Cross–cultural acceptability of interventions that may increase control at the end of life in people with dementia

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Caregivers, policy makers, researchers, students, residents and relatives work together to improve the quality of care and quality of life for vulnerable older people. The UNC-ZH is a regional platform, inspirator and learning network for innovation in long-term care. Research, education and training, and practice are closely related.

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Contents

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General introduction

A few years ago when I was visiting my family in East Asia, I asked S, a lovely lady in her late 70s, whether she had any preferences for her future care in case she becomes unable to make her own decisions. At that time, she has already witnessed more relatives deteriorate with dementia. "Oh, but I wouldn't want to make my own decisions anyway. My son will decide for me, whether my brains still work well or not." I was surprised, because she did decide on her own to undergo surgery for a tumor the year before. "Well, I would rather they didn't tell me about the illness. It was really stressful to make the decision and to think about the possibility of dying. If something like that happens again, just operate on me and lie to me that I would only need a minor intervention under narcosis. People are different," she said, "My husband wanted to know every detail of his medical care. I don't."

The complexity of control: people are different, cultures are different

Erich Fromm described a paradox in his book 'escape from freedom': while personal choice provides us with freedom and potentials for self-realization, it also brings anxiety and burdensome responsibility which people tend to escape from (1). On the other hand, according to another psychologist Ernest Becker, stiving for control can also be a means to deny death and escape from existential anxiety (2). People differ in how much control they would like to have over their lives. In the case of lady S, she was more comfortable handing over control to her family, while her husband attempted to retain it himself.

On a broader level, people with different cultural and historical backgrounds may have different tendencies when it comes to control. In the western world, control is seen as essential for a good death (3, 4). This emphasis on autonomy and personal control can be traced back to the start of modernity in the seventeenth century (5). However, in societies where values of modernity were introduced later and are less firmly rooted, control may not be the primary concern. In collective cultures, filial piety, for example, is an important value (6). This entails taking care of the parents, including taking over the responsibility and control of their medical decisions (7). Religious emphasis on sanctity of life, as well as historical events such as the Nazi regime also leave

marks on how certain countries perceive as appropriate amount of control that a person or their physicians can take (8).

Control in end-of-life care for people with dementia

Additional challenges and controversies around control exist in end-of-life care for people with dementia. Dementia is a neurocognitive syndrome currently affecting 55 million people worldwide, with more than half living in low-and middle-income countries (9). It is estimated that the number of people that live and die with dementia doubles each five years (10). At the end of life, control of the individual includes making preparations for death, influencing the time and place of dying, and managing distressing symptoms (4). These may all be very challenging for people with dementia because of the impairments in cognitive functions, decision-making, and communication (11), and changes in wishes as the disease progresses (12).

Interventions that may increase control

Several interventions may increase control at the end of life for people with dementia, including advance care planning (ACP), the use of technology to monitor distressing symptoms at the end of life, and euthanasia. ACP entails discussing "goals and preferences for future medical treatment and care" (13). There are diverse approaches to ACP. An approach focusing on making concrete treatment orders may help people gain more control over the medical treatments and distressing symptoms at the end of life, while an approach focusing on exploring values and generating global care goals leaves some room for family and healthcare professionals to decide on specific treatments. Both approaches allow people with dementia to prepare for future care and death and express their wishes when they are still able to consider and communicate what they want. Monitoring technology may help people gain control over distressing symptoms by detecting signs of discomfort, since people with dementia at the end of life are often no longer able to express themselves (14, 15). Euthanasia provides people with the possibility of controlling the timing and place of death, and end unbearable suffering brought by dementia or other comorbid conditions (16). In some countries, decisional capacity before

administration is required, which excludes people in later stages of dementia from euthanasia (17). In others, an advance euthanasia directive may provide people with an opportunity to exercise control over their future death (18).

These interventions may be received with diverse attitudes and controversies given the complexity of control in end-of-life care for people with dementia. Many current studies focus on the perspective of physicians, who are usually the ones carrying out the interventions. Regarding ACP, research suggest that physicians face moral challenges that influence their willingness to conduct these conversations with people with dementia (19). An examination of their ethical considerations throughout the ACP process, from initiation to enacting the plans, is needed to tailor suitable approaches of ACP for people with dementia. Studies on euthanasia demonstrated that physicians are less acceptive of euthanasia for people with dementia than the general public (20) and research on this topic has mainly been limited to countries where euthanasia is legal (20, 21). As more countries are debating and legalizing euthanasia (17), acceptability of physicians from countries with a variety of legalization is worth investigating. In terms of technology, although rapid development is taking place in devices that monitor possible distress (22, 23), a first step still needs to be set in mapping the available technologies that may be useful for the end of life. The acceptability of promising technologies can then be tested among the stakeholders.

Aims and outline of this dissertation

The aim of this dissertation is to provide insight into the acceptability of interventions that may increase control at the end of life for people with dementia. The research questions are:

1. Are advance care planning, the use of monitoring technology, and euthanasia acceptable in end-of-life care for people with dementia?
2. Are there cross-cultural differences in acceptability of these interventions?

Chapter 2 comprises the protocol of the CONT-END study: attempts to Control the End of Life in People with Dementia. This mixed-method vignette study investigates the acceptability of two approaches of ACP, the

use of monitoring technology at the end of life, and euthanasia among people with dementia, family caregivers, and physicians in six countries.

Chapters 3 and 4 report the results of the CONT-END study. Using interview data, **Chapter 3** examines the perspectives of Dutch and US physicians on two approaches of ACP for people with dementia. The following question was answered: What are ethical considerations of physicians from two high-income countries (the US and the Netherlands) on ACP for people with dementia? **Chapter 4** presents the quantitative results regarding the acceptability of euthanasia for people with dementia among physicians from six countries. The following questions were addressed: 1) Is euthanasia acceptable for people with dementia from the perspective of physicians in these six countries? 2) Are there differences in acceptability of euthanasia for people with dementia from the perspective of physicians between the countries? 3) Which personal characteristics of physicians are associated with the acceptability of euthanasia for people with dementia?

Chapter 5 and 6 investigate the role of monitoring technology in end-of-life care for people with dementia. With a scoping review, **Chapter 5** addresses the following questions: 1) What noninvasive monitoring technologies are available or under development that identify discomfort and distressing symptoms which can occur at the end of life? 2)What is known about the clinimetric properties (e.g., validity, reliability, sensitivity, specificity, responsiveness) of these technologies? 3) What is known about the acceptability and feasibility of these technologies for persons with limited communication? **Chapter 6** presents a first step in exploring the acceptability of a well-developed technology, Bispectral Index monitoring (BIS), in end-of-life care for dementia, using focus groups with people with dementia and family caregivers living in the Netherlands. The following questions were investigated: Is BIS at the end of life of people with dementia acceptable from the perspective of people with dementia and their family caregivers? In which situations it is considered acceptable and why?

The dissertation is concluded with a general discussion in **Chapter 7**, with summarized findings, methodological considerations, and recommendations for the practice and future research.

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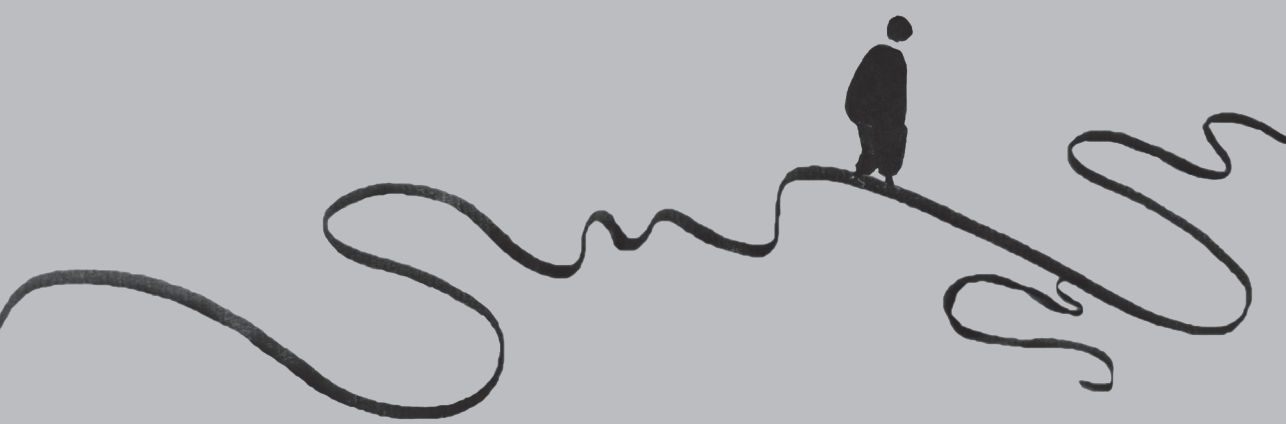

Interventions that may increase control at the end of life in persons with dementia: The cross-cultural CONT-END acceptability study protocol and pilot-testing

Smaling HJA, Jingyuan X, Nakanishi M, Shinan-Altman S, Mehr DR, Radbruch L, Gaertner J, Werner P, Achterberg WP, van der Steen JT.

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Abstract

Background: Interventions such as advance care planning (ACP), technology, or access to euthanasia may increase the sense of control over the end of life. In people with advanced dementia, the loss of cognitive and physical function limits the ability to control care. To date, little is known about the acceptability of these interventions from the perspective of persons with dementia and others involved. This study will examine the cross-cultural acceptability, and factors associated with acceptability, of four end-of-life interventions in dementia which contain an element of striving for control. Also, we report on the development and pilot testing of animation video vignettes that explain the interventions in a standardized manner.

Methods: Cross-sectional mixed-methods vignette study. We assess acceptability of two ACP approaches, technology use at the end of life and euthanasia in persons with dementia, their family caregivers and physicians in six countries (Netherlands, Japan, Israel, USA, Germany, Switzerland). We aim to include 80 participants per country, 50 physicians, 15 persons with dementia, and 15 family caregivers. After viewing each animation video, participants are interviewed about acceptability of the intervention. We will examine differences in acceptability between group and country and explore other potentially associated factors including variables indicating life view, personality, view on dementia and demographics.

In the pilot study, participants commented on the understandability and clarity of the vignettes and instruments. Based on their feedback, the scripts of the animation videos were clarified, simplified and adapted to being less slanted in a specific direction.

Discussion: In the pilot study, the persons with dementia, their family caregivers and other older adults found the adapted animation videos and instruments understandable, acceptable, feasible, and not burdensome. The CONT-END acceptability study will provide insight into cross-cultural acceptability of interventions in dementia care from the perspective of important stakeholders. This can help to better align interventions with preferences. The study will also result in a more fundamental understanding

as to how and when having control at the end of life in dementia is perceived as beneficial or perhaps harmful.

Trial registration: The CONT-END acceptability study was originally registered at the Netherlands Trial Register (NL7985) at 31 August, 2019, and can be found on the International Clinical Trials Registry Platform.

Background

The central theme in what is regarded as a good death in western countries, is control (1). Attempts to exert control at the end of life are emotionally charged and controversial. This is obvious from controversies around interventions such as euthanasia and assisted dying. In dementia, retaining control is inherently difficult due to cognitive decline. Issues with end-of-life care may be complicated by impaired decisional capacity and decreased ability to express preferences or complaints such as pain.

Palliative care assumes that anticipating and preparing for the end of life is beneficial (2, 3) and advance care planning (ACP) for the end of life is part of it. ACP involves discussing and documenting the desired direction of the patient's care with patients and their family caregivers, thereby providing some control over current and future care. Positive effects of ACP on end-of-life care with dementia have been reported (4, 5). However, dementia decreases the ability to imagine future situations, and coping (well) with dementia implies that preferences can change substantially (6). For example, people's prior perceptions of whether they will be enjoying life with moderate or severe dementia can be inaccurate. Also, the course of the disease cannot be predicted accurately (3). If the perceived control turns out to be unrealistic or does not match desired levels or negatively impact relationships, perceived control can cause more distress than the perception of no control at all (7). So, ACP in dementia is not without its challenges.

Despite many barriers to initiating ACP with persons with dementia (8, 9), some work indicates that ACP is acceptable in dementia care (5). However, much less is known about whether persons living with dementia prefer a specific approach to ACP. For example, people might prefer to detail specific

future treatments or they might simply prefer to discuss their goals and values regarding future care. In this study, we focus on the acceptability of two ACP approaches when applied to dementia care (10, 11). The first ACP approach focuses on advance treatment orders in detail and thus capitalises on being in control. The second ACP approach focuses on setting global goals of care and coping with disease.

While ACP may provide some control over future decisions, there are interventions at the end of life that may provide more sense of control. At one extreme, people choosing assisted dying or euthanasia can dictate the time, place and manner of their death. Since 2002, Dutch law has regulated euthanasia with the Termination of Life on Request and Assisted Suicide Act, which legalized the ending of life by physicians at the request of patients suffering unbearably without hope of relief. The same year, Belgium adopted a law on euthanasia that is largely similar to the Dutch law (12). Canada has legalized suicide assistance or euthanasia by physicians or nurse practitioners in 2016 (13, 14). Euthanasia can also be legally practiced in Luxembourg, Colombia, Spain, some states of Australia, and in New Zealand. Physician-assisted suicide (PAS), not euthanasia, is legal in Switzerland, in a handful of US states and, more recently, in Austria. In Germany, the Federal Constitutional Court has overturned the prohibition of 'business-like' suicide assistance in the penal code in 2020, making it legally available again to commit suicide with the voluntary help of third parties (15).

The debate on legalizing euthanasia and PAS is controversial. Complete consensus seems to be unachievable due to incompatible normative frameworks that clash(16). Differences in attitudes towards ending life upon request have been associated with differences in countries' economic, religious and health-related factors (17). Based on a 48-country survey study, there appears a rough West-East division in euthanasia acceptance among the European public, with relatively high acceptance in Western European countries compared to low to moderate acceptance in the other countries (18). Public support for euthanasia and PAS in the US ranges between 47%-69%, with higher public support for euthanasia than PAS (19). The Netherlands is a country among the top in Europe with regard to public euthanasia acceptance (18, 19). A total

of 60% of the Dutch public agree euthanasia is acceptable for people with advanced dementia. Interestingly, far fewer physicians consider performing euthanasia in this population acceptable, only 8-24% (20). In Japan, views about the acceptance of euthanasia, in general, vary greatly depending on the study population (21-24). So far, however, research about the acceptability of euthanasia across all these nations has primarily focussed euthanasia in general and on family caregivers, 'the public' or physicians. Much less is known about how acceptable people with dementia find euthanasia.

Technological advances in medicine imply patients, family caregivers and physicians need to make increasingly difficult end-of-life decisions. The growing use of technology in healthcare raises new questions such as, if, when and how the use of technological aids can affect the dying process. For example, distressing symptoms are common at the end of life in persons with dementia (25). Patients' self-report of discomfort is considered the "gold standard" (26). However, in the terminal phase, patients may not be able to self-report their symptoms. This implies a loss of control in expressing their discomfort and needs and having to rely on others to observe discomfort. Automated pain and discomfort detection by continuous monitoring of facial expressions, activity and vital signs is being developed and may also be available for the dying (27, 28). Nurses may then respond to technical signals from a distance rather than using bedside observations alone. As such devices are developed and implemented in care, it is important to understand the views of persons with dementia, their family caregivers and physicians about the use of monitoring technology (e.g. medical devices that can recognize distress) at the end of life.

To optimize care for persons with dementia, physicians need to understand differing attitudes toward end-of-life care and which factors to consider when discussing end-of-life decisions with persons with dementia and families from diverse backgrounds. Acceptability of interventions that increase control may vary by life view and personality. Control may be helpful in some cases. Early research in psychology for example, found that beliefs about having (some) control promote adjustment with life-threatening disease (29, 30). With uncontrollable disease, however, acceptance in the sense of ability to tolerate the nature of the disease can help redirect personal goals, change

personality in a positive way and strengthen relationships (31). Control or goal engagement is the opposite, in a way, to acceptance or letting go. However, it is more complicated than that. For example with aging, people adjust goals to what is feasible which buffers their sense of control (32). Moreover, both control and acceptance can improve wellbeing. Also, manageability, together with comprehensibility and meaningfulness allows people to better cope with adversities (33, 34). More generally, there is a need for research to address the complexities and underlying question of how and when attempts at retaining control over the end of life is beneficial and acceptable for whom, and to explain individual and possible cross-national differences.

In this study, the perspectives of persons with dementia, their family caregivers, and physicians in six countries (Netherlands, Japan, Israel, US, Germany, Switzerland) will provide insight into the cross-cultural acceptability in dementia care of two ACP approaches, the use of monitoring technology at the end of life, and euthanasia.

Objectives

The primary objective is to investigate the acceptability of the four interventions (i.e., whether the participants would want the interventions at the end of life: persons with dementia for themselves, family caregivers for their relative, and whether physicians would use it at request). The secondary objectives include examining differences in acceptability between groups and countries, and to explore associations between acceptability and other participant characteristics (e.g., demographics, variables indicating life view such as religion, and personality variables such as coping style). We use open-ended questions in the interviews to examine qualitatively possible ambiguity regarding being in control through the interventions and in what situations and why the participants feel the interventions are or are not acceptable.

Methods

The Attempts to CONTrol the END of life in people with dementia (CONT-END) acceptability study was originally registered at the Netherlands Trial Register (NL7985) at 31 August, 2019, and can be found on the International

Clinical Trials Registry Platform. The study has a cross-sectional mixed-methods design with participants evaluating intervention vignettes and completing a survey. The vignette scripts, storyboards and early versions of the animation videos were pilot-tested between March and June 2020. Data for the CONT-END acceptability study are collected in the Netherlands, US, Germany, Switzerland, Japan and Israel. The study will be conducted according to the principles of the Declaration of Helsinki (Fortaleza, Brazil, October 2013).

An independent Ethics Advisory Committee was installed as a requirement of the funder, which included representatives from most participating countries in the study, including one member of the Alzheimer Association, to ensure that ethical issues that may arise are also treated in a manner that is sensitive to the international differences. The main remit is to review documents and to monitor the project's progress from an ethics point of view. The Ethics Advisory Committee members do not receive compensation for their time and are not otherwise involved in the study.

Selection on countries

The interventions offer different levels of control and their acceptability may vary between countries, groups and individuals. The countries in this study were selected based on literature about large differences in end-of-life care, access to means to exercise control and norms regarding autonomy, technology and sanctity of life (35-45).

First, there may be differences in acceptability of the ACP interventions between countries. This is based on literature about patient autonomy versus relational autonomy or influence of the family or professional caregiver on end-of-life decision making, and legalisation of assisted suicide and not euthanasia in Switzerland and US states (e.g., (35)). Physicians in Germany have much decision-making authority (45). Physicians in the Netherland are more "paternalistic" than in the US regarding end-of-life treatment decisions in dementia (46). However, in the Netherlands there is also a focus on self-management with health even proposedly defined as "the ability to adapt and to self-manage" (47).

Second, inhabitants of technology-minded countries with aggressive life-prolonging treatment and infrequent withholding of treatment at the end of life to allow a "natural course" might be most in favour for using technology in the dying. By contrast, in the Netherlands, less aggressive care is common in dementia at the end of life (e.g. low antibiotic use and invasive rehydration) (48-50), as is withholding life-prolonging treatment if it does not improve quality of life (51). Rates of withholding treatment may be comparable in Switzerland (43, 52). Further, three countries are known for technological advances: Israel, Japan and the US. These countries are also known for high rates of feeding tubes in people with advanced dementia (36, 38, 39).

Third, a number of publications (36, 44) have shown that sanctity of life is an important value in end-of-life decision making in Israel and Japan. Germany is distinct within Europe for low acceptance of euthanasia (45). In the Netherlands, on the other hand, euthanasia is legal when fulfilling certain criteria, and the country was at the forefront of euthanasia legislation (41, 45).

Hypotheses

For the acceptability of the interventions per group, we expect that the ACP intervention with detailed advance treatment orders will be most often acceptable and euthanasia least often acceptable in physicians. No hypotheses on acceptability rated by persons with dementia compared to the other groups are formulated because not enough is known about their views on this matter to formulate specific hypotheses. With regard to acceptability by country, we hypothesize that the ACP intervention with detailed advance treatment orders will be most often acceptable in countries where patients have high autonomy in decision making about medical procedures and care, and where people may feel they need a defence against medical overtreatment, while sanctity of life is not necessarily a dominant principle (in particular, the US). Technology for symptom monitoring when unable to self-report, such as use of cameras in the dying phase, is expected to be most often acceptable in technology-minded countries (Japan, Israel and US). Euthanasia may be most often acceptable in countries that have euthanasia or PAS regulation already in place for a while (in particular the Netherlands and Switzerland) and the least acceptable in countries where ending life is highly controversial (Germany, Israel and Japan).

For the explorative analyses, we expect demographics, variables indicating life view such as religion, view on dementia, attitudes regarding life-prolonging treatment and death and dying, and variables indicating personality such as coping strategy to be associated with acceptability of the interventions. These aspects of life view and personality are selected because they may relate to control. In explaining diversity in acceptability of ACP, individual differences may be more important than differences between countries and respondent groups (hypothesized based on a study in physicians in the UK and the Netherlands; (53)), with those tending to planning as a coping strategy more likely to find the interventions acceptable. Contrary, it could be that people with higher death anxiety are less likely to find the interventions acceptable, as it has been related to fewer preparations for death in people with advanced cancer (54, 55).

Participants

We initially aimed to include a total of 900 participants from six countries (Netherlands, US, Japan, Israel, Germany, Switzerland), comprising 300 persons with (early) dementia, 300 family caregivers and 300 physicians. From each country, we planned to recruit 50 dyads of persons with dementia and their family caregivers, and 50 physicians. Recruitment procedures for persons with dementia, their family caregivers and physicians are adapted for each participating country in close collaboration with our local partners. We amended the participant target due to difficulty recruiting persons with dementia and family caregivers (see paragraph 'Adjustments to protocol').

We work with healthcare professionals, primarily physicians working in memory clinics and hospitals, to recruit dyads of a person with dementia and their family caregiver. We also recruit via general practitioners (GPs) and dementia case managers. When persons with dementia visit their physician, the physician will offer an information package to eligible participants. Participants can then: a) directly contact the research team, or b) inform their physician about their decision. The physician will then ask for permission to forward the contact information of the pair to the research team.

For the recruitment of the physicians, the study is announced via relevant webpages and newsletters of local professional networks and educational institutions. The researchers also directly contact physicians who are already in their professional network by email to inform them about the study. The researchers send physicians who are interested an information package about the study and call them to explain the study in more depth and to schedule an appointment for the assessment.

The inclusion criteria for the person with dementia are: 1) has a diagnosis of irreversible dementia established by a physician; 2) has been informed about and is aware of their diagnosis; 3) has a family caregiver who is willing to participate in the study; 4) has decision-making capacity and is able to communicate through sufficient memory and language; 5) is able to understand and sign the consent form; 6) has adequate vision and hearing (can be achieved by using corrective lenses and hearing aid if required); and 7) consents to participate.

There is no formal capacity test to avoid feelings of failure if that would result in denying participation. We rely on the clinician's estimation of whether people have capacity to decide to participate in the study and are able to do so. If needed, we provide the referring clinicians with three relevant items of the Dementia Severity Rating Scale to aid clinical judgement of the capacity to give meaningful responses in the interview (56). For the 'Memory' item a score of ≤2, 'Speech and Language' item a score of ≤3, and 'Ability to make decisions' item a score of ≤2 indicate sufficient ability for the purpose of this study. If the person with dementia is currently affected by a severe psychiatric disorder (e.g., major depression, schizophrenia, substance abuse, post-traumatic stress disorder) as diagnosed by a psychiatrist, psychologist, or physician, or if the participant is expected to die in a few weeks, they are excluded.

Family caregivers can participate if 1) they are willing and able to participate in the study; 2) the person with dementia they care for is willing and able to participate; 3) are ≥18 years old. Physicians can participate if they practice a specialty that includes provision of end-of-life care for persons with dementia. Depending on the country, the specialty could be primary care physicians

such as GPs, elderly care physicians, geriatricians, geriatric psychiatrists, neurologists, and palliative care physicians.

Study setting

The study setting differs for the person with dementia and their family caregiver versus physicians. Ideally, the assessment with the person with dementia and their family caregiver takes place at the local research site, at their home or the practice of their healthcare professional. This can be at a memory clinic, hospital, or their physician's practice. The assessment with the physicians will take place at their office or online via videocall.

Procedure

Participation in the study consists of a one-time assessment of 60 (physicians) to 90 minutes (person with dementia and family caregiver). During the assessment, the participants view four animation videos (range duration 1:53 to 4:51 minutes depending on the intervention and language). After each video, they are interviewed. The order of the two ACP-videos and the Technology video is randomized by an independent statistician. Due to the potential sensitivity of the topic, the Euthanasia video is shown last. The participants also complete a brief survey with items about attitudes concerning the end of life, views on dementia, decision-making, coping, and demographic information. Table 1 gives an overview of all the instruments and items in the survey. If needed, a translator is present during the assessment.

The in-person assessment with the person with dementia and their family caregiver is conducted by two researchers or one researcher and a volunteer. Volunteers and translators are trained by the research team in advance. After finishing the assessment, the pair is debriefed and receives information about what to do if they feel distressed afterwards related to the assessment.

Sample size calculation

The number of participants is determined by the primary objective of the trial (acceptability). We will use logistic regression analyses and before the COVID-pandemic, we aimed at a total of (6 countries x 3 groups) x 50 = 900 respondents for sufficient power according to the 10 events per

variable rule of thumb, for a minimum acceptability or non-acceptability rate of 10%. Therefore, with percentages of 10% and up, power would suffice to assess differences between 6 countries and 3 respondent groups. Testing of associations with other characteristics, i.e. life view and demographic and personality characteristics, is exploratory. Also see paragraph 'Adjustments to protocol'.

Table 1 Overview of the instruments per group.

Constructs	Items in the survey	Respondent group		
		Person with dementia	Family caregiver	Physician
Attitudes towards the end of life	· 4 items from the Death Anxiety Questionnaire (58)	X	X	X
	· one item of each of the five subscales from the Death Attitude Profile-Revised (DAP-R) (59, 60)	X	X	X
	· Item about general level of comfort with talking about the end of life (11)	X	X	X
Caregiver burden	Zarit Burden Interview, 6-item version (ZBI-6) (61-65)		X	
Concerns about future	Three items from the subscale 'Preparation for end of life' of the Quality of life at the end of life (QUAL-E) (68)	X		
Coping styles	Brief COPE subscales: Use of instrumental social support; Active coping; Denial; Use of emotional social support; Acceptance; Planning; Religious coping (69, 70)	X	X	X
Decision-making	· Is your relative capable of taking decisions on medical treatments by themselves? (11)		X	X
	· Does your relative's faith or spiritual background influence decisions about care and treatment? (11, 71)			
	· Medical decision making (11)			X
Dementia	· Dementia diagnosis	O		
	· Quick Dementia Rating System (QDSR) - cognitive subscale (72)	O		

Table 1 Overview of the instruments per group. (continued)

Constructs	Items in the survey	Respondent group		
		Person with dementia	Family caregiver	Physician
Demographic variables	Age, gender, educational level, country of birth, religious background, worked in healthcare, relation to person with dementia, living situation of person with dementia, work status family caregiver	O	X	X
Goals of care	• The most important goal of [your relative's] health care is to preserve my [his/her] life as long as possible, even if that requires treatments that may cause pain or discomfort. (11)	X	X	
	• When you think about the goals of care for your relative, which of the following do you most strongly consider? what you think your relative would probably want for themselves, what you want for your relative, what you think the physician of your relative wants for themselves, and don't know		X	
Illness cognition	Rating of the following statements:			
	• Dementia is a disease you can die from. (11, 37)	X	X	X
	• Dementia is a normal part of the ageing process. (73, 74)	X	X	X
	• Palliative care applies from the time of diagnosis to the stage of severe dementia. (75)			X
Illness perception	Brief Illness Perception Questionnaire (IPQ-B) - one item from the Consequence, Personal Control, Illness concern and Emotional representation dimensions (76-78)	X		
Interpersonal closeness	Inclusion of other in the self scale (IOS) (79)		X	
Locus of control	4-item version of the Locus of Control scale (IE-4) (80)	X	X	X

Table 1 Overview of the instruments per group. (continued)

Constructs	Items in the survey	Respondent group		
		Person with dementia	Family caregiver	Physician
Mood	2-item Patient Health Questionnaire depression module (PHQ-2) (81)	X	X	
		O		
Personal experiences with dementia	Have you personally experienced a family member or friend having advanced dementia at the end of their life? (82)	X	X	X
Preparedness	Item about preparedness for the end of life of relative (83)		X	
Work experience	Specialty, additional palliative training, work setting, years of experience with dementia care (82)			X

Note: X = fills in questions about themselves, O = questions about person with dementia filled in by family caregiver.

Adjustments to protocol

Due to COVID-19 hitting the world in the beginning of 2020, the start of the data collection was postponed to July 2020 and is extended till 2023.The COVID restrictions caused severe delays in the data collection. Healthcare providers were hesitant to join the study both as a participant and to assist in the recruitment of persons with dementia and their family caregivers due to the increased workload and wanting to protect their patients. Therefore, adjustments were made to the protocol. The recruitment strategies for persons with dementia and family caregivers were expanded to recruiting through dementia cafes and social media. In the US, an online service of patients who have volunteered to participate in research studies (Research Match) and electronic resources were used to identify additional persons with dementia. When identified from the electronic record, their physician was asked if it is acceptable to contact the patients and caregivers. A telephone screening script was developed to check whether the person with dementia and family caregiver met our inclusion criteria.

After completing the data collection of the Dutch and US physicians, and after interviewing 15 dyads of person with dementia and family caregiver in the

Netherlands, we decided to reduce the number of interviews to 15 per country per group. This was because 50 dyads was no longer considered feasible within the remaining study time and because we found data saturation in the Dutch data was reached after 12-15 interviews (57). For physicians, we decided to offer a full self- report online version of the assessment after 15 interviews, where they can view the animation videos themselves and then indicate whether they find each intervention acceptable. Open text fields are provided for an optional explanation of the answers. In general, this online option was not deemed feasible for the dyads (e.g., limitations in digital-literacy, availability of technology for online meeting, etc.), and not approved of by the Dutch ethics committee due to the potential sensitive topics. For the dyads, the focus will thus be on the qualitative data.

For the adjusted protocol a new power calculation was performed. We will use logistic regression analyses and expect that collecting physician data (n=50) in a total of 6 (countries) results in 300 physician respondents. Power depends strongly on the type of intervention as this has varied, so far in data collected in the Netherlands, the US and Japan, from acceptable for almost all (advance care planning interventions) to acceptable for closely around half. According to the 10 events per variable rule of thumb, for 7 variables, with 300 respondents, 70 events suffice for acceptability in ratios close to half of respondents, but would not suffice for interventions that are (not) acceptable for the large majority of the respondents. However, examining associations with acceptability is less relevant for interventions which are endorsed or rejected by the great majority.

Primary study parameter(s)

The primary outcome is acceptability of the interventions, assessed during the interview. The two primary acceptability measures are: (1) whether the participant finds the intervention acceptable for dementia care, and (2) whether they want the intervention for themselves. This means, whether persons with dementia want it for themselves, family caregivers for their relative and whether physicians would use it at request. The primary outcome is a categorical variable with three categories ('yes', 'no' and 'don't know' as a valid answering option).

Secondary study parameters

The secondary outcomes will be assessed using the survey. Table 1 provides an overview of the instruments per group. When not available, the forward-backward translation technique was used to translate the instruments in all languages necessary for the current study (i.e. Dutch, English, German, Japanese and Hebrew). The instruments were translated to each new language by two native speaking researchers independently. They compared their translations and came to a consensus, followed by back-translation by a professional, independent translator. The translation was reviewed by the two researchers and discussed with a third person, the principal investigator or coordinating local partner. The professional translator and original authors were consulted for any remaining specific questions.

To assess attitudes towards the end of life, we use the death anxiety questionnaire (58) as an indicator of a general or global fear of death as a whole. The response options are *strongly disagree* (1), *disagree* (2), *agree* (3) and *strongly agree* (4), and we added *I don't know* as an additional option. A sum-score can be calculated by summing the scores of the items with a high score reflecting more anxiety about dying. Also, we selected one item of each of the five subscales of the Death Attitude Profile-Revised (DAP-R) (59, 60) to assess attitudes towards death. including: '*The prospect of my own death arouses anxiety in me*' (Fear of death), '*I avoid thinking about death altogether*' (Death Avoidance), '*Death is neither good nor bad*' (Neutral Acceptance), '*I look forward to a life after death*' (Approach Acceptance), and '*I see death as a relief from the burden of this life*' (Escape Acceptance). We will look at the individual items. The seven response categories were reduced to five to match those of the death anxiety questionnaire. Additionally, we use a single item asking the participants about their general level of comfort with talking about the end of life with the response options *very comfortable*, *somewhat comfortable*, *somewhat uncomfortable*, *very uncomfortable*, *don't know* (11).

To assess caregiver burden, we use the shortened 6-item version of Zarit's well-tested caregiver burden interview (ZBI-6) (61-65). Items are scored on a five-point scale, with a cut-off score of ≥13 considered as a clinically significant burden (66). The items are added up to create a sum-score.

The three items from the subscale 'Preparation for end of life' from the Quality at the end of life in terminal patients (QUAL-E) (67, 68) are used to indicate concerns of the person with dementia about the future after they have died. The items are scored on a 5-point Likert scale ranging from *not at all* to *completely*. The items are added up to create a subscale score.

To assess coping strategies in all three groups, we use the Brief COPE subscales Active coping, Planning, Using instrumental support, Using emotional support, Denial, Acceptance, and Religion (69, 70). Each subscale contains two items that are scored from 1 (*not doing it at all*) to 4 (*doing it a lot*). The items are added up to create the subscale score.

We will use two items about medical decision making. The family caregiver is asked whether their relative is capable of taking decisions on medical treatments by themselves using the response option *yes*, *sometimes or in part*, *no* and *I don't know* (11). Next, they are asked to indicate whether their relative's faith or spiritual background influences decisions about care and treatment using the categories *yes strongly*, *yes somewhat*, *no*, *I don't know* (11, 71). The physicians are asked to rate the item *When you think about the goals of future care for your patients with dementia, which of the following do you most strongly consider?* Using the response options *what you think your patient would probably want for themselves*, *what the family/loved one of the patient wants*, *what you as the physician of your patient wants for them* and *don't know* (11). We will look at the individual items.

The family caregiver is asked about the type of dementia and the month and year of the diagnosis. As an indicator of the stage of dementia, we will ask the family caregiver to complete the cognitive subscale of the Quick Dementia Rating System (QDRS) (72). This subscale corresponds to the Mini Mental State Examination classifications (28-30, 24-27, 18-23, 10-17 and 0-9)). The cognitive subscale consist of 4 domains: memory and recall, orientation, decision making & problem solving, and language & communication abilities. Each domain has five possible answers, with higher numbers reflecting more severe cognitive symptoms. The items of QDRS are added up to create a sum-score.

The family caregiver and person with dementia are asked to indicate the extent to which they (dis)agree with the following statement: *The most important goal of [your relative's] health care is to preserve my [his/her] life as long as possible, even if that requires treatments that may cause pain or discomfort* using a scale ranging from *strongly agree* (1) to *strongly disagree* (5). *Don't know* (9) is also a valid option (11). The family caregiver is also asked to indicate which they most strongly consider when thinking about the goals of care for their relative using the categories *what you think your relative would probably want for themselves, what you want for your relative, what you think the physician of your relative wants for themselves,* and *don't know.*

Illness cognition refers to the dementia. All three groups are asked to rate the extent they agree with two statements: *Dementia is a disease you can die from* (11, 37) and *Dementia is a normal part of the ageing process* (73, 74) using the response options *strongly agree* (1) to *strongly disagree* (5) and *Don't know* (9). Physicians will also be asked to rate the statement *Palliative care applies from the time of diagnosis to the stage of severe dementia* using similar response categories (75).

Illness perception also refers to the dementia. The person with dementia is asked to rate four selected items of Brief Illness Perception Questionnaire (IPQ-B) (76-78) that are relevant to our research questions. The four items consist of one item from the Consequence, Personal Control, Illness concern and Emotional representation dimensions. The items are scored using a 11-point (0-10) Likert-type scale with higher scores reflecting more negative perceptions. The items are added up to create a sum-score.

Inclusion of other in the self (IOS) was assessed using the IOS Scale (79). This is a single-item, pictorial measure of relationship closeness. It consists of seven pairs of circles, one that includes the word *self* and one that includes the word *other,* that overlap to different degrees. Family caregivers are invited to select the pair that best describes their relationship with the person with dementia.

Locus of control (i.e., personal belief about whether outcomes of behaviour are determined by one's actions or by forces outside one's control) is measured

using the 4-item locus of control scale (IE-4) (80). The items are scored on a scale ranging from *doesn't apply at all (1)* to *completely applies (5)*. Higher scores on Internal Locus of Control of Reinforcement (Item 1 and 2) relate to higher levels of internality (internal control), while higher scores on External Locus of Control of Reinforcement (Item 3 and 4) relate to higher externality (external control). Internal and External Locus of Control are calculated separately.

To assess possible depression in the person with dementia and their family caregiver, the 2-item Patient Health Questionnaire depression module (PHQ-2) (81) is used. The PHQ-2 asks about the frequency of depressed mood and anhedonia over the past 2 weeks, scoring each as *not at all* (0) to *nearly every day* (3). The time frame was adjusted to one month, as we were interested in mood over a longer period of time. Additional to rating their own mood, the family caregiver is asked to rate the mood of their relative using these two items.

The item *Have you ever accompanied a member of your family or friend suffering from advanced dementia at the end of their life* is used to measure personal experience with dementia (82). The item is scored using *yes* (1) or *no* (0).

The family caregiver is asked about their preparedness for the end of life of their relative using the item *If your relative were to die soon, how prepared would you be for their death* (83). We adjusted the 3 response options to a 7-point scale ranging from 1 (*not prepared at all*) to 7 (*prepared as much as possible*) to allow for greater precision (84).

Demographic information includes age, gender, educational level, country of birth, religious background, worked in healthcare, relation to the person with dementia, living situation of the person with dementia, and work status of the family caregiver. The family caregiver provides the demographic information about the person with dementia. For physicians, we also ask details about their work experience; specialty, additional palliative training, work setting, years of experience with dementia care (82).

Finally, the members of the CONT-END acceptability study research team are asked to fill in a questionnaire about their own attitudes and views

regarding the study and acceptability of the four interventions to increase transparency and their reflective awareness. This will be done at the beginning and after the data collection.

Pilot testing of the instruments

The pilot testing of the items for the survey was conducted in the Netherlands. During a face-to-face visit, the survey for people with dementia was read out loud to one person with dementia (female). Her family caregiver (female) examined the survey for family caregivers. Six people aged over 65 years (five females, one male) received the digital version of the survey for family caregivers. One of them (female) also evaluated the survey for people with dementia digitally. The participants were asked to indicate whether the items were easy to understand and whether they were confronting. Most items were considered clear and not confronting. Items from validated questionnaires were not adjusted despite occasional comments from the participants. The time and effort needed to fill in the survey was also acceptable. Some participants commented that it was difficult to choose one option when they had a nuanced view. Minor adjustments were made in the instructions and response options (for example, changing "agree" and "disagree" if not the endpoint of the scale into "somewhat agree" and "somewhat disagree" for the questions on attitudes about the end of life).

Development of the animation videos

With a professional media production group, Knowledge Media Research Centre, we developed video vignettes to explain each intervention in a standardized manner, aiming at a neutral stance, not slanted to either acceptance or non-acceptance. We choose animation videos to support understanding with visual and audio cues. Each video includes a brief introduction, an example and a summary of the main aspects of the intervention. To facilitate orientation, each video has its own colour. Further, a mnemonic for each video in the form of a hand-out with screenshots summarizes the content of the animation video for the persons with dementia and their family caregivers. The handout about euthanasia is supplemented with a sheet explaining local rules and explanation of differences with locally better-known PAS or palliative sedation.

The animation videos were developed iteratively navigating the following steps: step 1, developing the scripts; step 2, reviewing, pilot-testing and refining the scripts; step 3, reviewing, pilot-testing and refining the animation videos; step 4, translating and adapting the animation videos into other languages.

Step 1: Developing the scripts. The initial scripts of the animation videos were developed in English. The scripts were written with the goals in mind that they should be applicable in all six countries and understandable for all three groups of participants in this study.

Step 2: Reviewing, pilot-testing and refining the scripts. The initial scripts were reviewed by the CONT-END research team, consisting of an elderly care physician, GP, epidemiologist, communication expert, psychologists, and anthropologist. Next, the partners from the other countries were consulted on whether cultural adjustments were needed. This resulted in minor changes, for example, to replace "euthanasia" in the American and German context with "termination of life on demand" and "Aktive Sterbehilfe". The independent international Ethics Advisory Committee reviewed the scripts as well. For the euthanasia video, they suggested emphasizing the hypothetical nature of the video to avoid misunderstanding in countries where active euthanasia is illegal. All feedback was discussed within the research team and adjustments were made to the scripts.

The scripts were then translated into Dutch following the forward-backward technique and read out loud during home visits to four pairs of persons with early dementia (three female, one male) and their family caregivers (three female, one male). The family caregivers were the partner or adult children of the persons with dementia. The participants were recruited through GPs. Participants were asked to comment on whether the scripts were easy to understand, neutral, and whether they were confronting. Based on the feedback from the participants, the scripts were thoroughly revised; the language and plot of the videos were simplified, overly positive words, such as "valuable", were changed into neutral words and the difference between the two ACP interventions was clarified. The English scripts were adjusted accordingly.

Step 3: Reviewing, pilot-testing and refining the animation videos. Based on the updated scripts, Dutch and English animation videos were developed and produced by a team of experts from Knowledge Media Research Centre and a freelance animation artist. The Dutch animation videos were pilot-tested digitally due to COVID-19 related restrictive measures. Eight Dutch participants (five female, three male) with experience with dementia or an age above 65 viewed the animation videos. They were recruited through the Regional Older people Advisory Board connected to the Leiden University Medical Center (LUMC) and via the researchers' network. In general, the participants found the videos clear and easy to follow. Some participants pointed out that the videos gave the impression that all discomfort could be detected by the technology, and that there were no obstacles for euthanasia once all criteria are met. Potentially confronting elements in the videos were also discussed, for example, the animation of an inflated lung reminded some people of a COVID19-infection.

The English version of the euthanasia animation video was reviewed by the Ethics Advisory Committee. They suggested adding hand-outs and making the euthanasia procedure more clear for non-Dutch viewers. The English technology video was presented at the Alzheimer's Association International Conference 2020 (85) to collect feedback from a professional audience. They deemed the animation video suitable. All feedback gathered from this step was discussed within the research team and yet more minor adjustments in scripts and animation videos were made.

Before and after the pilot-testing, readability tests were performed for the scripts with an online tool (available at: https://www.webfx.com/tools/readable/check.php). The results suggested that almost all of the updated scripts (rated as grade 9 to 10) were more easily readable than the initial versions (grade 10 to 13). The updated script about technology had an average level of grade 9 and should be easily understood by 14 to 15 year-olds. The other three updated video scripts were rated as grade 10, which should be easily understood by 15 to 16 year-olds.

Step 4: Translating and adapting the animation videos into other languages. The English scripts were translated into Hebrew, German, and Japanese using

the same forward-backward translation process as for the Dutch scripts. The translated scripts were reviewed by the local partners and at least two older adults (>65 years) from each country to check whether anything in the scripts was too confrontational or difficult. (Cultural) adjustments in wordings were made when necessary. The Dutch research team and the local partners provided feedback on the timing of the animation videos and approved of the final versions.

Data analyses

Descriptive statistics will be used to present the acceptability of the four interventions. The internal consistency of the scales will be calculated using Cronbach's alpha. Descriptive statistics will be calculated to describe the demographics of the respondent groups per country.

We will use logistic regression analyses with acceptability of the intervention as the dependent variable to examine differences in acceptability between group and countries. '*Do not know*' as a response option is often ignored and excluded from the denominator. A dichotomous variable will be create with a denominator of 'acceptable versus not acceptable plus do not know' . The analyses will be unadjusted and adjusted for the most important life view or personality parameter (religion for euthanasia, planning for the other interventions). We will explore associations between acceptability and participant characteristics (gender, educational level, age, severity of cognitive impairment for persons with dementia, and palliative care training for physicians) and personality (locus of control, coping), depression, medical decision making, professional or personal experience with dementia, physician's comfort with end-of-life conversations, and caregiver burden, and life view (religion, death anxiety/attitude, preparedness for end of life, priority quality vs. quantity of life, illness cognition). For this, we will use stepwise backward regression analyses. The analyses will be done with and without adjustment for country and group (forced in the stepwise regression analyses).

Qualitative data from the interviews will be used to map possible ambiguity regarding being in control through the interventions, and as to why and in what situation the participant feels the interventions are acceptable. A content

analysis regarding acceptability of the interventions will be conducted. Additionally, across all interviews, we will conduct a thematic analysis on perceptions of control. Data collection and data analysis will be executed iteratively. Coding is supported by the software program ATLAS.ti.

Data management and monitoring

To protect participant privacy, the data will receive a unique identification code with linkage keys to be stored securely separately from the data. Names and other information that could directly identify the participant are therefore omitted. As long as it is necessary to trace data to an individual participant, the participant identification code list per country will be maintained to enable linking the data to a particular participant. This will be until the data has been fully cleaned and no new cleaning issues have arisen.

Participants can choose to fill in the survey digitally or on paper. We will use a secure certified online program for the digital questionnaires, Castor (Amsterdam, The Netherlands). The data from the paper survey will be entered in the online program by the researcher. We will subject 10% of the data to a random audit by a second researcher to test the accuracy of quantitative data entry of the paper survey and forms. The audio files of the interviews will be deleted after they have been transcribed and the transcripts have been checked. Data will be entered and stored using a secure data server. To allow for cross-national comparison, the study will be performed in non-EU countries according to the same protocol that is acceptable for use in the EU countries.

Dissemination

The findings will be submitted to relevant peer-reviewed scientific journals and national and international conferences within the field. We will share the results with key stakeholders involved in both homecare and long-term care of persons with dementia to help improve clinical practice. The animation videos are available from the PI upon reasonable request after conclusion of the data collection.

Discussion

In this study examined the perspectives of persons with dementia, their family caregivers and physicians in six countries (Netherlands, Japan, Israel, US, Germany, Switzerland) to provide insight into the cross-cultural acceptability in dementia care of two ACP approaches, the use of monitoring technology at the end of life, and euthanasia. We anticipated and experienced practical and operational issues in conducting the study. First, due to COVID-19 restrictive measures, more assessments with physicians will be conducted online than initially anticipated. The online assessment offers more flexibility, possibly lowering the threshold for physicians to participate in the study and allowing the research teams to collect data simultaneously in multiple countries. While the COVID-19 pandemic may make it difficult to find physicians who have time to participate in a study, it also highlights the importance of timely ACP and monitoring distress signals at the end of life, possibly motivating physicians to share their opinions about these interventions. Second, we strive to conduct the assessments with the person with dementia and their family caregiver in person. It could be that the person and family caregiver are reluctant to receive visitors, even if allowed. The online option with these groups will also be offered as a last resort option after consultation with the local institutional review board and based on the judgement of the family caregiver if this would be a feasible option for their relative. Third, the recruitment of persons with dementia matching our inclusion criteria may be challenging in countries where dementia is generally diagnosed in a late stage of the disease.

The study limits professional caregivers' perceptions to those of physicians and nurse practitioners with medical responsibilities whereas nurses have a role in providing these interventions as well. Further, data will not be collected simultaneously in all countries and groups; as a result of the sequential cross-sectional design, we cannot adjust for possible trends over time.

Strengths of this study include the cross-cultural aspect, comparing the perspectives of persons with dementia, family caregivers, and physicians, the sample size, mixed-method design, and initiative to increase the researchers' transparency and their reflective awareness. The animation videos were developed using input of international experts, have been pilot-tested,

and have been reviewed and approved by an independent Ethics Advisory Committee. This study will contribute to a more fundamental understanding of how acceptable a range of interventions differing in level of control offered is, and more generally, as to how and when having control at the end of life in dementia is perceived as beneficial. This facilitates aligning interventions with preferences and will help improve dementia care.

Declarations

Ethics approval and consent to participate
For the Netherlands, the CONT-END acceptability study has been approved by the Medical Ethics Committee - Leiden The Hague Delft (NL72354.058.19). For the US, the Institutional Review Board University of Missouri – Columbia reviewed and approved the study (2046522). For Japan, the study protocol has been approved by the Ethics Committee Tohoku University Graduate School of Medicine (2021-1-1105; approved revision 2022-1-1081). The Ethics Committee of the School of Social Work at Bar Ilan University has approved of the study protocol for Israel (012213). The Ethics Committee of Nord-West and Central Swiss approved the study (2022-00630). In Germany, the Ethics Committee of the Rheinische Friedrich-Wilhelms-Universität Bonn approved the study (304/22).

The protocol of the pilot study has been reviewed by the Medical Ethics Committee - Leiden The Hague Delft (METC LLD), and they declared it to be exempt from the Medical Research Involving Human Subjects Act (WMO), protocol number: N19.098. Informed consent will be obtained from all participants.

Consent for publication
Not applicable

Availability of data and materials
The data that support the findings of the pilot study are available upon reasonable request and with permission of the principal investigator: Jenny van der Steen PhD, email jtvandersteen@lumc.nl.

Competing interests
The authors declare that they have no competing interests.

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Authors' contributions
JS conceived the study, and was responsible for the design of the study and was advised by all other authors (HS, XJ, MN, SSA, DM, LR, JG, PW, WA). JS and HS were the main contributors to the writing of the manuscript. XJ wrote the sections about the development of the animation videos. XJ and HS collected the pilot study data. XJ analysed and interpreted the results of the pilot study. All authors (HS, XJ, MN, SSA, DM, LR, JG, PW, WA, JS) contributed to the development of the animation videos. All authors read and approved the final manuscript.

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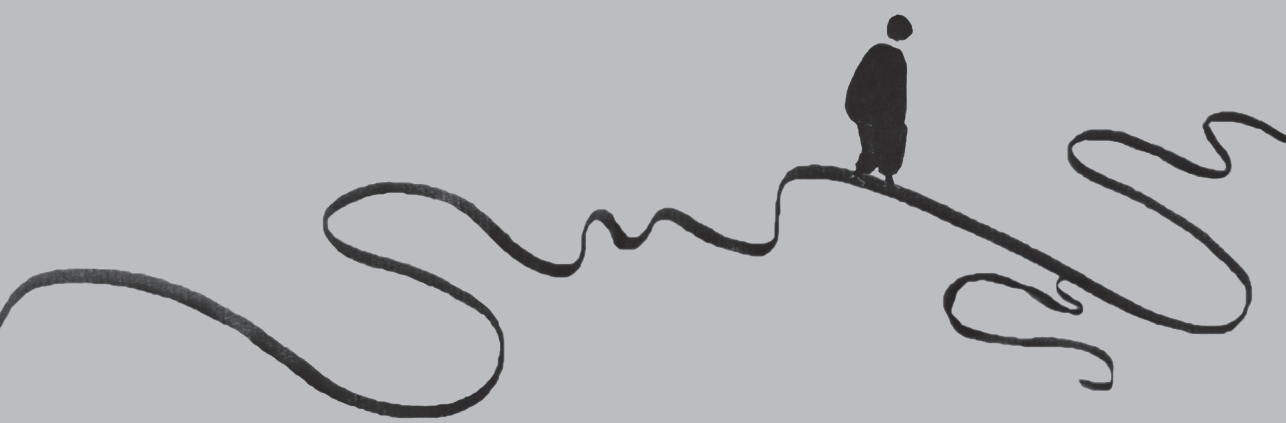

Advance care planning with people living with dementia: ethical considerations of physicians in the United States and the Netherlands

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Abstract

Objectives: Advance care planning (ACP) is important but complex with people living with dementia. This study aims to explore ethical considerations of physicians around ACP for dementia in two high-income countries (United States and the Netherlands).

Methods: In this qualitative study, semi-structured interviews were conducted with Dutch and American physicians from specialties that provide end-of-life care for people with living dementia. Their considerations regarding ACP for people living with dementia were solicited after short animation video vignettes on two approaches to ACP, one focused on concrete treatment orders, and the other on setting global care goals. Interview transcripts were analyzed using thematic analysis with elements of reflexive thematic analysis to identify ethical considerations.

Results: Interviews with 50 Dutch physicians and 47 American physicians and 3 nurse practitioners generated three themes of ethical considerations: 1) Respecting the autonomy of the person with dementia, 2) Rationality as the basis for decisions and subsequent actions, and 3) Minimizing burden and suffering.

Discussion: The complexity of ACP for people living with dementia is reflected in the challenges within each ethical consideration and the tensions between them, especially between autonomy and rationality. We recommend an approach to ACP that balances the ethical considerations, focusing on the values of the people living with dementia and allowing flexibility in future decision-making to take the current best interest of the person into account.

Introduction

Advance care planning (ACP) is regarded as a crucial part of care for people living with dementia (Timmons et al., 2022), aimed at improving goal-concordant care and quality of life (Kelly et al., 2019). ACP is defined as "a process of communication about future care and treatment preferences, values and goals with the person with dementia, family, and the health care team, preferably with ongoing conversations and documentation" (van der Steen et al., 2024b). The process of ACP has evolved from focusing on documenting treatment orders, such as do-not-resuscitate orders, to including goals-of-care conversations (Im et al., 2024; van der Steen et al., 2024a). Physicians may take different approaches to ACP on this continuum, depending on personal preferences and the setting they work in (Smaling et al., 2023; Flo et al., 2016).

In both the United States and the Netherlands, ACP is recommended for people living with dementia (Fazio et al., 2018; van der Steen et al., 2023), and treatment refusals in advance directives are legally recognized (van der Steen et al., 2023; NIH National Institute on Aging, 2022). In the United States (US), ACP is covered by Medicare, which is a federal health insurance covering people with disabilities and those 65 years old and above (U.S. Centers for Medicare & Medicaid Services, n.d.). It often focuses on discussing and completing documents such as a living will, a health care power of attorney, and medical orders for life-sustaining treatment (NIH National Institute on Aging, 2022), facilitated by forms such as MOLST (Martin & McDonald, 2014) or dementia-specific directives (Gaster et al., 2017; Gaster & Pope, 2024). A variety of physician and advanced practice nursing specialties may initiate ACP discussions. In the Netherlands, ACP discussions can be initiated by the general practitioner or specialists in the hospital, but they are most often initiated and reviewed regularly by physicians specialized in caring for older adults (formal name of the specialty: "elderly care physician") in nursing homes upon admission as they take over the (generalist) medical care from the GP (van der Steen et al., 2023). While physicians specialized in caring for older adults may also support GPs in consultations for older people in community-based practice, geriatricians' practice is hospital-based. Common topics of

ACP in the Netherlands include general care goals and concrete decisions such as hospital admission (Ter Brugge et al., 2022).

For people living with dementia, decreasing decisional capacity due to the illness and the importance of engaging family make ACP a complex and ethically challenging process for physicians (Keijzer-van Laarhoven et al., 2020). As physicians usually lead ACP conversations and provide treatment that may depend on decisions made during ACP, understanding their views about the process and how ACP should inform care can provide important insights on this challenging process. Previous studies mainly focused on more practical issues such as timing, resources, and challenges in assessing cognitive capacity (Wendrich-van Dael et al., 2020; Tjia et al., 2023; Perin et al., 2021) or ethical considerations that influence physicians' willingness to engage in ACP (Keijzer-van Laarhoven et al., 2020). A broader examination of ethical considerations by physicians about the whole process of ACP, from initiation to activation of previously made decisions, will add a deeper understanding of ACP in this population.

Thus, this study aims to explore ethical considerations of physicians from two high-income countries with different practice patterns (the United States and the Netherlands) on ACP for people living with dementia. The results of the current study may guide future training and the development or refinement of healthcare policy.

Methods

Study design

This qualitative study is part of the CONT-END (Attempts to CONTrol the END of life in people with dementia) project on end-of-life care for people living with dementia, which investigated the acceptability of four interventions for people living with dementia from the perspectives of people living with dementia, family caregivers, and physicians from six countries (Smaling et al., 2023). The four interventions investigated in the CONT-END project included two approaches of advance care planning, the use of monitoring technology at the end of life, and euthanasia. The current study only included the data on advance care planning from Dutch and American physicians and

was guided by a reflexive approach to thematic analysis (Braun & Clarke, 2021). Data collection took place between July 2020 and December 2022. The study was registered at the Netherlands Trial Registration (NL7985) on 31 August, 2019, and is currently available on the International Clinical Trial Registry Platform (NL-OMON26073). The study received ethics approval from the local Dutch medical ethical board (METC-LLD, NL72354.058.19, 10 April 2020) and the Institutional Review Board of the University of Missouri (2046522, 3 December 2021). All participants signed an informed consent form. Participants received gift cards for their participation (25 euros in the Netherlands, 100 dollars in the United States). The consolidated criteria for reporting qualitative research (COREQ) checklist was used to report the methods and results of this study (Tong et al., 2007).

Participants

We aimed to include 50 physicians in each country through convenience sampling. Physicians practicing in a specialty that could include the provision of end-of-life care for people living with dementia were eligible, as were American nurse practitioners in these specialties if they assumed responsibility for medical treatment. Examples of specialties included family medicine, internal medicine, geriatric medicine, older adult care, palliative medicine, and neurology. In the United States, physicians and nurse practitioners were recruited and informed of the study through the email lists of the American Geriatrics Society and the American College of Physicians – Missouri section, emails to selected practitioners at the University of Missouri School of Medicine , personal contacts of the authors, and snowballing. In the Netherlands, only physicians were approached via email through the networks of Leiden University Medical Center (LUMC) , including the general practitioner network Extramural LUMC Academic Network (ELAN) , the academic long-term care network University Network for the Care Sector South Holland (UNC-ZH) , and the Specialist training program for care for older adults (SOOL) . Potential participants were provided with additional information on request. After receiving signed informed consent, researchers scheduled an interview.

Data collection

Participants were introduced to the subject of the interview by watching two short animated video vignettes on ACP, along with two other vignettes of the CONT-END project (Smaling et al., 2023). The vignettes on ACP described approaches focusing on either making concrete treatment decisions, such as resuscitation and hospital admission (Dutch: 3min21sec, English: 3min27sec), or getting to know the person and establishing important care goals such as maximizing comfort (Dutch: 2min52sec, English: 2min49sec). The ACP vignettes were played in a random order, one after the other (Smaling et al., 2023). After each video, participants answered questions on 1) the acceptability of the approach to ACP presented in the vignettes for people living with dementia, and 2) whether they were willing to use the approach upon request of the person with dementia or their family caregivers. After both ACP videos, participants expressed whether they preferred one of the approaches for their patients with dementia or for themselves if they developed dementia. They also explained their reasons and possible exceptions. The whole interview process was anticipated to take 50 minutes to complete. Answering questions about ACP took roughly half of this time. Interviewers included two psychologists experienced in qualitative research, a U.S. research assistant with a background in biology and psychology, and Dutch graduate students in medicine (2 female, 1 male) and psychology (1 female). The first author (X. J.) conducted interviews in both countries. Students were trained by the first author with extensive feedback. Most interviews were performed online via Zoom, except for two Dutch interviews, which took place via the telephone, and one face-to-face due to technical problems with Zoom or preference of the participants. Prior to the interview, participants also answered an online questionnaire about their demographics and work experience, which took around 10 minutes to complete.

Data analyses

We used descriptive statistics, analyzed with SPSS 29 (IBM, 2024), to characterize the study sample and the acceptability of and preference for the presented ACP approaches in both countries. Interviews were transcribed verbatim without a member check (Morse, 2015). Thematic analysis was

facilitated by Atlas.ti 23 (2024). The analysis resembles a codebook approach of thematic analysis, with elements of reflexive thematic analysis (Braun & Clarke, 2021). A codebook was developed to facilitate coding by multiple team members, which consisted of X. J., H. S. , and graduate students in medicine (2 female, 2 male) or psychology (1 female). Most students who performed the interviews were also involved in coding. An initial codebook was developed after H. S. and X. J. independently coded three Dutch interviews. Each subsequent interview was coded by two researchers independently. Regular consensus meetings were held, and the codebook was fine-tuned and expanded throughout the process. Students without coding experience first coded a training set consisting of three interviews and were coached on the job by the first author. The coding of the American interviews started after all the Dutch interviews were coded. The coding was largely inductive, while the structure of the codebook was influenced by the interview questions, and some researchers kept the theoretical framework of acceptability by Sekhon and colleagues in mind while coding (Sekhon et al., 2017). After all coding was performed, the first author gathered similar codes into code groups and generated initial categories and themes together with M. P. and J. T. S. . The themes were discussed and revised reiteratively with input from X. J., D. R. M., H. S., M. P., and J. T. S . They have all been involved in qualitative research and research in end-of-life with dementia. The authors represented the two countries and several relevant clinical fields, such as family medicine and palliative medicine.

Positionality of authors

X. J. and H. S. are full-time researchers with degrees in psychology. D. R. M. is a family physician, geriatrician, and palliative care physician in the United States. M. P. is a general practitioner in the Netherlands. W. A. is a physician specialized in caring for older adults in the Netherlands. K. T. B. and K. M. are medical students in the United States. J. T. S. is a full-time researcher with a background in epidemiology. X. J., D. M., P.M., H. S, J. T. S., K. T. B., and W.A. have previous experience in qualitative research. The medical doctors in the team all have extensive experience conducting ACP with people living with dementia. The other authors have no direct experience in conducting ACP but have had regular conversations with people living with dementia

through interviews about ACP in the context of research. Among the authors, X. J., D. R. M., and M. P. consider ACP focusing on important goals much more suitable for people living with dementia than ACP focusing on making concrete treatment orders. This may have influenced the way we interpreted the data.

Results

Fifty Dutch physicians, 47 American physicians, and three American nurse practitioners participated in the study. The interviews lasted an average of 57 minutes (IQR 50-63). The sample characteristics are presented in Table 1. More than half of the participants were female. Most Dutch participants were physicians specialized in caring for older adults who mainly practiced at nursing homes or outpatient settings, while the specialties of the American participants were more diverse, with the great majority practicing at hospitals. Around half of the participants had training in palliative care after medical school. Most had cared for multiple people living with dementia at the end of life in the last year. The majority of the American participants practiced in the state of Missouri (n = 20, 40%) or New York (n = 10, 20%). All Dutch participants practiced in the province South-Holland. Forty-nine (98%) Dutch participants and 38 (76%) American participants were moderately or very comfortable talking about end-of-life with people living with dementia and their family caregivers. Forty-six (92%) Dutch participants and 49 (98%) American participants indicated that they would most strongly consider the wishes of the person with dementia, compared to wishes of the family or the physician, when considering future care goals for people living with dementia.

Across both countries, there was strong agreement that both forms of ACP were acceptable for people living with dementia or upon request of the person with dementia or their family. Among the 50 Dutch physicians, 43-46 (86-92%) answered "yes" to these three questions for concrete treatment orders, and 48-49 (96-98%) found the important goals approach acceptable for people living with dementia or by request of the person with dementia or family. In the United States, the numbers were 43-49 (86-98%) and 48-50 (96-100%), respectively. In both countries, either approach was preferred by at least a

one-third of the participants, both for people living with dementia (concrete treatment orders: 17 (34%) in the Netherlands, 18 (36%) in the United States; important goals: 21 (42%) in the Netherlands, 23 (46%) in the United States) and for the physicians themselves if they had dementia (concrete treatment orders: 16 (32%) in the Netherlands, 20 (40%) in the United States; important goals: 26 (52%) in the Netherlands, 21 (42%) in the United States). The other physicians (8-12 (16-24%) in the Netherlands, 9 (18%) in the United States) stated that they did not have a preference.

Ethical considerations

Analysis generated three major themes representing the ethical considerations of professionals when conducting ACP with people living with dementia and when interpreting the decisions made during ACP. The themes and subthemes are presented in Figure 1.

Respecting the autonomy of the person with dementia

Many participants acknowledged that ACP is about the wishes of the person with dementia. Therefore, they considered supporting their autonomy to be one of the key considerations. Participants mentioned that whenever possible, it is essential to let people living with dementia be the decision-makers. This means that their wishes should be heard and taken into account.

> *"[I would've] preferred to hear from the patients themselves what they think about it [their medical decisions]."* (Dutch physician in training to become a physician specialized in caring for older adults, age 31)

This also included respecting the wishes of people living with dementia of not participating in an ACP conversation. When family caregivers were included in ACP conversations, some participants said to pay attention to whether they truly represent the interests of the person with dementia. A number of participants would only include families in ACP conversations in the presence of the person with dementia, or with their permission.

Table 1. Sample characteristics

	The Netherlands (N = 50)	USA (N = 50)
Female, % (N)	70 (35)	52 (26)
Age, median (IQR)	48 (34-59)	33 (28 - 45)
Medical specialty[a], % (N)		
Family physician	24 (12)	24 (12)
Physician specialized in caring for older adults	52 (26)	6 (3)
Geriatrician	2 (1)	2 (1)
Palliative care physician	0 (0)	10 (5)
Nurse practitioners	0 (0)	6 (3)
Specialist in training		
Older adult care	22 (11)	0 (0)
Internal medicine	0 (0)	14 (7)
Other[b]	2 (1)	18 (9)
Other[c]	0 (0)	8 (4)
Place of practice[d], % (N)		
Home	46 (23)	26 (13)
Nursing home	74 (37)	44 (22)
Hospital	8 (4)	82 (41)
Hospice	16 (8)	26 (13)
Private	0 (0)	18 (9)
Received training in palliative care after basic medical training, % (N)	42 (21)	54 (27)
Years of experience caring for people with dementia, median (IQR)	18 (4-25)	4 (1-11)
Number of patients with dementia died last year, % (N)		
0	8 (4)	18 (9)
1-4	16 (8)	36 (18)
5-9	36 (18)	16 (8)
10-19	20 (10)	16 (8)
20 or more	20 (10)	14 (7)
Personal experience with family or friends having advanced dementia at the end of life, % (N)	48 (24)	60 (30)

[a] One physician in each country had more than one specialty.
[b] Examples of other specialties of physicians in training included for palliative care, neurology, and geriatrics
[c] Other specialties included neurologist, internal medicine, emergency physician, and ophthalmologist.
[d] Physicians could practice in multiple locations.

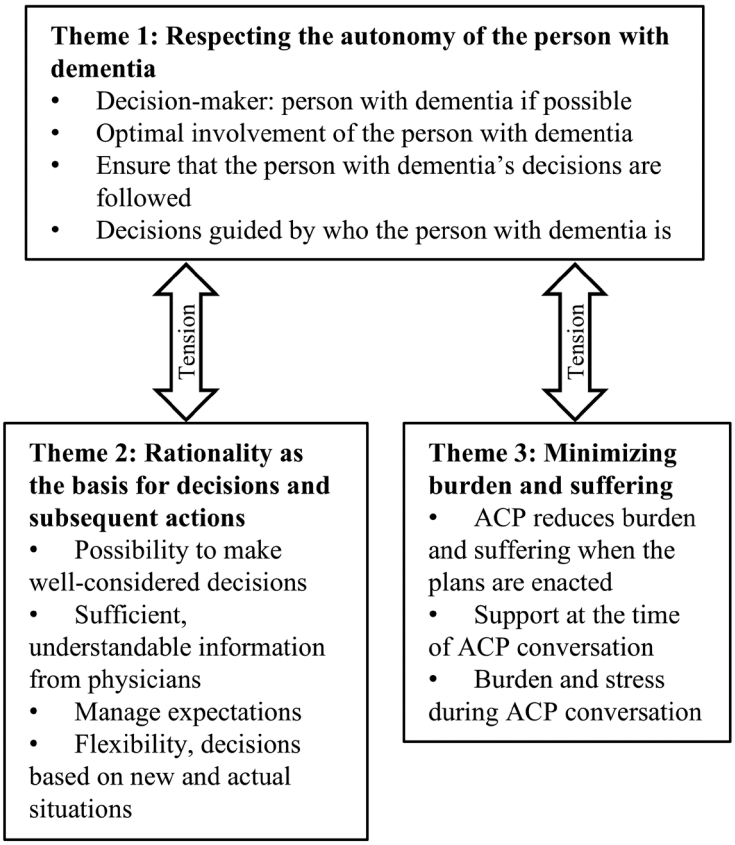

Figure 1. Ethical considerations of physicians in ACP for people with dementia

To maximize autonomy and decision-making for people living with dementia, participants suggested several ways to improve patient involvement. For example, physicians can initiate and encourage the conversation, make ACP easier by discussing important goals rather than concrete decisions, or let people living with dementia and their families prepare questions before the conversation.

"It should be scheduled […] And so, they know they're about what they're going to be coming in to discuss when they come in. And that way they can choose to bring whatever family member they want in with them. And they

can think about their questions and read about it a little more before they come in." (US general practitioner, age 30)

Some argued for a societal culture that favors ACP, which could be achieved by, for example, public education. A few participants acknowledged, however, that ACP may not be acceptable for some people living with dementia from non-Western cultures.

If concrete decisions are made by the person with dementia during ACP, several participants mentioned that the wishes might not be honored by the family or physicians, but many participants found it important to ensure that these decisions are followed.

"In one [of the approaches] you have a very concrete record of what they do and do not want. Then there is no room for discussion or interpretation afterwards." (Dutch physician in training to become a physician specialized in caring for older adults, age 31)

A number of participants recognized that the ACP conversation itself helps to get all stakeholders on the same page and increases the chance of the decisions being followed.

"So that the family knows how the patient feels. Otherwise, ehm, if the family doesn't know then the family might choose something different for the patient, even though the patient has things written down." (US geriatrician, age 37)

Participants noted that the chance of the decisions of the person with dementia being followed would be enhanced by making the decisions specific, documenting them clearly, and communicating the decisions well with all professionals involved. Some American participants also emphasized the importance of legal aspects, such as assigning and involving a legal representative in the ACP and using a legal document.

Physicians also considered it important that medical decisions be guided by who the patient is. Some participants stated that knowing what is important for the patient was salient, and not to only focus on medical issues during ACP. Some suggested starting the ACP conversations with discussions about

important goals, which will subsequently inform concrete decisions either during the ACP or in the future.

> *"I think what it would give you is it gives you ehm, a better sense of ehm, what the patient's values are so you can match future treatment decisions to those goals in, in a way that actually works better than just a, a checklist."* (US geriatrician, age 51)

Rationality as the basis for decisions and subsequent actions

Many participants emphasized that decisions and actions resulting from ACP need to be based on careful considerations and be clinically appropriate. Decisions were seen as well-considered if they are made beforehand, and by a person that has decisional capacity and not influenced by psychiatric conditions or strong emotions. Capacity of the person with dementia is a crucial requirement for many physicians to conduct ACP with them, especially when making concrete decisions, but also to establish important goals.

> *"Ehm, no, I think if they're not able to you know, repeat back or tell you those risks and those benefits [then ACP is not acceptable]."* (US resident in cardiology, age 27)

> *"With dementia that is often still a bit of denial so to speak that you are actually that old and vulnerable."* (Dutch general practitioner, age 57)

Most of these participants did not mention the possible fluctuation of capacity. Many participants emphasized conducting ACP in an early stage, while others recognized the possibility to conduct the conversation as dementia progresses.

> *"[…] some people just still understand a lot. Especially when the subject is the end of life."* (Dutch general practitioner, age 63)

To help people living with dementia make well-considered decisions, some participants stressed the importance of providing sufficient and understandable information during the ACP. They expressed the importance of giving clear explanations adapted to the capacity of the person with dementia.

> *"I also think, very often it's also very [good] to use examples, so it's clearer to people oh this is what you mean. It's the same with the resuscitation, where*

people often think, oh then you're just going to press on my chest a few times and then I'll go on with my life. Well of course it doesn't work like that. So that's how I explain, what resuscitation is and what it involves." (Dutch physician specialized in caring for older adults, age 38)

Participants also suggested choosing an approach that is easier for the person with dementia. A few participants considered the less abstract discussion about concrete decisions to be easier. For many others, it was talking about important goals, which does not require an understanding of medical interventions and their consequences.

"And when we have the patient or family explicitly saying yes, no to very particular medical interventions, ehm, it, it, it's, it's assuming that they know everything there is about those medical interventions which they don't. They can't. Ehm, I, I actually acknowledge even myself as a doctor, if I, if someone asked me if I wanted ECMO [extracoporeal membrane oxygenation], for instance, […] if I'm ever in a situation where I need that, I very much want someone who knows about ECMO to look at what matters to me in life and to say, is there a good chance that this treatment will allow these goals to be met." (US geriatrician, age 33)

In addition to providing information, a number of participants argued that expectation management is part of ACP. This would prevent medically futile decisions based on unrealistic expectations. We observed cultural differences in perspectives on being directive. Dutch participants were more comfortable guiding the decisions. American participants were often more reserved in influencing ACP decisions.

"For people with dementia who are already living in the nursing home, I usually say, well, I don't think it's helpful to resuscitate. And then I explain it, but then I actually more or less indicate that I have already made that decision. […] I don't explain it as a choice." (Dutch physician specialized in caring for older adults, age 37)

"I would. At the end of the day, I would probably let the patient make that decision and treat them according to how they wish." (US family physician, age 28)

Many participants stated that some flexibility is required to ensure rational and suitable decisions, as both a person's condition and their preferences could change over time.

> *"Yes we did put cross there at the time [that the person still wanted to be taken to the hospital], but now they can't even survive the ride to the hospital in an ambulance."* (Dutch physician specialized in caring for older adults, age 62)

> *"Their needs and wishes may have changed completely."* (Dutch physician specialized in caring for older adults, age 62)

Some participants handled this problem of changing situations and wishes by making agreements less specific and more widely applicable, for example, by establishing goals rather than concrete treatment orders. Dutch participants, especially those with more experience, argued that physicians should be entitled to overrule decisions that no longer suit new situations. These experienced physicians also expressed more comfort in making decisions based on care goals, while many of their early-career colleagues expressed a wish to rely on clear decisions made in advance. American participants often mentioned that they would engage the ethics committee when previous decisions were absent or unsuitable, because, without specific direction, treatment could only be withheld in very rare cases.

> *"In the US you are presumed to want everything done until proven otherwise. […] I could tell you two examples in my career where the physicians decided, we are not going to offer CPR for this patient, even though we don't have some decision maker telling us that. But that is here very rare. […] It's the tradition, it's the culture, it's the medical legal system, it's physicians being risk-averse."* (US emergency physician and palliative care physician, age 67)

Minimizing burden and suffering

According to many participants, one of the key reasons to conduct ACP is to minimize burden and suffering in the future.

> *"In the US we tend to do things to people at the end of life that are invasive, painful and not helpful, and people need to impose restrictions to avoid*

unnecessary pain and suffering." (US emergency physician and palliative care physician, age 67)

However, participants also expressed concerns over the possible burden and stress that the ACP conversation itself could induce. They therefore suggested several strategies to support the person with dementia and minimize the burden during ACP conversations, such as involving a supportive family caregiver.

Many participants were convinced that ACP will not only reduce future suffering and futile treatment for the person with dementia, but also reduce the stress and burden for decision-making of family caregivers and physicians.

"It is very difficult for eh, a family member to say no to a treatment which is available, you know? […] this would be a time for the physician to gently remind them and say, you remember our conversation with Anna? What she said, she wanted comfort and if we're going to do this, this, this, this could provide her pain or suffering." (US internist, age 65)

They indicated that the decisions would be easier to make if the family caregivers and physicians felt the assurance that they were following the wishes of the person with dementia.

However, many participants recognized that people living with dementia and family caregivers may experience emotional distress during ACP conversations because of the sensitive topic of the end of life or because of conflicts and differences of opinion within the family. A few physicians said that they would support the people living with dementia and family as much as possible, by introducing the topic gently, including a supportive family caregiver, letting a physician who already has a trusting relationship with the person with dementia conduct the ACP session, and incorporating a calm and patient-oriented attitude.

"So I think, trying to approach ehm, death and morbidity with a calm and peaceful attitude sometimes helps patients realize that at some point, death is okay too." (US family physician, age 29)

If the person with dementia was still likely to be stressed by the ACP conversation, some participants would choose to postpone it, only talk with the family, or forgo the conversation.

> *"When people become very restless and tense when you talk about the end of life or about the future. Some people get very scared. […] So then, then I keep it very short."* (Dutch physician specialized in caring for older adults, age 37)

Discussion

This study identified three key ethical considerations for Dutch and American physicians regarding ACP for people living with dementia: "respecting the autonomy of the person with dementia", "rationality as the basis for decisions and subsequent actions", and "minimizing burden and suffering". Each of these considerations presents its own challenges, and they can conflict with each other. The main tension arises between autonomy and rationality. Prioritizing autonomy of the person with dementia requires strict adherence to all the concrete decisions made during ACP, which may conflict with the flexibility to make decisions based on the actual clinical situations that might arise. Strict observance of autonomy also potentially conflicts with the principle of minimizing suffering when prior decisions conflict with the current best interest. These tensions are also recognized in a review as a major barrier to physicians conducting ACP with people living with dementia (Keijzer-van Laarhoven et al., 2020).

The results suggest that ACP for people living with dementia is a complex quest for balance between conflicting ethical considerations. Autonomy, rationality, and minimizing suffering highly resemble the key principles of autonomy, beneficence, and nonmaleficence in clinical ethics (Varkey, 2021). The possible solution for the tension among them may also be comparable. According to Varkey (2021), the only ethically defensible option when autonomy conflicts with beneficence is to allow physicians to make medical decisions on behalf of a person when they lose capacity, taking into account their previously expressed values and current best interest. It is unjustifiable to focus solely on one of the principles, either by neglecting the patient's wishes to

prioritize beneficence or refraining from using the physician's full knowledge to benefit the patient in order to maximize autonomy (Varkey, 2021). This balance between the ethical considerations therefore requires flexibility in carrying out advance decisions made during ACP. This flexibility needs to be recognized and discussed with people living with dementia and family caregivers to avoid false promises (Beck et al., 2017).

The necessity for flexibility requires a shift in the purpose of ACP from increasing goal-concordant care (Malhotra, 2023; Morrison et al., 2021; Sallnow et al., 2022) to enhancing overall well-being. Current evidence regarding whether ACP leads to goal-concordant care is inconsistent (Dixon et al., 2017; Kelly et al., 2019; Wendrich-van Dael et al., 2020), and we believe that this aim may not serve to meet the most important needs of people living with dementia. Research shows that only a small group of people with mild dementia expressed a need to make plans and take control of their lives (Hill et al., 2017). Instead, ACP aimed at goal-concordant care may primarily serve the needs of family caregivers who feel uncertain about making decisions for the person with dementia (Poole et al., 2018), and physicians who require documentation to mitigate legal risks associated with restricting or withdrawing life-sustaining treatments (Fleuren et al., 2020; Keijzer-van Laarhoven et al., 2020). The latter underscores the main difference observed in this study between the American and Dutch physicians in their willingness to make decisions based on the best interest of the person with dementia. This was also recognized in another interview study on decisions in people living with dementia and pneumonia, which found that physicians in the United States, unlike physicians in the Netherlands, were at times hesitant to decide in the patient's best interest out of fear for disciplinary action that families could take against them (Helton et al., 2006). These needs may also explain some physicians' preference for an ACP approach focused on making concrete treatment orders. For people living with dementia, the most pressing needs are support in coping with and accepting the disease, and respect (Miranda-Castillo et al., 2013; Shiells et al., 2020; van der Roest et al., 2007). These needs gradually shift to comfort and contact in later stages and the end of life (Fleuren et al., 2020; Shiells et al., 2020). New goals of ACP should therefore focus on facilitating well-being and adjustment for both people living with

dementia (Dixon et al., 2018; Morrison et al., 2021), and their family caregivers (Malhotra et al., 2024). The aim of ACP should extend beyond improving care at the very end of life to the longer journey of "living with dying" (Abel et al., 2020). The first step in achieving this is to start ACP with discussions of current concerns and values of the person with dementia (van der Steen, 2024b).

Future research should investigate elements of ACP that help clarify values of the person with dementia and ways to document and communicate these values to best inform future care. Techniques to facilitate acceptance of future changes and unpredictability in the context of ACP warrant exploration. Since medical personnel have reported challenges in providing sufficient psychological support for people living with dementia (Tetrault et al., 2023), training could be developed or part of ACP could be delegated to co-workers, such as social workers, chaplains, and psychologists, who have more expertise in discussing values and facilitating adjustment (Hickman et al., 2023). Policy can be modified to protect physicians from legal risks when making in-the-moment decisions, especially when concluding a treatment is futile for the patient. Furthermore, studies should explore the needs of physicians who prefer making concrete treatment orders in ACP, and how these needs can be addressed within an ACP approach focusing on the discussion of values. Finally, the perspectives of other stakeholders in ACP, such as people living with dementia, family, and other healthcare professionals, should also be investigated and compared to the findings of the current study.

A strength of this study was the inclusion of physicians from diverse specialties across two countries, who shared their rich experiences and various perspectives. Soliciting their opinions with two ACP vignettes facilitated the expression of detailed personal experience and reflections on different approaches to ACP with people living with dementia. The rigor of the study was further enhanced by the reflexivity and triangulation of researchers with extensive clinical and research experiences in both countries. A limitation was that physicians with an interest in palliative care may be more likely to participate. This might explain the high acceptability of ACP among the participants. The difference in work experience and work setting between

participants from the two countries may partly explain the more directive role that Dutch physicians take in ACP. Further, the participants from the United States practiced in a few states. Generalization of their views to physicians working in other states should be done with caution. Lastly, due to their professional training and experience, participants in this study may have primarily considered medical care and the physical domain of well-being. However, end-of-life care should be multi-disciplinary, and attention should also be paid to psychological, social, and spiritual well-being in ACP (Fetherston et al., 2018).

In conclusion, Dutch and American physicians illustrated three themes representing ethical considerations that play significant roles in ACP for people living with dementia. ACP remains a complex process that requires weighing and balancing of ethical principles. We advocate for an ACP approach centered on the discussion of values of the person with dementia while allowing for a certain degree of flexibility in future decision-making.

Declarations

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Conflict of Interest
The authors report no conflict of interest.

Data Availability
The data of this study are not publicly available due to privacy concerns. The study was preregistered at the Netherlands Trial Registration (NL7985) on 31 August, 2019, currently available on the International Clinical Trial Registry Platform.

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Author Contributions

XJ was involved in study concept and design, acquisition of subjects and data, analysis and interpretation of data, and preparation of manuscript. DM was involved in the acquisition of subjects, analysis and interpretation of data, and preparation of manuscript. MP was involved in the analysis and interpretation of data, and preparation of manuscript. KB was involved in the acquisition of subjects and data, analysis and interpretation of data, and preparation of manuscript. KM was involved in the analysis and interpretation of data, and preparation of manuscript. WA was involved in study concept and design, analysis and interpretation of data, and preparation of manuscript. HS, was involved in study concept and design, acquisition of subjects and data, analysis and interpretation of data, and preparation of manuscript. JS was involved in study concept and design, analysis and interpretation of data, and preparation of manuscript. All authors approved of the final draft.

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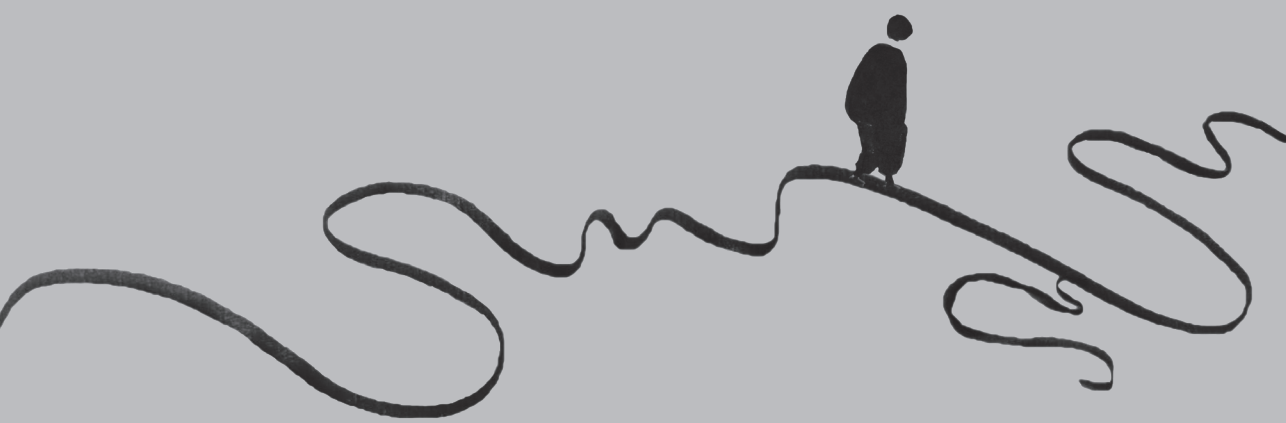

Acceptability of euthanasia for people with dementia: perspectives of clinicians from six countries

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Abstract

Objectives: Euthanasia for people with dementia is controversial and clinicians should decide how to respond to euthanasia requests. We aimed to investigate clinicians' perspectives on the acceptability of euthanasia for people with dementia, and differences between countries and personal characteristics potentially associated with acceptability.

Design, Setting, Participants, Measurements: Cross-sectional vignette study as part of the CONT-END studies, in which we conducted interviews with clinicians from the Netherlands, Switzerland, Germany, USA, Japan, and Israel online or in-person, and logistic regression analyses to assess associations with acceptability.

Results: Participants included 202 physicians and three nurse specialists who assumed similar medical responsibilities. Acceptability was higher in the Netherlands (66%) than in other countries (23-44%, OR 0.16-0.41, p = 0.003-0.03). Dutch clinicians were more often willing to perform euthanasia upon request of a person with dementia (58%) than clinicians in other countries (18-34%, OR 0.16-0.17, p = 0.007-0.03), except for Israel (40%, OR 0.48, p = 0.07). Two coping styles, planning (OR 0.77, 95% CI [0.59, 1.00]) and religious coping (OR 0.71, 95% CI [0.60, 0.84]), were associated with lower acceptability of euthanasia. Being religious (OR 0.47, 95% CI [0.24, 0.93]), training in palliative care (OR 0.48, 95% CI [0.26, 0.91]), and using emotional social support as coping style (OR 0.77, 95% CI [0.62, 0.95]) were associated with lower willingness to perform euthanasia upon request of a person with dementia.

Conclusions: Clinicians' perspectives on the acceptability of euthanasia for people with dementia varied across countries and individuals, with diversity related to coping styles, training in palliative care, and religion.

Objective

Euthanasia is defined as a medical professional actively ending a person's life with medical means such as injection (1). It is equivalent to the clinician-administered form of medical assistance in dying (MAID) or practitioner-administered form of voluntary assisted dying (VAD), but does not include self-administered assisted dying, also named physician assisted suicide (PAS) (2). Euthanasia is legal or decriminalized in the Netherlands, Belgium, Luxembourg, Canada, Colombia, Spain, Portugal, New Zealand, Australia, and Ecuador, and is undergoing fierce debate in others (3-6). Euthanasia is possible for people with dementia in the Netherlands, Belgium, Luxembourg, Canada, and Colombia, mostly restricted to people with mild dementia who still have decision-making capacity (2). Although physicians generally prefer PAS to euthanasia (1), the diminishing capacity in people with dementia to communicate a wish to die and to take the medication by themselves imply that they risk being unable to access PAS in later stages (7). This creates additional challenges and an added layer of controversy around euthanasia . Previous research in Belgium suggested that physicians consider euthanasia less acceptable for people with dementia compared to those with other diseases (8). Interest in the possibility of euthanasia for people with dementia is growing (9) with the rising number of people dying with dementia (10), legalization of euthanasia in more countries (11), and an increasingly positive public opinion towards euthanasia in high-income countries (12). Insights into the opinions of clinicians from both countries where euthanasia is legal and illegal may inform social debates and policymaking, because clinicians are usually responsible for responding to euthanasia requests. A limited number of studies on euthanasia specifically for people with dementia reported lower acceptability by clinicians than the general public (8, 13-15). The acceptability has increased over time (15) and is positively associated with some clinicians' personal characteristics, such as being young, male, not having strong religious beliefs, and no training in palliative care (8, 13-15). However, research on clinicians' perspectives on the acceptability of euthanasia for dementia mainly focused on countries where euthanasia is legal (8, 14-15).

The current study investigates clinicians' views on the acceptability of euthanasia in six high-income countries with different legal statuses of euthanasia and other end-of-life options (Table 1). The research questions were: 1) Is euthanasia acceptable for people with dementia from the perspective of clinicians in these six countries? 2) Are there differences in acceptability of euthanasia for people with dementia from the perspective of clinicians between the countries? 3) Which personal characteristics of clinicians are associated with the acceptability of euthanasia for people with dementia?

Table 1. Legal status of euthanasia and other end-of-life options in the participating countries

Country	Euthanasia	Physician assisted suicide	Withdrawal of life-sustaining intervention
The Netherlands (11)	Decriminalized	Legal	Legal
Switzerland (11)	Not legal	Legal	Legal
Germany (11)	Not legal	Legal	Legal
United States (11)	Not legal	Legal in some states[a]	Legal
Japan (16)	Not legal	Not legal	Unclear[b]
Israel (17)	Not legal	Not legal	Not legal

[a] Physician assisted suicide is legal in the states of Oregon, Washington, Montana, Vermont, California, Colorado, Hawaii, New Jersey, Maine, and New Mexico. Also in Washington, D.C.

[b] A relevant legislative bill is not yet submitted to the National Diet due to opposition.

Methods

Study design

We conducted a mixed-methods vignette study in the Netherlands, Switzerland, Germany, USA, Japan, and Israel. Clinicians, people with dementia, and family caregivers participated in a one-time assessment including a questionnaire on personal characteristics and a semi-structured interview on the acceptability of euthanasia, advance care planning, and the use of symptom monitoring technology for people with dementia as part of the CONT-END study (18). Each topic was prompted by a brief animation video. This article reports on clinicians' acceptability rating of euthanasia following

the STROBE checklist for cross-sectional studies. The data were collected between July 2020 and January 2024.

Participants

Clinicians eligible to participate primarily included physicians with a specialty that could include end-of-life care for people with dementia. American nurse specialists from these disciplines who assume a similar level of medical responsibility as general practitioners were also included. We recruited participants through email lists and websites of the research institutes, through professional networks, and using professional connections of the authors (Supplementary Table S1) (18).

Instruments

The research team developed the animation videos with input from local collaborators, people with dementia, and older adults (18). The video illustrating the procedure and requirements for euthanasia ranged from 2 minutes 59 seconds (English) to 4 minutes 20 seconds (Japanese). The videos were translated and back-translated. Minor cultural-sensitive adjustments were described in the protocol paper (18). To prevent confusion with physician assisted suicide, we used the expression "termination of life on demand" in the US, Israel, and Japan. In Germany and Switzerland, we used "Aktive Sterbehilfe", literarily meaning active assistance in dying as the preferred term. If during the interview, the participant seemed to confuse the concept of euthanasia with physician assisted suicide or withdrawal of life-sustaining treatments, the interviewer clarified that we were studying the active ending of a person's life by medical professionals with, for example, as injection.

Acceptability was assessed using the questions: 1) Do you consider euthanasia acceptable for people with dementia? 2) Would you use euthanasia for a patient with dementia at their request? 3) Do you think your colleagues would find euthanasia acceptable to use for a patient with dementia at their own or their family caregiver's request? 4) Would you use euthanasia for a patient with dementia at their family caregiver's request? 5) Would you want euthanasia for yourself if you had dementia? 6) Do you think euthanasia is currently legal where you practice? In countries other than the Netherlands,

the first five questions were accompanied with the assumption "suppose it was legal". Participants were asked to indicate an answer of yes/no/don't know, before they elaborated on their considerations. Primary outcome variables were whether euthanasia is considered acceptable for people with dementia from the perspective of clinicians and whether they would use it at request of a person with dementia. Since performing euthanasia at request of the family caregiver is not legal nor desirable, we did not include this as a primary outcome.

Personal characteristics included demographics, professional experience, and attitudes relevant to end-of-life care. Collected demographics consisted of age, sex, religion, and country of birth or ethnicity. During the analysis, religion was grouped into not religious (atheist, agnostic, humanist, or no specific religious background) and a group containing all other options (e.g. Catholic, Protestant, Hindu, other).

Professional experience was assessed as specialization, place where they treat people with dementia, years of experience in dementia care, whether palliative training was received after basic medical training (yes/no), number of patients with dementia who died in the last year (0/1-4/5-9/10-19/20+) and whether the participant had personally experienced a family member or friend with advanced dementia at the end-of-life (yes/no). Specialties were grouped into older person-related specialties (elderly care physician, geriatrician, psycho-geriatrician, dementia care nurse practitioner and geriatric clinical nurse specialist) and other (e.g., general practitioner, internal medicine, neurologist).

Further, we assessed comfort to talk about the end of life with people with dementia (4-point scale), comfort to talk about the end of life in general (4-point scale, don't know), and the perspective (patient/caregiver/clinician) that is the mostly strongly considered relating to goals of future care for people with dementia (18, 19). The Locus of Control scale (IE-4) (20) comprised four items, two for internal and two for external locus of control scaled 1 to 5. Illness cognition (knowledge of dementia) was covered by 1) "dementia is a disease you can die from" (19, 21); 2) "dementia is a normal part of the ageing process" (20); and 3) "palliative care applies from the time of diagnosis to the stage of severe dementia" (21); each statement was rated on a 1-5 scale (18) and

don't know was a valid option. Attitudes towards death were measured by the 4-item Death Anxiety Questionnaire (24) and 5 items of the Death Attitude Profile-Revised (DAP-R) (25, 26) selected from the DAP-R subscales fear of death, avoidance of death, neutral acceptance of death, convergent acceptance of death, and escapist acceptance of death. Answers were scored on a 1-4 scale and a don't know option. Coping styles were measured by relevant 2-item subscales of the Brief COPE (27, 28), including active coping, planning, use of instrumental social support, use of emotional social support, denial, acceptance, and religious coping scored 1-4.

Procedures

The assessment generally consisted of 10 min for the online questionnaire, followed by 50 min for the interview. We sent a link to the online questionnaire in Castor electronic data capture (EDC; Castor, the Netherlands) via email. During the online interview, participants viewed four animation videos, each describing an intervention (i.e., two approaches to advance care planning, monitoring technology, and euthanasia) (18), and after each, answered questions about the acceptability of the interventions. The video about euthanasia was shown last due to the topic's potential sensitivity. In the Netherlands, four interviews were conducted via the telephone and one face-to-face due to technical problems with video calling or preference of the participant. To make up for delays due to the pandemic, after data collection in the Netherlands and the US was completed, we offered a fully self-reported online version in the other countries after the first 15 interviews.

Statistical analysis

We initially aimed to include 50 clinicians from each country, forming a total of 300. The power analysis was based on the larger CONT-END program to detect differences in acceptability of four interventions between 6 countries and 3 groups of participants (18). For euthanasia, 70 events of (not) acceptable would provide sufficient power, with an estimation of a 50% acceptability rate which is lower than other interventions investigated in the CONT-END program (18).

SPSS 29 and R 4.3.1 were used for the statistical analysis. Missing data were assumed to be missing at random and were treated with pairwise deletion in the exploratory analysis. The option don't know was given an average score, for example 3 on a 1-5 scale. To check the influence of the data collection methods, a sensitivity analysis was performed on the main outcome measures of the Israeli data, which included the most participants who responded to the self-reported online version.

Regression analyses were performed separately for two dependent variables: 1) whether the clinicians considered euthanasia acceptable for people with dementia, and 2) whether they would use it at request of a person with dementia. To address the research question of whether there were differences between countries, we used logistic regression with and without adjustment for age, gender, and religion. To explore associations of personal characteristics with each dependent variable, we first determined that there was a significant clustering effect by country (29). We then conducted regressions for potentially associated variables adjusted for clustering by country as part of a two-level model. Those variables with a p-value of less than 0.2 were then entered in a two-level model (countries with random intercept and personal characteristics) (30), which was trimmed by backwards regression on the personal characteristics. Wald statistics with an alpha of 0.05 were used in the backward selection. Analyses for the two-level models were conducted using the R package Ime4.

We recognize the problem of overfitting (31) and model instability (32) produced by backward regression, so we performed a sensitivity analysis with Lasso regression with the R package glmmLasso, which compensates for possible overfitting by applying a penalty to the correlation coefficients, shrinking those of irrelevant variables to 0 (32). The optimal strength of penalty (lambda) was determined based on Bayesian information criterion. The optimal lambda of 18 was used for the regression on the acceptability of euthanasia for people with dementia, and a lambda of 22 for the regression on the willingness to use euthanasia upon request of a person with dementia.

Ethics

The study protocol is published and approved by the institutional review board or ethics committee in all country sites (18). The study is registered at the Netherlands Trial Registration (NL7985) on 31 August, 2019, currently available on the International Clinical Trial Registry Platform (NL-OMON26073). All participants provided written informed consent. Participants received gift cards for their participation. The amount was decided together with the local researcher based on common practice for similar studies (the Netherlands and Germany 15 euros, Switzerland 30 Swiss Franc, US 100 dollars, Japan 2000 yen, Israel 110 Israeli New Shekel).

Results

Demographics

A total of 202 physicians and 3 nurse specialists participated (Table 2, Supplementary Table S2). Due to the use of large email lists, websites and snowballing during recruitment, it was not possible to estimate the number of potential participants reached by the recruitment strategies. Around half of the participants (54%) were female, with more males from Japan (21 of 25; 84%) and more females from Germany 16 of 17 (94%). A great majority of participants (84%-100%) were born in the country where they practice medicine except for Switzerland (5 of 13; 39%). The participants from the US were mostly (90%) non-Hispanic Caucasian or Asian. A third of the overall participants were not religious. Clinicians practicing a specialty related to older people accounted for a third of all participants, with a higher percentage from the Netherlands (76%) than other countries (6%-26%). A great majority of the participants (81%) had cared for patients with dementia who died in the last year. The interviews lasted a median of 45 minutes (IQR 38 - 52, range 16 – 99) excluding the time viewing the animation videos.

Four single data points, each from a different participant, were missing because of refusal to answer a question by the participant, or because the interviewer forgot to ask a question. These missing data were about the acceptability of euthanasia for the participant themselves (one Dutch participant), legality of euthanasia (another Dutch participant and a German participant), and a question about planning as coping strategy (another Dutch participant).

Table 2. Characteristics of participants

	Overall (N = 205)	Netherlands (N = 50)	Switzerland (N = 13)	Germany (N = 17)	USA (N = 50)	Japan (N = 25)	Israel (N = 50)
Gender, % (N)							
Female	54 (110)	70 (35)	62 (8)	94 (16)	52 (26)	16 (4)	42 (21)
Male	46 (95)	30 (15)	38 (5)	6 (1)	48 (24)	84 (21)	58 (29)
Age, median, (interquartile range: IQR), range	42 (33-54) 26-78	48 (34-59) 26-76	46 (44-60) 36-69	46 (38-60) 26-62	33 (28-45) 26-71	48 (41-56) 30-66	36 (33-45) 26-78
Born in the country where they currently worked, % (N)	87 (134)	92 (46)	39 (5)	94 (16)	-	100 (25)	84 (42)
Religion, % (N)							
Not religious	31 (63)	46 (23)	39 (5)	29 (5)	26 (13)	60 (15)	4 (2)
Christian	34 (70)	52 (26)	62 (8)	65 (11)	40 (20)	12 (3)	4 (2)
Jewish	18 (36)	0 (0)	0 (0)	6 (1)	6 (3)	0 (0)	64 (43)
Muslim	7 (15)	0 (0)	0 (0)	0 (0)	2 (1)	0 (0)	28 (14)
Polytheist and other	10 (21)	2 (1)	0 (0)	0 (0)	26 (13)	28 (7)	0 (0)
Specialty, % (N) (more possible)							
Older person related specialties	34 (69)	78 (39)	15 (2)	6 (1)	32 (16)	8 (2)	18 (9)
Other	66 (136)	22 (11)	85 (11)	94 (16)	68 (34)	92 (23)	82 (41)
Place of practice, % (N) (more possible)							
Hospital	54 (110)	8 (4)	69 (9)	47 (8)	82 (41)	36 (9)	78 (39)
Nursing home	45 (93)	74 (37)	38 (5)	41 (7)	44 (22)	52 (13)	18 (9)
Home	41 (84)	46 (23)	23 (3)	53 (9)	26 (13)	64 (16)	40 (20)

Other (hospice, private, clinic, daycare center)	37 (76)	16 (8)	54 (7)	24 (4)	54 (27)	60 (15)	30 (15)
Years of experience in dementia care, median (IQR), range	8 (3-20) 0-44	19 (4-25) 2-38	15 (10-22) 5-40	8 (5-14) 1-31	4 (1-11) 0-44	15 (9-20) 2-30	4 (2-10) 0-40
Training in palliative care, % (N)	52 (106)	42 (21)	85 (11)	35 (6)	54 (27)	76 (19)	44 (22)
Number of their patients with dementia who died in the last year, % (N)							
0	9 (19)	8 (4)	8 (1)	0 (0)	18 (9)	4 (1)	8 (4)
1-4	34 (70)	16 (8)	15 (2)	41 (7)	36 (18)	28 (7)	56 (28)
5-9	25 (51)	36 (18)	23 (3)	35 (6)	16 (8)	32 (8)	16 (8)
10-19	17 (34)	20 (10)	39 (5)	12 (2)	16 (8)	6 (3)	6 (3)
20 or more	15 (31)	20 (10)	15 (2)	12 (2)	14 (7)	14 (7)	14 (7)
Personal experience with a family member or friend having advanced dementia at the end of their life, % (N)	56 (114)	48 (24)	69 (9)	65 (11)	60 (30)	56 (14)	52 (26)

Note: In the US, ethnicity instead of country of birth was collected and reported in the text. In Switzerland, most clinicians who were born outside of the country are from Germany.

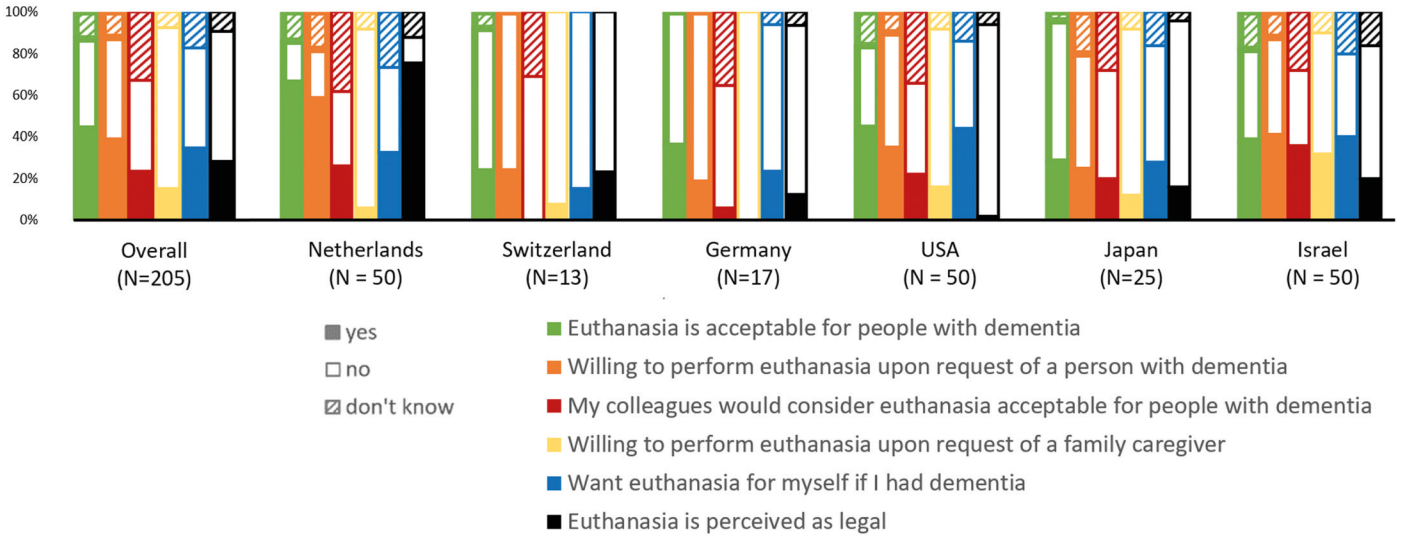

Figure 1. Acceptability of euthanasia for people with dementia from the perspective of clinicians

Acceptability of euthanasia

In total, 44% of the participants considered euthanasia acceptable for people with dementia, ranging from 23% in Switzerland to 66% in the Netherlands (Figure 1; Supplementary Table S3). Over one third (38%) of the clinicians were willing to perform euthanasia upon request of a person with dementia; ranging from 18% in Germany to 58% in the Netherlands. Twenty-three percent thought that their colleagues would consider euthanasia acceptable. Fifteen percent of participants were willing to perform it upon request of a family caregiver, ranging from none (Germany) to 32% (Israel). More (35%) of the participants would want euthanasia for themselves if they had dementia. Some clinicians in each of the countries believed that euthanasia for people with dementia was legal in their practice, up to 76% in the Netherlands. Sensitivity analysis with Israeli participants suggested that there might be some differences between those who attended interviews and those who completed the self-reported online version, although in different directions (acceptable: 47% and 34%, willing to perform upon patient request: 26% and 46% respectively).

Differences in acceptability between countries

Table 3 shows that the acceptability of euthanasia for people with dementia was higher in the Netherlands than in any of the other countries in unadjusted analysis; the differences were still significant for Switzerland and Japan after the adjustment for age, gender, and religion. Clinicians from other countries except for Israel were also less likely than Dutch clinicians to be willing to perform euthanasia upon request of a person with dementia, with or without adjustment for age, gender and religion. Considering the covariates in this analysis, clinicians who were not religious were more likely to consider euthanasia acceptable for people with dementia (OR 2.49; 95% CI [1.21, 5.13]), and willing to conduct it upon request of a person with dementia (OR 2.20; 95% CI [1.06, 4.55]).

Personal characteristics and acceptability

From the bivariable associations with the acceptability of euthanasia for people with dementia, adjusted for the clustering effect of country, we retained ($p < 0.20$): religion, practicing in the hospital, practicing in nursing homes, the perspective to consider most strongly when talking about goals of future care (patient/clinician/family), internal locus of control, avoidance of death, neutral acceptance of death, convergent acceptance of death, and five coping styles (planning, use of instrumental social support, use of emotional social support, denial, and religious coping) (Supplementary Table S4). From the bivariate associations with the willingness to perform euthanasia upon request of a person with dementia, adjusted for the clustering of country, the following variables were retained ($p < 0.20$): age, religion, training in palliative care, number of deceased patients with dementia in the last year, practicing in the hospital, practicing in nursing homes, practicing in clinics or daycare centers, avoidance of death, convergent acceptance of death, and four coping styles (use of instrumental social support, use of emotional social support, denial, and religious coping). Gender, specialization, comfort to talk about the end of life with people with dementia, comfort to talk about the end of life in general, years of experience in dementia care, personal experience with dementia at the end of life, and illness cognition did not show bivariable associations with the two main outcomes and were not included in the models.

Multivariable selection (Table 4) identified the coping styles planning (OR 0.77; 95% CI [0.59, 1.00]) and religious coping (OR 0.71; 95% CI [0.60, 0.84]) as independently associated with the acceptability of euthanasia for people with dementia. The willingness to use euthanasia upon request of a person with dementia was associated with not being religious (OR 2.12; 95% CI [1.07, 4.20]), no training in palliative care (OR 0.48; 95% CI [0.26, 0.91]), and less use of emotional social support as coping style (OR 0.77; 95% CI [0.62, 0.95]). The more conservative lasso regression retained only religious coping in both models.

Table 3. Associations between country and acceptability of euthanasia, unadjusted and adjusted for age, gender, and religion (N=205)

Country	Acceptable for people with dementia from clinicians' perspective					Willing to perform it upon request of a person with dementia				
		Unadjusted		Adjusted			Unadjusted		Adjusted	
	N (%)	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	N (%)	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Netherlands	33 (66)	1	-	1	-	29 (58)	1	-	**1**	-
Switzerland	3 (23)	**0.16 (0.04-0.64)**	**0.01**	**0.15 (0.04-0.64)**	**0.01**	3 (23)	**0.22 (0.05-0.89)**	**0.03**	**0.22 (0.05-0.95)**	**0.04**
Germany	6 (35)	**0.28 (0.09-0.89)**	**0.03**	0.31 (0.09-1.00)	0.05	3 (18)	**0.16 (0.04-0.61)**	**0.008**	**0.17 (0.04-0.68)**	**0.01**
USA	22 (44)	**0.41 (0.18-0.91)**	**0.03**	0.48 (0.20-1.17)	0.11	17 (34)	**0.37 (0.17-0.84)**	**0.02**	**0.33 (0.13-0.82)**	**0.02**
Japan	7 (28)	**0.20 (0.07-0.57)**	**0.003**	**0.17 (0.05-0.52)**	**0.002**	6 (24)	**0.23 (0.08-0.67)**	**0.007**	**0.17 (0.05-0.54)**	**0.003**
Israel	19 (38)	**0.32 (0.14-0.72)**	**0.006**	0.46 (0.18-1.12)	0.11	20 (40)	0.48 (0.22-1.07)	0.07	0.51 (0.20-1.32)	0.17

Notes: OR = odd ratio, CI = confidence interval. AIC of the models were 277 (acceptability unadjusted), 277 (acceptability adjusted), 269 (willingness unadjusted), and 266 (willingness adjusted) respectively. Results with $p < 0.05$ are bolded.

Table 4. Independent associations with acceptability of euthanasia

	OR (95% CI)	*P*-value	Wald
Acceptability of euthanasia for people with dementia from clinicians' perspective			
Religious coping (scale 2-10)	0.71 (0.60, 0.84)	<0.001	16.23
Planning as coping (scale 2-10)	0.77 (0.59, 1.00)	0.05	3.93
Willingness to use euthanasia upon request of people with dementia			
Use of emotional social support as coping (scale 2-10)	0.77 (0.62, 0.95)	0.02	5.60
Training in palliative care (no as reference)	0.49 (0.26, 0.91)	0.02	5.18
Not religious (reference: choosing and affiliation other than atheist, agnostic, humanist, or no specific religious background)	2.12 (1.07, 4.20)	0.03	4.68

Note: Country random effect variance (variance, SE): 0.16 (0.40) for the model on acceptability of euthanasia for people with dementia and 0.17 (0.41) for the model on willingness to use euthanasia upon request of people with dementia. Model fit values (AIC, BIC, Log-likelihood) were 261, 275, -127 for the first model and 262, 278, and -126 for the second model respectively.

Conclusions

Across the six countries, 44% of the clinicians considered euthanasia acceptable for people with dementia. Thirty-eight per cent expressed willingness to perform euthanasia upon request of a person with dementia. Dutch clinicians were more likely to consider euthanasia acceptable compared to Swiss and Japanese clinicians. They were also more likely to be willing to perform euthanasia compared to Switzerland, Germany, US, and Japan. Exploratory analysis showed that more use of the coping styles planning and religious coping were associated with lower acceptability of euthanasia for people with dementia. Willingness to perform euthanasia upon request of a person with dementia was associated with reporting no religion, no training in palliative care, and less use of emotional social support as coping style.

Consistent with previous research, Dutch clinicians reported the highest acceptability compared to other countries (12). Since the Netherlands is the only country in this study where euthanasia has been decriminalized, we cannot disentangle influence of legality in country comparisons. The overall acceptability in our study is higher than in a Dutch survey in 2016 with 1147 physicians (13), but similar to a survey in 2017 with 136 Quebec physicians (14).

This might be due to potential selection bias in smaller studies. Participants of our study, for example, perceived themselves to be more accepting of euthanasia than their colleagues. Generalization of the results should therefore be done with caution. The results of this study suggest that opinions on euthanasia for people with dementia are diverse. Policy may need to consider the wishes and needs of clinicians both for and against this practice.

The questions of this study also did not specify factors such as capacity and the stage of dementia that clinicians might find important in deciding on acceptability of euthanasia for people with dementia. Previous research indicated that Dutch clinicians were more conservative when the dementia advances, while Belgian clinicians showed the opposite attitudes (8). There is tension between respecting the autonomy of the person with dementia who requested euthanasia earlier because they consider living with advanced dementia involves unbearable suffering versus protecting vulnerable incompetent individuals by properly assessing their current suffering and avoiding undue influence from relatives (8, 34). Future research and societal discussions are needed to find ways that mitigate this tension.

This study brought new insights on the potential role of coping style in the acceptability of euthanasia, building on previous knowledge that emotional burden is an important determinant of the willingness to perform euthanasia (35). Surprisingly, planning as a coping strategy of clinicians was negatively associated with the acceptability of euthanasia, which is usually a result of the person with dementia planning for their death. The mechanism of associations between coping strategies and acceptability of euthanasia may need to be explored in future research.

In line with prior research which focused on people with advanced dementia, we found that clinicians who report a religion (8, 13-14) or training in palliative care (14) were less likely to consider euthanasia acceptable. Palliative care training may bring more knowledge and skills to relieve suffering (14), and palliative care does not include hastening death by its current definition (36). Contrary to earlier studies, age (8, 14), gender (13) and practicing in a hospital (14) or nursing home (13) were not significantly associated with acceptability after the adjustment for other personal characteristics, possibly due to limited

sample size of the current study. These results imply that if adherence to religion and rates of palliative care changes, we may observe a shift in clinicians' acceptability of euthanasia for people with dementia. Globally, the percentage of people with religion is relatively stable (37), but as palliative care is being promoted (38), clinicians might show more reservation in providing euthanasia for people with dementia. On the other hand, the general public, who have a more positive attitude towards euthanasia, still has poor understanding of palliative care (12, 39). We recommend improving access to palliative care and public education on options to alleviate unbearable suffering, such as palliative sedation, in order to facilitate better informed decision making and to ease tensions between divergent attitudes of clinicians and the public.A strength of the study is the comparison between six high-income countries which shows the diversity of attitudes towards euthanasia for people with dementia and adds to the limited literature on this topic of growing importance. The exploration of a variety of personal characteristics indicated understudied factors associated with acceptability. We recruited a sample interested in end of life or palliative care in dementia, not in particular or only interested in euthanasia. Future research may compare the opinions of frontline clinicians with those of ethical and legal experts. A limitation of the study is that the planned sample size was not reached in Switzerland, Germany, and Japan after exhausting the recruitment possibilities within the duration of the study. The willingness of clinicians to participate in the study was limited due to heavy clinical duties during Covid. To ensure the understanding of the concept of euthanasia, we provided clear explanations in the animation video and clarification of interviewers. However, we cannot rule out that some participants might still have based their answers on a broader conceptualization with may include physician assisted suicide and withdrawal of life-sustaining interventions. This may have resulted in a higher acceptability rate and a number of participants perceiving euthanasia to be legal in their country when it is not. Lastly, no low- and middle-income countries were included. The acceptability in these countries, where the majority of people living with dementia in the world reside (40), can be examined in future studies. Different results may be expected in countries with a less comprehensive healthcare systems and higher religiosity .

In summary, close to half of clinicians from the Netherlands, Switzerland, USA, Germany, Japan, and Israel considered euthanasia acceptable for people with dementia. Dutch clinicians reported the highest acceptability. In this international study, not being religious, training in palliative care, and several coping strategies were associated with acceptability. These factors can be taken into consideration in policy on euthanasia for people with dementia.

Declarations

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Author contributions
JS, XJ, HS, MN, SA, LR, JG, WA, and DM were involved in the conception and design of the study. All authors contributed to the acquisition of subjects. XJ and HS were involved in the acquisition of data. XJ, HS, MN, DM, and JS analyzed and interpreted the data. XJ drafted the manuscript. All authors critically reviewed the manuscript and approved of the final version. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Data Sharing Statement

The data is currently unavailable because the authors have not finished using them for their own purposes.

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Supplementary Table S1. Recruitment strategies per country

Country	Recruitment strategies	Areas of recruitment
The Netherlands	Email through the networks of Leiden University Medical Center (LUMC), including the general practitioner network Extramural LUMC Academic Netwerk (ELAN), the academic long-term care network University Network for the Care sector South Holland (UNC-ZH), and the Specialist training program for "Elderly Care" Medicine (SOOL).	South Holland
Switzerland	Personal contacts of the authors, snowballing	Whole country
Germany	Personal contacts of the authors and students, snowballing	Noordrijn-Westfalen and Nedersaksen
USA	Email lists of the American Geriatrics Society and the American College of Physicians – Missouri section, emails to selected practitioners at the University of Missouri School of Medicine, personal contacts of the authors, snowballing.	Mainly Missouri and surrounding states, snowballing also reached New York and Texas
Japan	Website of Tohoku University, personal contacts of the authors and students, snowballing	Whole country, mainly Tohoku and Nagasaki
Israel	Personal contacts of the authors, snowballing	Whole country

Supplementary Table S2. Characteristics of participants cont.

	Overall (N = 205)	Netherlands (N = 50)	Switzerland (N = 13)	Germany (N = 17)	USA (N = 50)	Japan (N = 25)	Israel (N = 50)
Comfort talking about end-of-life care for people with dementia and family caregivers, % (N)							
Very comfortable	42 (85)	66 (33)	62 (8)	18 (3)	42 (21)	28 (7)	26 (13)
Moderately comfortable	42 (86)	32 (16)	38 (5)	71 (12)	34 (17)	56 (14)	44 (22)
Moderately uncomfortable	16 (32)	2 (1)	0 (0)	12 (2)	20 (10)	16 (4)	30 (15)
Very uncomfortable	1 (2)	0 (0)	0 (0)	0 (0)	4 (2)	0 (0)	0 (0)
Comfort talking about the end of life in general, % (N)							
Very comfortable	48 (98)	54 (27)	69 (9)	29 (5)	58 (29)	36 (9)	38 (19)
Somewhat comfortable	31 (63)	40 (20)	31 (4)	35 (6)	22 (11)	36 (9)	26 (13)
Somewhat uncomfortable	19 (38)	4 (2)	0 (0)	35 (6)	18 (9)	24 (6)	30 (15)
Very uncomfortable	2 (4)	2 (1)	0 (0)	0 (0)	2 (1)	2 (1)	2 (1)
I don't know	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	4 (2)
Perspective most strongly considered relating to goals of future care, % (N)							
Person with dementia	81 (165)	92 (46)	100 (13)	82 (14)	98 (49)	68 (17)	52 (26)
Family caregiver	9 (18)	2 (1)	0 (0)	12 (2)	2 (1)	32 (8)	12 (6)
What I as physician wish for the person with dementia	6 (13)	0 (0)	0 (0)	6 (1)	0 (0)	0 (0)	24 (12)
Don't know	4 (9)	6 (3)	0 (0)	0 (0)	0 (0)	0 (0)	12 (6)
Internal locus of control (scale 2-10), median (IQR), range	8 (7-8) 3-10	8 (7-8) 6-10	7 (6-8) 4-9	8 (8-9) 6-10	8 (6-8) 3-10	7 (6-7) 5-10	8 (7-8) 3-10
External locus of control (scale 2-10), median (IQR), range	5 (4-6) 2-10	5 (4-6) 3-8	5 (4-5) 3-7	5 (3-6) 3-6	5 (4-6) 2-8	5 (4-5) 3-7	5 (5-6) 3-10

Supplementary Table S2. Characteristics of participants cont. (continued)

	Overall (N = 205)	Netherlands (N = 50)	Switzerland (N = 13)	Germany (N = 17)	USA (N = 50)	Japan (N = 25)	Israel (N = 50)
Illness cognition (scale 3-15), median (IQR), range	12 (11-14) 4-15	12 (11-14) 6-15	13 (11-15) 11-15	13 (12-14) 8-15	13 (11-14) 4-15	12 (11-12) 8-14	11 (9-12) 5-15
Attitudes towards death, median (IQR), range							
Death anxiety (scale 4-20)	9 (6-11) 4-16	8 (5-11) 4-15	9 (6-11) 5-13	9 (2) 4-13	7 (6-12) 4-16	9 (2) 5-13	10 (8-12) 4-14
Fear of death (scale 1-5)	2 (1-3) 1-5	2 (1-3) 1-3	2 (1-3) 1-4	2 (2-3) 1-4	2 (1-3) 1-4	2 (1-3) 1-4	2 (2-3) 1-5
Avoidance of death (scale 1-5)	1 (1-2) 1-5	1 (1-1) 1-4	1 (1-2) 1-2	2 (1-2) 1-3	2 (1-3) 1-5	2 (1-2) 1-4	2 (1-3) 1-5
Neutral acceptance of death (scale 1-5)	3 (3-4) 1-5	4 (3-4) 1-5	4 (3-4) 2-5	3 (3-4) 2-4	3 (3-4) 2-5	4 (3-4) 2-5	3 (3-4) 2-5
Convergent acceptance of death (scale 1-5)	2 (1-4) 1-5	2 (1-3) 1-5	2 (1-3) 1-5	2 (1-4) 1-5	3 (1-5) 1-5	2 (1-4) 1-5	3 (1-4) 1-5
Escapist acceptance of death (scale 1-5)	2 (1-3) 1-5	1 (1-3) 1-5	2 (1-3) 1-5	1 (1-2) 1-3	2 (1-3) 1-5	2 (1-3) 1-5	2 (1-3) 1-5
Coping Styles (scale 2-10), median (IQR), range							
Active coping	7 (6-8) 4-8	6 (6-7) 4-8	7 (6-8) 6-8	7 (6-8) 4-8	7 (6-8) 4-8	6 (6-7) 5-8	7 (6-8) 5-8
Planning	7 (6-8) 3-8	7 (6-8) 3-8	7 (6-8) 4-8	7 (7-8) 5-8	7 (6-8) 4-8	7 (6-8) 5-8	7 (6-8) 4-8

Supplementary Table S2. Characteristics of participants cont. (continued)

	Overall (N = 205)	Netherlands (N = 50)	Switzerland (N = 13)	Germany (N = 17)	USA (N = 50)	Japan (N = 25)	Israel (N = 50)
Use of instrumental social support	6 (5-7) 2-8	6 (5-6) 2-8	6 (5-8) 4-8	6 (5-7) 4-8	6 (5-7) 2-8	6 (5-6) 4-8	6 (5-7) 2-8
Use of emotional social support	6 (5-7) 2-8	6 (5-6) 3-8	7 (6-8) 4-8	7 (6-7) 4-8	6 (4-6) 2-8	6 (5-6) 4-8	6 (4-7) 2-8
Denial	2 (2-3) 2-8	2 (2-2) 2-3	2 (2-3) 2-4	3 (2-4) 2-5	2 (2-2) 2-4	2 (2-3) 2-4	3 (2-4) 2-8
Acceptance	6 (6-7) 2-8	7 (6-7) 4-8	6 (3-7) 2-8	6 (6-7) 5-8	6 (6-8) 4-8	6 (6-7) 5-8	6 (6-8) 3-8
Religious coping	4 (3-6) 2-8	3 (2-5) 2-8	4 (3-5) 2-7	4 (2-5) 2-7	4 (3-7) 2-8	4 (3-5) 2-7	5 (3-6) 2-8

Supplementary Table S3. Acceptability of euthanasia among physicians in six countries as presented in Figure 1

	Overall (N = 205)	Netherlands (N = 50)	Switzerland (N = 13)	Germany (N = 17)	USA (N = 50)	Japan (N = 25)	Israel (N = 50)
Euthanasia is acceptable for people with dementia from physician's perspective, N (%)							
Yes	90 (44)	33 (66)	3 (23)	6 (35)	22 (44)	7 (28)	19 (38)
No	89 (43)	10 (20)	9 (69)	11 (65)	20 (40)	17 (68)	22 (44)
Don't know	26 (13)	7 (14)	1 (8)	0 (0)	8 (16)	1 (4)	9 (18)
Willing to perform euthanasia upon request of a person with dementia, N (%)							
Yes	78 (38)	29 (58)	3 (23)	3 (18)	17 (34)	6 (24)	20 (40)
No	102 (50)	12 (24)	10 (77)	14 (82)	28 (56)	14 (56)	24 (48)
Don't know	25 (12)	9 (18)	0 (0)	0 (0)	5 (10)	5 (20)	6 (12)
Whether my colleagues would consider euthanasia acceptable for people with dementia, N (%)							
Yes	48 (23)	13 (26)	0 (0)	1 (6)	11 (22)	5 (20)	18 (36)
No	90 (44)	18 (36)	9 (69)	10 (59)	22 (44)	13 (52)	18 (36)
Don't know	67 (33)	19 (38)	4 (31)	6 (35)	17 (34)	7 (28)	14 (28)
Willing to perform euthanasia upon request of a family caregiver, N (%)							
Yes	31 (15)	3 (6)	1 (8)	0 (0)	8 (16)	3 (12)	16 (32)
No	159 (78)	43 (86)	12 (92)	17 (100)	38 (76)	20 (80)	29 (58)
Don't know	15 (7)	4 (8)	0 (0)	0 (0)	4 (8)	2 (8)	5 (10)
Want euthanasia for myself if I had dementia, N (%)							
Yes	71 (35)	16 (33)	2 (15)	4 (24)	22 (44)	7 (28)	20 (40)
No	98 (48)	20 (41)	11 (85)	12 (71)	21 (42)	14 (56)	20 (40)
Don't know	35 (17)	13 (27)	0 (0)	1 (6)	7 (14)	4 (16)	10 (20)
Missing	1 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Supplementary Table S3. Acceptability of euthanasia among physicians in six countries as presented in Figure 1 (continued)

	Overall (N = 205)	Netherlands (N = 50)	Switzerland (N = 13)	Germany (N = 17)	USA (N = 50)	Japan (N = 25)	Israel (N = 50)
Whether euthanasia is perceived as legal, N (%)							
Yes	57 (28)	37 (76)	3 (23)	2 (13)	1 (2)	4 (16)	10 (20)
No	127 (62)	6 (12)	10 (77)	13 (81)	46 (92)	20 (80)	32 (64)
Don't know	19 (9)	6 (12)	0 (0)	1 (6)	3 (6)	1 (4)	8 (16)
Missing	1 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Supplementary Table S4 Bivariable associations between clinician's personal characteristics and acceptability of euthanasia, adjusted for clustering of country

	Acceptability of euthanasia
Personal characteristics	**Fixed effect (level 1)**
	OR (80% CI)*, *p*-value
Age	1.00 (0.99, 1.02), 0.93
Sex (female as reference)	1.03 (0.69, 1.53), 0.92
Not religious (reference: choosing and affiliation other than atheist, agnostic, humanist, or no specific religious background)	**2.25 (1.46, 3.48), 0.02**
Specialization (older people related specialties as reference)	0.76 (0.46, 1.26), 0.49
Training in palliative care (no as reference)	0.83 (0.57, 1.21), 0.53
Comfort to talk about the end of life with people with dementia	0.85 (0.65, 1.11), 0.45
Years of experience in dementia care	1.01 (0.99, 1.03), 0.55
Number of deceased patients with dementia in the last year (0 as reference)	
1-4	1.23 (0.73, 2.08), 0.61
5-9	1.19 (0.73, 1.94), 0.65
10-19	1.17 (0.76, 1.81), 0.64
20 or more	0.86 (0.58, 1.28), 0.63
Practicing in hospital	**0.41 (0.26, 0.65), 0.01**
Practicing in nursing home	**0.36 (0.14, 0.94), 0.17**
Practicing in home setting	1.73 (0.77, 3.87), 0.38
Practicing in other settings (clinic or day care)	0.72 (0.48, 1.08), 0.31
Personal experience with dementia at the end of life (no as reference)	0.90 (0.62, 1.31), 0.71
Most strongly considered perspective relating to goals of future care for people with dementia (patient as reference)	
Family	**0.41 (0.19, 0.90), 0.15**
Myself as physician	0.67 (0.28, 1.59), 0.55
Don't know	**4.41 (1.49, 13.08), 0.08**
Comfort talking about the end of life in general	0.82 (0.65, 1.03), 0.27
Internal locus of control	**1.21 (1.03, 1.42), 0.13**
External locus of control	1.00 (0.86, 1.17), 0.97
Illness cognition	1.00 (0.92, 1.09), 0.95

for people with dementia from clinicians' perspective	Willingness to use euthanasia upon request of people with dementia	
Random effect (level 2: country)	**Fixed effect (level 1)**	**Random effect (level 2: country)**
Variance (SE) of intercept	OR (80% CI)*, *p*-value	Variance (SE) of intercept
0.22 (0.47)	**0.98 (0.96, 1.00), 0.10**	0.24 (0.49)
0.22 (0.47)	1.21 (0.81, 1.80), 0.53	0.24 (0.49)
0.23 (0.49)	**2.16 (1.39, 3.36), 0.03**	0.27 (0.52)
0.14 (0.38)	1.51 (0.89, 2.55), 0.31	0.37 (0.60)
0.20 (0.45)	**0.53 (0.36, 0.78), 0.03**	0.18 (0.43)
0.19 (0.44)	1.08 (0.82, 1.42), 0.72	0.24 (0.49)
0.21 (0.45)	0.99 (0.97, 1.01), 0.46	0.25 (0.50)
0.23 (0.48)		0.19 (0.44)
	1.36 (0.80, 2.30), 0.46	
	1.44 (0.89, 2.34), 0.34	
	0.96 (0.61, 1.51), 0.90	
	1.97 (1.32, 2.94), 0.03	
0.00 (0.00)	**0.56 (0.36, 0.88), 0.10**	0.00 (0.00)
0.17 (0.42)	**0.40 (0.16, 0.98), 0.19**	0.23 (0.48)
0.51 (0.71)	0.52 (0.23, 1.18), 0.31	0.15 (0.39)
0.18 (0.43)	**0.60 (0.39, 0.91), 0.13**	0.16 (0.40)
0.21 (0.46)	1.15 (0.78, 1.69), 0.64	0.24 (0.48)
0.16 (0.39)		0.22 (0.47)
	1.00 (0.49, 2.06), 1.00	
	1.05 (0.46, 2.40), 0.94	
	1.08 (0.43, 2.73), 0.91	
0.20 (0.45)	0.97 (0.77, 1.23), 0.88	0.22 (0.47)
0.21 (0.46)	1.00 (0.85, 1.18), 1.00	0.22 (0.47)
0.22 (0.47)	1.11 (0.95, 1.30), 0.42	0.20 (0.45)
0.22 (0.47)	0.96 (0.88, 1.05), 0.55	0.21 (0.46)

Supplementary Table S4 Bivariable associations between clinician's personal characteristics and acceptability of euthanasia, adjusted for clustering of country (continued)

	Acceptability of euthanasia
Personal characteristics	**Fixed effect (level 1)**
Attitude towards death	
Death anxiety	1.00 (0.94, 1.07), 0.98
Fear of death	0.89 (0.73, 1.08), 0.45
Avoidance of death	**1.26 (1.02, 1.55), 0.15**
Neutral acceptance of death	**1.27 (1.04, 1.55), 0.12**
Convergent acceptance of death	**0.87 (0.77, 0.98), 0.14**
Escapist acceptance of death	0.87 (0.73, 1.04), 0.33
Coping style	
Active coping	0.89 (0.75, 1.05), 0.38
Planning	**0.79 (0.67, 0.93), 0.06**
Use of instrumental social support	**0.82 (0.72, 0.94), 0.07**
Use of emotional social support	**0.84 (0.74, 0.96), 0.09**
Denial	**0.78 (0.62, 0.98), 0.15**
Acceptance	0.99 (0.85, 1.15), 0.95
Religious coping	**0.71 (0.64, 0.79), <0.001**

*80% confidence interval was reported because the variables were selected for the backward regression based on the criteria $p < 0.20$. Results with $p < 0.20$ are bolded.

for people with dementia from clinicians' perspective	Willingness to use euthanasia upon request of people with dementia	
Random effect (level 2: country)	**Fixed effect (level 1)**	**Random effect (level 2: country)**
0.22 (0.47)	1.01 (0.94, 1.08), 0.91	0.23 (0.48)
0.20 (0.45)	0.84 (0.69, 1.03), 0.25	0.21 (0.46)
0.27 (0.52)	**1.25 (1.02, 1.54), 0.17**	0.26 (0.51)
0.22 (0.47)	1.20 (0.98, 1.47), 0.25	0.22 (0.47)
0.21 (0.46)	**0.82 (0.72, 0.93), 0.04**	0.24 (0.49)
0.21 (0.46)	1.10 (0.92, 1.31), 0.49	0.22 (0.47)
0.21 (0.45)	0.85 (0.72, 1.01), 0.21	0.21 (0.46)
0.18 (0.42)	0.86 (0.73, 1.01), 0.24	0.18 (0.43)
0.19 (0.44)	**0.85 (0.74, 0.98), 0.12**	0.20 (0.45)
0.20 (0.45)	**0.76 (0.66, 0.87), 0.01**	0.19 (0.44)
0.17 (0.41)	**0.77 (0.61, 0.97), 0.14**	0.19 (0.44)
0.22 (0.47)	1.09 (0.94, 1.27), 0.46	0.22 (0.47)
0.20 (0.45)	**0.77 (0.69, 0.86), 0.002**	0.23 (0.48)

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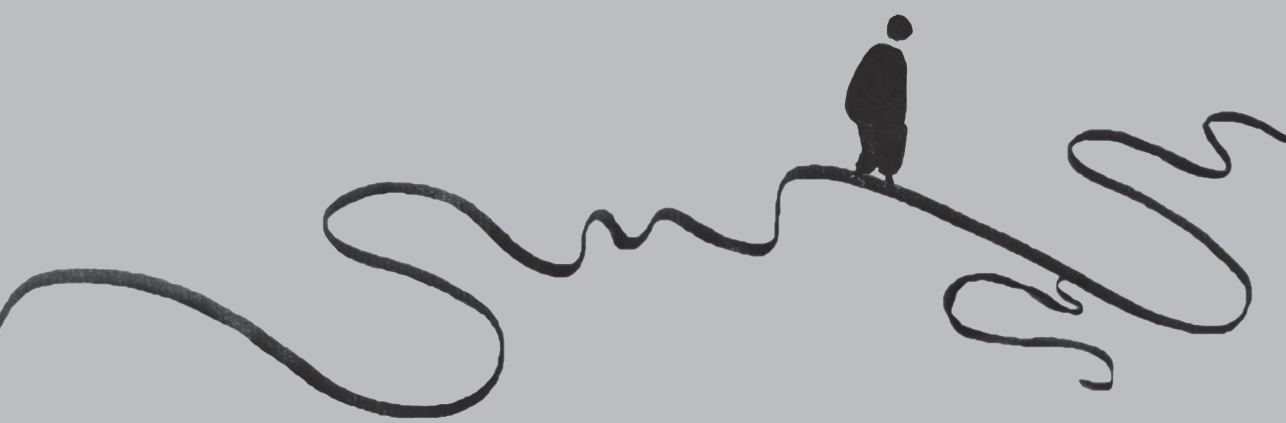

Noninvasive monitoring technologies to identify discomfort and distressing symptoms in persons with limited communication at the end of life: A scoping review

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Abstract

Background: Discomfort and distressing symptoms are common at the end of life, while people in this stage are often no longer able to express themselves. Technologies may aid clinicians in detecting and treating these symptoms to improve end-of-life care. This review provides an overview of noninvasive monitoring technologies that may be applied to persons with limited communication at the end of life to identify discomfort.

Methods: A systematic search was performed in nine databases, and experts were consulted. Manuscripts were included if they were written in English, Dutch, German, French, Japanese or Chinese, if the monitoring technology measured discomfort or distressing symptoms, was noninvasive, could be continuously administered for 4 hours and was potentially applicable for bed-ridden people. The screening was performed by two researchers independently. Information about the technology, its clinimetrics (validity, reliability, sensitivity, specificity, responsiveness), acceptability, and feasibility were extracted.

Results: Of the 3,414 identified manuscripts, 229 met the eligibility criteria. A variety of monitoring technologies were identified, including actigraphy, brain activity monitoring, electrocardiography, electrodermal activity monitoring, surface electromyography, incontinence sensors, multimodal systems, and noncontact monitoring systems. The main indicators of discomfort monitored by these technologies were sleep, level of consciousness, risk of pressure ulcers, urinary incontinence, agitation, and pain. For the end-of-life phase, brain activity monitors could be helpful and acceptable to monitor the level of consciousness during palliative sedation. However, no manuscripts have reported on the clinimetrics, feasibility, and acceptability of the other technologies for the end-of-life phase.

Conclusions: Noninvasive monitoring technologies are available to measure common symptoms at the end of life. Future research should evaluate the quality of evidence provided by existing studies and investigate the feasibility, acceptability, and usefulness of these technologies in the end-of-life setting.

Guidelines for studies on healthcare technologies should be better implemented and further developed.

Introduction

Discomfort and distressing symptoms in the last two weeks of life are common. (1-6) Based on reviews of people dying with dementia and cancer, many may experience pain (12%-96%), difficulty breathing (8%-83%), fatigue (22%-93%), incontinence (32%-65%), and anxiety (6%-57%). (2, 6) Studies in intensive care units (ICU), hospital general wards, nursing homes, and among the general public reported similar percentages of these symptoms, with the addition of agitation (12% - 71%), (4, 5, 7) sleep disturbances (18% - 56%), (7, 8) nausea (9% - 59%), (4, 8) delirium (75% - 91%), (3, 9, 10) fever (16% - 61%), and (4, 8) pressure sores (16% - 42%). (3, 4) To relieve health-related suffering at the end of life, which is a core task of palliative care, (11) it is essential to identify these distressing symptoms in a timely manner.

However, timely recognition of discomfort and distressing symptoms may be challenging at the end of life. People who are dying may have difficulties expressing their discomfort due to fatigue, sedation, delirium, cognitive impairment, loss of consciousness or communication problems such as aphasia. (6, 12, 13) In current practice, the identification of discomfort and distressing symptoms relies upon observations of professional caregivers and family. (14) However, observation may not be the most accurate measurement of discomfort (15, 16), and continuous observation of discomfort by staff is not feasible, (17) so alternatives are needed. Implementing noninvasive monitoring technologies may aid in the early detection of discomfort and distressing symptoms at the end of life.

Various technologies that monitor distressing symptoms have already been developed, for example, actigraphy to monitor agitation, (19) systems to detect stress based on facial expressions,(20) and various devices to monitor nociception. (21) In addition to directly monitoring distressing symptoms, monitoring technologies such as the bispectral index (BIS) may also help detect discomfort by monitoring the level of consciousness of people who receive palliative sedation due to refractory distress. (22-24) However, knowledge

about which technologies may be useful in the end-of-life context is lacking because most of these technologies have not been specifically developed for this setting, and previous reviews mainly focused on populations that were still mobile (25-28) and could self-report their symptoms. (29, 30)

This review aims to generate an overview of noninvasive monitoring technologies that may be applied to people with limited communication at the end of life to identify discomfort and distressing symptoms. The results may provide a useful reference for clinicians who consider implementing technology in the end-of-life care of people with limited communication. Our main research question was: What noninvasive monitoring technologies are described in the literature that may be useful in identifying discomfort and distressing symptoms in persons with limited communication at the end of life? The subquestions were as follows: 1) What noninvasive monitoring technologies are available or under development that identify discomfort and distressing symptoms which can occur at the end of life, 2) What is known about the clinimetric properties (e.g., validity, reliability, sensitivity, specificity, responsiveness) of these technologies, and 3) What is known about the acceptability and feasibility of these technologies for persons with limited communication?

Methods

A scoping review was chosen since the goal was to provide a broad view of technologies to identify discomfort and distressing symptoms in persons with limited communication at the end of life rather than to generate clinical guidance for a specific technology. (31, 32) This review was conducted in accordance with the Joanna Briggs Institute methodology for scoping reviews and reporting followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses extension for scoping review (PRISMA-ScR) checklist. (33) The protocol for this scoping review was registered in the Open Science Framework (24 February 2022, Registration number: E6M8B). (34)

Search Methods

Manuscripts were included if they described a noninvasive technology that may be used to continuously (i.e., for at least 4 hours) monitor discomfort

and distressing symptoms in people at the end of life. The technology needed to serve as a direct or indirect measure of discomfort, potentially distressing symptoms, or level of consciousness. In studies with human subjects, participants must be at least 18 years old. The manuscript had to be written in English, Dutch, German, French, Japanese, or Chinese. The manuscript was excluded if the monitoring technology fully relied on self-report, was applied in the study to all participants during an invasive procedure only, was applied in infants or children only, it was an animal study or a review, no information on the technology was provided, or if the full text article was not available. Technologies that were judged by the screening researchers as not applicable to bed-ridden persons were also excluded, for example technologies that require input from a GPS tracker or step counts. People with limited communication at the end of life include persons who have difficulties expressing their discomfort due to fatigue, sedation, cognitive impairment, or communication problems (e.g. aphasia).(12) This is operationalized in the search by also including populations in similar situations as people with limited communication at the end of life, where they are bedridden and noncommunicative, for example people with dementia, aphasia, profound intellectual disability, and people in critical care. Noninvasive is defined in this review as no penetration in the body of the person with solid material, while weak electric currents, weak laser lights or ultrasounds may be used. (18)On 16 March 2021, a search was conducted in PubMed, MEDLINE (OVID), Embase (OVID), Emcare (OVID), Web of Science, Cochrane Library, PsycINFO (EbscoHOST), Academic Search Premier (EbscoHOST), and Google Scholar. On 23 February 2023, an update search was performed in the same databases. In cooperation with a trained librarian (JWS), a detailed search strategy was composed. The query consisted of the combination of the following three concepts:

- death, end-of-life phase, terminal care, elderly, critical care, profound disability, bedridden persons, nonmobile persons, dementia, aphasia
- activity monitors, activity trackers
- (dis-)comfort, distress, agitation, pain assessment, pressure ulcers, quality of life, breathing difficulty, anxiety, sleep disturbances, fatigue, nausea, delirium, fever, incontinence, sedation depth

For these concepts, all relevant keyword variations were used, not only keyword variations in the controlled vocabularies of the various databases but also the free text word variations of these concepts. The search strategy was optimized for all consulted databases, taking into account the differences in the various controlled vocabularies as well as the differences in database-specific technical variations (e.g., the use of quotation marks). The complete search strategy is available as an appendix to the registered protocol. (34) After data extraction, six experts were consulted for additional, potentially missing information about new technologies under development. The experts were from the Interdem Taskforce Assistive Technologies and professional network of the authors.

Source of evidence screening and selection

After removing duplicates, each title and abstract was independently screened by two researchers. Full-text articles were retrieved after the first screening round, and each article was assessed for eligibility by two independent reviewers. Consensus meetings were held to discuss discrepancies.

Data extraction

Data extraction was performed using a form developed and pilot-tested by the research team. Extracted data were checked by a second researcher, and regular consensus meetings were held to discuss doubts and discrepancies. The following data were extracted from the included articles: author, year of publication, language, country, participants, type of technology, model and brand, and indicators of discomfort monitored by the technology. For studies that described the development of a technology, the aim of the study and the details of the technology (e.g., sensors, parameters) were extracted. For studies mentioning clinimetrics, acceptability, or feasibility of the technology, this information was also extracted, together with the study design and other instruments that were used in the study. The extracted data were then synthesized into tables and narrative summaries for each type of technology. An often used threshold for acceptable clinimetrics is at least 70% for sensitivity, specificity, and area under the curve (AUC). (35, 36)

Results

The flow chart of the screening process is presented in Figure 1. A total of 229 manuscripts were included. Table 1 shows that most manuscripts were written in English by researchers in North America or Europe. The number of publications on this topic has shown exponential growth over the past 3 decades. Based on the bodily functions and signals that are measured, the monitoring technologies included in this review were grouped into 8 categories, of which actigraphy and multimodal systems such as polysomnography accounted for more than half of the included manuscripts. Table 2 lists the identified monitoring technologies for each indicator of discomfort. Multiple technologies measured sleep, pain, and agitation. No technologies monitored difficulty breathing, nausea, or fever. Many monitored sleep disordered breathing, but not the subjective experience of difficulty breathing.

We briefly illustrate each type of monitoring technology and the main findings from the studies regarding the clinimetrics (see Supplement I), acceptability, and feasibility (see Supplement II). Supplement III summarizes manuscripts that did not report clinimetrics, acceptability, or feasibility, mainly because the technology was implemented as standard measurement instruments. The models and brands of the technologies, the settings and the study populations are listed in Supplements I-III.

Actigraphy

Actigraphy uses accelerometers to measure movements with a band or pads that are attached to the wrist, ankle, neck, mattress, (37) or integrated in a garment. (38) The data are usually processed by built-in software. Several researchers developed their own algorithms with machine learning to analyze the construct of interest, for example, agitation, body position or sleep/wake states, using movement data. (38-40) In approximately half of the manuscripts, actigraphy was used as a standard measurement for sleep. When discrepancies were observed between actigraphy results and observations or self-reports, authors of recent manuscripts favored actigraphy as a standard, objective measurement. (41, 42)

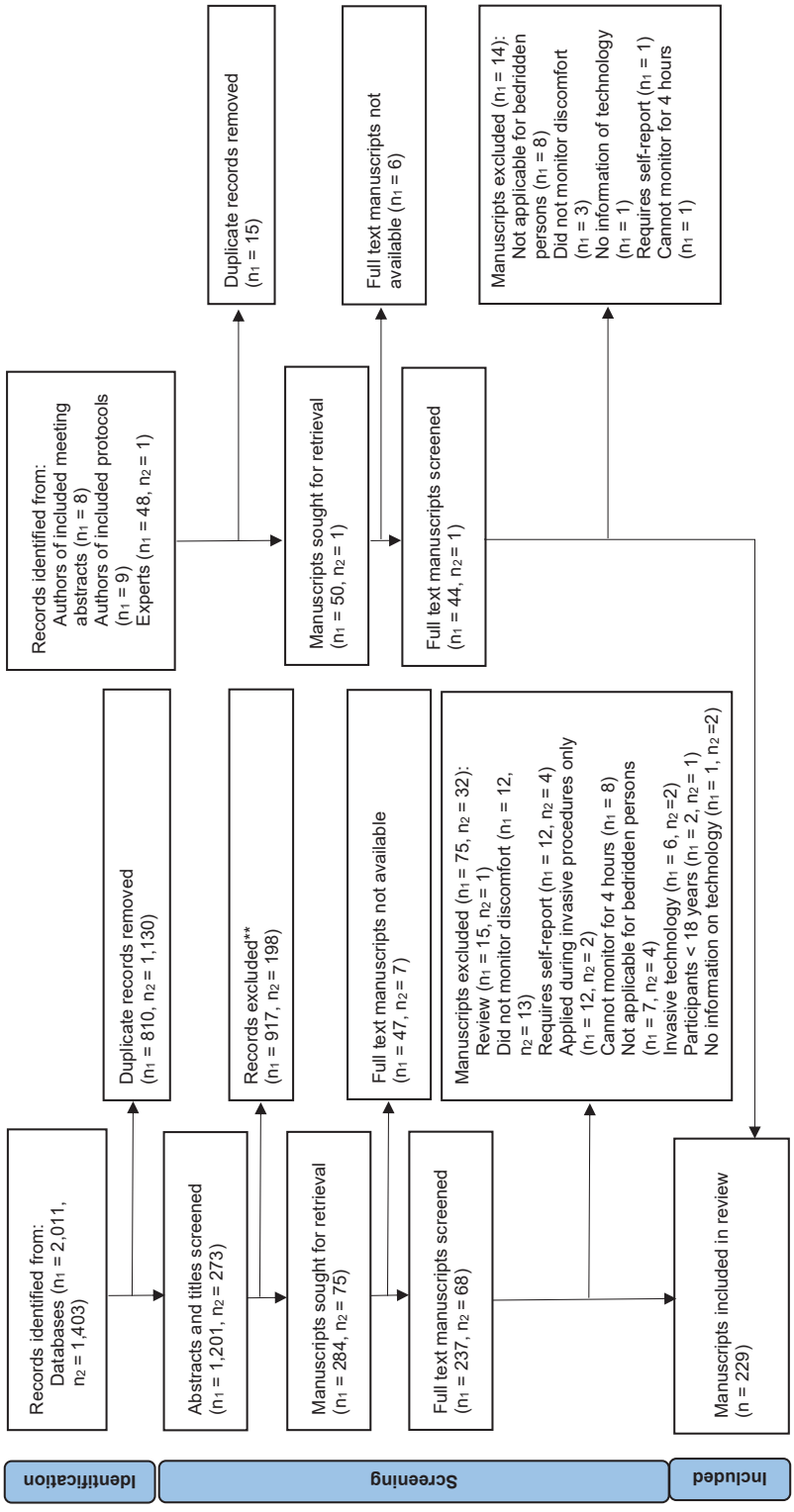

Figure. 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram.

Note: n_1 = first search in 2021, n_2 = update search in 2023

Table 1 Typology of the included manuscripts

	Number of manuscripts	Percentage
Languages		
English	220	96%
Chinese	4	2%
Dutch	2	1%
Japanese	2	1%
German	1	<1%
Countries		
United States of America	63	28%
Canada	13	6%
Netherlands	12	5%
Italy	11	5%
France	9	4%
Germany	9	4%
Japan	9	4%
Australia	8	3%
United Kingdom	8	3%
Belgium	7	3%
China	7	3%
South Korea	7	3%
Finland	5	2%
Spain	5	2%
Switzerland	3	1%
Brazil	2	1%
Denmark	2	1%
India	2	1%
Greece	2	1%
Mexico	2	1%
New Zealand	2	1%
Portugal	2	1%
Singapore	2	1%
Other countries	8	3%
Two or more countries[a]	29	13%

Table 1 Typology of the included manuscripts (continued)

	Number of manuscripts	Percentage
Year of publication		
1991-1995	4	2%
1996-2000	13	6%
2001-2005	15	7%
2006-2010	31	14%
2011-2015	41	18%
2016-2020	79	25%
2021-2023[b]	46	20%
Monitoring technologies		
Actigraphy	57	25%
Brain activity monitors	25	11%
Bispectral Index (BIS)	15	
Other Electroencephalography (EEG)-based[c, d]	9	
Sedation monitor (concept)	1	
Electrocardiography (ECG)[c]	12	5%
Electrodermal activity (EDA) monitor	8	3%
Surface electromyogram (sEMG)	2	1%
Incontinence sensors	11	5%
Multi-modal systems[e]	96	42%
Polysomnography (PSG)	75	
With environmental sensors	6	
Other multi-modal systems	14	
Non-contact monitoring systems[f]	21	9%
Pressure mats	9	
Video/facial expression analysis	4	
Infrared	2	
Radar	3	
Multiple sensors	3	

Table 1 Typology of the included manuscripts (continued)

	Number of manuscripts	Percentage
Aim of studies[g]		
No technology-related aims (the technology is applied as standard measurement)	91	39%
Development of the technology	38	17%
Feasibility/pilot study of the technology	51	22%
Validation of the technology	65	28%

Note: Total number of included manuscripts = 229.
[a]The main countries involved were the USA (11 manuscripts), China (8 manuscripts), Finland (6 manuscripts), and the Netherlands (6 manuscripts). The countries involved in specific manuscripts can be found in etables 1-3 in the supplements.
[b]Manuscripts published before March 13, 2023 were included.
[c]3 manuscripts used both Electroencephalography and Electrocardiography to monitor people under sedation.
[d]Other electroencephalogram-based technologies refer to traditional EEGs and other technologies which use EEG electrodes.
[e]Multi-modal systems use a combination of different technologies within one integrated system or algorithm.
[f]Non-contact monitoring systems use sensors that do not have direct contact with the person being monitored.
[g]16 articles had multiple aims.

Table 2 Summary of monitoring technologies per indicator of discomfort

Indicator of discomfort	Types of monitoring technology[a]
Vital signs	Multi-modal systems[b] – other multi-model systems Non-contact monitoring systems[c] – radar
Arrhythmia	Electrocardiography (ECG)
Consciousness/depth of sedation	Actigraphy Brain activity monitors - bispectral index scale (BIS) Brain activity monitors – other electroencephalogram (EEG)-based technologies
Sleep, including sleep disordered breathing	Actigraphy Brain activity monitors - BIS Brain activity monitors – other EEG-based technologies ECG Multi-modal systems[b] – PSG Multi-modal systems[b] – with environmental sensors Multi-modal systems[b] – other multi-model systems Non-contact monitoring systems[c] – pressure mats Non-contact monitoring systems[c] – infrared Non-contact monitoring systems[c] – radar Non-contact monitoring systems[c] – multiple sensors
(Risk of) pressure ulcers	Actigraphy Non-contact monitoring systems[c] - pressure mats
Urinary incontinence	Incontinence sensors Multi-modal systems[b] – with environmental sensors
Pain	Brain activity monitors - BIS Brain activity monitors – other EEG-based technologies ECG Electrodermal activity (EDA) monitor Surface electromyogram (sEMG) Multi-modal systems[b] – other multi-model systems Non-contact monitoring systems[c] – video/facial expression analysis
Agitation	Actigraphy Multi-modal systems[b] – with environmental sensors Multi-modal systems[b] – other multi-model systems Non-contact monitoring systems[c] – video/facial expression analysis Non-contact monitoring systems[c] – multiple sensors
Anxiety	ECG Multi-modal systems[b] – with environmental sensors Multi-modal systems[b] – other multi-model systems

Table 2 Summary of monitoring technologies per indicator of discomfort (continued)

Indicator of discomfort	Types of monitoring technology[a]
Stress	Actigraphy Brain activity monitors – other EEG-based technologies ECG EDA monitor Multi-modal systems[b] – other multi-model systems
Significant moments	Multi-modal systems[b] – other multi-model systems
Emotions	Non-contact monitoring systems[c] – video/facial expression analysis
(Motor subtypes of) delirium	Actigraphy Brain activity monitors - BIS Brain activity monitors – other EEG-based technologies Multi-modal systems[b] – with environmental sensors Multi-modal systems[b] – other multi-model systems
Thermal comfort	Non-contact monitoring systems[c] – infrared
Mental fatigue	Multi-modal systems[b] – other multi-model systems

Note: [a]Cateogries and subcategories (if applicable) of technologies are presented.
[b]Multi-modal systems use a combination of different technologies within one integrated system or algorithm.
[c]Non-contact monitoring systems use sensors that do not have direct contact with the person being monitored.

Clinimetrics

Although there were some mixed results for different models of actigraphy, showing that it could underestimate sleep time in the ICU (40) or overestimate this in people with Huntington's or Alzheimer's Disease compared to polysomnography, (43, 44) and it could be less accurate when the participants had sleep disordered breathing, (45) in general, it demonstrated acceptable sensitivity and specificity of identifying sleep-wake states in ICU patients (40), older adults in nursing homes (46) and people with dementia. (47)

Actigraphy measurement could recognize agitated behaviors (39), distinguish between groups of higher and lower agitation in people with dementia in long-term care facilities or hospital, (48, 49) and was correlated with observational scales for agitation such as the Cohen-Mansfield Agitation Inventory in people with dementia. (49, 50) The correlation with the Neuropsychiatric Inventory was found only in some articles (49) but not in others (48). Among nursing home residents with dementia, actigraphy

demonstrated acceptable discriminant validity compared with the Mini-Mental State Examination, which measured a different concept. (51) Most of these studies were performed in people with dementia who were still mobile. In one study among ICU patients, who may be more similar to people at the end of life, actigraphic data also correlated with observations of agitation using the Richmond Agitation Sedation Scale. (52)

The devices had good precision and sensitivity when used to monitor the risk of pressure ulcers in the hospital (38) and could reduce the chances of patients developing pressure ulcers in the ICU. (53) Actigraphy could recognize stress in nursing home residents with acceptable accuracy but lower precision and sensitivity. (54)

In summary, for populations that are similar to people at the end of life, actigraphy has demonstrated good clinimetrics in monitoring sleep, agitation, and risk of pressure ulcers but is not precise in recognizing stress.

Feasibility and acceptability

Actigraphy was feasible for multiday continuous measurement of older adults with intellectual disability (55) and people with dementia. (49) Although community-dwelling older adults found it easy to use, (56) it can be confusing for some people with less cognitive capacity. (57) The battery life could also be improved. (44, 56) No manuscripts reported on the feasibility and acceptability of actigraphy in bed-ridden participants with limited communication.

Brain activity monitors

Electronic activity of the brain can be measured by electroencephalography. It traditionally uses electrodes with gel attached to the head. Portable versions with few electrodes have been developed. (58)

Bispectral Index (BIS)

BIS is a specific type of device that uses EEG signals to measure the depth of sedation. BIS consists of a sticker on the forehead with four EEG electrodes connected to a small monitor that displays a number ranging from 0 to 100. It has been implemented in the ICU and palliative care units. (59, 60)

Clinimetrics

Sedation indices measured by BIS correlated with those measured by standard EEG in the ICU. (61) BIS scores increased during painful procedures in patients with traumatic brain injury in the ICU (62). It also correlated with PSG and could discriminate between deep and light sleep in healthy adults; (63) however, it was only weakly correlated with self-reported sleep quality in ICU patients. (64) BIS monitoring with density spectral was tested for the detection of delirium in hospitals. Its accuracy was comparable to that of the 3-minute Diagnostic Interview for Confusion Assessment Method and was more accurate in people with dementia than in those without cognitive impairment. (65)

In summary, limited research has been performed on the clinimetrics of BIS. The preliminary results showed that it may have the potential to detect pain and delirium, as well as to monitor sedation and sleep. (61-65)

Feasibility and acceptability

In a study in the ICU, BIS was deemed not possible to implement in a quarter of the eligible participants due to delirium, other medical procedures, discomfort of the sensors or displacement of the sensors. (64) One case study suggested that BIS was helpful for nurses to titrate medication for palliative sedation in the ICU and to educate the family. It reassured the family that the patient died comfortably, and they were pleased to see BIS fluctuations when talking to the patient. (66) Thus, BIS is not always feasible, but it can be acceptable and helpful when it is.

Other electroencephalography (EEG)-based technologies

In recent years, EEG sensors have been developed into more user-friendly forms of dry electrodes, (58) a headband (67) or an earplug. (68) In two older studies, EEG was used to objectively measure sleep. (69, 70) Two recent studies used EEG to objectively monitor the depth of sedation. (71, 72)

Clinimetrics

Compared to PSG, EEG-based technologies showed good accuracy in determining sleep stages in healthy adults (68) and could distinguish sleep and

wake in ICU patients. (73) Good AUC was reported for delirium diagnosis in the ICU. (74) Preliminary results showed differences in EEG signals during stress in healthy adults (67) and pain in people with dementia residing in long-term care settings. (58)

Feasibility and acceptability
A portable device to measure sleep was deemed feasible in the ICU. (73) An EEG-based headband was acceptable for long-term care residents with dementia, while properly positioning the device was challenging. (58) No manuscript reported on the acceptability of other EEG-based technologies.

The concept of sedation monitors

Feasibility and acceptability
An interview study showed that family and professional caregivers considered it acceptable to use monitors during palliative sedation as an objective measurement of sedation and pain, which could reassure the family and guide titration. (75)

Electrocardiography (ECG)
ECG is the measurement of the electronic activity of the heart. Traditionally, electrodes are attached to the torso and connected to a monitor. Among the manuscripts included in this review, the number of electrodes varied between 3 and 12, and the devices could be portable. (76, 77) Heart rate data can also be extracted from smart watches. (78) ECG was used as a standard measurement for arrhythmia (79) and stress. (78, 80, 81)

Clinimetrics
Indices derived from ECG signals correlated with self-rated pain among patients taking physical therapy after surgery (76) and sleep apnea among people with suspected sleep disordered breathing measured by standard PSG. (77) When ECG indications of pain differed from observation, a recent study with patients under palliative sedation favored the ECG measurement and concluded that it was more objective. (72) No studies reported the clinimetrics of ECG in people at the end of life.

Feasibility and acceptability

It was feasible to use ECG to monitor stress in the workplace. (82) After surgery, patients were more satisfied with ECG monitoring for atrial fibrillation than observation. (83)

Electrodermal activity (EDA) monitors

By placing electrodes on the skin, electrodermal activity monitors measure the skin conductance, which drops as the sweat glands are activated by the sympathetic nervous system, indicating stress. (84) It is best measured at the palms and feet, where the sweat glands are dense. An older version of the portable EDA monitor included sensors on two fingers and hardware bound to the arm, (84) while newer versions can take the form of a ring (85) or a sock. (86) EDA monitors have been tested with healthy adults and people in the ICU.

Clinimetrics

EDA measurement has been shown to be more sensitive than vital signs and BIS measurements in detecting pain in sedated patients in the ICU. (87) Among healthy volunteers, tt had good sensitivity, specificity and accuracy in detecting stress (86, 88) and could discriminate between stress and cognitive load. (84)

Feasibility and acceptability

EDA sensors integrated into the sock were feasible for most participants in a study with intellectual disabilities. (88) Factors that hindered the implementation were other garments, such as compression socks, and the participants removing the device.

Surface electromyography (sEMG)

Surface electromyography monitors muscle activity by attaching electrodes on the surface of the skin. Sensors of an older version needed to be attached to a monitor, which hanged in a holster at the waist. (89) A new device integrated multiple sensors into one soft mask and used Wi-Fi to transfer data directly

from the sensor nodes to the server. (90) Only two studies on sEMG were identified in this review.

Clinimetrics

sEMG signals at the shoulder did not seem to be different for people experiencing cervical pain from those without pain. (89) However, facial expressions monitored by sEMG were different for neutral and painful faces in the laboratory setting. (90)

Feasibility and acceptability

No manuscripts have reported on the feasibility and acceptability of sEMG.

Incontinence monitors

Incontinence monitors are systems to monitor urinary incontinence events so that caregivers would only need to change the incontinence materials when an event takes place. Sensors measuring moisture or temperature change are attached to or built into incontinent materials. One device integrated the sensors into the fabric of a mat on top of the mattress. (91) The more recent and commercially available sensors are usually disposable. Data can be transmitted wirelessly to a web portal or mobile app.

Clinimetrics

Although there seemed to be high false positive and false negative rates in earlier systems tested in the laboratory and acute care rehabilitation wards for older adults, (92, 93) more recent manuscripts reported favorable results in the laboratory setting. (94) The incontinence monitors could also reduce urine leakage and the use of incontinence materials in nursing homes. (95, 96) However, some of these reports may need to be interpreted with caution since they were published by the manufacturers.

Feasibility and acceptability

The incontinence sensors did not seem to disturb the patients since they reported not feeling the sensors in laboratory tests. (92) An earlier system was challenging to implement due to several technical problems and the

unwillingness of experienced staff to change their routine in rehabilitation wards. (93) A recent pilot study reported positive reactions of family caregivers and staff in nursing homes. They appreciated the fact that the device helped save time and reduced the occasions where the clients were disturbed unnecessarily. (96)

Multimodal systems

Systems combining different sensors that monitor different bodily functions are grouped into the category multimodal systems.

Polysomnography (PSG)

Standard polysomnography uses multiple parameters (EEG, electro-oculogram, EMG, ECG, oxygen saturation, body position, snoring, airflow and breathing measurements) to monitor sleep. (97) It is considered the gold standard for diagnosing disordered breathing during sleep (e.g., obstructive sleep apnea), which is how it was used in most included manuscripts. Traditionally, PSG is administered by a technician at a sleep laboratory, but portable home monitoring systems have been developed, using only some of the sensors to monitor sleep quality or breathing. (98-100) New portable systems can take the form of a headband, (101) a wristband, (102) a collar around the neck, (103) or a ring. (104) PSG has been used in diverse populations, including adults with sleep problems and nursing home residents with dementia.

Clinimetrics

Portable PSG systems were reported to have good reliability, sensitivity and specificity in diagnosing obstructive sleep apnea among outpatients with heart or lung problems compared with standard PSG (98, 103, 105, 106) but may produce false positives when compared with clinician judgment in the post anesthesia care unit (107) or may produce false negatives when compared with traditional PSG among people using positive airway pressure. (108) It was recommended to lower the cutoff score when using portable PSG to detect hypopnea events. (108) Minute ventilation, measuring the tidal volume and respiration rates with only two chest leads, was effective in detecting respiratory depression in the post anesthesia care unit. (100) With the help of machine

learning models, new potable PSG systems have also demonstrated accuracy in measuring sleep stages in healthy adults. (104) In summary, portable PSG systems had good clinimetrics in monitoring sleep disordered breathing and sleep stages.

Feasibility and acceptability

Portable PSG systems may have occasional technical failure (109-111) but were evaluated as easy to use, comfortable, and did not interfere with sleep among healthy adults, those with sleep apnea, and people with bipolar disorder. (111-113)

With environmental sensors

In recent years, environmental sensors to assess light, sound, humidity, and barometric pressure have been combined with actigraphy to monitor agitation and uncover its environmental determinants in people with dementia in their homes or institutions. (114-116) Sometimes cameras (116, 117), door sensors, pressure mats, and EDA sensors (116) were also used in the systems. Other systems monitored anxiety, (118) delirium, (117) sleep, and urinary incontinence (119). In most of the included manuscripts, data from the various sensors were not yet integrated in a system and needed to be synchronized and processed by the researchers. These systems have been tested with people with dementia and older adults in the ICU.

Clinimetrics

Factors associated with agitation or delirium were identified. For people with dementia, environmental factors (i.e., temperature, pressure, and humidity) strongly correlated with agitation annotated by nurses or family caregivers, although the predictors were specific to each participant. (115) Another study indicated that the combination of actigraphy, skin temperature, and EDA data predicted agitation the best for people with dementia. (116) In the ICU, older adults with delirium differed from those without delirium in facial expressions, movements, postures, visitation frequency, environmental light and sound at night. (117)

Feasibility and acceptability

Studies concluded that their systems were feasible for monitoring people with dementia at a rehabilitation institute (116) and critically ill patients in the ICU. (117) The challenges were Wi-Fi connections (114), trouble-shooting for the installation via the phone, (119) and that people with dementia can take off the sensors when agitated. (120)

Other multimodal systems

Several systems combined ECG, respiration monitors, EDA, sEMG, skin temperature, and breath temperature to monitor the activation of the sympathetic nervous system, which was indicative of pain, (121) mental stress, (122) anxiety, (123) agitation, (124) or significant moments (125) in different studies. In most studies, the sensors were implemented separately, but several studies integrated the sensors into a chest belt, (124) a wristband, (126) or a system worn on the fingertip. (125) New algorithms for analyzing the data were proposed. (127) These multimodal systems have mainly been tested in the laboratory with healthy adults (128, 129) but also with older adults with or without dementia. (124, 125)

Clinimetrics

The multimodals systems could produce accurate measurements of physiological signals, such as ECG, photoplethysmography and respiration signals, changes in heart rate, skin temperature, and EDA, similar to conventional instruments in adults and older adults tested in the laboratory setting. (124, 129) Compared with self-report, the systems had an acceptable accuracy in classifying pain into three severity categories in healthy adults in the laboratory, (121) had good clinimetrics in detecting moderate to severe pain among patients in the ICU, but the results were not optimal when the pain was milder. (130) They could detect significant moments, (125) agitation and aggression in people with dementia, (126, 131) and correlated with mental fatigue (132) and stress in healthy adults. (122, 128) One system could indicate anxiety with high precision but low specificity compared to self-report and observation in healthy adults. (123) In summary, multimodal systems had

good clinimetrics in detecting pain and had some preliminary positive results in monitoring agitation and stress.

Feasibility and acceptability
A chest belt integrating EDA, heart rate, and skin temperature measurements was rated by community-dwelling older adults with a score of 2.7 out of 3 for appearance and 2.8 out of 3 for comfortability. (124) In another study with healthy adults in the laboratory, the authors reported EEG signals to be poor when participants moved. (123)

Noncontact monitoring systems

Pressure mats
Pressure mats are mattresses or films with integrated sensors (e.g., piezoelectric sensors(133)) to measure pressure. They do not need to have direct contact with the person since they can be used under a mattress topper or sheet. Pressure mats can be used to measure the body position and movement on the bed, which can be useful for preventing pressure ulcers. (134) Micromovements measured by pressure mats can be used to monitor sleep stages and sleep disordered breathing. (135, 136) Pressure mats have been tested with healthy adults in the laboratory and were implemented as standard measurements in nursing home residents with dementia, people with sleep apnea, and patients in the ICU and intermediate care units.

Clinimetrics
While older models of pressure mats needed the addition of a percutaneous oxygen saturation sensor to accurately detect sleep disordered breathing, (137) a new model was very accurate on its own compared to PSG in the laboratory among outpatients with sleep problems. (133) Clinimetrics of the pressure mats in measuring other indicators of discomfort were not reported in the included manuscripts.

Feasibility and acceptability
A study in 2009 showed that pressure mats were feasible to use in the ICU for 48 hours. (138)

Video/facial expression analysis

Several algorithms have been developed to recognize agitation, emotions, and pain by analyzing videos taken by commercially available cameras. Using remote photoplethysmography (rPPG), some systems can also estimate heart rhythm based on the change in light transmission and reflection of the skin due to changes in blood flow. (139)

Clinimetrics

The systems could detect faces and facial expressions most of the time, even when they were moving, as in simulated videos, (140) or partially covered, as during group activity with people with Mild Cognitive Impairment. (141). They could recognize grimaces in simulated videos and emotions in people with mild cognitive impairment and were moderately to highly correlated with manual scoring of pain based on facial expressions in community-dwelling older adults and nursing home residents with dementia. (139, 142)

Feasibility and acceptability

No manuscripts have reported on the feasibility and acceptability of these systems.

Infrared

Infrared sensors register the infrared waves emitted by warm objects. It can be used to monitor skin temperature and motion, which are further analyzed by researchers to indicate thermal comfort (143) and sleep stages. (144) The sensor can be installed in front of the participants or above their beds. The systems have been tested in healthy adults and nursing home residents.

Clinimetrics

A model to analyze the thermal comfort of nursing home residents was reliable. A lower temperature of the nose indicated feeling cold. (143) Compared to a commercially available bed sensor, the infrared system was able to detect waking states better than other stages of sleep in healthy adults. (144)

Feasibility and acceptability

No manuscripts have reported on the feasibility and acceptability of these systems.

Radar

Radar systems monitor the shape and position of objects by emitting radio frequency waves and receiving reflections. By monitoring the small movements of the chest, radar systems can detect vital signs such as heart rate (145) and respiration rate. (146) Breathing and location can be used to monitor sleep quality. (147) The radar system can be installed on the wall or above the person being monitored. The systems have been tested in healthy adults.

Clinimetrics

Radar systems have demonstrated high accuracy in monitoring respiration rate, (146) heart rate, (145) sleep time, and sleep efficiency (147) in healthy adults.

Feasibility and acceptability

No manuscripts have reported on the feasibility and acceptability of these systems.

Multiple sensors

Only a few studies have experimented with the use of multiple noncontact sensors. Sleep or agitation was monitored using (infrared) cameras, acoustic sensors, and pressure mats in healthy adults, people with COVID-19, community-dwelling older adults, and people with dementia. (148-150)

Clinimetrics

The clinimetrics of systems using multiple noncontact sensors were not yet optimal. Radar and pressure mats overestimated total sleep time and sleep accuracy in the laboratory among community-dwelling older adults. (149) The reliability of the measurements of heart rate and respiration rate of healthy adults and people with dementia differed depending on the setting.

(148) Infrared cameras and a pressure mat complimented each other in their registration of movement of patients with COVID-19. (150)

Feasibility and acceptability

In the study with people with dementia in the emergency department and a geriatric-psychiatric ward, few disruptions occurred during the measurements, and one out of 19 participants with dementia refused to be monitored. (148)

Discussion

A variety of monitoring technologies are available to monitor discomfort and distressing symptoms that can occur at the end of life, including actigraphy, brain activity monitoring, ECG, EDA monitoring, surface EMG, incontinence sensors, multimodal systems, and noncontact monitoring systems. Although there were no validation studies in the end-of-life setting, the clinimetrics of selected technologies, especially actigraphy and portable polysomnography, have been researched and were satisfactory in other settings. Relatively few manuscripts have reported on the feasibility and acceptability of these technologies, and even fewer have been conducted in the end-of-life setting, except for brain activity monitors, which have been reported to be acceptable for palliative sedation. In the other settings, the technologies were deemed feasible most of the time. Challenges for feasibility included positioning of the device, signal quality during movement, problems with Bluetooth or Wi-Fi connections, battery life, and the device being taken off due to agitation.

This review demonstrated the rapid development of monitoring technologies, and we share the expectations of others that user-friendly systems with small, wireless, and noncontact sensors or smart garments will soon be available as minimally invasive options to monitor a wide range of discomfort and distressing symptoms in end-of-life care. (27, 151, 152) Currently, promising research is being conducted on the monitoring of a variety of indicators of discomfort with technology. Specifically, the depth of sedation may be monitored using brain activity monitors; sleep/wake states using actigraphy, brain activity monitors, portable PSG, infrared sensors, and radar; sleep disordered breathing using portable PSG, actigraphy, pressure mats,

and ECG; risk of pressure ulcers using actigraphy; urinary incontinence using incontinence monitors; agitation using actigraphy and multi-modal systems; pain using brain activity monitors, ECG, EDA, multi-modal systems, facial expression analysis; delirium using brain activity monitors, and multimodal systems with environmental sensors; stress using brain activity monitors, EDA, multi-modal systems; fatigue using multi-modal systems; and thermal comfort using infrared sensors. However, we are not yet able to make recommendations for clinical practice due to limited research in this setting. Many studies included in this review contained a small sample, some technologies were only validated by the development team, and previous reviews on specific types of technologies, such as urinary incontinence monitors and BIS, reported very low quality of evidence. (153, 154) The included feasibility studies only focused on technical aspects and employed diverse, often unclear endpoints, which was also the case in a previous review on e-health in geriatric rehabilitation. (155)

More attention is needed to examine the clinimetrics, feasibility, and acceptability of the technologies with solid study designs, a sample to generate enough power for the proposed analyses, and standardized outcome measurements. The Health Technology Assessment (HTA) core model may be a useful tool to guide future studies in systematically evaluating technologies from multiple dimensions. It provides a list of relevant research questions, corresponding outcome measurements and possible sources of information. (156) However, this model primarily guides the synthesis of evidence instead of primary research. For the latter, more detailed instructions would be needed. For example, with the note that the cutoffs for good clinimetrics should not be fixed but depend on the goal of the technology, (157) more information is needed on how to determine these standards. With the accelerated development in the field of healthcare technology, we recommend better implementation of existing evaluation guidelines and further development of the guidelines to directly guide the design of primary studies.

This review has a few limitations and strengths. Many of the included manuscripts were not about the end-of-life setting, and we did not evaluate the quality of the studies. Commercially available technologies without scientific studies were also not systematically searched for. These were beyond the aim of

our scoping review. Since the search terms were in English, manuscripts in other languages without an English title or abstract were not included. Despite these limitations, the authors believe that this review identified most monitoring technologies that were already applied or developed for settings similar to the end of life. We implemented an elaborate search strategy consisting of broad search terms, including manuscripts in multiple languages and gray literature, and conducted an expert consultation to include technologies that are still under development. To the best knowledge of the authors, this is the first review on noninvasive monitoring technologies that may be applied to the end of life, where people are often bed-ridden and have limited communication abilities. Future research is needed to assess the methodological quality of the studies, to identify potentially useful technologies for the end of life, to further develop them and validate them in this setting and to compare different technologies measuring the same symptoms.

Conclusions

This review provides an overview for clinicians, researchers and technology developers of noninvasive technologies that can potentially be used to monitor discomfort and distressing symptoms in persons with limited communication at the end of life. A variety of technologies are available to monitor symptoms such as sleep, level of consciousness, risk of pressure ulcers, urinary incontinence, agitation, and pain. Clinimetrics and feasibility in non-end-of-life settings were promising, while acceptability studies were scarce. Future research should evaluate the usefulness, acceptability and feasibility of the identified technologies in end-of-life care, further develop the technologies and validate them in this setting. Guidelines for studies on healthcare technologies should also be developed.

Declarations

Ethics approval and consent to participate

Not applicable. This study did not involve human participants. No ethics approval was needed according to the Dutch Medical Research Involving Human Subjects Act.

Consent for publication
Not applicable.

Availability of data and materials
Data are available upon reasonable request to the corresponding author.

Competing interests
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Authors' contributions

HS, JTS, and XJ conceptualized the review. JWS performed the literature search. HS contacted the experts. XJ and HS were involved in the screening and data extraction. XJ drafted the manuscript. HS, JTS, JWS, and WA revised the manuscript. All authors read and approved the final manuscript.

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Supplements of "Noninvasive monitoring technologies to identify discomfort and distressing symptoms in persons with limited communication at the end of life: A scoping review"

eTable 1 Manuscripts reporting clinimetrics of the monitoring technologies to detect distress and discomfort

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Actigraphy				
Alam	2019	USA	Pebble watch (Pebble Technology, Corp., Taiwan), Pixie app	Agitation
Bankole	2012	USA	TEMPO 3.1 (developed by University of Virginia)	Agitation
Chikhaoui	2016	Canada	Shimmer3 GSR (Shimmer, Dublin, Ireland)	Agitation and aggression
Grap	2011	USA	Basic Motionlogger (Ambulatory Monitoring Inc, Ardsley, NY)	Agitation

Aim of study	Methods: Study design; Participants (age, disease, setting); Procedures	Clinimetrics of the technology (validity, sensitivity, reliability, specificity, responsiveness)
To predict agitation of people with dementia using multiple-instance learning models.	Quantitative cross-sectional study with 10 older adults with mild to severe dementia living at home. Participants wore the Pebble watch for 30 days. Agitation events were marked by family caregivers.	Accuracy: 76% - 87%. F-score: 0.69-0.73. Area under the receiver-operating characteristic curves (AUC): 0.78-0.92, indicating significantly higher true positive rates compared with single instance learning models.
To validate the Body Sensor Network (BSN) in measuring agitation.	Quantitative cross-sectional study with 6 older adults with dementia in nursing homes. Each participant wore the devices in the morning, afternoon and evening for 3 hours per session. The Cohen-Mansfield Agitation Inventory (CMAI), the Aggressive Behavior Scale (ABS) and the Mini-Mental State Examination (MMSE) were assessed at each session.	Convergent validity (BSN vs. CMAI and ABS): acceptable for morning sessions, less for afternoon and evening sessions. Discriminant validity (BSN vs. MMSE): strong. Secondary validation (Teager scores calculated from the BSN measurements during agitation vs. pre- and post-agitation): strong support
To compare Microsoft Kinect sensor and actigraphy in detecting aggressive and agitation behaviors, and to develop and validate corresponding algorisms.	Quantitative cross-sectional study with 10 adults. They performed aggressive and agitated behaviors wearing the device. All actions were performed 5 times.*	The algorism developed by the researchers using actigraphic data could recognize aggressive and agitated behaviors (F-Measure = 0.85 – 0.94)
To differentiate behavioral states common in the critically ill population.	Quantitative cross-sectional study with 30 adult healthy volunteers in the laboratory. Participants wore the device on the wrist and ankle and simulated states of calmness, restlessness, and agitation for 10 minutes.	The average movement is significantly different among the three states and between wrist and ankle measurements.

eTable 1 Manuscripts reporting clinimetrics of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Knuff	2019	USA	wGT3x+ activity monitors (Actigraph, LLC, Pensacola, FL)	Agitation
Mahlberg	2007	Germany	Actiwatch (Cambridge Neurotechnology Ltd, Cambridge, UK)	Agitation
Nagels	2006	Belgium	Basic motion-logger (Ambulatory monitoring, New York, USA)	Agitation
Raj	2014	USA	Actiwatch 2 (Phillips Respironics, Andover, MA)	Agitation/ sedation
Valembois	2015	France	Vivago (Vivago Oy, Espoo, Finland)	Aberrant motor behavior

Aim of study	Methods: Study design; Participants (age, disease, setting); Procedures	Clinimetrics of the technology (validity, sensitivity, reliability, specificity, responsiveness)
To evaluate the feasibility and validity of actigraphy as a measurement of agitation in dementia.	Quantitative cross-sectional study. 20 older adults with dementia living in long-term care facilities wore the wristband continuously for a minimum of 24 hours and maximum of 7 days.	Significant difference in motor activity between the low- and high-agitation groups. Most actigraphic data, except for night time measurements, significantly correlated with the CMAI (r = 0.74 - 0.77, p < 0.001) and the Neuropsychiatric Inventory (NPI, r = 0.47 - 0.56, p = 0.01 – 0.04)
To evaluate the actigraphy in measuring day-night rhythm disturbances and agitated behavior.	Randomized controlled trial with 24 older adults with dementia and agitated behavior in a geriatric psychiatry unit. 14 received medication, 10 received placebo. Control group: 10 young and 10 older healthy subjects. The device was worn for at least two weeks. The NPI was scored before and after the treatment period.	The actigraphic agitation is significantly lower in the treatment group compared to placebo and healthy control groups. No correlation between actigraphy and NPI.
To assess the association between the actigraphic measure of agitation and a validated scale.	Quantitative cross-sectional study with 110 older adults recently diagnosed with dementia. The device was worn for 48 hours. CMAI was rated by nurses during staff briefings. *	Significant association between actigraphic measures and CMAI (F = 126.75, p < 0.001).
To determine the usefulness of actigraphy to measure sedation/agitation in the ICU.	Quantitative cross-sectional study with 86 adults in the ICU of a tertiary care center. Actigraphy was worn for 60 or 70 minutes. The Richmond Agitation Sedation Scale (RASS) was scored every 10 minutes.	Actigraphic data associated with sedation/agitation level as assessed by RASS.
To evaluate the usefulness of actigraphy to measure disorders in motor behavior.	Quantitative cross-sectional study with 183 older adults, of which 126 had dementia admitted to an intermediate care unit in the hospital. The device was worn for 10 days. Apathy, aberrant motor behavior, agitation and anxiety were evaluated with the NPI.	Motor activity measured by the actigraphy was lower in patients with apathy (p = 0.008 - 0.05, depending on time of the day), and was greater in those with aberrant motor behavior (p = 0.003 - 0.04 depending on time of the day). No correlation with agitation and anxiety was observed.

eTable 1 Manuscripts reporting clinimetrics of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Anusha	2021	India	Not reported	Risk of pressure ulcers and agitation
Cicceri	2020	Italy	developed by the researchers	Risk of pressure ulcers
Minteer	2020	USA	PUMP1 and PUMP2, developed by the authors	Risk of pressure ulcers
Pickham	2018	USA	Leaf Patient Monitoring System (Leaf Healthcare, Inc., San Francisco, CA)	Risk of pressure ulcers
Alessi	1999	USA	Wrist activity monitor (Augmentech Inc., Pittsburgh, PA)	Sleep
Brooks	1993	USA	Actigraph (Ambulatory Monitoring, Inc., Ardsley, NY)	Sleep

Aim of study	Methods: Study design; Participants (age, disease, setting); Procedures	Clinimetrics of the technology (validity, sensitivity, reliability, specificity, responsiveness)
To validate the use of accelerometer on the mattress to monitor movement on the bed.	Quantitative non-randomized experimental study in the laboratory. The number of participants was not reported. Accelerometers were placed on the mattress and the participants performed several actions on it, including sitting up, rolling over, and slightly moving the limbs.	The algorithm categorized the activity with a 100% accuracy for a single participant. 92% accuracy when the system was trained with the accelerometer on more locations on the bed. When the system was trained with seven different beds, the accuracy on an eighth bed was 82%.
To design and implement a wearable sensor system to prevent pressure ulcers with deep learning.	Quantitative cross-sectional study. 6 adult patients wore a hospital gown with integrated sensors in the medicine department. The body position was monitored. The proposed deep learning method was compared with two machine learning models.	The precision was between 99% and 100%. The sensitivity was between 93% and 100%.
To test the accuracy of PUMP1 (garment sensors) and PUMP2 (bed sensors) in detecting body repositioning.	Quantitative cross-sectional study with 10 immobile patients in the hospital. They were monitored by both devices for 10 ± 2 hours. The data was compared to body repositioning events identified from a video footage.	Both PUMP1 and PUMP2 captured repositioning movement with 85% reliability. False positives: 2 events for PUMP1, 1 for PUMP2. False negatives: 11 events for PUMP1, 7 for PUMP2.
To assess the effectiveness of Leaf on preventing pressure ulcers.	Randomized controlled trial. Among 1,312 patients in ICU, 659 wore a Leaf monitor which helps providers know whether the patient has turned recently.	Patients with Leaf had significantly less chance of pressure ulcers (OR=0.33, 95% CI [0.12, 0.90]). The staff complied to the turning scheme of these patients more (67% vs. control=51%, $p < 0.005$).
To evaluate the effect of daytime physical activity and night time environment on sleep and agitation.	Quantitative cross-sectional study with 29 older adults with incontinence living in nursing homes. The monitor was worn on the wrist for 5 nights during the night.	Wrist activity monitors had a sensitivity of 95.5% and a specificity of 82.0% monitoring sleep-wake status, compared to behavioral observations.
To evaluate the sensitivity of the actigraph to detect insomnia treatment effects.	Quantitative cross-sectional study with 9 older adults with insomnia, without dementia. They wore the actigraph for one night at home.	Change in total sleep time measured by actigraphy correlates with the sleep log ($r = 0.69$, $p = 0.04$). No correlations between the two measurements in changes of time to sleep onset, wake after sleep onset and sleep efficiency.

eTable 1 Manuscripts reporting clinimetrics of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Delaney	2021	Australia	Actiwatch Spectrum Plus (Phillips Respironics Inc, Murrysville, PA)	Sleep
van Someren	2007	Netherlands	Actiwatch and Sleep 5 software (Cambridge Neurotechnology, Cambridge, UK)	Sleep
Gibson	2019	New Zealand	Actiwatch-2. Software: Actiware 2015, Version 6 (Mini Mitter, Respironics)	Sleep
Maskevich	2017	Australia	Actiwatch Spectrum Pro (Philips Respironics, Murrysville, PA), Jawbone UP2 and Fitbit One	Sleep
Stavitsky	2010	USA	Actiwatch AW-64 (Mini Mitter, Sunriver, Orlando)	Sleep

Aim of study	Methods: Study design; Participants (age, disease, setting); Procedures	Clinimetrics of the technology (validity, sensitivity, reliability, specificity, responsiveness)
To evaluate the feasibility and reliability of actigraphy to monitor sleep compared with polysomnography (PSG).	Quantitative cross-sectional study. 80 adult patents in the ICU were monitored for 24 hours.	Agreement in identifying sleep and wake states compared with PSG (69.4%; K = 0.386, $p < 0.05$), with a moderate level of sensitivity (65.5%) and specificity (76.1%). Amongst non-ventilated patients: specificity 83.7%; sensitivity 56.7%. Moderate correlation with PSG reported total sleep time ($r = 0.359$, $p < 0.05$, underestimated) and wakefulness ($r = 0.371$, $p < 0.05$, overestimated).
To investigate the reliability of actigraphy sleep monitoring depending on the recording duration.	Quantitative cross-sectional study with 10 adults with insomnia living at home and 12 older adults with dementia at group-care facilities. Participants wore the device continuously for 20 days.	Reliability: 59% - 97%, increasing with the recording duration. The authors recommended at least 7 days of monitoring for reliable data.
To evaluate the reliability of actigraphy to score sleep patterns.	Quantitative cross-sectional study with 15 older adults with dementia and their family caregivers. Both groups wore the device at home for one week and used an event marker to register relevant events such as bedtime.	People with dementia: Sleep: sensitivity: 87%, specificity: 80% Wake: sensitivity 77%, specificity: 61% Family caregiver: Sleep: sensitivity: 90%, specificity: 93% Wake: sensitivity 92%, specificity: 57%
To validate the monitoring devices for sleep measurement.	Quantitative cross-sectional study with 7 adult Huntington's gene carriers. They wore the devices overnight while undergoing a PSG at the laboratory.	All the actigraphy devices are less accurate than PSG and overestimate sleep time by more than an hour and sleep efficiency by 15%. The researchers concluded that they are sufficient to estimate general sleep-wake patterns.
To compare self-report with actigraphic data on sleep quality	Quantitative cross-sectional study with 30 community-dwelling adults with Parkinson's Disease and 14 normal control participants. The device was worn 24 hours a day for 7 days at home. Sleep diaries were kept for the same period.	Actigraphic data of sleep quality correlated with self-report in the Parkinson group but not in the control group.

eTable 1 Manuscripts reporting clinimetrics of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
McClure	2020	USA	BioStamp nPoint (MC10, Inc., Lexington, MA, USA)	Sleep – disordered breathing
Mehra	2008	USA	Sleepwatch-O (Ambulatory Monitoring, Inc., Ardsley, NY)	Sleep
Mokhtaran	2022	Italy	Fitbit Charge 3 (Fitbit Inc., San Francisco, California)	Sleep

Aim of study	Methods: Study design; Participants (age, disease, setting); Procedures	Clinimetrics of the technology (validity, sensitivity, reliability, specificity, responsiveness)
To develop an analysis system to detect breathing patterns.	Quantitative non-randomized experimental study with 100 healthy adults in the laboratory. Participants simulated central sleep apnea, coughing, obstructive sleep apnea, sighing, and yawning, while being monitored with wireless sensors on the chest and abdomen.	F1 score was 92% for normal breathing, 87% for central sleep apnea, 72% for coughing, 51% for obstructive sleep apnea, 57% for sighing, and 63% for yawning.
To examine the association between actigraphic measures and PSG-determined sleep-disordered breathing (SDB) and/or periodic limb movement disorder (PLMD).	Quantitative cross-sectional study with 455 older women living in the community. The device was worn for three 24-hour periods. The PSG was administered for one night at their home by staff.	Poor sleep efficiency measured by wrist actigraphy was associated with SDB (OR = 2.43, 95% CI: 1.43-4.14) and PLMD (OR = 2.36, 95% CI: 1.34-4.15). Reduced sleep duration was also associated with SDB (OR = 3.18, 95% CI: 1.51-6.68) and PLMD (OR = 3.77, 95% CI: 1.78-7.95).
To explore the use of Fitbit to monitor sleep quality.	Quantitative cross-sectional study with 26 adults with obstructive sleep apnea. Participants were observed by standard PSG and Fitbit simultaneously for three nights in the hospital (baseline, before treatment, after treatment).	Fitbit correlated with PSG in the estimation of total sleep time (r = 0.8-0.9, p < 0.001), sleep efficiency (r = 0.8-0.9, p < 0.001), the percentage of four sleep stages (r = 0.5-0.9, p = 0.001-0.03). Sensitivity: 90%-93% Specificity: 56%-59% Accuracy: 59%-61% The measurement of Fitbit improved after the treatment for obstructive sleep apnea. The authors concluded that it is less able to measure abnormal sleep patterns.

eTable 1 Manuscripts reporting clinimetrics of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Svetnik	2021	USA	Garmin Vivosmart	Sleep
Kikhia	2016	Sweden, Greece, Netherlands	Philips sensor DTI-2 (Philips Research, Eindhoven, The Netherlands)	Stress
Brain activity monitors - Bispectural Index (BIS)				
Arbour	2015	Canada	BIS VISTA bilateral BIS (Aspect Medical Systems, Newton, MA)	Pain
Arbour	2015	USA	BIS A-2000 XP (Aspect Medical Systems, Inc. Norwood, MA)	Sedation
Dahaba	2011	Australia, China	BIS-Vista version 1.4 (Aspect Medical Systems, Newton, MA)	Sleep

Aim of study	Methods: Study design; Participants (age, disease, setting); Procedures	Clinimetrics of the technology (validity, sensitivity, reliability, specificity, responsiveness)
To investigate the usefulness of a wearable in measuring treatment effects of insomnia in people with dementia.	Randomized experimental study with 285 older adults with Alzheimer's disease and insomnia. During insomnia treatment of four weeks, participants were instructed to wear the device all the nights at home. Three overnight measurements with standard PSG were performed in the laboratory at screening, baseline, and at the end of the treatment.	Compared to PSG, the device overestimated total sleep time (e.g., placebo baseline = 412 min for watch and 265 min for PSG) and underestimated the change in total sleep time before and after treatment.
To validate the sensor system in recognizing stress.	Quantitative cross-sectional study with 6 older adults living in nursing homes. Participants wore the device when they are awake for 2 months. Observation notes were made by the staff.	With sampling rate of an hour and stress level threshold of 3: precision: 19%, recall: 48%, accuracy: 76%
To validate BIS in pain detection of people with traumatic brain injury.	Quantitative cross-sectional study with 25 critically ill adults in the ICU with acute traumatic brain injury and altered level of consciousness. They were monitored 1 min before, during, and 15 min after turning and non-invasive blood pressure measurements. Pain behaviors were observed.	BIS measurements increased during turning (nociceptive) but not during non-invasive blood pressure measurements (non-nociceptive). Only BIS of the right hemisphere correlates with pain behavior and only for people with left-sided traumatic brain injury ($r = 0.99$, $p < 0.001$).
To evaluate the predictive value of BIS in determining level of burst suppression during drug-induced coma, compared with EEG.	Quantitative prospective, observational cohort study with 4 adults in the ICU under drug-induced coma. 33 hours of monitoring was performed in total.	BIS value, BIS suppression ratio, and BIS burst counts had medium to strong correlations with EEG burst counts.
To assess whether BIS can quantify sleep depth.	Quantitative cross-sectional study with 10 healthy sleep-deprived adults. Participants were monitored during one sleep.*	BIS value showed a temporal decline corresponding to sleep stages. The lowest score was about 40.

eTable 1 Manuscripts reporting clinimetrics of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Giménez	2017	Spain	BIS A-2000 XP Monitor (Aspect Medical Systems, Inc. Norwood, MA) with Quatro Sensors	Sleep
Pedrao	2020	Brazil	BIS™ Vista Monitoring System (Covidien LLC, Mansfield, United States)	Sleep
Luo	2021	USA	BIS-VISTA with density spectral array (Aspect Medical Systems, Inc. Norwood, MA)	Delirium
Brain activity monitors – other electroencephalography (EEG)-based technologies				
Haenggi	2004	Switzerland	EMMA (Department of Clinical Neurophysiology, Kuopio University Hospital, Kuopio, Finland)	Sedation
Lee	2022	South Korea	Amp GS5001 (SOSO H&C, Kyungpook University, Daegu, Korea)	Delirium

Aim of study	Methods: Study design; Participants (age, disease, setting); Procedures	Clinimetrics of the technology (validity, sensitivity, reliability, specificity, responsiveness)
To assess the feasibility and reliability of BIS for sleep monitoring.	Quantitative cross-sectional study with 12 healthy adults. Sleep was measured with PSG and BIS both at baseline and after sleep deprivation at the laboratory.	BIS value was highly correlated with the hypnogram and could discriminate between deep and light sleep.
To test the feasibility of using BIS to evaluate sleep in critically ill patients.	Quantitative cross-sectional study with 29 critically ill patients on ICU. BIS monitoring was performed for a whole night (12 hours). The participants filled in the Richards-Campbell Sleep Questionnaire (RCSQ) the next morning.	Total sleep volume, total sleep time, and continuous sleep volume measured by BIS were weakly correlated with the RCSQ depth of sleep domain score, overall sleep quality domain score, and total score. Total volume, total time, and continuous volume were moderately correlated with the occurrence of awakenings domain score of RCSQ.
To evaluate the use of BIS to identify delirium.	Quantitative cross-sectional study with 40 adults with delirium and 83 adults without delirium. Participants were monitored for 20 minutes at the hospital that they were recruited from.	BIS with density spectral array was similar to the 3-minute Diagnostic Interview for Confusion Assessment Method in identifying delirium. Visual inspection of the density spectral array was not associated with delirium.
To explore the use of long latency evoked potential (EP) in measuring depth of sedation.	Quantitative cross-sectional study with 10 healthy adults under sedation. EP, which is the brain activity 100ms after a standard auditory stimuli, was measured in different stages of sedation based on the Ramsay Sedation Score.	The brain activity 100ms after a standard auditory stimuli (EP) decreased as the depth of sedation increased.
To test a compact EEG device as diagnostic tool for delirium by analysing differences in EEG signals in patients with and without delirium both before and after spinal surgery.	Quantitative cross-sectional study with 37 older adults who had spinal surgery. EEG measurements were performed before, one week after and three months after the surgery in the hospital or outpatient clinic. Delirium was diagnosed by a psychiatrist. Patients with delirium were compared to those without.	Compared to the group without delirium, people with delirium showed more increase in the H-beta waves (19%, $p = 0.003$), gamma (19%, $p = 0.006$) waves, the tension index (8%, $p = 0.011$), and more decrease in the theta waves (–23%, $p = 0.016$) one week after the surgery.

eTable 1 Manuscripts reporting clinimetrics of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Urdanibia-Centelles	2021	Denmark	NicoletOne™ Version 5.71 (Nicolet, Natus Medical Incorporated)	Delirium
Nakamura	2020	UK	Not reported	Sleep - stages
Vacas	2016	USA	SedLine Brain Function Monitor (Masimo Corp., Irvine, California)	Sleep - stages
Pu	2021	Australia	MUSE 2 (InteraXon Inc., Toronto ON, Canada)	Pain
Roh	2012	South Korea	developed by the authors	Stress

Aim of study	Methods: Study design; Participants (age, disease, setting); Procedures	Clinimetrics of the technology (validity, sensitivity, reliability, specificity, responsiveness)
To compare visual analysis and automatic analysis of continuous EEG in diagnosing delirium in septic patients.	Quantitative cross-sectional study with 102 older adults with sepsis in the ICU. Delirium was evaluated six times per day with the Confusion Assessment Method in the ICU.	Delirium was associated with several parameters of the continuous EEG. The AUC is slightly higher for visual analysis (88%) than automatic analysis (74%). The authors concluded that the automatic analysis can complement the visual analysis in delirium diagnosis.
To investigate the validity of in-ear EEG monitoring of sleep.	Quantitative cross-sectional study with 22 adult participants. Sleep was monitored by both the in-ear EEG and PSG for a whole night in their homes.	Accuracy in five sleep stage classification: 74% compared to PSG (k = 0.61).
To validate the device in laboratory setting and to test the feasibility of its use in the ICU.	Quantitative cross-sectional study with three adult outpatients in the laboratory and 23 ICU patients. The system was validated against PSG in the laboratory, where participants were monitored for one night. The mean recording time in the ICU was 19.1 hours.	The system could distinguish sleep from wakefulness and the transition between sleep stages, although the latter is less accurate.
To assess the feasibility of a headband EEG to monitor pain in long-term care residents with dementia.	Quantitative cross-sectional study with 4 older adults with dementia and chronic pain in a long-term care facility. Each participant was monitored for 10 minutes. The Pain Assessment in Advanced Dementia (PAINAD) scale was administered before and after the measurement.	The detrended fluctuation analysis of EEG signals fluctuated in participants experiencing pain, but not in the participant without pain.
To develop a portable system to measure stress and mental state.	Quantitative non-randomized experimental study with 10 healthy adults in the laboratory. For 10 minutes, participants wore a headband and did three stressful tasks with rest in between.	Compared to the resting state, the largest lyapunov exponent value (the physiological marker for stress and mental state) decreased to 0.734 and the standard deviation of heart rate variability (HRV), also derived from EEG data, increased to 73ms during stressful tasks.

eTable 1 Manuscripts reporting clinimetrics of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Electrocardiography (ECG)				
De jonckheere	2014	France	Developed by the authors	Pain
Grasso	2018	USA	Mortara H12 (Mortara Instrument, Milwaukee, Wis, USA)	Sleep – apnea
Li	2022	China	myBeat-WHS-1 (Union Tool Co., Ltd., Japan)	Stress
Miranda	2017	USA	HxM Bluetooth chest belt (Zephyr)	Anxiety
Electrodermal activity (EDA) monitors				
Aslanidis	2018	Greece	Med Storm Pain Monitor System (MED Storm® Innovation AS, Oslo, Norway)	Pain

Aim of study	Methods: Study design; Participants (age, disease, setting); Procedures	Clinimetrics of the technology (validity, sensitivity, reliability, specificity, responsiveness)
To present an ambulant device which monitors pain with HRV analysis.	Quantitative cross-sectional study with 12 adults having physical therapy after surgery. Pain was scored with the Visual Analogue Scale (VAS) during the first and second therapy session.	The HRV was correlated with the VAS (r = - 0.50, p = 0.002). HRV was lower in the VAS > 30 subgroup than in the VAS ≤ 30 one (p=0.002).
To evaluate the portable ECG system in its detection of sleep disordered breathing compared to standard PSG.	Quantitative prospective cohort study with 30 adult patients with the suspicion of sleep disordered breathing. The ECG monitor and PSG were worn simultaneously overnight in the laboratory.	ECG parameters correlated with PSG parameter of apnea (r = 0.77 - 0.81). The ECG system was accurate and sensitive but relatively imprecise in detecting the severity of the apnea.
To use a wearable ECG monitor to measure workplace stress in nurses.	Quantitative cross-sectional study with 17 healthy nurses during one work day at the hospital. Participants wore the device and filled in the Chinese Nurses Stress Response Scale (CNSRS) after work.	The HRV parameters were correlated with time, work and rest phases, postures, and subscales of the CNSRS (physiological reaction, irritability, social phobia, and fatigue).
To present a system to detect internal states of anxiety during caregiving tasks.	Quantitative non-randomized experimental study with 10 healthy adults in the laboratory. During 30 min sessions, participants had a relaxation stage and performed cognitive therapy tasks with a simulated person with dementia. Video recordings of each 30s of the session were coded by the participants for the presence of anxiety.	Using inter beat interval as classification feature, the accuracy of the model was 73%.
To monitor electrodermal activity changes during pain.	Quantitative cohort study with 25 adult patients under sedation in the ICU. Participants were monitored for four hours. During a 10-second pain stimulus, electrical dermal activity changes in the palm were measured and compared to observation, BIS, cardiovascular and respiratory measurements.	EDA monitoring was more sensitive to pain compared to cardiovascular, respiratory and BIS measurements.

eTable 1 Manuscripts reporting clinimetrics of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
De Vries	2022	Netherlands	Sentisock (Mentech, Eindhoven, the Netherlands)	Stress
Leborgne	2023	Netherlands	Developed by the author	Stress
Setz	2010	Switzerland	Emotion Board (developed by the authors)	Stress
Surface electromyogram (sEMG)				
Carlson	1996	USA	BioPrompt 3000 (Physical Health Devices)	Pain

Aim of study	Methods: Study design; Participants (age, disease, setting); Procedures	Clinimetrics of the technology (validity, sensitivity, reliability, specificity, responsiveness)
To validate the sock-integrated EDA sensor in monitoring stress.	Quantitative non-randomized experimental study with 28 healthy adults in the laboratory. Measurements were taken at baseline, during mental stress and physical stress in a 75 min session. Sock-integrated EDA data was compared to wrist EDA measured by Empatica E4 and self-report of the participants using the Self-Assessment-Manikin scale.	Sentisock: F1-score: 0.84, sensitivity: 81%, specificity: 86%, balanced accuracy: 83% Empatica E4: F1-score: 0.83, sensitivity: 81% , specificity: 84%, balanced accuracy: 82%
To develop a sock garment to detect stress in people with intellectual disabilities.	Quantitative non-randomized experimental study. Sixty adults with severe intellectual disabilities in long-term care facilities tried on the garment. It was not clear whether the experiment was conducted with other participants in the laboratory, where the sock sensor was compared with Empatica E4 (Empatica Inc, Boston, USA) during sitting, walking, standing, and doing math.	The signal quality was good for neural and stable positions, but more noise was present during movement. The sock sensors recognized EDC changes in stressful situations with an accuracy of 85%.
To investigate accuracy of EDA in discriminating stress from cognitive load.	Quantitative randomized controlled trial with 33 healthy adults in the laboratory. Participants went through a 2-hour stress session with social and cognitive stress, as well as a 2-hour cognitive load session.	Maximum accuracy of discriminating stress from cognitive load: 83%
To determine whether there is difference in ambulatory sEMG signals in the upper trapezius muscle for people with and without pain.	Quantitative case-control study with 10 adult participants with cervical pain and 10 adult participants without pain. Participants were monitored by the ambulatory device in their normal life for three consecutive days during daytime.	No difference in sEMG signals was found between the group with pain and the group without.

eTable 1 Manuscripts reporting clinimetrics of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Yang	2018	China, Finland, Austria, France, and Sweden	Developed by the authors	Pain
Incontinence sensors				
Boerakker	2022	Netherlands	Abena Nova (Abena Group, Denmark), WeSense (Seneca Sense Technologies, Canada)	Incontinence
Cusick	2003	UK	Developed by the authors	Incontinence
Ouslander	1998	USA	Not reported	Incontinence
Not reported (This manuscript is the device website)	2022	Denmark	TENA Identifi Sensor Wear (Essity Hygiene and Health AB, Denmark)	Incontinence
Tekcin	2022	Tekcin	Developed by the authors	Incontinence

Aim of study	Methods: Study design; Participants (age, disease, setting); Procedures	Clinimetrics of the technology (validity, sensitivity, reliability, specificity, responsiveness)
To present a facial expression monitoring system for automatic pain assessment.	Quantitative non-randomized experimental study with one healthy adult in the laboratory. The participant mimicked painful expressions, which were compared to frowning and neutral expressions. The duration of the measurement was not reported.	Muscle activities in the face during painful expressions and neutral expressions could be differentiated.
To investigate the use of intelligent incontinence material in nursing homes.	Mixed-methods pilot study with 25 older adults in nursing homes with urinary incontinence. Abena Nova and WeSense were compared to the regular incontinence material.	Abena Nova reduced the use of incontinence materials by 34%, WeSense reduced it by 16%.
To develop and test an incontinence sensor.	Quantitative cross-sectional study with volunteers. No details on the participants were reported. A total of 71 events were simulated, of which 20 simulated incontinence events.*	5 false-positive events, 2 false negatives events. The authors concluded that the system met the technological requirements.
To investigate the relationship between incontinence and sleep disruption.	Quantitative cross-sectional study with 73 older adults in nursing homes. Night-time incontinence was recorded both by a device and by staff.	The records of the device (wet/dry status) coincide with the records made by staff.
To report customer results.	Quantitative cross-sectional study with 324 adults. Further details not reported.*	Leakage was reduced by 66%, Time saved (per client per year): 86.7 hours, incontinence material changes reduced by 22%, toilet visits reduced by 6%, urine loss reduced by 14%, rubbish reduced by 36%. Clients can use materials with less absorption capacities.
To develop a humidity sensor to measure urinary incontinence.	Quantitative non-randomized experimental study in the laboratory. No participants were involved. The sensor was tested in a humidity chamber and water was dripped on it to measure the change in resistance.	In the humidity chamber, the resistance decreased as the humidity increased. Change in resistance of the sensor was measurable with 0.1ml of water dripped on it.

eTable 1 Manuscripts reporting clinimetrics of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Toba	1996	Japan	Not reported	Incontinence
Van der Hurk	1998	Netherlands	Developed by the authors	Incontinence
Wang	2009	USA	Developed by the authors	Incontinence
Multi-modal systems - polysomnography (PSG)				
Koley	2013	India	Alice LE (Philips Respironics)	Sleep - apnea

Aim of study	Methods: Study design; Participants (age, disease, setting); Procedures	Clinimetrics of the technology (validity, sensitivity, reliability, specificity, responsiveness)
To evaluate the effects of wearing a thin-film urinary drainage sensor in the incontinence material on urinary quality of life and nursing work hours.	Mixed-method cross-sectional study with 4 older adults with urinary incontinence in long-term care facility. Incontinence materials were changed regularly (4 times a day) and as needed (as soon as possible after sensor detection) for 4 days each. The wetting times were compared. Working time was recorded and asked through a caregiver questionnaire.	Incontinence material wetting time was reduced from 1 hour 21 ± 11 minutes with the regular change to 9±1 minutes with the sensor. Total working time increased from 52 minutes to 90 minutes because of the change of the sensors.
To evaluate the applicability and validity of the Urine Leakage Recording Device.	Quantitative non-randomized experimental study with 5 older adults. Participants were instructed to turn and void during the experiment. 3 human assessors scored the data generated from the device to determine incontinence events. This was compared with the self-report of participants. The setting was probably laboratory, but not stated in the manuscript.	Interscorer reliability: 0.92. True positive events: 5.3 out of 10, False positive events: 9.3. The authors concluded that the device was not useful.
To validate the system to record urinary leakage in women doing intense physical activities.	Quantitative non-randomized experimental study with one adult woman. The sensitivity of the sensor was first tested in the laboratory with a burette dropping urine onto it. Then the participant wore the device during a 25-minute jog, releasing urine at the end.	The lab test suggested that the sensor could always detect a leakage of more than 0.5ml. The jogging experiment demonstrated that the sensitivity of the sensor was not influenced by sweat disturbance.
To develop an algorism to detect apnea or hypopnea events using airflow data from PSG.	Quantitative cross-sectional study with 36 adult participants with a variety of diseases. 28 participants received one recording session for a night. 8 participants had repeated test. Recordings were conducted at a Center for sleep disorders. The algorism results were compared with full PSG.	Accuracies of event detection: hypopnea: 92%, apnea: 95%, and combined 97%.

eTable 1 Manuscripts reporting clinimetrics of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Supe	2017	USA	Capnostream 20 Bedside Monitors (Covidien, Needham, Massachusetts, USA)	Hypopnea
Koskinen	2021	Finland	Collare (Nukute Ltd, Finland)	Sleep - apnea
Makinen	2022	Finland	Collare (Nukute Ltd, Finland)	Sleep - apnea
Rotariu	2013	Romania	Developed by the authors	Sleep - apnea
Jungquist	2019	USA	ExSpiron 1Xi Minute Ventilation Monitor (Respiratory Motion)	Hypopnea
Acebo	1991	USA	Home monitoring system, brand not reported	Sleep -apnea

Aim of study	Methods: Study design; Participants (age, disease, setting); Procedures	Clinimetrics of the technology (validity, sensitivity, reliability, specificity, responsiveness)
To implement continuous monitoring to identify alarm conditions of respiratory distress.	Quantitative cross-sectional study with 25 adult patients with obstructive sleep apnea on a post anesthesia care unit. The time of the monitoring ranged from a few hours to several days.	True positive rate: 57%, compared with clinician judgement. True negative rate: 100%.
To validate the Nukute Collare in diagnosing sleep apnea.	Mixed-methods cross-sectional study with 71 adults with or without sleep apnea. Collare measurement was compared with standard PSG.*	91% sensitivity, 97% specificity, 91% positive predictive value, 97% negative predictive value, and 0.9-1.0 balanced accuracy.
To validate the Nukute Collare in screening sleep apnea.	Quantitative cross-sectional study with 41 adults. Collare measurement was compared with standard PSG.*	Accuracy of diagnosing sleep apnea automatically: 88% - 95%, accuracy of automatically classifying apnea severity: 76%.
To develop a system to monitor sleep apnea using wireless sensor nodes.	Quantitative cross-sectional study with 3 patients in the hospital. The patients simulated apnea events to test the system.	Simulated apnea events were detected by the system and alarms were triggered.
To compare Minute ventilation, capnography, and pulse oximetry in identifying respiratory depression and to develop and algorism for early detection.	Quantitative cross-sectional study with 48 adult participants in the post anesthesia care unit. The participants were the devices during their whole stay in the unit.	Minute ventilation and capnography were both effective in detecting respiratory depression, while pulse oximetry was not. A machine learning model could predict an opioid-induced respiratory depression event 10 min in advance with 80% accuracy.
To investigate the reliability and validity of measures of sleep and apnea using the home sleep monitoring system.	Quantitative cross-sectional study with 14 adults (Study 1) and 8 older adults living in nursing facilities (study 2). Study 1: One night, together with standard PSG in the Sleep Disorders Center. Study 2: Four weekly 24-h recordings were made on successive weeks at the participants' homes.	Study 1: Significant agreement was found for each sleep measure and the apnea index between the home monitoring system and standard PSG. Study 2: There were significant individual differences, and the measurement is reliable for each sleep measure and the number of apneas.

eTable 1 Manuscripts reporting clinimetrics of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Buyse	2023	Belgium	Hospital PSG, model and brand not reported	Sleep -apnea
Ravishankar	2014	India and USA	ICU bedside monitors, brand not reported	Hypopnea
Li	2021	China, USA	Nox-T3 (Nox Medical, Reykjavik, Iceland)	Sleep – disordered breathing
To	2021	China	Nox-T3 (Nox Medical, Reykjavik, Iceland)	Sleep - apnea
Xu	2017	China	Nox-T3 (Nox Medical, Reykjavik, Iceland)	Sleep - apnea

Aim of study	Methods: Study design; Participants (age, disease, setting); Procedures	Clinimetrics of the technology (validity, sensitivity, reliability, specificity, responsiveness)
To investigate whether lowering the cut-off scores for type 3 portable monitoring would benefit the diagnosis and treatment of obstructive sleep apnea.	Quantitative cross-sectional study with a database of 865 adults who started continuous positive airway pressure. Apnea-hypopnea index (AHI) of both the in-hospital PSG and portable monitoring were simulated from the existing data. Calculations of negative tests were performed with different Portable monitoring- respiratory event index (PM-REI) cut-of scores.	Portable monitoring underestimated the hypopnea events by 15 events/ hour, compared to in-hospital PSG. Lowering the PM-REI cut-off score for portable monitoring reduced the negative test rate from 57% to 34%.
To develop an algorithm to detect respiratory distress.	Quantitative cross-sectional study using ICU patient records. Preliminary analysis: 50 records with acute respiratory failure and 48 records without. Extended analysis: 157 records with no acute respiratory distress.	True Positive Rate: 88-92%; False Positive Rate: 6-12%. The algorithm would be able to detect respiratory instability when existing systems would not.
To evaluate the portable monitor in diagnosing sleep disordered breathing.	Quantitative cross-sectional study with 84 adults with chronic heart failure. Participants were monitored at home for one night. Another measurement was conducted with both PSG and the portable monitor in the laboratory.	Diagnosing sleep disordered breathing at ≥ 5 AHI events per hour: 87% sensitivity, 77% specificity. Detecting of Cheyne-Stokes respiration: 95% sensitivity, 91% specificity, compared to PSG.
To test the reliability of Nox-T3 in diagnosing sleep apnea in people with major diseases.	Quantitative cross-sectional study with 74 adults with psychiatric illnesses, stroke, ischemic heart diseases, chronic kidney diseases or other major diseases, suspected of having obstructive sleep apnea. Participants were simultaneously monitored by standard PSG and Nox-T3 overnight for at least four hours in the hospital.	Nox-T3 respiratory event index was significantly lower than the PSG AHI. Nox-T3 can reliably diagnose obstructive sleep apnea, but can underestimated the severity.
To validate the portable monitor in the diagnosis of sleep apnea.	Quantitative cross-sectional study with 80 adults. Participants were monitored at home for one night. Another measurement was conducted with both PSG and the portable monitor in the laboratory.	At ≥ 5 AHI events per hour: 95% sensitivity, 69% specificity. At ≥ 15 AHI events per hour: 93% sensitivity, 85% specificity, compared to standard PSG

eTable 1 Manuscripts reporting clinimetrics of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Wang	2015	China	Oximeter (Konica Minolta, Japan)	Sleep - apnea
Chang	2019	China, USA	PM, Nox-T3 (Nox Medical, Reykjavik, Iceland)	Sleep -apnea
Alvarez	2017	Spain	Reslink™ module (ResMed Inc. SanDiego, CA)	Sleep - hypopnea
Ganglberger	2022	USA	Respiration belt: AirGo (brand not reported), standard PSG: Natus System (brand not reported)	Sleep -apnea
Tedeschi	2013	Italy	Somtè PSG (Compumedics, Abbotsford, Victoria, Australia)	Sleep - apnea

Aim of study	Methods: Study design; Participants (age, disease, setting); Procedures	Clinimetrics of the technology (validity, sensitivity, reliability, specificity, responsiveness)
To evaluate the use of oximeter in diagnosing obstructive sleep apnea.	Quantitative cross-sectional study with 244 patients with obstructive sleep apnea hypopnea syndrome in the hospital. Participants were monitored overnight with both an oximeter and a full PSG.	Oximeter demonstrated a sensitivity of 68% and a specificity of 73% in diagnosing obstructive sleep apnea hypopnea syndrome, compared with PSG.
To evaluate a portable monitor in diagnosing obstructive sleep apnea.	Quantitative cross-sectional study with 90 adults with chronic obstructive pulmonary disease. Participants were monitored at home for one night. Another measurement was conducted with both PSG and the portable monitor in the laboratory.	95% sensitivity and 78% specificity in diagnosing obstructive sleep apnea compared to a standard PSG.
To evaluate the reliability of the built-in software compared to ventilatory Polygraphy.	Quantitative cross-sectional study with 26 adults with stable obesity hypoventilation syndrome under nocturnal non-invasive ventilation. Participants were monitored at home for a full night.	The built-in analysis is reproducible and reliable to assess quality of non-invasive ventilation when compared with Polygraphy ($r^2 = 0.71$, $p < 0.001$), but is less consistent than manual scoring.
To develop an algorithm to detect sleep-related respiratory abnormalities measured by a wearable device.	Quantitative cross-sectional study with 404 overweight adults. Participants were monitored with both devices for at least one night in the laboratory.	The AHI from the PSG, labeled by experts, correlated with those predicted by models using data from the respiration belt and oxygen saturation ($r = 0.96$), respiration-only ($r = 0.78$), and saturation only ($r = 0.93$). The AUCs were 94%, 86%, and 82% for the receiver operating characteristic curves, and 48%, 32%, and 51% for the precision-recall curves.
Compare home unattended portable monitoring and automatic continuous positive airway pressure titration to an attended in-laboratory program.	Randomized controlled trial with 131 adults with high suspicion of obstructive sleep apnea. 66 participants received home monitoring and 65 received in-laboratory standard PSG.	Reliability: 97% for the home portable monitoring. 2 out of 66 recordings had low quality.

eTable 1 Manuscripts reporting clinimetrics of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Polese	2013	Brazil	Stardust II® (Philips Respironics, Inc., Murrysville, PA, USA)	Sleep - apnea
Lazazzera	2022	France	UpNEA (developed by the authors)	Sleep - apnea
Kang	2012	China	WatchPAT (Itamar Medical, Israel)	Sleep - apnea
Lachenmeier	2022	Germany	SleepU (Wellue Health, Shenzhen Viatom Technology Co., Ltd., Shenzhen, China)	Sleep - dyspnea

Aim of study	Methods: Study design; Participants (age, disease, setting); Procedures	Clinimetrics of the technology (validity, sensitivity, reliability, specificity, responsiveness)
To evaluate the effectiveness of a type 3 portable monitor.	Quantitative cross-sectional study with 43 older participants. Sleep was assessed for two nights, one at home with the portable monitor (Stardust), the other at the hospital with Stardust and standard PSG.	No difference in the apnea–hypopnea index values between the portable and standard PSG. Good correlation between standard PSG and portable monitor (r=0.67) and the combination (r=0.84). The area under the receiver operator curve indicated good sensitivity and a positive predictive value for AHI with cutoffs of 5, 15, and 30 and good specificity and negative predictive value for AHI values above 15.
To present a system aimed to predict respiratory and cardiovascular disorders. UpNEA was part of the whole system.	Quantitative cross-sectional study with 96 adults with apnea/hypopnea syndrome in a hospital. Participants wore the glove-life device for a night. It was not reported with which device the results were compared. One healthy adult also wore the device for four nights.*	Within the patient group, the device detected central and obstructive apnea or hypopnea with a sensitivity of 73% - 87%, a specificity of 55% - 68%, and an accuracy of 65% - 72%. The data from the healthy adult showed a specificity of the device in detecting apnea or hypopnea was 96%.
To validate WatchPAT in diagnosing obstructive sleep apnea hypopnea syndrome.	Quantitative cross-sectional study with 35 adults complaining of snoring. Participants were monitored with Watch PAT and standard PSG simultaneously in the laboratory.	The apnea hypopnea index registered by WatchPAT correlated with PSG (r = 0.96, p < 0.001). Sensitivity = 92%, specificity = 100%. Accuracy is lower in patients with a high BMI.
To present a case where wearable oximetry device with haptic feedback was used to treat sleep disturbances in a person with lung cancer.	Case report with a home-dwelling older adult with lung cancer and sleep disturbances due to drops of oxygen saturation during sleep. The device vibrated when the oxygen saturation dropped. The recording of one whole night was reported.	The detection of decrease in oxygen saturation was reliable. By waking the patient with the vibration, events of oxygen saturation drop were reduced, so did sleep disturbances and anxiety symptoms associated with them.

eTable 1 Manuscripts reporting clinimetrics of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Arnal	2020	France	Dreem Headband (developed by the authors)	Sleep - stages
Cooray	2021	UK	Signals from standard PSG (model and brand not reported)	Sleep – stages and rapid-eye-movement sleep behavioral disorder (RBD)
Hirnoven	1997	Finland	8-channel 9000-11 recorder (Oxford Medilog)	Sleep - stages
Altini	2021	Finland	Oura Ring, Gen2M (Oura Health Ltd, Oulu, Finland)	Sleep - stages

Aim of study	Methods: Study design; Participants (age, disease, setting); Procedures	Clinimetrics of the technology (validity, sensitivity, reliability, specificity, responsiveness)
To validate the Dreem Headband, containing EEG, pulse oximetry and accelerometer in determining sleep stages.	Quantitative cross-sectional study with 25 healthy adults at a sleep center. The sleep stages determined by Dreem Headband was compared with standard PSG.	The error of Dreem Headband compared with standard PSG: EEG signals: 10% - 16% Heart rate: 1.2 ± 0.5 beats per minute Breathing frequency: 0.3 ± 0.2 cycles per minute Respiration rate variability: 3.2 ± 0.6%
To develop a RBD screening tool with minimal sensors.	Quantitative cross-sectional study with 50 adults with RBD and 50 healthy controls. Participants were monitored for one night with standard PSG for one night. The results of the algorithm were compared to results based an earlier algorithm using EEG, electrooculogram (EOG), and EMG.	The optimal model combined EOG and EMG and could classify sleep stages with 0.57 ± 0.19 kappa (3 stage) and detect RBD detection with an accuracy of 90% (sensitivity 88% and specificity 92%).
To develop an algorism to score drowsiness and sleep onset.	Quantitative cross-sectional study. An algorism was developed based on 30 min recording at sleep onset of seven healthy adult participants and a 6-hour daytime recording, including drowsy and sleep episodes, of seven adult patients with obstructive sleep apnea syndrome was used to test the algorism. *	Total agreement between the visual and computer scorings: 92% Non-REM sleep: 64% sensitivity, 82% specificity. Drowsy stages: 19% sensitivity, 61% specificity. Alpha activity detection: 5% sensitivity, 11-13% specificity.
To test the accuracy of sleep stages determination by Oura Ring, combined with machine learning.	Quantitative cross-sectional study with 106 adults. In total, 440 nights of sleep were monitored by Oura Ring and standard PSG. Some of the recordings took place at home, the setting of other recordings was not reported. Machine learning models were build using different numbers of parameters derived from Oura Ring signals.	Accuracy for 2-stage detection (sleep, wake) with accelerometer data was 94%. Including other parameters (temperature, HRV, and circadian features) increased the accuracy to 96%. Accuracy for 4-stage detection (light NREM sleep, deep NREM sleep, REM sleep, and wake) with accelerometer data was 57%. Including other parameters increased the accuracy to 79%.

eTable 1 Manuscripts reporting clinimetrics of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Ghorbani	2022	Singapore	Oura Ring, Gen2 and Gen3 (Oura Health Ltd, Oulu, Finland)	Sleep - stages
Kinnunen	2020	Finland	Oura Ring Gen3 (Oura Health Ltd, Oulu, Finland)	Sleep -heart rate
Multi-modal systems - with environmental sensors				
Au-Yeung	2020	USA	Ambient sensors: model not reported (NYCE Sensors, Vancouver, BC), Pressure mats: model not reported (Emfit, Finland), Actigraphy: Actiwatch Spectrums (Philips Respironics, Murrysville, PA), Environmental sensors: Thunderboard Sense 2- SLTB004A (Silicon Labs, Austin, TX)	Agitation
Bankole	2020	USA	BESI system (developed by the authors)	Agitation

Aim of study	Methods: Study design; Participants (age, disease, setting); Procedures	Clinimetrics of the technology (validity, sensitivity, reliability, specificity, responsiveness)
To compare two generations of Oura Ring algorithms in classifying sleep stages.	Quantitative cross-sectional study with 58 healthy adults, each went through 3 nights of home monitoring with standard PSG and Oura Ring.	Gen3 accuracy: 92.6%, sensitivity: 94.9% (0.03), specificity: 78.5%. Gen3 algorithm outperformed Gen2 and is comparable with PSG in measuring sleep latency, light sleep, rapid eye movement, and wake after sleep onset durations.
To validate the Oura Ring in monitoring nocturnal heart rate.	Quantitative cross-sectional study with 49 healthy adults. Recordings were made at home with both the Oura Ring and an ECG during the night.	High correlation between the Oura Ring and ECG on the average heart rate ($r^2 = 0.996$) and HRV ($r^2 = 0.980$).
To provide a proof of concept of monitoring and predicting agitation in memory care facilities with by monitoring the activity, sleep, and the environment (temperature, light, sound, humidity).	Quantitative case study with one adult with dementia in a memory care unit. The participant was continuously monitored by the system for 138 days. Agitation was recorded by nurses.	Sleep, total activity, humidity, ambient sound during the night, humidity and light and in the living room of the previous evening correlated with the presence of agitation at night ($p < 0.05$)
To develop and validate a home monitoring system for agitation and its environmental triggers in people with dementia. The system includes an actigraphy and environmental sensors for acoustic, light, humidity, barometric pressure, and movement.	Mixed-method study with two healthy volunteers and 12 community-dwelling people with dementia and their family caregivers. The BESI system was first tested in the laboratory and then applied in each home of the people with dementia for 30 days. Family caregivers recorded the activities and agitation events of the people with dementia.	Environmental factors (temperature, pressure, and humidity) strongly correlated with agitation ($r = 0.70$ to 0.85, $p = 0.05$). However, the predictors were person-specific.

eTable 1 Manuscripts reporting clinimetrics of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Khan	2019	Canada	Developed by the authors	Agitation
Davoudi	2019	USA	Developed by the authors	Delirium
Multi-modal systems – other multi-modal systems				
Chen	2019	Singapore	Study 1: chest-worn biosensor (model and brand not reported), Study 2: Everion® CD, analyzed by the Biovitals™ analytics platform	Change in vital signs, hypoxia

Aim of study	Methods: Study design; Participants (age, disease, setting); Procedures	Clinimetrics of the technology (validity, sensitivity, reliability, specificity, responsiveness)
To develop a system to automatically detect agitation in people with dementia. The proposed system includes actigraphy, EDA monitor, pressure mat, video cameras, environmental motion sensors, and door sensors.	Quantitative cross-sectional study with two older adults with dementia at a rehabilitation institute. The participants were monitored for 15 and 13 days respectively. Agitation episodes were noted by nurses. Different algorithms were tested using different combinations of sensor data.	The highest AUC (89%) was achieved by combining actigraphy, skin temperature, and EDA data.
To pilot test a system that includes a camera, three actigraphy, a light sensor, and a microphone in the ICU.	Quantitative cross-sectional study with 17 older adults in the surgical ICU, nine of them had delirium. Participants were monitored continuously for a maximum of seven days.	Participants with and without delirium significant differed in facial expressions, functional status entailing extremity movement and postures, and environmental factors including the visitation frequency, light and sound pressure levels at night.
To present an analytic platform to monitor the changes in vital signs, including heart rate, respiration rate and activity.	Quantitative non-randomized experimental studies. The first study used data of 26 older adults with heart failure after discharge. They were monitored for seven to 60 days. Disturbance was added by the researchers to a few days of the data to validate the system. In the second study, 50 healthy adults wore the device for four days in their daily life and for two hours in a hypobaric chamber where they performed controlled exercises. The Biovitals results of daily life was compared with those in the chamber.	Study 1: The system could recognize randomly added disturbance to the data with an AUC of 80%-94%. Study 2: The system could distinguish the daily life from the hypobaric chamber condition with an AUC of 99%, a sensitivity of 91%, and a specificity of 98%.

eTable 1 Manuscripts reporting clinimetrics of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Ramirez-Moreno	2021	Mexico	Ultracortex "Mark IV" EEG headset, (OpenBCI, New York, NY, USA) Empatica E4 (Empatica, Milano, Italy)	Mental fatigue
Gelinas	2021	Canada	Nociception Level (NOL) Index PMD200™ (Medasense Biometrics Ltd, Ramat Gan, Israel)	Pain
Jiang	2019	Finland, USA, Austria	Developed by the authors	Pain

Aim of study	Methods: Study design; Participants (age, disease, setting); Procedures	Clinimetrics of the technology (validity, sensitivity, reliability, specificity, responsiveness)
To develop a model to detect mental fatigue in workplace.	Quantitative non-randomized experimental study with 17 healthy adults in the laboratory. Participants were monitored for 30s with eyes open, 30s with eyes closed, and four minutes during an auditory oddball task. Correlations to self-reported mental fatigue levels (using the fatigue assessment scale) were calculated to find the best predictors.	EEG features correlated with the self-report of mental fatigue. The parameters measured by Empatica E4 did not have statistically significant correlations. The best model using three EEG features had an accuracy of 88%.
To test a system to monitor pain in patients after an operation. The device is worn on the finger and monitors EDA, and heart rate.	Quantitative non-randomized experimental study with 70 participants in the ICU after cardiac surgery. The NOL index calculated by the system was compared to self-reports of pain and anxiety (0-10 numeric rating scale), as well as observation of pain using the Critical-Care Pain Observation Tool (CPOT) measured before and during a non-nociceptive procedure and before, during, and after a nociceptive procedure.	The NOL index was higher during nociceptive procedures and correlated with self-reported pain intensity and unpleasantness. It did not correlate anxiety and CPOT. The NOL recognized pain with a self-reported intensity above 1 (out of 10) with an AUC of 70%, sensitivity of 76%, and specificity of 61%. For pain intensity above 5, the AUC was 74%, the sensitivity was 85%, and the specificity was 75%.
To develop a system to continuously monitor pain by measuring respiration rate, heart rate, EDA, and face sEMG.	Quantitative non-randomized experimental study with 30 healthy participants in the laboratory. Participants received electrical or thermal pain stimuli on the forearm of ring finger while being monitored by the system. The monitoring results were compared to self-report of no pain, mild pain, or moderate/severe pain based on a VAS.	They system could classify pain in three severity categories with an accuracy of 70.6%. Respiration rate, heart rate, EDA correlate more strongly with pain intensity than face sEMG.

eTable 1 Manuscripts reporting clinimetrics of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Lai Kwan	2019	Canada	Triple Point Sensor (TPS) (ought Technology Ltd.)	Significant moments
Miranda	2016	USA	Heart rate: Hxm (Zephyr); EDA: Empatica E3; EEG: Muse band	Anxiety
Rajasekaran	2011	USA	Portable Autonomous Multisensory Intervention Device (PAMID, developed by the authors)	Agitation
Spasojevic	2021	Canada	Empatica E4	Agitation

Aim of study	Methods: Study design; Participants (age, disease, setting); Procedures	Clinimetrics of the technology (validity, sensitivity, reliability, specificity, responsiveness)
To present a system which detects significant moments of people with dementia and their family caregivers by measuring EDA, skin temperature, and heart rate.	Quantitative cross-sectional study with three older people with dementia and their family caregivers. Participants wore the sensor during 45-min sessions of a movement program for 8 times. Significant moments, carrying physical, emotional, or interpersonal significance, were detected by the system and participants were asked to watch 20s recordings of these moments and evaluate whether these were significant or memorable.	The agreement between the automatic detection and subjective report was 70%.
To describe an experiment eliciting anxiety in informal caregivers for people with dementia, while measuring heart rate, EDA, and EEG.	Quantitative non-randomized experimental study with 10 healthy adults in the laboratory. During 30 min sessions, participants had a relaxation stage and performed therapy with a simulated person with dementia. The level of anxiety was recorded by the participants and researchers. Models were developed using the physiological parameters to predict the presence of anxiety.	The average precision of different models using EDA and inter-beat interval was 78%. The best model used only inter-beat interval, reaching a precision of 80%. Specificity was 38% on average and 47% for the inter-beat interval model.
To test the reliability of the chest belt which integrated measurements for heart rate, skin temperature and EDA, and to evaluate its appearance and comfortability.	Quantitative non-randomized experimental study with six community-dwelling older adults in the laboratory. During a 40-minute experiment, participants took four sets of STROOP tests while being monitored by the device and conventional instruments.	PAMID was sensitive in detecting changes in heart rate, skin temperature and EDA.
To detect agitation in people with dementia using a multi-modal wearable device which monitored movement, blood volume pulse, EDA, and skin temperature.	Quantitative cross-sectional study with 17 people with dementia in a dementia unit. Participants wore the device in day time for a maximum of two months. Agitation events were noted with observation through video cameras.	Multi-modal prediction models were better than single-model ones. The best model had an AUC of 82%. Skin temperature was the least relevant signal.

eTable 1 Manuscripts reporting clinimetrics of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Choi	2012	USA, Qatar	Developed by the authors	Stress
Wijsman	2011	Netherlands	Developed by the authors	Stress
Wu	2012	South Korea	Developed by the authors	Stress
Non-contact monitoring systems - pressure mats				
Boissy	2011	Canada	Developed by Université de Sherbrooke, Québec, Canada	(risk of) pressure ulcer
Dietz-Terjung	2020	Germany	VitaLog (SWGSportwerkGmbH&Co. KG, Dortmund, Germany)	Sleep – disordered breathing

Aim of study	Methods: Study design; Participants (age, disease, setting); Procedures	Clinimetrics of the technology (validity, sensitivity, reliability, specificity, responsiveness)
To validate a system to distinguish stress from relaxation by monitoring respiration, HRV, EDA, and sEMG.	Quantitative non-randomized experimental study with 10 healthy adults in the laboratory. During a 48-minute experiment, participants performed various mentally stressful tasks, with deep breathing in between.	The system could distinguish mental stress from relaxation with a classification rate of 81%, a true positive rate of 87%, and a true negative rate of 71%.
To find physiological parameters that can best predict mental stress. ECG, respiration, EDA, and sEMG were measured.	Quantitative non-randomized experimental study with 30 healthy adults in the laboratory. During an experiment of around 20 minutes, the participants performed three cognitive tasks with time pressure and distraction. Social stress was also induced. Resting periods were scheduled between the tests.	Using seven physiological features, the system could distinguish stressful periods from rest periods with an accuracy of 80%.
To test the effectiveness of stress reduction training with a wearable biofeedback system, consisting of ECG, Pulse rate, respiration, ambient and breath temperature measurements.	Quantitative non-randomized experimental study with 67 adults in the laboratory and during a 3-week biofeedback training for stress reduction. For the validation of the device, several adults were measured by it and a commercially available PolyG-A system in the laboratory.	The proposed device produced similar ECG, photoplethysmography and respiration signals compared to the commercial system. HRV and pulse rate variability were extracted accurately.
To present the functioning of two type of carbon nano tube films (multi-layered vs purified) in detecting pressure.	Quantitative experimental study without participants. The electrical and mechanical properties of the films were tested.	The loosely woven, multi-layered film had lower sensitivity (resistance change was 8 times higher) compared to the purified film. The purified film was less affected by the mechanical noise of the testing system (noise ratio 5% vs. 50%).
To assess the accuracy of VitaLog in estimating respiratory rate variability.	Quantitative cross-sectional study with 103 adults referred to the sleep lab. The VitaLog data were compared to nasal flow signal obtained by PSG.*	The VitaLog estimation of respiration rate variability had a correlation of $r = 0.99$ and a bias of 0.2 inhale-exhale cycles per minute compared with nasal flow signal. The Mann-Whitney U test showed no significant difference between participants with or without sleep disturbed breathing.

eTable 1 Manuscripts reporting clinimetrics of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Kobayashi	2012	Japan	SD-101 (manufacturer not reported); Percutaneous oxygen saturation (SpO2)sensor: SX Module SX-2007 (Kenzmedico Co. Ltd., Saitama, Japan)	Sleep – apnea
Motoi	2009	Japan	Developed by the authors	Sleep – apnea and hypopnea
Non-contact monitoring systems – video/facial expression analysis				
Becouze	2007	New Zealand	Camera: Canon IXUS 40 digital camera; Algorithm developed by the authors	Agitation
Palestra	2020	Italy	RGB cameras; Algorithm developed by the authors	Emotions

Aim of study	Methods: Study design; Participants (age, disease, setting); Procedures	Clinimetrics of the technology (validity, sensitivity, reliability, specificity, responsiveness)
To investigate whether adding a SpO2 measurement increases the accuracy of recognizing mild to moderate obstructive sleep apnea syndrome by SD-101.	Quantitative cross-sectional study with 60 adult patients from an out-patient clinic. Overnight sleep was simultaneously monitored by PSG and SD-101 at the laboratory.	Adding SpO2 measurement improved the accuracy of the SD-101 for OSAS detection for AHI >15 (sensitivity: 97% vs. 88%; specificity: 90.5 % vs. 85.7 %, compared to the SD-101 alone). The SD-101 measurements significantly correlated with the PSG data (SD-101 alone: $r = 0.871$, $p < 0.0001$; SD-101 with SpO2: $r = 0.965$, $p < 0.0001$). Bland–Altman plots showed a smaller dispersion for the SD-101 with SpO2 than for the SD-101 alone.
To study the applicability of non-contact sensors in a hospital room. Only the results about the pressure mat were presented in this manuscript.	Quantitative cross-sectional study with two adults with sleep apnea in the hospital. Participants were monitored for one night with both the pressure mat under the pillow and a standard PSG.	There was good agreement on the number of apnea or hypopnea events per hour between the pressure mat and the PSG.
To develop an algorithm to detect grimacing independent of the head movement.	Quantitative non-randomized experimental study with two simulated videos of the face, one grimacing and the other with a neutral expression.	The algorithm could successfully track the reference point on the forehead and identify the face area when the head was moving. The grimacing level determined by the system corresponded with observation.
To evaluate a robot-facilitated memory training in its effects of engaging the participants.	Quantitative cross-sectional study with 21 adults with Mild Cognitive Impairment. Videos of an hour were taken during robot-facilitated group memory training sessions and emotions were identified by automatic facial expression analysis.	The system could detect all faces, including partially covered faces (success rate 56%), and recognize emotions reliably when the face was detected.

eTable 1 Manuscripts reporting clinimetrics of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Castillo	2020	Canada	Algorithm: FaceReader version 8 (Noldus Technology Information)	Pain
Rezaei	2021	Canada	Algorithm developed by the authors	Pain
Non-contact monitoring systems - infrared				
Casaccia	2019	Italy	Passive InfraRed motion sensor (brand not reported)	Sleep - stages
Tejedor	2020	Spain	Camera: FLIR E60bx	Thermal comfort

Aim of study	Methods: Study design; Participants (age, disease, setting); Procedures	Clinimetrics of the technology (validity, sensitivity, reliability, specificity, responsiveness)
To validate the FaceReader in its estimation of pain and heart rate.	Quantitative cross-sectional study with pre-existing video recordings of two older long-term care residents with dementia and two community dwelling older adults. FaceReader automatically analysed pain based on facial expressions and estimated the heart rate. Pain was also manually scored using the Facial Action Coding System (FACS) and heart rate was estimated with the well-established Video Magnification (VM) algorithm.	FaceReader rating of pain scores strongly correlated with FACS during and around facial pain expression (r = 0.99 – 1.00). Its heart rate estimation strongly correlated with VM (r = 0.99 – 1.00).
To develop a technology to automatically recognize pain in long-term care facilities.	Quantitative experimental study with pre-existing video recordings of the faces of 25 adults with shoulder injury, 47 community-dwelling older adults, and 48 older adults with severe dementia in long-term care facilities. Automatic recognition of pain was compared with Prkachin and Solomon Pain Index (PSPI), scored by trained human annotators.	The algorithm outperformed baseline in recognizing pain. Pain prediction with the final model correlated with PSPI (r = 0.48 – 0.70), had an average precision of 0.71 (people with dementia) and 0.84 (in older adults without dementia). The AUC was 0.85 – 0.86.
To test the possibility of classifying sleep stages using infrared signal.	Quantitative case report on 25 nights of sleep data of one healthy adult. The sleep stages classified by the Passive InfraRed system was compared to the sleep pattern measured by a Ballistocardiographic bed sensor (Nokia Sleep bed sensor) under the mattress.	Passive InfraRed sensor could detect the waking states (R = 0.67 - 0.86, R^2 = 0.45 - 0.69) better than REM (R = 0.40, R^2 = 0.16), deep sleep (R = -0.03, R^2 = 0.00). and light sleep (R = 0.61, R^2 =0.37).
To propose a model to determine indoor thermal comfort for nursing home residents.	Quantitative case study with 15 older adults in a nursing home during winter. Participants were monitored for five minutes. A thermal questionnaire was filled in by the participants.	The proposed numerical model was reliably. The temperature of the nose could reliably indicate feeling cold. The self-report of the participants was concluded as not reliable.

eTable 1 Manuscripts reporting clinimetrics of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Non-contact monitoring systems - radar				
Hsu	2017	USA	EZ-Sleep (developed by the authors)	Sleep
Resuli	2021	USA	Vayyar radar system	Sleep -respiration rate
Schnellenberge	2020	Germany	Developed by the authors	Vital signs
Non-contact monitoring systems - multiple sensors				
Dimitrievski	2021	Macedonia, Portugal, Spain	Piezoelectric sensor: (Angelcare, Montreal, QC, Canada), passive infrared sensors (Sunfounder, Shenzhen, China)	Sleep

Aim of study	Methods: Study design; Participants (age, disease, setting); Procedures	Clinimetrics of the technology (validity, sensitivity, reliability, specificity, responsiveness)
To present a radio-based sleep monitor.	Quantitative cross-sectional study with 10 healthy community-duelling adults. More than 100 nights of sleep was monitored by EZ-Sleep and compared to a wearable SleepProfiler and sleep diary.	Compared to SleepProfiler, the EZ-Sleep had an average error of 3.15 min in estimating time in bed, 10.3 min in total sleep time, 4.9 min in sleep latency, 8.2 min in wake after sleep onset, and 2.8% in sleep efficiency. EZ-Sleep can simultaneously monitor more than one people, although there can be a little disturbance if two people are sleeping close to each other.
To test the accuracy of respiration rate estimation in different sleeping positions with a radio frequency sensor.	Quantitative non-randomized experimental study with five healthy adults in a laboratory. Participants took different sleeping positions, each for at least six minutes. The radio frequency based estimation of breathing was compared with a respiration belt.	The accuracy of respiration estimation by the radar system was 92% in back postures, 84% in side postures, 76% in stomach position, 90% with a blanket covering the participant, 87% when sleeping on the back with the face turned sideways, and 86% in the sitting position.
To present a dataset with radar signals of the vital signs with synchronized reference.	Quantitative non-randomized experimental study with 30 healthy adults in the laboratory. Participants lay on a tilted table and five scenarios triggering the automatic nervous system and hemodynamics were simulated. Radar recording of the chest was conducted simultaneously with ECG, impedance cardiogram, and blood pressure.	The interbeat-intervals measured by the radar highly correlated with the ECG data ($r = 0.96$, $p < 0.001$)
To present a non-invasive system that monitors movement during sleep, aiming to detect sleep disturbances due to COVID-19.	Quantitative cross-sectional study with adults with COVID-19 in the hospital. Participants were monitored for eight hours.	Data from the Piezoelectric sensor correlated with the infrared sensors ($r = 0.32$ - 0.43). The five infrared sensors also correlated with each other ($r = 0.83$). There was built-in delay in the infrared sensors and oscillation in the piezoelectric sensor, but these could be adjusted with the post-processing of the data.

eTable 1 Manuscripts reporting clinimetrics of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Ravindran	2023	UK	Radar: Somnofy (VitalThings, Norway); Pressure mats: Withings Sleep Analyser (WSA, Withings, France), Emfit-QS (Emfit Ltd, Finland)	Sleep
Kroll	2020	Germany	Camera: Mini-Webcam (Conrad Electronics SE, Hirschau, Germany); Acoustic sensor: ME32 (Olympus Imaging Europa GmbH, Hamburg, Germany) Pressure mat: SafeBed IP system (Emfit® Ltd., Vaajakoski, Finland)	Agitation

Note: Adults = mean age between 18 and 65; Older adults = mean age over 65;
ICU = intensive care unit
References can be found in Supplement IV.
*The setting was not reported.

Aim of study	Methods: Study design; Participants (age, disease, setting); Procedures	Clinimetrics of the technology (validity, sensitivity, reliability, specificity, responsiveness)
To compare three non-contact sleep monitors with PSG and actigraphy (Actiwatch Spectrum).	Quantitative cross-sectional study with 35 older adults, some with sleep apnea. Participants used the non-contact devices at their own homes for 8-14 days and had one overnight measurement with all the devices in the laboratory.	Compared to PSG, all three devices overestimated total sleep time (bias > 90 min) and sleep efficiency (bias > 13 %), and underestimated wake after sleep onset (bias > 50 min). Bedside radar accurately measured sleep onset latency (bias < 6 mins) while the under-mattress devices overestimated it (bias >16 mins). These performances were less optimal than actigraphy. The bedside radar performed better in discriminating sleep vs wake (Matthews Correlation Coefficient (MCC) [mean and 95% CI] = 0.63 [0.57 0.69]) than the under-mattress devices (MCC = 0.41 [0.36 0.46]; Emfit-QS = 0.35 [0.26 0.43]). Accuracy of identifying REM and Light sleep was poor for all three devices, but deep sleep was predicted with moderate accuracy (MCC >0.45) by both Somnofy and Withings Sleep Analyser.
To validate the non-contact monitoring system and a tent-like shelter for people with dementia.	Quantitative cross-sectional study with six healthy adult volunteers in the laboratory and 19 patients, most of whom had dementia, in the emergency department and a geriatric-psychiatric ward. Participants were monitored for two hours, the first hour without the tent-like shelter, the second hour with it.	In the laboratory test, the measurement of heart rate was reliable between the first and second hour, but that of respiration rate was not. The camera and mattress registration of movement complimented each other. The measurements in the emergency department and geriatric-gerontopsychiatric ward were reliable.

eTable 2 Manuscripts reporting on the acceptability or feasibility of the monitoring technologies to detect distress and discomfort

Actigraphy				
First author	**Year**	**Country**	**Monitoring technology (model and brand)**	**Symptom monitored**
Knuff	2019	USA	wGT3x+ activity monitors (Actigraph, LLC, Pensacola, FL)	Agitation
Favela	2020	Mexico	Fitbit Charge 2 HR, Fitbit Alta (Fitbit Inc, CA, USA)	Behavioral symptoms of dementia
LeBlanc	2022	USA	MisFit Shine	Sleep

Aim of study	Methods: Study design; Participants being monitored; Setting; Procedures; Participants evaluating the technology;	Acceptability or feasibility of the technology
To evaluate the feasibility and validity of actigraphy as a measurement of agitation in dementia.	Quantitative cross-sectional study. 20 older adults with dementia living in long-term care facilities wore the wristband continuously for a minimum of 24 hours and maximum of 7 days. Feasibility was evaluated by the researchers.	Actigraph monitors recorded for almost 1 week. Agitation severity did not influence compliance. The authors concluded that multi-day continuous actigraphic monitoring is feasible.
To evaluate an intervention program lead by a social robot.	Mixed methods non-randomised experimental study with 10 older adults in a long-term care facility. The wristwatch form of actigraphy was worn for 54 days on average. Feasibility was evaluated by the researchers.	One participant refused to wear the device at night. Two other participants needed persuasion to take the device off for charging. One participant feared losing or damaging the device and discontinued wearing it. The other participants did not experience anxiety about the device.
To describe the experience of using a sleep monitor for sleep self-management.	Qualitative study with 25 community-dwelling older adults with sleep disturbances. The participants wore the device for four weeks and received an interview afterwards.	Regarding the device, participants could understand how it worked and considered it easy to use. The plain design was appreciated, although some participants wanted the device to look more like a watch and found it bothersome having to tap it to see the time. The device was comfortable and light-weighted. The wrist clamp and battery life could be improved. There was concern about privacy of the data and some did not trust the results of the device. Both financial and time costs were important issues to consider. More than half of the participants had the intention to continue using the device.

eTable 2 Manuscripts reporting on the acceptability or feasibility of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Svetnik	2021	USA	Garmin Vivosmart	Sleep
Van Dijk	2012	Netherlands	Actiwatch AW7 (Cambridge Neurotechnology Ltd, Cambridge, UK)	Sleep
Brain activity monitors – Bispectural Index (BIS)				
Gambrell	2005	USA	Not reported	Depth of sedation

Aim of study	Methods: Study design; Participants being monitored; Setting; Procedures; Participants evaluating the technology;	Acceptability or feasibility of the technology
To investigate the usefulness of a wearable in measuring treatment effects of insomnia in people with dementia.	Randomized experimental study with 285 older adults with Alzheimer's disease and insomnia. During insomnia treatment of four weeks, participants were instructed to wear the device all the nights at home. Three overnight measurements with standard polysomnography (PSG) were performed in the laboratory at screening, baseline, and at the end of the treatment. The challenges of using the device were reported by the researchers.	74% of the participants had usable data of the device, which is at least three nights of measurements in a week. The challenges were patient compliance, battery life and Bluetooth connectivity between the watch and tablet.
To evaluate the feasibility of using actigraphy to monitor sleep in older people with intellectual disability.	Quantitative cross-sectional study. 563 older adults with intellectual disability wore the actiwatch continuously for a maximum of 14 days. Feasibility was evaluated by the researchers.*	A successful measurement was obtained from 200 (35%) of the participants. Unsuccessful measurements were mainly due to problems wearing the device and incomplete bedtime information. 354 (92%) of those who started wearing the device wore it for more than 7 days.
To present a case where the BIS monitor is used successfully in the ICU.	Case study of a 78-year-old woman with intraventricular haemorrhage. She was monitored in the last few hours of her life in the ICU. The nurse and family expressed their opinions on the device.	The nurse saw BIS as an additional tool to help titration and to educate the family. The family is more confident of a comfortable death and are pleased to see the BIS values fluctuate when they talked to the patient.

eTable 2 Manuscripts reporting on the acceptability or feasibility of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Pedrao	2020	Brazil	BIS™ Vista Monitoring System (Covidien LLC, Mansfield, United States)	Sleep
Brain activity monitors – other electroencephalography(EEG)-based technologies				
Pu	2021	Australia	MUSE 2 (InteraXon Inc., Toronto ON, Canada)	Pain
Vacas	2016	USA	SedLine Brain Function Monitor (Masimo Corp., Irvine, California)	Sleep - stages
Brain activity monitors – the concept of sedation monitors				
Six	2020	Belgium	Not reported	Sedation

Aim of study	Methods: Study design; Participants being monitored; Setting; Procedures; Participants evaluating the technology;	Acceptability or feasibility of the technology
To test the feasibility of using BIS to evaluate sleep in critically ill patients.	Quantitative cross-sectional study with 29 lucid patients in ICU. BIS monitoring was performed for a whole night (12 hours). The participants filled in the Richards-Campbell Sleep Questionnaire (RCSQ) the next morning. The feasibility was evaluated by the researchers.	Among 49 patients who were eligible for the study, seven refused to participate, two could not be monitored because of delirium, five could not be monitored because of other procedures they underwent, five dropped out because of discomfort of the sensors or displacement of the sensors. The authors concluded that BIS had limited feasibility in lucid patients in the ICU.
To assess the feasibility of a headband EEG to monitor pain in long-term care residents with dementia.	Quantitative cross-sectional study with 4 older adults with dementia and chronic pain in a long-term care facility. Each participant was monitored for 10 minutes. The Pain Assessment in Advanced Dementia (PAINAD) scale was administered before and after the measurement.	The device was acceptable to people with dementia and no participant tried to remove the device. No discomfort was reported. Appropriately positioning the device was challenging.
To validate the device in laboratory setting and to test the feasibility of its use in the ICU.	Quantitative cross-sectional study with three adult outpatients in the laboratory and 23 ICU patients.	The system is feasible in the ICU.
To investigate what influences professional caregivers and family members' attitudes towards the use of monitors during continuous sedation until death.	Qualitative interview study with 20 professional caregivers and 15 family members of patients in a palliative care setting.	Family members and professional caregivers found the use of monitors during continuous sedation until death acceptable because this would be a more objective assessment of consciousness and pain, which gave reassurance to family and guides titration for the professional caregivers.

eTable 2 Manuscripts reporting on the acceptability or feasibility of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Electrocardiography (ECG)				
Li	2022	China	myBeat-WHS-1 (Union Tool Co., Ltd., Japan)	Stress
Tao	2021	China, United Arab Emirates, Bahrain	Not reported	Atrial fibrillation
				EEG
Tiihonen	2008	Finland	Developed by the authors	Depth of sedation

	Aim of study	Methods: Study design; Participants being monitored; Setting; Procedures; Participants evaluating the technology;	Acceptability or feasibility of the technology
	To use a wearable ECG monitor to measure workplace stress in nurses.	Quantitative cross-sectional study with 17 healthy nurses during one work day at the hospital. Participants wore the device and filled in the Chinese Nurses Stress Response Scale (CNSRS) after work. The feasibility was evaluated by the authors.	The authors concluded that it was feasible to use the portable device to monitor stress in nurses in their work environment.
	To improve diagnostic efficiency of severe fever with thrombocytopenia syndrome bunyavirus (SFTSV) complicated by atrial fibrillation	Quantitative randomized controlled study with 200 older adults with SFTSV and hypertrophic cardiomyopathy in the hospital and 20 healthy adults. After surgery for cardiac sympathetic block, patients were randomly assigned to a monitoring group using ECG, supported by a new algorithm, or a routine observation group to monitor atrial fibrillation. Patients reported their satisfaction.	Patients were significantly more satisfied with the ECG atrial fibrillation monitoring technology than clinical observation ($p < 0.05$).
and ECG			
	To develop and validate a portable device to measure the depth of sedation with auditory event-related potentials (ERP).	Quantitative cross-sectional study with four healthy adults in the laboratory. Technical validation of the device was performed. ERP, EEG, ECG, and somatosensory-evoked potentials were measured. The quality of the signals were evaluated by an experienced neurophysiologist.	ERP and somatosensory-evoked potential measurements generated distinct responses. The quality of the signal recordings was good. The noise amplitudes were acceptable. The interface was easy to use. (Note: The study reported results of the technical validation, but no clinimetrics.)

eTable 2 Manuscripts reporting on the acceptability or feasibility of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Electrodermal activity (EDA) monitors				
Leborgne	2023	Netherlands	Developed by the author	Stress
Incontinence sensors				
Boerakker	2022	Netherlands	Abena Nova (Abena Group, Denmark), WeSense (Seneca Sense Technologies, Canada)	Incontinence
Nikoletti	2004	Australia	Not reported	Incontinence

Aim of study	Methods: Study design; Participants being monitored; Setting; Procedures; Participants evaluating the technology;	Acceptability or feasibility of the technology
To develop a sock garment to detect stress in people with intellectual disabilities.	Quantitative non-randomized experimental study. Sixty adults with severe intellectual disabilities in long-term care facilities tried on the garment. It was not clear whether they also participated in the experiment. The feasibility was evaluated by the researchers.	Of the 60 clients, 48 accepted and wore the sock. The others did not wear it due to other garments necessary for their comfort, such as compression socks, or due to repeated behavior resulting in removing the clothing. The researchers concluded that the sock was comfortable and user-friendly for most people with intellectual disabilities.
To investigate the use of intelligent incontinence material in nursing homes.	Mixed-methods pilot study with 25 older adults in nursing homes with urinary incontinence. Abena Nova and WeSense were evaluated by the clients, family caregivers, and staff.	The clients did not feel the presence of extra sensors in the incontinence material. Family caregivers valued less dirty laundry and less unnecessary care moments. The staff reported that the technology is time-saving and they could trust it. The downsides were that the bowel incontinence is not measured and that the sensors are sometimes difficult to attach.
To evaluate an incontinence alarm in acute elderly care setting.	Mixed-method study with 41 older adults on acute care rehabilitation wards. Incontinence was monitored for 72 hours for each patient.	Numerous problems were reported: false alarms, false negatives, shorter transmission range than claimed by the manufacturer, the need to recharge frequently, and sensors being discarded with pads. Resolving these issues was time-consuming and frustrating for staff and patients. There was resistance of experienced staff to learn the technology and to change personal routines.

eTable 2 Manuscripts reporting on the acceptability or feasibility of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Toba	1996	Japan	Not reported	Incontinence
Van der Hurk	1998	Netherlands	Developed by the authors	Incontinence
Multi-modal monitoring systems – polysomnography (PSG)				
Abdenbi	2002	France	CID 102 and CID 108 (CIDELEC, Sainte-Gemmes-sur-Loire, France)	Sleep
Koskinen	2021	Finland	Collare (Nukute Ltd, Finland)	Sleep - apnea

Aim of study	Methods: Study design; Participants being monitored; Setting; Procedures; Participants evaluating the technology;	Acceptability or feasibility of the technology
To evaluate the effects of wearing a thin-film urinary drainage sensor in the incontinence material on urinary quality of life and nursing work hours.	Mixed method cross-sectional study with 4 older adults with urinary incontinence in nursing homes. Participants were asked about the comfort of the sensors once a day for four days. Nursing staff filled in a survey about the burden.	Among the 16 responses from the older adults, 14 (87.5%) were "not at all uncomfortable," 2 (12.5%) were "it does not bother me". 3 out of 4 nursing staff commented that the interruption of other working activities led to reduced efficiency. They didn't perceive the changing and cleaning of the incontinence materials as burdensome.
To evaluate the applicability and validity of the Urine Leakage Recording Device.	Quantitative non-randomized experimental study with 5 older adults. Participants were instructed to turn and void during the experiment. The experimenter evaluated the operation of the device. The setting was likely a laboratory, but not reported in the manuscript.	No restriction nor inconvenience was reported by the participants. The device was easy to operate.
To evaluate an ambulatory sleep monitoring set-up.	Quantitative cross-sectional study with 25 adults with possible sleep apnea. 15 had both 102 (respiratory recordings) and 108 (full polysomnographic recordings) at home for one night. 10 had CID 102 set up at the hospital and recorded at home.	Technical failures occurred in 2/15 with CID 108. No failure with CID 102.
To validate the Nukute Collare in diagnosing sleep apnea.	Mixed-methods cross-sectional study with 71 adults with or without sleep apnea. Collare measurement was compared with standard PSG. Participants filled in a questionnaire to evaluate the device.*	45 out of 71 measurements were completed valid. Most participants (93%) considered Collare easy to use, 85% reported that it did not disturb their sleep, 90% did not feel pain or tenderness in the neck after the measurement, 75% considered Nukute Collare more comfortable than the standard PSG, 85% said that they would use it again.

eTable 2 Manuscripts reporting on the acceptability or feasibility of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Morales	2012	USA	ResCare AutoSet™ (ResMed, Sydney, Australia)	Sleep - apnea
Silvia	2014	USA	M1 (SleepImage, Denver, CO, USA)	Sleep - insomnia
Lazazzera	2022	France	UpNEA (developed by the authors)	Sleep - apnea
Multi-modal monitoring systems – with environmental sensors				
Au-Yeung	2020	USA	Ambient sensors: model not reported (NYCE Sensors, Vancouver, BC), Pressure mats: model not reported (Emfit, Finland), Actigraphy: Actiwatch Spectrums (Philips Respironics, Murrysville, PA), Environmental sensors: Thunderboard Sense 2-SLTB004A (Silicon Labs, Austin, TX)	Agitation

Aim of study	Methods: Study design; Participants being monitored; Setting; Procedures; Participants evaluating the technology;	Acceptability or feasibility of the technology
To assess the feasibility of a two-stage screening procedure for obstructive sleep apnea syndrome (OSAS).	Quantitative cross-sectional study with 452 older adults in the community. Participants conducted an overnight home recording of nasal pressure on their own, kept a diary and received a separate, standard PSG.	Complete data on 442 of 452 (98%) home recordings
To evaluate a brief sleep intervention and to investigate the feasibility and effectiveness of sleep monitoring of the M1 device.	Quantitative cross-sectional study with 8 adults with bipolar disorder. Participants wore the device for two seven-night periods at home and kept a sleep diary. They filled in a M1 acceptability questionnaire after each week of wearing the device.	The M1 device was evaluated as easy to use, easy to apply and did not interfere with the participants' sleep. The device was worn for at least two nights by all participants and on average 6.12 and 5.50 days in each week. The willingness to wear the device again declined after the second week, but was still high.
To present a system aimed to predict respiratory and cardiovascular disorders. UpNEA was part of the whole system.	Quantitative cross-sectional study with one healthy adult. The participant wore the glove-life device for four nights and reported on its comfort.*	The device did not cause discomfort to the participant.
To provide a proof of concept of monitoring and predicting agitation in memory care facilities with by monitoring the activity, sleep, and the environment (temperature, light, sound, humidity).	Quantitative case study with one adult with dementia in a memory care unit. The participant was continuously monitored by the system for 138 days. Agitation was recorded by nurses. The feasibility was evaluated by the researchers.	Ambient motion sensors functioned well with no technical problems. Sleep was successfully monitored for 91 out of 137 nights due to Wi-Fi problems or the participant not sleeping on the bed. Actigraphy was off-wrist 2% of the time. Environmental data was successfully collected 48% of the time.

eTable 2 Manuscripts reporting on the acceptability or feasibility of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Khan	2019	Canada	Developed by the authors	Agitation
Davidoff	2022	Belgium, Netherlands	Wearables: Chill+, LYS (LYS Technologies), Blooloc tracker; Pressure mat: EMFIT QS (EMFIT, Finland); Environmental sensors: Metatracker (MbientLab), micrphone: Nokia 6.1 Android phone, Blooloc	Anxiety
Davoudi	2019	USA	Developed by the authors	Delirium
Rose	2015	USA	Tab-like bed sensor: Wireless Identification and Sensing Platform (WISP, brand not reported); Watch: Technology-Enabled Medical Precision Observation (TEMPO, brand not reported); Incontinence sensor: DryBuddy (brand not reported) Microphone: model and brand not reported	Sleep, agitation, and urinary incontinence

Aim of study	Methods: Study design; Participants being monitored; Setting; Procedures; Participants evaluating the technology;	Acceptability or feasibility of the technology
To develop a system to automatically detect agitation in people with dementia. The proposed system includes actigraphy, EDA monitor, pressure mat, video cameras, environmental motion sensors, and door sensors.	Quantitative cross-sectional study with two older adults with dementia at a rehabilitation institute. The participants were monitored for 15 and 13 days respectively. Agitation episodes were noted by nurses. Different algorithms were tested using different combinations of sensor data. The feasibility was evaluated by the authors.	The system was feasible to monitor people with dementia.
To pilot test a system that identifies physiological markers and contextual triggers of agitation in people with dementia. EDA, heart rate, activity, skin temperature, light, sleep, position of the participant, and environmental sound were monitored.	Quantitative cross-sectional study with older adults with dementia with severe behavioral symptoms in a neuropsychiatric ward. The number of participants was not reported. Agitation was scored by the nurse at nine random moments per day using the Pittsburgh Agitation Scale and the Richmond Agitation Sedation Scale.	Some participants took off the wearables when they were most agitated. Connectivity problems and some rooms not installing the devices complicated the data collection. Synchronizing all the data was intensive and errors lead to loss of data.
To pilot test a system that includes a camera, three actigraphy, a light sensor, and a microphone in the ICU.	Quantitative cross-sectional study with 17 older adults in the surgical ICU, nine of them had delirium. Participants were monitored continuously for a maximum of seven days. The feasibility was evaluated by the authors.	The system was feasible to monitor critically ill patients in the ICU.
To investigate the feasibility and acceptability of the wireless devices, including a tab-like bed sensor, a smart watch, an incontinence sensor, and a microphone, in community-dwelling people with dementia.	Quantitative cross-sectional study with 50 community-dwelling older adults with dementia. Participants were monitored for five to seven days. Family caregivers set up the devices with help from the study team via the phone and they received an interview about the feasibility after the study.	Minimal effort was required to operate the system, but it was still challenging for caregivers who were not very familiar with technology. Troubleshooting via the phone was challenging, but reviewing the data helped. Adding another bedside receiver solved problems with the incontinence sensors. Bowel incontinence complicated the measurement.

eTable 2 Manuscripts reporting on the acceptability or feasibility of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Multi-modal monitoring systems – other multi-modal systems				
Iaboni	2022	Canada	Empatica E4 (Empatica)	Agitation and aggression
Rajasekaran	2011	USA	Portable Autonomous Multisensory Intervention Device (PAMID, developed by the authors)	Agitation
Miranda	2016	USA	Heart rate: Hxm (Zephyr); EDA: Empatica E3; EEG: Muse band	Anxiety
Non-contact monitoring systems – pressure mats				
Sakai	2009	Japan	KINOTEX sensor (NITTA Corp. Osaka, Japan)	Risk of pressure ulcers

Aim of study	Methods: Study design; Participants being monitored; Setting; Procedures; Participants evaluating the technology;	Acceptability or feasibility of the technology
To develop personalized machine learning models for detecting behavioral and psychological symptoms of dementia (BPSD). The device monitored motion, blood volume pulse, EDA, and skin temperature.	Quantitative cross-sectional study with 17 older adults with dementia and BPSD in a dementia care unit. Participants wore the Empatica wristband for eight weeks during waking hours. Agitation and aggression events were annotated by trained nurses.	The models could recognize the presence of motor agitation (median Area under the receiver-operating characteristic curves (AUC) = 90%), verbal aggression (median AUC = 86%), and physical aggression (median AUC = 82%)
To test the reliability of the chest belt which integrated measurements for heart rate, skin temperature and EDA, and to evaluate its appearance and comfortability.	Quantitative non-randomized experimental study with six community-dwelling older adults in the laboratory. During a 40-minute experiment, participants took four sets of STROOP tests while being monitored by the device and conventional instruments. The appearance and comfort of the device were evaluated by the participants.	The appearance of the device was rated 2.7 out of 3, and the comfortability was rated 2.8 out of 3.
To describe an experiment eliciting anxiety in informal caregivers for people with dementia, while measuring heart rate, EDA, and EEG.	Quantitative non-randomized experimental study with 10 healthy adults in the laboratory. During 30-min sessions, participants had a relaxation stage and performed therapy with a simulated person with dementia. The level of anxiety was recorded by the participants and researchers. Models were developed using the physiological parameters to predict the presence of anxiety. The feasibility was evaluated by the authors.	When participants moved during the sessions, EEG signal was poor. No reliability information was reported about the other sensors.
To examine the feasibility of using continuous interface pressure monitoring to prevent pressure ulcers in the ICU.	Quantitative cross-sectional study with 30 postoperative patients in the ICU. They were monitored for up to 48 hours.	Continuous monitoring of the intensity and duration of whole-body interface pressure using the KINOTEX sensor is feasible in intensive care patients.

eTable 2 Manuscripts reporting on the acceptability or feasibility of the monitoring technologies to detect distress and discomfort (continued)

First author	Year	Country	Monitoring technology (model and brand)	Symptom monitored
Non-contact monitoring systems – multiple sensors				
Kroll	2020	Germany	Camera: Mini-Webcam (Conrad Electronics SE, Hirschau, Germany); Acoustic sensor: ME32 (Olympus Imaging Europa GmbH, Hamburg, Germany) Pressure mat: SafeBed IP system (Emfit® Ltd., Vaajakoski, Finland)	Agitation

Note: Adults = mean age between 18 and 65; Older adults = mean age over 65; ICU = intensive care unit.
References can be found in Supplement IV.
*The setting was not reported.

Aim of study	Methods: Study design; Participants being monitored; Setting; Procedures; Participants evaluating the technology;	Acceptability or feasibility of the technology
To validate the non-contact monitoring system and a tent-like shelter for people with dementia.	Quantitative cross-sectional study with six healthy adult volunteers in the laboratory and 19 patients, most of whom had dementia, in the emergency department and a geriatric-gerontopsychiatric ward. Participants were monitored for two hours, the first hour without the tent-like shelter, the second hour with it.	There were little perturbations during the measurements in the emergency department and geriatric-gerontopsychiatric ward. One out of 19 measurements did not take place because of non-cooperation of the patient.

eTable 3 Manuscripts in which the clinimetrics, acceptability or feasibility of the technologies that monitor distress and discomfort were not reported (the technology is either used as standard measurement or is newly developed)

First author	Year	Country	Monitoring technology (model and brand)
Actigraphy			
Burnett-Zeigler	2018	USA	Not reported
Godfrey	2009	UK, Ireland	activPAL Professional (PAL Technologies Ltd, Glasgow, UK)
Mahlberg	2007	Germany	Actiwatch (Cambridge Neurotechnology Ltd, Cambridge, UK)
Blytt	2017	Norway	Actiwatch Spectrum (Philips Respironics Inc, Murrysville, Pennsylvania)
Buratti	2021	Italy	Actiwatch Spectrum or Actiwatch-2 (Philips Respironics Inc, Murrysville, Pennsylvania)
Jaiswal	2023	USA	Actiwatch Spectrum Plus (Phillips Respironics Inc, Murrysville, Pennsylvania)
Wilcox	2019	Canada	Actiwatch Spectrum Plus (Phillips Respironics, Bend, Oregon, USA)
Hoekert	2006	Netherlands	Actiwatch (Cambridge Neurotechnology Ltd., Cambridge, U.K.)
Meadows	2010	UK	Actiwatch (Cambridge Neurotechnology Ltd, Cambridge, UK)
Most	2012	Netherlands	Actiwatch (Cambridge Neurotechnology Ltd., Cambridge, UK)
van Someren	2019	Netherlands and Italy	Actiwatch (Cambridge Neurotechnology Ltd, Cambridge, UK)
de Feijter	2021	Netherlands	Actiwatch AW4 (Cambridge Neurotechnology Ltd, Cambridge, UK)
van den Berg	2008	Netherlands	Actiwatch AW4 (Cambridge Neurotechnology Ltd, Cambridge, UK)
van den Berg	2009	Netherlands	Actiwatch AW4 (Cambridge Neurotechnology Ltd, Cambridge, UK)
Kazui	2017	Japan	Actiwatch-L (Mini Mitter Co., Inc.-Respironics, Inc. Co. Bend, Oregon, USA)
Rowe	2010	USA	Actiwatch-L (Mini Mitter Co., Inc.-Respironics, Inc. Co. Bend, Oregon, USA)
Leary	1998	Ireland	Accelerometer (Gaewihler Electronics, Hombrechtikon, Switzerland)
van Hilten	1994	Netherlands and Canada	Activity monitor (Gaehwiler Electronic, CH-8634, Hombrechtikon, Switzerland)

Symptom monitored	Participant population and setting
Stress	Adults with depressive symptoms*
Delirium (motor subtypes)	Adults receiving palliative care in hospice
Agitation	Older adults with Alzheimer's disease from a geriatric psychiatry unit
Sleep	Older adults with or without dementia, living in nursing homes
Sleep	Older adults with Alzheimer's disease, mild cognitive impairment, or no cognitive impairments living at home
Sleep	Adults in the ICU, with or without delirium
Sleep	Adults in the hospital, after discharge from the ICU where they received at least 3 days of mechanical ventilation
Sleep	Older adults with dementia living in group care facilities
Sleep	Older adults both institutional care residents and community dwelling poor sleepers
Sleep	Older adults with Alzheimer's disease and control group*
Sleep	Older adults*
Sleep	Adults and older adults living at home
Sleep	Older adults living at home
Sleep	Older adults living at home
Sleep	Older adults with Lewy Body dementia and control group*
Sleep	Adults who take care of their family members with dementia at home
Sleep	Adults: hypertensive patients and control group*
Sleep	Older adults with Parkinson's disease and control group at an outpatient neurology department

eTable 3 Manuscripts in which the clinimetrics, acceptability or feasibility of the technologies that monitor distress and discomfort were not reported (the technology is either used as standard measurement or is newly developed) (continued)

First author	Year	Country	Monitoring technology (model and brand)
Guarnieri	2020	Italy	Fitbit Flex (Fitbit Inc., San Francisco, California)
Yesavage	2020	USA	Motionwatch (Ambulatory Monitoring Inc., Ardsley, New York)
Mulin	2011	France	Micro- Mini MotionLogger (Ambulatory-Monitoring, Inc., Ardsley, New York)
Currie	2003	Canada	Mini-motion logger actigraph units (Ambulatory Monitoring Inc., Ardsley, New York)
Watanabe	2002	Japan	Mini Motion Logger (Ambulatory Monitoring Inc., Ardsley, New York)
Kotschet	2023	Australia	Parkinson's Kinetigraph (PKG, Global Kinetics Corporation™, Australia)
Jones	2020	Australia	SenseWear Professional 8.0 (Temple Healthcare, BodyMedia, Inc.)
Spira	2017	USA	SleepWatch-O (Ambulatory Monitoring Inc., Ardsley, New York)
Yaffe	2007	USA	Sleepwatch-O (Ambulatory Monitoring Inc., Ardsley, New York)
Cabanel	2020	Germany	SOMNOwatch system (Somnomedics, Randersacker, Germany)
Westerberg	2010	USA	Not reported
Elías	2020	USA	Not reported
Brain activity monitors – Bispectural Index (BIS)			
Barbato	2017	Australia	Bispectral Index monitor (Covidien Pty Ltd.), with Quatro sensors.
Bass	2019	USA	Not reported
De Deyne[o]	1998	Belgium	Aspect A-1000 EEG analyser (Aspect, Natick, USA)
Monreal-Carrillo	2017	USA	BIS Vista Bilateral Monitoring System 1.2 (Aspect Medical Systems, Inc. Norwood, MA, USA)
Quraishi	2011	USA	BIS (Aspect Medical Systems, Inc. Norwood, MA)

Symptom monitored	Participant population and setting
Sleep	Adults and older adults with Alzheimer's disease or amnestic Mild Cognitive Impairment in a multicenter setting
Sleep	Older adults with Alzheimer's disease*
Sleep	Older adults with Alzheimer's disease, with or without apathy*
Sleep	Adults: insomnia patients and control group*
Sleep	Older adults with or without hypertension living at home
Sleep	Adults with Huntington's disease
Sleep	Older adults with dementia and sleep problems*
Sleep	Older adults living at home
Sleep	Older adults. Data was taken from a previous study about osteoporotic fractures*
Sleep	Older adults: memory clinic patients
Sleep	Older adults with amnestic Mild Cognitive Impairment and control group living at home
Sleep	Older adults: ICU survivors
Sedation and comfort	Adult patients at the end of life in palliative care units of the hospital
Sedation and pain	Adults in the ICU
Sedation	Adult patients with a Ramsay sedation score of 6 in the ICU
Sedation	Adults on palliative sedation in the hospital
Sedation	Adult with locked-in syndrome in the ICU

eTable 3 Manuscripts in which the clinimetrics, acceptability or feasibility of the technologies that monitor distress and discomfort were not reported (the technology is either used as standard measurement or is newly developed) (continued)

First author	Year	Country	Monitoring technology (model and brand)
Brain activity monitors – other electroencephalography (EEG)-based technologies			
Espie	1998	UK	Walter-Graphtex System and Oxford Medilog 9000-II ambulatory system
Sato	2002	USA, Japan	Not reported
Electrocardiography (ECG)			
Estrada	2000	USA	78720 ASDN system (Hewlett Packard)
Gerber	2019	Switzerland	Carescape Monitor B650 (GE Healthcare, Little Chalfont, United Kingdom)
Gerber	2019	Switzerland	Carescape Monitor B650 (GE Healthcare, Little Chalfont, United Kingdom)
Park	2022	Korea	Apple Watch Series 4, 5, or 6 smartwatch (Apple Inc)
EEG and ECG			
Six	2019	Belgium	EEG: NeuroWave Systems Inc. ECG: ANI (Mdoloris Medical Systems SAS)
Six	2021	Belgium	EEG: NeuroWave Systems Inc. ECG: ANI (Mdoloris Medical Systems SAS)
Electrodermal activity (EDA) monitors			
Jusilla	2018	Finland	Moodmetric smart ring (Vigofere Oy, Finland)
Massot	2010	France	EmoSense (developed by the authors, based on Programmable Systemon-Chip, Cypress MicroSystems, Inc.)
Melander	2018	Sweden, Norway	Discrete Tension Indicator (DTI-2) (Philips Research); Empatica E4 (Empatica Incorporation)
Quad Industries	2022	Netherlands	Model not reported, developed by Mentech (the Netherlands) and Quad Industries (Belgium)
Incontinence sensors			
Fischer	2019	Austria	Developed by the authors
Wai	2008	Singapore	Developed by the authors
Multi-modal systems – Polysomnography (PSG)			
Bell	1996	USA	Model 8-16 EEG machines (Grass Instruments)

Symptom monitored	Participant population and setting
Sleep	Adults with severe or profound intellectual disability and epilepsy. Assessment was performed in the hospital and at home.
Sleep	Older adults in the community.
Arrhythmia	Adults in non–intensive-care telemetry unit
Stress	Critically ill adults in the ICU
Stress	Healthy adults. The experiment was conducted in the ICU environment.
Stress	Healthy nurses during cardiopulmonary resuscitation training
Depth of sedation and pain	Older adult in the palliative care unit undergoing palliative sedation
Depth of sedation and pain	Older adults undergoing palliative sedation until death
Stress	No participants. The manuscript presented the design of a system
Stress	Healthy blind adults in an urban space
Stress	Older adults with dementia in nursing homes
Stress	No participants. The manuscript presented a printed electronic patch for people with severe intellectual disability.
Incontinence, occupancy of the bed	No participants. The manuscript reports the development of the electronic system.
Incontinence	No participants. The manuscript reports the design of the system.
Sleep	Older healthy adults at a sleep laboratory

eTable 3 Manuscripts in which the clinimetrics, acceptability or feasibility of the technologies that monitor distress and discomfort were not reported (the technology is either used as standard measurement or is newly developed) (continued)

First author	Year	Country	Monitoring technology (model and brand)
Bugalho	2019	Portugal	XLTEK-TREX (Natus Medical Inc., Middleton, USA)
Bugalho	2019	Portugal	XLTEK-TREX (Natus Medical Inc., Middleton, USA)
Cooke	2009	USA	Embla recording system (Flaga Medical Devices/ Medcare, Reykjavik, Iceland)
Dew	2003	USA	Not reported
Dijkstra	2019	Belgium	BrainnetMorpheus (MEDATEC)
Djonlagic	2019	USA, Germany	Compumedics Siesta Portable PSG (Abottsville, Australia)
Eisensehr	2001	Germany	A digital 32-channel system (Brainlab, Schwarzer, Munich, Germany)
Fanfulla	2011	Italy	N-S 7000 (Embla, Denver, CO, USA)
Fleming	2015	USA	ExSpiron (Respiratory Motion, Inc. USA)
Gelber	2015	USA	Not reported
Gebran	2009	Canada	AR-B1831 single-board-computer (Accroser Technology Co. Ltd., Cypress, California)
Herring	2020	USA	Not reported
Heude	1996	France	Schwarzer ED24 (Madhaus, Germany)
Jiang	2013	China, Italy	Polysmith 5.0 (Nihon Khoden, U.S.)
Joo	2011	South Korea	ApneaLink (ResMed, Australia)
Kim	2017	South Korea	Embla™ N7000 (Embla, Reykjavik, Iceland)
Kim	2011	South Korea	Embla S7000 (Medcare system, NY)
Kardiol	1999	Germany	4-channel recording system, brand not recorded
Koo	2019	USA	Not reported
Lankford	2008	Canada, USA	Not reported
Low	2012	USA	Not reported

Symptom monitored	Participant population and setting
Sleep	Older adults with dementia, Parkinson Disease, or ideopathic rapid eye movement (REM) sleep behavior disorder at a sleep laboratory
Sleep	Older adults with REM sleep behavior disorder at a sleep laboratory
Sleep	Older adults with Alzheimer's disease and obstructive sleep apnea at home and at a sleep laboratory
Sleep	Healthy older adults at a sleep laboratory
Sleep - Isolated REM sleep without atonia	Adults with sleep problems at a sleep laboratory
Sleep - stages	Older adults with or without cognitive impairment at home
Sleep - REM behavioral disorder	Older adults with Parkinson Disease and adults without Parkinson Disease at a sleep laboratory
Sleep	Older adults in the step-down units after ICU discharge
Hypopnea	Adult with obstructive sleep apnea in post-anesthesia care unit
Sleep - disordered breathing	Older adults without moderate or severe dementia at home
Sleep – narcolepsy episodes	No participants. The manuscript introduces a prototype of the devices.
Sleep - insomnia	Older adults with Alzheimer's Disease and insomnia at a sleep laboratory
Sleep	Adults with snoring and daytime somnolence at a laboratory
Sleep	Adults with VCIND (vascular cognitive impairment, no dementia), stroke or healthy controls at sleep laboratory
Sleep - apnea	Older adults with acute cerebral infarction and a healthy control group at a hospital
Sleep - disordered breathing and sleep disturbances	Older adults with or without asthma*
Sleep - apnea and hypopnea	Older adults with mild cognitive impairment and controls at a laboratory
Sleep - apnea	Adults with acute myocardial infarction in the ICU
Sleep - apnea	Older adults with acute stroke or transient ischemic attack in the hospital
Sleep	Adults and older adults with insomnia at a sleep laboratory
Sleep	Adults with insomnia, with or without Human Immunodeficiency Virus (HIV) at a sleep laboratory

eTable 3 Manuscripts in which the clinimetrics, acceptability or feasibility of the technologies that monitor distress and discomfort were not reported (the technology is either used as standard measurement or is newly developed) (continued)

First author	Year	Country	Monitoring technology (model and brand)
McCall	2006	USA	Not reported
Maglavera	2006	Greece	SENSATION Medical System (developed by the authors)
Martinez-Nicolas	2021	Spain	Thermochron iButton DS1921H (Maxim Integrated Products, Sunnyvale, CA), HOBO Pendant G Acceleration Data Logger UA-004–64 actimeter (Onset Computer, Bourne, MA). Standard PSG: model and brand not reported
Onen	2008	France	Embla digital portable recording system (Flaga hf., Reykjavik, Iceland)
Pao	2013	USA	Not reported
Patout	2019	UK	ALICE 5 (Philips-Respironics, Murrysville, PA, USA)
Piano	2017	Italy	Not reported
Piano	2015	Italy	Not reported
Pittsley	2005	USA	a modified Respitrace/Medilog portable recorder
Prasad	2016	USA	Embletta™ PDS system (Natus Neurology Inc., Middleton, WI)
Smith	2009	Australia	E series (Compumedics, Melbourne, Vic., Australia)
Soderstrom	2004	Sweden	Embla (Flaga hf Reykjavik, Iceland)
Targa	2020	Spain	Embletta (Embla, Canada); Sibelmed Exea Serie 5 (Sibel SAU, Spain); Alice 6 LDx (Philips Respironics, USA); ApneaLink (Resmed, Canada)
Terzaghi	2013	Italy	SD LTM 32 BS (Micromed, Treviso, Italy)
Várady	2002	Hungary	Not reported, algorism developed by the authors
Varri	2001	Finland, France	Not reported, scoring system developed by the authors
Walsh	2010	USA, UK, Germany	Not reported
Wang	2019	China	Embletta (Embla, Suffolk, UK) BI9800 (Biomedical Instruments Co., Ltd., Osaka, Japan)
Wilcock	2008	UK	Pulsox 3i (Minolta, USA)

Symptom monitored	Participant population and setting
Sleep - insomnia	Adults with insomnia at a sleep laboratory
Sleep	No participants. The manuscript presented a system and proposed its possible applications.
Sleep and circadian rhythm	Adults with or without sleep disordered breathing at home and in the hospital
Sleep - apnea	Older adults with possible sleep apnea at a sleep center
Sleep	Older adults with Lewy body dementia at a hospital
Respiration	Adult patients with chronic obstructive pulmonary disease (COPD) – obstructive sleep apnea overlap*
Sleep	Adult patients with Huntington Disease at a center for movement disorders
Sleep	Adult patients with Huntington Disease at a laboratory
Sleep - disordered breathing	Older adults at home
Sleep - apnea	Older adults with obstructive sleep apnea at home
Sleep - apnea	Adults with obstructive sleep apnea*
Sleep	Adults at home
Sleep - apnea	Older adults with Alzheimer's disease*
Sleep	Older adults with Lewy body dementia or Parkinson's Disease at a hospital
Sleep - apnea	Adults*
Sleep	No participants. The manuscript reports the development of an algorism.
Sleep	Older adults with insomnia at a laboratory
Sleep - apnea	Adults with or without obstructive sleep apnea at a hospital
Sleep - hypoxemia	Adults with advanced cancer in a specialist palliative care unit

eTable 3 Manuscripts in which the clinimetrics, acceptability or feasibility of the technologies that monitor distress and discomfort were not reported (the technology is either used as standard measurement or is newly developed) (continued)

First author	Year	Country	Monitoring technology (model and brand)
Xun	2019	China	Model not reported (Weinmann, Germany)
Zhang	2017	China, Germany	Alice 5 Diagnostic Sleep System (Philips Healthcare, Andover, USA)
Tateishi	1994	Japan	Fukuda SM28 (Fukuda, Tokyo, Japan)
Multi-modal systems – with environmental sensors			
Hoehn-Saric	2004	USA	Developed by other researchers, monitoring EDA, heart rate, activity level and ambient temperature
Multi-modal systems – other multi-model systems			
Hassan	2020	Pakistan, Saudi Arabia, Korea	Developed by the authors, including sEMG, EEG, and ECG
Non-contact monitoring systems - pressure mats			
Fukuda	2022	Japan	Nemuri Scan (Paramount Bed, Tokyo, Japan)
Higami	2019	Japan	Nemuri Scan (Paramount Bed, Tokyo, Japan)
Tong	2015	China	RS-611 (Beijing Xinxing Yangsheng Technology Co., Ltd.)
Peterson	2013	USA	Pressure mapping system (XSENSOR Technology Corporation, Calgary, Canada)
Sofronova	2021	Bulgaria	Developed by the authors

Note: Adults = mean age between 18 and 65; Older adults = mean age over 65; ICU = intensive care unit

References can be found in Supplement IV.

* The setting was not reported.

° This study aimed to test the feasibility, but did not report about it in the results or discussions.

Symptom monitored	Participant population and setting
Sleep – structure and hypoxia	Adults with obstructive sleep apnea monitored in the laboratory
Sleep – apnea and structure	Adults with snoring, with or without stroke history at a hospital
Sleep - apnea	Adults with coronary artery problems monitored in their normal daily life
Anxiety	Adults with panic disorder or general anxiety disorder and healthy controls in their own environment
Pain	No participants. The manuscript proposed a fog computer architecture for remote pain monitoring.
Sleep	Older adults with Lewy body dementia in nursing homes
Sleep	Older adults with Alzheimer's disease in nursing homes
Sleep – apnea and structure	Adults and older adults with obstructive sleep apnea-hypopnea syndrome*
Risk of pressure ulcers	Adults in intensive care and intermediate care units
Risk of pressure ulcers	One healthy adult. The manuscript reported the development of a an e-textile mat.

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Search strategy for "Noninvasive monitoring technologies to identify discomfort and distressing symptoms in persons with limited communication at the end of life: a scoping review"

Main topics: Non-invasive monitoring AND distressing symptoms.

Other topics: Dementia OR palliative care OR critically ill OR profound intellectual and multiple disability OR bedridden

Details of the search strategies for each database:

PubMed: 179
MEDLINE (OVID) 182
Embase (OVID) 184
Web of Science 186
Cochrane Library 188
Emcare (OVID) 191
PsycINFO (IEbscoHOST) 192
Academic Search Premier (EbscoHOST) 197
Google Scholar 201

PubMed:

(("Dementia"[Mesh] OR "Dementia"[tw] OR "dement*"[tw] OR "Alzheimer Disease"[tw] OR "Alzheimer*"[tw] OR "CADASIL"[tw] OR "Creutzfeldt-Jakob"[tw] OR "Creutzfeldt-Jakob Syndrome"[tw] OR "Diffuse Neurofibrillary Tangles with Calcification"[tw] OR "Frontotemporal Lobar Degeneration"[tw] OR "Huntington Disease"[tw] OR "Huntington*"[tw] OR "Kluver-Bucy"[tw] OR "Kluver-Bucy Syndrome"[tw] OR "Lewy Body"[tw] OR "Lewy Body Disease"[tw] OR "Pick Disease of the Brain"[tw] OR "Primary Progressive Aphasia"[tw] OR "Primary Progressive Nonfluent Aphasia"[tw] OR "Death"[Mesh] OR "dying"[tw] OR "end of life phase"[tw] OR "end of life"[tw] OR "end-of-life phase"[tw] OR "endoflife"[tw] OR "end-of-life"[tw] OR "Hospice and Palliative Care Nursing"[mesh] OR "Hospice Care"[Mesh] OR "Hospice Care"[tw] OR "Hospice Care"[tw] OR "Hospice"[tw] OR "Hospices"[Mesh] OR "Hospices"[tw] OR "palliat*"[tw] OR "Palliative Care"[Mesh] OR "Palliative Care"[tw] OR "Palliative Medicine"[mesh] OR "Palliative Phase"[tw] OR "Palliative Phases"[tw] OR "Palliative Stage"[tw] OR "Palliative Stages"[tw] OR "Palliative Supportive Care"[tw] OR "Palliative Surgery"[tw] OR "Palliative Therapy"[tw] OR "Palliative Treatment"[tw] OR "Palliative Treatments"[tw] OR "Terminal Care"[Mesh] OR "Terminal Care"[tw] OR "terminal stage"[tw] OR "elderly"[ti] OR "critical care"[mesh] OR "critical care"[tw] OR "intensive care"[tw] OR "Critical Illness"[Mesh] OR "Critical Illness"[tw] OR "critically ill"[tw] OR (("profound"[tw] OR "profound*"[tw]) AND ("Disabled Persons"[Mesh] OR "Intellectual Disability"[Mesh])) OR (("profound"[tw] OR "profound*"[tw]) AND ("intellectual"[tw] OR "intellectualism"[tw] OR "intellectually"[tw]

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MEDLINE (OVID)

(exp "Dementia"/ OR "Dementia".mp OR "dement*".mp OR "Alzheimer Disease".mp OR "Alzheimer*".mp OR "CADASIL".mp OR "Creutzfeldt-Jakob".mp OR "Creutzfeldt-Jakob Syndrome".mp OR "Diffuse Neurofibrillary Tangles with Calcification".mp OR "Frontotemporal Lobar Degeneration".mp OR "Huntington Disease".mp OR "Huntington*". mp OR "Kluver-Bucy".mp OR "Kluver-Bucy Syndrome".mp OR "Lewy Body".mp OR "Lewy Body Disease".mp OR "Pick Disease of the Brain".mp OR "Primary Progressive Aphasia". mp OR "Primary Progressive Nonfluent Aphasia".mp OR exp "Death"/ OR "dying".mp OR "end of life phase".mp OR "end of life".mp OR "end-of-life phase".mp OR "endoflife".mp OR "end-of-life".mp OR exp "Hospice AND Palliative Care Nursing"/ OR exp "Hospice Care"/ OR "Hospice Care".mp OR "Hospice Care".mp OR "Hospice".mp OR exp "Hospices"/ OR "Hospices".mp OR "palliat*".mp OR exp "Palliative Care"/ OR "Palliative Care".mp OR exp "Palliative Medicine"/ OR "Palliative Phase".mp OR "Palliative Phases".mp OR "Palliative Stage".mp OR "Palliative Stages".mp OR "Palliative Supportive Care".mp OR "Palliative Surgery".mp OR "Palliative Therapy".mp OR "Palliative Treatment".mp OR "Palliative Treatments".mp OR exp "Terminal Care"/ OR "Terminal Care".mp OR "terminal stage". mp OR "elderly".ti. OR exp "critical care"/ OR "critical care".mp OR "intensive care".mp OR exp "Critical Illness"/ OR "Critical Illness".mp OR "critically ill".mp OR (("profound" OR "profound*").mp AND (exp "Disabled Persons"/ OR exp "Intellectual Disability"/)) OR (((("profound" OR "profound*") AND ("intellectual" OR "intellectualism" OR "intellectually" OR "intellectuals") AND ("multiple" OR "multiples")).mp AND (("disabilities" OR "disability").mp OR exp "disabled persons"/ OR "disabled persons".mp OR "disabled".mp OR "disablement".mp OR "disablements".mp OR "disabling".mp OR "disablity".mp)) OR exp "Bedridden Persons"/ OR "Bedridden".mp OR "Non-Mobile Person".mp OR "Non-Mobile Persons".mp) AND (("activity monitor" OR "activity monitors" OR "activity monitoring" OR "activity tracker" OR "activity trackers" OR "activity tracking" OR "Ambulatory Monitor*" OR "Ambulatory Monitoring" OR "Electronic Skin").ti. OR (("monitor*" OR "monitoring"). ti. AND (exp *"Telemedicine"/ OR "telemed*".ti. OR "telehealth*".ti. OR "technol*".ti.)) OR "monitoring app".ti. OR "monitoring application".ti. OR "monitoring applications".ti. OR "monitoring apps".ti. OR "monitoring device".ti. OR "monitoring devices".ti. OR "monitoring

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OR "delirious".ti. OR exp *"Fever"/ OR "fever".ti. OR exp *"Urinary Incontinence"/ OR "Incontinence".ti. OR "incontinen*".ti. OR "Sedation depth".ti. OR "Sedation depths".ti. OR "Depth of sedation".ti.)

Embase (OVID)

((exp *"Dementia"/ OR ("Dementia" OR "dement*" OR "Alzheimer Disease" OR "Alzheimer*" OR "CADASIL" OR "Creutzfeldt-Jakob" OR "Creutzfeldt-Jakob Syndrome" OR "Diffuse Neurofibrillary Tangles with Calcification" OR "Frontotemporal Lobar Degeneration" OR "Huntington Disease" OR "Huntington*" OR "Kluver-Bucy" OR "Kluver-Bucy Syndrome" OR "Lewy Body" OR "Lewy Body Disease" OR "Pick Disease of the Brain" OR "Primary Progressive Aphasia" OR "Primary Progressive Nonfluent Aphasia").ti,ab OR exp *"Death"/ OR exp *"Terminal Care"/ OR exp *"Hospice"/ OR exp *"Palliative Therapy"/ OR ("dying" OR "end of life phase" OR "end of life" OR "end-of-life phase" OR "endoflife" OR "end-of-life" OR "Hospice and Palliative Care Nursing" OR "Hospice Care" OR "Hospice Care" OR "Hospice Care" OR "Hospice" OR "Hospices" OR "Hospices" OR "palliat*" OR "Palliative Care" OR "Palliative Care" OR "Palliative Medicine" OR "Palliative Phase" OR "Palliative Phases" OR "Palliative Stage" OR "Palliative Stages" OR "Palliative Supportive Care" OR "Palliative Surgery" OR "Palliative Therapy" OR "Palliative Treatment" OR "Palliative Treatments" OR "Terminal Care" OR "Terminal Care" OR "terminal stage").ti,ab OR "elderly".ti OR exp *"Intensive Care"/ OR exp *"Critical Illness"/ OR exp *"critically ill patient"/ OR ("critical care" OR "critical care" OR "intensive care" OR "Critical Illness" OR "Critical Illness" OR "critically ill") OR (("profound" OR "profound*").ti,ab AND (exp *"Disabled Person"/ OR exp *"Intellectual Impairment"/)) OR (("profound" OR "profound*") AND ("intellectual" OR "intellectualism" OR "intellectually" OR "intellectuals") AND ("multiple" OR "multiples") AND ("disabilities" OR "disability" OR "disabled persons" OR "disabled persons" OR "disabled" OR "disablement" OR "disablements" OR "disabling" OR "disablity")).ti,ab OR exp *"Bedridden Patient"/ OR ("Bedridden" OR "Non-Mobile Person" OR "Non-Mobile Persons").ti,ab) AND (("activity monitor" OR "activity monitors" OR "activity monitoring" OR "activity tracker" OR "activity trackers" OR "activity tracking" OR "Ambulatory Monitor*" OR "Ambulatory Monitoring" OR "Electronic Skin").ti. OR (("monitor*" OR "monitoring").ti. AND (exp *"Telemedicine"/ OR "telemed*".ti. OR "telehealth*".ti. OR "technol*".ti.)) OR "monitoring app".ti. OR "monitoring application".ti. OR "monitoring applications".ti. OR "monitoring apps".ti. OR "monitoring device".ti. OR "monitoring devices".ti. OR "monitoring technologies".ti. OR "monitoring technology".ti. OR exp *"Monitoring, Ambulatory"/ OR exp *"Monitoring, Physiologic"/ OR exp *"Ambulatory Monitoring"/ OR exp *"Physiologic Monitoring"/ OR "Noninvasive device".ti. OR "Non-invasive device".ti. OR "Noninvasive devices".ti. OR "Non-invasive devices".ti. OR "Noninvasive monitoring device".ti. OR "Noninvasive monitoring device".ti. OR "Non-invasive monitoring device".ti. OR "Noninvasive monitoring devices". ti. OR "Noninvasive monitoring devices".ti. OR "Non-invasive monitoring devices".ti. OR "Noninvasive monitoring technologies".ti. OR "Noninvasive monitoring technologies".ti. OR "Non-invasive monitoring technologies".ti. OR "Noninvasive monitoring technology". ti. OR "Noninvasive monitoring technology".ti. OR "Non-invasive monitoring technology". ti. OR "Noninvasive monitoring".ti. OR "Non-invasive monitoring".ti. OR "Noninvasive technologies".ti. OR "Non-invasive technologies".ti. OR "Noninvasive technology".ti. OR "Non-invasive technology".ti. OR "Outpatient Monitor*".ti. OR "Outpatient Monitoring".

ti. OR "Portable Electronic Application".ti. OR "Portable Electronic Applications".ti. OR "Portable Software Application".ti. OR "Portable Software Applications".ti. OR "Smart watch".ti. OR "Smart watches".ti. OR "Smartwatch".ti. OR "Smartwatches".ti. OR "tracker".ti. OR "trackers".ti. OR "wearab*".ti. OR "wearable activity tracker".ti. OR "wearable activity trackers".ti. OR "wearable activity tracking".ti. OR "Wearable Device".ti. OR "Wearable Devices".ti. OR "Wearable Electronic Device".ti. OR exp *"Wearable Electronic Devices"/ OR exp *"wearable computer"/ OR "Wearable Electronic Devices".ti. OR "Wearable Technologies".ti. OR "Wearable Technology".ti. OR "wearable".ti. OR "wearables".ti. OR "noninvasive body sensor".ti. OR "noninvasive body sensors".ti. OR "non invasive body sensor".ti. OR "non invasive body sensors".ti. OR "body sensor".ti. OR "body sensors".ti. OR "wristband sensor".ti. OR "wristband sensors".ti. OR "wearable computing".ti. OR "wearable computer".ti. OR "wearable computers".ti. OR "point-of-care App".ti. OR "point-of-care Apps".ti. OR "point-of-care Application".ti. OR "point-of-care Applications".ti. OR "facial recognition technology".ti. OR "face recognition technology".ti. OR "Point-of-Care Technology".ti. OR "Point-of-Care Techn*".ti. OR "HUME".ti. OR "ePAT".ti. OR " electronic pain assessment".ti. OR ("BIS" AND "bispectral").ti. OR "bispectral index".ti. OR exp *"Consciousness Monitor"/ OR exp *"Consciousness Monitors"/ OR exp *"Biosensing Techniques"/ OR (exp *"Facial Expression"/ AND (exp *"Point-of-Care Systems"/ OR exp *"Point of Care System"/)) OR (((("noninvasiv*" OR "non invasiv*" OR "unobtrusiv*" OR "portable").ti. OR exp "Mobile Applications"/ OR exp *"Mobile Application"/) AND "monitor*".ti.) OR "Painchek".mp OR "Paincheck".mp OR "automated facial analysis".mp OR "automated facial recognition".mp OR "automated facial expression analysis".mp) AND (("discomfort" OR "discomfort*").ti. OR exp *"Psychological Distress"/ OR exp *"distress syndrome"/ OR "distressing symptoms".ti. OR "distressing symptom".ti. OR "distressing".ti. OR "distress".ti. OR exp *"Patient Comfort"/ OR "comfort".ti. OR "comfort*".ti. OR exp *"Psychomotor Agitation"/ OR exp *"Restlessness"/ OR "agitation".ti. OR "agitat*".ti. OR "restlessness".ti. OR "restless*".ti. OR "hyperactivity".ti. OR "hyperactiv*".ti. OR "akathisia".ti. OR exp *"Pain"/ OR "pain".ti. OR exp *"Pain Measurement"/ OR "pain assessment".ti. OR exp *"Stress, Psychological"/ OR exp *"Mental stress"/ OR "stress level".ti. OR "stress levels".ti. OR "pressure ulcer".ti. OR "pressure ulcer".ti. OR "life quality".ti. OR exp *"quality of life"/ OR "quality of life".ti. OR "breathing difficulty".ti. OR "difficulty breathing".ti. OR "difficult breathing".ti. OR "labored breathing".ti. OR "laboured breathing".ti. OR "Shortness of Breath".ti. OR "Breath Shortness".ti. OR "Breathlessness".ti. OR exp *"Dyspnea"/ OR "Dyspnea".ti. OR exp *"Anxiety"/ OR "Anxiety".ti. OR "Nervousness".ti. OR "Hypervigilance".ti. OR "Anxiousness".ti. OR exp *"Sleep Disorder"/ OR exp *"Sleep Wake Disorders"/ OR "sleep disturbances".ti. OR "sleep disturbance".ti. OR exp *"Fatigue"/ OR "fatigue".ti. OR exp *"Nausea"/ OR "nausea".ti. OR "nauseous".ti. OR exp *"Delirium"/ OR "delirium".ti. OR "delirious".ti. OR exp *"Fever"/ OR "fever".ti. OR exp *"Urinary Incontinence"/ OR exp *"Urine Incontinence"/ OR "Incontinence".ti. OR "incontinen*".ti. OR "Sedation depth".ti. OR "Sedation depths".ti. OR "Depth of sedation".ti. OR exp *"anesthesia level"/))

Web of Science

(TS=("Dementia" OR "Dementia" OR "dement*" OR "Alzheimer Disease" OR "Alzheimer*" OR "CADASIL" OR "Creutzfeldt-Jakob" OR "Creutzfeldt-Jakob Syndrome" OR "Diffuse Neurofibrillary Tangles with Calcification" OR "Frontotemporal Lobar Degeneration" OR

"Huntington Disease" OR "Huntington*" OR "Kluver-Bucy" OR "Kluver-Bucy Syndrome" OR "Lewy Body" OR "Lewy Body Disease" OR "Pick Disease of the Brain" OR "Primary Progressive Aphasia" OR "Primary Progressive Nonfluent Aphasia" OR "Death" OR "dying" OR "end of life phase" OR "end of life" OR "end-of-life phase" OR "endoflife" OR "end-of-life" OR "Hospice and Palliative Care Nursing" OR "Hospice Care" OR "Hospice Care" OR "Hospice Care" OR "Hospice" OR "Hospices" OR "Hospices" OR "palliat*" OR "Palliative Care" OR "Palliative Care" OR "Palliative Medicine" OR "Palliative Phase" OR "Palliative Phases" OR "Palliative Stage" OR "Palliative Stages" OR "Palliative Supportive Care" OR "Palliative Surgery" OR "Palliative Therapy" OR "Palliative Treatment" OR "Palliative Treatments" OR "Terminal Care" OR "Terminal Care" OR "terminal stage" OR "elderly" OR "critical care" OR "critical care" OR "intensive care" OR "Critical Illness" OR "Critical Illness" OR "critically ill" OR (("profound" OR "profound*") AND ("Disabled Persons" OR "Intellectual Disability")) OR (("profound" OR "profound*") AND ("intellectual" OR "intellectualism" OR "intellectually" OR "intellectuals") AND ("multiple" OR "multiples") AND ("disabilities" OR "disability" OR "disabled persons" OR "disabled persons" OR "disabled" OR "disablement" OR "disablements" OR "disabling" OR "disablity")) OR "Bedridden Persons" OR "Bedridden" OR "Non-Mobile Person" OR "Non-Mobile Persons") AND TS=("activity monitor" OR "activity monitors" OR "activity monitoring" OR "activity tracker" OR "activity trackers" OR "activity tracking" OR "Ambulatory Monitor*" OR "Ambulatory Monitoring" OR "Electronic Skin" OR (("monitor*" OR "monitoring") AND ("Telemedicine" OR "telemed*" OR "telehealth*" OR "technol*")) OR "monitoring app" OR "monitoring application" OR "monitoring applications" OR "monitoring apps" OR "monitoring device" OR "monitoring devices" OR "monitoring technologies" OR "monitoring technology" OR "Monitoring, Ambulatory" OR "Monitoring, Physiologic" OR "Noninvasive device" OR "Non-invasive device" OR "Noninvasive devices" OR "Non-invasive devices" OR "Noninvasive monitoring device" OR "Noninvasive monitoring device" OR "Non-invasive monitoring device" OR "Noninvasive monitoring devices" OR "Noninvasive monitoring devices" OR "Non-invasive monitoring devices" OR "Noninvasive monitoring technologies" OR "Noninvasive monitoring technologies" OR "Non-invasive monitoring technologies" OR "Noninvasive monitoring technology" OR "Noninvasive monitoring technology" OR "Non-invasive monitoring technology" OR "Noninvasive monitoring" OR "Non-invasive monitoring" OR "Noninvasive technologies" OR "Non-invasive technologies" OR "Noninvasive technology" OR "Non-invasive technology" OR "Outpatient Monitor*" OR "Outpatient Monitoring" OR "Portable Electronic Application" OR "Portable Electronic Applications" OR "Portable Software Application" OR "Portable Software Applications" OR "Smart watch" OR "Smart watches" OR "Smartwatch" OR "Smartwatches" OR "tracker" OR "trackers" OR "wearab*" OR "wearable activity tracker" OR "wearable activity trackers" OR "wearable activity tracking" OR "Wearable Device" OR "Wearable Devices" OR "Wearable Electronic Device" OR "Wearable Electronic Devices" OR "Wearable Electronic Devices" OR "Wearable Technologies" OR "Wearable Technology" OR "wearable" OR "wearables" OR "noninvasive body sensor" OR "noninvasive body sensors" OR "non invasive body sensor" OR "non invasive body sensors" OR "body sensor" OR "body sensors" OR "wristband sensor" OR "wristband sensors" OR "wearable computing" OR "wearable computer" OR "wearable computers" OR "point-of-care App" OR "point-of-care Apps" OR "point-of-care Application" OR "point-of-care Applications" OR "facial recognition technology" OR "face recognition technology" OR "Point-of-Care Technology" OR "Point-

of-Care Techn*" OR "HUME" OR "ePAT" OR " electronic pain assessment" OR ("BIS" AND "bispectral") OR "bispectral index" OR "Consciousness Monitors" OR "Biosensing Techniques" OR ("Facial Expression" AND "Point-of-Care Systems") OR (("noninvasiv*" OR "non invasiv*" OR "unobtrusiv*" OR "portable" OR "Mobile Applications") AND "monitor*") OR "Painchek" OR "Paincheck" OR "automated facial analysis" OR "automated facial recognition" OR "automated facial expression analysis") AND TI=("discomfort" OR "discomfort*" OR "Psychological Distress" OR "distressing symptoms" OR "distressing symptom" OR "distressing" OR "distress" OR "Patient Comfort" OR "comfort" OR "comfort*" OR "Psychomotor Agitation" OR "agitation" OR "agitat*" OR "restlessness" OR "restless*" OR "hyperactivity" OR "hyperactiv*" OR "akathisia" OR "Pain" OR "pain" OR "Pain Measurement" OR "pain assessment" OR "Stress, Psychological" OR "stress level" OR "stress levels" OR "pressure ulcer" OR "pressure ulcer" OR "life quality" OR "quality of life" OR "quality of life" OR "breathing difficulty" OR "difficulty breathing" OR "difficult breathing" OR "labored breathing" OR "laboured breathing" OR "Shortness of Breath" OR "Breath Shortness" OR "Breathlessness" OR "Dyspnea" OR "Dyspnea" OR "Anxiety" OR "Anxiety" OR "Nervousness" OR "Hypervigilance" OR "Anxiousness" OR "Sleep Wake Disorders" OR "sleep disturbances" OR "sleep disturbance" OR "Fatigue" OR "fatigue" OR "Nausea" OR "nausea" OR "nauseous" OR "Delirium" OR "delirium" OR "delirious" OR "Fever" OR "fever" OR "Urinary Incontinence" OR "Incontinence" OR "incontinen*" OR "Sedation depth" OR "Sedation depths" OR "Depth of sedation"))

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(("Dementia" OR "Dementia" OR "dement*" OR "Alzheimer Disease" OR "Alzheimer*" OR "CADASIL" OR "Creutzfeldt Jakob" OR "Creutzfeldt Jakob Syndrome" OR "Diffuse Neurofibrillary Tangles with Calcification" OR "Frontotemporal Lobar Degeneration" OR "Huntington Disease" OR "Huntington*" OR "Kluver Bucy" OR "Kluver Bucy Syndrome" OR "Lewy Body" OR "Lewy Body Disease" OR "Pick Disease of the Brain" OR "Primary Progressive Aphasia" OR "Primary Progressive Nonfluent Aphasia" OR "Death" OR "dying" OR "end of life phase" OR "end of life" OR "end of life phase" OR "endoflife" OR "end of life" OR "Hospice and Palliative Care Nursing" OR "Hospice Care" OR "Hospice Care" OR "Hospice Care" OR "Hospice" OR "Hospices" OR "Hospices" OR "palliat*" OR "Palliative Care" OR "Palliative Care" OR "Palliative Medicine" OR "Palliative Phase" OR "Palliative Phases" OR "Palliative Stage" OR "Palliative Stages" OR "Palliative Supportive Care" OR "Palliative Surgery" OR "Palliative Therapy" OR "Palliative Treatment" OR "Palliative Treatments" OR "Terminal Care" OR "Terminal Care" OR "terminal stage" OR "elderly" OR "critical care" OR "critical care" OR "intensive care" OR "Critical Illness" OR "Critical Illness" OR "critically ill" OR (("profound" OR "profound*") AND ("Disabled Persons" OR "Intellectual Disability")) OR (("profound" OR "profound*") AND ("intellectual" OR "intellectualism" OR "intellectually" OR "intellectuals") AND ("multiple" OR "multiples") AND ("disabilities" OR "disability" OR "disabled persons" OR "disabled persons" OR "disabled" OR "disablement" OR "disablements" OR "disabling" OR "disablity")) OR "Bedridden Persons" OR "Bedridden" OR "Non Mobile Person" OR "Non Mobile Persons"):ti,ab,kw AND ("activity monitor" OR "activity monitors" OR "activity monitoring" OR "activity tracker" OR "activity trackers" OR "activity tracking" OR "Ambulatory Monitor*" OR "Ambulatory Monitoring" OR "Electronic Skin" OR (("monitor*" OR "monitoring") AND ("Telemedicine" OR "telemed*" OR "telehealth*" OR "technol*")) OR

"monitoring app" OR "monitoring application" OR "monitoring applications" OR "monitoring apps" OR "monitoring device" OR "monitoring devices" OR "monitoring technologies" OR "monitoring technology" OR "Monitoring, Ambulatory" OR "Monitoring, Physiologic" OR "Noninvasive device" OR "Non invasive device" OR "Noninvasive devices" OR "Non invasive devices" OR "Noninvasive monitoring device" OR "Noninvasive monitoring device" OR "Non invasive monitoring device" OR "Noninvasive monitoring devices" OR "Noninvasive monitoring devices" OR "Non invasive monitoring devices" OR "Noninvasive monitoring technologies" OR "Noninvasive monitoring technologies" OR "Non invasive monitoring technologies" OR "Noninvasive monitoring technology" OR "Noninvasive monitoring technology" OR "Non invasive monitoring technology" OR "Noninvasive monitoring" OR "Non invasive monitoring" OR "Noninvasive technologies" OR "Non invasive technologies" OR "Noninvasive technology" OR "Non invasive technology" OR "Outpatient Monitor*" OR "Outpatient Monitoring" OR "Portable Electronic Application" OR "Portable Electronic Applications" OR "Portable Software Application" OR "Portable Software Applications" OR "Smart watch" OR "Smart watches" OR "Smartwatch" OR "Smartwatches" OR "tracker" OR "trackers" OR "wearab*" OR "wearable activity tracker" OR "wearable activity trackers" OR "wearable activity tracking" OR "Wearable Device" OR "Wearable Devices" OR "Wearable Electronic Device" OR "Wearable Electronic Devices" OR "Wearable Electronic Devices" OR "Wearable Technologies" OR "Wearable Technology" OR "wearable" OR "wearables" OR "noninvasive body sensor" OR "noninvasive body sensors" OR "non invasive body sensor" OR "non invasive body sensors" OR "body sensor" OR "body sensors" OR "wristband sensor" OR "wristband sensors" OR "wearable computing" OR "wearable computer" OR "wearable computers" OR "point of care App" OR "point of care Apps" OR "point of care Application" OR "point of care Applications" OR "facial recognition technology" OR "face recognition technology" OR "Point of Care Technology" OR "Point of Care Techn*" OR "HUME" OR "ePAT" OR " electronic pain assessment" OR ("BIS" AND "bispectral") OR "bispectral index" OR "Consciousness Monitors" OR "Biosensing Techniques" OR ("Facial Expression" AND "Point of Care Systems") OR (("noninvasiv*" OR "non invasiv*" OR "unobtrusiv*" OR "portable" OR "Mobile Applications") AND "monitor*") OR "Painchek" OR "Paincheck" OR "automated facial analysis" OR "automated facial recognition" OR "automated facial expression analysis"):ti AND ("discomfort" OR "discomfort*" OR "Psychological Distress" OR "distressing symptoms" OR "distressing symptom" OR "distressing" OR "distress" OR "Patient Comfort" OR "comfort" OR "comfort*" OR "Psychomotor Agitation" OR "agitation" OR "agitat*" OR "restlessness" OR "restless*" OR "hyperactivity" OR "hyperactiv*" OR "akathisia" OR "Pain" OR "pain" OR "Pain Measurement" OR "pain assessment" OR "Stress, Psychological" OR "stress level" OR "stress levels" OR "pressure ulcer" OR "pressure ulcer" OR "life quality" OR "quality of life" OR "quality of life" OR "breathing difficulty" OR "difficulty breathing" OR "difficult breathing" OR "labored breathing" OR "laboured breathing" OR "Shortness of Breath" OR "Breath Shortness" OR "Breathlessness" OR "Dyspnea" OR "Dyspnea" OR "Anxiety" OR "Anxiety" OR "Nervousness" OR "Hypervigilance" OR "Anxiousness" OR "Sleep Wake Disorders" OR "sleep disturbances" OR "sleep disturbance" OR "Fatigue" OR "fatigue" OR "Nausea" OR "nausea" OR "nauseous" OR "Delirium" OR "delirium" OR "delirious" OR "Fever" OR "fever" OR "Urinary Incontinence" OR "Incontinence" OR "incontinen*" OR "Sedation depth" OR "Sedation depths" OR "Depth of sedation"):ti,ab,kw) OR (("Dementia" OR "Dementia" OR "dement*" OR "Alzheimer Disease" OR "Alzheimer*" OR "CADASIL"

OR "Creutzfeldt Jakob" OR "Creutzfeldt Jakob Syndrome" OR "Diffuse Neurofibrillary Tangles with Calcification" OR "Frontotemporal Lobar Degeneration" OR "Huntington Disease" OR "Huntington*" OR "Kluver Bucy" OR "Kluver Bucy Syndrome" OR "Lewy Body" OR "Lewy Body Disease" OR "Pick Disease of the Brain" OR "Primary Progressive Aphasia" OR "Primary Progressive Nonfluent Aphasia" OR "Death" OR "dying" OR "end of life phase" OR "end of life" OR "end of life phase" OR "endoflife" OR "end of life" OR "Hospice and Palliative Care Nursing" OR "Hospice Care" OR "Hospice Care" OR "Hospice Care" OR "Hospice" OR "Hospices" OR "Hospices" OR "palliat*" OR "Palliative Care" OR "Palliative Care" OR "Palliative Medicine" OR "Palliative Phase" OR "Palliative Phases" OR "Palliative Stage" OR "Palliative Stages" OR "Palliative Supportive Care" OR "Palliative Surgery" OR "Palliative Therapy" OR "Palliative Treatment" OR "Palliative Treatments" OR "Terminal Care" OR "Terminal Care" OR "terminal stage" OR "elderly" OR "critical care" OR "critical care" OR "intensive care" OR "Critical Illness" OR "Critical Illness" OR "critically ill" OR (("profound" OR "profound*") AND ("Disabled Persons" OR "Intellectual Disability")) OR (("profound" OR "profound*") AND ("intellectual" OR "intellectualism" OR "intellectually" OR "intellectuals") AND ("multiple" OR "multiples") AND ("disabilities" OR "disability" OR "disabled persons" OR "disabled persons" OR "disabled" OR "disablement" OR "disablements" OR "disabling" OR "disablity")) OR "Bedridden Persons" OR "Bedridden" OR "Non Mobile Person" OR "Non Mobile Persons"):ti,ab,kw AND ("activity monitor" OR "activity monitors" OR "activity monitoring" OR "activity tracker" OR "activity trackers" OR "activity tracking" OR "Ambulatory Monitor*" OR "Ambulatory Monitoring" OR "Electronic Skin" OR (("monitor*" OR "monitoring") AND ("Telemedicine" OR "telemed*" OR "telehealth*" OR "technol*")) OR "monitoring app" OR "monitoring application" OR "monitoring applications" OR "monitoring apps" OR "monitoring device" OR "monitoring devices" OR "monitoring technologies" OR "monitoring technology" OR "Monitoring, Ambulatory" OR "Monitoring, Physiologic" OR "Noninvasive device" OR "Non invasive device" OR "Noninvasive devices" OR "Non invasive devices" OR "Noninvasive monitoring device" OR "Noninvasive monitoring device" OR "Non invasive monitoring device" OR "Noninvasive monitoring devices" OR "Noninvasive monitoring devices" OR "Non invasive monitoring devices" OR "Noninvasive monitoring technologies" OR "Noninvasive monitoring technologies" OR "Non invasive monitoring technologies" OR "Noninvasive monitoring technology" OR "Noninvasive monitoring technology" OR "Non invasive monitoring technology" OR "Noninvasive monitoring" OR "Non invasive monitoring" OR "Noninvasive technologies" OR "Non invasive technologies" OR "Noninvasive technology" OR "Non invasive technology" OR "Outpatient Monitor*" OR "Outpatient Monitoring" OR "Portable Electronic Application" OR "Portable Electronic Applications" OR "Portable Software Application" OR "Portable Software Applications" OR "Smart watch" OR "Smart watches" OR "Smartwatch" OR "Smartwatches" OR "tracker" OR "trackers" OR "wearab*" OR "wearable activity tracker" OR "wearable activity trackers" OR "wearable activity tracking" OR "Wearable Device" OR "Wearable Devices" OR "Wearable Electronic Device" OR "Wearable Electronic Devices" OR "Wearable Electronic Devices" OR "Wearable Technologies" OR "Wearable Technology" OR "wearable" OR "wearables" OR "noninvasive body sensor" OR "noninvasive body sensors" OR "non invasive body sensor" OR "non invasive body sensors" OR "body sensor" OR "body sensors" OR "wristband sensor" OR "wristband sensors" OR "wearable computing" OR "wearable computer" OR "wearable computers" OR "point of care App" OR "point of care Apps" OR

"point of care Application" OR "point of care Applications" OR "facial recognition technology" OR "face recognition technology" OR "Point of Care Technology" OR "Point of Care Techn*" OR "HUME" OR "ePAT" OR " electronic pain assessment" OR ("BIS" AND "bispectral") OR "bispectral index" OR "Consciousness Monitors" OR "Biosensing Techniques" OR ("Facial Expression" AND "Point of Care Systems") OR (("noninvasiv*" OR "non invasiv*" OR "unobtrusiv*" OR "portable" OR "Mobile Applications") AND "monitor*") OR "Painchek" OR "Paincheck" OR "automated facial analysis" OR "automated facial recognition" OR "automated facial expression analysis"):ti,ab,kw AND ("discomfort" OR "discomfort*" OR "Psychological Distress" OR "distressing symptoms" OR "distressing symptom" OR "distressing" OR "distress" OR "Patient Comfort" OR "comfort" OR "comfort*" OR "Psychomotor Agitation" OR "agitation" OR "agitat*" OR "restlessness" OR "restless*" OR "hyperactivity" OR "hyperactiv*" OR "akathisia" OR "Pain" OR "pain" OR "Pain Measurement" OR "pain assessment" OR "Stress, Psychological" OR "stress level" OR "stress levels" OR "pressure ulcer" OR "pressure ulcer" OR "life quality" OR "quality of life" OR "quality of life" OR "breathing difficulty" OR "difficulty breathing" OR "difficult breathing" OR "labored breathing" OR "laboured breathing" OR "Shortness of Breath" OR "Breath Shortness" OR "Breathlessness" OR "Dyspnea" OR "Dyspnea" OR "Anxiety" OR "Anxiety" OR "Nervousness" OR "Hypervigilance" OR "Anxiousness" OR "Sleep Wake Disorders" OR "sleep disturbances" OR "sleep disturbance" OR "Fatigue" OR "fatigue" OR "Nausea" OR "nausea" OR "nauseous" OR "Delirium" OR "delirium" OR "delirious" OR "Fever" OR "fever" OR "Urinary Incontinence" OR "Incontinence" OR "incontinen*" OR "Sedation depth" OR "Sedation depths" OR "Depth of sedation"):ti)

Emcare (OVID)

((exp *"Dementia"/ OR ("Dementia" OR "dement*" OR "Alzheimer Disease" OR "Alzheimer*" OR "CADASIL" OR "Creutzfeldt-Jakob" OR "Creutzfeldt-Jakob Syndrome" OR "Diffuse Neurofibrillary Tangles with Calcification" OR "Frontotemporal Lobar Degeneration" OR "Huntington Disease" OR "Huntington*" OR "Kluver-Bucy" OR "Kluver-Bucy Syndrome" OR "Lewy Body" OR "Lewy Body Disease" OR "Pick Disease of the Brain" OR "Primary Progressive Aphasia" OR "Primary Progressive Nonfluent Aphasia").ti,ab OR exp *"Death"/ OR exp *"Terminal Care"/ OR exp *"Hospice"/ OR exp *"Palliative Therapy"/ OR ("dying" OR "end of life phase" OR "end of life" OR "end-of-life phase" OR "endoflife" OR "end-of-life" OR "Hospice and Palliative Care Nursing" OR "Hospice Care" OR "Hospice Care" OR "Hospice Care" OR "Hospice" OR "Hospices" OR "Hospices" OR "palliat*" OR "Palliative Care" OR "Palliative Care" OR "Palliative Medicine" OR "Palliative Phase" OR "Palliative Phases" OR "Palliative Stage" OR "Palliative Stages" OR "Palliative Supportive Care" OR "Palliative Surgery" OR "Palliative Therapy" OR "Palliative Treatment" OR "Palliative Treatments" OR "Terminal Care" OR "Terminal Care" OR "terminal stage").ti,ab OR "elderly".ti OR exp *"Intensive Care"/ OR exp *"Critical Illness"/ OR exp *"critically ill patient"/ OR ("critical care" OR "critical care" OR "intensive care" OR "Critical Illness" OR "Critical Illness" OR "critically ill") OR (("profound" OR "profound*").ti,ab AND (exp *"Disabled Person"/ OR exp *"Intellectual Impairment"/)) OR (("profound" OR "profound*") AND ("intellectual" OR "intellectualism" OR "intellectually" OR "intellectuals") AND ("multiple" OR "multiples") AND ("disabilities" OR "disability" OR "disabled persons" OR "disabled persons" OR "disabled" OR "disablement" OR "disablements" OR "disabling" OR "disablity")).ti,ab OR exp *"Bedridden Patient"/ OR

("Bedridden" OR "Non-Mobile Person" OR "Non-Mobile Persons").ti,ab) AND (("activity monitor" OR "activity monitors" OR "activity monitoring" OR "activity tracker" OR "activity trackers" OR "activity tracking" OR "Ambulatory Monitor*" OR "Ambulatory Monitoring" OR "Electronic Skin").ti. OR (("monitor*" OR "monitoring").ti. AND (exp *"Telemedicine"/ OR "telemed*".ti. OR "telehealth*".ti. OR "technol*".ti.)) OR "monitoring app".ti. OR "monitoring application".ti. OR "monitoring applications".ti. OR "monitoring apps".ti. OR "monitoring device".ti. OR "monitoring devices".ti. OR "monitoring technologies".ti. OR "monitoring technology".ti. OR exp *"Monitoring, Ambulatory"/ OR exp *"Monitoring, Physiologic"/ OR exp *"Ambulatory Monitoring"/ OR exp *"Physiologic Monitoring"/ OR "Noninvasive device".ti. OR "Non-invasive device".ti. OR "Noninvasive devices".ti. OR "Non-invasive devices".ti. OR "Noninvasive monitoring device".ti. OR "Noninvasive monitoring device".ti. OR "Non-invasive monitoring device".ti. OR "Noninvasive monitoring devices". ti. OR "Noninvasive monitoring devices".ti. OR "Non-invasive monitoring devices".ti. OR "Noninvasive monitoring technologies".ti. OR "Noninvasive monitoring technologies".ti. OR "Non-invasive monitoring technologies".ti. OR "Noninvasive monitoring technology". ti. OR "Noninvasive monitoring technology".ti. OR "Non-invasive monitoring technology". ti. OR "Noninvasive monitoring".ti. OR "Non-invasive monitoring".ti. OR "Noninvasive technologies".ti. OR "Non-invasive technologies".ti. OR "Noninvasive technology".ti. OR "Non-invasive technology".ti. OR "Outpatient Monitor*".ti. OR "Outpatient Monitoring". ti. OR "Portable Electronic Application".ti. OR "Portable Electronic Applications".ti. OR "Portable Software Application".ti. OR "Portable Software Applications".ti. OR "Smart watch".ti. OR "Smart watches".ti. OR "Smartwatch".ti. OR "Smartwatches".ti. OR "tracker".ti. OR "trackers".ti. OR "wearab*".ti. OR "wearable activity tracker".ti. OR "wearable activity trackers".ti. OR "wearable activity tracking".ti. OR "Wearable Device". ti. OR "Wearable Devices".ti. OR "Wearable Electronic Device".ti. OR exp *"Wearable Electronic Devices"/ OR exp *"wearable computer"/ OR "Wearable Electronic Devices". ti. OR "Wearable Technologies".ti. OR "Wearable Technology".ti. OR "wearable".ti. OR "wearables".ti. OR "noninvasive body sensor".ti. OR "noninvasive body sensors".ti. OR "non invasive body sensor".ti. OR "non invasive body sensors".ti. OR "body sensor".ti. OR "body sensors".ti. OR "wristband sensor".ti. OR "wristband sensors".ti. OR "wearable computing". ti. OR "wearable computer".ti. OR "wearable computers".ti. OR "point-of-care App".ti. OR "point-of-care Apps".ti. OR "point-of-care Application".ti. OR "point-of-care Applications". ti. OR "facial recognition technology".ti. OR "face recognition technology".ti. OR "Point-of-Care Technology".ti. OR "Point-of-Care Techn*".ti. OR "HUME".ti. OR "ePAT".ti. OR " electronic pain assessment".ti. OR ("BIS" AND "bispectral").ti. OR "bispectral index".ti. OR exp *"Consciousness Monitor"/ OR exp *"Consciousness Monitors"/ OR exp *"Biosensing Techniques"/ OR (exp *"Facial Expression"/ AND (exp *"Point-of-Care Systems"/ OR exp *"Point of Care System"/)) OR ((("noninvasiv*" OR "non invasiv*" OR "unobtrusiv*" OR "portable").ti. OR exp "Mobile Applications"/ OR exp *"Mobile Application"/) AND "monitor*".ti.) OR "Painchek".mp OR "Paincheck".mp OR "automated facial analysis".mp OR "automated facial recognition".mp OR "automated facial expression analysis".mp) AND (("discomfort" OR "discomfort*").ti. OR exp *"Psychological Distress"/ OR exp *"distress syndrome"/ OR "distressing symptoms".ti. OR "distressing symptom".ti. OR "distressing". ti. OR "distress".ti. OR exp *"Patient Comfort"/ OR "comfort".ti. OR "comfort*".ti. OR exp *"Psychomotor Agitation"/ OR exp *"Restlessness"/ OR "agitation".ti. OR "agitat*". ti. OR "restlessness".ti. OR "restless*".ti. OR "hyperactivity".ti. OR "hyperactiv*".ti. OR

"akathisia".ti. OR exp *"Pain"/ OR "pain".ti. OR exp *"Pain Measurement"/ OR "pain assessment".ti. OR exp *"Stress, Psychological"/ OR exp *"Mental stress"/ OR "stress level".ti. OR "stress levels".ti. OR "pressure ulcer".ti. OR "pressure ulcer".ti. OR "life quality".ti. OR exp *"quality of life"/ OR "quality of life".ti. OR "breathing difficulty".ti. OR "difficulty breathing".ti. OR "difficult breathing".ti. OR "labored breathing".ti. OR "laboured breathing".ti. OR "Shortness of Breath".ti. OR "Breath Shortness".ti. OR "Breathlessness".ti. OR exp *"Dyspnea"/ OR "Dyspnea".ti. OR exp *"Anxiety"/ OR "Anxiety".ti. OR "Nervousness".ti. OR "Hypervigilance".ti. OR "Anxiousness".ti. OR exp *"Sleep Disorder"/ OR exp *"Sleep Wake Disorders"/ OR "sleep disturbances".ti. OR "sleep disturbance".ti. OR exp *"Fatigue"/ OR "fatigue".ti. OR exp *"Nausea"/ OR "nausea".ti. OR "nauseous".ti. OR exp *"Delirium"/ OR "delirium".ti. OR "delirious".ti. OR exp *"Fever"/ OR "fever".ti. OR exp *"Urinary Incontinence"/ OR exp *"Urine Incontinence"/ OR "Incontinence".ti. OR "incontinen*".ti. OR "Sedation depth".ti. OR "Sedation depths".ti. OR "Depth of sedation".ti. OR exp *"anesthesia level"/))

PsycINFO (EbscoHOST)

(TX("Dementia" OR "Dementia" OR "dement*" OR "Alzheimer Disease" OR "Alzheimer*" OR "CADASIL" OR "Creutzfeldt-Jakob" OR "Creutzfeldt-Jakob Syndrome" OR "Diffuse Neurofibrillary Tangles with Calcification" OR "Frontotemporal Lobar Degeneration" OR "Huntington Disease" OR "Huntington*" OR "Kluver-Bucy" OR "Kluver-Bucy Syndrome" OR "Lewy Body" OR "Lewy Body Disease" OR "Pick Disease of the Brain" OR "Primary Progressive Aphasia" OR "Primary Progressive Nonfluent Aphasia" OR "Death" OR "dying" OR "end of life phase" OR "end of life" OR "end-of-life phase" OR "endoflife" OR "end-of-life" OR "Hospice and Palliative Care Nursing" OR "Hospice Care" OR "Hospice Care" OR "Hospice Care" OR "Hospice" OR "Hospices" OR "Hospices" OR "palliat*" OR "Palliative Care" OR "Palliative Care" OR "Palliative Medicine" OR "Palliative Phase" OR "Palliative Phases" OR "Palliative Stage" OR "Palliative Stages" OR "Palliative Supportive Care" OR "Palliative Surgery" OR "Palliative Therapy" OR "Palliative Treatment" OR "Palliative Treatments" OR "Terminal Care" OR "Terminal Care" OR "terminal stage" OR "elderly" OR "critical care" OR "critical care" OR "intensive care" OR "Critical Illness" OR "Critical Illness" OR "critically ill" OR (("profound" OR "profound*") AND ("Disabled Persons" OR "Intellectual Disability")) OR (("profound" OR "profound*") AND ("intellectual" OR "intellectualism" OR "intellectually" OR "intellectuals") AND ("multiple" OR "multiples") AND ("disabilities" OR "disability" OR "disabled persons" OR "disabled persons" OR "disabled" OR "disablement" OR "disablements" OR "disabling" OR "disablity")) OR "Bedridden Persons" OR "Bedridden" OR "Non-Mobile Person" OR "Non-Mobile Persons") AND TI("activity monitor" OR "activity monitors" OR "activity monitoring" OR "activity tracker" OR "activity trackers" OR "activity tracking" OR "Ambulatory Monitor*" OR "Ambulatory Monitoring" OR "Electronic Skin" OR (("monitor*" OR "monitoring") AND ("Telemedicine" OR "telemed*" OR "telehealth*" OR "technol*")) OR "monitoring app" OR "monitoring application" OR "monitoring applications" OR "monitoring apps" OR "monitoring device" OR "monitoring devices" OR "monitoring technologies" OR "monitoring technology" OR "Monitoring, Ambulatory" OR "Monitoring, Physiologic" OR "Noninvasive device" OR "Non-invasive device" OR "Noninvasive devices" OR "Non-invasive devices" OR "Noninvasive monitoring device" OR "Noninvasive monitoring device" OR "Non-invasive

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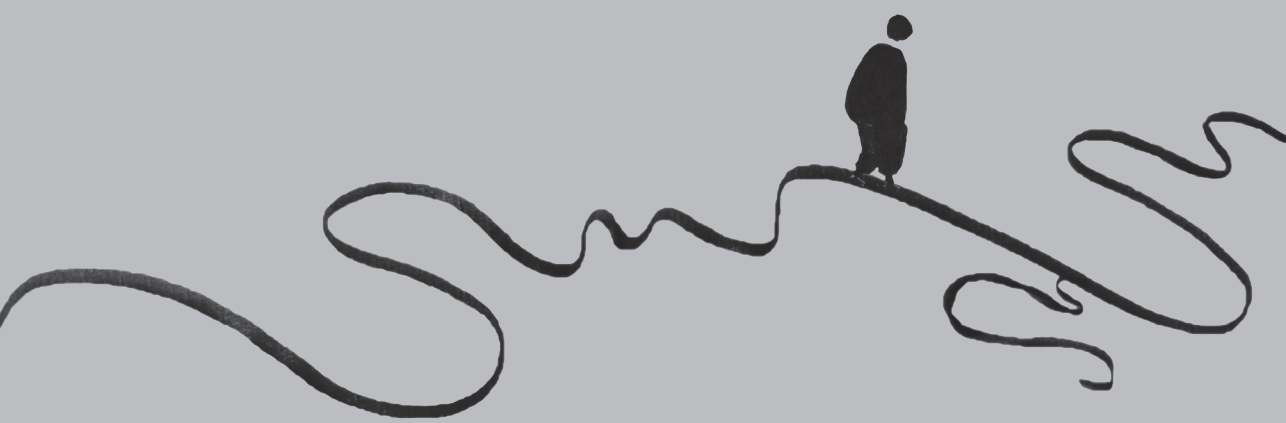

Acceptability of Bispectral Index monitoring in end-of-life care for dementia

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Abstract

BACKGROUND: Assessing consciousness might benefit the care for people with Alzheimer's disease and other types of dementia at the end of life by indicating distressing symptoms and moments of awareness. This could guide symptom control and increase interaction with the person with dementia.

OBJECTIVE: This study aims to investigate the acceptability of a biosignal measurement of consciousness, the Bispectral Index monitoring (BIS), for persons with dementia at the end of life.

METHODS: Qualitative study using focus groups and interviews with demonstrations of BIS monitoring, with 17 individuals with dementia and 24 family caregivers. Qualitative content analysis was based on the theoretical framework of acceptability.

RESULTS: People with dementia did not find BIS monitoring bothersome, yet acceptability varied across participants and situations. Family caregivers considered BIS acceptable for medical situations such as palliative sedation and pain assessment. Perceived effectiveness, ethicality, and usefulness considerations underpinned reasons and concerns around acceptability.

CONCLUSIONS: Potential end-users expressed diverse attitudes towards BIS monitoring in dementia end-of-life care. If BIS or similar technologies are to be implemented in the future, care must be taken to ensure that the device has sufficient added value, that the person with dementia and family are well informed, and that the technology does not replace human care. Future research should investigate its efficacy and feasibility in the situations that were deemed acceptable.

Introduction

Monitoring the level of consciousness of people with dementia may help maximize comfort and improve their quality of life at the end of life. End of life with dementia includes people in a comatose state and those with severely impaired decision-making, although controversy on this definition is ongoing [1, 2]. In this state, self-reporting of distressing symptoms is often no longer possible, while as many as 63% of people with dementia in palliative care and between 22% and 85% of people with dementia in nursing homes may be in pain [3, 4]. A change in consciousness may be used as an indicator of possible discomfort and guide symptom control [5]. Moreover, identifying moments of awareness [6], which are often unexpected [7, 8], may provide valuable opportunities to engage with people with advanced dementia [7].

Currently, evaluation of consciousness is mainly based on clinical observation [9]. Although observational scales are reliable in the end-of-life care context [10], their validity is questioned [11]. For example, people in palliative care who are evaluated as being unconscious based on the rating of these scales, may actually still be conscious enough to experience discomfort [12]. Researchers question the accuracy and objectivity of observation because the signs of consciousness in this population are often subtle and unclear [13]. Objective, valid measurement of biosignals of consciousness using portable devices identified in a recent review [14] may provide an alternative option.

One potentially useful technology to measure consciousness is the Bispectral Index (BIS) monitor. BIS measures neuromuscular and superficial cortical activity through electrodes placed on the forehead. Its main variable, the BIS index, consists of a single number computed from a complex algorithmic equation based on the electroencephalography (EEG) data of a large sample of healthy adult subjects undergoing general anesthesia [15]. Its value can range from 0 (complete EEG suppression) to 100 (fully awake). This non-invasive, bedside technology is routinely used during surgery to monitor the depth of anesthesia and is found to be acceptable and potentially useful for palliative sedation to detect discomfort and help titrate the medication [16-18]. The BIS index scores showed more variations in lower levels of consciousness compared to observational scales that had only one or two categories [19, 20], indicating

that BIS may be better at discriminating levels of consciousness in deeper sedation.

Research on the use of BIS monitoring with people with dementia is limited. One study showed that the baseline BIS level for people with dementia was lower [21], but the effect of sedatives on the decline of BIS index was similar to people without dementia [22]. The feasibility of BIS monitoring has been demonstrated in people with severe dementia during dental treatment with sedation [23], and it was generally tolerated by nursing home residents [24]. Thus, there is potential for the use of BIS monitoring in people with dementia.

However, it is not known whether people with dementia and their family caregivers are interested in, or would find it relevant or even acceptable, to apply BIS monitoring in end-of-life care for people with dementia. It is crucial to systematically examine the attitudes of stakeholders before deciding whether to devote more resources to validating and implementing the device in this setting [25-27] In this study, the theoretical framework of acceptability (TFA) developed by Sekhon and colleagues [25] was used to assess the acceptability of the application of BIS monitoring in various situations in end-of-life care for people with dementia. TFA is the first comprehensive framework for healthcare interventions developed based on an umbrella review. It consists of seven component constructs: 1) affective attitude, 2) burden, 3) perceived effectiveness, 4) ethicality, 5) intervention coherence, 6) opportunity costs, and 7) self-efficacy. According to TFA, acceptability can be examined before the person participates in an intervention (prospective), during the intervention (concurrent), and after going through the intervention (retrospective).

This study examines the prospective acceptability of BIS monitoring at the end of life of people with dementia from the perspective of people with dementia and their family caregivers. We investigate in which situations it is considered acceptable and why.

Materials and methods

Study design

In this qualitative study, focus groups and interviews were conducted between August 2022 and January 2023 with family caregivers and people with dementia. Focus groups were chosen because the study aimed to gain an understanding of collective attitudes, and the group dynamic may stimulate more diversity in opinions [28, 29]. To maximize participation of people with dementia, a few people with dementia were interviewed individually or in pairs instead of collectively in the focus group setting. This research was grounded in a constructivist paradigm, aimed at understanding the subjective opinions of the participants and taking into account the situation and lens of the researchers [30]. The COREQ guideline was followed to report this study [31].

Participants

Participants were people with dementia, current family caregivers, and former family caregivers. All participants provided informed consent for this study. Current family caregivers were included because they represent the population that would be involved in decision-making regarding the actual implementation of BIS monitoring for people with dementia. Former family caregivers could contribute to the discussion with their experience of situations at the end of life, when the level of consciousness was not clear. All participants had decision-making capacity. In order to take part in the study, people with dementia needed to be aware of their dementia diagnosis and have enough language, memory and hearing abilities to participate in an interview or group discussion in Dutch. Current family caregivers had to provide care to a person living with dementia for at least two hours a month. Former family caregivers had to have provided care to a person with dementia who died within the past five years. These criteria were included in the informed consent form.

Family caregivers were recruited through the Dutch Alzheimer's Association and the University Network of the Care Sector South Holland (UNC-ZH) academic long-term care network. Current and former caregivers who were registered at the Dutch Alzheimer's Association panel received an invitation from the association asking their permission to be approached by the researchers. The researchers then sent an email about the study and the informed consent form to those who were interested, followed by a phone call to address any questions. Additionally, former family caregivers were approached by healthcare professionals affiliated with the long-term care network. Healthcare professionals contacted potential participants via phone or email and sent them the information letters with informed consent forms. For the recruitment of people with dementia, researchers first contacted healthcare professionals who worked at daycare programs of institutions associated with the long-term care network. People with dementia who attended these programs were approached in person by the researchers or healthcare professionals. Participants and healthcare professionals who helped with the recruitment were informed of the inclusion criteria in order to assess eligibility. All participants were encouraged to contact the research team if they had any questions. Recruitment stopped when the research team involved in data collection (XJ, HS, JTS and students) agreed that no new information related to the research questions emerged from the last focus group. Data saturation on the code level was confirmed later during data analysis: 99% of the codes were generated before the last focus group, which was with persons with dementia [32].

Procedures

Each focus group had one main moderator and one researcher supporting the process. One focus group was conducted by a single researcher due to unforeseen circumstances. Focus groups were scheduled to last 90 minutes, including a short break. Individual or duo interviews were conducted by a single researcher, and aimed to last no longer than 60 minutes. The moderators and interviewers included experienced female researchers with a background in psychology (HS, XJ) or epidemiology (JTS) and experience in qualitative research, female master students with a background in psychology, and a male

master student in medicine. They all received training in conducting interviews and focus groups. Focus groups and interviews were performed face-to-face as much as possible, in long-term care facilities (n = 6), conference centers (n = 2), or the home of the person with dementia (n = 1). One focus group with family caregivers was conducted online to include participants who were not able to participate in face-to-face groups. In the majority of the focus groups and interviews, only the participants and researchers were present. In one interview a family member was present to support the person with dementia. During one focus group at a daycare center, a few other people with dementia and two staff members were in the same large room due to limited space. They conducted quiet activities on their own and did not participate in the focus group.

A semi-structured topic guide (Supplement I) and standard operating procedure (SOP) were developed. There were slight differences between the guide and SOP for people with dementia and those for family caregivers. In the initial plan, current and former caregivers were to participate in separate focus groups, so everyone could feel free to express their opinions to people in similar situations and so current caregivers would not be confronted with distressing experiences of former caregivers around the death of the relative with dementia. However, some groups were mixed due to a misunderstanding about whether the relative with dementia was still alive. Despite initial concerns, no negative experiences were reported from the first mixed group. Instead, the input from different perspectives led to lively discussion. As a result, the study team decided to no longer separate the two groups for easier logistics.

All focus groups and interviews started with an introduction round and the researchers explaining the aims of study and their roles within the meeting. Participants were asked whether there were situations in which they would like to know the consciousness level of people with dementia. The BIS device was then demonstrated, either live or with an instruction video. Researchers explained that the BIS device monitors brain activity, which indicates the level of consciousness. They also mentioned that it is already being used during surgery. In most face-to-face focus groups and interviews participants had the opportunity to try on the BIS monitor and share their experiences

and first impressions of the device. If the device produced a beeping sound, researchers explained this indicated that the signal quality from the sensors was inadequate. For family caregivers, additional questions were asked about the advantages and disadvantages of BIS monitoring for people with dementia. Next, participants were asked in what situations they would find the use of BIS acceptable to monitor consciousness of people with dementia. The research team provided five standard situations, which were generated based on past research and the functionality of BIS monitors. The situations included during natural sleep of people with dementia, recovering from surgery in the hospital, severe dementia in the nursing home, the last days/hours of life, and palliative sedation. Participants were also encouraged to suggest other situations. To stimulate discussion, the proposed situations were not restricted to the end of life or a specific setting. In order to minimize experiences of failure, all situations proposed by the participants, no matter whether they were realistic for BIS monitors or not, were noted and subsequently discussed in the focus groups. Finally, each situation that was mentioned was displayed on one poster or screen and participants were invited to indicate whether they considered BIS monitoring acceptable by sticking colored post-it notes (red=not acceptable, green=acceptable) on the posters, voting online or replying verbally. After that, they elaborated on their opinions.

The focus groups and interviews were audio recorded and transcribed verbatim. Field notes were made by the assistants during the focus group and interview about the acceptability of the situations. Immediately afterwards, salient observations and reflections of the researchers on the interaction with participants were discussed between the moderator and assistant and added to the field notes. Member checking was not performed.

All participants completed a brief demographics questionnaire before or immediately after the focus group or interview. Care providers of the day centers helped complete the demographics for some participants with dementia. (Former) family caregivers also provided the demographic data of their (deceased) relatives with dementia.

Data analysis

The number of stickers or votes for each BIS monitoring situation were counted and recorded in the field notes. The opinions of people with dementia were derived from their answers in the transcripts, as they did not always manage to use sticky notes to indicate their preference. Situations proposed by the participants which were similar but phrased differently across the groups were combined during the analysis. Since many situations were generated, they were grouped into day-to-day and medical situations, depending on whether the situation was related to medical procedures, symptom assessment, and medical decision-making.

The transcripts were analyzed using combined inductive and deductive approaches of qualitative content analysis, addressing the question as to why participants considered BIS monitoring (not) acceptable [33, 34]. After open coding, the codes were grouped according to TFA [25]. An initial structure of the code tree was established based on the research questions and impressions from the data and observations. This was discussed between XJ, HS, JTS, and a female master student in medicine. Open coding was then conducted by XJ and the female master student to capture as much as possible the meanings conveyed by the participants. The two researchers independently coded one focus group of family caregivers and generated initial codes. They discussed any discrepancies and reached consensus on the code book. The codes were organized into groups such as pros, cons, and suggestions. The code book was checked by HS and JTS for clarity. XJ and YS independently coded the first focus group again based on this code book and reached consensus. They subsequently coded the other focus groups and interviews independently and held consensus meetings per two or three transcripts. During the consensus meetings, they discussed their differences in coding until they reached agreement and modified the codes and groups in the code book. Atlas.ti 22 (Scientific Software Development GmbH, Berlin) was used to support the coding. After all the data were coded, XJ grouped the codes in categories largely based on TFA [25]. When the theory did not fit the data, new categories were constructed, or the interpretation of existing categories was modified. This analysis was discussed with HS and JTS. The data from the field notes were also summarized under corresponding categories.

Ethical considerations

The study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and later amendments. All participants signed an informed consent form. People with dementia were encouraged to discuss participation in the study with healthcare professionals and their family caregivers before deciding whether to participate. All participants were informed that they would each receive a gift card of 20 euros. In practice, 13 people with dementia received gift cards worth 24 euros which were available at the time. The study was deemed exempt from the Dutch Medical Research Involving Human Subjects Act (WMO) by the ethics commission for non-WMO studies Leiden University Medical Center Division 3 (reference No. 22-3004, 04-04-2022).

Results

Demographics

Seventeen people with dementia participated in three face-to-face focus groups and two interviews. To overcome a language barrier, one participant was interviewed in the presence of his family caregiver for language support. Two other participants were interviewed together. Twelve current caregivers and 12 former caregivers participated in four face-to-face focus groups and one online focus group. An additional three current caregivers withdrew before the focus groups, due to personal issues (n = 2) or an unspecified reason (n = 1). Focus groups lasted between approximately 80 and 120 minutes. Focus groups with family caregivers took longer than those with people with dementia. Interviews lasted between 46 and 61 minutes. Table 1 presents the sample characteristics.

The former family caregivers reported the death of the persons with dementia occurred on average 26.7 months before the study (SD 17.5, range 8 – 54 months). Three of the current caregivers were caring for a relative with dementia born outside the Netherlands (two from West-European countries, one from South Asia). Half of the current caregivers indicated the person with dementia was able to express pain or discomfort, and a third of former caregivers reported their ability to do so in the last week of life. Based on the remarks in the questionnaire, however, it is worth noting that not all caregivers

were certain about the accuracy of their observation of discomfort in their relatives.

When BIS monitoring is considered acceptable

Situations for possible use of the BIS monitor in dementia care and their acceptability are presented in Table 2. A number of day-to-day and medical situations were suggested by participants. These suggested applications mostly aimed at ensuring the comfort of people with dementia, improving contact with them, and informing medical decisions. People with dementia suggested fewer applications than family caregivers.

Table 1 Sample characteristics

	Person with dementia (N = 17)	**Current caregiver (N = 12)**	**Former caregiver (N = 12)**
Age in years: Mean (SD) or median (IQR), range	84.9 (7.4), 72 – 99	69.0 (13.0), 41- 89	67.0 (65.0 -71.5), 59 – 89
Female, N (%)	7 (41)	7 (58)	6 (50)
Country of birth: N (%)			
the Netherlands	13 (76)	12 (100)	12 (100)
Other*	4 (24)	0	0
Education†, N (%)			
Low	13 (76)	6 (50)	4 (33)
Medium	3 (18)	1 (8)	1 (8)
High	1 (6)	5 (42)	7 (58)
Type of dementia person cared for, N (%)			
Alzheimer's	11 (65)	7 (58)	5 (42)
Parkinson's	1 (6)	0 (0)	0 (0)
Vascular	0 (0)	5 (42)	6 (50)
Frontal-temporal	0 (0)	1 (8)	3 (25)
Korsakov	0 (0)	1 (8)	0 (0)
Don't know or not diagnosed	5 (29)	0 (0)	0 (0)

Table 1 Sample characteristics (continued)

	Person with dementia (N = 17)	Current caregiver (N = 12)	Former caregiver (N = 12)
Living situation of the person with dementia, N(%)			
Alone	6 (35)	0	
With caregiver or other housemates	10 (59)	6 (50)	
Sheltered housing	1 (6)	0	
Long-term-care facility	0	6 (50)	
Relationship with the person with dementia, N(%)			
Partner		9 (75)	8 (67)
Son/daughter		3 (25)	3 (25)
Niece/nephew/cousin		0 (0)	1 (8)
Hours per week spent on caregiving (in the last week of the person's life), median (IQR), range		22 (5-53), 2-168	35 (24-43), 5-120

Note: M = mean, SD = standard deviation, IQR = interquartile range

* Other countries of birth included a West-European country and two former Dutch colonies in South-America and Asia.

† The level of education based on the aggregated International Standard Classification of Education: Low= 8 years or less of primary and special primary education; prevocational secondary education; lower secondary vocational training and assistant's training. Medium= upper secondary education, (basic) vocational training, middle management and specialist education. High= higher education, 4-year education at universities of applied sciences and research universities; doctoral degree programs at research universities. All levels of secondary vocational training ("middelbaar beroepsonderwijs" in Dutch) were classified as Low in this study. [35,36]

Table 2 Acceptability of Bispectual Index monitoring in specific situations in palliative care for dementia

Situations	People with dementia			Family caregivers		
Day-to-day situations	Yes	No	Missing*	Yes	No	Missing*
Situations proposed by researchers						
In natural sleep	8	4	5	10	12	2
Severe dementia in nursing home	7	2	8	15	7	2
Last days/hours of life	8	3	6	16	4.5†	3
Situations proposed by participants‡						
During contact moments	n/a	n/a	n/a	9	5	2
When the person with dementia is noncommunicative	3	1	2	7	1	3
When staff does not know the person with dementia well	n/a	n/a	n/a	7	2	0
In home situation, to know someone's level of awareness	n/a	n/a	n/a	6	0	0
To know how aware the person with dementia is of their action when they exercise autonomy	n/a	n/a	n/a	3	0	3
Medical situations						
Situations proposed by researchers						
Recovering from operation in the hospital	5	6	7	19	4.5†	0
Palliative sedation	5	4	8	17	3	4
Situations proposed by participants‡						
To detect pain/discomfort	1	0	1	19	1	0
To detect psychological suffering	n/a	n/a	n/a	3	2	0
To detect deterioration of physical condition	n/a	n/a	n/a	4	0	2
To help make important medical decisions	n/a	n/a	n/a	4.5†	0	0

Table 2 Acceptability of Bispectual Index monitoring in specific situations in palliative care for dementia (continued)

Situations	**People with dementia**			**Family caregivers**		
Day-to-day situations	Yes	No	Missing*	Yes	No	Missing*
Acute situations, e.g., transient ischemic attack or cerebrovascular accident	n/a	n/a	n/a	4	0	0
To monitor the progression of dementia	2	0	0	3	1	0

* Missing values refer to cases in which participants did not express their opinions, said that they did not know or seemed not to understand the question.
† One participant put down half a sticker, explaining that she considered it only partially acceptable (half of a green sticker) or unacceptable (half of a red sticker).
‡ The situations proposed by the participants of a focus group were discussed in the particular focus group. Therefore, the number of votes varied per situation. The situations proposed by the researchers were discussed in all focus groups and interviews.

The acceptability of BIS monitoring differed depending on the situation. Around half of the people with dementia could not understand or imagine the situations or express an opinion on acceptability. The other participants with dementia had diverse opinions. The majority of participants considered BIS monitoring acceptable in day-to-day situations, while the acceptability was more controversial in medical situations. As for family caregivers, they generally considered BIS monitoring acceptable in most situations discussed, especially in medical situations such as when the person with dementia is recovering from surgery in the hospital or using the device to detect pain and discomfort. Opinions differed regarding the use of BIS in day-to-day situations, for example to monitor natural sleep or people with severe dementia in the nursing home. The situations proposed by other participants were deemed acceptable by a larger proportion of participants compared to those suggested by the researchers. In total, 39 (41 %) votes by people with dementia across all situations were acceptable, 20 (21%) unacceptable, and 37 (39%) were missing. For family caregivers, the votes were 146.5 (70%) acceptable, 43 (20%) not acceptable, and 21 (10%) missing.

Why BIS monitoring is considered (not) acceptable

The opinions regarding the acceptability of BIS monitoring are summarized in Table 3. They were categorized according to the TFA domains, including affective attitude, burden, ethicality, intervention coherence, opportunity costs, and perceived effectiveness. Several modifications were made to the categories and their definitions to fit the data. Two inductive categories were generated, namely feasibility and usefulness. For the category "perceived effectiveness", subcategories were generated to illustrate various aspects of effectiveness of BIS, including monitoring symptoms, facilitating communication, decision-making and improving care, and facilitating acceptance. The TFA category "self-efficacy" was not included in the analysis because no comments were related to it. This is probably because BIS does not require much action from the people with dementia or family caregivers themselves. The definition of the category "burden" was modified from "the perceived amount of effort that is required to participate in the intervention" to "perceived amount of difficulties, disturbance, and effort for the person with dementia, the family, and healthcare professionals". The implementation of BIS does not require much effort from the receivers, but participants suggested that it may be burdensome in other ways and may affect other groups such as the family and professionals.

We observed that the opinions of family caregivers and people with dementia largely overlapped, although those raised by family caregivers were more elaborate. While both groups made many comments about the effectiveness and usefulness of BIS, they expressed few concerns about opportunity costs. Some other comments made by people with dementia were more general, for example a negative attitude of seeing no added value, or a positive attitude towards the device without further elaboration: *"Oh, look! How nice!"* (Person with dementia, female, age 92). We observed that some people with dementia and a few family caregivers had difficulty understanding the questions and imagining the situations being discussed. Some were preoccupied by their immediate concerns, such as curing dementia or measuring its progression. *"Yes, if it is really necessary, I would do it....to get better, you understand?"* (Person with dementia, male, age 99).

Table 3 Acceptability of Bispectral Index monitoring in palliative care for dementia – comments organized according to the theoretical framework of acceptability

Categories	Codes positive attitudes	Codes negative attitudes	Codes neutral attitude
Affective attitude (how a person feels about the intervention)	Gives peace to the family	Emotionally difficult to accept a device around the end of life	No reason not to use it
	Acceptable, without explanations[§]	*The person with dementia is anxious about the results of the measurement*[§]	No impression and no opinion[‡]
	Interest in the device[‡]		Technology is the unavoidable future[‡]
Burden (perceived amount of difficulties, disturbance, and effort for the person with dementia, the family, and healthcare professionals)*	The sensor is soft and not irritating	The beeping or the sensor can be disturbing for people with dementia	
	Easy to use[‡]	Extra work for the staff[‡]	
	Small device[‡]		
Ethicality (extent to which the intervention matches a person's value system)	It is the right of the person with dementia[‡]	Dangerous to let a machine make important decisions	Consent is needed from the family and person with dementia
	Family and physician are responsible for understanding how the person with dementia might feel[‡]	May lead to less care for people with a lower level of consciousness[‡]	*The results should be communicated to the person with dementia*[§]
		Should not be used to compensate for insufficient care or to substitute human care[‡]	*Privacy is not a concern*[§]

Table 3 Acceptability of Bispectral Index monitoring in palliative care for dementia – comments organized according to the theoretical framework of acceptability *(continued)*

Categories		Codes positive attitudes	Codes negative attitudes	Codes neutral attitude
			Use may not be justified if only for the benefits of the family or the researchers‡	
Intervention coherence (extent to which the person understands how the intervention works)			*Difficult to understand how the device works§*	
			The family may not use the device correctly due to lack of understanding and capacity‡	
Opportunity costs (extent to which benefits, profits or values must be given up to engage in the intervention)			Costs‡	
Perceived effectiveness (extent to which the intervention is perceived as likely to achieve its purpose)	Monitoring symptoms†	Helps monitor the person with dementia when family or staff are not available	It may not be able to accurately monitor pain, consciousness, and sleep	*Actions should be taken after symptoms are monitored§*
		Objectively monitors discomfort, consciousness, and sleep quality	Does not directly monitor pain‡	
		Helps detect the start of the dying process	Does not monitor overall wellbeing, physical condition, progression of dementia, or content of consciousness‡	
			The output is difficult to interpret‡	

Table 3 Acceptability of Bispectral Index monitoring in palliative care for dementia – comments organized according to the theoretical framework of acceptability *(continued)*

Categories		Codes positive attitudes	Codes negative attitudes	Codes neutral attitude
	Facilitating communication†	Helps noncommunicative persons	May further reduce interaction if the person is labeled noncommunicative or does not react due to unwillingness rather than capability ‡	
	Decision-making and improving care †	Helps improve comfort	*Does not help to cure dementia, thus no value is perceived*§	
		Helps professionals understand the situation to provide better, personalized care and treatment		
		Helps family and visitors adjust their interaction with the person with dementia		
		Helps indicate whether the person with dementia is able to make decisions§		
	Facilitating acceptance†	*Acceptable if it helps the person with dementia to accept the dementia diagnosis*§		
		Helps the family accept the approaching death‡		

Table 3 Acceptability of Bispectral Index monitoring in palliative care for dementia – comments organized according to the theoretical framework of acceptability *(continued)*

Categories	Codes positive attitudes	Codes negative attitudes	Codes neutral attitude
Feasibility (the extent to which it is practical and feasible to use the device)†		Difficult to have good signal quality†	
		May be pulled off by the person with dementia†	
		Might not work with agitated people†	
Usefulness (the extent to which there is a perceived need to use the technology)†		No added value	
		Observation is sufficient to determine whether the person with dementia is able to participate in conversations, their stage of dementia, and the start of the dying phase	
		The staff will provide enough monitoring	
		Other existing devices are sufficient	
		No need for the device if the person can still understand and communicate	
		No need for the device if there is no specific indication	

Table 3 Acceptability of Bispectral Index monitoring in palliative care for dementia – comments organized according to the theoretical framework of acceptability *(continued)*

Categories	Codes positive attitudes	Codes negative attitudes	Codes neutral attitude
		No need for the device when the person cannot react normally anyway[§]	
		Observation is sufficient to determine how the person with dementia feels and whether they are asleep[‡]	
		The professionals should be able to determine the medication dosage by themselves[‡]	
		No need for the device because the family do not want to know about the level of awareness[‡]	
		No need for the device if the person does not want to live if no longer aware[‡]	

Note: The category self-efficacy from the theoretical framework of acceptability did not apply to our data.

* The definition was adjusted to fit the data of this study.

† This category or subcategory was constructed based on the data of this study.

[‡] These comments were made by family caregivers only.

[§] The comments in *italics* were made by people with dementia only.

Affective attitude

The participants mostly had a neutral or positive impression of BIS monitoring. They showed much interest in the device by asking questions, trying it on, or touching the sensors. Two participants with dementia were a bit anxious because they thought that the device would evaluate their cognitive functioning. The family elaborated on their attitudes towards BIS monitoring in palliative care for people with dementia. For some, BIS may give them peace of mind by providing more monitoring and information. *"Some reassurance as well, you know. That it, well, that it's still there, the awareness."* (current caregiver, male, age 78). But for the end of life, some found it difficult to include the device. *"I don't want to see her hooked up to all sorts of tubes and stuff if it's not necessary ...I don't want that at that stage that is so intimate"* (former family caregiver, male, age 78).

Burden

Many thought that the sensors of BIS monitors would not be burdensome for people with dementia, because they were soft and not painful to attach. Participants who attached the sensors kept them on their foreheads between a few seconds to a few minutes. They did not give the impression that the sensors bothered them, although temporary red marks were left on some participants' foreheads after removing the sensors. *"Well, I don't really feel anything actually"* (person with dementia, male, age 99).

Others raised the concern that the device may still be disturbing for people with dementia because of the extra stimuli. *"Touching her head, that's absolutely not done. It would mean instant war, so to speak"* (former caregiver, male, age 65). The beeping sound for inadequate signal quality, which occurred often during the demonstration, was perceived as annoying.

Some family caregivers also worried that BIS monitors in the current form, although small and relatively easy to use, would increase the workload for the staff and would not be welcomed in busy hospitals and nursing homes. Extra personnel might be needed to keep an eye on the monitors, to operate the device if less educated personnel were unable to do so, and to deliver care when the device showed that care might be needed. One of them suggested: *"If you can use a final version, wirelessly, then you are also rid of that monitor...*

otherwise it won't work. Then you'd still have to have someone there" (former caregiver, male, age 78).

Ethicality

The main ethical concern raised by the participants was that the device should be used for the benefit of the person with dementia, rather than for the family, researchers, or staff. Thus, it should not be used to substitute care that needs to be provided by healthcare professionals. *"Yes you have to avoid that these kind of aids, ehm, well I don't want to say laziness, but a kind of efficiency tool. [...] if that's how it's going to work, well, then I have no desire to grow old"* (current caregiver, female, age 56). If used improperly, participants worried that it might lead to people who have a constant lower level of consciousness receiving less attention and care.

Participants discussed ethical implications of using the BIS monitor to help medical decision-making. While some were enthusiastic, others stated that it would be dangerous to rely too heavily on a machine for important decisions. *"- So maybe it's like extra support or something when you have to make a yes-or-no decision about euthanasia. I hope so, I certainly hope so. – It makes me nervous, a remark like that. I sincerely hope that no outside persons, based on a device like this, are ever allowed to arrive at a decision in a decision tree that this person has decreased awareness or no awareness, and we are either going to pull the plug now or we'll start palliative sedation with death as the goal, the person dies."* (current caregivers, female, age 71 and 56 respectively).

Participants who considered BIS monitoring acceptable stated that proper monitoring is the right of the people with dementia as well as the responsibility of healthcare professionals. When implemented, it was considered important to share enough information with the stakeholders. Both people with dementia and family caregivers stated that they would want healthcare professionals to ask their consent about using BIS and share the monitoring results with them. Privacy was only mentioned by two persons with dementia, saying that it was not a concern. *"- Oh everyone [is allowed to know how aware I am]. – Everyone yes. – Yes! I have no secrets from... It's my condition. So it is a good thing when*

people can know what my condition is" (persons with dementia, female, age 76, and male, age 72).

Intervention coherence

Concerns were raised by all groups of participants about adequate understanding of BIS monitoring. Some people with dementia thought that those being monitored would not understand how the device works and what it is used for. *"But that wouldn't help, you have to explain everything and people don't understand you... They will shout 'no!'"* (person with dementia, male, age 73). A former family caregiver (female, age 65) worried that it might be implemented in the wrong way if this was done by caregivers at home who did not know enough about how to use it.

Opportunity costs

Few comments related to things that need to be given up in order to use BIS monitoring. Only two family caregivers mentioned that the cost could be a concern for healthcare institutions to implement it.

Perceived effectiveness

Monitoring symptoms

The expectation of the BIS device being able to monitor symptoms that are of interest to the participants was one of the main arguments for the acceptability of using it in dementia care. Those who considered BIS acceptable saw its potential for monitoring sleep, pain, and the onset of dying. However, others questioned whether the device was capable of monitoring these symptoms and events. A few participants were mainly interested in other measurements, such as the stage of dementia or the prognosis. They did not consider BIS monitoring acceptable because it would not provide such information.

Participants mentioned several advantages of BIS related to symptom monitoring, for instance, that it provides non-biased, objective information: *"I think it's really helpful because one person says this and the other says that and well, the device measures exactly how it is."* (current caregiver, female, age 71), and that it can provide continuous monitoring when staff is not available, for example,

at night. However, other participants did not agree with the latter, arguing that staff should be on standby to take action when symptoms are detected.

Facilitating communication

Participants saw the potential of BIS monitoring for helping noncommunicative people with dementia express their feelings or helping others in their interaction with the person with dementia. *"Is it about that you know that it, your message, is received or not? Because I would really like that"* (former caregiver, male, age 62). One former family caregiver (male, age 65), however, raised the concern that this would reduce the willingness to make the effort to interact with people who are identified as having reduced communication ability, or with people who are conscious and capable of communication, but reluctant to do so, for example, due to a bad mood.

Decision-making and improving care

Many participants hoped that BIS monitoring would improve care and medical decision-making for people with dementia. *"If it's a device and it's in the hospital, and they can take action. Well great"* (person with dementia, female, age 76).

This can especially be helpful for staff who do not know the person with dementia well enough to provide personalized care. The family can also adjust their behavior based on the monitoring results *"What do and what don't you say in this room. It would be very good to know if there is still awareness, so you can leave the room and discuss it outside"* (former caregiver, male, age 65).

Facilitating acceptance

Participants suggested that BIS monitoring may provide more information and thus facilitate their acceptance of the situations they are in. Family caregivers indicated that BIS monitoring might help them accept the approaching death. *"That it would do make it easier for me to let go if I... could see that the level of awareness is also drastically reduced in the person with dementia"* (current caregiver, female, age 58). A person with dementia (female, age 82) said that the device would be valuable if it could help people with dementia accept their diagnosis, for example, by showing that their brain is not functioning well.

Feasibility

Several family caregivers raised concerns about the feasibility of the device due to problems with the signal quality and behavior of the people with dementia. As it was challenging to get good signal quality while there was good connection with the skin during the focus groups, the participants questioned whether it would work in practice. *"If it is so difficult to put it on correctly, then I would have some reservations, especially for people with dementia in the final phase"* (former caregiver, male, age 65). This may be of concern especially for people with dementia who are agitated. Family caregivers said that agitated people and those who do not want anything on their head, might pull the sensors off.

Usefulness

There were many comments questioning the usefulness of the device, in particular from persons who know about existing measures of communication, observation, and care and felt these sufficed. Based on the field notes, this may be partly related to difficulty imagining situations where communication or the observation of consciousness could be challenging. *"When someone is in pain. You can see it"* (former caregiver, female, age 59). When discussing the use of BIS monitoring to help titrate medication for palliative sedation, some participants expected healthcare professionals to be capable of doing that without the help of a monitoring device. One former family caregiver (male, age 78) even said that overmedication would be preferred to restless situations around the end of life. A current family caregiver (female, age 71) suggested that BIS monitoring would also not be necessary for people who would want to end their life before reaching the state of no longer being fully conscious.

The device would also not be useful if there is no need for extra information. For example, the device was not considered necessary if the person with dementia is in natural sleep and not experiencing any specific symptom that required attention and care. *"I think, like the person before me just said, that using it would only be a good idea for people who are very restless during the night."* (person with dementia, male, age 92). Some family caregivers did not want to know about the level of awareness in certain situations, for instance at the end of life.

Suggestions

The participants made several suggestions on the use or further development of the device (Table 4). Participants suggested making the data more accessible for remote monitoring and later viewing. The sensors could be made more user-friendly, for example wireless, and be attached more securely to the head. Interestingly, there seemed to be discrepancies on how long BIS monitoring should be used in people with dementia, ranging from a maximum of 30 minutes to around-the-clock monitoring.

TABLE 4 All suggestions on the use or possible future application and development of Bispectural Index monitoring in palliative care for dementia

To improve user experience of the family and professional caregivers:
Device should be linked to an app for the caregivers
Record the signals to be read later, so that it is not necessary to watch the monitor all the time
To improve user experience of the person being monitored:
*Should not be measured for too long**
Make the device wireless
Use camouflaged sensors, so that the view of people wearing them is less disturbing
Incorporate a hairband or headband to better secure the sensors on the head
Explain the goal of the device to the person with dementia in case they can still understand
To ensure effectiveness:
*Monitoring should continue for 24 hours a day**
Interpretation of the signals should be personalized, because each brain is different
Monitor regularly to indicate the progression of dementia
Compare measurements in rest and agitation

* The suggestions in *italics* were made by people with dementia. The other suggestions were made by family caregivers. No suggestions were made by both groups.

Discussion

This study examined when and why BIS monitoring is acceptable or unacceptable in end-of-life care for people with dementia. As for when BIS monitoring was acceptable, only a few people with dementia were able to evaluate the acceptability of BIS monitoring in specific situations, and their attitudes were diverse. Family caregivers were positive about its application in

most situations discussed in the study, such as during palliative sedation and for pain monitoring. Its use was more controversial for them in non-medical situations, such as during natural sleep. Participants elaborated on different aspects of why they considered BIS monitoring (not) acceptable, including affective attitude, burden, ethicality, intervention coherence, opportunity costs, and perceived effectiveness, feasibility and usefulness. In general, BIS monitoring was not perceived as burdensome, and some participants saw its potential for monitoring symptoms, facilitating communication, facilitating acceptance, and helping with decision-making and improving care. However, its added value was not evident for some participants. Other participants also saw room for improvement in the user-friendliness of the device.

Although family caregivers and some people with dementia saw the potential of implementing BIS monitoring in a number of situations, only some of these situations would actually be realistic given current BIS technology. Based on the design of the BIS monitor and the literature, it is currently possible to apply BIS in palliative care to help titrate medication during palliative sedation [37, 38], to monitor wakefulness during recovery in the hospital, to monitor natural sleep [39], and to indicate periods of alertness in the home or nursing home setting. There might be potential for using BIS monitoring in the detection of acute pain [40], to indicate emotional responsiveness during interaction [41], and to identify the start of the dying phase. Currently, it is beyond the functionality of BIS monitors to indicate the contents of consciousness, the progression of dementia, the deterioration of physical condition, and decision-making capacity.

Even though some of the participants' expectations may not be satisfied by the current possibilities of the BIS monitor, they may be indicative of other underlying needs that should be met. Family caregivers indicated the need for more information about the experience of their relative with dementia and support in decision-making. People with dementia expressed the need to be informed of the progression of their dementia. Measures need to be taken to address these needs, with or without the technology. For example, clinicians can ask whether there is a wish to periodically communicate the results of clinical observations on the stage of the disease to people with dementia and

family caregivers. They can also provide information on what this stage would mean to the people with dementia and give advice to family caregivers on communicating with the person. If preferred, simple neurological tests could also be offered.

The results of this study demonstrate diverse opinions of people with dementia and family caregivers on BIS monitoring, and they shed light on issues to consider in the further development and implementation of monitoring technologies in end-of-life care for dementia, including BIS, if its effectiveness is demonstrated in the future. Stakeholders should be well-informed, and care must be taken that the technology does not replace human care. It is important to explain its use to people with dementia and family, and clarify misunderstandings before the implementation in order to minimize anxiety and manage expectations. Moreover, our participants with dementia expressed mixed attitudes towards the acceptability of BIS monitoring. This is in line with recent reviews reporting that people with dementia or mild cognitive impairment saw the benefits of monitoring technologies, but had reservations about acceptability [42, 43]. Healthcare professionals should therefore only implement such technologies after obtaining consent, or pay close attention to any signs of resistance during its application. Participants of our study also expressed ethical concerns that technologies should not substitute humans in medical decision-making, which coincides with a conclusion in a recent review [44]. Therefore, we should exercise caution regarding using input from the device to make important decisions, and healthcare institutions should ensure the quality of care provided by human professionals and avoid using the device as a substitute to compensate for substandard care.

This study has implications for the refinement of TFA framework when applied in studies on monitoring technology in dementia care, especially if the technology being researched requires minimal input from the person being monitored, as was the case for BIS monitors. The component constructs self-efficacy and opportunity costs may not be applicable, and the explanations of the constructs should be formulated not only from the perspective of the person receiving the intervention, but also the family and healthcare professionals as crucial stakeholders in dementia care [45]. For example, the construct "burden"

was described in TFA as "the perceived amount of effort that is required to participate in the intervention" [25]. It could be modified into "the perceived amount of effort that is required for the person receiving the intervention, family caregivers, and healthcare professionals". Moreover, concepts that are closely related to acceptability, such as feasibility and usefulness were frequently mentioned by our participants and could be added to the framework.

Future research is needed to further investigate the use of BIS monitoring in end-of-life care. Since effectiveness and purposefulness are essential when applying technology in palliative care [44], future studies should evaluate the usefulness of BIS monitoring in situations deemed potentially acceptable by people with dementia and family caregivers in this study. Other crucial stakeholders, namely healthcare providers, should be involved. The device can also be improved to increase user-friendliness for a population outside the operation room and will need to be validated in people with dementia. Interestingly, the possible application of BIS monitoring to ensure unconsciousness in assisted dying [46] was not mentioned by our participants. This is worth future investigation because assisted dying is an important topic for end-of-life care in the Dutch context [47], and the number of people with dementia receiving assisted dying has been increasing in recent years [48]. Moreover, feasibility and efficacy studies in palliative care for people with dementia should be conducted, for example a pilot study among nursing home residents with advanced dementia [41]. Concurrent and retrospective acceptability should be assessed if BIS is implemented after further development.

This research has several strengths and weaknesses. The involvement of people with dementia provided us with valuable information on their experience with the device, which is sometimes different from the perspectives of family caregivers. People with dementia are underrepresented in research [49], while their voices are crucial in research aiming to improve their future care. The inclusion of both current and former family caregivers also contributed to the richness of the data. The sample included elements of cultural diversity. More than 23% of the participants with dementia were born in another country, which was more than in the general population [50]. At least one of the 12

family caregivers had a parent with a migration background, based on the information they gave about the person with dementia they cared for. A limitation was the use of abstract questions about imagined scenarios. We have simplified the questions and adjusted the procedure to make it less cognitively challenging for people with dementia. Previous research demonstrated the possibility of involving people with dementia in qualitative studies [51], and we found that this is facilitated by limiting abstract questions and focusing on direct experience of real situations. However, some participants still did not fully understand the questions and the technology. Moreover, the group setting may have potentially led to social desirability bias. We recognize that the acceptability expressed by the participant may not be the same as their actual decision to use the technology when introduced by a healthcare professional [27]. Therefore, caution is needed when interpreting the results. Despite the limitations, this study was the first to illustrate the attitudes of people with dementia and family caregivers regarding a technology that monitors the level of consciousness of people with dementia in palliative care.

Conclusion

In conclusion, opinions on the acceptability of BIS monitoring differed among people with dementia. Family caregivers considered BIS acceptable in medical situations in palliative care for people with dementia, such as palliative sedation and pain detection. Reasons as to why BIS monitoring was deemed acceptable included its potential to improve care and that it was not perceived as burdensome. Skepticism was expressed concerning its added value compared to existing measures of symptom monitoring and the risk of replacing human care with the technology. Future research should validate and examine the acceptability of BIS monitoring in practice. If it is implemented in dementia care in the future, professionals should make sure that the stakeholders are well-informed and that the tool is only used as a supplement to human care.

Declarations

Author contributions

Xu Jingyuan (Conceptualization; Methodology; Investigation; Formal analysis; Data curation; Writing – Original draft preparation; Project administration);

Hanneke J.A. Smaling (Conceptualization; Methodology; Investigation; Writing – Review & Editing; Supervision; Project administration); Albert Dahan (Resources; Writing – Review & Editing); Justin Chan (Methodology; Resources; Writing – Review & Editing); Jenny T van der Steen (Conceptualization; Methodology; Investigation; Writing – Review & Editing; Supervision; Funding acquisition)

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Conflict of interest
Jenny T. van der Steen is an Editorial Board Member of this journal but was not involved in the peer-review process of this article nor did she have access to any information regarding its peer-review. All other authors have no conflict of interest to report.

Data availability statement
The data supporting the findings of this study are not publicly available due to privacy and ethical restrictions.

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General discussion

Main research findings

The studies in this dissertation investigated acceptability of interventions that may increase the sense of control when applied in dementia care. The following research questions were addressed: 1) Are advance care planning (ACP), the use of monitoring technology, and euthanasia acceptable in end-of-life care for people with dementia? 2) Are there cross-cultural differences in acceptability of these interventions?

Chapter 2 describes the design of the CONT-END study, which investigated the acceptability of these interventions among people with dementia, family caregivers, and physicians in 6 countries. It also reports on the development of animation vignettes to explain ACP, monitoring technology, and euthanasia to participants of the CONT-END study. **Chapter 3** found that ACP for people with dementia was highly acceptable for physicians in the first two countries where we completed the data collection: the Netherlands and USA. Participants from both countries shared similar ethical considerations regarding ACP for people with dementia, which included respecting the autonomy of the person with dementia, rationality as basis of decisions and subsequent actions, and minimizing burden and suffering. Tension existed among these ethical principles, especially between autonomy and rationality. While prioritizing autonomy means strictly following previous decisions made by the person with dementia, prioritizing rationality indicates providing room for decision making based on the current situation, which can deviate from decisions made during ACP. We can conclude that ACP is acceptable in dementia care, at least according to physicians. There were little cross-cultural differences in the acceptability of ACP among two western, high-income countries.

The use of technology and euthanasia is more controversial. Differences in the acceptability of euthanasia were observed among countries and individuals. **Chapter 4** illustrates that euthanasia for people with dementia was acceptable for nearly half of the participating physicians in the Netherlands, Switzerland, Germany, US, Japan, and Israel. The acceptability was higher in the Netherlands compared to the other countries. Being religious, training in palliative care, and the coping styles planning, religious coping, and using

emotional social support were associated with lower acceptability. **Chapter 5** presents a scoping review which identified a wide range of noninvasive monitoring technologies to detect discomfort that may occur at the end of life. Most technologies were designed to monitor sleep, level of consciousness, risk of pressure ulcers, urinary incontinence, agitation, or pain. Potential application of these technologies in end-of-life care, however, was under-researched. No studies on clinimetrics, feasibility, and acceptability of the technologies were reported in this setting except for Bispectral Index monitoring (BIS). In a case study, this technology to measure the level of consciousness was perceived as helpful and acceptable during palliative sedation. Driven by further enquiry of the acceptability of BIS in end-of-life care for dementia, **Chapter 6** demonstrated diverse opinions among people with dementia and family caregivers in the Netherlands. For people with dementia, there were different opinions regarding acceptability, although the participants did not experience the sensors of BIS as bothersome. For most family caregivers, BIS was evaluated as acceptable for medical situations such as palliative sedation and pain assessment. Considerations underlying the acceptability related to perceived effectiveness, ethicality, and usefulness of the device. More research is needed to investigate whether there are cross-cultural differences in the acceptability of technology.

Theoretical considerations

Control in end-of-life care for people with dementia

All of the interventions investigated in this dissertation may influence the sense of control for people with dementia (Chapter 2). Control at the end of life can consist of making preparations for death, influencing the time and place of dying, and managing distressing symptoms (1). Although control is an important element in good end-of-life care in the western world (2), retaining total control is not possible or desirable for many people with dementia, through interventions both ahead of time and at the end of life. According to a recent review, people with dementia live for a median of 4.8 years after diagnosis (IQR 4.0-6.0; 66 studies) (3). Only less than a third of people with dementia reach the advanced stage of dementia (4). For people who do, the disease can take an average of 5.3 years from mild to the advanced

stage. (Q-statistic 0.39-0.42; 2 studies) (5). In earlier stages of dementia, attempts to increase control around the end of life may take the form of euthanasia, especially in countries where it is legal. However, since euthanasia for people with dementia is not considered acceptable by all physicians that participated in our study regardless of its legal status (Chapter 4), euthanasia may not be an option for many who wish to control their end of life in this manner. Control in earlier stages of dementia can also be exerted by making arrangements for future treatments and care through ACP. However, total control of future medical treatments is not desirable either. This is reflected in the acceptability of relevant interventions investigated in this dissertation. According to the Dutch and American physicians from our study, flexibility for in-the-moment decisions is required to weigh in the patient's best interest (Chapter 3). They argued that not all situations can be discussed in detail during ACP, and the situations and best medical decisions can change. At the end of life, control by the person with dementia may be enhanced by giving them a voice to communicate discomfort through monitoring technologies. Such technologies are still being developed (Chapter 5) (6), and people with dementia have demonstrated mixed attitudes towards BIS (Chapter 6) (7).

Previous research suggests that we still know little about attitudes towards control in people with dementia (8). The need for control may differ per person. Some people with dementia would prefer to focus on the current situation instead of the future, where the physical and mental level of functioning is difficult to know or imagine (9). Some people with dementia make adaptations to the new challenges in their lives, as a way to cope with the disease (10). Some researchers even argue that quality of life for people with dementia is defined by how well they cope and adapt to the situation (11). Only a small group of people with mild dementia from a British study expressed a wish to take control by making plans for the future (12). Thus, stakeholders in dementia care need to recognize that control may not be the most important issue. Interventions that aim to maximize control of the person with dementia, such as ACP focused on making concrete treatment orders, can be offered as an option but if the person with dementia does not want to participate, other intervention or support need to be provided. For the group for whom control is of critical importance, the limitations of retaining control at the end of life

may need to be addressed, such as explaining limitations of advance euthanasia directives.

Identity

Besides the possibility and desirability of control, the changing identity in dementia poses additional challenges in the exertion of control on a future end of life (13). Main components of identity, which is what makes any person to be themselves, includes personality traits (14), morality (13), and memory (15). As dementia progresses, the personality often changes towards more neuroticism, less extraversion, and less conscientiousness (16). Moral capacities can be damaged due to the dementia, leading to family members perceiving a change in the person with dementia (13). People with dementia in later stages may no longer be able maintain a continuous sense of identity based on past experiences and life story (17).

I support the opinion that instead of one single identity, people have "successive selves" which continuously change (18). It is questionable how legitimate it is to exercise absolute control over a future self, when this future self may in many ways be a different person. However, people typically cling to an illusion that their identity is continuous and consistent, and it is difficult to reconcile with changes in identity when planning for the future (19). It may be a role of ACP and public education to challenge the assumption of a continuous, consistent identity and facilitate the acceptance of change. For example, during ACP, some people with dementia may express a wish to end their life in certain future situations, like many Dutch participant with dementia of the CONT-END study. The healthcare professional engaged in the ACP can start a discussion on how the person with dementia sees themself in the future, and explain that many professionals observe an adaptation and change in attitudes of people with dementia as the disease progresses (Chapter 3). If the person with dementia expresses a fear for losing the self, it may be beneficial to explain that the experiential self remains even in later stages of dementia, which means that the person still experiences the world through their senses moment by moment, although this self may not be continuous (19). If people with dementia are open to the idea of a changing self and changing interests,

they can be encouraged to consider the moral responsibility of making prudent decisions, respecting the rights and agency of future selves (20).

Good death

One important aim of retaining control around the end of life and to provide interventions that are acceptable for the stakeholders is to ensure a good death (21). Essential elements of a good death in dementia include being pain-free, having comfort, peace and dignity, being surrounded by familiar things and people, person-centered communication, spirituality, having a completed life, and receiving only preferred interventions (22). These elements are similar to the definition of a good death in general (23). The interventions investigated in the CONT-END study mainly contribute to the first and last elements of a good death. However, the psychological and spiritual elements are also crucial components of a good death and should be addressed when there is a need (22, 24). This can be part of ACP, especially the approach of getting to know what is important for the person which we investigated in Chapter 3. However, this is not yet a wide-spread practice, as people with young-onset dementia made a suggestion in a recent study to include existential issues in ACP conversations (25). In Dutch end-of-life care, although spiritual caregivers are often involved, psychological and social services were used less frequently (26). In dementia care, psychologists are usually an integral part of the multidisciplinary team and often functions as the practitioner in charge together with a physician. I suggest that psychological care to be better integrated in the end-of-life care of other illnesses too. In the future, I believe, there is also a potential for technologies to assist caregivers in many routine tasks, such as monitoring the patient and helping with activities of daily living. Caregivers can thus use more of their time in providing human contact and attending to psychological and spiritual needs of the patient and family. The current generation of older people in Western countries may still feel uncomfortable for technology to assist with their activities of daily living, but the acceptance is higher in younger generations, suggesting a potential change in the future (27).

Methodological considerations

The strengths of the studies included in this dissertation were the involvement of a variety of perspectives on the controversial topics of end-of-life care for people with dementia. We not only involved voices from different countries, but also the different stakeholders including physicians, family caregivers, and most importantly, people with dementia.

Involvement of people with dementia in research

Patient and public involvement (PPI) in research is crucial because we ultimately want to provide care that address the needs of the most important stakeholders (28). In the CONT-END and BIS studies, the most important stakeholders are people with dementia. We strived to give voice to people with dementia by including them as participants, both in the actual study (Chapter 6) and during pilot testing (Chapter 2).

We faced many challenges recruiting people with dementia. Aside from the Covid-19 pandemic, a major obstacle we encountered was the well-meant protection from professional caregivers and also from family. Many perceived the topic as confronting and burdensome for people with dementia and protected them by not informing the people with dementia of this research. In some countries, like Israel, we were informed by our collaborator that people with dementia are generally protected from the news of their diagnosis, which make them ineligible to partake in the CONT-END study. Based on my experience while conducting the study, the concern of the protecting caregivers is not totally grounded. Although some potential participants refused to take part because they did not want to talk about the end of life or did not have room in their life for research, many agreed to participate when they were contacted directly by the researchers. Some interviews were indeed emotional for the participants, but they expressed that it was not more stressful than their current life with dementia. Many conveyed that they were very glad to be able to contribute in research on a subject that is of crucial importance for them. A number of participants also expressed gratitude for being able to talk about end-of-life topics freely and being listened to with full attention.

Another major obstacle was the timing of approaching people with dementia in research that require a substantial level of cognitive capacity. From our experience, the window is variable and can be small between receiving a dementia diagnosis to losing the capacity to contemplate on and articulate complicated issues such as ACP and euthanasia. In some countries, dementia is typically diagnosed late, which exacerbated the problem (29). Even when it is diagnosed timely, the current clinical criteria for the diagnosis of dementia require a considerable loss of cognitive capacity, which may already make it challenging to participate in an interview study (30). The turmoil of practical and emotional adjustments in the period directly after the diagnosis was also the reason for some people with dementia and family caregivers not to participate in our studies.

From our experience with tackling these challenges, I recommend better integrating research into dementia care. For example, memory clinics can register the willingness to be approached for research when a person gets a diagnosis. Informing people with dementia of potential research can be integrated into the tasks of professional caregivers, accompanied by sufficient training. Previous research suggested that training related to the research limited gate-keeping (31). Of course, the freedom to deny participation should be guaranteed. For research in late stage dementia, professional caregivers can also assist researchers to acquire consent of participation in advance (31).

Due to the difficulty in timing of involving people with dementia in research that require reasoning and elaboration of thoughts of people with dementia, I recommend that such research can include people with mild cognitive impairment (MCI) as well. A recent study showed that more than 90% of people with MCI ultimately progress to dementia (32). People with MCI are also experiencing cognitive decline and have thoughts about a possible future with dementia. The involvement of this group opens up the window of participation, although researchers should be aware that the experience and opinions of these participants may change as the disease progresses.

I also recommend more involvement of people with dementia in the whole research process. The role of the public and patients in research can range from listener, co-thinker, advisor, partner, to decision-maker (33). They

can be involved in one or more research stages (33). In our studies, people with dementia were mainly involved as listener and co-thinker during the execution phase of the research (28). We could have involved them more intensively throughout the research cycle as co-researchers instead of only participants. A review has demonstrated that this is feasible, for example by involving people with dementia in a lay advisory group or using interviews or focus groups to formulate a research agenda, co-create an intervention, or interpret qualitative data (34). However, the type of grant supporting the CONT-END study limited our options in involving people with dementia as co-researchers. I suggest funding bodies provide more room for public and patient involvement in all kinds of grants they provide. Researchers can also facilitate the involvement of people with dementia by building a trusting relationship, co-creating a clearly defined role, ensuring adequate resources, employing a flexible research design, valuing the lived experience of people with dementia, providing support if needed, and reflecting on their involvement (35). I hope that with these measures, more people with cognitive decline will get a chance to contribute to research and have their voice heard.

Mixed methods studies

The CONT-END study used a mixed methods methodology, combining interview with questionnaires, and closed questions with open-ended questions (Chapter 2). The quantitative data enabled us to compare the acceptability of the interventions across countries and groups of participants, as well as to explore factors that are related to the acceptability. The qualitative data helped us gain a deeper understanding of the reasons and situations where the participants considered a certain intervention (not) acceptable. Employing the mixed methods methodology in the CONT-END study provided us the possibility to answer a range of research questions that are not possible be answered by a qualitative or quantitative study alone (36).

However, I noticed that the mixed methods design posed limitations on the quality and efficiency of this particular study. We chose to formulate interview questions openly, so that instead of being restricted by specific situations described in the questions, participants could come up with important situations themselves of when the intervention was (not) acceptable.

However, in order to conduct quantitative comparisons in the CONT-END study, the questions need to be well-defined and the interpretations should be limited. Acceptability can be highly dependent on the specific situation, for example the stage of dementia, decisional capacity, and concomitant diseases (37). After the initial interviews, we realized that the participants interpreted the questions very differently and this made it challenging to interpret the quantitative results. We partially addressed it by specifying some concepts in the questions and adding them to a comprehensive guide for interviewers. Interviewers were instructed to redirect participants if they noticed that the participants had a different interpretation of the questions. However, this was not systematically checked for each participant, and some ambiguity remained in the interview questions. Thus, accurate interpretation of the quantitative results remains challenging.

We also met challenges of feasibility with the original concurrent design, collecting both qualitative and quantitative data from a single assessment. The power analysis based on the quantitative analysis resulted in 900 participants. This number is larger than what a qualitative study would require to reach data saturation. Although we decided to stop asking follow-up questions after reaching data saturation in each country and group, the interviews and subsequent data analysis were still time-consuming and had little added value. The study team then decided to provide a questionnaire-only version for physicians, so that they could view the video's and answer the questions on their own. This increased the efficiency of the study, limited the participant burden, and facilitated participation of busy physicians.

Upon reflection, I think that the CONT-END study could have benefited from a sequential design, so that the advantage of both approaches could be maximized, and the time could be spent efficiently. If I were to conduct the study again, I would have started with qualitative in-depth interviews with a small sample from each country to identify important reasons for and situations where the interventions were considered (not) acceptable. A questionnaire with more specific questions would be devised based on these situations, and distributed to a larger group of physicians and family caregivers.

This could have contributed to a more efficient use of the project time and better interpretable results from the quantitative data.

Positionality

The PhD trajectory has been a journey of continuous exploration and reflection on my positionality. I grew up in China and studied psychology in Hong Kong and Leiden. The education I received was largely based on (post-)positivism. There was a strong emphasis on gaining knowledge about an objective reality through quantitative methods, avoiding or reducing biases as much as possible during the investigation. While I recognize its value in natural sciences, I did not feel comfortable applying it to the subject that I'm interested in, which is the individual experience of human beings. Beyond the formal education, growing up in China also exposed me to idealistic views of the world from Buddhism. Although I do not adhere to any religious tradition, I felt affinity with the idea that each individual's subjective world is largely based on their unique perception and interpretation of their experiences.

I got into contact with constructionism through a sociology course during my Bachelor training, and later, in a course on qualitative research in the early phase of my PhD trajectory. I agreed with the epistemological assumption that knowledge in social sciences is created through human interactions (38). In the years afterwards, I experienced many internal conflicts reflecting on the research methods that I have used during my research, which were not all based on constructionism. I gradually realized that a key struggle was finding an ontological position between relativism and realism. My current reflection on this issue is that relativism and realism is not dichotomous, but a continuum. Objects of investigation vary in the extent they are affected by context and humans. The laws of physics, like gravity, are realities independent of the observer and human activity, although when the context drastically changes on a quantum scale, another set of laws will apply. Social phenomena are more dependent on human activities. Concepts of happiness, love, and end of life can be highly dependent on the social and historical context, while constantly being shaped by how people interact with each other and talk about these topics. Individual opinions on a certain topic can evolve continuously in the small context created by the interaction with the researcher.

My position in the CONT-END study is around the middle of the relativism-realism continuum, leaning slightly towards the realism side. This is based on my observation and assumption that most participants in this study seem to have a pre-existing general attitude towards topics like planning for future care, technology, and euthanasia. Although I recognize that their opinions can be more concretely formed during the participation in the study, influenced by how the interventions are portrait in the animation vignettes, how the interviewers ask the questions and how they respond to the answers. I also noticed that people who had more prior exposure to these interventions, especially experienced physicians, had stronger pre-existing views. A few other participants, however, developed new insights and modified or clarified their original view as they elaborated their opinions and gave deeper thoughts on these topics during the interviews. I recognize that we, investigators, play a role in the data that we get, but the opinions of the participants at the time of the study are also realities that are largely knowable and expressed.

The PhD journey has also helped me clarify my thoughts on agency. I interpret agency as the freedom to make choices and to act. It has been one of my core values, formed from frustrations and powerlessness growing up in an authoritarian environment. I have now gradually realized an accepted the limitations to it. I believe that our agency and number of available choices are limited by our cognitive and physical capacities, our societal context, and choices made by our previous selves.

I reflected on my own opinions on ACP, technology, and euthanasia throughout the study and observed them develop as I encountered the participants and literature. My view on ACP evolved from embracing it in all forms to seeing it as a way to communicate current values and needs. I began to adhere more value to the well-being of a later self. In a care context where there is enough attention to the needs of a person, and where maximum life extension is not the default, I even think that ACP may not always be necessary. My opinions towards technology changed from indifferent and slightly negative to more permissive, especially after finding monitoring systems in the review that do not require any contact with the person. I also changed my views on euthanasia from being totally supportive, from a respect to autonomy,

to more conservative, after hearing about the emotional burden it can have on physicians. During interviews, I tried to bracket my own views and react with a similar openness and curiosity towards all answers, although I noticed myself asking more questions when the opinion of the participant did not corresponded with mine. To facilitate reflexivity of the whole research team, I also set up a questionnaire for all investigators involved to reflect on their own opinions on the investigated topics and included such reflections in the training of all interviewers. Our opinions played a larger role in the presentation of the results and the recommendations that we give in the articles, for example the emphasis on leaving room for future decision making in Chapter 3.

Being a young, female researcher employed by a Dutch university with a Chinese appearance, I might have been seen as an outsider by most participants and it prompted them to explain their care system and cultural context in more details to me. I myself take an eclectic stance towards the cultures that I have lived in or am exposed to. Without feeling particular affiliations with any one of them. I observe and interact largely as an outsider. At the same time, being able to speak Dutch and English fluently, looking East-Asian in Japan, and being involved in the subject of dementia may have let participants to see me partly as an insider, enough to share their genuine view on the topics. Having lived long enough in both Asia and West-Europe, I also gained cultural experience that helped me understand participants' narratives as an insider. Many students and research assistants were also involved in this study, acting as insiders in interviews and during interpretation of data. This combination of insiders and outsiders allowed the study to enjoy the benefits of both.

Implications and recommendations

The results of this dissertation demonstrated that interventions that may increase the sense of control are controversial in the context of end-of-life care for people with dementia (Chapters 4 and 6). Even the highly acceptable intervention ACP entails complex ethical considerations with conflicting principles (Chapter 3). Therefore, interventions should be tailored for individual situations and preferences. Considerations and controversies surrounding the interventions and end-of-life care for people with dementia

can be made explicit for stakeholders to make more informed choices. Measures can be taken to support all stakeholders in the process of implementing the interventions when they are considered acceptable.

Implications for policy

I recommend policy to improve public awareness of end-of-life situations and choices in dementia. This is particularly relevant because ACP is recommended to start informally among the person with dementia and family (25). So quality information needs to be easily available before a healthcare professional gets involved in the discussion. In addition to making use of existing resources that encourage the discussion and documentation of treatment options and values (39-41), different views on identity can be presented to the public to stimulate reflection and formulation of their own thoughts. Campaigns can promote a realistic image of life in nursing homes, the end of life and the recognition that the needs of the person with dementia can change as the disease progresses. I believe that this may help people develop more realistic expectations, for example about moving to a nursing home or future euthanasia, and allow more flexibility when they or their family need to consider and document wishes for future care with dementia. This in turn will contribute to more suitable care at the end of life for people with dementia, and reduce ethical dilemmas of healthcare professionals and family.

I also recommend policy-makers to encourage the involvement of people with dementia in the development of technologies for end-of-life care. Our review found a large number of technologies that can potentially monitor distressing symptoms, but very limited research and application of monitoring technology in end-of-life care for dementia (Chapter 5). Our focus study on BIS monitoring demonstrated that some people with dementia and family were open to the use of technology in some, but not all situations at the end of life (Chapter 6). There is potential to better support care for people with dementia at the end of life with technology and suitable technologies need to be identified and further developed together with the stakeholders to best address their needs.

Furthermore, regulation should protect people who have lost capacity from interventions that they may not want to receive, including care technologies. In the Netherlands, this is regulated with the law Care and Coercion (in Dutch: Zorg en Dwang), which advises against interventions if there is no consent or if the person with dementia shows signs of resistance, and requires regular evaluation to find alternatives or reduce the involuntary care. However, practical challenges in the implementation are reported, and the rights of people who are not resisting against involuntary care may still be under-protected (42). Other countries that are designing or modifying similar laws can make use of the experiences in the Netherlands.

Implications for practice

To facilitate practitioners to deal with ethical challenges inherent in caring for people with dementia at the end of life, I recommend that they hold regular intervision sessions to discuss their doubts, reflect on their own value systems, and support each other. This can be done in a comprehensive moral case deliberation in groups with 8-12 participants (43), or in quick simple steps on a small scale (44).

I also recommend more involvement of psychologists and spiritual carers in end-of-life care. In my opinion, the fear of death and fear of discomfort can play an important role in the choices people make for their (future) care including end-of-life care (45). These fears should not be discarded as psychological disfunction and used as reasons to disqualify someone from making their own decision. Rather, as the existential psychotherapists stated, these fears can be opportunities to stare at our existence straight in the eyes and open possibilities of living a richer and more fulfilling life (46). I argue, as a psychologist myself, that my colleagues and spiritual carers can play a more important role in end-of-life care whenever possible, to prepare people by exploring their attitudes towards life and death, before they discuss and document their wishes regarding medical care with medical professionals. In my opinion, psychological intervention to facilitate acceptance and adjustment should be available and recommended when the fear for future deterioration is expressed as the main reason for an euthanasia request or an advance euthanasia directive.

Implications for education

Educational programs can prepare healthcare professionals for their future career by increasing their awareness and reflections on the complexities in end-of-life care for dementia. They can be introduced to the conflicting ethical principles, and the possible integration of more technologies in dementia care. Future healthcare professionals should be encouraged to reflect on their own values, theirs view on identity, good death, and technology in order to make conscious choices and state their personal preferences and limitations to their future clients.

Future research

The findings presented in this dissertation point to many directions for future research. For example, acceptability of interventions affecting the end of life for people with dementia should be examined among the stakeholders in middle- and low-income countries, and different cultural groups within one country. Studies can also be conducted to further develop and implement monitoring technologies to detect distressing symptoms at the end of life. My personal interest lies in exploring interventions that address the need of control, identity, and facilitate acceptance of death and decline in people with cognitive impairment. I'm interested in whether this acceptance would affect their choices for the end of life, and attitudes towards interventions investigated in this dissertation.

Recent reviews reported that psychological interventions (such as problem-focused and meaning-focused therapies) may have a positive effect on the acceptance of the disease, depression, and quality of life in people with cognitive impairment (47, 48). However, research on this topic is limited and the quality of many of the studies was low (47, 48). I suggest co-creating an intervention together with people with cognitive decline, case managers, and psychologists working with this population, aiming at reducing fear for future decline and enhancing the acceptance of uncertainties. The intervention can then be implemented in a randomized controlled trial. People with subjective cognitive decline and mild cognitive impairment can be recruited through patient organizations, memory clinics that receive consultations regarding cognitive decline, general practitioners, nurses, and other professional

caregivers who work with community-dwelling people with dementia. People who experience stress and fear for future decline can self-identify or be referred to this intervention by healthcare professionals. Depending on the country, psychologists, social workers, and case managers can be trained to provide the intervention, because they are trained to provide psychosocial interventions and usually work in an interdisciplinary team together with the medical care professionals who would perform the referral. The attitude towards future changes and decline, current quality of life, and goals of care can be measured as outcome. The intervention can start in one region in one country, for example the Netherlands. If successful, it can be expanded to other regions or combined with psychosocial interventions designed for family caregivers such as acceptance and commitment therapy (49). It may also be interesting to investigate whether such an intervention would be applicable to other cultures and countries.

Epilogue

Last year, I talked with the lovely East-Asian lady again about her wishes for the future "Now that I'm above 80, I accept death and do not mind talking about it at all," she said lightheartedly, "I think it helps my family if they know what I want". In the presence of her children, we went over her wishes and several common treatment options at the end of life. Her decisions were documented. It was challenging, however, to explain to her that we would not follow her wish to feed her a bunch of sleeping pills to end her life once she is too ill to take care of herself. She was not totally satisfied, but accepted our promise that we would do our best to ensure comfort and quality of life.

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8

Summary

Introduction (Chapter 1)

This dissertation examined the acceptability of interventions that may increase control at the end of life of people with dementia. Dementia progressively affects cognition, decision-making, communication and physical functioning. These changes make it difficult for people with dementia to retain control at the end of life by expressing preferences, making decisions, or communicating discomfort and distressing symptoms. However, maximum control at the end of life may not be universally desirable. Some people prefer to remain closely involved in decisions about their care, while others prefer to delegate decisions to family members or professionals. Cultural, religious, legal and historical contexts may also shape how much control is considered appropriate, and who is expected to exercise it. In order to provide person-centered care to people with dementia and to shape education and policies regarding interventions that influence control, it is important to investigate people's attitudes towards such interventions.

Several interventions may increase control at the end of life for people with dementia, including advance care planning (ACP), the use of technology to monitor distressing symptoms at the end of life, and euthanasia. Advance care planning entails communication about future care and treatment preferences, as well as values and goals of the person with dementia. ACP may help people with dementia express their wishes while they are still able to do so, thus exercising control over their care in the future. This dissertation investigated two ACP approaches, one focusing on concrete treatment orders (order-setting), and the other focusing on values and global care goals (goal-eliciting). Monitoring technology designed to monitor discomfort or distressing symptoms at the end of life may help people with dementia retain control over their well-being, and for family and physicians to monitor the symptoms when the person with dementia can no longer communicate it themselves. Euthanasia, where it is legally possible, may offer control over the timing and circumstances of death. It remains controversial in dementia care because the disease affects decision-making capacity and communication.

The aim of the dissertation was to provide insight into the acceptability of these interventions in end-of-life dementia care. Two research questions

guided the work: whether ACP, monitoring technology and euthanasia are acceptable in end-of-life care for people with dementia, and whether there are cross-cultural differences in their acceptability.

Chapter 2

Chapter 2 describes the protocol and pilot-testing of the CONT-END program, a cross-cultural mixed-methods vignette study on the interventions that may increase control at the end of life for people with dementia. The study was designed to assess the acceptability of the two ACP approaches, monitoring technology at the end of life and euthanasia. It included the perspectives of people with dementia, family caregivers and physicians in six countries: the Netherlands, Japan, Israel, the United States, Germany and Switzerland.

A central methodological feature of the CONT-END program was the use of short animated video vignettes. These vignettes explained the interventions in a standardized manner before participants were interviewed about acceptability. The study also collected information through questionnaire on demographic characteristics, life view, attitudes to dementia and dying, personality-related variables and professional background, depending on the participant group. A pilot testing was performed to check whether the vignettes and instruments were understandable, acceptable, feasible and not too burdensome. Based on participant feedback, the scripts were clarified, simplified and adjusted to be more neutral. The chapter therefore established the methodological foundation for the later empirical chapters.

Chapter 3

Chapter 3 reports the acceptability and ethical considerations on advance care planning for people living with dementia, from the perspectives of physicians in the United States and the Netherlands. The study included interviews with 50 Dutch physicians, 47 American physicians and three American nurse practitioners with medical responsibilities. Participants' views on two animation vignettes were included in this study: one about ACP focused on order-setting, such as resuscitation and hospital admission, and one about

ACP focused on getting to know the person and eliciting goals, such as maximizing comfort.

Both ACP approaches were regarded as acceptable by a large majority of participants in both countries. The analysis generated three ethical considerations that shaped physicians' views. The first was respecting the autonomy of the person with dementia. Physicians emphasized that, whenever possible, people with dementia should be heard and involved in decisions about their care, and that their preferences should remain central when families participate in ACP conversations. The second consideration was rationality as the basis for decisions and subsequent actions. Physicians did not view previously expressed wishes as the only relevant consideration; they also considered the clinical situation, feasibility, medical knowledge and the current best interests of the person with dementia. The third consideration was minimizing burden and suffering, both for the person with dementia and for those involved in care.

The chapter shows that ACP is ethically complex, even when it is generally acceptable. There is tension among the ethical considerations, especially between autonomy and rationality. Prioritizing autonomy may imply strict following of prior decisions, which may conflict with rationality based on current clinical judgment. This chapter therefore argues for an ACP approach centered on the values of the person with dementia, while allowing flexibility in future decision-making. Rather than treating ACP only as a way to secure goal-concordant care through fixed instructions, ACP should also support well-being, adjustment to dementia and communication among the person with dementia, family and professionals.

Chapter 4

Chapter 4 examines the acceptability of euthanasia for people with dementia from the perspective of clinicians in the six countries included in the CONT-END program. Differences in the acceptability between countries and associations between acceptability and personal characteristics were also investigated. Participants consisted of 202 physicians and three nurse specialists with similar medical responsibilities.

Across the six countries, 44% of the participants considered euthanasia acceptable for people with dementia, and 38% were willing to perform euthanasia upon request of a person with dementia. Acceptability was highest in the Netherlands, where 66% considered euthanasia acceptable. In the other countries, the proportion ranged from 23% to 44%. Dutch clinicians were also more often willing to perform euthanasia upon request of a person with dementia than clinicians in most other countries. We also found associations between acceptability and personal characteristics and coping styles. Planning as a coping style and religious coping were associated with lower acceptability of euthanasia. Willingness to perform euthanasia upon request of a person with dementia was associated with reporting no religion, no training in palliative care and less use of emotional social support as a coping style.

These findings show that opinions on euthanasia for people with dementia varied substantially between countries and individuals. Policy may need to consider the wishes and needs of clinicians both for and against this practice. Changes in the acceptability of euthanasia may be expected as palliative care becomes more widespread or when religiosity changes in a country. Research is needed to explore the mechanism of associations between coping strategies and acceptability of euthanasia.

Chapter 5

Chapter 5 presents a scoping review of non-invasive monitoring technologies that may identify discomfort and distressing symptoms in people with limited communication at the end of life. The review addressed the fact that people near the end of life may have difficulty expressing discomfort because of fatigue, sedation, delirium, cognitive impairment, loss of consciousness or communication problems. In current practice, recognition of discomfort often depends on observations by professional caregivers and family, but continuous observation is not always feasible.

The review comprised searches in nine databases and consultation of experts. Manuscripts were eligible when they described a non-invasive technology that measured discomfort, distressing symptoms or level of consciousness; could be administered continuously for at least four hours; and was potentially

applicable to bedridden people. Of 3,414 identified manuscripts, 229 met the eligibility criteria. The review identified a variety of technologies, including actigraphy, brain activity monitoring, electrocardiography, electrodermal activity monitoring, surface electromyography, incontinence sensors, multimodal systems and noncontact monitoring systems. The main indicators of discomfort measured by these technologies were sleep, level of consciousness, risk of pressure ulcers, urinary incontinence, agitation and pain.

The chapter concludes that many relevant technologies exist or are under development, but their application in end-of-life care remains under-researched. One study reported that brain activity monitors may be helpful and acceptable for monitoring level of consciousness during palliative sedation. For the other technologies, however, no manuscripts reported clinimetrics, feasibility or acceptability specifically in the end-of-life phase. It maps the field and identifies the need for future research to further develop monitoring technologies for end-of-life care, and to evaluate their usefulness, feasibility and acceptability in this context.

Chapter 6

Chapter 6 investigates the acceptability of Bispectral Index monitoring (BIS) in end-of-life care for dementia. BIS is a noninvasive bedside technology that uses brain activity to indicate level of consciousness. It is routinely used during surgery to monitor depth of anesthesia and may be relevant in palliative care, for example during palliative sedation or when consciousness and discomfort are difficult to assess. The study used focus groups and interviews with demonstrations of BIS monitoring and included 17 people with dementia and 24 family caregivers in the Netherlands.

The results show that people with dementia did not find the BIS sensors bothersome, but acceptability differed across participants and situations. Family caregivers generally considered BIS monitoring acceptable in medical situations, especially during palliative sedation and for pain assessment. Reasons for acceptability included the potential to improve care, support symptom monitoring, facilitate communication, assist decision-making and help family caregivers accept difficult situations.

At the same time, participants raised important concerns. Some questioned the added value of BIS compared with existing observation, communication and professional judgment. Others were concerned about feasibility, including signal quality and whether people with dementia would remove them if they are agitated or do not want sensors on their heads. The use of BIS was more controversial in non-medical situations, such as natural sleep. Participants also emphasized that the technology should not replace human care or human decision-making. The chapter concludes that BIS or similar technologies should only be implemented if they have sufficient added value, if people with dementia and family caregivers are well informed, and if the use of the technology remains supplementary to professional and family care. Future research should validate BIS monitoring in people with dementia and test its efficacy, feasibility and acceptability in the situations that participants considered most acceptable.

Discussion (Chapter 7)

Chapter 7 integrates and reflects on the findings, and discusses theoretical, methodological and practical implications. Returning to the topic of control, this chapter concludes that total control is indeed not possible or desirable for many people with dementia. ACP may increase control over future care, but physicians emphasized that future decisions require flexibility because circumstances and best interests may change. Monitoring technologies may support control by helping to detect discomfort when communication is limited, but the evidence base and acceptability remain incomplete. Euthanasia was not acceptable to many clinicians in the six-country study regardless of permissive legislation, leaving it inaccessible to many people with dementia as a means to exert control.

The discussion also addresses identity and the idea of a good death. Dementia can change memory, personality and moral capacities, which complicates the question of how far earlier wishes should travel in attempting to control future care. The dissertation suggests that ACP and education of the general public may help people reflect on possible changes in identity and accept uncertainty. A good death involves more elements than control, such

as being free from pain, comfort, dignity, familiar people and surroundings, person-centered communication, spirituality, a sense of completion and receiving preferred interventions. Although the interventions studied in this dissertation related to several of these elements, it is argued psychological and spiritual dimensions of a good death require attention in future research.

The methodological discussion highlights the importance and difficulty of including people with dementia in research on end-of-life care. The recruitment of people with dementia for studies in this dissertation was challenging. Professional and family caregivers sometimes acted as gatekeepers because they perceived the topic as too confronting or burdensome. The dissertation argues that this protection was not always supported by the actual experience of participants, many of whom valued the opportunity to contribute. Another challenge was timing: the period between diagnosis and loss of capacity to reflect on complex topics may be short or variable. The dissertation therefore recommends better integration of research into dementia care and more involvement of people with dementia throughout the research process.

For policy and practice, the dissertation recommends improving public awareness of end-of-life situations and choices in dementia, including realistic information about nursing home care, the changing needs of people with dementia and the limits of future control. It also recommends involving people with dementia in the development of technologies for end-of-life care and protecting people who have lost decision-making capacity from unwanted interventions, including non-preferred care technologies. For professionals, the dissertation recommends regular reflection on ethical dilemmas, for example through intervision or moral case deliberation, and greater involvement of psychologists and spiritual carers in end-of-life care to discuss fears and to facilitate living with uncertainties. For education, future healthcare professionals should be trained to reflect on conflicting ethical principles, their own values, identity, good death and the role of technology.

Conclusion

This dissertation shows that acceptability of interventions intended to increase control at the end of life for people with dementia varies. ACP was

generally acceptable to physicians yet ethically complex. Euthanasia was more controversial and acceptability varied substantially between physicians within and across countries. Monitoring technologies may support symptom recognition, but require further development, stronger evidence and careful implementation. End-of-life dementia care should therefore not aim to maximize control in a uniform way. Offering tailored control in an uncertain situation can be helpful, but foremost, we should strive to align care with the person's values, current needs, legal context and professional responsibilities.

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Nederlandse samenvatting

Introductie (Hoofdstuk 1)

Ín dit proefschrift onderzochten wij in hoeverre interventies die de controle aan het levenseinde van mensen met dementie zouden kunnen vergroten acceptabel zijn. Dementie tast geleidelijk het cognitief functioneren, vermogen om beslissingen te nemen, communicatie en fysieke mogelijkheden aan. Deze veranderingen maken het moeilijk voor mensen met dementie om aan het levenseinde controle te behouden door voorkeuren te uiten, beslissingen te nemen of ongemak en belastende symptomen te communiceren. Maximale controle aan het levenseinde is echter niet voor iedereen wenselijk. Sommige mensen willen nauw betrokken blijven bij beslissingen over hun zorg, terwijl anderen de voorkeur geven aan het delegeren van beslissingen aan familieleden of professionals. De culturele, religieuze, juridische of historische context kan eveneens invloed hebben op hoeveel controle passend wordt geacht en wie geacht wordt deze uit te oefenen. Om persoonsgerichte zorg te bieden aan mensen met dementie en om onderwijs en beleid vorm te geven rond interventies die controle beïnvloeden, is het belangrijk om attitudes ten aanzien van dergelijke interventies te onderzoeken.

Verschillende interventies kunnen de controle aan het levenseinde voor mensen met dementie vergroten, waaronder proactieve zorgplanning (ACP/PZP), het gebruik van technologie om onwelbevinden aan het levenseinde te monitoren, en euthanasie. Proactieve zorgplanning omvat communicatie over toekomstige zorg- en behandelvoorkeuren, evenals waarden en doelen van de persoon met dementie. ACP kan mensen met dementie helpen hun wensen te uiten zolang zij daartoe nog in staat zijn en zo controle uit te oefenen over hun toekomstige zorg. Dit proefschrift onderzocht twee ACP-benaderingen: één gericht op concrete behandelafspraken ("order-setting") en de ander gericht op waarden en belangrijke doelen ("goal-eliciting"). Monitoringtechnologie die is ontworpen om ongemak of belastende symptomen aan het levenseinde te detecteren, kan mensen met dementie helpen controle te behouden over hun welzijn. Deze technologie kan ook familie en artsen helpen symptomen te monitoren wanneer de persoon deze niet meer zelf kan communiceren. Euthanasie, waar wettelijk toegestaan, kan controle bieden over het tijdstip en de

omstandigheden van het overlijden. Het blijft controversieel in de dementiezorg omdat de ziekte wilsbekwaamheid en communicatievaardigheden beïnvloedt.

Het doel van het onderzoek in dit proefschrift was inzicht te bieden in hoe acceptabel deze interventies zijn in de zorg voor mensen met dementie rondom het levenseinde. Twee onderzoeksvragen stonden centraal: 1)of ACP, monitoringtechnologie en euthanasie acceptabel zijn in levenseindezorg voor mensen met dementie, en 2) of er culturele verschillen zijn in hoe acceptabel de interventies zijn.

Hoofdstuk 2

Hoofdstuk 2 beschrijft het protocol en de pilotstudie van het CONT-END-programma, een crossculturele mixed-methods vignettenstudie naar interventies die controle zouden kunnen vergroten bij het levenseinde van mensen met dementie. De studie beoordeelt hoe acceptabel de twee ACP-benaderingen, monitoringtechnologie aan het levenseinde en euthanasie worden gevonden. De studie omvatte de perspectieven van mensen met dementie, naasten en artsen uit zes landen: Nederland, Japan, Israël, de Verenigde Staten, Duitsland en Zwitserland.

Een belangrijke methode in het CONT-END-programma was het gebruik van korte animatievideo vignetten. Deze vignetten legden de interventies op gestandaardiseerde wijze uit voordat deelnemers werden geïnterviewd over hoe acceptabel zij de interventies vonden. In het onderzoek verzamelden wij daarnaast informatie via vragenlijsten over demografische kenmerken, levensbeschouwing, attitudes ten aanzien van dementie en de dood, copingstijlen en professionele achtergrond, afhankelijk van de deelnemersgroep. Een pilotstudie werd uitgevoerd om te beoordelen of de vignetten en instrumenten begrijpelijk, acceptabel, haalbaar en niet te belastend waren. Op basis van feedback van deelnemers werden de scripts verduidelijkt, vereenvoudigd en neutraler gemaakt. Het hoofdstuk vormt daarmee de methodologische basis voor de latere empirische hoofdstukken.

Hoofdstuk 3

Hoofdstuk 3 beschrijft hoe acceptabel men proactieve zorgplanning bij mensen met dementie vond vanuit het perspectief van artsen in de Verenigde Staten en Nederland, en welke ethische overwegingen een rol spelen. De studie omvatte interviews met 50 Nederlandse artsen, 47 Amerikaanse artsen en drie Amerikaanse verpleegkundig specialisten met medische verantwoordelijkheid. De deelnemers gaven hun mening over twee videovignetten. Één vignet gaat over ACP gericht op afspraken over behandelingen ("order-setting"), zoals wel of niet reanimeren en ziekenhuisopname. Het ander vignet gaat over ACP gericht op het leren kennen van de persoon en het achterhalen van doelen van zorg ("goal-eliciting"), zoals het maximaliseren van comfort.

Beide ACP-benaderingen werden door een grote meerderheid van de deelnemers in beide landen als acceptabel beschouwd. De analyse leverde drie ethische overwegingen op die de opvattingen van artsen dekten. De eerste was respect voor de autonomie van de persoon met dementie. De artsen benadrukten dat mensen met dementie, waar mogelijk, gehoord en betrokken moeten worden bij beslissingen over hun zorg.Hun voorkeuren moeten centraal blijven staan wanneer naasten deelnemen aan ACP-gesprekken. De tweede overweging was rationaliteit als basis voor beslissingen en daaropvolgende behandelingen. De artsen beschouwden eerder geuite wensen niet als de enige relevante factor; zij hielden ook rekening met de klinische situatie, haalbaarheid, medische kennis en het huidige belang van de persoon met dementie. De derde overweging was het minimaliseren van belasting en lijden, zowel voor de persoon met dementie als voor degenen die bij de zorg betrokken zijn.

Dit hoofdstuk laat zien dat ACP vanuit de ethiek bezien, complex is, zelfs wanneer het in het algemeen acceptabel wordt gevonden. Er bestaat spanning tussen de ethische overwegingen; vooral tussen autonomie en rationaliteit. Het prioriteren van autonomie kan betekenen dat eerdere beslissingen strikt moeten worden gevolgd, wat kan botsen met rationaliteit gebaseerd op actuele klinische beoordeling. Dit hoofdstuk pleit daarom voor een ACP-benadering die is gericht op de waarden van de persoon met dementie, terwijl flexibiliteit in toekomstige besluitvorming behouden blijft. In plaats van

ACP uitsluitend te zien als een middel om doelgerichte zorg te waarborgen via vaste instructies, zou ACP ook het welzijn, het aanpassen aan de dementie en de communicatie tussen de persoon met dementie, naasten en professionals moeten ondersteunen.

Hoofdstuk 4

In hoofdstuk 4 werd onderzocht hoe acceptabel euthanasie is voor mensen met dementie vanuit het perspectief van clinici in de zes landen die deelnamen aan het CONT-END-programma. Ook werden verschillen tussen landen onderzocht, en verbanden tussen de mate waarin euthanasie acceptabel werd gevonden enerzijds, en persoonlijke kenmerken anderzijds. De deelnemersgroep bestond uit 202 artsen en drie verpleegkundig specialisten met vergelijkbare medische verantwoordelijkheid.

In de zes landen vond 44% van de deelnemers euthanasie acceptabel voor mensen met dementie, en 38% was bereid euthanasie uit te voeren op verzoek van een persoon met dementie als het wettelijk toegestaan zou zijn. De mate waarin euthanasie acceptabel werd gevonden, was het hoogst in Nederland, met 66%. In de andere landen varieerde dit percentage tussen de 23% en 44%. Nederlandse clinici waren ook vaker bereid euthanasie uit te voeren op verzoek van een persoon met dementie dan clinici in de meeste andere landen. We vonden ook verbanden tussen hoe acceptabel men het vond met persoonlijke kenmerken en met copingsstijlen. Planning als copingstijl en religieuze coping waren geassocieerd met minder acceptabel vinden van euthanasie. Bereidheid om euthanasie uit te voeren op verzoek van een pesoon met dementie was geassocieerd met het niet hebben van een religie, geen training in palliatieve zorg en minder gebruik van emotionele sociale steun als copingstijl.

Deze bevindingen laten zien dat opvattingen over euthanasie voor mensen met dementie sterk variëren tussen landen en individuen. Beleid moet mogelijk rekening houden met de wensen en behoeften van clinici die zowel voor, als tegen euthanasie zijn. Veranderingen in hoe acceptabel euthanasie word gevonden, zijn te verwachten naarmate palliatieve zorg breder beschikbaar wordt gesteld of wanneer religiositeit in een land verandert. Onderzoek is

nodig om de mechanismen achter de verbanden tussen copingstijlen en hoe acceptabel men euthanasie vindt te verkennen.

Hoofdstuk 5

Hoofdstuk 5 is een scoping review van niet-invasieve monitoringtechnologieën die onwelbevinden en belastende symptomen kunnen identificeren bij mensen met beperkte communicatie aan het einde van hun leven. De review richtte zich op het feit dat mensen aan het levenseinde moeite kunnen hebben om onwelbevinden te uiten door vermoeidheid, sedatie, delier, cognitieve beperkingen, coma of communicatieproblemen. In de huidige praktijk is herkenning van onwelbevinden vaak afhankelijk van observaties door zorgverleners en familie, maar continue observatie is niet altijd haalbaar.

De review omvatte zoekopdrachten in negen databases en consultatie van experts. Manuscripten kwamen in aanmerking wanneer die een niet-invasieve technologie beschreven die onwelbevinden, belastende symptomen of bewustzijnsniveau mat; continu toepasbaar was gedurende ten minste vier uur; en potentieel toepasbaar was bij bedlegerige mensen. Van de 3.414 geïdentificeerde manuscripten voldeden er 229 aan de criteria. De review identificeerde verschillende soorten technologieën, waaronder actigrafie, hersenactiviteitsmonitoring, elektrocardiografie, elektrodermale activiteit, oppervlakte-elektromyografie, incontinentiesensoren, multimodale systemen en contactloze monitoringsystemen. De belangrijkste indicatoren van onwelbevinden die door deze technologieën werden gemetenwaren slaap, bewustzijnsniveau, risico op decubitus, urine-incontinentie, agitatie en pijn.

Het hoofdstuk concludeert dat veel relevante technologieën bestaan of in ontwikkeling zijn, maar dat hun toepassing in levenseindezorg onderbelicht blijft. Eén studie rapporteerde dat hersenactiviteitsmonitoringen nuttig en acceptabel kunnen zijn voor het monitoren van het bewustzijnsniveau tijdens palliatieve sedatie. Voor de andere technologieën rapporteerde geen enkel manuscript klinimetrie, haalbaarheid of hoe acceptabel ze zijn bij het levenseinde. De review brengt het veld in kaart en identificeert de noodzaak voor toekomstig onderzoek om monitoringtechnologieën verder te

ontwikkelen en te evalueren in hoeverre ze in deze context bruikbaar, haalbaar, en acceptabel zijn.

Hoofdstuk 6

In hoofdstuk 6 onderzochten wij hoe acceptabel Bispectral Index-monitoring (BIS) is in levenseindezorg voor dementie. BIS is een niet-invasieve technologie voor aan het bed die hersenactiviteit gebruikt om het bewustzijnsniveau aan te geven. Het wordt routinematig gebruikt tijdens operaties om de diepte van anesthesie te monitoren. Het kan ook relevant zijn in palliatieve zorg, bijvoorbeeld tijdens palliatieve sedatie of wanneer bewustzijn en ongemak moeilijk te beoordelen zijn. De studie maakte gebruik van focusgroepen en interviews waarin BIS-monitoring gedemonstreerd werd. Zeventien mensen met dementie en 24 naasten in Nederland namen deel aan de studie.

De resultaten laten zien dat mensen met dementie de BIS-sensoren niet hinderlijk vonden, maar het verschilde tussen deelnemers en situaties hoe acceptabel ze het gebruik van BIS vonden. Naasten vonden BIS over het algemeen acceptabel in medische situaties, vooral tijdens palliatieve sedatie en om pijn te signaleren. Redenen dat men BIS acceptabel vond, waren onder meer de potentiële verbetering van zorg, ondersteuning bij symptoommonitoring, het faciliteren van communicatie, ondersteuning bij besluitvorming en het helpen van naasten om moeilijke situaties te accepteren. Tegelijkertijd uitten deelnemers belangrijke zorgen. Sommigen betwijfelden de toegevoegde waarde van BIS in vergelijking met bestaande observatie, communicatie en professionele beoordeling. Anderen maakten zich zorgen over haalbaarheid, waaronder signaalkwaliteit en de vraag of mensen met dementie de sensoren zouden verwijderen als zij geagiteerd zijn of geen sensoren op hun hoofd willen. Het gebruik van BIS was controversiëler in niet-medische situaties, zoals natuurlijke slaap. Deelnemers benadrukten ook dat de technologie menselijke zorg of menselijke besluitvorming niet mag vervangen.

Het hoofdstuk concludeert dat BIS of vergelijkbare technologieën alleen moeten worden geïmplementeerd als zij voldoende toegevoegde waarde hebben, wanneer mensen met dementie en naasten goed geïnformeerd zijn, en als het gebruik van de technologie aanvullend blijft op de zorg door professionals en

familie. Toekomstig onderzoek kan BIS bij mensen met dementie valideren en testen hoe effectief, haalbaar en acceptabel BIS is in de situaties die de deelnemers het meest acceptabel vonden in deze studie.

Discussie (Hoofdstuk 7)

Hoofdstuk 7 integreert de bevindingen en omvat reflecties op theoretische, methodologische en praktische implicaties. Terugkerend naar het thema controle, is de conclusie dat totale controle inderdaad niet mogelijk of wenselijk is voor veel mensen met dementie. ACP kan controle over toekomstige zorg vergroten, maar artsen benadrukten dat toekomstige beslissingen flexibiliteit vereisen omdat omstandigheden en belangen kunnen veranderen. Monitoringtechnologieën kunnen controle ondersteunen door onwelbevinden te detecteren wanneer communicatie beperkt is, maar er is nog onvoldoende bewijs over hoe effectief, haalbaar, en acceptabel deze technologieën zijn in de context van levenseindezorg. Euthanasie werd door veel clinici in de zes landen niet acceptabel gevonden, ongeacht permissieve wetgeving, waardoor het voor veel mensen met dementie geen toegankelijke manier is om controle uit te oefenen.

De discussie gaat ook in op de concepten identiteit en een goede dood. Dementie kan geheugen, persoonlijkheid en morele beoordelingsvermogens aantasten, wat leidt tot de vraag in hoeverre de veranderde persoon dezelfde is als voorheen, en in hoeverre eerdere wensen richtinggevend moeten zijn voor toekomstige zorg. Dit proefschrift geeft aan dat ACP en voorlichting van het brede publiek zouden kunnen helpen bij het reflecteren op mogelijke veranderingen in identiteit en het leren accepteren van onzekerheid. Een goede dood is niet slechts een goed gecontroleerd proces, maar omvat ook geen pijn hebben, comfort, waardigheid, vertrouwde mensen in een vertrouwde omgeving, persoonsgerichte communicatie, spiritualiteit, een gevoel van afronding van het leven en het ontvangen van gewenste interventies. Hoewel de in dit proefschrift onderzochte interventies betrekking hadden op enkele van deze elementen, wordt betoogd dat de psychologische en spirituele dimensies van een goede dood meer aandacht verdienen in toekomstig onderzoek.

De methodologische discussie benadrukt het belang en hoe moeilijk het is om mensen met dementie te betrekken bij onderzoek naar levenseindezorg. De werving van mensen met dementie voor de studies in dit proefschrift vormde een uitdaging . Professionals en familie traden soms op als poortwachter en informeren de mensen met dementie niet over de studie, omdat zij het onderwerp als te confronterend of belastend beschouwden. Het proefschrift stelt dat deze bescherming niet altijd overeenkwam met de daadwerkelijke ervaring van deelnemers, van wie velen het waardeerden om bij te dragen. Een andere uitdaging was het moment om potentiële deelnemers te benaderen voor onderzoek: de periode tussen diagnose en verlies van capaciteit om op complexe onderwerpen te kunnen reflecteren kan kort zijn, of wisselend. Het is daarom aan te raden om onderzoek beter te integreren in de dementiezorg, zodat mensen met dementie beter betrokken kunnen worden gedurende het hele onderzoeksproces.

Voor beleid en praktijk is de aanbeveling gebaseerd op dit proefschrift om meer informatie te bieden aan het publiek over situaties en keuzes aan het levenseinde bij dementie, inclusief realistische informatie over verpleeghuiszorg, de veranderende behoeften van mensen met dementie en de grenzen aan controle over de toekomst. Het is ook aan te bevelen om mensen met dementie te betrekken bij de ontwikkeling van technologieën voor levenseindezorg en om mensen die wilsonbekwaam zijn voor beslissingen rondom hun zorg te beschermen tegen ongewenste interventies, waaronder niet-gewenste zorgtechnologieën. Voor professionals wordt regelmatige reflectie op ethische dilemma's aanbevolen, bijvoorbeeld via intervisie of moreel beraad. Ook raden we aan om de betrokkenheid van psychologen en geestelijk verzorgers in levenseindezorg te vergroten om zorgen en angsten te bespreken. Ze kunnen mensen helpen beter om te gaan met onzekerheid. Voor onderwijs zouden toekomstige zorgprofessionals moeten worden getraind in het reflecteren op conflicterende ethische principes, hun eigen waarden, identiteit, een goede dood en de rol van technologie.

Conclusie

Dit proefschrift laat individuele variatie zien in hoe acceptabel mensen interventies vinden die controle aan het levenseinde voor mensen met dementie

kunnen vergroten. ACP werd door artsen over het algemeen acceptabel gevonden, maar is ethisch gecompliceerd. Euthanasie was controversiëler en het varieerde sterk tussen landen en binnen landgrenzen hoe acceptabel artsen het vonden. Monitoringtechnologieën kunnen symptoomherkenning ondersteunen, maar vereisen verdere ontwikkeling, sterker bewijs en zorgvuldige implementatie. Levenseindezorg bij dementie moet daarom niet streven naar het maximaliseren van controle op uniforme wijze. Het aanbieden van interventies op maat om controle te bevorderen kan helpend zijn in een onzekere situatie, echter moeten we vooral streven naar zorg die aansluit bij de waarden, huidige behoeften, juridische context en professionele verantwoordelijkheid van individuen.

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About the author

Xu Jingyuan was born in China in 1994. She grew up in Xi'an until the age of eleven, after which she attended secondary school in Shanghai. Growing up in different environments sparked her early interest in people, culture, and the question of what gives life meaning. From a young age, she was driven by curiosity about human suffering, wellbeing, and existential questions, motivations that would later shape both her academic and professional path.

Between 2013-2017, Xu studied her Bachelor of Social Sciences at the University of Hong Kong, majoring in psychology with a minor in Spanish. Her bachelor thesis focused on the relationship between meaning in life and wellbeing in an intercultural context. Alongside her studies, she worked as a research assistant at the university and volunteered at Suicide Prevention Services in Hong Kong, where she supported older adults with emotional difficulties and suicide risk. While living in Hong Kong, she also came into contact with palliative and psychosocial care, which deepened her interest in supporting people during vulnerable phases of life.

Xu moved to the Netherlands in 2018 and completed the Master's programme in Clinical Psychology at Leiden University. During this period, she gained practical experience in several healthcare settings. At Raeger Autisme Centrum, she supported children with autism spectrum disorder and intellectual disability. At Stichting Philadelphia Zorg, she worked with older adults with intellectual disabilities. At MOB, she worked as a psychologist with older adults with a non-Western background in residential care locations, contributing to psychosocial care and the implementation of person-centred care. She also volunteered at Florence Caregroup with residents living with dementia and, from 2019 to 2022, at Issoria Hospice & Thuis, visiting people in the terminal phase of life and supporting both clients and their informal caregivers. These experiences strengthened her belief in the importance of compassionate, person-centered psychological support.

In 2020, Xu started her PhD research at the Department of Public Health and Primary Care of the Leiden University Medical Center. Her research focused on perspectives on acceptable care and controversial interventions

in dementia in the last phase of life within the international CONT-END program.

Currently, Xu works as a psychologist at GGZ-Reflection in Rijswijk, the Netherlands, where she treats adults with a broad range of mental health issues. In her current work, her focus has broadened from end-of-life care to improving the quality of life and psychological wellbeing of the wider adult population. She remains motivated by a desire to help people cope with emotional suffering, getting in touch with their own values, and live meaningful and fulfilling lives.