EXTRA Dementia and Geriatric Cognitive Disorders

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Original Research Article

Why Is It So Difficult to Evaluate Nursing Interventions in Dementia?

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Key Words
Health technology assessment · Dementia · Nursing interventions · Non-pharmacological studies

Abstract
Two recent health technology assessment (HTA) reports published in Germany focused on non-pharmacological interventions for patients with dementia. One of the major results was the poor methodological quality of the studies in this field. This paper concisely presents the main quantitative and qualitative findings of the HTA report published by the German Agency for HTA at the Institute of Medical Information and Documentation (dahta@DIMDI), followed by a detailed discussion of the major methodological problems observed for the inclusion criteria, interventions, the setting, number of patients included, duration of observation, comparators, clinical endpoints, health economics, and, most obvious, the impossibility of blinding and eliminating placebo effects for future clinical studies. We conclude with several suggestions addressing these challenges for future research in this field.

Introduction

Demographic changes will lead to an increasing number of patients with various forms of non-reversible dementia. Assuming a constant age-related prevalence, the number of demented patients in Germany is likely to double by 2050 [1]. No causal treatment of Alzheimer's dementia is available to date. Certain forms of early interventions such as changes in

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lifestyle or an active reduction of certain risk factors may effectively reduce the burden society will have to face, but from today's perspective, more research is needed on these issues. Cholinesterase inhibitors and memantine are available as symptomatic antidementia drugs, but their importance for the treatment is still a matter of some debate [2–5]. Therefore, the development, improvement, and evaluation of non-pharmacological interventions for patients and/or caregivers represent an important task, which needs to be addressed with greater resolve and sophistication.

The recent publication of two health technology assessment (HTA) reports in Germany – one from the German Institute for Quality and Efficiency in Health Care (IQWiG) [6] and the other issued by the German Agency for Health Technology Assessment at the Institute of Medical Information and Documentation (dahta@DIMDI) [7] – reflects the growing public and scientific interest in non-pharmacological approaches. Both reports conclude that the scientific rigor of the studies examined was poor compared to the more straightforward randomized controlled and double-blind trials which have become the gold standard of clinical psychopharmacology. The authors of both reports raised serious doubts about the validity of the studies on non-pharmacological interventions in dementia.

Two other reviews [8, 9] additionally accounted for interventions focusing on the caregivers and not the patients. Even though the evidence in this respect is stronger, both studies came to very similar conclusions. Olazarán et al. [8] state that, despite the high number of randomized controlled trials included in the analysis, the proportion of high-quality studies was low. Ayalon et al. [9] included only 3 randomized controlled trials (all of which evaluated caregiving interventions) and 6 single-case study designs.

From the existing literature, it appears unclear whether better-suited studies can be designed and carried out. Potential theoretical shortcomings and practical pitfalls need to be identified and overcome preferably before further resources are invested in new trials. Therefore, the results from one [7] of the HTA reports mentioned earlier form the basis for a detailed discussion of specific problems, which need to be taken into account when designing future studies that evaluate nursing interventions in dementia. In the present paper, we try to identify and address the challenges lying ahead of researchers in this field. By doing so, the goal is to spark a discussion about potential methodological advances in order to improve the rigor of future studies and also to highlight a necessary differentiation from pharmacological research.

To achieve this goal, the following Methods section illustrates the way relevant literature for this report was identified. The Results section then tries to focus on problems with study designs identified, while evaluating the available evidence. In the final chapter, the results are discussed and possible next steps towards a standardization of research in nursing interventions are highlighted.

Methods

To identify the relevant literature for the scope of the HTA report, the search consisted of three different approaches: a systematic database search (e.g. in PubMed), a hand search in selected specific journals, and a request for papers in the pipeline but yet unpublished that was sent to relevant German institutions and experts involved in dementia care research. Nevertheless, for the literature search, all international publications were considered. Only randomized trials with a minimum number of 30 or more participants were included. In order to be able to cope with the magnitude of existing therapies, only studies on interventions that could be grouped into validation therapy/emotion-oriented care, occupational therapy, sensory stimulation, relaxation techniques, reality orientation therapy, and reminiscence therapy

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Table 1. Short description of the interventions

Nursing intervention	Short description
Sensory stimulation (Snoezelen)	This technique combines mild sensory stimuli (visual, aural, tactile, and olfactory stimuli) with relaxation. This way, a harmonically designed environment is meant to avoid deprivation, assist in stress reduction, and reduce aggressive behavior. No physical or intellectual requirements exist. Multisensory stimulation emerged from the concept of Snoezelen. Specially equipped rooms are used to reinforce the senses. Other approaches also use sensory stimulation (e.g. music) but in general and not in such a comprehensive way [41].
Aromatherapy	Aromatherapy is also a sensory approach. Essential oils are used for massages, bathing, or room flavor. The procedure is assumed to reduce stress and pain, cultivate recreative sleep, and positively influence depressive illnesses. Aromatherapy may also form part of a multisensory approach [42].
Reality orientation therapy	In this therapy, information is memorized and the orientation concerning place, time, and persons is reinforced. The basic idea is to enable the patients to better recognize their environment and, therefore, to develop more self-control and self-confidence. The caregiver uses possibly every contact to involve the patients in a reality-oriented communication. Additionally, exercises (concerning for example date, weather, and name of meals) at a fixed schedule are done [43, 44].
Reminiscence therapy	This therapy stems from the older reality orientation therapy. The main subject is the patient's biography. Apart from talks, photographs, things, or even music from the patient's past are used. It can be an individual or a group therapy [45].
Validation therapy/ emotion-oriented care	Validation is a process of verbal and non-verbal communication. The way the patients perceive their environment and their feelings are not corrected but respected and affirmed (validated). The goals are, among others, an improved self-esteem, stress reduction, and improved communication skills. Emotion-oriented care is a combination of different approaches with validation being the core concept [43, 46].
Occupational therapy	The central aspects of the occupational therapy are activities of daily living, such as getting dressed, using the bathroom, climbing stairs, or bathing. An essential part is the adaption of the environment to the patient's diminishing abilities. Additionally, the day is structured with fixed times for meals, care-giving activities, and repeating leisure times [47].
Relaxation techniques	This is a general term for different techniques to reduce stress and relax. Often, autogenic training or progressive muscle relaxation are used. Autogenic training is a method of self-influence with the goal to induce relaxation. For progressive muscle relaxation, the muscles of certain body parts are alternately flexed and relaxed in order to induce relaxation [48].

were included following an expert panel discussion looking into the relative importance of different areas of possible interventions being performed in Western European countries. For a short description of the different interventions, refer to table 1. In most countries, these therapeutic concepts are carried out mainly by trained professionals (e.g. specialized nursing staff, psychologists, vocal or occupational therapists, etc.). Studies published before 1996 for the clinical part and before 1989 for the health economic part were excluded.

Table 2. Results of the clinical studies

References	Patient characteristics	Intervention	Controls	Setting	Patients	Measurement period	Endpoints	Results
Toseland et al. [10], 1997	Moderate-to-severe dementia based on the Short Portable Mental Status Questionnaire with behavioral occurrences (e.g. physical aggression, verbal insults)	Validation therapy/ emotion-oriented care in small groups	*Group 1:* activity classes *Group 2:* usual care	Inpatient care	n = 88 (lost to follow-up: 25%)	52 weeks: classes of 30 min, 4 times a week	– Multidimensional Observation Scale for Elderly Subjects – Cohen-Mansfield Agitation Inventory (for nurses and observer) – Geriatric Indices of Positive Behavior – Minimum Data Set – Resident Assessment Protocol	No differences between intervention and control groups (activity classes)
Schrijne-maekers et al. [11], 2002	Moderate-to-severe dementia with behavioral syndromes *Criteria:* – MMSE <21 – Dutch Behavior Rating Scale for Psychogeriatric Inpatients ≥30 – Resident for more than 2 months – Participant of an organized day care program of at least 5 and a half days a week	Validation therapy/ emotion-oriented care	Usual care	Inpatient care	n = 151 (lost to follow-up: 38%)	52 weeks	– Dutch Behavior Rating Scale for Psychogeriatric Inpatients – Geriatric Residents Goal Scale – Cohen-Mansfield Agitation Inventory – Activities of Daily Living Scale – Global Assessment of Functioning	No differences between intervention and control groups
Finnem et al. [12], 2005	Patients with dementia of AD type, mixed dementia of AD type, vascular dementia, and dementia syndrome (DSM-IV) *Criteria:* – Patients with dementia – Amnesic-confabulatory syndrome – Age ≥65 years – Care dependency – Resident for more than 1 month	Validation therapy/ emotion-oriented care	Usual care	Inpatient care	n = 194 (lost to follow-up: 25%)	24 weeks	– Cornell Scale for Depression in Dementia – Cohen-Mansfield Agitation Inventory – Geriatric Resident Goal Scale – Philadelphia Geriatric Center Morale Scale	Positive effects of the intervention on 2 of 7 endpoints
Gitlin et al. [13], 2001	Patients with AD and related symptoms *Criteria:* – Patients with dementia – Caregiver lives in the same household – Dependency in 2 or more activities of daily living – Difficulties of the caregiver	Occupational therapy	Usual care	Home care	n = 202 (lost to follow-up: 15%)	12 weeks	– Memory and Behavior Problems Checklist – Activities of daily living – Instrumental activities of daily living	Positive effects of the intervention on 1 of 3 endpoints
Gitlin et al. [14], 2003	Patients with dementia *Criteria:* – MMSE <24 or diagnosis of dementia	Occupational therapy	Usual care	Home care	n = 255 (lost to follow-up: 26%)	24 weeks	– Revised Memory and Behavior Problems Checklist – Activities of daily living – Instrumental activities of daily living	No difference between intervention and control groups
Dooley and Hinojosa [15], 2004	Patients with mild-to-moderate dementia *Criteria:* – MMSE ≥10 – Patient lives at home – Primary caregiver exists	Occupational therapy	Usual care	Home care	n = 40 (lost to follow-up: none)	8 weeks	– Physical Self-Maintenance Scale – Affect and Activity Limitation – Alzheimer's Disease Assessment	Positive effects of the intervention on 2 of 3 endpoints
Gitlin et al. [16], 2005	Patients with AD and related symptoms *Criteria:* – MMSE <24 or diagnosis of dementia	Occupational therapy	Usual care	Home care	n = 188 after 6 months (lost to follow-up: 33%)	52 weeks	– Number of memory-related behavioral occurrences	No differences between intervention and control groups

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Table 2 (continued)

References	Patient characteristics	Intervention	Controls	Setting	Patients	Measurement period	Endpoints	Results
Graff et al. [17], 2006	Patients with mild-to-moderate dementia *Criteria:* – Brief Cognitive Rating Scale 9–40 – Age ≥65 years – Patient lives at home – Primary caregiver exists	Occupational therapy	Usual care	Home care	n = 135 (lost to follow-up: 15%)	6 weeks	– Assessment of Motor and Process Skills – Process Scale – Interview of Deterioration in Daily Activities in Dementia – Performance Scale	Positive effects of the intervention on all endpoints
Baker et al. [18], 1997	Patients with AD, vascular or presenile dementia *Criteria:* – Patient lives at home – Primary caregiver exists – Participants had been referred to Elderly Severely Mentally III Service by a GP – Day care at least twice a week	Sensory stimulation (Snoezelen)	Activity classes	Home care, day care clinic	n = 31 (lost to follow-up: none)	4 weeks after intervention	– Rehab Rating Form – Behaviour and Mood Disturbance Scale – Behaviour Rating Scale – MMSE	Positive effects of the intervention on 2 of 4 endpoints
Baker et al. [19], 2001	Patients with moderate-to-severe dementia *Criteria:* – MMSE 0–17 – AD, vascular or mixed dementia type – Patient lives at home – Primary caregiver exists – Participants had been referred to Elderly Severely Mentally III Service by a GP – Day care at least twice a week	Sensory stimulation (Snoezelen)	Activity classes	Home care, day care clinic	n = 50 (lost to follow-up: none)	4 weeks	– Behaviour Mood Scale – Behaviour Rating Scale – MMSE – Cognitive Assessment Scale	No differences between intervention and control groups
Baker et al. [20], 2003	Patients with moderate-to-severe dementia *Criteria:* – MMSE 0–17	Sensory stimulation (Snoezelen)	Activity classes	Day care clinic and psycho-geriatric wards	n = 136 (lost to follow-up: 7%)	4 weeks	– MMSE – Behaviour Rating Scale – Clifton Assessment Procedures for the Elderly – Behaviour and Mood Disturbance Scale – Rehab Rating Form	No differences between intervention and control groups
Van Weert et al. [21], 2005	Patients with moderate-to-severe dementia *Criteria:* – Moderate to severe dementia (DSM-III-R) – Nursing care dependency	Sensory stimulation (Snoezelen)	Usual care	Inpatient care	n = 125 (lost to follow-up: 51%)	18 months	– Dutch Behavior Observation Scale for Psychogeriatric Inpatients – Cohen-Mansfield Agitation Inventory – Cornell Scale for Depression in Dementia	Positive effects of the intervention on 5 of 12 endpoints
Remington [22], 2002	Patients with mild-to-severe dementia *Criteria:* – Agitated behavior at least once a day (Cohen-Mansfield Agitation Inventory) – Age ≥60 years – Patients are able to hear and to feel with their hands	Sensory stimulation (music and massage)	Usual care	Inpatient care	n = 68 (lost to follow-up: none)	1 h after intervention	– Cohen-Mansfield Agitation Inventory – Ward Behavior Inventory – Confusion Inventory	Positive effects of the intervention on all endpoints
Ballard et al. [23], 2002	Patients with severe dementia *Criteria:* – Clinically significant agitation (Cohen-Mansfield Agitation Inventory) – Clinical Dementia Rating Scale stage 3	Sensory stimulation (aroma and massage) with Melissa cream	Sunflower-oil	Inpatient care	n = 72 (lost to follow-up: 1%)	4 weeks	– Cohen-Mansfield Agitation Inventory	Positive effects of the intervention on the primary endpoint

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Table 2 (continued)

References	Patient characteristics	Intervention	Controls	Setting	Patients	Measurement period	Endpoints	Results
Woods et al. [24], 2005	Patients with moderate-to-severe dementia *Criteria:* – AD according to DSM-IV – MMSE <20 – Stable medication for 1 month or more – Inpatient care for the last 2 months – Patients are mobile	Sensory stimulation (therapeutic touch)	*Group 1:* placebo *Group 2:* usual care	Inpatient care	n = 57 (lost to follow-up: none)	3 days	– Agitated Behavior Rating Scale	No differences between intervention and placebo control groups
Suhr et al. [25], 1999	Patients with mild-to-moderate AD *Criteria:* – Behavioral occurrences which reduce activities of daily living – Home care	Relaxation techniques (progressive muscle relaxation)	Alternative relaxation technique	Home care	n = 34 (lost to follow-up: 18%)	8 weeks	– Dementia Severity Rating Scale – Visual Retention Test – Controlled Oral Word Association Test – Beck Anxiety Inventory – Brief Psychiatric Rating Scale – Behavior Rating in Alzheimer's Disease	Positive effects of the intervention on 1 of 6 endpoints
Spector et al. [26], 2003	Patients with dementia according to DSM-IV *Criteria:* – MMSE 10–24 – Score 0 or 1 in questions 12 and 13 of Clifton Assessment Procedures for the Elderly – Behavior Rating Scale	Reality orientation therapy	Usual care	Inpatient care/day care	n = 201 (lost to follow-up: 17%)	7 weeks	– MMSE – Alzheimer's Disease Assessment Scale – Cognition – Holden Communication Scale – Clifton Assessment Procedures for the Elderly – Behavior Rating Scale – Quality of Life – Alzheimer's Disease Scale – Clinical Dementia Rating Scale – Cornell Scale for Depression in Dementia – Rating Anxiety in Dementia	Positive effects of the intervention on 3 of 8 endpoints
Onder et al. [27], 2005	Patients with dementia *Criteria:* – Of the National Institute of Neurological and Communicative Diseases and Stroke and the Alzheimer's Disease and Related Disorders Association – MMSE 13–28 – Donepezil for more than 3 months	Reality orientation therapy	Usual care	Home care	n = 156 (lost to follow-up: 15%)	25 weeks	– MMSE – Alzheimer's Disease Assessment Scale – Cognition – Neuropsychiatric Inventory – Barthel Index – Number of impaired instrumental activities of daily living	Positive effects of the intervention on 2 of 5 endpoints
Politis et al. [28], 2004	Patients with dementia according to DSM-IV *Criteria:* – Apathy – Global Deterioration Scale Score 3–5 – Short conversation or easy activity possible	Reminiscence therapy	Activity classes	Inpatient care	n = 37 (lost to follow-up: none)	4 weeks	– Apathy score of the Neuropsychiatric Inventory – Alzheimer's Disease-Related Quality of Life Scale – Cooper Ridge Activity Index	No differences between intervention and control groups
Lai et al. [29], 2004	Patients with dementia according to DSM-IV *Criteria:* – Communicative ability	Reminiscence therapy	*Group 1:* general communication *Group 2:* usual care	Inpatient care	n = 101 (lost to follow-up: 15%)	6 months	– Social Engagement Scale – Well-being/Ill-being Scale	No differences between intervention and control groups

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Results

Database

Altogether, 1,658 clinical, 665 health economic, and 35 studies dealing with ethical or legal topics were identified in the structured literature search. Following the assessment of the abstracts by two independent reviewers, 287 clinical and 213 health economic publications were included for a closer examination of their relevance for the subject. Finally, 20 clinical [10–29] and 6 health economic [30–35] publications met the inclusion criteria (details for the clinical part can be seen in table 2).

The 20 clinical publications presented results from 19 different studies from seven different countries. Of these 20 papers, 3 focused on validation therapy/emotion-oriented care, 5 on manual therapy, 2 each on reality orientation and reminiscence therapy, 1 on a technique aimed at relaxation, and 7 on sensory stimulation. The latter are divided into 4 studies based on Snoezelen, and 1 study each on aromatherapy, music/massage, and therapeutic touch. These therapies are described in table 1.

Ten studies reported no significant differences in comparing the intervention and the control group. The specific interventions in these studies were validation therapy/emotion-oriented care, manual therapy, sensory stimulation, reminiscence therapy, and relaxation. Seven studies reported positive results in some of the observed aspects. Finally, 3 publications showed favorable results in all measured endpoints for a program of manual therapy, aroma therapy, and music/massage, respectively. An excerpt of relevant study data is presented in table 2.

The identified publications presenting health economic findings were based on studies in four different countries. One study reported no significant differences in clinical outcomes but an increase in costs due to an occupational therapy program. A slower decline in the Mini-Mental State Examination (MMSE) score in participating patients was claimed by 2 Italian publications. However, the authors reported costs that omitted some important aspects of the intervention. The remaining 2 publications focused on a mix of interventions (an activity program and a special care program for still agile patients), therefore making it impossible to single out the effects of individual parts of the interventions.

Overall, the studies included in the review were of poor methodological quality with a wide range of inclusion criteria, implementation and conduct of the interventions, study periods, settings, choice and design of the control groups, the number of patients enrolled, and the observed endpoints. The results were even less favorable for the health economic studies, providing too little information for any reliable conclusion. In the following part, the aforementioned flaws of the studies will be presented in more detail.

Based on the results of and explanations given in the systematic review of nursing interventions in dementia, the intention is to highlight the identified methodological problems in order to foster a scientific discussion around the question: 'Why is it so difficult to conduct a scientifically sound study in the field of nursing interventions in dementia?'

Inclusion Criteria

While analyzing the publications for the systematic review, it became evident that many different instruments are used for the validation of a dementia diagnosis. Among the more frequently applied scales are the DSM-IV, the MMSE, the Clinical Dementia Rating Scale, and the Brief Cognitive Rating Scale. Unfortunately, there is still an ongoing controversial discussion on how all these scales can be linked or even transferred into one another. With that in mind, however, three categories (mild, moderate, and severe) are typically used to rate the severity of dementia. In addition to this rather rough estimation, the study population in most cases includes patients from different subgroups or even individuals without a diagno-

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sis of dementia. In connection with small patient cohorts, this hinders a separate calculation for each subgroup, therefore reducing the chance to identify groups of patients that are likely to benefit the most from an intervention.

Obviously, ethical and legal considerations need to play a major role before including patients into a study. This holds true for both pharmaceutical and non-pharmaceutical interventions. In the case of dementia, the autonomy of the participants is an issue, especially when thinking about informed consent to take part in a dementia study. So far, no standard for the inclusion has been established; therefore, these questions have to be raised for every single patient. Since, from a legal perspective, the patients will eventually lose their capacity to represent themselves, every single decision concerning the patient, and therefore also the decision to take part in a study, might also have to be taken by an appointed legal representative.

Interventions

In order to conduct an interventional study, the exact procedure has to be described first. For nursing interventions in dementia, the field of possible interventions is – as in other indications – quite diverse, and their differentiation is not always clear. An example might be music therapy, which is a single intervention but can also be subsumed as part of a sensory stimulation program.

The origin of these challenges goes as deep as to the fundamental underlying concepts for these interventions. In general, many different sensory, environmental, and cognitive treatments can be grouped under this topic. Some interventions are based on a complete shift in the way care is delivered, while others will be given only temporarily in class type forms. These differences may also have an influence on the amount of time and effort spent for a specific intervention.

Talking about similarities and differences between different approaches, a standard within specific interventions seems to be far from common. This makes it difficult to even compare treatments bearing the same name. Additionally, the way an intervention is delivered differs from one caregiver to another, which might sometimes be due to the need for specific adaptations of a program caused by the situation of one patient. However, another source for these differences might also be added requirements for caregivers. On the one hand, the study protocol often requires them to change their usual routine entailing a chance to possibly improve their work, while, on the other hand, they have to follow a tight schedule or they even (e.g. in case of family caregivers) might lack the necessary education.

As a result of these challenges, it should be worthwhile to define specific interventions in a stricter manner so that differences are reduced. Secondly, in order to alter or formalize the role of caregivers at the start of an intervention, this group needs to be given more training and time for them to learn, apply, and get used to the respective new method.

Setting

In outpatient as well as inpatient care, a wide array of different treatments is possible. Especially in an ambulatory setting, an additional objective of any intervention will be the reduction of the burden of care for family caregivers. A reduced burden of care might actually prolong the period of outpatient care, avoiding or at least delaying nursing home admissions. This may lead to a reduction in the direct costs for the social security system on the one hand, but potentially raises costs for family caregivers on the other. Interventions in both settings are of course worth to be investigated since the treatment usually takes place in an outpatient setting in early stages of the disease and is later shifted towards a higher degree of inpatient treatment. Studies in this field should account for differences in the environment or in the existing knowledge of the caregivers.

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The setting can also be biased by different study countries, leading to a wide variety of health care systems in which the intervention is applied. From the 19 clinical studies included in the aforementioned systematic review, 7 were conducted in the USA, 4 each in the Netherlands and Great Britain, and 1 each in Italy, Canada, and China. One study was conducted in Great Britain, the Netherlands, and Sweden at the same time. This further complicates an analysis of the different treatments.

Number of Patients Included and Duration of Observation

In comparison to studies with pharmacological interventions, the number of patients included was rather small and the duration of observation tended to be short. Only very few studies considered in our systematic review included more than 200 patients. The observation period differed substantially, ranging from a minimum of 1 h to a maximum of 52 weeks. This problem obviously also touches ethical and legal problems for the inclusion of patients as longer observation periods also translate into longer time spans for the control group without the presumably favorable intervention. However, it also raises an economic question since bigger and longer-lasting studies require more funding. On the other hand, a higher number of patients facilitates the detection of significant results. As a consequence, the outcomes of smaller and shorter studies are very likely to have a lower statistical and clinical level of evidence and resulting validity. For future studies, it has to be discussed what time horizon and number of patients are appropriate to show meaningful clinical and therapeutically relevant differences between the intervention and the control group.

Comparators

An additional aspect of differences is the choice of the respective comparator. Most studies analyzed in the systematic review compared the interventions with a standard care procedure, an alternative program, or a combination of these. What this 'standard of care' includes is not answered in any study. Hence, the same challenges as described for differences in the intervention also apply for the definition of the comparators since it is quite likely that the properties of the control groups will vary across studies. One question that has to be raised at this point is, if it is possible at all, to identify or agree on a standard of care. Usually, study results rely on differences in effects between the novel intervention and the standard of care at a given time in the respective field. Lacking this foundation complicates the interpretation of all study findings, even if the difference was positive in a respective study. Furthermore, studies comparing a novel intervention to standard care are more likely to yield significant results, which is not the case for studies with an alternative program for the controls group. In that case, the majority of studies report no significant differences between the two groups.

Additionally, the results for controls receiving standard care may also be diluted by external effects of an intervention on the comparators. One study mentioned possible positive effects on the controls because of a changed behavior of caregivers in an inpatient setting. This might have resulted from an increased attention and recognition for the work done in the hospital ward, as well as the availability of more time for patients in the control arm since the others were taken care of in the intervention. One possible interpretation for this finding could be that the effects are not caused by specific characteristics of the intervention itself but at least partly rest upon factors such as increased attention, devotion, and engagement.

Studies in the area of non-pharmacological interventions also have to deal with potentially huge confounding effects arising from the underlying pharmacological treatment patients receive. In this sense, results could be negatively biased even if the groups are well designed, and this factor has been accounted for by the researchers. On the other hand, an intervention might very well struggle with the fact that it has to add positive effects on top of the impact of an ongoing drug therapy.

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Clinical Endpoints

Evidence for disease-specific clinical endpoints derived by high-level controlled trials is requested by all drug authorization agencies. For the design of studies with a pharmaceutical agent, appropriate endpoints and respective validated instruments aiming at catching effects are more or less well known and accepted in dementia. For non-drug interventions, however, the issues of relevant outcomes, endpoints, and measures which might be used to collect data are different and challenging. In general, no specific guidance can be found in the literature on what to include in studies, and by looking at dementia as a broad group of different diseases, the available body of evidence gets sparser the lower the prevalence of the indication. Research in the area of dementia care covers a wide range of endpoints aiming at objectives as diverse as cognitive and linguistic capabilities, the capacity for remembering facts and things, agitation, social behavior, controlling aggressiveness or anxiety, overcoming apathy, dealing with depression (also by caregivers), coping with the mental burden in general, fitness for everyday life, and positively impacting the quality of life of patients and their caregivers. By doing so, a wide array of different questionnaires is utilized in practice – sometimes even to capture the same domains of interest. In most cases, these questionnaires have not been validated in a scientifically sound way, which, at the end, leads to using non-validated and probably inappropriate measures of which the results cannot be interpreted. A lot of research in this field has been done with respect to pharmacological interventions in dementia care. Such research also needs to be carried out for non-pharmacological interventions. One result of this might be a reduction of the range of different measures, which would allow for less complex comparisons of findings from different studies.

Health Economics

In almost every case, health economic information provided by authors in this field does not follow internationally accepted standards (for Germany, refer to [36]). The most basic questions, e.g. the adopted perspective, are not reported or discussed, not to mention a missing distinction between different types of costs and their quantities. Therefore, the transferability of results from one regulatory framework to another is strongly limited. Even within the respective health care system of a study, only limited economic implications can be inferred in most cases, as these flaws hinder the interpretation of the results. Researchers in this area should therefore start to adopt standards that are already well accepted in studies with pharmacological interventions, either internationally or at least in their respective country.

Discussion

The concept of evidence-based medicine has been introduced two decades ago and has been enhanced up to now. For pharmaceutical products, requirements for study protocols and their methodological backbone have been harmonized mainly driven by formal requirements imposed by market authorization agencies like the FDA and the EMEA. As a result, the quality of pharmaceutical trials and studies has increased dramatically with respect to their methodology as well as their presentation of the results in journal articles or other publications.

Since HTA agencies such as the NICE in England and Wales or the IQWiG and the DIMDI in Germany do not only assess drugs but increasingly also consider medical devices, procedures, and non-medical interventions (e.g. nursing interventions) for evaluation, it is only logical that it should at least be tried to apply and/or adopt the basic concepts of evidence-based medicine to these health interventions as well [37–39].

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Table 3. Next steps to identify a standard in studies for nursing interventions

Area	Challenge
Inclusion criteria	Identify and agree upon a common measurement for the diagnosis
Interventions/comparators	Thoroughly describe and, if possible, define standards for different interventions
Settings	Carefully and thoroughly describe the environment
Number of patients included and duration of observation	Concentrate on large-scale studies for interventions that have shown to be promising
Clinical endpoints	Identify and agree upon a common set of validated instruments
Health economics	Adopt established and accepted methods

In recent years, the methodological development focused primarily on pharmacological studies, which is why a widely accepted and sound framework exists. However, the gold standard concentrating on double-blind, controlled, and randomized settings obviously raises some major challenges for the conduct of studies in non-pharmacological interventions in demented patients. It is evident that in these indications at least health care providers and, to a great extent, also the people collecting the data can hardly be put in a blinded situation when conducting these studies. This can be seen as a major drawback, leading to the conclusion that, regardless of the setting, doubts about the true efficacy of an intervention will remain. The randomization of study subjects also raises problems, but these might be met by a randomization of study centers, where different study sites – be it an inpatient or outpatient setting – conduct only one kind of intervention. This way, every participating branch does something else, which is why even an unchanged treatment provides useful insight. Of course, this leaves plenty of room for possible biases of all different kinds, starting with selection biases or issues concerning different skills of the therapists. Nevertheless, all these problems that arise when benchmarking the quality of studies in this health care sector with the design of clinical trials for pharmaceuticals might not be overcome but at least be addressed with very rigorous transparency about the study design. On a separate note, some of the challenges just discussed are not exclusive to non-pharmaceutical interventions in dementia. A great majority of medical devices are also facing these hurdles, which will be addressed by HTA agencies in the near future.

For care interventions in dementia, only a limited amount of qualitatively good studies can be found (e.g. [17]), which, in turn, suggests that it is possible to conduct well-designed studies also in this field. Nevertheless, the majority of the publications is of poor quality; hence, there is still a lot of work ahead for researchers in this field. Table 3 gives an overview of useful next steps to achieve a common denominator for future studies.

Obviously, a major part of the problem is the lack of financial resources for this kind of research. Especially aspects like the number of included patients or the time of follow-up are affected by this problem, which cannot easily be solved in face of a low public interest. Nevertheless, a few of the other topics mentioned above (e.g. a standardization of the interventions and endpoints) could be solved or at least be worked on irrespective of the funding. The recent attempt by Moniz-Cook et al. [40] might serve as an example to identify valid outcome measures for dementia care.

In summary, it needs to be highlighted that, even though studies in this field show weaknesses on some basic requirements, this lack of evidence does not necessarily imply a lack of

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efficacy and efficiency of these non-pharmaceutical interventions. This finding only emphasizes the need for additional and methodologically robust studies that also take into account the circumstances under which dementia care is provided in their specific context.

The most obvious and striking problem with non-pharmacological interventions studied in patients with dementia is the impossibility of avoiding placebo and/or setting effects by systematic blinding. This methodological difficulty cannot be overcome by the most sophisticated designs as the interventions under scrutiny can be seen, heard, and felt. The latter sentence aims to point out the comparable simplicity of pharmacological studies and the notion that, by posing unrealistic barriers of methodological requirements for researchers in the field of nursing interventions, attempts at studying more ambitious and adequate methods of care will be hindered.

Arguments calling for fairness in enabling comparisons of different techniques, the necessities of an increasing population of dementia patients, and political as well as economic requirements make the development and, consequently, the deployment of sound methods unavoidable and urgent. This is also reasonable as it could provide a common ground for comparisons of different kinds of interventions. In the end, the goal has to be the identification of effective and efficient interventions for the increasing number of patients.

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