. In principle, physicians should base their decisions for or against treatment on the available evidence. Still, while the focus is on efficacy and effectiveness, according to Korenstein et al. [8], more research is needed to expand the evidence base about harms from treatments. For Lvm, this extends beyond patient-centered outcomes to financial or economic harms on the system level [10].

This analysis shows that Lvm in dementia care is widespread, occurs across sectors and providers, and is associated with higher costs. However, cross-sectional data alone cannot represent cause and effects. Longitudinal analyses are needed to confirm the findings and to include other outcomes, such as the effect on institutionalization, to examine group differences in nursing home admissions among community-dwelling PwD with and without Lvm. In addition to the costs and utilization of health resources, further research should consider the long- and short-term physical and psychological consequences and expand the evidence on (cost) effectiveness.

As diverse as the stakeholders and drivers of low-value dementia care are, solutions must be equally varied, such as implementing deprescribing interventions [47]. Therefore, multiple levers must be pulled to foster high-value care and treatments [3]. In times of increasing numbers of PwD and the associated growing socioeconomic burden on healthcare systems worldwide, more intersectoral research on low-value care is required to generate evidence about the causal effect of Lvm on patient-reported and health economic outcomes. Also, separate modularized solutions or interventions should be developed to prevent low-value care in outpatient and inpatient settings. Further research should provide quantitative evidence of the harm from low-value care to healthcare stakeholders to broaden the rational basis for decision making, especially for healthcare payers.

4.1 Limitations

This study used baseline data from the DelpHi-MV trial [20], resulting in limited generalizability. First, the data and related findings refer to a rural region in North-Eastern Germany and cannot simply be transferred to urban settings and the West or South. Nevertheless, due to the large primary care sample with GPs in a leading role, our findings are representative of other regions with community-dwelling PwD. Furthermore, primary data and utilization data were collected directly from the patients; other data sources, such as health insurers, were not accessible. However, we performed a standardized data assessment and obtained valid information on relevant clinical dimensions not usually available in secondary data analyses. The completeness and accuracy of information may be affected by the limited cognitive capacities of the participating PwD. Considering the clinical course of dementia disease, most study participants had mild cognitive impairments or early-stage dementia. However, to increase the validity of our data, we obtained additional information from care providers and caregivers in proxy interviews. In addition, the participating PwD were on average 80 years old and were community-dwelling. Therefore, findings cannot simply be transferred to PwD residing in institutions.

Clinical evidence-based guidelines and consensus-based expert publications were used to define low-value interventions, which leads to additional limitations. First, the present analysis does not cover all Lvm. Therefore, the demonstrated prevalence of Lvm is somewhat underestimated. The classification as low-value care also depends on the perspective. In the present analysis, the sources represent an expert perspective rather than the patient perspective regarding unwanted care. In addition, the respective recommendations overemphasize the clinical rationale while not reflecting the economic evidence [10]. A broader evidence base for Lvm must be included from the outset to implement effective strategies minimizing Lvm.

In addition, the results may be limited due to the use of the PRISCUS list [29]. In recent years, other evidence-based lists such as the FORTA [48] or EU(7)-PIM [49] lists, which are more contemporary, have been developed and published. However, the design of the DelpHi-MV trial [20] was developed earlier and targeted drug data collection according to the PRISCUS list [29], which remains a common tool in health services research to indicate potentially inappropriate drugs. However, demonstrated results might change if different lists are used. Further research is therefore needed to detect differences in Lvm and costs according to the other available Lvm lists.

Furthermore, although the PRISCUS list [29] is an explicit tool that offers practical advantages for large-scale epidemiologic studies by directly collecting or measuring

relevant data, it neglects clinical contextual factors and circumstances and individual patient needs [50, 51]. As a result, prescriptions may have been recorded as Lvm even though the treatment provided was appropriate, representing a conflict of goals already described by Schwartz et al. [52]. These clinical contextual factors were unknown in this analysis. Therefore, further research is needed to clarify on an individual patient level if Lvm represents an inappropriate medical treatment with an existing better alternative and if the association between Lvm, patient-reported outcomes, and costs remain significant.

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Declarations

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Code availability The authors can provide the STATA code upon request.

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