



## UvA-DARE (Digital Academic Repository)

### Clinical, economic and methodological studies in elderly patients with dementia and their informal caregivers

MacNeil Vroomen, J.L.

**Publication date**

2015

**Document Version**

Final published version

[Link to publication](#)

**Citation for published version (APA):**

MacNeil Vroomen, J. L. (2015). *Clinical, economic and methodological studies in elderly patients with dementia and their informal caregivers*.

**General rights**

It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

**Disclaimer/Complaints regulations**

If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: <https://uba.uva.nl/en/contact>, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.



## General Discussion

## GENERAL DISCUSSION

The focus of this thesis was on the evaluation of case management in dementia. However, we also investigated two other subjects important in dementia care, i.e. crisis and place of death. Crisis situations are common in dementia care. Crisis situations often lead to admission of a patient into an institution, although both patient and informal caregivers have a preference for care at home. Therefore, we tried to define crisis in dementia care and created an operational framework to summarize potential solutions from the perspective of different stakeholders. Next, we analyzed data from the Dutch statistics agency to assess which person level characteristics are associated with the place where persons with dementia die. The second part of the thesis focused on the evaluation of the case management models. We included a wide range of clinical outcome measures and economic outcome measures to compare the care models to each other. Finally, we sought to advance statistical methods in economic evaluations by testing the performance of different strategies for multiple imputation of cost-effectiveness data.

The general discussion is divided into three parts. First, we will review the main findings and conclusions of the papers included in this thesis. Second, we will discuss limitations and methodical issues of the papers included. Lastly, implications for practice and future research will be presented.

### Main findings and conclusions

*Is there a commonly accepted operational definition of dementia related crisis that can be used in clinical practice and future research?*

Based on a review of the literature we defined dementia related crisis as:

*“a process where there is a stressor(s) that causes an imbalance requiring an immediate decision which leads to a desired outcome and therefore crisis resolution. If the crisis is not resolved, the cycle continues.”*

The person with dementia, the caregiver, and the health support staff all have different perspectives on the definition of crisis and its resolution. From the literature, it becomes clear that crises come in all kinds of formats and that every crisis has a unique solution. Therefore, it is very difficult to prevent or plan for all crises even if there is a willingness to create a strategic plan. We used an operational framework to compile types of crisis stressors and recommendations from the crisis literature based on three different perspectives; the person with the dementia, the caregiver and the healthcare providers. Use of this framework will help caregivers, healthcare providers and researchers to identify interventions that may be useful in the management of crisis in dementia (Chapter 2: **Reviewing the definition of crisis in dementia care**).

*Which personal- level characteristics are associated with location of death for persons who died of dementia in the Netherlands?*

In this study among 17,814 people with dementia listed as a cause of death in 2006, we

showed that increased age, being single, living in an institution the year before death, and having an income below the median of 14,410 euros were all associated with an increased likelihood of dying in a long-term care facility compared to dying at home. We also showed that people were at higher risk of dying in a hospital rather than at home if they were between the ages of 75 to 84, single, lived in an institution the year before death and had an income below 14,410 euros. It is important to mention that the majority of the people in this study died in a long-term care facility and very few died at home or in hospital in contrast to studies in other countries (1,2). This is surprising because a year before death, over half of the population with dementia-related deaths were still living at home. Only 12% of the entire population was ever hospitalized the year before death. We found that hospitalization occurred more frequently in people who were male, younger than 85 years old, married or cohabitating, living at home, and had an income over the median. Considering the wish of persons with dementia and their informal caregivers to be able to die at home in combination with a nationwide policy to keep people at home as long as possible, it may be necessary to reorganize care to make this better possible in the future (Chapter 3: **The Dutch experience: People with dementia do not die in hospitals**).

*Were there differences at baseline between people with dementia and informal caregivers in the two case management models and the no case management model?*

In the COMPAS study, two case management models were compared with no access to case management. This was a prospective, observational, controlled, cohort study with follow-up every 6-months for 2 years. Community-dwelling participants were recruited in the Netherlands (n=521). The case management models were 1) the intensive case management model (ICMM) where case management is provided within one care organization and the linkage model (LM) where multiple case management organizations are present within one region. Since the COMPAS study was an observational study, there is an extra risk of bias. Therefore, we compared characteristics between the groups at baseline to evaluate the probability of bias. At baseline, persons with dementia in the case management models were often older, female, single, living alone, had a lower education, increased multi-morbidity and higher neuropsychiatric symptoms scores than those in the no access to case management group. Persons with dementia in the ICMM started in case management earlier than in the LM. Informal caregivers were often in their mid-sixties, female, and were family members which was comparable to other studies (3-5). These findings indicated that there possibly was confounding by indication present. Therefore, analysis of the study required the use of complex statistical methods such as propensity scores to adjust for baseline difference between groups (Chapter 5: **Two Dutch case-management models for dementia versus GP care: baseline results**).

*Does implementation of case management lead to better outcomes as compared to no access to case management?*

The COMPAS study was the first to evaluate clinical outcomes of dyads of persons with dementia and their primary informal caregiver receiving two types of case management

in comparison with dyads in a control group with no access to case management. The analyses showed no differences in neuropsychiatric (NPI) scores in persons with dementia between the control group, the intensive case management model (ICMM) and the Linkage model (LM). However, in informal caregivers, mental health according to the GHQ-12 was worse in the control group than in the ICM group. There was no difference in psychological health (GHQ-12 scores) between the LM group and the control group or the LM versus the IC group. The significant effect was lost when using the Bonferoni correction for multiple groups and when persons who switched groups during the study were excluded. In all groups at all measurements, mean GHQ-12 scores were above the suggested cut-off for the GHQ-12 of one to two points (6,7) which indicates that the informal caregivers were already at increased risk of mental health problems at the start of the study. Although we found no differences in primary outcomes, secondary outcomes showed a trend towards positive effects of case management compared to no case management. Total, met and unmet care needs were less in the ICMM group compared to the control group. Total met needs were less in the LM group versus the control group. This indicates that the control group had more needs overall than the intensive case management group. Mean utility scores for the informal caregiver were higher in the ICMM than the LM group (Chapter 6: **Comparison of clinical outcomes in community dwelling patients with dementia and their informal caregivers with and without case management: two year results of the COMPAS study**).

*Is the implementation of case management cost-effective in comparison with no access to case management?*

In the economic evaluation of the COMPAS study, there were no differences in QALYs, NPI scores or GHQ-12 scores between the 3 groups. Informal care costs were statistically significantly lower in the ICMM group compared to both the LM and the control group. We found that total costs were lowest for the ICMM followed by LM and finally the control group. However, differences in total costs were not statistically significant between groups. For the combined QALY score for dyads, the ICMM group was considered cost-effective in comparison with both the control group and the LM. The LM was considered cost-effective in comparison with the control group for the combined QALY, but in this case cost savings were accompanied by a small decrease in QALYs. For patient QALYs, the difference was small for all comparisons and not statistically significant. Based on these results, ICMM and LM were cost-effective in comparison with control. For the NPI and GHQ outcomes, both case management models appeared to be cost-effective in comparison with the control group (Chapter 7: **The cost-effectiveness of two forms of case management compared to a control group for persons with dementia and their informal caregivers from a societal perspective**).

*Which multiple imputation strategies work best in an economic evaluation?*

In this study, we evaluated the performance of different multiple imputation strategies and complete case analysis (CCA) for scenarios with varying rates of missing data in costs and effects in a pragmatic economic evaluation. We showed that for all rates of missing

data, multiple imputation strategies performed better than CCA. The results of the CCA, Multiple Imputation-Predictive Mean Matching (MI-PPM) and the two-step MI were all influenced by the amount of missing data. With a larger amount of missing data, the Log MI-PMM deviated the least from the reference analysis (RA) for the cost difference, cost standard error, incremental net benefit (INB) and its standard error, and the probability that intervention treatment was considered cost-effective in comparison with the control treatment at a willingness to pay of 30,000 euros per QALY. Therefore, the Log MI-PMM is considered most appropriate to impute missing cost and effect data. However, when considering QALYs the MI-PMM performed best since it deviated the least from the RA with increasing amounts of missing data. Overall, the Log-MI-PMM was least affected by the amount of missing data (Chapter 8: **Comparing Multiple Imputation strategies for zero-inflated cost data: which method works best?**).

### **Methodological considerations and limitation**

#### *Study design*

The observational design of the COMPAS study may have led to baseline differences as well as selection bias. We tried to overcome this in the analyses by using propensity scores weighting for all analyses. We chose to use a generalized boosted model for the estimation of the propensity score weights because we had three groups (8). Propensity scores techniques summarize all the variables where baseline imbalances exist into a single score which is advantageous over regression-based, covariate-adjustment techniques which risk affecting the precision of the treatment effect with too many covariates (8). As we were comparing multiple groups, we took a conservative estimate ( $p$ -value less than  $0.05/3=0.017$ ) by using a Bonferoni correction although this resulted in a loss of power.

Another design issue was that there may have been confounding by indication, meaning that persons in the control group may have had access to case management outside their region and general practitioners may have selectively referred patients with dementia to case management. Based on our results, the control group was younger and had less co-morbidity at baseline. However, because of the observational nature and the length of time required to recruit people into this study it is difficult to know whether this can be explained by confounding by indication. We attempted to address this potential bias by randomly calling participating general practitioners to ask if they ever sent persons with dementia to case management outside of their region and how they handled patients with dementia that exhibited complex neuropsychiatric behavioural symptoms. Based on the baseline results and consulting with the general practitioners, we decided to use techniques to adjust for selection bias such as a propensity score (8).

#### *Recruitment*

As the majority of regions provide people with dementia case management, it was hard to recruit sufficient persons from control regions. The Dutch Ministry of Healthcare stipulated in 2008 that “any form of case management” had to be part of usual care for persons with dementia in all regions in the Netherlands at the end of 2011. By 2011, case management

was available in the majority of regions and sub regions although there were still regions where case management was not yet implemented or had limited capacity. We tried to overcome the sample size issue by oversampling in the two case management arms.

During recruitment there was a considerable group of informal caregivers that did not want to participate because they felt overburdened. Participants were followed for two years with a low dropout rate. Study participants worsened considerably in GHQ-12 scores over the two year study duration to levels comparable to the refusers who did not want to participate at baseline. This may have led to further selection bias due to the possibility that the informal caregivers who declined to participate may have been more burdened compared to study participants.

#### *Switchers*

Approximately 14% of the participants in this study switched into or out of case management over time. However, a sensitivity analysis in which we excluded these participants and evaluated general health and neuropsychiatric symptoms, led to the same results as the primary analysis indicating that there was no difference in primary outcomes between groups.

#### *Regions and case management models*

We put regions of case management together based on similarities in 2010. Over the last five years dementia care has changed in the Netherlands through changes in case management policy and at the organizational level. It is possible that one region was more successful in implementing case management than another region but based on the study design it is difficult to detect if there were differences between regions within the models themselves. Also, it is possible that the organisation of case management has changed over time. However, it was not possible to evaluate this in this study.

#### *Primary outcomes*

In our design, we made sure to use outcomes that have been used before in previous case management studies. Primary outcomes were neuropsychiatric symptoms in persons with dementia and the psychological health of the caregiver. It could be disputed that these are subjective outcomes that are not or of little interest to the people involved in daily practice such as the general practitioner, case managers, informal caregivers and the persons with dementia. However, we think that these outcomes are predictive of adverse outcomes in both the person with dementia and the informal caregiver. Previous studies have shown that adverse outcomes such as institutionalization of the person with dementia or the development of mental disorders in the informal caregiver are associated with high costs (9-12). Additionally, we included a vast amount of secondary outcomes which in combination with the primary outcomes allowed us to glimpse into the lives of the informal caregivers and the persons with dementia. Although “hard” outcomes like institutionalization are maybe easier to interpret, it can be difficult to interpret what longer stays in the community mean for people involved in the care for persons with dementia. Delayed institutionalization may be beneficial to persons with dementia but perhaps at the cost of the health of the informal caregiver. This was one of the reasons for choosing

the GHQ-12 and the NPI as primary outcomes and use more objective outcomes such as institutionalization as secondary outcomes.

#### *Missing data*

Missing data is always an issue in clinical studies, not only in observational designs. This study ran for two years in very vulnerable patients, burdened carers and was conducted with multiple interviews and questionnaires, and, therefore, some missing data was inevitable. The use of multilevel analyses with an adjustment for time allowed use of all available data and to estimate effects over time. However, in the economic evaluation due to the cumulative nature of costs, one missing cost group will result in a failure to calculate total costs resulting in a loss of important information. This is also a problem for the calculation of Quality-Adjusted-Life-Years (QALYs) which is based on the area under the curve calculation of utility scores over time. In order to maximize the information available that we had we decided to use multiple imputation in the economic evaluation.

#### *Strengths*

The COMPAS study has several strengths. In this study, persons with dementia and their informal caregivers were followed over a period of 2 years. This is a relatively long period of time and provides good insight into the course of NPI scores of the persons with dementia and the mental health of the informal caregiver along with resource utilization and quality of life. Despite this long period of follow-up, dropout levels were relatively low. Another strength is that the case management models were implemented for many years previous to the start of this study. Therefore, the results have high external validity. The wide range of secondary outcomes assessed in this study provides relevant insights into the problems of persons with dementia and their informal caregivers. The use of multilevel analyses with an adjustment for time allowed us to use all available data and to estimate effects over time. The economic evaluation was from a societal perspective and also included informal care costs strengthening the results of the economic evaluation.

### **Implication for research and practice**

#### *Future directions for the management of crisis in dementia*

Having defined dementia crisis and created a framework in dementia care, we used this framework to compile crisis stressors, and recommendations from the literature based on multiple perspectives. Recommendations for persons with dementia in the community include increased contact with the general practitioner to control comorbid conditions [like diabetes therapy], case manager consultations, caregiver support and education. Nursing home staff need to be aware of the environmental, physical and psychological needs of persons with dementia and the needs of their caregivers. Additionally, constructive communication with the extended family is essential. From the literature, it becomes clear that crises come in all kinds of formats and that every crisis has a unique solution. Therefore, it is very difficult to prevent or plan for all crises even if there is a willingness to create a strategic plan.

We recommend future research to use our operational framework for crisis in a dementia care setting, for example by evaluating records based on dementia crisis support.

This could help identify if there are stressors associated with hospitalization, hospital preparedness, providing patient support, and caregiver guidance. After its validation in the various care settings, we recommend that the framework be used in the planning of care services and research. The framework may also have the potential to attach costs to crisis situations. This would allow for a monetary estimation of avoiding or handling crisis situations in dementia care.

#### *Future directions in location of death research for persons with dementia*

It is current policy that central and local government enable older people to stay longer at home potentially enabling them to die in their most preferred location. However, it is unclear if these plans will create a cycle of vulnerable people going in and out of hospital every time there is a crisis at home. Policy-makers should focus on the current and future types of support required for death at home for persons with dementia. At this time initiatives are already being set up, such as nursing home physicians doing consultations at home and offering 24 hour coverage.

#### *Future directions of case management*

It is widely accepted in literature that prolonged high stress levels in caregivers is one of the most important risk factor for nursing home admission (10,13). Our study showed that all caregivers experienced high psychological stress. Therefore, increased focus on more effective caregiver support is recommended.

When we look at effective ways to deal with caregiver burden there have been no obvious solutions. Some interventions are more effective in certain subgroups of informal caregivers, so it is important to align the support to needs and characteristics of the caregivers (14). In a review by Brodaty et al. (15), it was concluded that non-pharmacological interventions taught to family caregivers could reduce the frequency and severity of disturbing behavioral and psychological symptoms of dementia as well as improve caregiver responses to these behaviors.

From previous meta-analyses and systematic reviews, we know that intervention programs that focus on both the caregiver and person with dementia were often more effective in delaying long stay care admittance than those in usual care, although to a lesser extent in improving caregivers' mental health (16,17). The most successful interventions used either psycho-educational or psychotherapeutic approaches, addressed multiple stressors, were better adapted to the individual needs of the caregivers, and provided a higher amount and intensity of support (17,18). A review by Pinguart and Sørensen (19) found that psychoeducational interventions have the widest-ranging effects, but only if they call for active participation of the informal caregiver. Case managers are the ideal candidates to implement these interventions and to help the informal caregiver and the person with dementia as they try and provide individualized care (20). In a recent Cochrane review of case management, the authors found quality of life was higher in caregivers that had case managers involved in the care for their loved ones. In the COMPAS study we found the quality of life of caregivers was higher in the Intensive case management model than in the linkage model and control groups. Identifying which components of case

management that are associated with increased quality of life could allow increased focus on more effective case management interventions (21).

#### *Future research on economic evaluation of case management*

The COMPAS study may provide evidence that the intensive case management model is cost-effective when compared to dyads without access to case management, and other forms of case management, as it appears to decrease informal care hours. Although both cost and effect differences were not statistically significant between case management models and in comparison with control, there seems to be a trend towards lower costs and better NPI and GHQ-12 scores in the case management groups as compared to control. When looking more closely at the case management models, the ICM model seems to be in favour of the LM. Although this study cannot provide firm evidence due to its observational nature, this study provides important information for persons with dementia and their informal caregivers, healthcare providers and policy makers.

## REFERENCES

1. Sleeman KE, Ho YK, Verne J, Gao W, Higginson IJ. Reversal of English trend towards hospital death in dementia: a population-based study of place of death and associated individual and regional factors, 2001-2010. *BMC Neurol.* 2014;14:59.
2. Teno JM, Gozalo PL, Bynum JP, et al. Change in end-of-life care for Medicare beneficiaries: site of death, place of care, and health care transitions in 2000, 2005, and 2009. *Jama.* Feb 6 2013;309(5):470-477.
3. Callahan CM, Boustani MA, Unverzagt FW, et al. Effectiveness of collaborative care for older adults with Alzheimer disease in primary care: a randomized controlled trial. *Jama.* May 10 2006;295(18):2148-2157.
4. Kisely SR, Goldberg DP. The effect of physical ill health on the course of psychiatric disorder in general practice. *Br J Psychiatry.* Jun 1997;170:536-540.
5. Dias A, Dewey ME, D'Souza J, et al. The effectiveness of a home care program for supporting caregivers of persons with dementia in developing countries: a randomised controlled trial from Goa, India. *PLoS One.* 2008;3(6):e2333.
6. Goldberg DP, Oldehinkel T, Ormel J. Why GHQ threshold varies from one place to another. *Psychol Med.* Jul 1998;28(4):915-921.
7. Goldberg DP, Gater R, Sartorius N, et al. The validity of two versions of the GHQ in the WHO study of mental illness in general health care. *Psychol Med.* Jan 1997;27(1):191-197.
8. McCaffrey DF, Griffin BA, Almirall D, Slaughter ME, Ramchand R, Burgette LF. A tutorial on propensity score estimation for multiple treatments using generalized boosted models. *Stat Med.* Aug 30 2013;32(19):3388-3414.

9. Schwarzkopf L, Menn P, Kunz S, et al. Costs of care for dementia patients in community setting: an analysis for mild and moderate disease stage. *Value Health*. Sep-Oct 2011;14(6):827-835.
10. Eska K, Graessel E, Donath C, Schwarzkopf L, Lauterberg J, Holle R. Predictors of institutionalization of dementia patients in mild and moderate stages: a 4-year prospective analysis. *Dement Geriatr Cogn Dis Extra*. 2013;3(1):426-445.
11. Haro JM, Kahle-Wroblewski K, Bruno G, et al. Analysis of burden in caregivers of people with Alzheimer's disease using self-report and supervision hours. *J Nutr Health Aging*. Jul 2014;18(7):677-684.
12. Costa N, Ferlicq L, Derumeaux-Burel H, et al. Comparison of informal care time and costs in different age-related dementias: a review. *Biomed Res Int*. 2013;2013:852368.
13. Alzheimer's Disease International. *World Alzheimer Report 2013. Journey of Caring: An analysis of long-term care for dementia*. London: Global Observatory for Ageing and Dementia Care, Health Service and Population Research Department, King's College London; September 2013 2013.
14. Van Mierlo LD, Meiland FJ, Van der Roest HG, Droes RM. Personalised caregiver support: effectiveness of psychosocial interventions in subgroups of caregivers of people with dementia. *Int J Geriatr Psychiatry*. Jan 2012;27(1):1-14.
15. Brodaty H, Arasaratnam C. Meta-analysis of nonpharmacological interventions for neuropsychiatric symptoms of dementia. *Am J Psychiatry*. Sep 2012;169(9):946-953.
16. Smits CH, de Lange J, Droes RM, Meiland F, Vernooij-Dassen M, Pot AM. Effects of combined intervention programmes for people with dementia living at home and their caregivers: a systematic review. *Int J Geriatr Psychiatry*. Dec 2007;22(12):1181-1193.
17. Brodaty H, Green A, Koschera A. Meta-analysis of psychosocial interventions for caregivers of people with dementia. *J Am Geriatr Soc*. May 2003;51(5):657-664.
18. Zarit S, Femia E. Behavioral and psychosocial interventions for family caregivers. *Am J Nurs*. Sep 2008;108(9 Suppl):47-53; quiz 53.
19. Pinquart M, Sorensen S. Helping caregivers of persons with dementia: which interventions work and how large are their effects? *Int Psychogeriatr*. Dec 2006;18(4):577-595.
20. Khanassov V, Vedel I, Pluye P. Case management for dementia in primary health care: a systematic mixed studies review based on the diffusion of innovation model. *Clin Interv Aging*. 2014;9:915-928.
21. Reilly S, Miranda-Castillo C, Malouf R, et al. Case management approaches to home support for people with dementia. *The Cochrane database of systematic reviews*. 2015;1:CD008345.