

What research we no longer need in neurodegenerative disease at the end of life: the case of research in dementia

Jenny T van der Steen, PhD; * prof. Claire Goodman, PhD

Affiliations

JTvdS: see below

CG: Claire Goodman, Professor of Health Care Research, Centre for Research in Primary and Community Care, University of Hertfordshire AL10 9AB, UK. Tel: +44 (0)1707 281331;
Email: c.goodman@herts.ac.uk

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*Corresponding author:

Jenny T. van der Steen, PhD. VU University Medical Center, EMGO Institute for Health and Care Research, Department of General Practice & Elderly Care Medicine, Van der Boechorststraat 7, 1081 BT Amsterdam, The Netherlands. Tel: +31-20-4449694; Fax: +31-20-4448234;
Email: j.vandersteen@vumc.nl

A complete silence. That was what we got back from the European experts that had been energetically discussing research priorities in palliative care in neurodegenerative disease (ND) until a short while ago.¹ The chair, an entertaining professor with good manners, must have felt the unease and quickly refocused the group to their task. But, wasn't this the best question of all day? What research we no longer need? As scientists able to consider different perspectives, shouldn't we have some idea of what research is, by contrast, no longer necessary?

Palliative care research, and research with people who have ND *and* are at the end of their life is by definition, difficult. Making choices is a sensitive issue, but funds are limited. Therefore, we take a counterpoint to the research agenda recently reported by EU Joint Programme-Neurodegenerative Disease Research (JPND),¹ and consider whether there are studies we no longer need or are low priority, taking the example of dementia.

The growth of palliative care research for people with dementia

At the end of life or earlier, people with dementia may benefit from palliative care. Some evidence suggests that hospice care or a palliative approach improves families' satisfaction with care although benefits for patients are less clear.²⁻⁵

Early research from the US (80-ies)⁶ focused on the development of hospice for people with dementia. In the UK, early work described care and symptoms (90-ies).^{7,8} Research in dementia at the end of life has exponentially increased since the turn of the century, with more countries developing research programmes⁹⁻¹¹ and narrative reviews appearing in a variety of specialty journals. Although high-quality evidence of effects or effective elements of palliative care in dementia is still sparse, currently, there is a consensus that it is helpful in the advanced stages.¹²

We are arguably at a turning point as different research disciplines that have had a limited exposure to research on palliative care in dementia (for example, social gerontologists, psychogeriatricians, ethicists and health services researchers) recognize that they have an important contribution to make. One challenge is how to expand the involvement of the research community and build capacity while ensuring that research is not inadvertently duplicated.. The burgeoning of qualitative research on the experience of becoming a person with dementia is a vivid example of how a research question that is recognised as important can inadvertently lead to avoidable duplication. A systematic review of qualitative research reviewed 126 papers and concluded that the common statement that the person with dementia's voice is not heard is not true if applied to white educated people who live with a carer.¹³ What might be the equivalent situation at the opposite end of the disease trajectory?

How to improve design and theory and build a sound evidence base

We suggest how to progress research on dementia at the end of life (online Box 1) by focusing on three broad areas of concern and s. These are (1) the use and contribution of theory, (2) the limitations of particular research designs and (3) how the evidence base develops and is applied. We first illustrate the three areas in how research on advance care planning (ACP) is approached and then discuss other examples addressing the three areas separately.

Research on ACP is "hot." It is seen as the means by which professionals in partnership with patients and their families can address the uncertainties that arise at the end of life, especially when patients cannot participate in decision making.^{10,14} To develop theory (1), we need to compare long-term effects of different advance care planning interventions (1a in Box 1). Pragmatic approaches are needed because patients with dementia will, at some point, no longer be able to revise their plans.

However, without sufficient breadth of understanding to support how ACP is introduced throughout the disease trajectory, we cannot design more sophisticated research (2b). Research also needs to address unintended consequences of planning ahead^{10,15,16} (3a) and interventions need to be sensitive to time, place, culture and particular populations. Furthermore, we need full reports of “negative” findings to avoid duplication, but also replication of the best studies in different settings (3c). For example, using the same instruments, we found that families’ understanding of prognosis in the Netherlands was unrelated to aggressive treatment as found in the US.¹⁷ However, we neglected to report in full this important dissonant finding, only reporting it in a single sentence in the discussion of a paper addressing a different research question.¹⁸ The findings do suggest that family education may work better in one country than in the other, and this example shows how an emphasis on “positive findings” and lack of full reporting of replication, risks compromising the evidence base.

The use and contribution of theory

We do not need more research that concludes palliative care for people with dementia is complex and context specific, which does not help build theory (Box 1, area 1). Too often, research for people with dementia at the end of life borrows the assumptions of what is good care from cancer models, whilst simultaneously acknowledging their limitations. It does not discuss or analyse what elements are transferable and which are not.¹⁹ We should consider what is already known about interventions that ameliorate the impact of frailty, old age, other chronic-progressive diseases and implementation research in long-term care. For example, research on continuity of care for people with long-term conditions is highly relevant for how palliative care for people with dementia is delivered over time.²⁰

In contrast to the often a-theoretical approaches of ACP research, the example of research on spirituality has arguably given too much to theorizing and too little to implementation (Box 1, 1b). Research on what spiritual care is, needs to consider how and if integration into palliative care models achieves better outcomes for patients and their caregivers.

The limitations of uni-dimensional research design or analysis

Although it may be appropriate for countries with no tradition of research in the area, the international research community should be increasingly wary of studies that describe the challenges of symptom assessment in advanced dementia, family burdens, or staff knowledge of palliative care and conclude that more research or single-solution interventions are needed (Box 1, 2a). Palliative care research, particularly for populations whose dying trajectory is protracted, faces particular challenges in establishing causality. If it is not possible to establish causality or effectiveness^{9,21} then we need to expand our portfolio of research methods (2b). Most palliative care interventions are multi component. We should be able to pinpoint relevant findings and determine which findings are generalizable, or at least show potential, and which do not, for example, through adequately powered parallel studies, mediator analyses or thorough evaluation of implementation.²²

In dementia research it is problematic researching highly selected populations, such as those limited to the terminal or severe disease stages or truncation in prospective studies that is not anchored in the disease trajectory (Box 1, 2c). It does not reflect the fact that many people die with dementia as a concomitant disease as well as from it, and that the dying trajectory is intrinsically uncertain, with palliative care needs arising along the disease trajectory. A narrow focus does not allow for studying changes in the course of the disease and the nature of optimal palliative care and anticipating changes and needs in each phase. Further, given what we know about the significance

of transitions through stages and settings, studies in single settings can only offer a partial account. For example, contrasting interventions in home care and long-term care has important benefits in terms of informing future policy.

Implementation based on a sound evidence base

In general, we may focus too much on innovative research (Box 1, 3a). Replication, not only collaborative parallel studies but also independent replication, is needed to understand generalizability of findings.²³ How else do we know if the researchers' enthusiasm affected their independence or critical distance and subsequently the reporting and publication of these studies? Optimism bias relates to distorted evidence or the reporting of "promising" results that need further testing.²⁴ We do not need research that is implemented too soon without replication with valuable learning lost in the process, or is not published in full or remains unpublished because of "neutral" or "negative findings."²⁵ Publication bias is an issue also in qualitative research, where striking or clear findings are over reported.²⁶ To advance the wider evidence base on palliative care, we may evaluate reporting bias in palliative care research and incentives for replication studies and publishing "negative" findings.

Conclusion

We took dementia as an example to indicate what research in palliative care in ND we no longer need, considering the use of theory, study design, and the wider evidence base. Poorly designed, stand-alone descriptive, uncontrolled and underpowered studies or those not targeting the right questions or that remain unpublished are always a waste of resource.²⁷ To develop palliative care in ND, in addition to a trans-setting and trans-stages-of-disease approach, we need a trans-disease approach. We need a cross fertilization in research ideas and approaches to understand how palliative care principles should be applied in different diseases. A programmatic approach covering a series of interlocking studies may help to efficiently build capacity and design the studies we need.¹⁹

This is not an attack on colleagues and we are aware that some of the research we state is no longer needed, we have recently undertaken. The platform of JPND to generate a trans-European research agenda for palliative care in ND was the trigger, an opportunity to consider what we have learnt. To suggest that some research is no longer needed, should be a cause for celebration. Our reflections complement the JPND report¹ and hopefully support palliative care research for people with ND and their caregivers, that leads to cross-national and interdisciplinary collaborations and building the next generation of research.

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References

1. EU Joint Programme – Neurodegenerative Disease Research (JPND). <http://www.neurodegenerationresearch.eu/initiatives/jpnd-alignment-actions/palliative-care/>
Palliative and end-of-life care research in neurodegenerative diseases. A report of the JPND Action group. [Report will be posted on the website soon]
2. Shega JW, Hougham GW, Stocking CB, et al. Patients dying with dementia: experience at the end of life and impact of hospice care. *J Pain Symptom Manage* 2008; 35(5): 499-507.
3. Teno JM, Gozalo PL, Lee IC, et al. Does hospice improve quality of care for persons dying from dementia? *J Am Geriatr Soc* 2011; 59(8): 1531-1536.
4. Cohen LW, van der Steen JT, Reed D, et al. Family perceptions of end-of-life care for long-term care residents with dementia: differences between the United States and the Netherlands. *J Am Geriatr Soc* 2012; 60(2): 316-322.
5. van Soest-Poortvliet MC, van der Steen JT, de Vet HCW, et al. Comfort goal of care and end-of-life outcomes in dementia: a prospective study. *Palliat Med* under review.
6. Volicer L, Rheaume Y, Brown J, et al. Hospice approach to the treatment of patients with advanced dementia of the Alzheimer type. *JAMA* 1986; 256(16): 2210-2213.
7. Lloyd-Williams M. An audit of palliative care in dementia. *Eur J Cancer Care (Engl)* 1996; 5(1): 53-55.
8. McCarthy M, AddingtonHall J, Altmann D. The experience of dying with dementia: a retrospective study. *Int J Geriatr Psychiatry* 1997; 12: 404-409.
9. van der Steen JT. Dying with dementia: what we know after more than a decade of research. *J Alzheimers Dis* 2010; 22(1): 37-55.
10. van der Steen JT, van Soest-Poortvliet MC, Hallie-Heierman M, et al. Factors associated with initiation of advance care planning in dementia: a systematic review. *J Alzheimers Dis* 2014; 40(3): 743-757.
11. Goodman C, Evans C, Wilcock J, et al. End of life care for community dwelling older people with dementia: an integrated review. *Int J Geriatr Psychiatry* 2010; 25(4): 329-337.
12. van der Steen JT, Radbruch L, Hertogh CM, et al; European Association for Palliative Care (EAPC). White paper defining optimal palliative care in older people with dementia: a Delphi study and recommendations from the European Association for Palliative Care. *Palliat Med* 2014; 28(3): 197-209.
13. Bunn F, Goodman C, Sworn K, et al. Psychosocial factors that shape patient and carer experiences of dementia diagnosis and treatment: a systematic review of qualitative studies. *PLoS Med* 2012; 9(10): e1001331.
14. Denning KH, Jones L, Sampson EL. Advance care planning for people with dementia: a review. *Int Psychogeriatr* 2011; 23(10): 1535-1551.
15. Mathie E, Goodman C, Crang C, et al. An uncertain future: the unchanging views of care home residents about living and dying. *Palliat Med* 2012; 26(5): 734-743.
16. Robinson L, Dickinson C, Bamford C, et al. A qualitative study: professionals' experiences of advance care planning in dementia and palliative care, 'a good idea in theory but ...'. *Palliat Med* 2013; 27(5): 401-408.
17. Mitchell SL, Teno JM, Kiely DK, et al. The clinical course of advanced dementia. *N Engl J Med* 2009; 361(16): 1529-1538.

18. van der Steen JT, Onwuteaka-Philipsen BD, Knol DL, et al. Caregivers' understanding of dementia predicts patients' comfort at death: a prospective observational study. *BMC Med* 2013 Apr 11; 11: 105.
19. Brazil K, Ozer E, Cloutier MM, et al. From theory to practice: improving the impact of health services research. *BMC Health Serv Res* 2005 Jan 7; 5: 1.
20. Parker G, Corden A, Heaton J. Experiences of and influences on continuity of care for service users and carers: synthesis of evidence from a research programme. *Health Soc Care Community* 2011; 19(6): 576-601.
21. Sampson EL, Ritchie CW, Lai R, et al. A systematic review of the scientific evidence for the efficacy of a palliative care approach in advanced dementia. *Int Psychogeriatr* 2005; 17(1): 31-40.
22. Higginson IJ, Evans CJ, Grande G, et al; MORECare. Evaluating complex interventions in end of life care: the MORECare statement on good practice generated by a synthesis of transparent expert consultations and systematic reviews. *BMC Med* 2013 Apr 24; 11: 111.
23. Fanelli D. Redefine misconduct as distorted reporting. *Nature* 2013; 494(7436): 149.
24. Djulbegovic B, Kumar A, Magazín A, et al. Optimism bias leads to inconclusive results-an empirical study. *J Clin Epidemiol* 2011; 64(6): 583-593.
25. McGauran N, Wieseler B, Kreis J, et al. Reporting bias in medical research - a narrative review. *Trials* 2010; 11: 37.
26. Petticrew M, Egan M, Thomson H, et al. Publication bias in qualitative research: what becomes of qualitative research presented at conferences? *J Epidemiol Community Health* 2008; 62(6): 552-554.
27. Sleeman KE, Murtagh FE. Increasing the value of research in palliative care. *Palliat Med* 2014; 28(10): 1165-1166.