Integrative Reactivation and Rehabilitation to Reduce Multiple Psychiatric Symptoms of Psychogeriatric Patients and Caregiver Burden

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Supplement 1: Integratieve reactivering en rehabilitatie (IRR)
(Tijdschrift voor Verpleeghuisgeneeskunde, Vol 34, no 1/2009)

Supplement 2: De relatie van psychiatrische functiestoornissen met cognitie, activiteiten dagelijks leven (ADL) en biografische gegevens
(Tijdschrift voor Geriatrie en Gerontologie, Vol 38, 2007)

Chapter

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General summary

1.   Introduction

In psychogeriatric patients who suffer from cognitive impairment or dementia, there is 80% prevalence of two or more psychiatric symptoms; e.g. depression, anxiety, paranoia, aggression. [1-4]. Multiple psychiatric symptoms (MPS) have negative effects on cognitive functioning and quality of life. They are a burden for the caregiver; about 70-80% of caregivers is moderately to heavily burdened. Furthermore, MPS predict the patient's admission to a nursing home. [3, 5-10] Moreover, these topics are among the top three of problems experienced by dementia patients and their caregivers. [10] In actuality, in usual nursing home care psychotropic drugs are widely used to treat MPS of psychogeriatric patients in spite of limited effects and potentially harmful side effects e.g. (a)typical antipsychotics. [2, 11-12] There is a lack of integrative psychotherapeutic programmes even though reports in literature indicate that for individual psychiatric symptoms, e.g. depression, anxiety, psychotherapeutic treatment may be effective. [13-18] However, psychotherapeutic interventions focussing on MPS in psychogeriatric patients who suffer from cognitive impairment or dementia are complex due to their multiplicity in combination with cognitive disorders, somatic co-morbidity, and social problems (e.g. relationships, loneliness). [19-20]

P.M.: For further literature references see specific chapters.

2.   Palliative care in chronic psychogeriatrics; a case study

A case study is presented about the relevance of psycho-social interventions for providing palliative care in the end of life phase of psychogeriatric patients with functional psychiatric co-pathology. The case study describes in detail the psycho-social intervention process as performed in a reactivation unit in a 'psychiatric skilled' Dutch nursing home. The know-how, is highly relevant to tune palliative care to the needs and abilities of the patient. The application of the four main-dimensions of the method of Dynamic System Analysis (particularly Cognitive functions, Psychological functions, Social context and Biology) can stimulate professionals to use an integral perspective both to the psycho-social needs of terminal psychogeriatric patients and their relatives and to the biological aspects. (Bakker, 1997) To establish the value of the DSA method for providing palliative care to psychogeriatric patients with functional psychiatric co-pathology scientific research is recommended to determine the prognostic profile of patients who benefit most from an actual palliative care programme.

3.   Psychogeriatric reactivation in an psychiatric-skilled nursing home; a clinical-empirical exploration

The chronic and diverse cognitive function disorders of psychogeriatric patients often occur in conjunction with mood and behavioural disorders (functional-psychiatric pathology), social problems and somatic comorbidity in addition to functional disability (Rubin and Kinscherf, 1989; Teri et al., 1990; Bozzola et al., 1992; Chatterjee et al., 1992; Ballard et al., 1995). [1] This complex co-pathology suggests that there is a need for specific intervention programmes (Colerick and George, 1986; Steele et al., 1990; McNaughton et al., 1995). The interventions aim at (re)gaining of stabilizing the ability to function autonomously and at enhancing the patients' quality of life (Mortimer et al., 1992; Gray and Fenn, 1993).

It is very important that the outcome of such interventions be measured (Lyons et al., 1997; Bakker and Das, 1996) and that the data is used to identify those patients who benefit most (Rubenstein et al., 1964; Colerick and George, 1986; Narain et al., 1988).

The objective of this study was to identify prognostic characteristics for the probability of discharge of psychogeriatric patients with functional-psychiatric pathology, in order to optimize patient selection for the reactivation programme.

Methods and materials. A retrospective, clinical, empirical study in a Dutch psychiatric nursing home. A group of 102 patients, consecutively enrolled in a psychogeriatric reactivation programme and who met the inclusion and exclusion criteria, was retrospectively examined. The general, functional and diagnostic characteristics were assessed at baseline.

Results. The general characteristics of the reactivation programme patients were not of prognostic value. However, functional characteristics (GDS, HI and ADL score) were prognostically important. In addition, diagnostic characteristics were identified within the following four domains; cognitive function disorder, psychiatric function disorders, caregiver system, and somatic co-morbidity. The prognostic value of the specific diagnostic classification of cognitive function disorders (with the exception of delirium) was irrelevant.

Conclusion. Prognostic modeling, specifically of positive change on severity of multiple psychiatric function disorders of psychogeriatric patients who suffer from cognitive impairment or dementia and on both general burden and competence of caregivers was feasible. The inclusion of a broader range of psychogeriatric patients i.e. lower or higher scores on MMSE and BI, in combination with specific interventions to enhance cognitive functioning, seems justified. Applying three decision rules all resulted in IRR as indicated intervention. Although the performances of the prognostic models found was considered moderate, this strategy is promising. Therefore, designing and conducting a study tailored to timely identifying psychogeriatric patients who likely benefit from an enriched IRR programme is recommended, preferably in a large scale multicentred study comprising a sufficient sample size..

4. Life expectancy following psychogeriatric reactivation

The mortality rate of psychogeriatric patients with cognitive function disorders (e.g. delirium, dementia, Korsakov, amnestic and other cognitive disorders) is higher than that of the normal population (1-3). Apart from the somatic pathology, cognitive dysfunctions often occur in conjunction with psychiatric function disorders, e.g. mood and behavioural disorders (4-8). These disorders are not only related to a decreased quality of life and the need for long-term care, but also to a diminished life-expectancy (9-13). In order to identify patients who may potentially benefit most from specific intensive interventions aimed at reducing the negative effects of the psychiatric function disorders. It is of clinical interest to determine prognostic indicators which may predict survival in these psychogeriatric patients. In order to optimize medical decision making, it is clinical relevant that patients who may benefit form intervention programmes are immediately identified (on admission).

In this clinical-empirical exploration the first objective was to estimate the life expectancy of patients having participated in the psychogeriatric reactivation programme. The second objective was to identify prognosticators of survival on admission.

Participants: Psychogeriatric patients (N=75), suffering from very mild to moderate cognitive function disorders in conjunction with psychiatric function disorders. Intervention: Interdisciplinary reactivation programme.

Measurements: General, functional and diagnostic patient characteristics assessed on admission for the psychogeriatric reactivation programme, and survival rate after discharge over a period of 7 years.

Results: The probability of survival for patients who were discharged from the psychogeriatric reactivation programme to their own homes or to a residential home with restricted support ('independent' group, N=53) was higher (1/HR=3.2) than for patients who were discharged to a nursing home ('dependent' group, N=22). The median survival period of the reference group (community-dwelling elderly people) was 95 months, that of the 'independent' group 35 months and that of the 'dependent' group 13 months. For the reactivated patients (N=75), gender, the Global Deterioration Scale, psychiatric function disorders and somatic comorbidity were of prognostic value. It was possible to account for 32% of the variance in survival after discharge.

Conclusion: The survival rate of the 'independent' group of patients was obviously higher (1/HR=3.2) than that of the 'dependent' group. There was no overlap in 95% CI of the median survival period after discharge. The results suggest that with respect to survival the two groups of psychogeriatric patients who participated in the reactivation programme differed definitely. Additionally, patients belonging to the 'independent' group had a greater chance to benefit form a reactivation programme. The prognostic patient characteristics for survival belonged to five domains (i.e. gender, cognitive function disorders, psychiatric function disorders, somatic comorbidity and caregiver system). The five dimensions are of clinical interest for optimizing the selection of patients who may derive most benefit from

a reactivation programme. The development of a valid prognostic instrument is a prerequisite for optimal medical decision making for such intervention pro-grammes, as is the analysis of cost-effectiveness.

5. Prevalence of psychiatric function disorders in psychogeriatric patients at referral to nursing home care; The relation to cognition, activities of daily living and general details

Systematic research shows that the prevalence of non-cognitive, psychiatric function disorders (PFDs) in psychogeriatric patients staying in a nursing home or home for the elderly percentages varies from 70% to 80%. It is not evident whether and to which degree the PFDs were present at the moment of referral or if the patients had acquired the PFDs during their length of stay in a nursing home or a home for the elderly. Aalten et al. (2003b) reported that of the patients who attended a policlinic for cognitive function disorders, 90% had PFDs. Literature on the prevalence of PFDs in psychogeriatric patients suffering from cognitive function disorders at the moment of referral to nursing home care is rather scarce.

PFDs play an important role in psychogeriatrics. They have negative effects on the quality of life of the psychogeriatric patients and also put a great burden on the caregiver system. In addition, these prognostic factors are important for early admission to an institution (nursing home) as well as for the outcome of psychogeriatric intervention programmes. For assessing psychiatric disorders in psychogeriatric patients Cummings et al. (1994) developed in the 1990s a valid and reliable instrument - the Neuropsychiatric Inventory (NPI). This instrument has already been applied in many studies (Aalten, 2004, 2003; Lyketsos et al., 2001; Wood et al., 2000). A Dutch version has been constructed and validated by Kat et al. (2002).

However, the relation of the PFDs as assessed by the NPI to the hallmarks of psychogeriatric patients - the cognitive function disorders and the related handicaps in activities of daily living (ADL) - is not obvious (Aalten, 2004; Tran et al., 2003). The same implies to relevant general details such as gender, age, marital status, domicile and type of primary caregiver. For the referral of psychogeriatric patients suffering from PFDs to specific intervention programmes it is of clinical interest to optimize the medical decision making process. To that end, insight in the at-referral prevalence and co-occurence of the PFDs and their relation to the cognitive function disorders and ADL handicaps is of relevance, combined with general details.

The objectives of this study were: (1) To estimate the prevalence and co-occurrence of PFDs in psychogeriatric patients suffering from cognitive function disorders at referral to clinical as well as non-clinical (transmural) psychogeriatric programmes; (2) It is expected that PFDs , both total and individual, are positively related to the cognitive function disorders as well as the ADL-handicaps; (3) Exploratively, the structure of the interrelationship of PFDs, cognitive function

disorders and ADL handicaps will be analysed. In addition, the general details and the structure to be identified will be described.

Methods: We studied patients aged $\geq$ 65 years (N=487), who were suspected to suffer from cognitive function disorders (MMSE $\leq$ 29) and were referred to trans-/intramural nursing home care in the Nieuwe Waterweg Noord region. General details, i.e. gender, age, marital status, domicile, primary caregiver, as well as PFDs (the Neuropsychiatric Inventory, NPI), cognition (MMSE) and ADL (Barthel Index, BI) were assessed.

Results: Mean score NPI was 3.6 (SD=2.3). Of the patients, 91.7% scored one or more NPI symptom; 81.6% two or more. Depression (43.9%), apathy (43.1%), anxiety (41.6%) and agitation/aggression (31.2%) had a high prevalence. The performance of the logistic regression models for total NPI score with MMSE, BI separately as well as combined with general details was minor. The results of the regression analyses for the individual NPI symptoms showed comparable low R^2 values; the explained a small proportion of the variance. However, in the PRINCALS analysis the MMSE and BI highly correlated with the cognitive dimension, and the NPI with the psychiatric dimension. The model fit was good; 82.6% of the variance was explained.

Conclusion: At the moment of referral to nursing home care, the prevalence and co-occurrence of PFDs was high. The four main NPI symptoms were depression, apathy, anxiety and agitation/aggression. NPI scores (total and per symptom) were relatively independent from MMSE, BI and general details. The PFDs – measured by the NPI – were a dimension on their own. Therefore, in psychogeriatrics it is of clinical relevance to think and act in terms of dimensions. Irrespective of a more rational psychopharmaceutical regime, this opens the door to the regular psychiatric domain for (psycho)therapeutic strategies, e.g. for depression and anxiety adapted to the kind and level of the cognitive function disorder of the psychogeriatric patient.

6.   Integrative psychotherapeutic nursing home programme to reduce multiple psychiatric symptoms of psychogeriatric patients and caregiver burden; a randomized controlled trial

Integrative psychotherapeutic programmes in nursing home care have never been tested in large-scale comprehensive studies.[10, 16, 27 - 30] For these reasons, we developed an integrative psychotherapeutic programme based on a problem-solving theoretical framework, called integrative reactivation and rehabilitation (IRR). In this chapter we reported the results of a RCT designed to test the effectiveness of IRR to reduce MPS in psychogeriatric patients who suffer from cognitive impairment or dementia, and burden of the caregiver. IRR was compared with UC in terms of mean differences on MPS and caregiver burden.

Participants: N = 168 (81 IRR; 87 UC). Patients had to meet DSM IV classification of dementia or amnestic disorders or other cognitive disorders. Additional inclusion criteria: MMSE $\geq$ 18 and $\leq$ 27; Barthel Index (BI) $\geq$5 and $\leq$ 19; Neuropsychiatric Inventory (NPI) $\geq$ 3.

Measurements: Primary outcome variable was MPS (NPI). Furthermore, caregiver burden and competence were measured. Assessments: T1 (intake), T2 (end of treatment), T3 (six months follow-up). Cohen's-d (C-d) was computed for mean differences (ITT). For confounding RRM was applied.

Results: From the perspective of the caregiver, in short term IRR showed up to 34% surplus effects on MPS; NPI-symptoms: 1.31 lower (C-d –0.53; P < 0.00) and NPI-sum-severity: 11.16 lower (C-d –0,53; P < 0.00). In follow-up effects sustained. On burden and competence of caregiver IRR showed surplus effects (up to 36%): N-emD: 3.78 (C-d –0.44; P < 0.01) and CB: 17.69 (C-d –0.63; P < 0.00) lower; CCL: 6.26 (C-d 0.61: P < 0.00) higher. In follow-up effects enlarged up to 50%. In RRM results demonstrated to be stable.

Conclusion: From the perspective of the caregiver, the application of IRR, based on person-oriented and problem-solving principles, was significantly two times more effective than usual care in reducing multiple psychiatric symptoms of psychogeriatric patients who suffer from cognitive impairment or dementia. On MPS of the patient, IRR showed a surplus diminishing effect at the end of treatment up to 34 %, and 30 % in six month follow-up. Moreover, IRR had a large positive effect on burden of the caregiver at end of treatment; up to 36%. In long term the surplus diminishing effect on burden of the caregiver even increased up to 50 %, while usual care had no effect at all. Moreover, one may expect that in countries with less well developed psychogeriatric nursing home care than in the Netherlands the surplus effect of IRR will be even substantially larger. This is an important and clinical relevant result, because both problems belong to the top three of experienced problems of dementia patients and their caregivers. Considering all available evidence, we recommend that usual (inter)national psychogeriatric nursing home care and perhaps other forms of care too incorporate integrative psychotherapeutic treatment. The same applies to the education programmes of the various involved disciplines. Future studies have to be performed to strenghten the evidence, preferably as blinded RCTs.

7.　Effect modification of integrative psychotherapeutic nursing home programme to reduce multiple psychiatric symptoms of psychogeriatric patients and caregiver burden; a randomized controlled trial

In the previous chapter we reported the results of a RCT designed to test the effectiveness of IRR to reduce MPS in psychogeriatric patients who suffer from cognitive impairment or dementia, and burden of the caregiver.

After all, it is clinically relevant to investigate whether specifically long term effects of IRR were modified by the level of cognitive functioning of the patient at baseline i.e. memory and selfcare and/or by type of dementia i.e. vascular dementia and alzheimer dementia.

The objective of this clinical-empirical study was to identify and estimate, whether long term effects of IRR on the two most relevant outcome variables (severity of the multiple psychiatric symptoms of the patient and general burden of the caregiver) were modified by cognitive functioning (memory and selfcare) and/ or by type of dementia (vascular and alzheimer).

Measurements: Primary outcome variable was MPS of the patient assessed by NPI.

Secondary outcome variables were caregiver burden and cognitive functioning. Assessments after intake (T1) and at six months follow-up (T3).

Statistics: Cohen's-d (C-d) was computed for mean differences. To predict long term improvement on MPS and caregiver burden multiple linear regression analysis was applied. As measure of model performance, multiple correlation squared (MR^2) was used.

Results: At six months follow-up, the severity of MPS of psychogeriatric patients showed significant effects with a moderate size in favour of IRR (9.91 lower than in UC). General caregiver burden was 24.76 lower, significantly in favour of IRR. Long term effects of IRR on severity of MPS, as well as on general burden of the caregiver were not significantly modified by level of cognitive functioning or type of dementia.

Conclusion: IRR was an integrative psychotherapeutic nursing home programme based on person-oriented and problem-solving principles. The significant beneficial effects of IRR compared to UC were not modified by level or type of cognitive disorders. This means that beneficial effects of IRR on the severity of multiple psychiatric symptoms of the patient and burden of the caregiver extended to a wide group of psychogeriatric patients who suffer from cognitive impairment or dementia, and their caregivers. Maybe a broader range of patients i.e. (psycho) geriatric patients suffering from a lower level of cognitive functioning and/or different type of cognitive disorder, can benefit from the IRR programme as well. These are important and clinical relevant results, because both topics are among the top three of problems experienced by dementia patients and their caregivers. [10] Considering all available evidence, usual psychogeriatric nursing home care and perhaps other forms of care as well, can now incorporate integrative psychotherapeutic treatment. The same applies to the education programmes of the various disciplines which are involved. Future studies have to be performed to strenghten the evidence, preferably as blinded RCTs.

8. Benefit of integrative psychotherapeutic nursing home programme to reduce multiple psychiatric symptoms of psychogeriatric patients and caregiver burden after six months follow-up; a randomized controlled trial

In this chapter we presented the results of a re-analysis of the effectiveness of IRR in terms of percentages of clinically relevant improved psychogeriatric patients who suffer from cognitive impairment or dementia as well as caregivers. The primary analysis regarded the mean differences between IRR and UC on continuous data of the primary and secondary outcome variables.

After all, it is relevant to estimate the percentages of patients and caregivers who showed clinically relevant improvement in IRR compared to usual care, especially at six months follow-up. Moreover, using an intention to treat (ITT) strategy offers the opportunity to calculate risk ratio's (RRs) and numbers needed to treat (NNTs), which can be compared to those of other interventions.[31, 32] At the end, performing a complete cases analysis (CC) allows a more realistic insight in the efficacy of IRR compared to usual care. Specifically, if there was a relatively high natural dropout, which is a well-known phenomenon in research on frail elderly. [17, 23 - 30] In case of no significant differences between dropouts in both arms of the study, results of a CC-analysis may present a more accurate estimation of the potential benefit of IRR. At the end, only patients and caregivers who fully participated in IRR programme can benefit completely of the offered interventions. In this re-analysis study - following Cummings - minimally, clinically relevant improvement was defined as more than 30 % improvement compared to the baseline value of the primary outcome variable, i.e. NPI-sum-severity. [33, 34] This corresponds well -in this study as well as in general- with a half standard deviation or more of the baseline value. [35, 36] The objective of this clinical-empirical study was to re-analyse the RCT with respect to long term benefit of IRR compared to UC in terms of percentages of clinically relevant improved patients on psychiatric symptoms and of caregivers on burden.

Measurements: Primary outcome variable: change in MPS after six months follow-up with NPI. Secondary outcome variables: Caregiver burden and competence by NPI-emotional distress, Caregiver burden, and Caregiver Competence List. Assessments after intake (T1); after six months follow-up (T3).

Statistics: Intention to treat-analysis on RRs (incl. NNTs) and complete cases analysis (CC) on ORs based on percentages of improved patients and caregivers ($\geq$ 0.5 sd of baseline value).

Results: IRR showed a significant positive effect on NPI-cluster hyperactivity (RR 2.64;

95% CI: 1.26 to 5.53; NNT: 4.07). For psychogeriatric patients who fully completed IRR the results were more pronounced with significant ORs of 2.80 on number of NPI-symptoms and 3.46 on NPI-sum-severity; in IRR up to 76 % patients improved . Regarding caregiver burden, competence of caregiver turned out to be significant beneficial in IRR (RR 2.23; 95% CI: 1.07 to 4.62; NNT 5.07). In complete cases analysis the ORs of percentages of improved caregivers were

significantly in favour of IRR on emotional distress, general burden and competence (range ORs: 2.40 to 4.18) with high percentages of improved caregivers up to 71%.

Conclusion: At six months follow-up IRR showed a significantly higher probability of clinically relevant improvement with a relatively small NNT (four) on multiple psychiatric symptoms in psychogeriatric patients who suffer from cognitive impairment or dementia. The results (76% improved patients) were more pronounced for those who fully completed the IRR programme. The same applies to the higher probability of IRR to improve NPI-related and general burden as well as competence of the caregiver (NNT of five and for those who fully participated 71% improved caregivers). Compared to donepezil, memantine and CBT, the NNTS of IRR were relatively low. Considering all available evidence, usual (inter)national multidisciplinary nursing home care and likely ambulant care programmes are advised to incorporate integrative psychotherapeutic treatment as well as psychiatric strategies. Future studies have to be performed to strenghten the evidence, preferably as blinded RCTs.

9. To identify prognostic factors for a favourable long-term outcome of an integrative psychotherapeutic nursing home programme to reduce multiple psychiatric symptoms of psychogeriatric patients and caregiver burden; a clinical-empirical study

In the previous chapter we explored the differences between IRR and UC on the percentages of clinically relevant improved psychiatric patients who suffer from cognitive impairment or dementia as well as caregivers ; $\geq$ half sd of the baseline value. [33 - 36] In this chapter the objective was to identify prognostic factors which can predict the likelihood of patients and caregivers to benefit from IRR and which patients from UC. In addition to the identification of these prognostic factors, it is of clinical interest to optimize medical decision making, mainly as decision making is often based on irrational factors. [37 - 39] In literature many decision rules are considered. [40 - 43] In this study three decision rules will be applied. The first decision rule (highest Mean Average-rule) is aimed to calculate the average percentage improvement in either intervention. The second rule concerns to minimize the maximum possible loss ('MINIMAX'-rule); this latter rule attempts to avoid the risk of missing benefit by comparing the highest difference between the interventions on each score over all outcome variables; than choose for the intervention with the lowest loss of benefit. The third decision rule concerns the 'MAXIMIN'-rule which implies that the patient will be assigned to the intervention with the lowest level of avoidable risk by comparing the difference between the interventions of the lowest score on all outcome variables.

The objective of the clinical-empirical study was to identify prognostic potentialities of biographic characteristics as well as all baseline variables on five selected

outcome variables. Three of the selected outcome variables showed a significant effect in the RCT i.e. severity of multiple psychiatric symptoms of the patient registrated by the caregiver, general burden and competence of the caregiver. Memory and self-care of the patient were two important background outcome variables. The prognostic potentialities were applied to long term (after six months follow-up). In addition, as the number of outcome variables equaled five, we have explored opportunities for building models to optimize decision making, in which the performances of MEAN AVERAGE, MINIMAX- , and MAXIMIN-decision rules were compared.

Measurements: Primary outcome variable was MPS of the patient. In view of clinically relevant background information of the effect of IRR, burden and competence of the caregiver and cognitive functioning (i.e. memory and self-care) of the patient were selected as secondary outcome variables. Two assessments: T1 (intake) and T3 (six months follow-up).

Statistics: Improvement was defined as a difference of a half sd or more of the baseline value. To identify prognostic potentialities of baseline characteristics logistic regression analysis was applied. To optimize decision making three decision methods were selected from literature and applied.

Results: In the overall combined prognostic models alzheimer dementia showed significant prognostic qualities for improvement on NPI-sum-severity (OR 3.01). The same holds true for IRR on general burden and competence of caregiver (OR 2.29 and 3.34). The prognostic models for NPI-sum-severity as well as competence showed a substantial explained variance (R^2 0.39 respectively 0.23). The others, especially for memory and self-care, were low. In general, the robustness of the prediction models was stable. Applying three decision rules, IRR resulted on five outcome variables as indicated.

Conclusion: Prognostic modeling, specifically of positive change on severity of multiple psychiatric function disorders of psychogeriatric patients who suffer from cognitive impairment or dementia and on both general burden and competence of caregivers was feasible. The inclusion of a broader range of psychogeriatric patients i.e. lower or higher scores on MMSE and BI, in combination with specific interventions to enhance cognitive functioning, seems justified. Applying three decision rules, all resulted in IRR as indicated intervention. Although the performances of the prognostic models found was considered moderate, this strategy is promising. Therefore, designing and conducting a study tailored to timely identifying (psycho)geriatric patients who likely benefit from an enriched IRR programme is recommended, preferably in a large scale multicentred blinded study comprising a sufficient sample size.

10.   Economic evaluation of an integrative psychotherapeutic nursing home programme to reduce multiple psychiatric symptoms of psychogeriatric patients and caregiver burden; a randomized controlled trial

Irrespective of beneficial clinical effects it is important to take into account the economic aspects, an economic evaluation.[33-36] In this paper we report the results of an economic evaluation of a RCT in which IRR was compared to usual multi-disciplinary nursing home care. The two objectives of this economic evaluation were to assess the cost-utility as well as the cost-effectiveness on six outcome variables of IRR compared to usual care (UC).

Measurements: Primary outcome variable: change in MPS after six months follow-up with NPI. Secondary outcome variables: General burden of the caregiver (CB), competence of caregiver (CCL), cognitive functioning (MMSE), selfcare (BI) and quality of life (EQ5D) of the patient. There were two assessments: after intake (T1) and after six months follow-up (T3). Measurements of costs were conducted every 8 weeks from the moment of inclusion (T0) over the preceding last four weeks (TiC-P). The economic evaluation spans an interval from the start of intervention (T1) up until 40 weeks.

Statistics: Monte Carlo Markov Chain (MCMC) approach to impute the missing values.

The cost-utility was evaluated by relating the difference in direct medical costs per patient receiving either IRR or UC to the difference in terms of Quality Adjusted Life Years gained (QALY), which yielded a cost per QALY estimate.

Complete case analysis (CC) was applied in comparison of the differences in total costs combined with the differences in effects i.e. Incremental Cost-Effectiveness Ratio (ICER).

Results: Applying multiple imputation (MI), at 40 weeks, IRR turned out to be significantly more (cost-)expensive than UC; the costs for IRR were € 4.572,-- (i.e. € 53,-- per day) higher than those for UC (95 % CI: 364.24 to 8797.76). At the same time the number of QALYs was 0.02 lower (non-significant) in IRR (95% CI:-0.10 to 0.05).

So, in the MI analysis after 40 weeks UC could achieve the same amount of QALYs, albeit at significant lower costs. According to the ICER-method IRR was significantly more effective on NPI-sum-severity of the patient (€ 320,-- per point), caregiver burden (€ 130,-- per point) and caregiver competence (€ 540,-- per point). Irrespective of type of intervention improved patients were significantly more (cost-)expensive with respect to NPI-sum-severity of the patient, general burden of the caregiver and competence of the caregiver. Improving seemed inextricably related to more costs, together with relatively high numbers of improved patients and caregivers in IRR. On NPI-sum-severity, general burden and competence of the caregiver comprised after six month follow-up clearly more significantly improved patients and caregivers than UC.

Conclusion: On QALYs, no significant differences were found, while total medical costs of psychogeriatric patients in IRR were significantly higher. In contrast, fully participating patients and their caregivers improved in IRR significantly more on mean scores of the primary outcome variable i.e. severity of multiple psychiatric symptoms of the patient and of the secondary outcome variables i.e. general caregiver burden and competence of the caregiver, with ICERS varying from

€ 130.-- to € 540.--. The large discrepancy between QALYs and ICERs found in this study on psychogeriatric patients may mean a drawback in cost-utility studies in psychogeriatrics. It demands further research on validation of EQ5D in intervention studies with psychogeriatric patients. Considering all available evidence, the surplus costs of IRR may be considered acceptable when the beneficial effects were taken into account on the high societal costs of suffering from multiple psychiatric symptoms of psychogeriatric patients and high burden of caregivers.To optimize the cost-utility and cost-effectiveness of IRR, the construction of a tool enabling to identify suitable psychogeriatric patients and caregivers for IRR is of high economical and clinical interest. Such a tool would contribute to optimize medical decision making based on an economical evaluation.

11.   General summary

In this dissertation the (cost-)effectiveness is tested of an integrative psychotherapeutic nursing home programme (IRR) to reduce multiple psychiatric symptoms of psychogeriatric patients who suffer from cognitive impairment or dementia as well as burden of caregivers. From the perspective of the caregiver, IRR showed a two times larger mean reduction on number and severity of psychiatric symptoms of psychogeriatric patients than usual nursing home care; actually up to 61% reduction after six months follow up. Of the patients who fully completed the IRR programme up to 76% improved 30% or more compared to their scores at baseline. In addition, mean burden of caregivers reduced up to 50% after six months follow-up, while usual care had no effect at all. Of the caregivers who fully completed the IRR programme up to 71% improved 30% or more compared to their scores at baseline. The surplus total costs for improvement were relatively low i.e. € 53,-- per day (about half of a CVA-unit: € 102,--). As in psychogeriatric patients who suffer from cognitive impairment or dementia the prevalence of two or more psychiatric symptoms is 80% and 70-80% of caregivers are moderately to heavily overburdened, implementation of integrative psychotherapeutic treatment in multidisciplinary usual nursing home care for psychogeriatric patients should be facilitated. In addition, future studies have to be performed to strengthen the evidence, preferably as blinded RCTs with a long follow-up period.

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P.M.: For further literature references see specific chapters.

Algemene samenvatting

1.   Inleiding

De prevalentie van twee of meer psychiatrische symptomen zoals depressie, angst, paranoia en agressie bij psychogeriatrische patiënten die lijden aan cognitieve stoornissen of dementie is 80%. Multipele psychiatrische symptomen (MPS) be-invloeden het cognitief functioneren en de kwaliteit van leven van deze patiënten in negatieve zin. Ze betekenen tevens een belasting voor hun mantelzorgers; on-geveer 70 tot 80% van de mantelzorgers voelt zich matig tot zwaar belast. Verder zijn MPS belangrijke voorspellers van een verpleeghuisopname. Deze thema's staan in de top drie van meest ervaren problemen bij dementiepatiënten en hun mantelzorgers.

Het gebruik van psychofarmaca voor de behandeling van MPS bij psychoge-riatrische patiënten is wijdverbreid. In de praktijk blijkt echter de werking van deze medicijnen beperkt en hebben ze vaak schadelijke bijwerkingen, zoals (a) typische antipsychotica. Integratieve psychotherapeutische programma's worden bijna niet aangeboden bij psychogeriatrische patiënten.

Uit eerder onderzoek is gebleken, dat als er sprake is van individuele psychi-atrische symptomen zoals depressie en angst, psychotherapeutische behande-ling effect kan hebben. Echter, psychotherapeutisch interveniëren op de MPS bij psychogeriatrische patiënten die lijden aan cognitieve stoornissen of dementie is gecompliceerd. Dit heeft enerzijds te maken met de complexiteit van de psychia-trische aandoeningen zelf, en anderzijds met cognitieve stoornissen, somatische co-morbiditeit en sociale problemen, zoals relatieproblemen en eenzaamheid. Om deze redenen ontwikkelden en onderzochten wij een integratief psychothe-rapeutisch verpleeghuiszorgprogramma genaamd: Integratieve Reactivering en Rehabilitatie (IRR).

In deze nederlandstalige, algemene samenvatting presenteren wij de samenvattin-gen van een casusbeschrijving, enkele observationele studies en een Randomized Controlled Trial (RCT). Verder worden methodologische vraagstukken, implicaties voor professionals, managers en beleidsmedewerkers en tot slot aanbevelingen ter verbetering van IRR behandeld. Dit hoofdstuk sluit af met een samenvatting.

2.   Palliatieve zorg in de chronische psychogeriatrische zorg: een gevalsbeschrijving

Aan de hand van een gevalsbeschrijving wordt de relevantie aangetoond van psycho-sociale interventies binnen de palliatieve zorg in de laatste levensfase van psychogeriatrische patiënten lijdend aan multipele psychiatrische symptomen. De gevalsbeschrijving is een gedetailleerde weergave van het psycho-sociale in-terventieproces zoals plaatsvindt op de reactiveringsafdeling van een Nederlands psychogeriatrisch verpleeghuis. Wij publiceerden in 2009 een update van de be-schrijving van IRR. Deze publicatie is toegevoegd als bijlage 1 aan deze disserta-tie.

Specifieke deskundigheid is zeer relevant om de palliatieve zorg goed af te stemmen op de noden en behoeften van de betreffende patiënt. Door toepassing van de vier hoofd-dimensies van de Dynamische Systeem Analyse, d.w.z. Cognitief functioneren, Psychologische functies, Sociale omgeving en Somatiek, worden professionals ondersteund om een integraal perspectief te hanteren, dat gericht is op de behandeling van zowel de psycho-sociale behoeften van terminale psychogeriatrische patiënten en hun familieleden, als de somatiek. (Bakker, 1997)

Om de waarde van de DSA-methode bij palliatieve zorg aan psychogeriatrische patiënten met multipele psychiatrische symptomen aan te tonen, is verder wetenschappelijk onderzoek gewenst. Op basis van onderzoek kan een prognostisch profiel worden ontwikkeld voor psychogeriatrische patiënten lijdend aan multipele psychiatrische symptomen uitgaande van wie het meest gebaat is bij een specifiek programma voor palliatieve zorg.

3. Psychogeriatrische reactivering in een psychogeriatrisch verpleeghuis; een klinisch-empirisch, explorerend onderzoek

De cognitieve functiestoornissen van psychogeriatrische patiënten zijn divers en chronisch van aard. Ze treden vaak op in samenhang met stemmings- en gedragsproblemen (multipele psychiatrische symptomen), sociale problemen en somatische comorbiditeit en leiden vaak tot functionele beperkingen (Rubin and Kinscherf, 1989; Teri et al., 1990; Bozzola et al., 1992; Chatterjee et al., 1992; Ballard et al., 1995).

Vanwege deze complexe co-pathologie bestaat er een grote behoefte aan specifieke interventieprogramma's (Colerick and George, 1986; Steele et al., 1990; McNaughton et al., 1995). Deze interventies zijn gericht op het (opnieuw) verkrijgen of het stabiliseren van de autonomie van de patiënt en/of en het verhogen van diens kwaliteit van leven (Mortimer et al., 1992; Gray and Fenn, 1993). Het is van belang dat de effectiviteit van dergelijke programma's wordt onderzocht (Lyons et al., 1997; Bakker and Das, 1996) en dat de resultaten ervan worden gebruikt om dìe patiënten te selecteren die hierbij het meest gebaat zijn (Rubenstein et al., 1964; Colerick and George, 1986; Narain et al., 1988).

Het doel van dit onderzoek was om bij psychogeriatrische patiënten met multipele psychiatrische symptomen prognostische kenmerken vast te stellen die bepalend zijn voor de kans op ontslag uit een psychogeriatrisch reactiveringsprogramma. Op deze manier kan de selectie van patiënten die gebaat zijn bij een dergelijk reactiveringsprogramma worden geoptimaliseerd.

Onderzoeksmethode: Een retrospectief, klinisch, empirisch onderzoek in een Nederlands verpleeghuis. Een groep van 102 patiënten, die verspreid over de tijd deelnamen aan een psychogeriatrisch reactiveringsprogramma en die voldeden aan de in- en exclusiecriteria, werd retrospectief onderzocht. De biografische, functionele en diagnostische kenmerken werden gemeten bij start van de interventie.

Resultaten: De biografische kenmerken van de patiënten in het reactiveringsprogramma bleken geen prognostische betekenis te hebben. Echter, functionele kenmerken zoals GDS, HI en ADL-score bleken wel van prognostische betekenis. Diagnostische kenmerken werden onderscheiden op vier domeinen: cognitieve functiestoornissen, psychiatrische symptomen, sociale omgeving (mantelzorg) en somatische co-morbiditeit. De diagnostische classificatie van cognitieve functiestoornissen (uitgezonderd delirium) bleek nauwelijks van prognostische belang.

Conclusie: Het reactiveringsprogramma lijkt veelbelovend voor kwetsbare oudere psychogeriatrische patiënten met multipele psychiatrische symptomen, maar zonder ernstige cognitieve functiestoornissen of ernstig tekortschietende zelfzorg. Het bleek mogelijk om op basis van opnamekenmerken een inschatting te maken van de kans op ontslag. In een volgend onderzoek zouden functionele en diagnostische patiëntkenmerken prospectief moeten worden geregistreerd. Om hun prognostische belang met meer zekerheid aan te tonen dient een wetenschappelijk onderzoek volgens een RCT te worden uitgevoerd.

4.   Levensverwachting na psychogeriatrische reactivering

Het sterftecijfer van psychogeriatrische patiënten met cognitieve functiestoornissen (bijv. delirium, dementie, Korsakov, amnestische en andere cognitieve stoornissen) is hoger dan dat van de normale populatie (1 – 3). Onafhankelijk van de somatische pathologie, spelen naast de cognitieve functiestoornissen vaak ook psychiatrische functiestoornissen, zoals stemmings- en gedragsproblemen een rol. Deze stoornissen houden niet alleen verband met een lagere kwaliteit van leven en de behoefte aan langdurige zorg, maar ook met een kortere levensverwachting. Om de patiënten te onderscheiden die naar verwachting het meest gebaat zijn bij specifieke, intensieve interventies, die gericht zijn op het terugdringen van de negatieve gevolgen van multipele psychiatrische symptomen, is het van klinisch belang om prognostische indicatoren te bepalen die de overlevingsduur van deze patiënten kunnen voorspellen. Om de medische besliskunde te optimaliseren is het van klinisch belang dat patiënten die het meest gebaat zijn bij interventieprogramma's reeds bij aanvang (bijv. bij toewijzing) kunnen worden onderscheiden.

De eerste vraagstelling van dit klinisch-empirisch, explorerende onderzoek was het meten van de levensverwachting van patiënten die hadden deelgenomen aan het psychogeriatrisch reactiveringsprogramma. De tweede vraagstelling betrof het bij opname identificeren van prognostische determinanten voor overleving.

Onderzoeksgroep: Psychogeriatrische patiënten (N=75) met lichte tot matige cognitieve functiestoornissen en multipele psychiatrische symptomen. De interventie was een interdisciplinair psychogeriatrisch reactiveringsprogramma.

Metingen: Biografische, functionele en diagnostische patiëntkenmerken werden geregistreerd bij opname in het psychogeriatrische reactiveringsprogramma. De overlevingsduur werd na ontslag over een periode van zeven jaar gemeten.

Resultaten: De kans op overleven voor de patiënten die uit het psychogeriatrisch reactiveringsprogramma naar huis of een verzorgingshuis werden ontslagen (de 'onafhankelijke' groep, N=53) was groter (1/HR=3.2) dan voor patiënten die werden doorgeplaatst naar een verpleeghuis (de 'zorgafhankelijke' groep, N=22). De mediaan van de overlevingsduur van de controle groep (thuiswonende ouderen) was 95 maanden; die van de 'onafhankelijke' groep 35 maanden en de mediaan van de 'zorgafhankelijke' groep was 13 maanden. Voor de gereactiveerde patiënten (N=75), waren sekse, de score op de Global Deterioration Scale, psychiatrische functiestoornissen en somatische co-morbiditeit van prognostisch belang. Van de variantie in overleving na ontslag kon 32% door deze prognostische determinanten worden verklaard.

Conclusie: De overlevingsduur van de 'onafhankelijke' groep patiënten was duidelijk langer (1/HR=3.2) dan van de 'zorgafhankelijke' groep. Er was geen overlap in de 95% betrouwbaarheidsintervallen van de mediaanwaarde van de overlevingsduur na ontslag. De resultaten laten zien dat met betrekking tot de overlevingsduur er fundamentele verschillen bestonden tussen de twee groepen psychogeriatrische patiënten die aan het reactiverings-programma deelnamen. Daarnaast hadden de patiënten uit de 'onafhankelijke' groep een grotere kans om baat te hebben bij het reactiveringsprogramma. De prognostische kenmerken die van betekenis waren voor de overlevingsduur konden worden ingedeeld in vier dimensies [(cognitieve functiestoornissen, psychiatrische symptomen, somatische co-morbiditeit en sociale omgeving (het mantelzorg-systeem)]. Deze vier dimensies zijn van klinisch belang voor de selectie van patiënten die de meeste baat hebben bij het reactiveringsprogramma. De ontwikkeling van een valide prognostisch instrument is een voorwaarde voor optimale medische besliskunde op het terrein van dergelijke interventieprogramma's, evenals de analyse van de kosteneffectiviteit.

5. Prevalentie van psychiatrische symptomen bij psychogeriatrische patiënten bij verwijzing naar verpleeghuiszorg; de relatie met cognitie, activiteiten dagelijks leven en biografische kenmerken

Bij systematisch onderzoek naar de prevalentie van niet-cognitieve, multipele psychiatrische symptomen (MPS) bij psychogeriatrische patiënten in een verpleeg- of verzorgingshuis worden percentages tussen de 70% en de 80% gevonden. Het is niet duidelijk òf, en in welke mate, er sprake was van deze MPS bij verwijzing naar verpleeghuiszorg en evenmin of de patiënten gedurende hun verblijf in verpleeg- of verzorgingshuis MPS ontwikkelden. Aalten et al. (2003b) vonden dat er bij 90% van de patiënten die een polikliniek voor cognitieve functiestoornissen bezochten sprake was van MPS. Er is nog weinig onderzoek gedaan naar de prevalentie van MPS bij psychogeriatrische patiënten met cognitieve functiestoornissen op het moment van verwijzing naar verpleeghuiszorg. MPS spelen een

belangrijke rol in de psychogeriatrie. Ze hebben een negatief effect op de kwaliteit van leven van de psychogeriatrische patiënt en zijn tevens belastend voor het mantelzorgsysteem. Bovendien zijn het belangrijke prognostische factoren voor zowel vroegtijdige opname in een instelling (verpleeghuis), als voor het al dan niet succesvol zijn van psychogeriatrische interventieprogramma's. Om bij psychogeriatrische patiënten psychiatrische stoornissen te kunnen meten, ontwikkelde Cummings et al. (1994) in de negentiger jaren een betrouwbaar en valide instrument: de Neuropsychiatrische Vragenlijst (NPI). Dit instrument is reeds in verschillende onderzoeken gebruikt (Aalten, 2004, 2003; Lyketsos et al., 2001; Wood et al., 2000). Een Nederlandstalige versie is door Kat et al. (2002) ontworpen en gevalideerd. Echter, de relatie tussen de met de NPI gemeten MPS en de meest opvallende eigenschappen van psychogeriatrische patiënten, zoals cognitieve functiestoornissen en gerelateerde beperkingen in activiteiten dagelijks leven, is niet direct duidelijk (Aalten, 2004, Tran et al., 2003). Hetzelfde geldt voor biografische kenmerken als sekse, leeftijd, burgerlijke staat, woonplaats en de hoedanigheid van de mantelzorger. Met het oog op de verwijzing van psychogeriatrische patiënten met MPS naar specifieke interventieprogramma's, is het van klinisch belang om het proces van medische besliskunde te optimaliseren. Ten behoeve hiervan is inzicht nodig zowel in de prevalentie, respectievelijk het tegelijkertijd optreden van MPS als hun relatie met cognitieve functiestoornissen en ADL-beperkingen, in combinatie met biografische kenmerken.

De vraagstellingen in dit onderzoek waren:
1. Het meten van de prevalentie en het tegelijkertijd optreden van MPS bij psychogeriatrische patiënten met cognitieve functiestoornissen op het moment van verwijzing naar klinische en transmurale psychogeriatrische programma's;
2. De verwachting dat MPS, afzonderlijk en in totaal, sterk samenhangen met cognitieve functiestoornissen en ADL-beperkingen;
3. Een exploratieve analyse van de structuur van de onderlinge samenhang tussen MPS, cognitieve functiestoornissen en ADL-handicaps.

Tenslotte zullen het belang van biografische kenmerken en de gevonden structuur worden beschreven.

Onderzoeksmethode: Onderzocht werden patiënten vanaf 65 jaar (N=487), bij wie vermoedelijk sprake was van cognitieve functiestoornissen (MMSE < 29) en die werden verwezen naar trans- of intramurale verpleeghuiszorg in de regio Nieuwe Waterweg Noord.

Geregistreerd werden biografische kenmerken zoals sekse, leeftijd, burgerlijke staat, woonplaats en zorgwaarnemer. Verder werden MPS (Neuropsychiatrische Vragenlijst, NPI), cognitie (MMSE) en ADL (Barthel Index, BI) gemeten.

Resultaten: De gemiddelde score op de NPI was 3.6 (SD=2.3). Het percentage patiënten dat één of meer NPI symptomen vertoonde was 91.7%. De prevalentie van depressie (43.9%), apathie (43,1%), angst (41,6%) en agitatie/agressie (31,2%)

was hoog. De voorspellingswaarde van de logistische regressie modellen van de totale NPI-score door MMSE, BI afzonderlijk en in combinatie met biografische kenmerken was laag. Regressie- analyse van de individuele NPI-symptomen leidde tot een vergelijkbaar resultaat met lage R^2-waarden; slechts een beperkt deel van de variantie werd verklaard. Echter in de PRINCALS-analyse bleken MMSE en BI hoog gecorreleerd op de cognitieve dimensie en de NPI op de psychiatrische dimensie. De 'model-fit' was goed; 82,6% van de variantie werd verklaard.

Conclusie: Op het moment van verwijzing van psychogeriatrische naar verpleeghuiszorg is de prevalentie van multipele psychogeriatrische symptomen (MPS) hoog. Verder treden ze vaak in onderlinge samenhang op. De vier belangrijkste NPI-symptomen zijn depressie, apathie, angst en agitatie/agressie. NPI-scores (totaal en per symptoom) blijken relatief onafhankelijk te zijn van MMSE, BI en biografische kenmerken. De MPS die werden gemeten door de NPI vormden een aparte dimensie. Om die reden is het in de psychogeriatrie van klinisch belang om te denken en te handelen in termen van dimensies. Onafhankelijk van een weloverwogen psychofarmaca beleid, opent dit de weg naar het reguliere psychiatrische domein van (psycho)therapeutische strategieën; bijvoorbeeld voor de behandeling van angst en depressie met aanpassingen voor het type cognitieve stoornis en het niveau van cognitief functioneren van de psychogeriatrische patiënt.

Om meer zekerheid te verkrijgen over de stabiliteit van deze bevindingen hebben wij in 2007 een replicatiestudie uitgevoerd bij een andere doelgroep, namelijk patiënten van een geheugenpoli in het ziekenhuis. Deze publicatie is toegevoegd als bijlage 2 aan deze dissertatie. De resultaten waren in nog iets sterkere mate terug te vinden in dit replicatie-onderzoek dan in de oorspronkelijke studie.

6. Een integratief psychotherapeutisch verpleeghuisprogramma om meervoudige psychiatrische symptomen bij psychogeriatrische patiënten en de belasting van mantelzorgers te verminderen; een gerandomiseerd en gecontroleerd onderzoek.

Er is nauwelijks grootschalig onderzoek gedaan naar de resultaten van integratieve psychotherapeutische programma's in de verpleeghuiszorg. Om deze reden ontwikkelden wij een integratief psychotherapeutisch programma, genaamd Integratieve Reactivering en Rehabilitatie (IRR), dat gebaseerd is op een persoonsgeoriënteerd en probleemoplossend theoretisch kader. In dit hoofdstuk wordt gerapporteerd over de resultaten van een RCT, opgezet om de effectiviteit van IRR op MPS bij psychogeriatrische patiënten die lijden aan cognitieve functiestoornissen of dementie en op de belasting van hun mantelzorgers te meten. IRR werd vergeleken met reguliere (verpleeghuis)zorg (UC) wat betreft gemiddelde verschillen op aantal en ernst van de MPS en mantelzorg-belasting.

Onderzoeksgroep: N = 168 (81 IRR; 87 UC). De patiënten moesten voldoen aan de criteria van de DSM IV-classificatie van dementieën, amnestische stoornissen

en overige cognitieve stoornissen. Overige inclusiecriteria waren: MMSE $\geq$ 18 en $\leq$ 27; Barthel Index (BI) $\geq$ 5 en $\leq$ 19; Neuropsychiatrische (NPI) $\geq$ 3.

Metingen: De primaire uitkomstvariabele was MPS gemeten met de NPI (aantal en ernst van de symptomen). Verder werden als secundaire uitkomstvariabelen de belasting en competenties van de mantelzorgers gemeten. De metingen vonden plaats op T1 (intake), T2 (einde behandeling), T3 (zes maanden na einde behandeling). Over de gemiddelde verschillen werd Cohen's-d (C-d) berekend (ITT). Om te corrigeren voor confounding werd Random Regression Modelling (RRM) toegepast.

Resultaten: Vanuit het perspectief van de mantelzorger had IRR op de korte termijn een 34% surplus effect op de MPS van de patiënt; aantal NPI-symptomen was 1.31 lager (C-d –0.53; p<0.00) en de totale ernst-score NPI van de patiënt was 11.16 lager (C-d –0.53; p<0.00). Op de lange termijn werden vergelijkbare resultaten gemeten. Verder had IRR eveneens een surplus verlagend effect op de belasting en surplus verhogend effect op de competenties van de mantelzorgers (tot 36% meer): 'NPI-emotionele belasting': 3.78 (C-d –0.44; p,0.01) lager en de 'algemene belasting': 17.69 (C-d –0.63; p<0.00) lager. 'Competenties': 6.26 (C-d 0.61: p<0.00) hoger. Op de lange termijn namen de positieve effecten toe tot 50%. Bij de RRM-analyse bleven deze resultaten behouden.

Conclusie: IRR is een integratief psychotherapeutisch verpleeghuiszorgprogramma, gebaseerd op persoons-georiënteerde en probleemoplossende principes. IRR bleek vanuit het perspectief van de mantelzorger in vergelijking met reguliere zorg significant twee keer zo effectief te zijn om multipele psychiatrische symptomen bij psychogeriatrische patiënten die lijden aan cognitieve stoornissen of dementie te verminderen. IRR had een surplus effect op de MPS bij de patiënten; nl. een extra reductie van 34% aan het einde van de behandeling en van 30% zes maanden na einde behandeling. Bovendien had IRR een groot extra positief effect op de belasting van de mantelzorger aan het einde van de behandeling; nl. oplopend tot 36%. Op de lange termijn liep het surplus reducerend effect op de belasting van de mantelzorger op tot 50%, terwijl de reguliere zorg hierop vrijwel geen effect had. Het is te verwachten dat het surplus effect van IRR in andere landen met minder ver ontwikkelde psychogeriatrische verpleeghuiszorg dan in Nederland zelfs nog groter is.

Het gaat hier om een belangrijke en klinisch relevante bevinding, omdat beide problemen (MPS van de patiënt en belasting van de mantelzorger) in de top drie staan van door dementiepatiënten en mantelzorgers als meest ernstig ervaren problemen. Alle bewijs tot nu toe overziend, zouden reguliere (inter)nationale extra- en intramurale verpleeghuiszorg en mogelijk ook andere zorgvoorzieningen integratieve psychotherapeutische behandeling in hun aanbod moeten opnemen. Hetzelfde geldt voor opleidingsprogramma's ten behoeve van de diverse betrokken disciplines. Toekomstige onderzoeken om de bewijskracht te versterken, dienen bij voorkeur uit te worden gevoerd als geblindeerde RCT's.

7. **Effectmodificatie van een integratief psychotherapeutisch verpleeghuiszorgprogramma om multipele psychiatrische symptomen bij psychogeriatrische patiënten en de belasting van mantelzorgers te verminderen: een gerandomiseerd, gecontroleerd onderzoek**

In het vorige hoofdstuk werd gerapporteerd over de resultaten van een RCT, die was opgezet om de effectiviteit van IRR op MPS bij psychogeriatrische patiënten die lijden aan cognitieve stoornissen of dementie en op de belasting van de mantelzorger te onderzoeken.

Het is van klinisch belang om te onderzoeken of met name de lange termijn effecten van IRR beïnvloed worden door de bij de start van het onderzoek gemeten ernst van de cognitieve functiestoornissen bij de patiënt (met name het geheugen, de zelfzorg) en/of het type dementie, met name vasculaire of Alzheimer dementie.

De vraagstelling binnen dit klinisch-empirische onderzoek was te onderzoeken of de lange termijn effecten van IRR op de belangrijkste twee uitkomstvariabelen (ernst van de multipele psychiatrische symptomen van de patiënt en de algemene belasting van de mantelzorger) werden beïnvloed door de ernst van de cognitieve functiestoornissen (geheugen en zelfzorg) en/of door type dementie (vasculair of Alzheimer) en in welke mate hiervan sprake was.

Metingen: De primaire uitkomstvariabele was de ernst-score op de NPI van de patiënt. De NPI was afgenomen bij de mantelzorger. De secundaire uitkomstvariabelen waren de belasting van de mantelzorger en het cognitief functioneren. De metingen vonden plaats bij start onderzoek (T1) en zes maanden na einde behandeling (T3).

Statistische analyse: Om de gemiddelde verschillen te berekenen werd gebruik gemaakt van Cohen's-d (C-d). Om de verbeteringen op de MPS en de belasting van de mantelzorg op de lange termijn te kunnen voorspellen werd gebruik gemaakt van multiple lineaire regressie.

Het kwadraat van de multiple correlaties (MR²) werd gebruikt als maat voor de model performance.

Resultaten: Zes maanden na einde behandeling bleek er een significant gunstig effect op de ernst van MPS bij psychogeriatrische patiënten (9.91 lager dan in de reguliere zorg). De algemene belasting van de mantelzorger was 24.76 keer lager, significant in het voordeel van IRR. De lange termijn effecten van IRR op zowel de ernst van de MPS van de patiënt, als de algemene belasting van de mantelzorger, werden niet significant beïnvloed door de ernst van de cognitieve functiestoornissen of het type dementie van de patiënt.

Conclusie: IRR bestond uit een integratief psychotherapeutisch verpleeghuiszorgprogramma, gebaseerd op persoons-georiënteerde en probleemoplossende principes. De significant gunstige effecten van IRR in vergelijking met de reguliere zorg werden niet beïnvloed door ernst of type cognitieve stoornis. Dit betekent dat de gunstige effecten van IRR op de ernst van de multipele psychiatrische symptomen van de patiënt en de belasting van de mantelzorg van toepassing zijn

op een brede groep psychogeriatrische patiënten en hun mantelzorgers. Wellicht kan een bredere doelgroep (psycho)geriatrische patiënten profiteren van IRR, met name patiënten lijdend aan ernstigere functiestoornissen (MMSE $\geq$ 12 - < 18) of andere type cognitieve stoornissen (bijv. CVA-gerelateerd of na een ongeval). Het gaat hier om een belangrijke en klinisch relevante bevinding, omdat beide problemen in de top drie staan van de door dementiepatiënten en hun mantelzorgers als meest ernstig ervaren problemen. Al het beschikbare bewijs overziend, zouden reguliere (inter)nationale extra- en intramurale verpleeghuiszorg en mogelijk ook andere zorgvoorzieningen, integratieve psychotherapeutische behandeling in hun aanbod moeten opnemen. Hetzelfde geldt voor opleidingsprogramma's ten behoeve van de diverse betrokken disciplines.

8. Baat van een integratief psychotherapeutisch verpleeghuis-programma om multipele psychiatrische symptomen bij psychogeriatrische patiënten en de belasting van mantelzorgers te verminderen zes maanden na einde behandeling; een gerandomiseerd, gecontroleerd onderzoek

In dit hoofdstuk worden de resultaten gepresenteerd van een heranalyse van de effectiviteit van IRR in termen van percentages klinisch-relevant verbeterde psychogeriatrische patiënten die lijden aan cognitieve stoornissen of dementie en mantelzorgers. In de primaire analyse werden de gemiddelde verschillen vergeleken tussen IRR en reguliere (verpleeghuis)zorg (UC), gebruik makend van de continue data van de primaire en secundaire uitkomstvariabelen.

Met name voor de lange termijn (zes maanden follow-up) is berekening relevant van het percentage psychogeriatrische patiënten en mantelzorgers bij wie sprake is van een klinisch-relevante verbetering na IRR in vergelijking met de reguliere zorg.

Verder biedt het gebruik van een 'intention-to-treat' (ITT)-strategie de mogelijkheid om 'risk ratio's' (RR's) en het aantal patiënten 'needed to treat' (NNT's) te berekenen, waardoor een vergelijking kan worden gemaakt met andere interventies. Uiteindelijk kan een 'complete cases analysis' (CC) een meer realistisch beeld opleveren van de werkzaamheid van IRR in vergelijking met de reguliere zorg. Een dergelijke analyse is relevant bij een relatief hoge uitval en dit is een bekend fenomeen in het ouderenonderzoek. In het geval dat er tussen de twee condities in het onderzoek geen significante verschillen in uitval zijn, kunnen de resultaten van een CC-analyse een preciezere schatting geven van het potentiële profijt van IRR. Immers alleen de patiënten en mantelzorgers die het IRR-programma in zijn geheel hebben doorlopen profiteren ten volle van de aangeboden interventies. In deze heranalyse werd in navolging van Cummings een minimaal klinisch relevante verbetering gedefinieerd als een verbetering van meer dan 30% ten opzichte van de startwaarde van de primaire uitkomstvariabele. In dit onderzoek was dit de NPI-score, afgenomen bij de mantelzorger. In het algemeen, maar ook in dit on-

derzoek komt dit overeen met een halve standaard deviatie of meer, ten opzichte van de startwaarde. De doelstelling van dit klinisch-empirische onderzoek was een heranalyse van de data uit de RCT met betrekking tot de lange termijn effecten van IRR in vergelijking met de reguliere zorg. Deze heranalyse betrof de percentages klinisch-relevant verbeterde patiënten en mantelzorgers, respectievelijk met betrekking tot psychiatrische symptomen en belasting/gevoel van competentie.

Metingen: De primaire uitkomstvariabele: verandering gevoel van competentie in MPS, gemeten met behulp van de NPI, zes maanden na einde behandeling. Secundaire uitkomstvariabelen: belasting en competenties van mantelzorgers, respectievelijk gemeten met de NPI-emotionele belasting, Algemene belasting en Gevoel van Competentielijst. De metingen vonden plaats bij start onderzoek (T1) en zes maanden na einde behandeling (T3).

Statistiek: Een 'intention-to-treat' analyse van RR's (incl. NNT's) en een 'complete cases analysis' (CC) van OR's, gebaseerd op het percentage verbeterde patiënten en mantelzorgers (≥ 0.5 sd van de startwaarde).

Resultaten: IRR had een significant positief effect op het NPI-cluster hyperactiviteit (RR 2.64: 95% CI: 1.26 tot 5.53; NNT: 4.07). Bij psychogeriatrische patiënten die het IRR-programma helemaal hadden doorlopen kwamen de resultaten nog duidelijker naar voren, met significante OR's van 2.80 op het totaal aantal NPI-symptomen en 3.46 op de NPI-totale ernst-score. IRR leidde bij 76% van de patiënten tot een significante klinische verbetering.

Met betrekking tot de secundaire uitkomstvariabele belasting van de mantelzorger bleek de kans op verbetering op het gevoel van competentie van mantelzorgers significant hoger bij IRR (RR 2.23; 95% CI: 1.07 to 4.62; NNT 5.07). In de 'complete cases analysis' wezen de OR's van de percentages verbeterde mantelzorgers op een significant gunstig effect van IRR. Het ging hier om de emotionele belasting, de algemene belasting en het gevoel van competentie (range OR's: 2.40 tot 4.18); met hoge percentages klinisch-relevant verbeterde mantelzorgers tot 71%.

Conclusie: Zes maanden na einde behandeling leidde IRR tot een significant hogere kans op klinisch-relevante verbetering van multipele psychiatrische symptomen bij psychogeriatrische patiënten die lijden aan cognitieve stoornissen of dementie. Een relatief kleine NNT (vier) bleek nodig. De resultaten (76% verbeterde patiënten) kwamen duidelijker naar voren bij patiënten die het IRR-programma volledig hadden doorlopen. Hetzelfde gold voor de hogere kans op verbetering in IRR van de aan de NPI gerelateerde emotionele belasting, de algemene belasting en het gevoel van competentie van de mantelzorger (NNT van vijf en voor degenen die het gehele programma volgden 71% verbeterde mantelzorgers). Vergeleken met donepezil (NNT: 10), memantine (NNT: 3-8) en cognitieve gedragstherapie (NNT: 5-10) waren de NNT's van IRR laag. Al het beschikbare bewijs overziend, zouden binnen de reguliere (inter)nationale, multidisciplinaire verpleeghuiszorg en vergelijkbare ambulante zorgprogramma's zowel integratieve psychotherapeutische behandeling als in de psychiatrie gebruikelijke strategieën moeten worden geïncorporeerd. Hetzelfde geldt voor opleidingsprogramma's ten behoeve van de

diverse betrokken disciplines. Toekomstige onderzoeken om de bewijskracht te verstreken dienen bij voorkeur uitgevoerd te worden als geblindeerde RCT's.

9.   Identificatie van prognostische factoren voor een gunstig lange-termijn effect bij psychogeriatrische patiënten en mantelzorgers die een integratief psychotherapeutisch verpleeghuisprogramma doorliepen, gericht op mulitpele psychiatrische symptomen en mantelzorg-belasting; een klinisch-empirisch onderzoek

Het vorige hoofdstuk was een verkenning van de verschillen tussen IRR en reguliere zorg (UC) met betrekking tot de percentages klinisch-relevant verbeterde psychogeriatrische patiënten die lijden aan cognitieve stoornissen of dementie en mantelzorgers. Een klinisch-relevante verbetering werd gedefinieerd als minimaal een halve sd van de startwaarde. De vraagstelling van dit hoofdstuk betrof de identificatie van prognostische factoren die kunnen voorspellen welke psychogeriatrische patiënten en mantelzorgers baat zullen hebben bij IRR dan wel bij UC. Naast de identificatie van deze voorspellers, is het van klinisch belang om de medische besliskunde te optimaliseren, te meer omdat medische besliskunde nogal eens gebaseerd is op irrationele overwegingen. In de literatuur is sprake van een veelvoud aan beslisregels. In dit onderzoek worden drie beslisregels toegepast. De eerste beslisregel (de regel van het hoogste algemeen gemiddelde) betreft de berekening van het gemiddelde percentage verbetering van elke afzonderlijke interventie. De tweede beslisregel is gericht op het minimaliseren van het maximaal mogelijke verlies (de 'MINIMAX'-regel); deze regel beoogt het risico te verkleinen om een positief effect te missen en doet dit door het hoogste verschil tussen de interventies op iedere score voor alle uitkomstvariabelen met elkaar te vergelijken; en dan te kiezen voor de interventie die het minste verlies aan baat laat zien. De derde beslisregel is de 'MAXIMIN'-regel, die voorschrijft dat de patiënt moet worden verwezen naar de interventie met het laagste vermijdbare risico en dit doet door een vergelijking tussen de interventies te maken op basis van de laagste score op alle uitkomstvariabelen.

De doelstellingen van dit klinisch-empirisch onderzoek waren de identificatie van het prognostisch gehalte van zowel de biografische kenmerken als de 'baseline'-kenmerken van vijf geselecteerde uitkomstvariabelen. In de RCT werd op drie van de geselecteerde uitkomstvariabelen een significant effect gemeten; nl. de door de mantelzorger beoordeelde ernst van de multipele psychiatrische symptomen (MPS) bij de patiënt, de algemene belasting en het gevoel van competentie van de mantelzorger. Geheugen en zelfzorg van de patiënt waren twee belangrijke achtergrondvariabelen. Het prognostisch gehalte werd gemeten op de lange termijn (d.w.z. zes maanden na einde behandeling). Vervolgens werd de mogelijkheid verkend om op basis van de vijf uitkomstvariabelen een model te bouwen waarmee de medische besliskunde zou kunnen worden geoptimali-

seerd. Hierbij werden de MEAN AVARAGE-regel, de MINIMAX en MAXIMIN-beslisregels toegepast.

Metingen: De primaire uitkomstvariabele betrof de bij de patiënten gemeten MPS. Met het oog op klinisch-relevante achtergrond informatie over het effect van IRR werden de belasting en gevoel van competentie van de mantelzorger, cognitief functioneren van de patiënt geselecteerd als secundaire uitkomstvariabelen. Metingen werden gedaan op T1 (intake) en T3 (zes maanden na einde behandeling).

Statistiek: Verbetering werd gedefinieerd als een verschil van een halve sd of meer ten opzichte van de startwaarde. Om het prognostisch gehalte van de 'baseline'-kenmerken te identificeren werd gebruik gemaakt van logistische regressie. Om de medische besliskunde te optimaliseren werden uit de literatuur drie beslisregels geselecteerd en toegepast.

Resultaten: In het meest uitgebreide, gecombineerde prognostische model bleek Alzheimer dementie significant voorspellend te zijn voor verbetering op de NPI-totale ernst-score (OR 3.01). Hetzelfde gold voor IRR met betrekking tot algemene belasting en competentie van de mantelzorgers. De prognostische modellen voor zowel NPI-totale ernst-score als competentie van mantelzorgers hadden een verklaarde variantie van R^2 0.39, respectievelijk 0.23. Bij de overige modellen was de verklaarde variantie laag, met name bij geheugen en zelfzorg. In het algemeen was "double-cross validation" de robuustheid van de predictieve modellen stabiel. Bij toepassing van drie beslisregels op de vijf uitkomstvariabelen bleek IRR steeds de meest aangewezen interventie.

Conclusie: Als het gaat om het voorspellen van positieve veranderingen in de ernst van de gemeten multipele psychiatrische symptomen van de patiënt en van de algemene belasting en het gevoel van competentie van mantelzorgers, bleek prognostisch modelleren haalbaar. Inclusie van een bredere groep patiënten, met name (psycho)geriatrische patiënten met lagere of hogere MMSE of BI-scores in combinatie met specifieke cognitieve interventies, lijkt gerechtvaardigd. Toepassing van de drie beslisregels leidde tot IRR als de meest succesvolle interventie. Het tijdig identificeren van psychogeriatrische patiënten die optimaal baat hebben bij IRR is van groot klinisch belang. Hoewel het verklarend gehalte van de prognostische modellen in deze studie tamelijk bescheiden was, lijkt deze strategie veelbelovend. Om deze reden is de opzet en uitvoering van een onderzoek aangewezen dat gericht is op het construeren van een prognosticum om tijdig patiënten te identificeren die bij een verbeterde versie van IRR de meeste kans op verbetering hebben. Een dergelijk onderzoek zou idealiter volgens een geblindeerde en grootschalige opzet, met deelname van verschillende instellingen moeten plaatsvinden, zodat een steekproef van voldoende omvang beschikbaar is.

10. **Economische evaluatie van een integratief psychotherapeu-tisch verpleeghuisprogramma om multipele psychiatrische symptomen bij psychogeriatrische patiënten en de belasting van mantelzorgers te verminderen; een gerandomiseerd, gecontroleerd onderzoek**

Los van gunstige klinische effecten van een behandeling is het ook van belang een analyse te maken van de hieraan verbonden economische aspecten. In dit hoofd-stuk rapporteren wij de resultaten van een economische analyse van een RCT, waarin IRR werd vergeleken met reguliere multidisciplinaire (verpleeghuis)zorg. De twee doelstellingen van deze economische analyse waren de kosten-baten-ana-lyse en de kosteneffectiviteit, van respectievelijk IRR in vergijking met reguliere zorg (UC), berekend op basis van zes uitkomstvariabelen.

Metingen: De primaire uitkomstvariabele was de verandering in de met de NPI gemeten MPS van de patiënt zes maanden na einde behandeling. Secundaire uitkomstvariabelen: algemene belasting van de mantelzorger (CB), gevoel van competentie van de mantelzorger (CCL), cognitief functioneren (MMSE), zelf-zorg (BI) en kwaliteit van leven (EQ5D) van de patiënt. Metingen vonden plaats op het moment van de intake (T1) en zes maanden na einde behandeling (T3). Kostenmetingen vonden vanaf de inclusie-datum (T0) achtwekelijks plaats en hadden steeds betrekking op de voorafgaande vier weken (TiC-P). De kostenef-fectiviteits-analyse besloeg het interval tussen start behandeling (T1) en de onder-zoeksduur tot 40 weken.

Statistiek: De Monte Carlo Markov Chain (MCMC) benadering werd gebruikt om te corrigeren voor ontbrekende waarden. De kosten-baten analyse werd ge-maakt door het verschil in directe, per patiënt gemaakte medische kosten van IRR respectievelijk UC te vergelijken met het verschil in verworven levensjaren met een goede kwaliteit ('Quality Adjusted Life Years'; QALY). Op basis hiervan werd een berekening gemaakt van de kosten per geschatte QALY.

Een 'Complete case analysis' (CC) werd gebruikt om verschillen in totale kos-ten te vergelijken, gecombineerd met verschillen in effecten, uitgedrukt in een zogenoemde Incremental Cost-Effectiveness Ratio; ICER.

Resultaten: Bij toepassing van multipele imputatie (MI) bleek IRR na 40 weken significant duurder (medische kosten) dan UC; de kosten van IRR waren € 4.572,-- (€ 53,-- per dag) hoger dan die van UC (95%: betrouwbaarheidsinterval: 364.21 tot 8797.76). Tegelijkertijd was het aantal QALYs 0.02 lager (niet-significant) bij IRR (95% betrouwbaarheidsinterval:-0.10 tot 0.05). Dit betekent dat in de MI-analyse UC na 40 weken eenzelfde aantal QALY's kon realiseren, weliswaar tegen signi-ficant lagere kosten. Volgens de ICER-methode bleek IRR significant kosteneffec-tiever met betrekking tot de NPI-totale ernst-score (€ 320,-- per punt), algemene belasting (€ 130,-- per punt) en competentie van de mantelzorger (€ 540,-- per punt). Gebaseerd op de 'complete cases'-analyse, bleek verder dat, los van type behandeling, verbeterde patiënten, met betrekking tot ernst van de psychiatrische symptomen, significant hogere kosten hadden gemaakt. Verbetering ging onlos-makelijk gepaard met hogere kosten. Hierbij was tegelijkertijd sprake van een

relatief hoger aantal verbeterde patiënten en mantelzorgers in de IRR-conditie.

Conclusie: Wat betreft QALY's werden er geen verschillen gevonden, terwijl in IRR de totale medische kosten van psychogeriatrische patiënten significant hoger waren.

In tegenstelling tot de QALY-benadering bleken de psychogeriatrische patiënten die het gehele IRR-programma gevolgd hadden, significant te verbeteren wat betreft gemiddelde scores op de primaire uitkomstvariabele multipele psychiatrische symptomen van de patiënt en op de secundaire uitkomstvariabelen, algemene belasting van de mantelzorger en competentiegevoel van de mantelzorger, met ICER's tussen de € 130,-- en € 540,--. Het grote verschil tussen de QALY- en ICER-benadering betekent mogelijk een terugslag voor kosten-baten analyses in de psychogeriatrie. Dit vraagt om verder onderzoek naar de validiteit van de EQ5D bij interventiestudies met psychogeriatrische patiënten. Verder vonden wij dat ongeacht het type interventie de verbeterde patiënten significant hogere medische kosten hadden. De reden zou kunnen zijn dat verbeterde patiënten langer leven (zie hoofdstuk 4). Al het beschikbare bewijs overziend, zijn de surplus kosten van IRR acceptabel, gelet op de positieve effecten op de hoge sociaal-economische kosten die verbonden zijn aan het lijden aan multipele psychiatrische symptomen door psychogeriatrische patiënten en de hoge belasting bij hun mantelzorgers. Om de kosten-batenanalyse en de kosteneffectiviteit van IRR te optimaliseren, is de constructie van een instrument nodig om psychogeriatrische patiënten en hun mantelzorgers te identificeren die baat hebben bij IRR. Een dergelijk instrument draagt bij aan het optimaliseren van medische besliskunde, gebaseerd op een economische evaluatie.

11.   Methodologische vraagstukken

In deze paragraaf worden de sterke en zwakke punten van respectievelijk de casusbeschrijving, de explorerend-observerende studies en de RCT-studies besproken. Een sterk punt van de casusbeschrijving was de gedetailleerde beschrijving van de inhoud en de uitvoerbaarheid van het reactiveringsproces. De casusbeschrijving was illustratief voor een potentieel gunstig effect van een multidisciplinair en integratief psychotherapeutisch verpleeghuisprogramma, gebaseerd op een persoonsgeoriënteerd en probleemoplossend theoretisch kader. De resultaten uit de explorerende verkenningen lieten duidelijk de klinische relevantie zien van een multidimensionale aanpak, bestaande uit de dimensies 'cognitief functioneren', 'psychologisch/psychiatrisch functioneren', 'sociale omgeving' en 'somatiek'. Daarnaast bleek uit het observationele onderzoek dat psychogeriatrische patiënten die een delirium hadden doorgemaakt niet profiteerden van IRR. Verder werd onomstotelijk duidelijk dat een groot aantal psychogeriatrische patiënten lijdt aan multipele psychiatrische symptomen. In het explorerende en observationele onderzoek was de steekproefomvang van beschikbare patiëntgegevens en het aantal patiënten en mantelzorgers relatief groot. Gebaseerd op de resultaten van het ex-

plorerende onderzoek kon de RCT in vergelijking met de literatuur zowel goed worden georganiseerd als daadwerkelijk worden uitgevoerd. In de RCT was de steekproefomvang van deelnemende patiënten en mantelzorgers ruim, vergeleken met andere interventiestudies.

Voor zover ons bekend is deze RCT één van de eerste waarin de effectiviteit van een multidisciplinaire en integratief psychotherapeutische behandeling in een verpleeghuissetting werd onderzocht. Multidisciplinaire zorg, inclusief psycho-farmacologische behandeling, is in veel verpleeghuizen beschikbaar met name in Nederland. De resultaten uit deze RCT onderstrepen echter dat bij de behandeling en zorg voor psychogeriatrische patiënten die aan multipele psychiatrische symptomen lijden en hun mantelzorgers psychotherapeutische kennis, die gebaseerd is op probleemoplossende principes van belang is. Een belangrijke vraag is welke ingrediënten van IRR relevant waren voor de geboekte resultaten. In de literatuur worden de volgende ingrediënten aangemerkt als cruciale factoren voor gunstige effecten in de (psycho)geriatrie: persoonsgeoriënteerd, probleemoplossend theoretisch kader, integratie van psychotherapeutische deeltechnieken, een optimistische houding, gecombineerde behandeling van patiënt én mantelzorger, een multidisciplinaire benadering en een strenge methodologische opzet. We denken dat het IRR programma deze cruciale ingrediënten bevat. Er zou meer aandacht besteed kunnen worden aan cognitieve aspecten door het IRR-programma uit te breiden met expliciete cognitieve (geheugen-, oriëntatie- en zelfzorg-) training en ondersteunende interventies eventueel in combinatie met het voorschrijven van cognitie-ondersteunende geneesmiddelen. Verder zou nog een grotere groep (psycho)geriatrische patiënten met een lager niveau van cognitief functioneren en een ander type cognitieve stoornis kunnen profiteren van een tweede generatie-versie van IRR. Tenslotte zou een verbeterde versie van het geautomatiseerde behandelplan en het GAS-score systeem de uitvoering van het IRR programma voor professionals kunnen vergemakkelijken. Een grote groep psychogeriatrische patiënten en hun mantelzorgers kan er profijt van hebben als 'cure- and-care' programma's zoals IRR beschikbaar komen. Dit speelt des te meer, omdat uit onderzoek naar effectmodificatie naar voren kwam dat type dementie of niveau van cognitief functioneren (MMSE $\geq$ 18 and BI $\geq$ 5) geen modificerend effect had op de resultaten voor de ernst van de multipele psychiatrisch symptomen of de belasting van de mantelzorger.

De klinische relevantie van de gevonden effecten van IRR is hoog kijkend naar de top drie van ervaren problemen bij dementie in Nederland, nl. psychiatrische symptomen, belasting van de mantelzorger en vrees voor opname in een verpleeghuis. Derhalve zou psychotherapeutische kennis een geïntegreerd onderdeel moeten worden in de opleidingsprogramma's van betrokken disciplines. In het deel van het proefschrift dat gaat over de lange termijn effecten, wordt aangetoond dat volledige deelname aan het IRR-programma de kans op daadwerkelijke verbetering bij zowel patiënt als mantelzorger vergroot. Dit onderstreept nog eens de noodzaak meer aandacht te besteden aan de negatieve gevolgen van weigering

van deelname of uitval uit psychogeriatrisch onderzoek. Dit is des te belangrijker, daar bekend is dat zelfs in longitudinaal onderzoek zonder interventie het uitvalspercentage voor deze groep patiënten in het algemeen erg hoog is (tot 40%). In wezen geeft dit de kwetsbaarheid weer van patiënten die op het punt staan te worden opgenomen in een verpleeghuis. In dit onderzoek waren er geen significante verschillen tussen de aantallen uitgevallen patiënten, de baseline kenmerken of de duur van deelname in beide condities. Selectieve uitval binnen één van de twee condities van de RCT is dan ook onwaarschijnlijk. Als uitgegaan werd van patiënten en mantelzorgers die het hele programma hadden doorlopen, wees het surplus resultaat binnen IRR vergeleken met UC duidelijk op de werkzaamheid van dit programma. Een sterk punt in het prognostische deel van het proefschrift was dat de onderscheiden modellen relatief stabiel bleken, ondanks de beperkte steekproefomvang van dit onderzoek. Bovendien lieten de modellen een substantiële performance zien voor zowel de ernst van de multipele psychiatrische symptomen bij de psychogeriatrische patiënt als voor het gevoel van competentie van de mantelzorger. De toepassing van drie geselecteerde beslisregels was een ander sterk punt van het prognostisch deel van de dissertatie; alle drie kwamen uit op IRR als eerste keuze. Voor een economische evaluatie werden de directe medische kosten van de patiënten berekend. Het gevolg van uitval voor de resultaten en de consequenties van de verschillende statistische strategieën kon worden aangetoond door gebruik te maken van QALY en de ICER-methode. Met de ICER-methode bleek bij IRR de kans op verbetering op drie klinisch-relevante uitkomstvariabelen, nl. psychiatrische symptomen, mantelzorg belasting en competentie, duidelijk hoger, maar ook duurder.

Beperkingen

Wat waren nu de beperkingen van dit proefschrift, in het bijzonder de casusbeschrijving, de explorerende en observationele onderzoeken en de RCT? De casusbeschrijving is per definitie een N= 1 onderzoek, zonder een vergelijking in termen van een voor- en nameting. Een dergelijke casus levert alleen een common sense-inzicht en klinische logica op over de relevantie van het IRR-programma. Het is echter een belangrijke eerste stap in de opzet en de uiteindelijke verwezenlijking van een RCT. Een beperking van de observationele onderzoeken was het ontbreken van aangetoond effect en van oorzakelijke verbanden. Desondanks kan dergelijk onderzoek tot belangrijke vooronderstellingen leiden of de basis vormen voor hypothesen die in een later uit te voeren RCT of gecontroleerd onderzoek kunnen worden getoetst. Met betrekking tot de RCT, is de generaliseerbaarheid van de resultaten een belangrijk discussiepunt. Ongeveer 50% van de voor deelname geschikte psychogeriatrische patiënten en mantelzorgers weigerde deelname aan het onderzoek. Het overgrote deel van deze weigerachtige patiënten woonde samen met een echtgeno(o)t(e). Het belangrijkste motief voor weigering was de angst te worden opgenomen als het lot de patiënt zou indelen bij de IRR-conditie. Vrees voor verpleeghuisopname is nummer drie in de top drie van ervaren pro-

blemen binnen de dementiezorg in Nederland. Daarom is het van belang om een kortdurend (ambulant) programma te ontwikkelen dat gericht is op het wegnemen van deze vrees voor opname.

Verder was de follow-up duur in deze studie zes maanden. De gunstige effecten van de patiënten bleven gehandhaafd en van de mantelzorgers namen ze toe. Het is echter een klinisch relevante vraag of de effecten blijvend zijn over een langere periode. Verder onderzoek hiernaar is noodzakelijk.

Een andere beperking van de RCT was dat de onderzoeksmedewerkers niet blind waren voor het type interventie. Zij gingen persoonlijk bij patiënten en mantelzorgers op (huis)bezoek en waren dus op de hoogte van het verblijf en de behandelgeschiedenis van de betrokken patiënten. In een klinisch onderzoek als dit was blindering niet haalbaar. Om de effecten van andere bronnen van observator bias of een gebrek aan interbeoordelaar betrouwbaarheid zo klein mogelijk te maken werden de onderzoeksmedewerkers zorgvuldig getraind in het op de juiste manier afnemen van de onderzoeksinstrumenten. Uiteindelijk is de vraag relevant of de resultaten van deze RCT in het algemeen verstoord zijn door bias. Bij de baseline-meting bleek er slechts één significant verschil (somatisch co-morbiditeit) te bestaan tussen de twee condities. Zelfs tussen de aantallen uitvallers waren er geen significante verschillen. Bovendien kwamen de resultaten in de RRM-analyses, waarin gecorrigeerd was voor baseline-waarde en uitval, overeen met die in de niet gecorrigeerde Cohen's-d analyses. Kortom, naar onze mening is het onwaarschijnlijk dat de resultaten uit de RCT aan een hoge mate van bias onderhevig zijn geweest, maar een effect van ongeblindeerde meting kan niet worden uitgesloten.

Met betrekking tot de resultaten op de primaire uitkomstvariabele NPI [gemiddelde verschillen, RR's (inclusief NNT's) en OR's] kan de klinische relevantie van de bevindingen zowel in de continue als de dichotome data (klinisch relevant verbeterd) worden aangetoond. Er is enige discussie mogelijk over het vraagstuk welke grootte van een effect beschouwd kan worden als klinisch relevant. De Vet en Norman adviseren een halve standaarddeviatie als minimaal klinische relevante verandering in gezondheidszorgonderzoek. Er is niet veel literatuur beschikbaar over de minimaal klinische relevante verandering in de NPI-score, uitgezonderd de artikelen van Cummings zelf. Ter beantwoording van deze vraag is verder onderzoek nodig. Echter, het surplus-effect van IRR dat met betrekking tot de gemiddelde verschillen en de percentages klinisch relevant verbeterde patiënten en mantelzorgers in deze RCT werd gevonden was relatief groot.

Een ander discussiepunt betreft de verschillen in NPI-scores indien deze werden afgenomen bij een verzorgende uit het team of bij de mantelzorgers. De trend van de scores was hetzelfde en de Pearson correlatie was significant en nam toe door de tijd (at T3: r=0.48; p=<0.001). Hoe kan het verschil in NPI-score verklaard worden? Ten eerste was de mantelzorger een stabiele factor vanaf het inclusiemoment tot aan het einde van de behandeling en van de zes maanden 'follow-up'. Verder hadden de mantelzorgers in aanvulling op de informatie die zij ontvin-

gen van het verzorgenden team langduriger individuele contacten met de patiënt. Volgens de literatuur zou hun inschatting meer overeenkomen met de behoeften, de opvattingen en de gevoelens van de patiënt. De data die verzameld werden bij het verzorgingsteam in beide condities waren niet continu; de onderzoekers interviewden bij het verzamelen van NPI-data verschillende verzorgenden van het team. De vraag is dus bij wie de NPI moet worden afgenomen om adequate gegevens over de multipele psychiatrische symptomen van de patiënt te verkrijgen? Bij het verzorgenden team, de mantelzorger of beiden? Bij verder onderzoek moet aan dit probleem aandacht worden besteed. Vooralsnog bleek de mantelzorg-NPI gevoelig voor zowel veranderingen in het aantal multipele psychiatrische symptomen als in de ernst ervan. Wij adviseren in ieder geval altijd ook bij de mantelzorger te meten.

Met betrekking tot de kwaliteit van leven werd, vergeleken met de klinisch relevante instrumenten zoals NPI, CB en CCL, op het EQ5D-instrument een relatief beperkt effect gevonden. In beide condities werd bij kleine aantallen psychogeriatrische patiënten en mantelzorgers een verbetering op de EQ5D gevonden. De relatief lage gevoeligheid van de EQ5D beperkte de bruikbaarheid voor de 'cost-utility'-analyse in termen van QALY's. Deze bevinding is conform de resultaten uit eerder onderzoek naar de relatie van kwaliteit van leven metingen en metingen van psychiatrische symptomen, zoals met de NPI door Ballard, Katona en Wimo. Een aangepast meetinstrument voor 'cost-utility'-onderzoek geschikt voor psychogeriatrische patiënten moet nodig worden ontwikkeld.

Een ander vraagstuk in dit 'cost-utility'- en kosteneffectiviteitsonderzoek heeft betrekking op het feit dat alleen de directe medische kosten van de patiënt werden geïnventariseerd. Andere patiëntgerelateerde kosten, de kosten van de mantelzorger en ook eventuele baten werden niet meegenomen. Het verdient aanbeveling om een meer omvattende methode van kostenevaluatie te ontwikkelen die uitgebreider is.

Tenslotte, volgens de door de Cochrane Collaboration geaccepteerde GRADE-systematiek (Grading of Recommendations Assessment, Development and Evaluation) kunnen de kwaliteit van het bewijs en de kracht van de aanbevelingen van deze RCT als gematigd sterk beschouwd worden, mede gelet op de hierboven besproken beperkingen.

12.   Implicaties voor professionals, managers en beleidsmakers

Met betrekking tot de implicaties die de bevindingen uit dit proefschrift voor professionals kunnen hebben, denken wij met name aan het invoeren van psychotherapeutische kennis in de gangbare psychogeriatrische zorg en in opleidingsprogramma's voor professionals zoals verzorgenden, artsen, psychologen, fysiotherapeuten, ergotherapeuten, maatschappelijk werkenden, enz.

Het gaat er in de behandeling niet zozeer om meer te doen, maar om een andere behandeling te geven, zoals bijvoorbeeld persoonsgeoriënteerde en psychotherapeutische, op een probleemoplossend kader gebaseerde interventies. Verder is onderzoek nodig naar een optimale implementatiestrategie voor IRR om toepassing van IRR op grote schaal mogelijk te maken. Daarnaast is het klinisch relevant om een tweede generatie IRR te ontwikkelen, aangevuld met cognitie-verbeterende interventies, inclusief een prognostisch instrument om interventies zodanig te optimaliseren dat multipele psychiatrische symptomen bij patiënten en overbelasting bij de mantelzorg kunnen worden verminderd.

Zoals benadrukt wordt in de resultaten uit het Nationale Dementie Programma in Nederland is er sprake van een hoge lijdensdruk zowel als gevolg van de psychiatrische aspecten bij de patiënten als de belasting van de mantelzorger. De laatste lijdt met name onder verregaande beperkingen en een verminderd welbevinden, dit geldt zelfs voor 80% van de mantelzorgers. Voor professionals geldt dat als zij zich psychotherapeutische strategieën, die gebaseerd zijn op een probleemoplossend theoretisch kader en op een persoonsgeoriënteerde benaderingswijze, eigen maken dit hen in staat stelt hun vaardigheden te vergroten om betere resultaten te boeken. Dit maakt voor hen het werken in dit specifieke domein aantrekkelijker. Gelet op de demografische ontwikkelingen is dat van groot sociaal-economisch belang.

Met betrekking tot onderzoek binnen ZonMw programma's, zoals het Nationaal Programma Ouderenzorg (NPO), is een belangrijke implicatie de ontwikkeling van een gevoelig kwaliteit van leven-instrument, dat strookt met andere klinisch relevante uitkomstmaten. Het vraagstuk een meetinstrument te ontwikkelen voor kwaliteit van leven bij (psycho)geriatrische patiënten, dat geschikt is voor de evaluatie van 'cost-utility' van interventies (QALYs), moet worden opgelost en verdient een hoge prioriteit. Verder zou moeten worden geïnvesteerd in de ontwikkeling van een passende werkwijze om patiëntgegevens over de multipele psychiatrische symptomen te verzamelen bij de psychogeriatrische patiënt zelf, het behandelteam en/of de mantelzorger. Daarnaast is de ontwikkeling van een economisch model dat alle relevante kosten en baten omvat, zodat een interventieprogramma vanuit economisch perspectief kan worden geëvalueerd, een andere belangrijk item in toekomstige ZonMw onderzoeksprogramma's. Vanuit een internationaal perspectief, uitgaande van de beschikbare bewijzen uit deze RCT en de reviewliteratuur, zouden interventiestudies betreffende psychiatrische symptomen bij psychogeriatrische patiënten bij voorkeur onderdelen van integratieve psychotherapeutische interventies moeten bevatten, namelijk als deel van de index-interventie of van de controle-conditie, ook bij medicijnonderzoek. Met andere woorden; dit zou de standaardnorm moeten zijn.

Voor zowel managers als beleidsmakers is het van belang om te weten dat verbetering in zowel gangbare verpleeghuiszorg als IRR in het algemeen tot significant hogere kosten leidde dan wanneer er geen sprake was van verbetering.

Uitgaand van het ongunstigste scenario waarin IRR slechts € 53,-- duurder is dan gangbare zorg - en dit is ongeveer gelijk aan de helft van de kosten van een CVA-unit (€102,--) - zou de implementatie van IRR gefaciliteerd moeten worden bijvoorbeeld door een aanpassing van de zorgzwaarte pakket (ZZP)-systematiek, waarin bijv. ZZP-9 – gericht op revalidatie in het verpleeghuis - beschikbaar zou moeten zijn voor rehabilitatie en revalidatie van multipele psychiatrische symptomen bij psychogeriatrische patiënten en mantelzorgbelasting. In deze context is het relevant om deel uit te maken van de veelbelovende ontwikkeling om Geriatrische Revalidatie een plek buiten de AWBZ te geven, namelijk onder te brengen in de zorgverzekeringswet op basis van een zogenaamde diagnose behandelcombinatie (DBC).

Met betrekking tot de ZZP's is het ook van belang zich te realiseren dat bij een gangbare ZZP-classificatie van een psychogeriatrische patiënt niet automatisch tegemoet wordt gekomen aan de behoefte aan psychotherapeutische zorg die nodig is om de lijdensdruk van patiënt en mantelzorger te verlichten. Patiënten met een grote variëteit in ZZP's bleken op basis van de inclusiecriteria geschikt voor deelname aan IRR. Bovendien was de correlatie tussen ZZP-7 (manifeste psychiatrische stoornis) en actuele NPI-scores laag. Een belangrijke aanbeveling is dan ook deze discrepanties te registreren en te bewaken om de consequenties hiervan zowel voor de dagelijkse praktijk als voor het overheidsbeleid duidelijk te kunnen maken. Als een volgende stap is het ontwikkelen van een specifiek 'evidence-based' prognostisch instrumentarium haalbaar. Naar onze mening zouden beleidsmakers de huidige kloof tussen het op economische maatstaven gebaseerde ZZP-classificatiesysteem en de robuuste klinische onderzoeksinstrumenten die gebruikt worden voor de inclusie van patiënten in passende zorg- en behandelprogramma's moeten dichten.

Wij adviseren managers en beleidsmakers zich te richten op de inhoud en de methodologische aspecten van psychotherapeutische zorg en behandeling voor patiënten en mantelzorgers opdat deze kunnen worden geïntegreerd binnen de gangbare speerpunten in financiën en beleid binnen de gezondheidszorg.

Tenslotte is aparte aandacht nodig voor het verbeteren van de kwaliteit van zorg in de chronische verpleeghuiszorg met betrekking tot de behandeling van multipele psychogeriatrische symptomen. Hoewel uit de RCT bleek dat reguliere verpleeghuiszorg – veelal belevingsgericht - een reductie van $\pm$ 30% geeft van de klachten, lijkt een grotere reductie haalbaar door (deel)technieken van IRR te gebruiken. Wij hebben bijvoorbeeld succesvol het concept van de 'gedragsconsulente' geïntroduceerd in de chronische verpleeghuiszorg. Hij/zij is opgeleid in het toepassen van diagnostiek en psychotherapeutische interventies, afgeleid van het IRR-programma. Verder kan de belasting van de mantelzorger aanzienlijk worden verminderd door systeemtherapietechnieken van IRR te gebruiken. Uiteraard behoeven deze ontwikkelingen verder wetenschappelijk onderzoek.

13. Aanbeveling tot verbetering van IRR

Wat zijn nu de mogelijkheden om de gunstige effecten van IRR te vergroten? Gebaseerd op de door ons uitgevoerde studie concluderen wij dat de effecten van IRR reeds gunstig zijn, maar nog verder kunnen worden verbeterd. Ten eerste zou een voorafgaand programma, bijvoorbeeld in de vorm van dagbehandeling, moeten worden ontwikkeld om de angst voor opname te verminderen. Een andere aanbeveling is de ontwikkeling van een goed prognostisch algoritme om de klinische besliskunde zodanig te verbeteren dat psychogeriatrische patiënten en mantelzorgers die het meest gebaat zijn bij IRR op voorhand kunnen worden onderscheiden. Met betrekking tot het programma zelf zou meer aandacht moeten worden besteed aan cognitie-verbeterende interventies, een onderscheid tussen korte en lange duur van IRR, in het bijzonder met betrekking tot de behandeling van persoonlijkheidsstoornissen, en verder zouden specifieke interventieprotocollen voor vaak voorkomende psychiatrische symptomen als depressie, angst en apathie moeten worden ontwikkeld. Bovendien zou een uitgebreid ambulant vervolgprogramma relevant kunnen zijn om de behandelresultaten te laten beklijven. Daarnaast zou een grootschalige, geblindeerde RCT moeten worden opgezet en uitgevoerd met een bredere studiegroep. De doelen van een dergelijke studie zouden enerzijds moeten zijn om de belangrijkste therapeutische elementen van de tweede generatie IRR op te sporen en anderzijds om een robuust prognosticum te construeren met het oog op het comprimeren van het IRR-programma tot een minder complexe interventie voor een specifieke doelgroep, patiënten met cognitieve stoornissen. Als gevolg hiervan kan IRR kosteneffectiever worden.

14. Samenvatting

In deze dissertatie werd de (kosten)effectiviteit onderzocht van een integratief psychotherapeutisch verpleeghuisprogramma (IRR) om multipele psychiatrische symptomen bij psychogeriatrische patiënten die lijden aan cognitieve stoornissen of dementie en de belasting van mantelzorgers te verminderen. IRR bleek vanuit het perspectief van de mantelzorger een tot twee keer zo grote gemiddelde reductie van het aantal en de ernst van de psychiatrische symptomen van de patiënten als de reguliere zorg te bewerkstelligen. Zes maanden na einde behandeling was er feitelijk sprake van een reductie van 61%. Vanuit het perspectief van het verzorgenden team waren de effecten niet significant, hoewel deze in dezelfde richting wezen en significant correleerden. Hierbij was bovendien sprake van een toenemende mate van correlatie door de tijd heen. Verder leidde IRR zes maanden na einde behandeling tot een vermindering in belasting van de mantelzorgers van max. 50%, terwijl de reguliere zorg hier nauwelijks effect op had.

Het surplus aan totale kosten van IRR was relatief laag, nl. € 53,-- per dag. Het aantal te behandelen patiënten om een klinisch relevant effect te behalen (NNT) was laag (=4-5) vergeleken met donezepil (=10) en memantine (=3-8). Verder bleken de gunstige effecten niet beïnvloed te worden door het type dementie of het

niveau van cognitief functioneren. Op basis van de GRADE-systematiek van de Cochrane Collaboration kunnen de aanbevelingen van deze RCT als gematigd sterk worden beschouwd.

Omdat 80% van de psychogeriatrische patiënten last heeft van multipele psychiatrische symptomen en 70 tot 80% van de mantelzorgers matig tot zwaar overbelast is, bevelen wij de implementatie aan van integratieve psychotherapeutische interventies in de multidisciplinaire reguliere – veelal belevingsgerichte - verpleeghuiszorg. Professionals, onderzoekers, managers en politici dienen aandacht te besteden aan psychotherapeutische trainingsprogramma's, kwaliteit van leven onderzoek, persoonsgeoriënteerd en inhoudgeoriënteerd management en aanpassing van de ZZP-classificatiesystematiek. Toekomstig onderzoek met het doel de 'evidence' van de (kosten)effectiviteit van persoonsgeoriënteerde en probleemoplossingsgerichte psychotherapeutische interventies te versterken, is noodzakelijk en dient bij voorkeur als geblindeerde RCT te worden uitgevoerd met een lange follow-up periode.

Chapter

1

General introduction

About 80% of psychogeriatric patients who suffer from cognitive impairment or dementia have two or more psychiatric symptoms and about 70-80% of caregivers are moderately to severely burdened [1-5].

As a consequence of the increasing prevalence and incidence of cognitive impairment and dementia in all aging societies, these two problems will demand urgent attention of healthcare professionals, managers and policymakers. The more as multiple psychiatric symptoms (MPS) play an important role in psychogeriatrics. There is overwhelming scientific evidence that they have many related negative secondary effects. For the patients there are negative effects on cognitive functioning, quality of life, and they predict admission to a nursing home. Furthermore, MPS put a high burden on the caregiver. Moreover, psychiatric symptoms and burden of the caregiver are the two as most problematic experienced phenomena in dementia, by patients as well as by caregivers [6]. All in all, MPS play a key role in psychogeriatrics [3-10].

In contrast, evidence based know-how concerning effective treatment and support is rather limited [11, 12]. Even more, terminology, definitions and underlying concepts vary widely e.g. BPSD (behavioural and psychological symptoms in dementia), problem behaviour, neuropsychiatric symptoms, and psychiatric symptoms [2, 3, 13-15]. The intriguing question is which factor(s) underlie(s) MPS of psychogeriatric patients who suffer from cognitive impairment or dementia e.g. neurological disease, general somatic disease, pain, and/or regular psychiatrics [2, 4, 15-18]. In actuality, for treatment of MPS of psychogeriatric patients the use of psychotropic drugs is widespread in nursing home care in spite of limited effects and potentially harmful side effects e.g. (a)typical antipsychotica [19, 20]. On the other hand, literature indicates that on individual psychiatric symptoms particularly depression and anxiety psychotherapeutic treatment may be effective, specifically if they are based on a problem-solving theoretical framework [11, 12, 21-23]. However, psychotherapeutic interventions on MPS of psychogeriatric patients who suffer from cognitive impairment of dementia are complex due to their multiplicity in combination with cognitive disorders, somatic co-morbidity, and social problems. [10, 24] Furthermore, a psychotherapeutic programme in a nursing home setting has never been tested in a large-scale comprehensive study [11, 25-27]. For these reasons, we developed and tested an integrative psychotherapeutic nursing home programme called: integrative reactivation and rehabilitation (IRR). The psychotherapeutic interventions were based on a person-oriented and problem-solving theoretical framework [11, 28].

In this dissertation we describe the process of the development of IRR and the findings of the tests, consisting of observational studies as well as a randomized controlled trial (RCT).

As an introduction, in chapter two the performance of psychotherapeutic interventions in the multidisciplinary IRR programme is described. In this chapter the theoretical background of the IRR programme is elucidated. The principles of the Dynamic System Analysis- (DSA) method are introduced. The DSA method emphasizes the unique experience of the psychogeriatric patient who suffers

from cognitive impairment or dementia. In addition to biological factors the DSA method emphasizes the importance of the subjective experience of the patient as well as the caregiver, the psychological abilities, the functional-psychiatric pathology and of the social context. Specific attention is given to the psychodynamics combined with and adapted to the actual cognitive disorders. Four main dimensions are distinguished by the DSA method, i.e. Cognition, Psychological functions, Social context and Biology. In short, DSA is an integrative psychosocial, biological method. Furthermore, in this chapter the IRR programme itself is more extensively introduced and described. To illustrate the performance of the IRR programme a case study is presented. We published an update of the description of IRR in 2009. This publication in a peer-group reviewed Dutch journal with an English abstract is added to this dissertation as a supplement (1). In two consecutive observational studies we explored which psychogeriatric patients and caregivers had potential benefit from the IRR programme. In the two studies presented in respectively chapters three and four we examined which prognostic factors play an important role in patient's discharge after participation in IRR as well as survival after discharge. We wanted to know which prognostic factors were crucial for the probability of discharge as well as survival, in order to optimize patient selection for the IRR programme. Furthermore, these descriptive studies were an explorative evaluation of the (relative) importance of the four main dimensions of the DSA method. The two studies were important preparatory steps in order to perform a randomized controlled trial to evaluate the (cost-)effectiveness of the IRR programme. In addition to that, it was relevant to estimate the prevalence of multiple psychiatric symptoms as well as their relation to other important aspects of psychogeriatric patients. Therefore, chapter five focusses on a study of the prevalence and co-occurences of MPS in psychogeriatric patients and their relation to memory and self-care. Also, theoretical aspects of underlaying factors of MPS are addressed. The results give insight in the prevalence and clinical relevance of MPS and related burden of caregivers. Another intriguing question is which factors underlie MPS, as measured by the Neuro-psychiatric Inventory of Cummings (1994).[15] From a neurological explanation one should expect to find powerful significant relations between NPI-score and cognitive tests like MMSE. From a more psychotherapeutic perspective, one should expect that the NPI-scores are a dimension on their own with just minor correlations with cognitive functions, i.e. memory and selfcare. To be sure about the stability of the findings in this study we also performed a replication study in 2007 in a different target group, i.e. patients of a memory policlinic. This study is publised in a peer-group reviewed Dutch journal with an English abstract and is added as a supplement (2) to this dissertation. The next logical step was to evaluate the effects of IRR compared to usual care. A RCT is the standard to meet. It is important to look at mean differences, effect modification as well as clinically relevant improvement and number needed to treat (NNT). Furthermore, prognostic modelling is important in combination with decision rules for optimizing clinical decision making in order to select the patients and caregivers who benefit most from IRR. In the chapters six to nine

we present the results of the randomized controlled trial, i.e. the mean effects of IRR compared to usual care, modifying effects, clinical relevant improvement and number needed to treat, and finally prognostic models for a favourable long term effect of IRR in combination with decision making rules. From an economical perspective the question is, what are acceptable costs for improvement (cost-effectiveness) and what is the cost-utility of IRR? So, in chapter ten an economic evaluation based on QALYs and ICERS is presented. Chapter eleven consists of the general discussion.

In overview, step by step, supported and guided by the results of the different consecutive studies the IRR programme – an integrative psychotherapeutic nursing home programme to reduce multiple psychiatric symptoms of psychogeriatric patients and caregiver burden – is developed and at last tested in a RCT. A strong point in this approach is that the findings are derived from related but not identical samples; so, the findings are (relatively) robust, especially in combination with a replication study, which confirmed the original findings. A disadvantage may be the gradual transitions in definitions and the differences in target group. The main findings of the thesis are summarized in chapter i (English version) and ii (Dutch version).

The content and main research question of the different chapters are as follows:

Chapter two: Description of the performance of the IRR programme; a case-study

Chapter three: Retrospective observational study to identify prognostic characteristics for the probability of discharge from IRR, in order to optimize patient selection for IRR

Chapter four: Prospective observational study to estimate life expectancy of psychogeriatric patients after following IRR. Furthermore, prognostic characteristics for survival were identified

Chapter five: Prospective observational study to estimate the prevalence and co-occurences of multiple psychiatric symptoms (measured by NPI) in psychogeriatric patients at referral to clinical as well as non-clinical nursing home care - the relation to cognitive function disorders (measured by MMSE) as well as activities of daily living (measured by Barthel index).

Chapter six: RCT to test in terms of mean differences the effectiveness of an integrative psychotherapeutic nursing home programme (IRR) compared to usual multidisciplinary nursing home care especially to reduce multiple psychiatric symptoms of psychogeriatric patients and burden of caregivers

Chapter seven: Post-hoc analysis of the RCT data to estimate whether long term beneficial effects of IRR on severity of MPS of psychogeriatric patients and general burden of caregivers were modified by level of cognitive function disorders and/or type of dementia

Chapter eight: Re-analysis of the RCT data to evaluate long term benefit of IRR compared to usual care in terms of clinically relevant (> 30% improved compared to baseline value) improved psychogeriatric patients and caregivers and numbers needed to treat.

Chapter nine: Post-hoc analysis of the RCT data to identify prognostic factors for a favourable long term effect of IRR for psychogeriatric patients and caregivers on five selected, responsive outcome variables

Chapter ten: Economic evaluation of the RCT with the objective to assess cost-utility as well as cost-effectiveness on six selected outcome variables of IRR compared to usual care. This evaluation creates the opportunity to mutual comparison of the effects of different healthcare programmes.

Chapter eleven: General discussion about the value of the findings of the RCT, methodological issues, and implications for professionals, managers and policymakers. This chapter ends with recommendations for implementation of IRR in usual psychogeriatric nursing home programmes and to offer professionals more access to education programmes of psychotherapeutic treatment skills. Furthermore, the possibilities to enhance the beneficial effects of IRR are discussed.

Chapter i and ii: Presentation of the main findings in a general summary in English as well as in Dutch.

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Palliative care in chronic psycho-geriatrics;
A case study[1]

1.   Introduction

Due to ageing of the Western population, there is a growing prevalence of chronic psycho-geriatric disorders like 'dementia of the Alzheimer type' and 'vascular dementia' (1 - 3). The genuine, though multifarious cognitive function disorders of psycho-geriatric patients co-occur often with mood and behavior disorders as well as with social problems. In case of palliative care, this complex co-pathology determines the wide range of psycho-social needs of individual psycho-geriatric patients and their social environment. In our psycho-geriatric reactivationprogram we are confronted with the special aspects of palliative care for this type of patients. About 25% of our total reactivation population dies during the course of the program; according to the literature this percentage is 13-32% (10 - 13). We found out that the method and expertise used in the reactivation program were relevant in arranging the palliative care of these patients in their terminal phase of life.

In this paper we will focus on our experience with palliative care of patients who deceased during the course the reactivation program. The psycho-geriatric reactivation is conducted in a Dutch 'psychiatric-skilled' nursing home. First we will present a case-study followed by an explanation about our reactivation program and the underlying method Dynamic System Analysis (D.S.A.). We will conclude with a discussion about the practice implications of D.S.A. for palliative care of psycho-geriatric patients with functional-psychiatric co-pathology.

2.   Case-study

2.1   Case history

Patiënt Mrs. M. was a 91 year old lady. In the early eighties she had suffered from a depression, since three years she had vivid nightmares related to second worldwar experiences. Three weeks before admission she suffered from a bronchopneumonia. After her protracted recovery Mrs. M. no longer wanted to go to the day-clinic; she stayed in bed almost all of the day. To the home-care team Mrs. M. showed increasing verbal and physical aggression. They had the impression that Mrs. M. didn't sleep much during the night. Her food and liquid intake was also below the minimum. She was admitted to the psycho-geriatric reactivation program because the circumstances and supportive system at home became insufficient. Mrs. M. agreed to admission.

2.2   Admission

We saw an anxious woman, looking her age, 55kg, lenght 1,67 m, mild dehydration and clear consciousness. She consented to the admission because: "at home it was miserable, maybe I can become strong again". From her visits to the day-clinic it

was known that she kept a distance from the other patients most of the time; Mrs. M. received a single room.

2.3 Observation and controlling phase

The first phase of the reactivation program developed reasonably well.

According to protocol multidisciplinary observations were conducted on four dimensions: cognitive, psychological and biological functions and social context.

With regard to cognitive functions the disorders of basic-skills proved to be mild and not extensive and varied somewhat over time (long-term and recent memory disorder, desorientation in place). There were no signs of delirium.

Concerning the psychological functions Mrs. M. suffered from severe functional-psychiatric pathology. She had symptoms of agitated depression, paranoia, and occasional outbursts of aggression. Her personality seemed broken up in multiple 'selves'. There was only a loose or no connection between them and she was not in control (dissociation). One self was strongly combined with vivid reminiscences of traumatic war events; another self showed a strong competent but dominant woman; yet another showed a caring, responsive motherly self, but there was also an overt aggressive, untouchable, intolerant self. The switch between the 'selves' took place without observable cue from outside. In communication with the team members Mrs M.'s overall attitude varied between a cooperative and a passive - submissive copingstyle. In her life history (hetero-anamnestic by her son) we found out that she was born in the Dutch East Indies, nowadays Indonesia. Her father died very early; she had hardly known him. Her spontaneous, caring East-Indian mother died at the age of 84. Until her wedding (when she was 32 years old) she had worked as a schoolteacher. During World War II she has been kept prison in a Japanese concentration camp together with her son. She did get a highly ambiguous position in the camp as the chief of a shed. She was responsible for order. On each disruption Mrs. M. became the same punishment as the perpetrator. She had undergo terrible tortures. She almost never spoke about them directly even now. Her son describes her (up to 3 or 4 years ago) as a dominant, very active, caring and positive woman, but nevertheless avoidant and introverted in emotional respect. This is a typical history for frail elderly patients with a complex post-traumatic stress disorder.

Concerning social context Mrs M. lived alone in a private apartment. Here husband died 6 years ago. Her 2 brothers and 2 sisters were all dead. Her only son payed a lot of attention to her and was the only important volunteer aid available.

With respect to her biological functions she had in 1995 a cerebral

vascular accident; she suffered from constipation, heart failure and a status after a recent bronchopneumonia. She was very tired and lacked stamina.

To control her behavior disorders (agitation, dominance and aggression) efforts were focused on establishing a cooperative relationship with her. This was ac-

complished by the nursing staff, music- and psychomotor-therapists, supported by psychopharmaca (a combination of paroxetine, pimozide and periciazine). The nursing staff used a so called 'All Bad/All Good' approach, which ideally implies that they make a maximum effort to give personal attention and to minimize regulating constraints, the latter, if inevitable, conducted by a nurse of another team. The main goals in this phase were to diminish the (negative effects of) personality-splitting and overt aggressive outbursts and to regulate the nightmare-based sleeping disorder.

2.4   Rehabilitation phase

In this second phase the psycho-geriatrician and psychologist had each weekly sessions with Mrs. M. to create (counter-) transference and to check and support her introspective abilities. Remarkable was the difference between lucide introspection in the present and the avoidance of the past. The interfering influence of the cognitive function disorders did not become clear. The music- and psychomotor therapists were looking now for cues to elicit the more positive 'selves' of Mrs. M. and to find ways to restore her defense mechanisms buffering against the traumatic life experiences. Her nightmares were under control. In short, the progress in regaining psycho-social abilities to autonomous functioning was slow. The extent of the underlying psychopathology as well as her frail somatic condition contributed to these limited results. Mrs. M. developed repeatedly a bronchopneumonia, with complaints of increasing heart failure. Her physical condition worsened and the cognitive functions deteriorated too. In the mean time the reactivation-team supported her only son in comprehending and working through his mothers behavior. The aim of discharge was unfeasible by now. Her son as a proxy decision-maker provided informed consent for changing the treatment policy to palliative care.

2.5   Palliative care

Because of her complex psycho-social disorders the actions of the multidisciplinary interventionplan were still indicated, but they served other goals. From now on they focused on the patients comfort. The specific aims were to support Mrs. M. and her son on the difficult pathway to her death, to minimize troublesome behavioral symptoms, emotional perceptions and reminiscences as well as the somatic discomforts, and to enhance positive feelings. A minister was added to the team and Mrs M. turned out to be sensitive to ritual forms of activities, especially religious ones. Predictable, controlled every day care routines, tuned by the staff to her preference's (e.g. washing procedure, kind of food and beverages, the furnishing of her single room, favorite music on tape, religious ceremonies, regular individual contacts bij team members) helped her to bear her

anxious, fearful reminiscences. This also gave her opportunities to be herself and to enjoy herself. Because of her progressive heart failure she was more and more confined to her bedroom. She stopped eating in spite of special meals, based on her desires and a few days later she stopped drinking. She talked about 'going with the Jews' and about her funeral. In spite of maximal compliance to her dominant and avoidant personality-traits, the multiple selves, as well as to the deteriorating cognitive functions, she sometimes had impulsive outbursts of aggression directed at members of de nursing team and at her son. However, most of the time she could calmly accept her fate. The son's perception of his mother and the perception by the treatment team were exchanged and tuned to each other for the sake of providing the best care. It helped him to cope with his new role –in the past his mother had made the decisions- the illness and near-death of his mother. It also helped him to evaluate his own live, (in)directly affected by his mother's traumatic war-experiences. He realized that he suffered from some 'second-generation' problems of traumatic war-experiences. He was advised to consult a psychologist himself.

At the end Mrs. M. was sleeping most of the time in her bed; sometimes she was restless and could not choose between bed or chair. The diazepam medication previously started was supplemented with a low dosis of morfine to relieve the pain. She reacted very well on this medication and a few days later she calmly died.

3.   Reactivation program

The psycho-geriatric reactivation program is designed to manage, functional-psychiatric and related social problems of psycho-geriatric patients with mild to moderate cognitive function disorders. The intervention program is tailored to the needs and abilities of the individual patient and aims at discharge (14). Discharge implies that the patients are returning to their home or go to an elderly-home like for assisted or independent living; this concerns aout 52% of the participating patients. The reactivation unit consists of 15 beds (five single rooms, one room with two beds, and two rooms with four beds). There is one living-room with a kitchenette. In addition, there are several therapy-facilities. The reactivation program is based on a multidisciplinary approach and intersects psychiatry and 'nursing-home' medicine. The program (duration 3-6 months) comprises integrated cure and care interventions, particularly therapy, nursing and welfare. Therapies - i.c. psychotherapy, music-/psychomotor therapy and somatotherapy- are predominantly directed toward reducing the severity of functional-psychiatric pathology and functional impairments which threaten autonomous functioning. The therapeutic team consists of: a psycho-geriatrician, music-/psychomotor-/creative therapists, a physical and occupational therapist, speech therapist and dietician. Nursing - i.c. rehabilitation, support, different behavioral therapy approaches, reality and orientation training and somatic care - attempts to uphold self-care and

coping strategies using individual and group support. Welfare – carried out by an occupational therapist, a minister, a social worker and volunteers - focuses on social activation and social support, and is directed towards consolidation of the (re-)gained abilities to autonomous functioning.

Furthermore, the reactivation process is characterized by the following three phases. The observation and control phase aims at managing dominant disorders within about four weeks, in particular for disorders detrimental to vital functions (e.g. sleeping pattern). The second rehabilitation phase focuses on (re-) establishing and stabilizing abilities to autonomous function by enhancing or restoring self-knowledge, self-control, self-care, development of new behavior, as well as adaptation. In the third, consolidation phase, the goal is to prepare for and work through the discharge. It is this third phase that changes in palliative care if the patients condition deteriorates to a terminal phase in the course of the program.

All disciplines are trained especially in conducting the method of Dynamic System Analysis. They followed courses (about 10 days) on secondary or college level offered by the foundation Psy-Ger-On.

4.   Integral psycho-social, biological method

The reactivation program is based on the method of Dynamic System Analysis. It is developed by Bakker (14, 15) specifically for interventions with psycho-geriatric patients with complex co-pathology. The method is inspired by the cybernetic system principles of Von Bertalanffy (16) and the theory of dissipative structures of Prigogine (17). Earlier, the basic system principles were transformed to general health care and psychiatry in the Netherlands by Querido (18), Lit (19), and Milders and Van Tilburg (20), respectively. The DSA method is elaborated and tested for psycho-geriatric reactivation (21). A computerized version is available as well. The DSA approach forms a counterbalance against the paramount importance of the biological orientation of the majority of (psycho-) geriatric scientific research, literature and practice. Next to biological factors the DSA method emphasizes the subjective experience of the unique individual patiënt, his/her psychological abilities as well as functional-psychiatric pathology and the social context. Specific attention is given to the psycho- dynamics in combination with cognitive function disorders. With regard to decisions about cure and care interventions the psychodynamic hypothesis is as important as the biological one. Recently two extensive cross-sectional studies - the Groningen Longitudinal Aging Study (GLAS) and the Maastricht Aging Study (MAAS) - confirmed the independent influence of psycho-social factors on autonomous as well as cognitive functioning, apart from the mutual interference with the biological factors (22-27). The DSA method applied to the psycho-geriatric reactivation program discriminates between four main-dimensions. The (dys)abilities, pathology and interventions can be ordered according to these four dimensions, taking into account their mutual interference. The dimensions are Cognitive functions (the basic skills, particularly memory, ori-

entation, language, praxis and gnosis), Psychological functions (the cognitive and emotional aspects of, particularly coping style, personality, perception, lif-events), Social context and Biology (see Figure 1). When the available personal power and the experienced personal burden are too much out of balance anxiety and stress will arise. Eventually this will trigger psychodynamic and biological processes as well as their accompanying pathological symptoms. Interventions can be directed both to minimize pathological symptoms and to support the personal power as well as to lower the experienced personal burden. An elaborated DSA diagram offers the multidisciplinary team a common language, that exceeds the boundaries of their own discipline. Moreover, DSA provides all the disciplines with the relevant, to psycho-geriatrics adapted, psychiatric knowledge and intervention techniques in addition to the well-known somatic and social aspects. For each patiënt there is a common integral intervention plan; sub-plans are derived for each discipline. All plans comprise relevant patient characteristics, goals, actions and their evaluation.
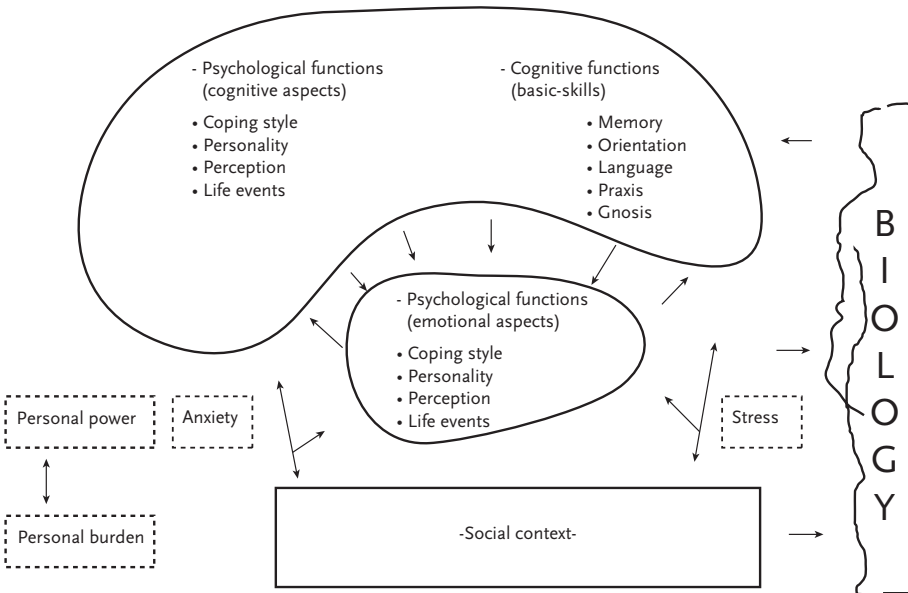
5. Practice implications of DSA

A delicate ethical subject for debate in palliative care of psycho-geriatric patients with more or less deteriorating cognitive functions is the transition from 'aggressive clinical management' to 'beneficience based clinical management'. The latter focuses on maximizing comfort of the patiënt instead of on recovery or extending life (2). A fundamental principle of palliative care is the provision of a patient –centered care, based on the patients perspective particularly every day routines (4). From the perspective of informed consent specific attention has to be payed

to the proxy decision-maker role of family member(s) (1,2). In concrete terms palliative care includes predominantly somatic interventions like oxygen, morphine, hygienic measures complemented with social support (1). For palliative care of psycho-geriatric patients in their terminal phase it is important not only to deal with the somatic aspects but also to understand the subjective feelings and mood of the patients (3,5); the more so if the patient is suffering from severe functional-psychiatric pathology as in the presented case- study. Applying the DSA method tot Mrs. M's situation, the insight in psychodynamics in combination with an empathic and gentle intuitive attitude made it possible to provide palliative care that fitted in to her varying needs. Her behavior was comprehended in terms of manifestations of a complex post-traumatic stress disorder with a depressive, paranoid and aggressive mood, dissociative symptoms, and both dominant and avoidant personality traits. To prevent desperate and unbearable suffering, to support the patient and/or to mitigate the psychiatric symptoms adequately it is important to recognize and understand these phenomena. To interpret the psycho-social phenomena of Mrs. M. as adaptations which regulated her painful reminiscences, made it possible for the team members to respond flexibly to her changing needs and every day routines all through the course of her illness. Moreover, for the multidisciplinary team the DSA method served as a clear handle to direct their professional interventions. The same holds true for the support of the social system i.c. the son in his role of proxy decision-maker and as second generation victim. It also offered a guideline for the type of psychopharmaca to be prescribed: paroxetine and periciazine for the depressive and aggressive symptoms, pimozide for controlling the vivid reminiscences / nightmares as well as the paranoid symptoms.

To look after the four main-dimensions of the DSA facilitates the professionals to weigh the pro's and cons of the transition from reactivation to palliative care within the same (DSA) framework (2,4). It prevents the use of a too narrow perspective in addressing the intense psychological as well as somatic problems occurring in palliative care with this type of psycho-geriatric patients (5). To realize a comprehensive informed consent, DSA provides the physician with a clear insight to explain to the patient or proxy decision-maker the prognosis with 'rigorous clinical management' in comparison with 'beneficence-based clinical management' i.c. palliative care.

The basic assumptions of the reactivation program seem to be of value to provide palliative care for psycho-geriatric patients with functional-psychiatric co-pathology. To establish its value for a palliative care program and to find out which patients benefit most from this kind of intensive palliative care program, scientific research is recommended. The research should focus on the determination of prognostic patiënt characteristics and the efficacy and cost-effectiviness of the actual used types of palliative care interventions (5,28).

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Psychogeriatric reactivation in a psychiatric-skilled nursing home:

A clinical-empirical exploration[1]

1.   Introduction

The chronic and diverse cognitive function disorders of psychogeriatric patients often occur in conjunction with mood and behavioural disorders (functional-psychiatric pathology), social problems and somatic comorbidity in addition to functional disability (Rubin and Kinscherf, 1989; Teri et al., 1990; Bozzola et al., 1992; Chatterjee et al., 1992; Ballard et al., 1995). This complex co-pathology suggests that there is a need for specific intervention programmes (Colerick and George, 1986; Steele et al., 1990; McNaughton et al., 1995). The interventions aim at (re) gaining or stabilizing the ability to function autonomously and at enhancing the patients' quality of life (Mortimer et al., 1992; Gray and Fenn, 1993).

It is very important that the outcome of such interventions are measured (Lyons et al., 1997; Bakker and Das, 1996) and that the data are used to identify those patients who benefit most (Rubenstein et al., 1964; Colerick and George, 1986; Narain et al., 1988).

The objective of this study was to identify prognostic characteristics for the probability of discharge of psychogeriatric patients with functional-psychiatric pathology, in order to optimize patient selection for the reactivation programme.

2.   Material and methods

2.1   Patients

Reactivation was tailored to psychogeriatric patients primarily suffering from (very) mild to moderate cognitive function disorders. These disorders fell into the following DSM-IV categories: dementia (not otherwise specified, nos), amnestic disorder (nos), cognitive disorder (nos), delirium (nos), and alcohol-induced persisting dementia/amnestic disorder. In addition, all patients exhibited functional-psychiatric pathology and loss of the ability to function autonomously. The patients were referred to the programme by ambulant mental health care services. The inclusion criteria for this study were that psychogeriatric disorders were accompanied by functional-psychiatric pathology and that the patients should be aged 65 and above. The exclusion criteria were: severe functional-psychiatric pathology (e.g. acute psychosis), severe cognitive function disorders and severe (life-threatening) somatic comorbidity. The regular independent referral committee for admission to nursing homes decided whether the reactivation programme was suitable for the individual patient.

2.2   Psychogeriatric reactivation

Psychogeriatric reactivation spans the fields of psychiatry and 'nursing home' medicine. The multidisciplinary programme (duration 3-6 months, in a 15-bed unit) comprised integrated interventions involving therapy, nursing and welfare.

Therapy (i.e. psychotherapy, expression therapy and somatotherapy) was predominantly directed towards improving clinical psychiatric symptoms as well as functional disabilities and to providing training in (adapted) life skills. Specific tools were developed to deal with refractory cognitive dysfunctions and personality disorders. Furthermore, the patients' social and somatic condition was optimized. The therapeutic team consisted of a psychogeriatrician, a clinical psychologist, music-/psychomotor-/creative therapists, a physiotherapist, an occupational therapist, a speech therapist and a dietician. The nursing team utilized supportive strategies and techniques (e.g. rehabilitation, cognitive training, behavioural therapy techniques and a medication programme) with the goal of stimulating and training patients to undertake selfcare. Welfare activities (provided by a welfare worker, clergyman, social worker and volunteers) focused on social activation and social participation, with the aim of conserving the patients' (re)gained ability to function autonomously. Members of staff from all disciplines were trained to conduct the intensive and integrated reactivation programme.

The reactivation process was characterized by three phases: (1) observation and control of dominant disorders, particularly disorders detrimental to vital functions; (2) (re)gaining or stabilizing the psychosocial abilities required for autonomous functioning and the enhancement of well-being and finally (3) preparing for and working through the patients' discharge.

2.3   Design

This was a retrospective, clinical, empirical study. Of the patients who were admitted to the psychogeriatric reactivation programme section of the 'DrieMaasStede', psychiatric-skilled nursing home at Schiedam, the Netherlands from 1989 to 1995, 102 met the inclusion/exclusion criteria.

2.4   Assessments

At baseline, details of the patients' gender, age, marital status and country of origin were recorded (SIG-information, 1995). At the same time, the patients' clinical status was assessed in terms of their prevailing functional and diagnostic characteristics (Mortimer et al., 1992; Lyons et al., 1997). The functional characteristics consisted of the Global Deterioration Scale (GDS, range 1-7), the Help Index (HI, range 0-12) and the Activities of Daily Life score (ADL, range 0-5) (Reisberg, 1982; Juva et al., 1994; SIG-information, 1995). The diagnostic characteristics were derived by having two experts complete an Functional Assessment List (FAL) comprising five domains (cognitive function disorder, functional-psychiatric pathology, caregiver system, traumatic experiences, and somatic comorbidity) (Bakker, 1997).

Finally, the duration of the reactivation programme and the date of discharge was recorded for each patient, the latter being the criterion that psychogeriatric reactivation had been beneficial to the patient in question. Discharge of the patient to a residential home for the elderly was authorized by the regular independent referral committee.

2.5   Procedure

Both the general and the functional data (HI, ADL) were routinely recorded (SIG-information, 1995). The diagnostic data were collected by a psychogeriatrician and a clinical psychologist, who independently completed the standardized FAL and GDS protocols after thorough examination of the patients' medical record (Severijns et al., 1990). The decision procedure was as follows: in the case of disagreement, the two experts attempted to reach consensus through discussion. If consensus could not be reached, the 'interest' variable was coded as missing.

2.6   Statistical analyses

Data were analyzed using the SPSS programme for Windows. The outcome variable was dichotomized (coded 1 for discharged patients or 0 for non-discharged patients). The patients' prognostic characteristics were identified by performing separate logistic regression analyses for each individual variable. Due to the sample size (N=102) and the exploratory nature of the study, variables were not entered simultaneously into the logistic model. The models were adjusted for gender, age and duration of the reactivation programme, to facilitate estimation of their prognostic value.

3. Results

Of the 102 patients, 52% (N=53) were discharged, 22% were transferred internally and 26% died during the reactivation period. The mean duration of treatment was 126 days (range 70-410 days). Of the discharged patients, 70% were transferred to a residential home for the elderly (either assisted-living or independent-living), 26% returned home and 4% went elsewere.

3.1   General characteristics

In respect of gender and age, the patient sample is similar to the distribution found in Dutch nursing homes (SIG-information, 1995). No prognostic differences were identified for gender, age, marital status, country of origin and treatment duration.

3.2   Functional characteristics

The patients' average score on GDS was 4.3 (SD=1.1), for HI and ADL 4.1 (SD=2.9) and 2.7 (SD=1.7), respectively.

Patients exhibiting a relatively low level of cognitive deterioration (GDS) had a high probability of discharge. Similarly, patients with a high level of self-care (HI, ADL) also had a greater chance of being discharged (table 1).

3.3   Diagnostic characteristics

The prognostic characteristics for discharge were identified, within four distinct domains. With respect to the domain of cognitive function disorder, patients with at least one registered cognitive dysfunction ('cognitive syndrome') had a low, though not significant, probability of being discharged. Of all the specific diagnostic classifications only Delirium (nos) showed a significant negative prognostic value (table 1.).

In the domain of functional-psychiatric pathology, patients with at least one emotional disorder had a decreased probability of discharge. The prognosis for patients with the characteristics of a paranoid personality disorder were highly unfavourable. In contrast, patients with a cooperative coping style had a discernibly better prognosis than submissive patients.

An inadequate caregiver system (outside the nursing home), characterized as having no children and/or having partner-relational problems, enhanced the probability of being discharged.

Of the somatic comorbidity, vitamin B (B_1, B_6 and B_{12} together) deficiency increased the probability of being discharged, in contrast to other somatic variables. Parkinsons' disease and cerebrovascular accident were, unexpectedly, not of prognostic value (table 1).

4.   Discussion

A literature search using the key words 'clinical-geriatric' and 'geronto-psychiatric' (treatment programmes) yielded only a limited number of empirical studies. These revealed that 34-62% of psychogeriatric patients are successfully discharged, and that 13-32% died during the programme (van Nieuwkerk, 1984; Liem et al., 1986; Narain et al., 1988; Koenig et al., 1992; Albronda et al., 1996). The results of our study are within the limits of these findings. Our patients were relatively old (mean age = 80.6) and had relatively unfavourable scores for functional characteristics. This indicates that they were referred for admission at a comparatively late stage (Narain et al., 1988; Teri et al., 1988; Eisdorfer et al., 1992; Muskens et al., 1992; Juva et al., 1994).

Tabel: 1   Prognostic power of functional and diagnostic characteristics for discharge of psycho-geriatric reactivation (adjusted for gender, age, duration of programme).

Functional and diagnostic characteristics	N[1]	OR	p (two-tailed)
Functional characteristics			
Global Deterioration Scale (1-7)	102	2.63	0.00
Help index (0-12)	102	1.23	0.01
ADL score (0-5)	102	1.39	0.01
Diagnostic characteristics			
Cognitive function disorder			
Delirium	17	0.10	0.004
'Cognitive syndrome[2]' ($\geq$1)	93	0.13	0.06
Functional-psychiatric pathology			
Emotion disorder ($\geq$1)	90	0.23	0.05
Depression (mixed)[3] ($\geq$1)	59	0.29	0.005
Somatoform disorder ($\geq$1)	22	2.60	0.08
Paranoid personality	6	0.14	0.08
Cooperative coping style	13	12.94	0.02
Submissive coping style	21	0.13	0.002
Caregiver system			
Insufficient caregiver system[4] ($\geq$1)	54	4.28	0.001
Somatic co-morbidity			
Vitamin B deficiencies	53	2.95	0.02
Severe wound	12	0.14	0.02
Urogenital system[5] ($\geq$1)	57	0.19	0.001
Cardiovascular/pulmonary system[6] ($\geq$1)	69	0.19	0.002

1)   N = number of patients with the relevant characteristic odds ratio.
2)   i.c. memory, orientation, praxis and language dysfuntions.
3)   i.c. agitated depression mixed with anxiety-panic and paranoia.
4)   i.c. no children and/or partner-relational problems.
5)   i.c. prostate, urogenital and kidney morbidity.
6)   i.c. decompensatio cordis, arrhythmias and conduction disturbances, hypertension and pulmonary morbidity.

Increasing emphasis is being given to the importance of recognizing the non-cognitive pathology of psychogeriatric disorders (Burns et al., 1990; Chatterjee et al., 1992; Teri et al., 1989, 1990; Rubin et al., 1987, 1989; Siegler et al., 1991). In the present study, the following characteristics of functional-psychiatric pathology were of great prognostic importance: a somatoform disorder, and agitated depression mixed with anxiety-panic and paranoia, a paranoid personality and an cooperative or submissive coping style.

An unexpected finding was that patients suffering from partner-relational problems and/or having no children (inadequate caregiver system) have a relatively high probability of being discharged. This could be attributed to the fact that they were treated in good time, which is supported by their relatively favourable self-care profile at admission. In contrast to acute conditions (e.g. myocardial

infarction, cerebrovascular accident, transient ischemic accident, pneumonia), chronic somatic morbidity was of prognostic relevance. This confirms the necessity of focusing on optimizing the patients' somatic condition.

It is of clinical interest to establish whether the beneficial effects can be attributed to the merits of the intervention programme. A randomized, controlled, parallel group design is therefore required, in which the effects of the intervention programme are compared to the effects of regular medical treatment.

5. Conclusion

Large numbers of psychogeriatric patients suffer from functional-psychiatric pathology, which goes hand in hand with a diminished ability to function autonomously and to maintain quality of life. Accordingly, timely intervention programmes are urgently needed.

The present clinical, empirical study found that the patients' clinical status at baseline (in terms of prevailing functional and diagnostic characteristics) was of important prognostic value for the probability of discharge from a psychogeriatric reactivation programme. The diagnostic characteristics were associated with the following four domains: cognitive function disorder, functional-psychiatric pathology, caregiver system and somatic comorbidity. The functional prognostic characteristics used in this study were GDS, HI and ADL.

The relatively high percentage of discharged patients in this study indicates that frail, elderly psychogeriatric patients with functional-psychogeriatric pathology can be successfully reactivated. Once data on the effective treatment ingredients are available, they can be adapted for similar programmes in day clinics, outpatient departments and intensive home care schemes. The development of a prognostic factor is a prerequisite for optimizing the assignment of patients to such programmes, as is the analysis of cost-effectiveness. Our group has designed a large-scale prospective study with a randomized, controlled, parallel group design to address these questions. This will then allow an evidence-based selection protocol to be specified.

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Life expectancy following psychogeriatric reactivation[1]

1.   Introduction

The mortality rate of psychogeriatric patients with cognitive function disorders (e.g. delirium, dementia, Korsakov, amnestic and other cognitive disorders) is higher than that of the normal population (1-3). Apart from the somatic pathology, cognitive dysfunctions often occur in conjunction with psychiatric function disorders, e.g. mood and behavioural disorders (4-8). These disorders are not only related to a decreased quality of life and the need for long-term care, but also to a diminished life-expectancy (9-13). In order to identify patients who may potentially benefit most from specific intensive interventions aimed at reducing the negative effects of the psychiatric function disorders, it is of clinical interest to determine prognostic indicators which may predict survival in these psychogeriatric patients. In order to optimize medical decision making, it is clinical relevant that patients who may benefit form intervention programmes are immediately identified (on admission).

In this clinical-empirical exploration the first objective was to estimate the life expectancy of patients having participated in the psychogeriatric reactivation programme. The second objective was to identify prognosticators of survival on admission.

2.   Patients and methods

2.1   Patients

Psychogeriatric reactivation was tailored to psychogeriatric patients primarily suffering from mild (or very mild) to moderate cognitive function disorders. The patients were referred to the programme by ambulant mental health care services. The inclusion criteria for this study were: (1) classified within the following DSM IV categories: dementia, amnestic disorder, other cognitive disorders and delirium; (2) psychiatric function disorders ($\geq$ 1); (3) referral for admission; (4) participation in (and discharged from) the reactivation programme, and (5) aged 65 or above.

The exclusion criteria for participation in the reactivation programme were: (1) severe psychiatric function disorders (e.g. acute psychosis); (2) severe cognitive function disorders (Global Deterioration Scale, GDS >6), and (3) (life-threatening) somatic comorbidity.

With regard to the probability of survival, we compared our patient group to a reference group of community-dwelling elderly people, matched by age and gender. For this purpose we used life expectancy tables for age and gender categories, produced by Statistics Netherlands (CBS), which are based on research into population stratifications.

The regular independent referral committee for admission to nursing and residential homes decided whether the reactivation programme was suitable for the patient. Furthermore it determined whether after discharge, referral to a residential home was feasible.

2.2   Psychogeriatric reactivation

Psychogeriatric reactivation spans the fields of psychiatry and nursing-home medicine (15). The reactivation programme (duration 3 to 6 months, in a 15-bed unit) comprised intensive interdisciplinary interventions involving treatment, rehabilitation, nursing, welfare and support of the caregiver system. Treatment was mainly directed towards improving psychiatric function disorders and somatic co-morbidity. Rehabilitation provided training in life skills necessary after discharge. The interventions were adapted to refractory cognitive disorders. Furthermore, the patients' social condition was optimised by welfare and family support.

The therapeutic team consisted of a psychogeriatrician, a clinical psychologist, music-/psychomotor-/creative therapists, a physiotherapist, an occupational therapist, a speech therapist and a dietician. The nursing team was trained in supportive strategies and techniques (e.g. cognitive training, behavioural therapy techniques, rehabilitation and a medication programme). The welfare activities (provided by a welfare worker, clergyman, social worker and volunteers) focused on social activation and social participation, aiming to maintain the patients' new (or regained) ability to function autonomously. The support of the caregiver system was provided by the clinical psychologist and the nursing team. Staff members from all disciplines were trained to conduct the intensive and integrated re-activation programme.

The reactivation process was characterized by three consecutive phases: (1) ob-servation and control of dominant psychiatric function disorders and somatic co-morbidity, particularly disorders and morbidity detrimental to vital functions; (2) achieving, regaining or stabilizing the psychosocial abilities required for autono-mous functioning and the enhancement of well-being and finally (3) preparing the patient for discharge.

2.3   Design

This was a prospective, clinical-empirical study. Of the 102 patients who participat-ed in the psychogeriatric reactivation programme section of the psychiatric-skilled nursing home 'DrieMaasStede', Schiedam, the Netherlands from 1989 to 1995, 75 met the selection criteria of this study.

2.5   Assessments

On admission, the patients' gender, age, marital status and country of origin were recorded (16). The patients' clinical status was assessed in terms of their prevail-ing functional and diagnostic characteristics (17,18). The functional characteristics consisted of the Global Deterioration Scale (GDS, range: 1-7), the Help Index (HI, range: 0-12) and Activities of Daily Life (ADL, range: 0-5) (19,20). The diagnostic characteristics were assessed by two experts (a psychogeriatrician and a clinical

psychologist), who completed a standardised Functional Assessment List (FAL) based on the DSM-IV and ICD-9. The FAL comprised five domains: general details, cognitive function disorders, psychiatric function disorders, somatic comorbidity and (caregiver) social system (21).

2.6   Procedure

Both the general and the functional data (HI, ADL) were routinely registered (16). After thorough examination of the patients' medical records (22) a psychogeriatrician and a clinical psychologist completed both the FAL and the GDS. The decision procedure was as follows: in the case of disagreement, the two experts attempted to reach consensus through discussion. If consensus could not be reached, the lack of consensus was recorded. Details of the duration of treatment and of location after discharge were recorded for each patient, following their discharge from the reactivation programme. Data concerning the deaths of participants were gathered by telephone and by consulting the Registry of Births, Marriages and Deaths.

2.7   Statistical analyses

To be able to compare survival rates after discharge, the study patients were divided into an 'independent' group being discharged home or to a residential home with restricted support and a 'dependent' group being discharged to a nursing home.

We used the Kaplan-Meier test for equality of survival distributions to make comparisons between the survival curves of the 'independent' group, the 'dependent' group and the reference group of community-dwelling elderly people. A log rank test was used to test the difference of survival distributions. Significance was set at $p<0.05$ (two-tailed).

To identify prognostic characteristics for survival after discharge, the Cox regression analyses were applied first to each individual variable (general, functional and diagnostic characteristics of the patients) assessed on the five domains. For efficiency reasons these results are not presented in this article. In the joined analyses of functional as well as diagnostic characteristics, characteristics with $p< 0.10$ (two tailed) in the separate analyses were entered simultaneously (backward elimination method). Next, in the combined analyses both functional and diagnostic characteristics meeting the p-values <0.05 (two tailed) were entered in the Cox regression analyses (backward elimination procedure). Regarding the explorative nature of this study the p-value was fixed at 0.05 (two tailed). The separate, joined and combined Cox regression analyses were adjusted for gender, age and type of discharge to facilitate estimation of their prognostic value.

The adjusted hazard ratio (HR) was used to measure performance. The more HR diverges from 1.0, the higher the prognostic value. A HR lower than 1 means a lower probability of death. All estimated parameters are presented with their 95% confidence intervals (CIs).

3. Results

Seventy-five patients participated in this study. Their mean age was 80 (range: 65-92; SD=6.74), 25% were men and 75% were women. In terms of marital status, 75% were single. The median duration of treatment was 122 days (range: 19-410). Of the 75 patients, 29% were discharged to a nursing home ('dependent' group; N=22) and 71% home or to a residential home with restricted support (the 'independent' group; N=53). Of the 'independent' group, 26% went to their own home, 70% to a residential home with restricted support and 4% went elsewhere.

3.1 Survival after discharge

The HR ratio for the 'independent' group of patients was 0.31, which implies that the estimated probability of survival is 3.2 times higher (1/HR) than that for the 'dependent' group. Statistical analysis showed that the medians of the three groups differed (log rank test=152.04; d.f.=2; p=0.00). The 95% CIs showed no overlap between the three groups ($median_{nurs}$=13 months; 95% CI: 3 to 22; $median_{ind}$ =35 months; 95% CI: 25 to 45; $median_{ref}$=95 months; 95% CI: 74 to 116).

3.2 Prognostic characteristics for survival after discharge

Of the general details, only gender (HR=3.07; 95% CI: 1.61 to 5.85) appeared to be significant; the probability of survival after discharge was three times higher for women than for men. Age was of no significance, nor were marital status and country of origin.

post-discharge survival
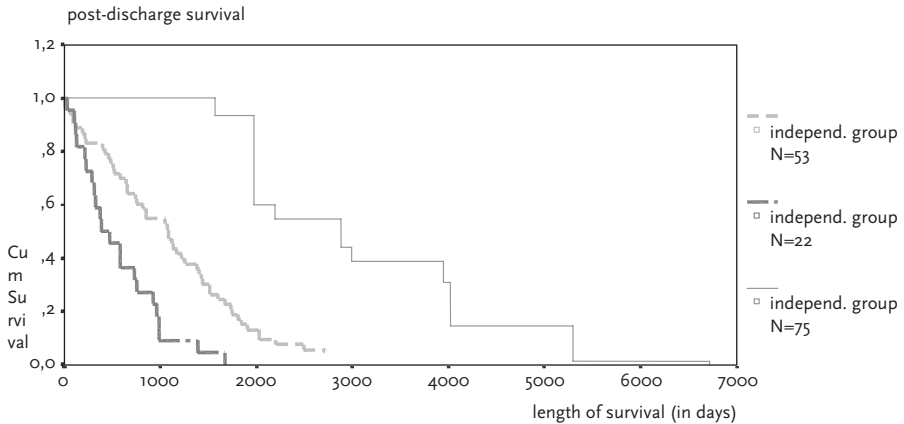
Fig. 1: Survival of the 'independent' and the 'dependent' group of psychogeriatric patients after discharge from a psychogeriatric reactivation programme in comparison with a reference group of community dwelling elderly (N=75).

3.3   Joined regression analyses of functional characteristics

The patients' average score on (GDS) was 4.2 (SD=1.3). The average scores on the HI and ADL were 3.5 (SD=2.7) and 2.4 (SD=1.7), respectively. In the joined Cox regression analyses for functional characteristics, adjusted for gender, age and type of discharge (see Table 1), only GDS was significant. Thus, patients who scored higher in GDS had a lower probability of survival than patients who scored lower.

3.4   Joined regression analyses of diagnostic characteristics

In the joined Cox regression analyses for diagnostic characteristics adjusted for gender, age and type of discharge, patient characteristics for the prognosis of survival after discharge were identified within the four domains: cognitive function disorders, psychiatric function disorders, somatic comorbidity and adequacy of the caregiver system.

Of the patients 7% were suffering from delirium, 32% from Alzheimers' disease, 33% from vascular dementia, 10% form Korsakov dementia and 18% belonged to mixed and not otherwise specified categories. The survival time was relatively short for patients with more severe characteristics of a cognitive function disorder ('cognitive syndrome'). Unexpectedly, no specific DSM IV diagnostic category except delirium (HR=3.02; 95% CI: 1.02 to 8.89) had any significant prognostic value in the separate analyses.

With respect to psychiatric function disorders, we measured the following characteristics on admission: 88% of all patients had one or more characteristics

Table 1. The hazard ratios of patient characteristics - assessed on admission - for survival after
discharge from a psychogeriatric reactivation programme, adjusted for gender, age and type of
discharge (d.f.=1).

Characteristics at intake	N[1]	HR[2]	SeHR[3]	95% CI for HR[4]	P (<)[5]
Joined analysis of functional characteristics					
gender (m=1, f=0)	19	2.45	1.37	1.33 to 4.52	.01
age	75	1.00	1.02	0.95 to 1.05	.97
type of discharge	75	0.48	1.40	0.25 to 0.94	.04
GDS	75	1.91	1.20	1.35 to 2.70	.001
Joined analysis of diagnostic characteristics					
gender (m=1, f=0)	19	3.43	1.37	1.84 to 6.39	.0001
age	75	0.98	1.02	0.93 to 1.03	.36
type of discharge	75	0.98	1.44	0.48 to 2.00	.95
'cognitive syndrome' [6]	66	1.20	1.08	1.03 to 1.40	.02
paranoia	15	2.17	1.42	1.09 to 4.33	.03
urogenital pathology[7]	37	2.01	1.27	1.26 to 3.22	.01
cardiopulmonary pathology[8]	45	1.53	1.17	1.13 to 2.08	.01
inadequate caregiver system[9]	45	0.55	1.33	0.32 to 0.97	.04
Combined analysis of diagnostic and functional characteristics					
gender (m=1, f=0)	19	3.07	1.39	1.61 to 5.85	.001
age	75	0.97	1.03	0.92 to 1.02	.28
type of discharge	75	1.00	1.45	0.49 to 2.06	1.00
GDS	75	1.58	1.20	1.09 to 2.27	.02
paranoia	15	2.19	1.41	1.11 to 4.30	.03
urogenital pathology	37	1.83	1.27	1.13 to 2.96	.02
cardiopulmonary pathology	45	1.56	1.17	1.14 to 2.12	.005
inadequate caregiver system	45	0.59	1.33	0.34 to 1.03	.07

[1] N=number of patients; [2] HR= hazard ratio; [3] Se$_{HR}$=standard errror of hazard ratio; [4] 95%CI=95% confidence intervals; [5] P=significance level; [6] i.e. memory-, orientation-, praxis- and language dysfunctions; [7] i.e. prostate, urogenital, and kidney morbidity; [8] i.e. decompensatio cordis, arrhythmias and conduction disturbances, hypertension, and pulmonary morbidity and [9] i.e. no children and/or partner-relational problems;.

of an emotional disorder (e.g. 76% of depression, 28% of fear or panic disorder and 20% of paranoia). Additionally, we identified one or more characteristics of a personality disorder in 48% of our patients. The joined Cox regression analyses for diagnostic characteristics showed that only paranoia was an unfavourable prognostic factor for survival after discharge. No other characteristics of emotional and personality disorders or coping style were of significant prognostic value. Characteristics of depression met a borderline significant value only in the separate analyses (HR= 2.05; 95% CI 0.99 to 4.24). In terms of somatic comorbidity, the degree of urogenital and cardiopulmonary pathology was a significant value for the probability of a relatively short survival. In this explorative study, common neurological disorders such as Parkinsons' disease and cerebrovascular accident were neither in the separate analyses nor in the joined analyses of diagnostic characteristics of prognostis value.

An inadequate caregiver system on admission, i.e. having no caring spouse and/ or children, was the only significant prognostic social factor for the probability of a relatively long survival.

3.5 Combined Cox regression analyses

The combined Cox regression analyses adjusted for gender, age and type of discharge showed that general, functional and diagnostic characteristics that were of prognostic significance for survival after discharge from the reactivation programme. Gender (men; HR=3.07), GDS (HR=1.58), paranoia (HR=2.19), somatic comorbidity (in this case: urogenital and cardiopulmonary pathology: HR=1.83 and 1.56 respectively) were not of prognostic significance. An inadequate caregiver system was the only factor in the analyses that may indicate a better prognosis (HR=0.59), though being borderline significant. The combined Cox regression model was able to account for 32% of the variance.

4. Discussion

First of all it has to be notified that the character of this study was explorative. That is the reason why the phenomenon of multiple testing was not taken into account. This limits the validity of the statistical inferences of this study. Therefore, we have presented the 95% CIs as well. In addition, there is a limitation to this explorative study due to the absence of a control group.

As expected, the probability of survival of the 'independent' group (being discharged home and to residential home) was higher (1/HR=3.2) than that of the 'dependent' group (being discharged to a nursing home). The data agree with the results of previous studies conducted in this field (23-26). The difference in survival between the 'independent' group (median=35 months) and the community-dwelling reference group (median=95 months) highlights the frailty of psychogeriatric patients suffering from cognitive function disorders in conjunction with psychiatric function disorders. This is in accordance with findings reported in the literature (1-3,13,27,28). As the 95% CIs of the median survival of the two reactivation groups did not show any overlap, the conclusion seems justified that they differed definitely. In the experimental phase of the intensive interdisciplinary programme it is from an ethical perspective important to select those patients who may benefit for a longer period from potentially favourable effects. Later on, if the effects hopefully have been proven to be favourable for this group of patients, further experimental research is ethically justified for psychogeriatric patients with a short(er) life expectancy, as well. Therefore, it is of high clinical interest to have an instrument to identify those patients who may benefit most from the psychogeriatric reactivation programme. Consequently, it is necessary to determine prognosticators of increased survival. Valid prognostic models may enable

clinicians to evaluate the outcomes of treatment of psychogeriatric patients following different kinds of intervention programmes and therefore improve medical decision-making (18).

On admission, women had a higher life expectancy than men. This is in accordance with findings reported in the literature (9,13,29-32). It is of clinical interest that, despite the wide range (mean 80; range 65-92 years), age was not of prognostic value for survival after discharge. So, age is not a relevant criterion for inclusion into the programme. This is supported by the findings of Mölsa et al. (33) in a community-based epidemiological investigation. In a previous study concerning the identification of prognostic characteristics for discharge, age was also non-significant (14), in contrast to studies by Alem et al. (9), Cohen-Mansfield et al. (10) and Koopmans et al. (31) on the survival of psychogeriatric patients after their admission to programmes in (non-psychiatric-skilled) nursing homes. This may be explained by differences in the effect in population characteristics as well as differences in the effect of the applied programmes or both.

According to the literature, high scores on HI and ADL have negative implications for survival (9,10,31,32,34). In the joined Cox regression analyses of functional characteristics, these characteristics turned out to be nonsignificant. A probable explanation is that GDS is a more powerful overall prognostic measure than the isolated HI and ADL.

Characteristics of a cognitive function disorder are of prognostic value for survival. In the elderly, they have been linked to a higher mortality risk, irrespective of age, education and somatic illnesses (1,3,28). The 'cognitive syndrome', which in our study comprised memory, orientation, praxis and language dysfunctions, was of significant prognostic value. The less patients suffered from a cognitive function disorder, the higher the probability for survival. The 'cognitive syndrome' was no longer significant in the combined Cox regression analyses. GDS, a functional measure for cognitive function disorders, was prognostically more powerful. GDS is a good candidate as inclusion criterion for cognitive function. In this study, all specific diagnostic classifications of cognitive function disorders according DSM IV were of no prognostic significance for survival after discharge; except for delirium (HR=3.02), though only in the separate analyses. This is in line with Mölsa (33), but in contrast to the findings of Koopmans et al. (31,35). In a previous study, delirium was a powerful negative prognostic factor for discharge from the reactivation programme (14). For future research it is to consider to exclude patients suffering from a deliriant episode from the reactivation programme.

With regard to psychiatric function disorders, many studies emphasize the importance of recognizing and treating non-cognitive function characteristics (4-6,8,36-40). Actually, they are considered to be more suitable for intervention. In our study paranoia, assessed on admission, was identified as the only psychiatric

function disorder that appeared to be prognostically significant for survival after discharge from the reactivation programme. The literature on this subject shows that the majority of patients, irrespective of hospitalization, with paranoid disorders have a poor prognosis (41). The inclusion of overtly paranoid patients in the reactivation programme should be made with great care. Another option is to adjust the programme more to paranoid patients. The most common psychiatric disorder in the elderly, late-life depression, together with dementia and physical dependency, is associated with mortality in continuing care for geriatric inpatients (11,12). Late-life depression associated with cardiovascular disease results in a mortality rate after discharge that is 2.6 times higher than the expected mortality rate (42). Surprisingly, in this study (with 76% of the patients showing characteristics of depression on admission), the HR of depression was 2.05, with a borderline significant value only in the separate analyses. Unexpectedly, the combined Cox regression analyses did not identify any depressive characteristic as risk factor for survival after discharge. In order to measure effects of the reactivation programme on depressive symptoms, it is of clinical importance to assess symptoms on admission as well as at discharge. Competing prognostic factors, particularly paranoid and cardiovascular characteristics, may also be of interest.

Chronic somatic comorbidity on admission, particularly urogenital and cardiopulmonary pathology, was an important (negative) prognosticator of survival after discharge. In contrast, acute conditions, e.g. myocardial infarction, cerebrovascular accident, and pneumonia (determined on admission) were insignificant, which is not in line with the studies by Koopmans et al. (31) and Mölsä et al. (1986) but they do support that of Dijk (30).

The importance of the treatment of somatic comorbidity in a psychogeriatric reactivation programme is stressed, particularly since the chronic somatic comorbidity was also prognostically important for the probability of discharge from the programme (14).

The inadequacy of the caregiver system as a positive prognosticator for survival seems contradictory to findings from other studies. Coe et al. (43) observed that the presence of a support system is positively related to survival. In our study, the inadequacy of the caregiver system was probably related to a relatively early admission to the reactivation programme, before the deterioration of autonomous functioning was too far advanced (44,45), since patients with an inadequate caregiver system tended to have relatively low scores for ADL, HI and GDS.

The combined Cox regression model for patient characteristics on admission - adjusted for gender, age and type of discharge - accounted for 32% of the variance found in survival rates after discharge. The percentage that could not be accounted for might be attributed to factors after admission such as novel events occurring between admission to the reactivation programme and death. Among these factors may be the reactivation programme itself, major new life events (i.e. the death of spouse), new psychiatric disorders and new somatic comorbidity.

Considering the foregoing clinical reflections of the findings of this study combined with those of previous studies we recommend future research on the cost-effectiveness of intervention programmes on psychiatric function disorders in psychogeriatric patients. In the experimental phase, the following aspects have to be taken into account.

To construct a prognostic instrument for optimal decision making considering the estimation of the probability of survival after treatment, it is recommended to address five domains: general details, cognitive function disorders, psychiatric function disorders, somatic comorbidity as well as adequacy of the caregiver system. Characteristics of gender, delirium, GDS, paranoia, cardiopulmonary and urogenital pathology as well as adequacy of the caregiver system seem to be important candidate factors.

In addition to survival, it is of clinical interest to estimate the effects of the psychogeriatric reactivation programme to quality of life (i.e. quality adjusted life year, QALY's) and the need for long-term care after discharge.

5.   Conclusion

As the mortality rate of psychogeriatric patients is high and the prevalence of psychogeriatric diseases will increase more and more, comprehensive intervention programmes tailored to cognitive and psychiatric function disorders of these patients are urgently needed. The first objective of this exploratory study was to estimate life expectancy of patients having participated in the reactivation programme, the second objective was to identify prognostic characteristics assessed on admission for survival after discharge. The patients (N=75) were admitted to the programme when they were on the verge of losing their ability to function autonomously.

To be able to compare survival rates after discharge, patients were divided into an 'independent' and a 'dependent' group. The estimated probability of survival of the 'independent' group of patients was obviously higher (1/HR=3.2) than that of the 'dependent' group. The median survival period showed no overlap. This suggests that with respect to survival the two groups of psychogeriatric patients who participated in the reactivation programme differed definitely. It is of high clinical interest to identify on admission those patients who have a greater chance to benefit more form the potentially favourable effects of the intensive interdisciplinary psychogeriatric reactivation programme.

In the combined Cox regression analyses, general, functional and diagnostic characteristics of patients, assessed on admission, were identified as prognostically relevant for the length of survival after discharge.

Of the general details, it appeared that women lived longer than men whereas age was not of relevance. Regarding four other domains, patients' survival was negatively related to GDS (cognition), paranoia, as well as to urogenital and cardiopulmonary pathology. An inadequate caregiver system was positively related to survival.

The development of a prognostic instrument is a prerequisite for optimal medical decision making for such intervention programmes, as is the analysis of cost-effectiveness. In order to draw firm conclusions, it is recommended that a large-scale study with a randomized, parallel-group design will be performed. Our research group have started such a research programme in July 2001.

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Prevalence of psychiatric function disorders in psychogeriatric patients at referral to nursing home care;

The relation to cognition, activities of daily living and general details[1]

1.   Introduction

Systematic research shows that the prevalence of non-cognitive, psychiatric function disorders (PFDs) in psychogeriatric patients staying in a nursing home or home for the elderly varies from 70% to 80%. It is not evident whether and to which degree the PFDs were present at the moment of referral or if the patients had acquired the PFDs during their length of stay in a nursing home or a home for the elderly. Aalten et al. (2003b) reported that of the patients who attented a policlinic for cognitive function disorders, 90% had PFDs. Literature on the prevalence of PFDs in psychogeriatric patients suffering from cognitive function disorders at the moment of referral to nursing home care is rather scarce.

PFDs play an important role in psychogeriatrics. They have negative effects on the quality of life of the psychogeriatric patients and also put a great burden on the caregiver system. In addition, these prognostic factors are important for early admission to an institution (nursing home) as well as for the outcome of psychogeriatric intervention programmes. For assessing psychiatric disorders in psychogeriatric patients Cummings et al. (1994) developed in the 1990s a valid and reliable instrument - the Neuropsychiatric Inventory (NPI). This instrument has already been applied in many studies (Aalten, 2004, 2003; Lyketsos et al., 2001; Wood et al., 2000). A Dutch version has been constructed and validated by Kat et al. (2002).

However, the relation of the PFDs as assessed by the NPI to the hallmarks of psychogeriatric patients - the cognitive function disorders and the related handicaps in activities of daily living (ADL) - is not obvious (Aalten, 2004; Tran et al., 2003). The same implies to relevant general details such as gender, age, marital status, domicile and type of primary caregiver. For the referral of psychogeriatric patients suffering from PFDs to specific intervention programmes it is of clinical interest to optimize the medical decision making process. To that end, insight in the at-referral prevalence and co-occurence of the PFDs and their relation to the cognitive function disorders and ADL handicaps is of relevance, combined with general details.

The objectives of this study were: (1) To estimate the prevalence and co-occurrence of PFDs in psychogeriatric patients suffering from cognitive function disorders at referral to clinical as well as non-clinical (transmural) psychogeriatric programmes; (2) It is expected that PFDs , both total and individual, are positively related to the cognitive function disorders as well as the ADL-handicaps; (3) Exploratively, the structure of the interrelationship of PFDs, cognitive function disorders and ADL handicaps will be analysed. In addition, the general details and the structure to be identified will be described.

2.   Material and methods

2.1   Patients

The study group comprised patients from the Nieuwe Waterweg Noord (NWN) region, who were referred to transmural and intramural nursing home care and who were suspected to suffer from cognitive function disorders (MMSE ≤ 29) and who were ≥ 65 years old (N=487). The patients were referred from ambulant mental healthcare service, hospital (neurologist), general practitioner or home care.

2.2   Design

This was a prospective observation study carried out in the NWN region, adjacent to Rotterdam, the Netherlands. The NWN region counts about 180,000 inhabitants; 16% of them were aged 65 and above. The observation period was from June 2001 to October 2002. The measurements were executed within a period of 1 month after the first contact with a professional of a nursing home or of the participating ambulant mental healthcare service.

The study was a part of a larger study comprising a randomized controlled trial with a parallel group design on cost-effectiveness of a psychogeriatric reactivation programme.

2.3   Assessments

At referral, the following general details of the patients were recorded: gender (women coded 1 and men coded 0), age (years), marital status (together coded 1 and alone coded 0), domicile (at home coded 1 and elsewhere coded 0), and type of primary caregiver (spouse coded 1 and other coded 0). The patients cognitive functional status was assessed with Mini Mental State Examination (MMSE) of which the range is 0-30 and 30 is normal (Folstein et al., 1975). The activity of daily living (ADL) status was assessed with the Barthel Index (BI) (de Haan et al., 1993) of which the range is 0-20 and 20 is normal). Both MMSE and BI are well known and widely used in (psycho)geriatrics. For assessing the PFDs the Neuro-Psychiatric Inventory (NPI, Cummings et al., 1994) was used (range 0-12; 0 is absence of symptoms). On each NPI-symptom the patient could score positively when he/she had showed that behaviour minimally once a week for the last 4 weeks. In this study the professionals were trained in applying all the assessment instruments.

2.4   Statistical analyses

For the categorical data the percentage was used as a measure of central tendency, while for the continuous data the mean was considered to be the measure of central tendency. The standard deviation was used as a measure of dispersion for both categorical and continuous data.

Bivariate categorical data were tested by the method of exact testing. Students' t test for unpaired samples was used to test for differences between two independent groups on continuous data.

When more than one predictor and/or confounding variable was used, the method of linear regression analysis was applied in case of continuous outcome variables, and logistic regression analysis was executed in case of binary outcome variables.

Regarding the method of linear regression analysis, the standardized regression coefficient of the individual variable was considered to be the measure of relative importance of the individual variable, whereas in case of logistic regression analysis the odds ratio of the individual variable was considered as a measure of relative importance, telling us how much more likely it is that the criterion variable (NPI symptom present, coded 1) has a higher level on general details, MMSE and BI than the criterion variable (NPI symptom absent, coded 0).

The 95% confidence intervals of both the unstandardized regression coefficients and the odds ratios of the individual predictor and/or confounding variables indicate the uncertainty region of the measures at issue.

The multiple correlation coefficient squared (R^2) and Nagelkerke R^2 are statistics used to quantify the proportion of variation explained by the model for the models of linear regression and logistic regression, respectively. All significance testing was fixed at 0.05 level of significance, two tailed.

The interrelationship of MMSE, BI and NPI was simultaneously examined with the method of non-metric principal component analysis. The computer algorithm is called PRINCALS (Gifi, 1985, 1981; Leeuw and Rijckevorsel, 1980). The purpose was to represent the interrelationship into a two-dimensional solution without substantial loss of information. Compared to the classical principal component analysis, the principal component analysis for non-metric data is characterized by the following advantages: the data are allowed to be of ordinal or even lower level, it enables to identify non-linearities between the variables of interest, and it enables visualizing differences, if there are any, of determinants on the two-dimensional solution. The percentage variance explained was considered to be the overall measure of model adequacy. The loadings of the individual variables indicate the degree of individual performance.

3. Results

Available patient scores from the NPI, MMSE and BI were analyzed.

Out of the 487 eligible patients 385 met this criterion. Regarding domicile, patients who met this criterion differed significantly from those who did not (p<0.001; 65 and 43%, respectively). This meant that more patients not living at home were excluded from the analysis due to missing data.

3.1 Characteristics at referral

Of the 385 patients 67.8% was female and 32.2% male (table 1). The mean age of women and men was 82.5 and 79.7 respectively (P<0.001). Of the men 65.8% were living with a spouse and of the women only 27.1% (P<0.001). At referral, 71.1% of men and 62.8% of women stayed at home (P<0.13). In 44.3% of men, the spouse was the primary caregiver whereas in women the percentage was 14.0 (P<0.001).

With respect to the MMSE, there was no significant difference between men and women (p<0.46). On the BI, men scored significantly higher (P<0.01) - in other words men were more ADL independent. On the NPI, there was no significant difference either (p<0.31). On the BI, men scored significantly higher (p<0.01) – in other words men were more ADL independent. So, compared to women at referral for clinical/non-clinical nursing home care, men were younger, were relatively ADL independent and lived together with their spouse, who also was the primary caregiver.

Of the patients 91.7% showed at least one symptom on the NPI (table 2); 81.6% two symptoms or more. Depression (43.9%) apathy (43.1%) followed by anxiety (41.6%) and agitation/aggression (32.2%) showed a high prevalence. On individual NPI symptoms women differed from men significantly on four symptoms. Relatively many women suffered from delusion, hallucination and anxiety; many men were agitated/aggressive.

The matrices of co-occurrence (table 3) demonstrate that overall depression with anxiety (25%) had the highest percentage of co-occurrence.

For women depression and anxiety (29%) had the highest percentage of co-occurrence, whereas for men agitation/aggression and irritability (25%). Women differed from men significantly on specific NPI symptoms with respect to the following co-occurrences: delusion/hallucination, delusion/depression, delusion/anxiety, delusion/irritability, hallucination/anxiety, hallucination/apathy, hallucination/irritability, anxiety/depression, anxiety/sleeping disorder and anxiety/eating disorder. On eight of the twelve NPI symptoms there was significant difference in co-occurrence between men and women. The percentages in women were higher. Looking from the perspective of the individual NPI symptoms in women, delusion had four significant co-occurrences, hallucination five, depression two, anxiety five, apathy one, irritability two, sleeping disorder two and at last eating disorder one. So, the percentage of co-occurrances was higher in women than in

men, principally of delusion, hallucination and anxiety. The other five significant different NPI symptoms were related to these three principal symptoms.

Table 1.   Patient characteristics: general details, MMSE, NPI and Barthel-index distinguished by gender

	Men	Women	Total	p-values (two-tailed)
Gender (%)	32.2	67.8	-	-
Age (years)	79.7 (s=7.5)	82.5 (s=6.6)	81.6 (s=7.0)	0.001[1]
Marital status - together (%)	65.8	27.1	60.5	0.001[2]
Domicile - at home (%)	71.1	62.8	65.5	0.13[2]
Primary caregiver - spouse (%)	44.3	14.0	23.6	0.001[2]
NPI (0-12)	3.5 (s=2.2)	3.7 (s=2.4)	3.6 (s=2.3)	0.31
MMSE (0-30)	18.4 (s=6.3)	17.0 (s=5.7)	17.4 (s=5.9)	0.46
Barthel (0-20)	15.1 (s=4.6)	13.7 (s=5.5)	14.8 (s=5.3)	0.006

[1] t-test for unpaired samples; two-tailed
[2] Fisher's exact (df=1); two-tailed

Table 2. NPI-symptoms distinguished by gender

	Men (N=124) %	Women (N=261) %	P< [1]	Total (N=385) %
Delusion	16.1	25.7	0.04	22.6
Hallucination	12.9	25.7	0.005	21.6
Agitation/aggression	38.7	27.6	0.04	31.2
Depression/Dysphoria	42.7	44.4	0.83	43.9
Anxiety	29.8	47.5	0.001	41.6
Euphoria	1.6	5.0	0.16	3.9
Apathy	46.8	41.4	0.32	43.1
Disinhibition	20.2	16.5	0.39	17.7
Irritability	41.9	34.5	0.18	36.9
Aberrant motor behaviour	21.0	22.6	0.79	22.1
Sleepdisturbance	19.4	25.7	0.20	23.6
Eatingdisorder	35.5	36.4	0.91	36.1
≥ 1 score	92,3	90,3	0.56	91,7
≥ 2 scores	80,8	83,1	0.67	81,6

[1] Fisher's Exact Test (2-sided; df=1)

Table 3. (Co-)occurences of NPI-symptoms in all patients and distinguished by gender

3.1. Matrix of (co-)occurences of NPI-symptoms in all patients (%) (n=385)

	delu	hal	agit	dep	anx	eufo	apath	disinh	irrit	repit	slpdis	eat d
delu	23											
hal	13	22										
agit	11	8	31									
dep	10	10	16	44								
anx	13	13	14	25	42							
eufo	2	1	1	1	2	4						
apath	12	11	17	22	22	2	43					
disinh	6	6	11	8	9	2	8	18				
irrit	11	10	21	20	18	2	19	10	37			
repit	8	7	9	11	14	2	14	6	11	22		
slpdis	11	10	11	13	12	1	12	5	11	8	24	
eat d	10	12	15	21	18	2	20	9	16	10	11	36

3.2. Matrix of (co-)occurences of NPI-symptoms in women (%) (n=261)

	delu	hal	agit	dep	anx	eufo	apath	disinh	irrit	repit	slpdis	eat d
delu	26											
hal	16	26										
agit	12	9	28									
dep	13	12	15	44								
anx	17	17	15	29	48							
eufo	2	1	2	2	2	5						
apath	13	14	16	21	23	2	41					
disinh	6	7	10	9	11	2	7	17				
irrit	14	12	18	20	20	2	17	11	35			
repit	9	8	8	13	16	2	12	6	11	23		
slpdis	13	13	11	14	15	1	12	5	12	9	26	
eat d	12	14	14	22	21	3	20	10	16	10	13	36

3.3. Matrix of (co-)occurences of NPI-symptoms in men (%) (n=124)

	delu	hal	agit	dep	anx	eufo	apath	disinh	irrit	repit	slpdis	eat d
delu	16											
hal	7	13										
agit	11	7	39									
dep	6	7	19	43								
anx	7	3	11	17	30							
eufo	2	1	1	0	0	2						
apath	8	6	20	23	19	1	47					
disinh	7	2	14	7	6	1	9	20				
irrit	7	4	25	19	15	1	23	10	42			
repit	7	4	10	8	11	2	18	6	11	21		
slpdis	7	5	11	9	6	1	11	4	10	6	19	
eat d	7	7	16	19	12	1	19	7	17	11	9	36

3.4. Significance testing of co-ocurrences between men and women[1,2])

	delu	hal	agit	dep	anx	eufo	apath	disinh	irrit	repit	slpdis	eat d
delu												
hal	• .01											
agit	.87	.70										
dep	• .05	.11	.47									
anx	• .01	•.001	.43	• .02								
eufo	1.00	1.00	1.00	.31	.19							
apath	.18	• .02	.32	.60	.51	.67						
disinh	.82	.07	.23	.70	.13	.67	.69					
irrit	• .04	• .01	.14	.90	.21	.67	.13	.86				
repit	.44	.14	.71	.18	.28	1.00	.16	1.00	1.00			
slpdis	.12	• .02	1.00	.19	• .02	1.00	.87	.80	.73	.32		
eat d	.11	.07	.65	.69	• .05	.29	.90	.46	.89	1.00	.31	

[1] exact testing, p-values (two-tailed)
[2] • = women higher percentage than men

3.2   Prognostics of total NPI score

To explore the prognostic relation of MMSE and BI to the NPI, the total NPI score was entered in a regression model with MMSE and BI as prognostic factors; this was followed by a combined analysis with the general details. In the first model with only MMSE and BI the MMSE was significant (p<0.01; B=-0.06; 95% CI: 0.10 to -0.02) (not presented). This meant that a lower score on the MMSE resulted on average in a higher NPI score, although the explained variance was minor (R^2=0.02). In the combined regression model in which general details were added (table 4), age (P<0.001) and MMSE score (P< 0.006) were of significant prognostic importance. This meant that being older and having a lower MMSE score was on average associated with a higher score on the NPI; also the performance of this model was low (R^2=.07).

Table 4. Regression Analysis of total NPI-score for MMSE, Barthel and general details

	B [1]	p-values	95% Confidence interval B	
Gender	0.52	0.07	-0.05	1.09
Age	-0.07	0.001	-0.10	-0.03
Marital status	-0.06	0.84	-0.70	0.57
Domicile	0.11	0.78	-0.63	0.84
Primary caregiver	0.39	0.20	-0.20	0.98
MMSE	-0.06	0.01	-0.11	-0.02
Barthel	-0.01	0.73	-0.06	0.04

R-Squared [2] =0.07

[1]   Unstandardized regression coefficients
[2]   Explained variance of the variables together

3.3   Prognostics of individual NPI symptoms

In order to analyse the relation of the MMSE and BI to NPI symptoms separately, logistic regression analyses were applied on each NPI symptom followed by similar analyses although adjusted for general details (table 5). It appeared that, in general, neither MMSE nor BI were of any prognostic value for NPI symptoms with the exception of delusion and hallucination. Both the MMSE and BI were of importance for delusion; the MMSE was also of prognostic value for hallucination. When the analyses were adjusted for general details, the MMSE appeared to be of no significant prognostic value at all. However, the BI had prognostic value for the following three symptoms: delusion (p<0.04), sleeping disorder (p<0.04) and eating disorder (P<0.05) in the sense that a low score on the BI was associated with delusion, sleeping and eating disorders.

Table 5.   Logistic Regression Analysis of NPI-symptoms as criterion variables

	Gender				age				marital status				domicile				primary caregiver				MMSE				Barthel				
			95% CI				95% CI				95% CI				95% CI				95% CI				95% CI				95% CI		
	OR[1]	p	low	up	OR	p	low	up	OR	p	low	up	OR	p	low	up	OR	p	low	up	OR	p	low	up	OR	p	low	up	R^2 Nagelkerke
Delusion	2.05	0.04	1.03	4.06	0.95	0.02	0.92	0.99	0.35	0.01	0.16	0.79	1.05	0.96	0.53	1.94	1.43	0.44	0.57	3.56	0.95	0.04	0.90	1.00	1.07	0.03	1.01	1.15	0.12
Hallucination	2.96	0.01	1.42	6.15	0.95	0.03	0.92	1.00	0.56	0.16	0.26	1.24	1.18	0.63	0.60	2.32	2.42	0.05	1.01	5.78	0.95	0.04	0.90	1.00	1.01	0.74	0.95	1.07	0.10
Agitation/agression	0.72	0.23	0.42	1.23	0.99	0.61	0.96	1.03	1.47	0.22	0.79	2.71	0.94	0.83	0.53	1.67	0.71	0.34	0.35	1.43	0.95	0.03	0.91	1.00	1.04	0.13	0.98	1.10	0.04
Depression/dysphoria	1.07	0.77	0.65	1.79	0.99	0.98	0.97	1.03	0.65	0.15	0.36	1.16	0.79	0.40	0.47	1.35	1.27	0.48	0.65	2.48	1.01	0.83	0.97	1.05	1.01	0.87	0.96	1.05	0.02
Anxiety	2.89	0.001	1.66	5.04	0.97	0.09	0.94	1.01	0.67	0.19	0.36	1.23	0.84	0.53	0.49	1.45	2.05	0.05	1.01	4.14	0.98	0.39	0.94	1.03	1.01	0.61	0.96	1.07	0.09
Euphoria	2.29	0.33	0.44	11.92	1.02	0.76	0.92	1.12	0.62	0.59	0.12	3.39	2.77	0.24	0.50	15.42	1.58	0.63	0.25	10.07	0.97	0.70	0.88	1.09	1.02	0.76	0.89	1.17	0.05
Apathy	0.86	0.55	0.51	1.43	0.97	0.21	0.95	1.01	1.30	0.36	0.74	2.31	0.94	0.83	0.56	1.60	0.64	0.18	0.33	1.24	0.99	0.62	0.95	1.03	0.97	0.23	0.93	1.02	0.03
Disinhibition	1.17	0.65	0.60	2.27	0.95	0.01	0.91	0.99	1.99	0.05	0.98	4.03	0.95	0.90	0.48	1.92	0.51	0.12	0.22	1.18	0.97	0.30	0.93	1.02	1.01	0.81	0.95	1.07	0.05
Irritability	0.91	0.72	0.54	1.53	0.96	0.04	0.93	1.00	1.31	0.36	0.73	2.34	1.36	0.27	0.79	2.36	0.77	0.44	0.39	1.50	0.98	0.22	0.94	1.02	0.99	0.90	0.95	1.05	0.04
Aberr. motor behavior	1.58	0.16	0.83	3.07	0.98	0.24	0.94	1.02	0.85	0.67	0.42	1.75	1.12	0.74	0.58	2.15	1.33	0.49	0.59	3.00	0.97	0.23	0.93	1.02	1.02	0.59	0.96	1.08	0.03
Sleep-disturbance	1.39	0.29	0.75	2.58	0.97	0.17	0.94	1.01	1.06	0.87	0.55	2.04	1.44	0.25	0.78	2.69	0.75	0.46	0.35	1.62	0.98	0.46	0.94	1.03	0.94	0.04	0.85	1.00	0.04
Eating disorder	0.88	0.66	0.52	1.52	1.01	0.72	0.97	1.04	0.63	0.14	0.34	1.16	2.48	0.01	1.39	4.42	0.96	0.91	0.48	1.93	0.98	0.38	0.94	1.02	0.95	0.07	0.91	1.00	0.05

1)   OR = odds-ratio adjusted for general details (gender, age, marital status, domicile and primary caregiver)

From the perspective of the NPI-symptoms themselves, the prognostic model for delusion demonstrated that gender (women), age (younger), marital status (alone) and the BI (higher score) were significant prognostic factors, though a small part of the variance was explained (R^2=0.12). For hallucination gender (women), age (younger) and primary caregiver (spouse) were of significant prognostic value, again with a small explanation of the variance (R^2=0.10). For anxiety there were three significant prognostic factors identified: gender (women), age (younger) and primary caregiver (spouse); the explained variance was small (R^2=0.09). Disinhibition had two prognostic factors: age (younger) and marital status (together) with a minor performance of the model (R^2=0.05). Irritability had one factor: age (younger) with a R^2 value of the model of 0.03. Sleeping disorder had one significant factor in the model (the BI; lower score) with a R^2 value of 0.04. Finally, the model for eating disorder had two significant factors: domicile (at home) and the BI (lower score); the explained variance equalled to R^2=0.05.

In order to get insight in the relation of the NPI to the MMSE, BI and general details, a principal component analysis for non-metric data, was performed (figure 1 and table 6). The MMSE and BI correlated with the cognitive dimension (dimension one) and NPI with the psychiatric dimension (dimension two) The model fit was good, as the percentage of variance explained by the two dimensions appeared to be 82,6%. Of the general details gender, marital status and type of caregiver were almost indifferent. Age (young) loaded mostly on the psychiatric dimension (two) and domicile (at home) on both dimensions.

Figure 1. Component loadings of NPI, MMSE and Barthel combined with general details
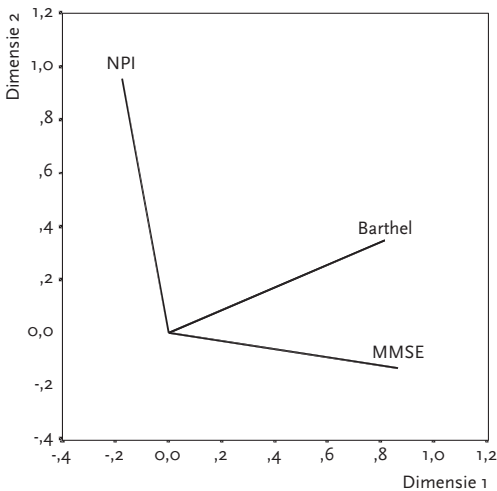
Table 6.   Dimensional loadings of NPI, MMSE and Barthel Index
            combined with general details

	Dimensional loadings	
	1	2
NPI	-0.18	0.96
MMSE	0.86	-0.13
Barthel Index	0.81	0.35
Age	-0.08	-0.23
Gender	-0.09	-0.01
Marital status	-0.03	0.04
Domicile	0.22	0.20
Primary caregiver	-0.04	0.06

Model-fit, total variance explained by NPI, MMSE and Barthel Index: 83%

4.   Discussion

The results demonstrate that at the moment of referral to clinical and transmural nursing home care the prevalence of PFDs as measured by the NPI was high (91% one or more symptoms) in psychogeriatric patients suffering from cognitive function disorders. This percentage was even higher than that measured (70-80%) within institutionalized psychogeriatric patients (Margallo-Lana et al., 2001; Tariot et al., 1993; Teri, 1989). It is in line with the data of the Maasbed study regarding a population referred to a policlinic for older patients with cognitive function disorders (Aalten et al., 2003; Kat et al., 2002). With respect to overall prevalence and the mean NPI score, men did not differ from women. In general depression, anxiety, apathy and agitation/aggression had a high prevalence. However, there were significant differences between men and women with respect to the prevalence and co-occurrences of specific NPI symptoms. For women delusion, hallucination and anxiety were the principal NPI symptoms; for men agitation/aggression and irritability. Accordingly, on the same level of cognitive disorder (MMSE score) at referral men and women expressed significant different PFDs. The same applied to ADL and general details. These results underline the divergent needs of men and women with respect to type of intervention. In addition, gender has to be taken into account for the construction of a prognosticum of specific intervention programmes tailored to the relevant PFDs.

The results of this study confirm the conclusion of the IPA European Regional Meeting in Geneva on the 4th of April 2003 that the psychiatric aspects of psychogeriatric patients need more scientific attention after years of relative neglect; not only neglect of the diagnostic aspects but also of the opportunities of (psycho)

therapy. Besides emotion- and demand-oriented care, small-scale housing and caregiver support, there is a need for psychiatric knowledge and skills tailored to the PFDs of psychogeriatric patients. All professionals in clinical as well as trans-mural psychogeriatric settings should be trained in the relevant psychiatric skills. For a variety of reasons, this is of great clinical interest. Literature shows currently about 50% if only for the actual psychopharmaceutical treatment prescriptions do not correspond to the type of the patients' psychiatric problems. (Pitkala et al., 2004; Dautzenberg et al., 2003; Margallo-Lana et al., 2001). Moreover, the PFDs are less difficult to influence positively than the cognitive and ADL function disorders (Legra and Bakker, 2002; Kipling, 1999; Koder, 1998; Beck and Stanley, 1997; Teri and Gallagher-Thompsom, 1991; Marston, 1991). Furthermore, they play a crucial role in many psychogeriatric issues. Besides the negative effects on the quality of life of the patients themselves (e.g. 46% depression, 45% anxiety, 46% apathy) the PFDs put a great burden on the caregiver system (e.g. 46% apathy, 33% agression, 39% irritability, 25% sleepdisturbance and 38% eating disorder). In addition, the PFDs e.g. depression and delusion (paranoid), are predictors of survival, specific somatic illnesses (brain/cardiovascular) as well as of outcome of intervention programmes. (Bakker et al., 2004; Beekman et al., 2004**).**

In this study we demonstrated the independent role of PFDs in psychogeriatric patients with respect to the cognitive (MMSE) and ADL (BI) status as well as the general details relevant in psychogeriatrics. There were a small number of significant bivariate and multiple (prognostic) relations, although with a minor performance. Consequently, MMSE, BI and NPI are each for themselves important for referral to clinical and transmural intervention programmes. Therefore, it is of clinical relevance to think and act in terms of dimensions. In psychogeriatrics patients will show divergent patterns of scores (also extreme ones) on the three instruments. For instance, with the stage-specific subdivisions of Cummings (Kaufer et al., 1998) of the MMSE (three subgroups: mild, moderate and severe) and a high/low division of the BI the possible number is 3 (MMSE) x 2 (BI) x 12 (NPI) = 72 patterns, even more if specific NPI symptom co-occurrences are taken into account.

An intriguing question is which factors underlie the PFDs, as measured by the NPI. Cummings argues for a neurological explanation. The same brain lesions and genetic mechanisms responsible for cognitive functions disorders should cause these PFDs. However, if this is the main cause one should expect to find more powerful significant relations between NPI and MMSE scores. Also general somatic diseases are candidates; there is a well-known significant prognostic relation between brain/cardiovascular disease, (subthreshold) depression and cognitive decline (Beekman et al., 2004). The same applies to the prognostic relation between a great number of severe somatic diseases and depression (Beekman et al., 1997). However, this is not known for other PFDs.

Another fascinating option is to explore the relation of PFDs with the psychiatric field itself; e.g. mood disturbances, somatoform disorders, anxiety disorders, stressful life events (actual and/or in the youth), personality disorders, neurotransmitter changes (independent of cognitive neurotransmitter changes). Irrespective of a more rational psychopharmaceutical regime this would open the door to verbal and non-verbal (i.e. expressive) psychotherapeutic interventions, adapted to the cognitive and ADL function disorders (Kennedy and Tanenbaum, 2000; Draper, 1998). In the literature, there are indications for the positive effect of adapted psychotherapeutic interventions particularly on depression and anxiety (Qazi et al., 2003; Scholey and Woods, 2003; Smalbrugge et al., 2003; Legra and Bakker, 2002; Gerson et al., 1999; Kipling et al., 1999; Koder, 1998; Teri and Gallagher-Thompson et al, 1991). As a matter of fact, in our ongoing randomized trial on cost-effectiveness of psychogeriatric reactivation, we tailored the intervention programme to the PFDs from a psychiatric viewpoint.

To find answers to these questions it is important to carry out further analyses on the dimensional structure of NPI (combined with MMSE/BI). The executed preliminary pattern analyses presented in figure 1 point in that direction. It is of relevance to compare the outcomes of these structure analyses of different NPI data sets available now. We are preparing to execute such analyses shortly.

5. Conclusions

At the moment of referral to intra- or transmural nursing home care, there is a high prevalence and co-occurrence of PFDs. On the same level of cognitive disorder (MMSE) the principal PFDs, irrespective of depression and apathy, differed between men and women, particularly delusion, hallucination, anxiety (more in women) and agitation/aggression and irritability (more in men). Men were also more ADL independent. With respect to common general details, men were relatively young, lived together with their spouse, who was often also the caregiver. The regression analyses demonstrated that the PFDs dimension was relatively independent of MMSE, BI and general details. In case of referral it is of relevance to think and act in terms of dimensions, instead of categories. Therefore, a prognostic instrument of psychogeriatric clinical and transmural programmes tailored to the patients with PFDs has to pay attention to these dimensions and relevant general details. The relatively independency of PFDs from the MMSE and BI opens the door to a more rational psychopharmaceutical regime, and to the regular psychiatric domain for psychotherapeutic strategies. These strategies, including scientific research, are of clinical interest because of the high prevalence of depression, anxiety, apathy and agitation/aggression in men and women suffering from cognitive impairments.

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Integrative psychotherapeutic nursing home programme to reduce multiple psychiatric symptoms of psychogeriatric patients and caregiver burden; A randomized controlled trial[1]

1.   Introduction

In psychogeriatric patients who suffer from cognitive impairment or dementia, there is an 80% prevalence of two or more psychiatric symptoms, e.g. depression, anxiety, paranoia, aggression. [1–5] Multiple psychiatric symptoms (MPS) have many related negative secondary effects. For the patients there are negative effects on cognitive functioning, quality of life and they predict admission to a nursing home. Furthermore, MPS are a burden for the caregiver. [3, 6-12] Moreover, these MPS are number one among the top three problems experienced by psychogeriatric patients and their caregivers. [13] In usual nursing home care, psychotropic drugs are widely used to treat the MPS of dementia patients despite of their limited effects and potentially harmful side-effects e.g. (a)typical antipsychotics. [2, 5, 14, 15] There is a lack of integrative psychotherapeutic programmes, even though reports in the literature indicate that for individual psychiatric symptoms, e.g. depression and anxiety, as well as caregiver burden, psychotherapeutic treatment may be effective in both nursing home and primary care settings. [16–19, 20-24] However, psychotherapeutic interventions focussing on the MPS of psychogeriatric patients who suffer from cognitive impairment or dementia are complex, due to their multiplicity in combination with cognitive disorders, somatic co-morbidity, and social problems (e.g. relationships, loneliness) [25, 26]. Furthermore, integrative psychotherapeutic programmes in nursing homes have never been evaluated in large-scale comprehensive studies. [10, 16, 27-30] For these reasons, we developed an unique integrative psychotherapeutic nursing home programme: integrative reactivation and rehabilitation (IRR). [31] In this paper we report on the results of a randomized controlled trial (RCT) designed to evaluate the effectiveness of IRR on the MPS of psychogeriatric patients who suffer from cognitive impairment or dementia and on caregiver burden.

2.   Materials and methods

2.1   Patients

The psychogeriatric patients were recruited from the urban region of Nieuwe Waterweg Noord (NWN), near Rotterdam in the Netherlands (approx. 180.000 inhabitants). The patients were referred from an (ambulant) mental health service (5.4%), a general hospital (13.8%), a memory clinic (6%) and general practitioners or primary healthcare services (75.1%). Before inclusion, all referred patients underwent a comprehensive geriatric assessment. The initial inclusion criteria were a DSM IV classification for dementia, amnestic disorders or other cognitive disorders. Additional inclusion criteria were: 1) age: $\geq$65 years; 2) cognitive functioning: MMSE $\geq$18 and $\leq$27 as well as Barthel Index (BI) $\geq$5 and $\leq$19; 3) psychiatric symptoms: Neuropsychiatric Inventory (NPI) 3 or more symptoms, and 4) informed consent. The exclusion criteria were: 1) delirium; 2) life-threatening somatic co-morbidity; 3) active coercive admission regime (according to psychiatric legislation), and 4) insufficient command of the Dutch language.

2.2   Design

The study was an open RCT, with a parallel group design and was performed from 2001 until 2006. Psychogeriatric patients who met the inclusion criteria were randomly and blindly assigned to either IRR or usual care (UC), with a randomization algorithm. In the first half of the study the assignment was in a ratio of 1 (IRR): 2 (UC). However, due to the limited numbers of eligible patients, time restrictions and financial limitations, in the second half of the study the ratio was reversed to 2 (IRR): 1 (UC). We finally included 168 patients (81 IRR and 87 UC). Patient's "Multiple Psychiatric Symptoms" was the primary outcome variable. In view of clinically relevant background information about the effects of IRR, 'burden' for the caregiver, 'cognitive functioning', 'quality of life' of the patient, and 'nursing home admission' were selected as secondary outcome variables. The assessments were carried out simultaneously in both groups at three measurement points: T1 (within two weeks after inclusion), T2 (at the end of the intervention, about three months after inclusion) and T3 (follow-up, six months after the end of the intervention). Furthermore, data were gathered by trained co-workers who were not members of the intervention team. The study protocol was approved by the Medical Ethics Committee of the Erasmus University Medical Centre.

2.3   Intervention

The IRR programme had a duration of 13 weeks, with clinical admission to a separate 15-bed specialized unit in a psychiatric-skilled nursing home. In addition to the usual multidisciplinary nursing home care, including psychotropic drugs treatment, the IRR also consisted of interventions for the MPS of the patient and family therapy for the caregiver. Cognitive and somatic functioning were also optimized (Figure 1). A more extensive description of the IRR programme has been published elsewhere. [31]

   A personal package of interventions was composed for each patient and caregiver, based on six dimensions. [10, 31] These six dimensions were: 'Emotion' (e.g. depression, anxiety, aggression), 'Personality' (e.g. characteristics of narcissism, borderline, dependency), 'Life events' (e.g. traumatic experiences such as war, incest, death of a spouse/child), 'Social functioning' (e.g. relationship problems with spouse/children, loss of pleasant social activities), 'Cognitive functioning' (e.g. problems with memory, self-care), and 'Somatic functional disorders' (e.g. impaired mobility, falls, polypharmacy, nutritional deficiency and intercurrent diseases). The following psychotherapeutic interventions based on a problem-solving theoretical framework, were available and written down in specific guidelines for each discipline: 1) diagnostic assessment, 2) counseling, 3) life-review, 4) interpersonal therapy, 5) (cognitive) behavioural therapy, 6) support in accepting behaviour and minimizing negative effects, 7) regression approach, temporarily accepting regression behaviour, 8) rehabilitation, 9) psycho-education, and 10) family therapy. [31] The interventions were mainly provided in a group, but when necessary individually.

With regard to the percentage of patients receiving each type of intervention (Table 1), it is important to realize that on average, the patients were treated for five functional psychiatric problems apart from the functional problems on the cognitive and somatic dimension. The interventions for these functional psychiatric problems were generally provided by four disciplines, but sometimes a discipline used more than one type of intervention during the different phases of the IRR programme. This makes the programme highly flexible and it is therefore possible to compose and provide a personal package of interventions for each patient and caregiver. After multidisciplinary consultation, the psycho-geriatrician - a nursing home physician with experience in psychiatric treatment - prescribed the interventions. The IRR team consisted of a nursing team, a psycho-geriatrician, a clinical psychologist, a social worker, a music therapist, a psychomotor therapist and a creative therapist, a physiotherapist, an occupational therapist, a speech therapist, a dietician and a welfare worker (Figure 1). Staff members were trained to systematically conduct the IRR programme. The progress of the patient/caregiver was monitored weekly, guided by the method of standardized goal attainment scaling (GAS: score range 1 to 7; 7 = independent (no help needed) [32].

Treatment compliance was continuously monitored during the course of the personal intervention plan for each patient/caregiver. Each week, all the disciplines had to deliver a written GAS score, based on functional progress during the therapy sessions. These scores were discussed in the multidisciplinary patient meeting and a consensus GAS score was determined. All the registered data were sent to the research team after the end of the treatment. Moreover, at the end of the IRR programme each discipline had to fill in an evaluation form about the course of the therapy, including active patient participation. These data are available from the first author.

Usual care (UC) consisted of a relatively high level of multidisciplinary nursing home care provided in the following settings: at home (25.3%), at home with mental healthcare (out-reaching) or psycho-geriatric day care/treatment (15.7%), in a home of assisted living (7.2%) and in a nursing home (51.8%). The multidisciplinary UC staff consisted of a nursing home physician or social geriatric physician, a psychologist, a paramedical team (physiotherapist, occupational therapist, speech therapist, welfare worker) and a nursing team (Registered Nurses, Certified Nurse Assistants and/or Nurse Assistants).

The UC was provided by different types of core multidisciplinary teams, each with a different theoretical framework, mostly emotion-oriented.

2.4   Assessments

The primary outcome variable was the number of 'MPS' assessed by number (0-12) as well as sum-severity (0-144, number x frequency x severity) using the Neuropsychiatric Inventory (NPI 12 item version). [33-35] The NPI was administered to the caregiver as well as one of the nurses in the nursing team. The following

secondary outcome variables were measured: 'burden' for the caregiver assessed with the 'NPI emotional distress' (N-emD: 0 to 60; 0 = no distress), the Caregiver Competence List (CCL: 28 to 112; 112 = optimal) [11, 36] and the Caregiver Burden (CB: 0 to 100; 0 = optimal). [37] To asses the 'cognitive functioning' of the patient, memory was measured with the Mini Mental State Exam (MMSE: 0 to 30; 30 = normal) [38] and self-care with the Barthel Index (BI: 0 to 20; 20 = normal). [39] The 'quality of life' of the patient was assessed with the MOS short-form general health survey (SF-20: 0 to 100; 100 = optimal) [40], EuroQol (EQ5D: – 0.59 to 1.0; 1.0 = optimal), and the visual analogue scale (VAS 'thermometer') for subjective health status (0 to 100; 100 = optimal) [41]. Admission to a nursing home was measured according to length of stay in days. The Global Deterioration Scale (GDS: 1-7; 1 = normal) was used to assess the risk of admission to a nursing home [42]. Somatic co-morbidity was assessed with the ICD-10, and the DSM IV disorders (axes I and II) were classified by a research psychiatrist. Finally, the following demographic data were collected from the patient and the caregiver: gender, age, marital status, family relationship, domicile and level of education.

2.5   Statistical analyses

Fisher's exact tests were used to estimate differences between IRR and UC on counts such as the number of deaths. Student's t test for unpaired samples was used to test for differences between IRR and UC on continuous data. To evaluate the effect of IRR compared to UC, the mean differences on the continuous outcome variables were calculated over time.

Cohen's-d was calculated to compare the different outcome variables. [43] According to the power calculation (-error fixed at 0.05 [two tailed] and -error fixed at 0.20), based on a 1:1 ratio, a sample size of 170 patients (85 IRR and 85 UC) is required. A Cohen's-d = 0.20 is regarded as a small effect, 0.50 as a moderate, albeit clinically relevant effect and 0.80 as a large effect. The 168 patients were randomly assigned to either IRR (N = 81) or UC (N = 87). The differences between the drop-outs in the two study groups, with regard to duration over time of participation in the programme, were determined by Cox-regression analysis. Hazard ratio (HR) was used as the measure of performance.

Random regression modelling (RRM) was performed to test for confounding by corresponding baseline scores, age, gender, somatic co-morbidity, and drop-out. RRM assumes that missing data are missing at random. The length of stay in a nursing home was estimated by Kaplan-Meier analysis. The 95% confidence intervals (CI) were provided where possible and relevant. As the outcome variables were substantially correlated, we assumed that the underlying structure of these variables actually represent three dimensions. Therefore, we have -level of 0.05 (two-tailed) divided by 3, implying that the corrected level of significance is actually 0.0167 (two-tailed). All statistical testing was performed according to the intention-to-treat (ITT) principle, and the statistical analyses were performed with SPSS, version 15, and SAS, version 9.2.

3.   Results

3.1   Characteristics of the study sample

The flow-chart (Figure 2) shows that, of the 336 eligible patients, 168 (50%) consented to participate. The non-participants did not differ significantly from the participants with regard to the inclusion criteria. The 168 patients were randomly assigned to either IRR (N=81) or UC (N=87). The differences between the two study groups in the number of drop-outs – the majority caused by death - were insignificant at all measurement points. Moreover, the drop-outs did not differ significantly with regard to any baseline assessment or length of time participating in the programme (Cox regression analysis: HR 1.21; P<0.54). With respect to biographical data, there were no significant differences between the two groups (Table 2). Mean somatic co-morbidity in the IRR group was significantly higher (IRR 5.6 [sd 2.6] ; UC 4.5 [sd 2.4] ; p<0.01). In our analyses we controlled for somatic co-morbidity. A mean GDS score 4.2 (sd 0.8) suggested that the study sample consisted of psycho-geriatric patients with mild cognitive impairment who were at risk for admission to a nursing home [44]. At T1 (Table 3) there were no significant mean differences between the IRR group and the UC group with the exception of the NPI cluster hyperactivity (mean difference 3.49; 95% CI: - 6.33 to - 0.59). [45, 46]

3.2   Effectiveness of IRR

Table 4a presents the results at the end of the treatment (T1-T2). On the primary outcome variable, the caregiver NPI showed significant effects, of a moderate size in favour of IRR. In the IRR group the mean number of NPI symptoms was 1.31 (sd 2.47) lower, and the NPI sum-severity was 11.16 (sd 21.02) lower than in the UC group, while in the UC group itself there was a reduction of 0.77 (sd 2.40), respectively 7.29 (sd 20.04). In a post-hoc analysis, the sum-severity of the NPI cluster hyperactivity (6.04; sd 9.28 lower) showed significant effects, of a moderate size in favour of IRR. Affective symptoms with a surplus reduction of 2.55 (sd 7.15) in the IRR group were marginally significant. On two measurements the effects on 'burden' for the caregiver were significant, and of a moderate size, in favour of IRR: general 'burden' (CB) was 17.69 (sd 28.05) lower, and 'competence' (CCL) was 6.26 (sd 10.31) higher in the IRR group than in the UC group, while in the UC group there was almost no effect. NPI emotional distress (N-emD) was significantly lower at 3.78 (sd 8.51). Of the other secondary outcome variables memory measured with the MMSE showed a marginally significant, minor effect in favour of IRR (1.13; sd 3.28 higher). In contrast, self-care (mean BI score) was marginally significant, 1.66 (sd 3.98) higher in favour of UC. There were no significant differences found with regard to 'quality of life' of the patient.

Table 4b presents the results at the six-month follow-up (T1 – T3). On the primary outcome variable the caregiver NPI showed marginally significant effects, of a

moderate size in favour of IRR. The number of NPI symptoms 1.02 (sd 2.32) was lower in the IRR group and the NPI sum-severity was 9.91 (sd 23.51) lower. Post-hoc analysis of the sum-severity of NPI clusters showed that hyperactivity had a significant, moderate to large effect in favour of IRR, i.e. 6.28 (sd 9.61) lower. With regard to 'burden' for the caregiver, the mean CB score was 24.76 (sd 28.29) lower, and the mean CCL score was 5.93 (sd 10.31) higher. The large effect on CB was significantly in favour of IRR, as was the moderate effect on CCL. UC had almost no effect. Furthermore, in the other secondary outcome variables there were no significant differences. Kaplan-Meier analysis showed that the length of stay in a nursing home did not differ significantly between the two groups (IRR mean 147.04 days; 95%CI:123.77 to 170.31, and UC mean 151.82 days; 95%CI:130.11 to 172.37; p<0.62).

3.3   Repeated measurement modeling

The random regression modelling (RRM) for repeated measurements was applied to test for confounding by corresponding baseline score of the outcome variables, age, gender, somatic co-morbidity and drop-out. We tested for time effect (T3) and intervention effect (IRR) (Table 5).

In general, the results confirmed the Cohen's-d calculations. The IRR had a significant effect, decreasing the number of caregiver NPI symptoms (b - 0.83; 95% CI -1.47 to –0.18). At T3 there was an additional significant effect. Furthermore, in the IRR group the caregiver NPI sum-severity demonstrated a marginally significant beneficial decrease (b - 5.10; 95% CI –9.79 to –0.40). On 'burden' for the caregiver, the N-emD and CB scores decreased significantly in the IRR group (b - 2.48; 95% CI –4.62 to –0.35 respectively b -16.09; 95% CI –24.24 to –7.94). The IRR had a significant increasing effect on 'competence' (b 6.18; 95% CI 3.41 to 8.95), while T3 was also positively significant. The results for the other secondary outcome variables ('cognitive functioning' and 'quality of Life') were also in line with the Cohen's-d calculations.

4.   Discussion

In this RCT we evaluated the effects of an integrative psychotherapeutic nursing home programme (IRR) to reduce multiple psychiatric symptoms and caregiver burden, compared to the usual, relatively highly developed multidisciplinary nursing home care that is provided in the Netherlands. From the perspective of the caregivers, the IRR had a significant and moderate to large surplus effect (up to 34%) in reducing the MPS of psychogeriatric patients who suffer from cognitive impairment or dementia in both short term and the long term. In fact, at the six-month follow-up there was a total reduction in MPS up to 46% in number and 61% in severity. Furthermore, with regard to caregiver burden and competence the IRR

had a large positive surplus effect (up to 36%) at the end of the treatment. During the follow-up the surplus effect even increased to a reduction of 50%, while usual care had hardly any effect at all.

The strength of this RCT was that, as far as we know, it is one of the first comprehensive studies, with a relatively large sample size, that addressed integrative psychotherapeutic treatment in a psychiatric skilled nursing home setting.[16,18, 27, 28, 30] Furthermore, RRM analysis showed that confounding – and in particular baseline scores and drop-out - had only a small modifying effect. Overall, the effects were stable.

However, this study had several limitations. First of all, the RCT was not blinded. Blinding was not feasible, because the trained co-workers had to visit the patients and caregivers personally, so they knew about the intervention, and because the caregivers and nurses were informed participants, they also knew about the intervention. The baseline assessments showed only slight differences between IRR and UC, except for somatic co-morbidity, so the information bias at baseline seems to be limited. However, future studies have to be performed, preferably as blinded RCTs. With regard to generalization of the results, it is important to note that 50% of the eligible patients were unwilling to participate in the study, and the main reason for refusal was fear of a clinical admission in case of allocation to the IRR group. In a post-hoc prognostic analysis, living together was not prognostic with regard to improvement on the primary outcome variable. Furthermore, the study sample included more patients with vascular dementia than with Alzheimer-type dementia, which is not in line with the study population in most epidemiological studies. This may be due to the inclusion criteria, i.e. suffering from both cognitive function disorders and three or more NPI symptoms. Patients with vascular dementia are expected to have more psychiatric problems, so they were over-represented in the present study. Nevertheless, in a post-hoc analysis the type of dementia showed no significant modifying effect, either on the MPS of the patient or on caregiver burden. Another issue is the relatively high percentage of drop-outs (up to 33%), the majority of which were caused by death. A high drop-out percentage is normal in geriatric research, even in observational studies, and basically, it reflects the vulnerability of psychogeriatric patients. [19, 47, 48] In this RCT there were no significant differences between drop-outs in the two groups and the confounding effect of drop-out in the RRM analysis was marginal.

Another issue that needs to be discussed is the difference between the scores on the nurse NPI and the caregiver NPI, though the trend was the same. First of all, the caregivers formed a stationary group from the moment of inclusion in the study until the end of the treatment and the six month follow-up. Furthermore, caregivers have more long-lasting individual contacts with the patient; in general their opinions correspond more with the actual needs, thoughts and feelings of dementia patients. [28, 49 - 53] In contrast, there was no continuity in the data from the nursing team in both groups; the trained co-workers had to ask different nurses within the nursing team for NPI data. This is an important issue that should be to addressed in future research projects.

How can the results of IRR be interpreted within the context of the literature? They confirm the indications in the literature that psychotherapeutic treatment for psychiatric symptoms in psychogeriatric patients are effective. [16 - 21, 27, 28, 30] Remarkable were the beneficial effects of IRR on the MPS of the patient, which are a relatively high burden for the caregiver i.e. hyperactivity cluster. [3, 45] The finding that there were contradictory effects of IRR on 'cognitive functioning' is in line with results reported in the literature. [1, 3, 51] The same holds true for quality of life and admission to a nursing home. [48, 54] With regard to the latter, it is a well-known fact that many factors other than patient factors play a dominant role in admission to an institution, i.e. formal co-operation between institutions, length of waiting lists, and geographical factors. An intriguing question is: which elements of IRR are the therapeutically effective components? We think that there are three possibilities. First, the application of well-known psychotherapeutic strategies, based on functional problem-solving principles, to both patient and caregiver problems. [16, 21, 30] Behavioural therapy was used most frequently (94.9%), followed by counseling (79.5%) and support (66.6%). Furthermore, 38.5% of the caregivers needed family therapy. Secondly, the tailor-made personal approach was important. In the literature the importance of a person-oriented approach is also emphasized. [16, 30, 55] In our study, the fact that psychogeriatric patients had an average of five functional psychiatric symptoms treated by a mean of four disciplines demonstrates the practical relevance and complexity of this issue. The IRR programme was found to be a successful method with which to manage this complexity. Finally, the systematical and strict methodological application of the IRR programme was another element that determined the surplus effect of the IRR. [29]. By Goal Attainment Scaling weekly, the person-oriented interventions for each patient and caregiver were monitored and, if necessary, adapted or modified. Furthermore, the individual interventions were described specifically per discipline in written guidelines.

5.   Conclusion

The application of an integrative psychotherapeutic nursing home programme (IRR), based on person-oriented and problem-solving principles, was significantly more effective than usual multidisciplinary nursing home care in reducing the multiple psychiatric symptoms of psychogeriatric patients who suffer from cognitive impairment or dementia as well as the burden on caregivers. One may therefore expect that in countries with less well developed psychogeriatric nursing home care than in the Netherlands the surplus effect will be substantially larger. This is an important and clinically relevant result, the more so because multiple psychiatric symptoms and caregiver burden are among the top three problems experienced by psychogeriatric patients and their caregivers. Considering all available evidence, we recommend that usual (inter)national nursing home care, and perhaps also other forms of psychogeriatric care, should incorporate integrative

psychotherapeutic treatment strategies. The same applies to the education pro-grammes for the various disciplines that are involved.

Future studies have to be performed to strengthen the evidence, preferably as blinded RCTs.

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Treatment components	**Disciplines**

Phase 1

Diagnostic assessment	Multidisciplinary

Phase 2

One of the following:

Interpersonal therapy	Psychologist		
Counseling	Psychogeriatrician	Psychologist	
Cognitive-behavioural therapy	Nurses	Therapists *)	Psychologist

One of the following:

Behavioural therapy	Nurses	Therapists *)	
Support	Nurses	Therapists *)	Welfare worker

Family therapy	Psychologist

Phase 3

Rehabilitation	Nurses	Occup therapist	Welfare worker

Support (discharge)	Social worker

***) for each patient, two or three of the following
    therapists are involved in the psychotherapeutic
    programme:**
psycho-motor therapist
music therapist
creative therapist
physiotherapist
occupational therapist

Figure 1. Typical IRR patient protocol

Eligible patients (n = 336)

Not randomized	n = 168
Refusal of referral/treatment	n = 152
Refusal of participation	n = 9
Reasons unknown	n = 7

Randomization
n = 168

IRR

UC

Intervention as allocated (n=81)
Did not receive standard
Intervention as allocated n = 1

Intervention as allocated (n=87)
Did not receive experimental
Intervention as allocated n = 1

Time 1:
available: n = 78
death: n = 2
refusal: n = 1
loss: n = 0
total drop out: n = 3
4 %

Time 1:
available: n = 83 [1]
death: n = 4
refusal: n = 0
loss: n = 0
total drop out: n = 4
5 %

Time 2:
available: n = 69
death: n = 10
refusal: n = 1
loss: n = 1
total drop out: n = 12
15 %

Time 2:
available: n = 77 [2]
death: n = 9
refusal: n = 0
loss: n = 1
total drop out: n = 10
12 %

Time 3:
available: n = 54
death: n = 24
refusal: n = 2
loss: n = 1
total drop out: n = 27
33 %

Time 3:
available: n = 64 [3]
death: n = 23
refusal: n = 0
loss: n = 0
total drop out: n = 23
26 %

[1] Fisher's Exact test for dropout * condition p 1.00 (two-tailed)
[2] Fisher's Exact test for dropout * condition p 0.49 (two-tailed)
[3] Fisher's Exact test for dropout * condition p 0.14 (two-tailed)

Figure 2. Flow chart discribing progress of patients through randomized controlled trial

Table 1. Psychotherapeutic treatment components, percentage of patients receiving IRR

	IRR
	n=81

Intervention types (percentages of patients)[1]

Diagnostic assessment	100.0%

Counselling	79.5%
Life-review	2.6%
Interpersonal therapy	48.7%
Cognitive-behavioral therapy	57.7%

Behavioral therapy	94.9%
Support	66.6%
Regression	3.8%

Rehabilitation	47.4%[2]
Support (discharge)	41.0%[3]

Psycho-education	6.4%
Family therapy	38.5%

[1]   Percentages are additional, not cumulative
[2]   Indicated in the (pre-)discharge phase
[3]   Support from social worker on discharge

Table 2. General details of participants, distinguished by intervention

	IRR	UC	
	n=81	n=87	p-value
Patient characteristics			
gender (females)	66.7%	62.1%	0.63[1]
age (in years), mean (sd)	79.8 (6.1)	81.5 (7.1)	0.10[2]
marital status: alone	77.8%	80.5%	0.71[1]
educational level: low	67.5%	68.7%	0.90[1]
domicile: at home	76.5%	66.7%	0.17[1]
primary caregiver: spouse	17.3%	13.8%	0.33[3]
DSM-IV dementia, (axis-I), count (%)			
dementia of the Alzheimer's type	18.5%	17.2%	0.84[1]
vascular dementia	23.5%	25.3%	0.86
dementia due to other conditions	16.0%	19.5%	0.69
amnestic/cognitive disorders	32.1%	31.0%	1.00
other	6.2%	2.3%	0.26
DSM-IV personality disorders (axis-II), count (%)	16.0%	9.2%	0.24
GDS-deterioration, mean (sd)	4.2 (0.7)	4.3 (0.9)	0,62[2]
somatic co-morbidity (ICD-10), mean (sd)	5.6 (2.6)	4.5 (2.4)	0.01[2]
Caregiver characteristics			
gender (females)	70.5%	61.7%	0.32[1]
age (in years), mean (sd)	58.6 (11.9)	58.9 (12.0)	0.86[2]
marital status: living together	91.4%	94.8%	0.52[1]
educational level: low	4.3%	2.6%	0.39[1]

[1]   Fisher's Exact Test (twotailed)
[2]   t-Test (twotailed)
[3]   Pearson Chi-square (twotailed)

Table 3. Level of outcome across time (T1, T2, T3) distinguished by intervention

	T1 (baseline measurement)									T2 (end of intervention)						T3 (six months follow-up)					
	IRR			UC			mean diff.	95%	CI	IRR			UC			IRR			UC		
	n	mean	sd	n	mean	sd	mean diff.	95%	CI	n	mean	sd	n	mean	sd	n	mean	sd	n	mean	sd
PRIMARY OUTCOME VARIABLE																					
Psychiatric function disorders patient																					
By caregiver																					
NPI-symptoms	72	5.92	2.35	76	5.23	2.16	-0.68	-1.41	0.05	62	3.97	2.19	66	4.59	2.40	49	3.49	2.16	51	3.84	2.11
NPI-sum-severity	72	35.90	21.84	76	29.68	20.12	-6.22	-13.05	0.62	62	18.26	14.74	66	22.50	15.10	49	15.84	13.81	51	18.61	19.52
NPI-clusters (sum-severity)																					
hyperactivity	72	11.82	9.94	76	8.33	7.68	-3.49	-6.39	-0.59	62	5.39	6.01	66	7.33	8.36	49	3.76	5.35	51	5.98	9.32
psychosis	72	6.68	7.08	76	5.80	7.48	-0.88	-3.24	1.49	62	3.55	5.55	66	2.92	4.56	49	2.59	4.25	51	2.88	5.34
affective symptoms	72	7.81	6.29	76	6.54	6.78	-1.27	-3.39	0.86	62	3.89	4.82	66	4.91	4.43	49	3.90	5.23	51	4.24	6.34
apathy	72	9.60	7.34	76	9.01	7.07	-0.58	-2.93	1.76	62	5.44	6.15	66	7.33	5.81	49	5.59	6.20	51	5.51	5.77
By nurse of nursing team																					
NPI-symptoms	76	4.36	1.69	56	3.82	2.02	-0.53	-1.19	0.13	68	3.88	1.88	72	3.21	1.94	52	3.46	1.96	61	3.25	2.09
NPI-sum-severity	76	23.57	13.97	56	20.79	17.48	-2.78	-8.40	2.84	68	17.50	13.47	72	16.11	14.25	52	17.51	15.33	61	15.30	14.75
SECONDARY OUTCOME VARIABLES																					
Caregiver burden																					
NPI-emotional distress (N-emD)	72	14.64	9.22	76	12.71	8.96	-1.93	-4.88	1.03	62	7.55	6.83	66	9.39	8.01	49	6.22	5.97	51	7.98	8.03
Caregiver burden (CB)	72	52.47	25.65	77	46.69	27.66	-5.79	-14.42	2.85	60	36.75	25.81	65	44.58	28.24	42	28.81	27.00	50	44.90	28.88
Competence (CCL)	72	84.62	14.24	77	86.58	14.46	1.96	-2.69	6.6	63	92.89	11.56	66	88.92	12.73	49	96.35	10.55	50	91.78	12.57
Cognitive functioning patient																					
MMSE	76	20.04	4.50	82	20.58	3.84	0.54	-0.77	1.85	63	20.48	4.51	72	19.67	4.35	51	19.46	5.44	60	19.50	4.99
Barthel Index (BI)	77	15.39	3.77	80	14.71	3.55	-0.68	-1.83	0.48	68	13.62	5.29	77	14.40	4.51	54	12.38	5.19	63	13.24	5.04
Quality of life of patient																					
SF-20 total	77	49.54	15.62	81	45.08	14.12	-4.46	-9.14	0.23	63	51.32	16.01	72	45.51	14.56	51	53.83	14.04	57	47.18	14.53
EQ5D patient	77	0.54	0.34	80	0.58	0.29	0.04	-0.06	0.14	62	0.59	0.32	67	0.57	0.29	45	0.62	0.36	62	0.55	0.32
Health status	76	67.54	15.74	77	69.16	15.99	1.62	-3.45	6.68	63	69.52	16.18	63	69.35	14.93	46	72.83	12.46	63	67.46	14.17

Table 4a. Differences [mean (sd) and Cohen's-d] in IRR and UC; end of treatment (T1 - T2)

	IRR n	UC n	mean IRR T1 - T2	mean UC T1 - T2	std. Deviation IRR	std. Deviation UC	mean diff UC-IRR	pooled sd	Cohen's d	p-value
PRIMARY OUTCOME VARIABLE										
Pychiatric function disorders of the patient										
By caregiver										
NPI-symptoms	62	66	2.08	0.77	2.53	2.40	-1.31	2.47	-0.53	0.003[1]
NPI-sum-severity	62	66	18.45	7.29	22.01	20.04	-11.16	21.02	-0.53	0.003[1]
NPI-clusters (sum-severity)										
hyperactivity	62	66	6.73	0.68	9.80	8.76	-6.04	9.28	-0.65	0.001[1]
psychosis	62	66	3.21	2.97	6.46	7.97	-0.24	7.28	-0.03	0.86
affective symptoms	62	66	4.40	1.85	6.81	7.46	-2.55	7.15	-0.36	0.05
apathy	62	66	4.11	1.79	8.54	7.24	-2.33	7.90	-0.30	0.10
By nurse of nursing team										
NPI-symptoms	67	49	0.31	0.39	2.10	2.42	0.07	2.24	0.03	0.87
NPI-sum-severity	67	49	4.75	1.39	15.71	17.22	-3.36	16.37	-0.21	0.29
SECONDARY OUTCOME VARIABLES										
Caregiver burden										
NPI-emotional distress (N-emD)	62	66	7.37	3.59	8.16	8.81	-3.78	8.51	-0.44	0.013[1]
Caregiver burden (CB)	59	65	17.34	-0.35	29.57	26.60	-17.69	28.05	-0.63	0.001[1]
Competence (CCL)	63	66	-7.92	-1.66	10.52	10.11	6.26	10.31	0.61	0.001[1]
Cognitive functioning of the patient										
MMSE	62	72	-0.23	0.90	3.13	3.41	1.13	3.28	0.34	0.05
Barthel Index (BI)	68	75	2.15	0.49	4.86	2.96	-1.66	3.98	-0.42	0.02
Quality of life of the patient										
SF-20 total	63	71	-0.83	0.14	13.22	13.06	0.97	13.14	0.07	0.67
EQ5D patient	62	65	-0.03	0.02	0.30	0.29	0.05	0.30	0.16	0.38
Health status	63	60	-0.51	-1.23	15.03	17.70	-0.73	16.38	-0.04	0.81

[1]   significant after correcting for multiple testing (p-value of < 0.0167)

Table 4b. Differences [mean (sd) and Cohen's-d] in IRR and UC; six months follow-up (T1 - T3)

	IRR	UC	mean		std. Deviation		mean diff	pooled sd	Cohen's d	p-value
	n	n	IRR T1 - T3	UC T1 - T3	IRR	UC	UC-IRR			
PRIMARY OUTCOME VARIABLE										
Psychiatric function disorders of the patient										
By caregiver										
NPI-symptoms	49	51	2.59	1.57	2.36	2.28	-1.02	2.32	-0.44	0.03
NPI-sum-severity	49	51	21.78	11.86	22.85	24.13	-9.91	23.51	-0.42	0.04
NPI-clusters (sum-severity)										
hyperactivity	49	51	8.27	1.98	9.43	9.78	-6.28	9.61	-0.65	0.001[1]
psychosis	49	51	4.24	3.04	5.52	7.82	-1.21	6.79	-0.18	0.38
affective symptoms	49	51	4.71	2.82	7.67	8.40	-1.89	8.05	-0.23	0.25
apathy	49	51	4.55	4.02	9.15	8.46	-0.53	8.80	-0.06	0.77
By nurse of nursing team										
NPI-symptoms	51	40	0.59	0.28	2.35	2.46	-0.31	2.40	-0.13	0.54
NPI-sum-severity	51	40	4.06	2.30	17.52	17.81	-1.76	17.65	-0.10	0.64
SECONDARY OUTCOME VARIABLES										
Caregiver burden										
NPI-emotional distress (N-emD)	49	51	8.73	5.08	8.49	10.13	-3.66	9.36	-0.39	0.06
Caregiver burden (CB)	42	50	24.76	0.00	31.16	25.65	-24.76	28.29	-0.88	0.001[1]
Competence (CCL)	49	50	-10.35	-4.42	10.35	10.27	5.93	10.31	0.58	0.005[1]
Cognitive functioning of the patient										
MMSE	51	60	1.25	1.07	4.17	3.91	-0.17	4.03	-0.04	0.83
Barthel Index (BI)	54	62	3.61	2.06	4.85	4.27	-1.55	4.55	-0.34	0.08
Quality of life of the patient										
SF-20 total	51	56	-1.98	-0.35	13.44	15.30	1.63	14.44	0.11	0.56
EQ5D patient	45	60	0.00	0.04	0.34	0.30	0.05	0.32	0.15	0.48
Health status	46	59	-2.22	1.86	14.85	17.04	4.08	16.12	0.25	0.20

1) significant after correcting for multiple testing (p-value of < 0.0167)

Table 5. Random regression modelling of intervention across time, adjusted for corresponding baseline assessment, gender, age, somatic co-morbidity and dropout

| | Random regression modelling of intervention across time | | | | | | | | |
| | intercept | | | time | | | intervention | | |
	effect size(b)	95% CI	p	effect size(b)	95% CI	p	effect size(b)	95% CI	p
PRIMARY OUTCOME VARIABLE									
Psychiatric function disorders of the patient									
By caregiver									
NPI-symptoms	3.50	-0.65 7.67	0.10	-0.54	-0.94 -0.14	0.01[b]	-0.83	-1.47 -0.18	0.01[1]
NPI-sum severity	24.72	-5.40 54.84	0.11	-2.78	-5.94 0.37	0.08	-5.10	-9.79 -0.40	0.03
By nurse of nursing team									
NPI-symptoms	1.31	-2.65 5.27	0.51	-0.05	-0.46 0.35	0.79	0.28	-0.34 0.90	0.38
NPI-sum severity	-1.29	-28.20 25.63	0.92	0.96	-2.23 4.15	0.55	-0.01	-4.29 4.27	1.00
SECONDARY OUTCOME VARIABLES									
Caregiver burden									
NPI-emotional distress (N-emD)	7.34	-6.27 20.96	0.29	-1.12	-2.35 0.11	0.07	-2.48	-4.62 -0.35	0.01[1]
Caregiver burden (CB)	33.43	-16.52 83.37	0.19	-2.56	-8.07 2.94	0.36	-16.09	-24.24 -7.94	0.01[1]
Competence (CCL)	29.66	11.56 47.77	0.01[b]	2.89	1.26 4.53	0.01[b]	6.18	3.41 8.95	0.01[1]
Cognitive functioning of the patient									
MMSE	3.31	-4.73 11.35	0.42	-0.82	-1.45 -0.20	0.01[b]	0.08	-1.06 1.23	0.88
Barthel Index (BI)	7.41	-0.85 15.68	0.08	-1.74	-2.46 -1.02	0.01[b]	-2.01	-3.29 -0.73	0.01[1]
Quality of life of the patient									
SF-20 total	21.40	-0.10 42.90	0.05	1.01	-1.66 3.68	0.46	3.29	-0.41 6.99	0.08
EQ5D patient	0.15	-0.37 0.68	0.57	-0.02	-0.07 0.04	0.59	0.04	-0.05 0.14	0.33
Health status	35.93	8.44 63.42	0.01[b]	-0.50	-3.18 2.17	0.71	1.57	-2.89 6.04	0.49

1)   Significant after correcting for multiple testing (p-value of < 0.0167)

Effect modification of an integrative psychotherapeutic nursing home programme to reduce multiple psychiatric symptoms of psychogeriatric patients and caregiver burden;
A randomized controlled trial[1]

1. Introduction

In psychogeriatric patients who suffer from cognitive impairment or dementia, there is 80% prevalence of two or more psychiatric symptoms; e.g. depression, anxiety, paranoia, aggression. [1 - 4]. Multiple psychiatric symptoms (MPS) have negative effects on cognitive functioning and quality of life. They are a burden for the caregiver, about 70-80% of caregivers is moderately to heavily burdened. Furthermore, MPS predict the patient's admission to a nursing home. [3, 5 - 10] Moreover, these topics are among the top three of problems experienced by dementia patients and their caregivers. [10] In actuality, in usual nursing home care psychotropic drugs are widely used to treat MPS of psychogeriatric patients in spite of limited effects and potentially harmful side effects e.g. (a)typical antipsychotics. [2, 11, 12] There is a lack of integrative psychotherapeutic programmes even though reports in literature indicate that for individual psychiatric symptoms, e.g. depression, anxiety, psychotherapeutic treatment may be effective. [13 - 16] However, psychotherapeutic interventions focussing on MPS in psychogeriatric patients who suffer from cognitive impairment or dementia are complex due to their multiplicity in combination with cognitive disorders, somatic co-morbidity, and social problems (e.g. relationships, loneliness). [17, 18]

Furthermore, integrative psychotherapeutic programmes in nursing homes have never been evaluated in large-scale comprehensive studies. [9, 13, 19 - 22] For these reasons, we developed an unique integrative psychotherapeutic programme: integrative reactivation and rehabilitation (IRR). [23] In a previous paper we reported on the results of the primary analysis of a RCT designed to evaluate the effectiveness of IRR on MPS of psychogeriatric patients and on caregiver burden. [24] From the perspective of the caregivers, the IRR had a significant and moderate to large surplus effect (up to 34%) in decreasing the MPS of psychogeriatric patients who suffer from cognitive impairment or dementia in both short term and long term. In fact, at the six-month follow-up there was a total reduction in MPS up to 46% in number and 61% in severity. Furthermore, with regard to caregiver burden and competence the IRR had a large positive surplus effect (up to 36%) at the end of the treatment. During the follow-up the surplus effect even increased to a reduction of 50%, while usual care had hardly any effect at all. As it is likely that type as well as severity of the dementia may influence the results, it is clinically relevant to investigate whether specifically long term effects of IRR were modified by the level of cognitive functioning of the patient at baseline and/or by type of dementia. [13 – 17, 20, 22]

The objective of this clinical-empirical study was to identify and estimate, whether long term effects of IRR on the two most clinically relevant outcome variables (severity of the multiple psychiatric symptoms of psychogeriatric patients and general burden of the caregivers) were modified by level of cognitive functioning (i.e. memory and self-care) and/or by type of dementia (i.e. vascular and alzheimer).

2.   Materials and methods

2.1   Patients

The psychogeriatric patients were recruited from the urban region of Nieuwe Waterweg Noord (NWN), near Rotterdam in the Netherlands (approx. 180.000 inhabitants). The patients were referred from an (ambulant) mental health service (5.4%), a general hospital (13.8%), a memory clinic (6%) and general practitioners or primary healthcare services (75.1%). Before inclusion, all referred patients underwent a comprehensive geriatric assessment. The initial inclusion criteria were a DSM IV classification for dementia, amnestic disorders or other cognitive disorders. Additional inclusion criteria were: 1) age: $\geq$65 years; 2) cognitive functioning: MMSE $\geq$18 and $\leq$27 as well as Barthel Index (BI) $\geq$5 and $\leq$19; 3) psychiatric symptoms: Neuropsychiatric Inventory (NPI) 3 or more symptoms, and 4) informed consent. The exclusion criteria were: 1) delirium; 2) life-threatening somatic co-morbidity; 3) active coercive admission regime (according to psychiatric legislation), and 4) insufficient command of the Dutch language.

2.2   Design

The study was an open RCT, with a parallel group design and was performed from 2001 until 2006. Patients who met the inclusion criteria were randomly and blindly assigned to either IRR or usual care (UC), with a randomization algorithm. In the first half of the study the assignment was in a ratio of 1 (IRR): 2 (UC). However, due to the limited number of eligible patients, time restrictions and financial limitations, in the second half of the study the ratio was reversed to 2 (IRR): 1 (UC). We finally included 168 patients (81 IRR and 87 UC). Patient's "Multiple Psychiatric Symptoms" was the primary outcome variable. In view of clinically relevant background information about the effects of IRR, 'burden' for the caregiver, 'cognitive functioning', 'quality of life' of the patient, and 'nursing home admission' were selected as secondary outcome variables. The assessments were carried out simultaneously in both groups at two measurement points: T1 (within two weeks after inclusion), and T3 (follow-up, six months after the end of the intervention). Furthermore, data were gathered by trained co-workers who were not members of the intervention team. The study protocol was approved by the Medical Ethics Committee of the Erasmus University Medical Centre.

2.3   Intervention

The IRR programme had a duration of 13 weeks with clinical admission to a separate 15-bed specialized unit of a psychiatric skilled nursing home. In addition to usual multidisciplinary nursing home care, including psychotropic drugs treatment. The IRR consisted of integrative psychotherapeutic interventions for MPS

of the patient and family therapy for the caregiver. The psychotherapeutic interventions were based on a problem solving theoretical framework. [22] A more extensive description of IRR programme has been published elsewhere. [23, 24]

Usual care (UC) consisted of a relatively high level of multidisciplinary nursing home care provided in the following settings: at home (25.3%), at home with mental healthcare (out-reaching) or psycho-geriatric day care/treatment (15.7%), in a home of assisted living (7.2%) and in a nursing home (51.8%).

The UC was provided by different types of core multidisciplinary teams, each with a different theoretical framework, mostly emotion-oriented.

2.4   Assessments

For the present study of effect modification, we have selected the following instruments out of a larger set of assessments. Multiple Psychiatric Symptoms (MPS) of the patient were assessed by means of the Neuropsychiatric Inventory (NPI 12 item version; NPI-sum-severity 0 to 144; 0 = no symptoms). [25, 26] The NPI was administered to the caregiver. General burden of the caregiver was assessed by Caregiver Burden ('CB': 0 to 100; 0 = optimal) [27]. For 'Cognitive functioning' of the patient, memory was measured by Mini Mental State Exam (MMSE: 0 to 30; 30 = normal) [28] and self care by Barthel Index (BI: 0 to 20; 20 = normal). [29] To assess the risk for being placed in a nursing home the Global Deterioration Scale (GDS: 1 to 7; 1 = normal) was used. [30] For registration of somatic co-morbidity the ICD-10 was used. Furthermore, the DSM IV disorders (axes I and II) were classified by a research psychiatrist. Finally, the following demographic data were collected from patient and caregiver: gender, age, marital status, family relationship, domicile and level of education.

2.5   Statistical analyses

To evaluate the effect of IRR compared with UC the mean differences of the outcome variables were calculated over time . Cohen's-d was calculated, allowing a comparison over different outcome variables. [31] According to the power calculation (-error fixed at 0.05 [two tailed] and -error fixed at 0.20) based on a 1:1 ratio a sample size of 170 patients (85 IRR and 85 UC) is required. A Cohen's-d = 0.20 is regarded as a small, 0.50 as a moderate, albeit clinically relevant and 0.80 as a large effect.

To predict long term improvement on the two outcome variables (NPI-sum-severity of the patient and General burden of the caregiver), the method of multiple linear regression analysis was applied. It is of specific clinical interest to identify and estimate whether the effect of intervention modified by predictor variables assessed at baseline i.e. MMSE, BI, vascular and Alzheimer's dementia [32 – 34]. The very meaning of effect modification is that the effect of Intervention, IRR and UC

respectively, depends on the baseline value of the relevant predictor variable. As measure of model performance, multiple correlation squared (MR^2) was used, once without and once with effect modification. The MR^2, theoretically varying between 0.0% and 100.0%, represents the percentage of variance explained. The effect modification would be of significance when the MR^2 including the effect modification was significant higher than MR^2 without effect modification. As individual measure of performance, the unstandardized and standardized regression weights, symbolized as b and ß respectively, were considered of relevance. All testing took place at 0.05 level of significance (two tailed). The statistical analyses were performed with SPSS, version 15.

3.   Results

3.1   Characteristics of the study sample

The flow-chart (Figure 1) shows that, of the 336 eligible patients, 168 (50%) consented to participate. The non-participants did not differ significantly from the participants with regard to the inclusion criteria. The 168 patients were randomly assigned to either IRR (N=81) or UC (N=87). The differences between the two study groups in the number of drop-outs – the majority caused by death - were insignificant at all measurement points. Moreover, the drop-outs did not differ significantly with regard to any baseline assessment or length of time participating in the programme (Cox regression analysis: HR 1.21; P<0.54). With respect to biographical data, there were no significant differences between the two groups (Table 1). Mean somatic co-morbidity in the IRR group was significantly higher (IRR 5.6 [sd 2.6] ; UC 4.5 [sd 2.4] ; p<0.01). In our analyses we controlled for somatic co-morbidity. A mean GDS score 4.2 (sd 0.8) suggested that the study sample consisted of psycho-geriatric patients with mild cognitive impairment who were at risk for admission to a nursing home. [30, 35] At T1 (Table 2) there were no significant mean differences between the IRR group and the UC group.

3.2   Effectiveness of IRR

Table 3 presents the results at six months follow-up (T1 – T3). On MPS, NPI-scores observed by the caregiver showed significant effects with a moderate size in favour of IRR.

In IRR the NPI-sum-severity score was 9.91 lower. Regarding 'Burden' of the caregiver, the mean CB score was 24.76 lower and significantly in favour of IRR with a large effect size. Furthermore, the cognitive outcome variables (MMSE, BI) showed no significant differences

3.3 Effect modification on improvement at six months follow-up (T1-T3)

Table 4 and 5 show that the long term effect of Intervention on NPI-sum-severity was not modified by level of cognitive functioning. Neither MMSE nor BI appeared to have modifying qualities. The results with type of dementia were similar. Neither vascular nor Alzheimer's dementia enabled modifying the long term effect of Intervention.

In addition, the long term effect of Intervention on general burden of the caregiver was not modified by cognitive functioning. Neither MMSE nor BI had the potentiality to modify the effect of Intervention. The findings were similar for type of dementia. Just as little as MMSE and BI, to both vascular and Alzheimer dementia could not be ascribed any modifying qualities. In addition, in supplementary explorative prognostic analyses we tested the interaction terms in combination with the main terms in the various prognostic models. The

p-values of all the interaction terms were above 0.25 (not presented). Of relevance is to mention that general burden improved in long term significantly more in IRR than in usual care. The same holds true for the improvement on NPI-sum-severity albeit marginally significant.

4. Discussion

In this study we investigated whether the long term effects of IRR were modified by the level of cognitive functioning and/or type of dementia. The results showed that whichever effect modification was taken into account, it did not matter. There was no significant modification of the beneficial effects of IRR on the severity of multiple psychiatric symptoms of psycho-geriatric patients or on general burden of the caregiver. The beneficial effects of the person-oriented, individual programme of IRR did not depend on the level of cognitive disorders or on type of dementia at baseline. This opens the door to explore what the limits are to benefit from IRR especially with respect to level of cognitive functioning. For reasons of the METC patient had to be capable to give an informed consent for participation in the RCT. So, the MMSE limit for inclusion was set at $\geq$18. However, in our clinical experience before the execution of the RCT, we had indications that the limit could be set at least at MMSE 12. This means that much more psychogeriatric patients and their caregivers may benefit from the IRR programme. With respect to the non-modifying effect of type of dementia it seems interesting to explore whether (psycho)geriatric patients suffering from a broader range of cognitive disorders like Cerebro Vascular Accident or crash accident may benefit from IRR. A previous empirical-clinical study (RCT) to the benefit of IRR compared to usual care showed that few patients and caregivers needed to be treated i.e. NNTs of four respectively five. [23] All in all, this means, that IRR was beneficial on clinically important disorders for a wide group of psychogeriatric patients who suffer from cognitive impairment or dementia and for caregivers [10.]

The strength of this study was that it was based on a relatively large sample size of participating patients [13, 16, 18, 20, 22]. Furthermore, there were no significant differences between dropout patients in both arms of the study and the confounding effect of dropout was marginally small. [23] What were the limitations of this study on effect modification? First of all, the post-hoc nature of the study is a limitation. There was no a priori hypothesis formulated concerning effect modification criteria. Furthermore, the RCT was not blinded. Blinding was not feasible, because the trained co-workers had to visit the patients and caregivers personally, so they knew the intervention history of the patients and because the caregivers and nurses were informed participants, they also knew about the intervention. The assessments at baseline showed just minor differences between IRR and usual care, except for somatic co-morbidity, so the information bias at baseline seems to be limited. However, future studies have to be performed, preferably as blinded RCTs. With regard to generalization of the results, it is of clinical relevance to keep in mind that 50% of the eligible patients were unwilling to participate in the study, and the main reason for refusal was fear of a clinical admission in case of allocation to the IRR group. However, in a post-hoc prognostic analysis living together showed no prognostic qualities with respect to improvement on the primary outcome variables.

Compared to literature, the results of IRR confirm the indications that psychotherapeutic treatment of psychiatric symptoms in psychogeriatric patients who suffer from cognitive impairment or dementia are effective. [13 – 16, 20, 22]

An intriguing question is which elements of IRR constitute the therapeutic effective components. However, in our study we could not analyze the different components separately, but carried it out as a clinical study on a combined complex intervention.

We think that there are three candidates which can explain the surplus effect of IRR for a broad range of psychogeriatric patients and their caregivers, i.e. the application of well-known psychotherapeutic strategies, based on functional problem-solving principles to both patient and caregiver problems, and the tailor made personal approach.[13, 22, 36, 37] Finally, the systematically and strict methodological application of the IRR programme was another element that determined the surplus effect of IRR. [21, 38]

5.   Conclusion

In conclusion, IRR was an integrative psychotherapeutic nursing home programme based on person-oriented and problem-solving principles. The significant beneficial effects of IRR on multiple psychiatric symptoms of psychogeriatric patients who suffer from cognitive impairment or dementia as well as on burden of caregivers were not modified by level of cognitive disorders or by type of dementia. The beneficial effects of IRR extended to a wide group of psychogeriatric patients and their caregivers. This means that within the limits of the in this study

applied inclusion criteria, the patients and caregivers had the same likelihood to benefit from the IRR programme. Maybe a broader range of patients i.e. (psycho) geriatric patients suffering from lower level of cognitive functioning and/or different type of cognitive disorder, can benefit from the IRR programme as well. This result is of great clinical interest, as both topics are among the top three problems experienced by dementia patients and their caregivers. Considering all available evidence, usual (inter)national psychogeriatric nursing home care and perhaps other forms of care as well, can now incorporate integrative psychotherapeutic treatment. The same applies to the education programmes for the various disciplines that are involved. Future studies have to be performed to strengthen the evidence, preferably as blinded RCTs.

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Eligible patients (n = 336)

Not randomized	**n = 168**
Refusal of referral/treatment	**n = 152**
Refusal of participation	**n = 9**
Reasons unknown	**n = 7**

**Randomization
n = 168**

IRR

UC

Intervention as allocated	**(n=81)**
Did not receive standard	
Intervention as allocated	n = 1

Intervention as allocated	**(n=87)**
Did not receive experimental	
Intervention as allocated	n = 1

Time 1:
available:	n = 78
death:	n = 2
refusal:	n = 1
loss:	n = 0
total drop out:	n = 3
	4 %

Time 1:
available:	n = 83 [1]
death:	n = 4
refusal:	n = 0
loss:	n = 0
total drop out:	n = 4
	5 %

Time 2:
available:	n = 69
death:	n = 10
refusal:	n = 1
loss:	n = 1
total drop out:	n = 12
	15 %

Time 2:
available:	n = 77 [2]
death:	n = 9
refusal:	n = 0
loss:	n = 1
total drop out:	n = 10
	12 %

Time 3:
available:	n = 54
death:	n = 24
refusal:	n = 2
loss:	n = 1
total drop out:	n = 27
	33 %

Time 3:
available:	n = 64 [3]
death:	n = 23
refusal:	n = 0
loss:	n = 0
total drop out:	n = 23
	26 %

[1] Fisher's Exact test for dropout * condition p 1.00 (two-tailed)
[2] Fisher's Exact test for dropout * condition p 0.494 (two-tailed)
[3] Fisher's Exact test for dropout * condition p 0.138 (two-tailed)

Figure 2. Flow chart discribing progress of patients through randomized controlled trial

Table 1. General details of participants, distinguished by intervention

	IRR n=81	UC n=87	p-value
Patient characteristics			
gender (females)	66.7%	62.1%	0.63[1]
age (in years), mean (sd)	79.8 (6.1)	81.5 (7.1)	0.10[2]
marital status: alone	77.8%	80.5%	0.71[1]
educational level: low	67.5%	68.7%	0.90[1]
domicile: at home	76.5%	66.7%	0.17[1]
primary caregiver: spouse	17.3%	13.8%	0.33[3]
DSM-IV dementia, (axis-I), count (%)			
dementia of the Alzheimer's type	18.5%	17.2%	0.84[1]
vascular dementia	23.5%	25.3%	0.86
dementia due to other conditions	16.0%	19.5%	0.69
amnestic/cognitive disorders	32.1%	31.0%	1.00
other	6.2%	2.3%	0.26
DSM-IV personality disorders (axis-II), count (%)	16.0%	9.2%	0.24
GDS-deterioration, mean (sd)	4.2 (0.7)	4.3 (0.9)	0,62[2]
somatic co-morbidity (ICD-10), mean (sd)	5.6 (2.6)	4.5 (2.4)	0.01[2]
Caregiver characteristics			
gender (females)	70.5%	61.7%	0.32[1]
age (in years), mean (sd)	58.6 (11.9)	58.9 (12.0)	0.86[2]
marital status: living together	91.4%	94.8%	0.52[1]
educational level: low	4.3%	2.6%	0.39[1]

[1] Fisher's Exact Test (twotailed)
[2] t-Test (twotailed)
[3] Pearson Chi-square (twotailed)

Table 2. Level of outcome across time (T1 - T3) distinguished by intervention

	range	high score = (+/-) [a]	T1 (baseline measurement)								T3 (six months follow-up)			
			IRR			UC			95% CI		mean diff.	IRR		UC	
			n	mean	sd	n	mean	sd				n	mean	n	mean
Psychiatric function disorders patient *(by caregiver)*															
NPI-sum-severity	0 to 144	(-)	72	35.90	21.84	76	29.68	20.12	-13.05	0.62	-6.22	49	15.84	51	18.61
Caregiver burden															
Caregiver burden (CB)	0 to 100	(-)	72	52.47	25.65	77	46.69	27.66	-14.42	2.85	-5.79	42	28.81	50	44.90
Cognitive functioning patient															
MMSE	0 to 30	(+)	76	20.04	4.50	82	20.58	3.84	-0.77	1.85	0.54	51	19.46	60	19.50
Barthel Index (BI)	0 to 20	(+)	77	15.39	3.77	80	14.71	3.55	-1.83	0.48	-0.68	54	12.38	63	13.24

[a]   + = high score is beneficial, - = high score is unfavourable

Table 3. Differences [mean (sd) and Cohen's-d] in IRR and UC; six months follow-up (T1 - T3)

	range	high score = (+/-) *	IRR n	UC n	mean IRR T1 - T3	mean UC T1 - T3	std. Deviation IRR	std. Deviation UC	mean diff UC-IRR	pooled sd	Cohen's d	p-value
SIX MONTHS FOLLOW-UP EFFECTS												
Psychiatric function disorders of the patient (by caregiver)												
NPI-sum-severity	0 to 144	(-)	49	51	21.78	11.86	22.85	24.13	-9.91	23.51	-0.42[1]	0.04
Caregiver burden												
Caregiver burden (CB)	0 to 100	(-)	42	50	24.76	0,00	31.16	25.65	-24.76	28.29	-0.88[1]	0,00
Cognitive functioning of the patient												
MMSE	0 to 30	(+)	51	60	1.25	1.07	4.17	3.91	-0.17	4.03	-0.04[2]	0.82
Barthel Index (BI)	0 to 20	(+)	54	62	3.61	2.06	4.85	4.27	-1.55	4.55	-0.34[2]	0.07

*) + = high score is beneficial; - = high score is unfavourable

Improvement OUTCOME VARIABLES	Determinants Cognitive functioning	b	95%CI		statistics Beta	95%CI		p-value	R squared	P F-change	t-value
NPI-sum-severity	Intercept	1,382	1,10	29,66				0,035	0,091	0,115	
	Intervention	8,726	-0,40	17,85	0,195	-0,01	0,40	0,061			1,899
	DSM_Vascular	2,086	-9,59	13,77	0,038	-0,17	0,25	0,724			0,355
	DSM_Alzheimer	10,825	-0,19	21,84	0,208	0,00	0,42	0,054			1,951
	Intercept	17,457	2,83	32,08				0,020	0,111	0,381	
	Intervention	3,213	-8,98	15,41	0,072	-0,20	0,34	0,602			0,524
	DSM_Vascular (D_V)	-5,216	-21,75	11,32	-0,094	-0,39	0,20	0,532			-0,627
	DSM_Alzheimer (D_A)	5,572	-9,63	20,77	0,108	-0,18	0,40	0,468			0,729
	Intervention*D_V	14,494	-8,55	37,54	0,197	-0,11	0,51	0,215			1,250
	Intervention*D_A	10,513	-11,26	32,28	0,149	-0,16	0,45	0,340			0,960
General caregiver burden	Intercept	3,524	-15,09	22,14				0,708	0,176	0,005	
	Intervention	24,182	11,97	36,39	0,394	0,20	0,59	0,000			3,938
	DSM_Vascular	-0,841	-16,08	14,39	-0,012	-0,23	0,20	0,913			-0,110
	DSM_Alzheimer	6,637	-8,16	21,43	0,094	-0,11	0,30	0,375			0,892
	Intercept	2,834	-16,09	21,76				0,676	0,196	0,355	
	Intervention	24,510	7,79	41,23	0,399	0,13	0,67	0,005			2,915
	DSM_Vascular (D_V)	-7,728	-29,27	13,81	-0,106	-0,40	0,18	0,477			-0,714
	DSM_Alzheimer (D_A)	11,971	-7,69	31,64	0,169	-0,10	0,44	0,229			1,211
	Intervention*D_V	12,754	-17,44	42,94	0,135	-0,18	0,45	0,403			0,840
	Intervention*D_A	-12,558	-41,91	16,79	-0,128	-0,42	0,17	0,397			-0,851

b=unstandardized regression coefficient

beta= standardized regression coefficient

p-value=significance leve adjusted for the other terms in the model

R-squared= explained variance by the model

p-value of F-change= significance level of the model with effect modification compared to the model without effect modification

Table 4. Long term improvement, yes/no effect modification of intervention, relevance of cognitive functioning and type of dementia

Improvement OUTCOME VARIABLES	Determinants Cognitive functioning	b	95%CI	95%CI	statistics Beta	95%CI	95%CI	p-value	R squared	P F-change	t-value
NPI-sum-severity	Intercept	17,552	2,919	32,185				0,019	0,062	0,203	1,84
	Intervention	8,544	-0,676	17,765	0,191	-0,01	0,39	0,069			
	MMSE	-0,584	-1,796	0,628	-0,101	-0,31	0,11	0,341			-0,957
	Intercept	17,640	2,877	32,402				0,020	0,062	0,885	1,827
	Intervention	8,531	-0,742	17,804	0,191	-0,01	0,40	0,071			
	MMSE	-0,681	-2,489	1,127	-0,118	-0,43	0,19	0,456			-0,748
	Intervention*MMSE	0,172	-2,188	2,532	0,022	-0,28	0,32	0,885			0,145
	Intercept	16,673	1,73	31,62				0,029	0,053	0,287	1,764
	Intervention	8,432	-1,06	17,93	0,188	-0,02	0,40	0,081			
	BI	-0,029	-1,52	1,47	-0,004	-0,21	0,20	0,969			-0,039
	Intercept	16,821	1,81	31,84				0,029	0,056	0,579	1,611
	Intervention	7,889	-1,84	17,62	0,176	-0,04	0,39	0,111			
	BI	-0,428	-2,50	1,64	-0,059	-0,34	0,22	0,682			-0,411
	Intervention*BI	0,849	-2,18	3,88	0,081	-0,20	0,37	0,579			0,557
General caregiver burden	Intercept	4,369	-14,52	23,26				0,647	0,167	0,003	3,924
	Intervention	24,003	11,85	36,16	0,391	0,20	0,59	0,000			
	MMSE	-0,274	-1,89	1,34	-0,034	-0,23	0,16	0,737			-0,337
	Intercept	3,816	-15,24	22,87				0,692	0,171	0,561	3,9
	Intervention	23,948	11,74	36,16	0,390	0,19	0,59	0,000			
	MMSE	0,222	-2,12	2,57	0,028	-0,26	0,32	0,851			0,189
	Intervention*MMSE	-0,925	-4,07	2,22	-0,084	-0,37	0,20	0,561			-0,584
	Intercept	10,957	-7,66	29,57				0,245	0,195	0,001	3,974
	Intervention	24,161	12,08	36,25	0,401	0,20	0,60	0,000			
	BI	-1,695	-3,71	0,32	-0,168	-0,37	0,03	0,098			-1,671
	Intercept	11,022	-7,72	29,76				0,246	0,195	0,864	3,656
	Intervention	23,780	10,85	36,71	0,394	0,18	0,61	0,000			
	BI	-1,827	-4,36	0,71	-0,181	-0,43	0,07	0,156			-1,432
	Intervention*BI	0,360	-3,81	4,53	0,023	-0,24	0,29	0,864			0,172

b=unstandardized regression coefficient
beta= standardized regression coefficient
p-value=significance leve adjusted for the other terms in the model
R-squared= explained variance by the model
p-value of F-change= significance level of the model with effect modification compared to the model without effect modification

Table 5. Long term inprovement, yes/no effect modification of intervention, cognitive functioning (MMSE) and activities of daily living (BI)

Benefit of integrative psychotherapeutic nursing home programme to reduce multiple psychiatric symptoms of psychogeriatric patients and caregiver burden after six months follow-up; A randomized controlled trial[1]

1)   Bakker TJEM, Duivenvoorden HJ, van der Lee J, Olde Rikkert MGM, Beekman ATF, Ribbe MW.

1.   Introduction

In psychogeriatric patients who suffer from cognitive impairment or dementia, there is an 80% prevalence of two or more psychiatric symptoms, e.g. depression, anxiety, paranoia, aggression. [1-5] Multiple psychiatric symptoms (MPS) have many related negative secondary effects. For the patients there are negative effects on cognitive functioning, quality of life and they predict admission to a nursing home. Furthermore, MPS are a burden for the caregiver. [3, 6-10] Moreover, these MPS are number one among the top three problems experienced by psychogeriatric patients and their caregivers. [10] In usual nursing home care, psychotropic drugs are widely used to treat the MPS of dementia patients despite of their limited effects and potentially harmful side-effects e.g. (a)typical antipsychotics. [11-13] There is a lack of integrative psychotherapeutic programmes, even though reports in the literature indicate that for individual psychiatric symptoms, e.g. depression and anxiety, as well as caregiver burden, psychotherapeutic treatment may be effective in both nursing home and primary care settings. [14-25] However, psychotherapeutic interventions focussing on the MPS of psychogeriatric patients are complex, due to their multiplicity in combination with cognitive disorders, somatic co-morbidity, and social problems (e.g. relationships, loneliness) [26, 27]. Furthermore, integrative psychotherapeutic programmes in nursing homes have never been evaluated in large-scale comprehensive studies. [17, 28-30] For these reasons, we developed an unique integrative psychotherapeutic nursing home programme: integrative reactivation and rehabilitation (IRR). [22] In this paper we report the results of a re-analysis of the effectiveness of IRR in terms of percentages of clinically relevant improved psychogeriatric patients and caregivers. The performed RCT was designed to test the effectiveness of IRR on MPS in psychogeriatric patients who suffer from cognitive impairment or dementia and on caregiver burden. The primary analysis regarded the mean differences between IRR and the control group (usual care) on continuous data of the primary and secondary outcome variables. The results of this analysis are published elsewhere. [23] From the perspective of the caregivers, the IRR had a significant and moderate to large surplus effect (up to 34%) in reducing the MPS of psychogeriatric patients who suffer from cognitive impairment or dementia in both short term and the long term. In fact, at the six-month follow-up there was a total reduction in MPS up to 46% in number and 61% in severity. Furthermore, with regard to caregiver burden and competence the IRR had a large positive surplus effect (up to 36%) at the end of the treatment. During the follow-up the surplus effect even increased to a reduction of 50%, while usual care had hardly any effect at all. After all, it is relevant to estimate the percentages of patients and caregivers who showed clinically relevant improvement in IRR compared to usual care, especially at six months follow-up. Moreover, using an intention to treat (ITT) strategy offers the opportunity to calculate risk ratio's (RRs) and numbers needed to treat (NNTs), which can be compared to those of other interventions. [31, 32] At the end, performing a complete cases analysis (CC) allows a more realistic estimation of the efficacy of IRR compared to usual care. Specifically, if there was a relatively high natural dropout, which is a well-known

phenomenon in research on frail elderly. [17, 23 - 30] In case of no significant differences between dropouts in both arms of the study, results of a CC-analysis may represent a more accurate estimation of the potential benefit of IRR. At the end, only patients and caregivers who fully participated in IRR programme can benefit completely of the available interventions. In this re-analysis study - following Cummings - minimally, clinically important improvement was defined as more than 30 % improvement compared to the baseline value of the primary outcome variable, i.e. NPI-sum-severity. [33, 34] This corresponds well -in this study as well as in general- with a half standard deviation or more of the baseline value. [35, 36] The objective of this clinical-empirical study was to re-analyse the RCT with respect to long term benefit of IRR compared to UC in terms of percentages of clinically relevant improved psychogeriatric patients on psychiatric symptoms and of caregivers on burden.

2. Material and Methods

2.1 Patients

The psychogeriatric patients were recruited from the urban region of Nieuwe Waterweg Noord (NWN), near Rotterdam in the Netherlands (approx. 180.000 inhabitants). The patients were referred from an (ambulant) mental health service (5.4%), a general hospital (13.8%), a memory clinic (6%) and general practitioners or primary healthcare services (75.1%). Before inclusion, all referred patients underwent a comprehensive geriatric assessment. The initial inclusion criteria were a DSM IV classification for dementia, amnestic disorders or other cognitive disorders. Additional inclusion criteria were: 1) age: ≥ 65 years; 2) cognitive functioning: MMSE ≥ 18 and ≤ 27 as well as Barthel Index (BI) ≥ 5 and ≤ 19; 3) psychiatric symptoms: Neuropsychiatric Inventory (NPI) 3 or more symptoms, and 4) informed consent. The exclusion criteria were: 1) delirium; 2) life-threatening somatic co-morbidity; 3) active coercive admission regime (according to psychiatric legislation), and 4) insufficient command of the Dutch language.

2.2 Design

The study was an open RCT, with a parallel group design and was performed from 2001 until 2006. The psychogeriatric patients who met the selection criteria were randomly and blindly assigned to either IRR or usual care (UC), using a randomization algorithm. In the first half of the study the assignment was in a ratio 1 (IRR): 2 (UC). Due to limited numbers of eligible patients and time restrictions of the study, in the second half the ratio was reversed to 2 (IRR): 1 (UC). The study included 168 patients (81 IRR and 87 UC). 'Multiple psychiatric symptoms' of the patient was the primary outcome variable. In view of clinically relevant background information of

the effects of IRR, 'Burden' of the caregiver, 'Cognitive functioning' and 'Quality of life' of the patient, as well as 'Nursing home admission' were selected as secondary outcome variables. The assessments were simultaneously executed in both groups of the study at two moments: T1 (within two weeks after intake) and T3 (follow-up; six months after end of intervention). Furthermore, data were gathered by trained co-workers, not members of this intervention team. The study was approved by the Medical Ethical Committee of the Erasmus University Medical Centre.

2.3 Intervention

The IRR programme had a duration of 13 weeks, with clinical admission to a separate 15-bed specialized unit in a psychiatric skilled nursing home. In addition to the usual multidisciplinary nursing home care, including psychotropic drugs treatment, the IRR also consisted of interventions to reduce the MPS of the psychogeriatric patient and family therapy for the caregiver. Cognitive and somatic functioning were also optimized (Figure 1). A more extensive description of the IRR programme has been published elsewhere. [22]

A personal package of interventions was composed for each patient and caregiver, based on six dimensions. [22, 23] These six dimensions were: 'Emotion' (e.g. depression, anxiety, aggression), 'Personality' (e.g. characteristics of narcissism, borderline, dependency), 'Life events' (e.g. traumatic experiences such as war, incest, death of a spouse/child), 'Social functioning' (e.g. relationship problems with spouse/children, loss of pleasant social activities), 'Cognitive functioning' (e.g. problems with memory, self-care), and 'Somatic functional disorders' (e.g. impaired mobility, falls, polypharmacy, nutritional deficiency and intercurrent diseases). The following psychotherapeutic interventions based on a problem-solving theoretical framework, were available and written down in specific guidelines for each discipline: 1) diagnostic assessment, 2) counseling, 3) life-review, 4) interpersonal therapy, 5) (cognitive) behavioural therapy, 6) support in accepting behaviour and minimizing negative effects, 7) regression approach, temporarily accepting regression behaviour, 8) rehabilitation, 9) psycho-education, and 10) family therapy. [22] The interventions were mainly provided in a group, but when necessary individually.

With regard to the percentage of patients receiving each type of intervention (Table 1), it is important to realize that on average, the patients were treated for five functional psychiatric problems apart from the functional problems on the cognitive and somatic dimension. The interventions for these functional psychiatric problems were generally provided by four disciplines, but sometimes a discipline used more than one type of intervention during the different phases of the IRR programme. This makes the programme highly flexible and it is therefore possible to compose and provide a personal package of interventions for each patient and caregiver. After multidisciplinary consultation, the psycho-geriatrician - a nursing home physician with experience in psychiatric treatment - prescribed

the interventions. The IRR team consisted of a nursing team, a psycho-geriatrician, a clinical psychologist, a social worker, a music therapist, a psychomotor therapist and a creative therapist, a physiotherapist, an occupational therapist, a speech therapist, a dietician and a welfare worker (Figure 1). Staff members were trained to systematically conduct the IRR programme. The progress of the patient/caregiver was monitored weekly, guided by the method of standardized goal attainment scaling (GAS: score range 1 to 7; 7 = independent (no help needed). [37] Treatment fidelity was continuously monitored during the course of the personal intervention plan for each patient/caregiver. Each week, all the disciplines had to deliver a written GAS score, based on functional progress during the therapy sessions. These scores were discussed in the multidisciplinary patient meeting and a consensus GAS score was determined. All the registered data were sent to the research team after the end of the treatment. Moreover, at the end of the IRR programme each discipline had to fill in an evaluation form about the course of the therapy, including active patient participation. These data are available from the first author. Usual care (UC) consisted of a relatively high level of multidisciplinary nursing home care provided in the following settings: at home (25.3%), at home with mental healthcare (out-reaching) or psycho-geriatric day care/treatment (15.7%), in a home of assisted living (7.2%) and in a nursing home (51.8%). The multidisciplinary UC staff consisted of a nursing home physician or social geriatric physician, a psychologist, a paramedical team (physiotherapist, occupational therapist, speech therapist, welfare worker) and a nursing team (Registered Nurses, Certified Nurse Assistants and/or Nurse Assistants).

The UC was provided by different types of core multidisciplinary teams, each with a different theoretical framework, mostly emotion-oriented.

2.4   Assessments

The primary outcome variable was the number of 'MPS' assessed by number (0-12) as well as sum-severity (0-144, number x frequency x severity) using the Neuropsychiatric Inventory (NPI 12 item version). [38, 39] The NPI was administered to the caregiver. The following secondary outcome variables were measured: 'burden' for the caregiver assessed with the 'NPI emotional distress' (N-emD: 0 to 60; 0 = no distress), the Caregiver Competence List (CCL: 28 to 112; 112 = optimal) [40] and the Caregiver Burden (CB: 0 to 100; 0 = optimal). [41] To asses the 'cognitive functioning' of the patient, memory was measured with the Mini Mental State Exam (MMSE: 0 to 30; 30 = normal) [42] and self-care with the Barthel Index (BI: 0 to 20; 20 = normal). [43] The 'quality of life' of the patient was assessed with the MOS short-form general health survey (SF-20: 0 to 100; 100 = optimal) [44], EuroQol (EQ5D: – 0.59 to 1.0; 1.0 = optimal), and the visual analogue scale (VAS 'thermometer') for subjective health status (0 to 100; 100 = optimal). [45] Admission to a nursing home was measured according to length of stay in days. The Global Deterioration Scale (GDS: 1-7; 1 = normal) was used to assess the risk of admission

to a nursing home [46]. Somatic co-morbidity was assessed with the ICD-10, and the DSM IV disorders (axes I and II) were classified by a research psychiatrist. Finally, the following demographic data were collected from the patient and the caregiver: gender, age, marital status, family relationship, domicile and level of education.

2.5   Statistical analyses

Fisher's exact tests were used to estimate differences between IRR and UC on counts such as the number of deaths. Student's t test for unpaired samples was used to test for differences between IRR and UC on continuous data. To evaluate the effect of IRR compared to UC, the mean differences on the continuous outcome variables were calculated over time. In this re-analysis of the RCT we tested in percentages the difference of improvement compared to baseline values between the two interventions (i.c. IRR and UC) in long term (follow-up; six months after the end of intervention: T_1-T_3). Following Cummings, improvement was defined as a difference of a half sd or more of the baseline value, corresponding to > 30 % improvement. [33 - 36] We calculated risk ratios (RRs) (in fact benefit ratios) for the estimation of the dichotomised change in favour of IRR for each outcome variable (Intention To Treat analysis/ ITT). Furthermore, the number needed to treat (NNT) was estimated in case of a significantly higher percentage of improvement in IRR compared to UC, and vice versa. To estimate the beneficial effect on patients and caregivers, who fully participated in the IRR programme, odds ratios (ORs) were calculated according a complete cases analysis (CC) using the data of patients who fully completed IRR respectively UC in long term. A risk ratio or odds ratio >1.0 was in favour of IRR. The differences between the drop-outs in the two study groups, with regard to duration over time of participation in the programme, were determined by Cox-regression analysis. Hazard Ratio (HR) was used as the measure of performance. The length of stay in a nursing home was estimated by Kaplan-Meier analysis. The 95% confidence intervals (CI) were presented. All significance testing was set at P<0.05 (two-tailed). The statistical analyses were performed with the software programme SPSS, version 15.

3.   Results

3.1   Characteristics of the study sample

The flow-chart (Figure 1) shows that, of the 336 eligible patients, 168 (50%) consented to participate. The non-participants did not differ significantly from the participants with regard to the inclusion criteria. The 168 patients were randomly assigned to either IRR (N=81) or UC (N=87). The differences between the two study groups in the number of drop-outs – the majority caused by death - were insignificant at all measurement points. Moreover, the drop-outs did not differ significantly

with regard to any baseline assessment or length of time participating in the pro-
gramme (Cox regression analysis: HR 1.21; P<0.54). With respect to biographical
data, there were no significant differences between the two groups (Table 2). Mean
somatic co-morbidity in the IRR group was significantly higher (IRR 5.6 [sd 2.6] ;
UC 4.5 [sd 2.4] ; p<0.01). In our analyses we controlled for somatic co-morbidity. A
mean GDS score 4.2 (sd 0.8) suggested that the study sample consisted of psycho-
geriatric patients with mild cognitive impairment who were at risk for admission
to a nursing home [47]. At T1 (Table 3.) there were no significant mean differences
between the IRR group and the UC group with the exception of the NPI cluster
hyperactivity (mean difference 3.49; 95% CI: - 6.33 to - 0.59). [48]

3.2   Long term improvement: risk ratios (RR)

Table 4 shows the estimated RRs and NNTs of improved patients at follow-up, six
months after end of intervention (T1-T3). On the primary outcome variable 'MPS',
all RRs were in favour of IRR, with up to 46% clinically improved patients; albeit
not one was statistically significant. Looking in more detail, on sum-severity of the
NPI-cluster hyperactivity IRR showed a significantly positive effect (RR 2.64; 95%
CI: 1.26 to 5.53; NNT: 4.07); with 40% improved patients in IRR. Furthermore, on
'Burden' of the caregiver the RR of competence (CCL) was 2.23 (95% CI: 1.07 to
4.62; NNT: 5.07) significantly in favour of IRR (with 36% improved caregivers).
General burden was marginally significant (RR 1.99; 95% CI: 0.95 to 4.17; NNT
6.25). 'Cognitive functioning' and 'Quality of life' showed no significant differ-
ences between the two arms. Kaplan-Meier analysis showed that the length of stay
in a nursing home did not differ significantly between IRR and UC (IRR mean
147.04 days and UC mean 151.82 days; P<0.62).

3.3   Long term improvement: complete cases analysis (CC)

Table 5 presents the estimated odds ratios (ORs) for improvement in long term
(T1-T3) of psychogeriatric patients and caregivers, who fully completed the inter-
vention in both groups of the RCT on MPS (number as well as sum-severity of
NPI-symptoms) IRR showed high significant odds ratios; OR: 2.80 (95 % CI: 1.22
to 6.42) respectively OR 3.46 (95 % CI: 1.48 to 8.12) with up to 76% improved
patients in IRR. Looking in more detail, the same holds true for NPI-sum-severity
of cluster hyperactivity (OR 5.50; 95 % CI: 2.32 to 13.01); with a high percentage
(65%) improved patients. Regarding 'Burden' of the caregiver, the ORs of the three
outcome variables were all three significantly in favour of IRR. On NPI-emotional
distress the OR was 2.40 (95 % CI: 1.05 to 5.49), on caregiver burden (CB) 4.18 (95
% CI: 1.74 to 10.04) and on competence (CCL) the OR was 3.73 (95 % CI: 1.61 to
8.64); with up to 71% improved caregivers. Of the other secondary outcome vari-
ables 'Cognitive functioning' and 'Quality of life', the ORs were insignificant.

4.   Discussion

In this study we re-analysed the data of the RCT with respect to long term benefit of IRR compared to usual care in terms of percentages of clinically relevant improved psychogeriatric patients on psychiatric symptoms and of caregivers on burden. At six months follow-up after the three months of treatment, the patients who were referred at IRR showed a higher likelihood of clinically relevant improvement on hyperactivity (RR 2.64) than patients referred at usual multidisciplinary nursing home care. The number needed to treat (four) was relatively small with a percentage improved patients of 40. If a patient fully completed the IRR programme, the likelihood of improvement was much more pronounced (ORs between 2.80 to 5.50) and the percentages of improved patients was high (up to 76%). With respect of caregivers, IRR showed a higher likelihood of improvement with relatively small NNTs (five) on competence (RR 2.23; up to 36% improved caregivers). Moreover, after a fully completed programme the ORs on competence and experienced burden varied between 2.40 to 4.18, with a high percentage of improved caregivers up to 71 %. These are important and clinically relevant results because MPS of dementia patients and burden of caregiver are the two as most problematic experienced phenomena in dementia care. [10, 49]

The beneficial long term effects of IRR on psychiatric symptoms of psychogeriatric patients and on the burden as well as the competence of caregivers are in line with the indications in literature that (adapted) psychotherapeutic interventions on individual psychiatric symptoms may be effective. [14 – 23, 50 - 55] The results of the re-analysis confirm those of the primary analyses based on the mean differences on continuous data. Moreover, the benefit of IRR was more pronounced, specifically when the fully completers were taken in account.

In addition, comparison of IRR on NNTs with donepezil, memantine as well as cognitive behaviour therapy showed that the NNTs of IRR were relatively low and in the same range i.e. donepezil NNT 10; memantine NNT 3-8; CBT NNT 5-10. [31, 32]

The strength of this re-analysis of the RCT-data was that, as far as we know, it was one of the first comprehensive studies with a relative large sample size, that addressed integrative psychotherapeutic treatment in a psychiatric-skilled nursing home setting. [17, 19, 21, 25 –28, 30] Furthermore, the surplus benefit for all patients who fully profited from the programme could be estimated. As the relatively large dropout group did not differ significantly between IRR and usual care on all relevant assessment parameters neither on participation interval, there was no question of selective dropout. The majority of dropout was caused by death. Besides, the phenomenon of high dropout percentages is well-known in geriatric research even in observation studies. [17, 23 - 30] Basically, it reflects the vulnerability of psychogeriatric patients suffering from multiple MPS rather than selective dropout as a consequence of the intervention at study, in this case IRR. What were the limitations of this re-analysis? First of all, the post-hoc nature of this re-analysis was a limitation. There was no a priori hypothesis formulated concerning the dichotomised improvement criteria. Furthermore, the RCT was not blinded. In a

clinical study like this, blinding is not feasible, because the trained co-workers had to visit the patients and caregivers personally, so they knew about the intervention, and because the caregivers were informed participants, they also knew about the intervention. As the assessments at baseline showed just minor differences between IRR and usual care, except for somatic co-morbidity, the information bias at baseline seems to be limited. However, future studies have to be performed, preferably as blinded RCTs. Regarding generalization of the findings of this RCT it is of clinical relevance to keep in mind that 50% of the eligible patients refused to participate. The core motive for refraining participation was fear of admission in case of assignment to IRR. However, in a post-hoc prognostic analysis living together showed no prognostic qualities with respect to improvement on the primary outcome variable. Furthermore, more patients were included with vascular dementia than with dementia of the Alzheimer type, which is not in line with most epidemiological studies. This may be an effect of the inclusion criteria i.e. suffering from both cognitive function disorders and three or more NPI-symptoms. As patients with vascular dementia are expected to have more psychiatric problems, they will be overrepresented in this study, as was the case. Nevertheless, in a post-hoc analysis type of dementia showed no significant modification effect on MPS on the patient or on caregiver burden. What are the therapeutic components of IRR? It is expected that after identification of the therapeutic components and developing them to a higher level of sophistication, the beneficial effects of IRR will increase.

To identify psychogeriatric patients and their caregivers with a relatively high likelihood to improve is another possibility to enlarge the beneficial effects of IRR. To that end, to optimize beneficial effects of IRR, the construction of a tool enabling the identification of suitable patients for IRR is of highly clinical interest. Such a tool contributes to optimize medical decision making.

5.   Conclusion

In conclusion, at six months follow-up IRR showed a significantly higher probability of improvement with a relatively small NNT (four) on multiple psychiatric symptoms in psychogeriatric patients who suffer from cognitive impairment or dementia. The results (76 % improved patients) were more pronounced for those who fully completed the IRR programme. The same applies to the higher probability of IRR to improve NPI-related and general burden as well as competence of the caregiver (NNT of five and for those who fully participated 71% improved caregivers). Compared to donepezil, memantine, and CBT the NNTS of IRR were relatively low. Considering all available evidence, usual (inter)national multidisciplinary nursing home care and likely ambulant care programmes are advised to incorporate integrative psychotherapeutic treatment as well as psychiatric strategies. Future studies have to be performed to strengthen the evidence, preferably as blinded RCTs.

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Treatment components	Disciplines

Phase 1

Diagnostic assessment	Multidisciplinary

Phase 2

One of the following:			
Interpersonal therapy	Psychologist		
Counseling	Psychogeriatrician	Psychologist	
Cognitive-behavioural therapy	Nurses	Therapists *)	Psychologist

One of the following:			
Behavioural therapy	Nurses	Therapists *)	
Support	Nurses	Therapists *)	Welfare worker

Family therapy	Psychologist

Phase 3

Rehabilitation	Nurses	Occup therapist	Welfare worker

Support (discharge)	Social worker

*) for each patient, two or three of the following
   therapists are involved in the psychotherapeutic
   programme:
psycho-motor therapist
music therapist
creative therapist
physiotherapist
occupational therapist

Figure 1. Typical IRR patient protocol

Not randomized	n = 168
Refusal of referral/treatment	n = 152
Refusal of participation	n = 9
Reasons unknown	n = 7

Randomization
n = 168

IRR | UC

Intervention as allocated **(n=81)**
Did not receive standard
Intervention as allocated n = 1

Intervention as allocated **(n=87)**
Did not receive experimental
Intervention as allocated n = 1

Time 1:
available: n = 78
death: n = 2
refusal: n = 1
loss: n = 0
total drop out: n = 3
4 %

Time 1:
available: n = 83 [1]
death: n = 4
refusal: n = 0
loss: n = 0
total drop out: n = 4
5 %

Time 2:
available: n = 69
death: n = 10
refusal: n = 1
loss: n = 1
total drop out: n = 12
15 %

Time 2:
available: n = 77 [2]
death: n = 9
refusal: n = 0
loss: n = 1
total drop out: n = 10
12 %

Time 3:
available: n = 54
death: n = 24
refusal: n = 2
loss: n = 1
total drop out: n = 27
33 %

Time 3:
available: n = 64 [3]
death: n = 23
refusal: n = 0
loss: n = 0
total drop out: n = 23
26 %

[1] Fisher's Exact test for dropout * condition p 1.00 (two-tailed)
[2] Fisher's Exact test for dropout * condition p 0.49 (two-tailed)
[3] Fisher's Exact test for dropout * condition p 0.14 (two-tailed)

Figure 2. Flow chart discribing progress of patients through randomized controlled trial

Table 1. Psychotherapeutic treatment ingredients, % performed among patients in IRR

	IRR
	n=81
Intervention types (percentages of patients)[1]	
Assessment	100.0%
Life-review	2.6%
Interpersonal therapy	48.7%
Counseling	79.5%
Cognitive-behavioral therapy	57.7%
Behavioral therapy	94.9%
Support	66.6%
Family therapy	38.5%
Regression	3.8%
Psycho-education	6.4%
Rehabilitation	47.4%[2]
Support (discharge)	41.0%[3]

[1]   Percentages are additional, not cumulative
[2]   Indicated in the (pre-)discharge phase
[3]   Support from social worker on discharge

Table 2. General details of participants, distinguished by intervention

	IRR	UC	
	n=81	**n=87**	**p-value**
Patient characteristics			
gender (females)	66.7%	62.1%	0.63[1]
age (in years), mean (sd)	79.8 (6.1)	81.5 (7.1)	0.10[2]
marital status: alone	77.8%	80.5%	0.71[1]
educational level: low	67.5%	68.7%	0.90[1]
domicile: at home	76.5%	66.7%	0.17[1]
primary caregiver: spouse	17.3%	13.8%	0.33[3]
DSM-IV dementia, (axis-I), count (%)			
dementia of the Alzheimer's type	18.5%	17.2%	0.84[1]
vascular dementia	23.5%	25.3%	0.86
dementia due to other conditions	16.0%	19.5%	0.69
amnestic/cognitive disorders	32.1%	31.0%	1.00
other	6.2%	2.3%	0.26
DSM-IV personality disorders (axis-II), count (%)	16.0%	9.2%	0.24
GDS-deterioration, mean (sd)	4.2 (0.7)	4.3 (0.9)	0,62[2]
somatic co-morbidity (ICD-10), mean (sd)	5.6 (2.6)	4.5 (2.4)	0.01[2]
Caregiver characteristics			
gender (females)	70.5%	61.7%	0.32[1]
age (in years), mean (sd)	58.6 (11.9)	58.9 (12.0)	0.86[2]
marital status: living together	91.4%	94.8%	0.52[1]
educational level: low	4.3%	2.6%	0.39[1]

[1]   Fisher's Exact Test (twotailed)
[2]   t-Test (twotailed)
[3]   Pearson Chi-square (twotailed)

Table 3. Level of outcome across time (T1, T3) distinguished by intervention

| | | | T1 (baseline measurement) | | | | | | | UC-IRR | | T3 (six months follow-up) | | | |
| | | | IRR | | | UC | | | | 95% CI | | IRR | | UC | |
	range	high score = (+/-)*	n	mean	sd	n	mean	sd	mean diff.			n	mean	n	mean
PRIMARY OUTCOME VARIABLE															
Psychiatric function disorders patient															
By caregiver															
NPI-symptoms	0 to 12	(-)	72	5.92	2.35	76	5.23	2.16	-0.68	-1.41	0.05	49	3.49	51	3.84
NPI-sum-severity	0 to 144	(-)	72	35.90	21.84	76	29.68	20.12	-6.22	-13.05	0.62	49	15.84	51	18.61
NPI-clusters (sum-severity)															
Hyperactivity	0 to 60	(-)	72	11.82	9.94	76	8.33	7.68	-3.49	-6.39	-0.59	49	3.76	51	5.98
Psychosis	0 to 36	(-)	72	6.68	7.08	76	5.80	7.48	-0.88	-3.24	1.49	49	2.59	51	2.88
affective symptoms	0 to 24	(-)	72	7.81	6.29	76	6.54	6.78	-1.27	-3.39	0.86	49	3.90	51	4.24
Apathy	0 to 24	(-)	72	9.60	7.34	76	9.01	7.07	-0.58	-2.93	1.76	49	5.59	51	5.51
SECONDARY OUTCOME VARIABLES															
Caregiver burden															
NPI-emotional distress (N-emD)	0 to 60	(-)	72	14.64	9.22	76	12.71	8.96	-1.93	-4.88	1.03	49	6.22	51	7.98
Caregiver burden (CB)	0 to 100	(-)	72	52.47	25.65	77	46.69	27.66	-5.79	-14.42	2.85	42	28.81	50	44.90
Competence (CCL)	28 to 112	(+)	72	84.62	14.24	77	86.58	14.46	1.96	-2.69	6.6	49	96.35	50	91.78
Cognitive functioning patient															
MMSE	0 to 30	(+)	76	20.04	4.50	82	20.58	3.84	0.54	-0.77	1.85	51	19.46	60	19.50
Barthel Index (BI)	0 to 20	(+)	77	15.39	3.77	80	14.71	3.55	-0.68	-1.83	0.48	54	12.38	63	13.24
Quality of life of patient															
SF-20 total	0 to 100	(+)	77	49.54	15.62	81	45.08	14.12	-4.46	-9.14	0.23	51	53.83	57	47.18
EQ5D patient	-0.59 to 1.0	(+)	77	0.54	0.34	80	0.58	0.29	0.04	-0.06	0.14	45	0.62	62	0.55
Health status	0 to 100	(+)	76	67.54	15.74	77	69.16	15.99	1.62	-3.45	6.68	46	72.83	63	67.46

*)   + = high score is beneficial; - = high score is unfavourable

1)   beneficial; 2) unfavourable

Table 4. (Endpoint analysis (ITT analysis) distinguished by intervention (long term)

	Endpoint analysis				
	long term (T1 - T3)				
	IRR (n=81)	UC (n=87)	Intention-To-Treat analysis		
	change	change	RR	95%CI		NNT
PATIENT OUTCOME VARIABLES						
Psychiatric function disorders patient						
By caregiver						
NPI-symptoms	0.43	0.28	1.56	0.82	2.98	
NPI-sum-severity	0.46	0.28	1.65	0.87	3.14	
NPI-clusters (sum-severity)						
hyperactivity	**0.40**	**0.15**	**2.64**	**1.26**	**5.53**	**4.07**
psychosis	0.30	0.26	1.12	0.57	2.20	
affective symptoms	0.32	0.22	1.47	0.74	2.93	
apathy	0.32	0.37	0.88	0.46	1.66	
SECONDARY OUTCOME VARIABLES						
Caregiver burden						
NPI-emotional distress (N-emD)	0.43	0.30	1.44	0.77	2.73	
Caregiver burden (CB)	0.32	0.16	1.99	0.95	4.17	6.25
Competence (CCL)	**0.36**	**0.16**	**2.23**	**1.07**	**4.62**	**5.07**
Cognitive functioning patient						
MMSE	0.09	0.12	0.75	0.27	2.07	
Barthel-index (BI)	0.10	0.07	1.43	0.47	4.31	
Quality of life patient						
SF-20 total	0.22	0.21	1.08	0.51	2.95	
EQ5D patient	0.14	0.10	1.31	0.51	3.35	
health status	0.20	0.18	1.08	0.50	2.32	

Table 5. Endpoint analysis (PP analysis) distinguished by intervention (long term)

	Endpoint analysis						
	long term (T1 - T3)						
	IRR (n=54)		UC (n=64)		complete cases analysis		
	n	change	n	change	OR	95% CI	
PATIENT OUTCOME VARIABLES							
Psychiatric function disorders patient							
By caregiver							
NPI-symptoms	49	0.71	51	0.47	2.80	1.22	6.42
NPI-sum-severity	49	0.76	51	0.47	3.46	1.48	8.12
NPI-clusters (sum-severity)							
hyperactivity	49	0.65	51	0.26	5.50	2.32	13.01
psychosis	49	0.49	51	0.45	1.17	0.53	2.57
affective symptoms	49	0.53	51	0.37	1.90	0.86	4.23
apathy	49	0.53	51	0.63	0.68	0.31	1.51
SECONDARY OUTCOME VARIABLES							
Caregiver burden							
NPI-emotional distress (N-emD)	49	0.71	51	0.51	2.40	1.05	5.49
Caregiver burden (CB)	42	0.62	50	0.28	4.18	1.74	10.04
Competence (CCL)	49	0.59	50	0.28	3.73	1.61	8.64
Cognitive functioning patient							
MMSE	51	0.14	50	0.17	0.79	0.28	2.26
Barthel-index (BI)	54	0.15	62	0.10	1.62	0.52	4.99
Quality of life patient							
SF-20 total	51	0.35	56	0.32	1.15	0.52	2.58
EQ5D patient	45	0.24	60	0.15	1.83	0.68	4.88
health status	46	0.35	59	0.27	1.44	0.62	3.31

To identify prognostic factors for a favourable long-term outcome of an integrative psychotherapeutic nursing home programme to reduce multiple psychiatric symptoms of psychogeriatric patients and caregiver burden;

A clinical-empirical study[1]

1.   Introduction

In psychogeriatric patients who suffer from cognitive impairment or dementia, there is an 80% prevalence of two or more psychiatric symptoms, e.g. depression, anxiety, paranoia, aggression. [1-5] Multiple psychiatric symptoms (MPS) have many related negative secondary effects. For the patients there are negative effects on cognitive functioning, quality of life, and they predict admission to a nursing home. Furthermore, MPS are a burden for the caregiver. [3, 6-12] Moreover, these MPS are number one among the top three problems experienced by dementia patients and their caregivers. [13] In usual nursing home care, psychotropic drugs are widely used to treat the MPS of psychogeriatric patients despite of their limited effects and potentially harmful side-effects e.g. (a)typical antipsychotics. [2, 5, 14,15] There is a lack of integrative psychotherapeutic programmes, even though reports in the literature indicate that for individual psychiatric symptoms, e.g. depression and anxiety, as well as caregiver burden, psychotherapeutic treatment may be effective in both nursing home and primary care settings. [16-19, 24] However, psychotherapeutic interventions focussing on the MPS of psychogeriatric patients who suffer from cognitive impairment or dementia are complex, due to their multiplicity in combination with cognitive disorders, somatic co-morbidity, and social problems (e.g. relationships, loneliness) [25, 26]. Furthermore, integrative psychotherapeutic programmes in nursing homes have never been evaluated in large-scale comprehensive studies. [10, 16, 27-30] For these reasons, we developed an unique integrative psychotherapeutic nursing home programme: integrative reactivation and rehabilitation (IRR). [31] In a previous paper we reported on the results of a randomized controlled trial (RCT) designed to evaluate the effectiveness of IRR in reducing the MPS of psychogeriatric patients who suffer from cognitive impairment or dementia and the burden of caregivers.

The findings of the RCT - based on mean difference between IRR and UC - have been published elsewhere. [32] In another publication we explored the differences between IRR and UC on the percentages of clinically relevant improved psychogeriatric patients and caregivers ; $\geq$ half sd of the baseline value. [33-36] In the current paper the objective was to identify prognostic factors which can predict the likelihood of patients and caregivers to benefit from IRR and which patients from UC. In addition to the identification of these prognostic factors, it is of clinical interest to optimize medical decision making, mainly as decision making is often based on irrational factors. [37-39] In literature many decision rules are considered. [40-43] In this study three decision rules will be applied. The first decision rule (highest Mean Average-rule) is aimed to calculate the average percentage improvement in either intervention. The second rule concerns to minimize the maximum possible loss ('MINIMAX'-rule); this latter rule attempts to avoid the risk of missing benefit by comparing the highest difference between the interventions on each score over all outcome variables; than choose for the intervention with the lowest loss of benefit. The third decision rule concerns the 'MAXIMIN'-rule which implies that the patient will be assigned to the intervention with the lowest level of avoidable risk by comparing the difference between the interventions of the lowest score on all outcome variables.

The objectives of the clinical-empirical study were to identify prognostic potentialities of diagnostic and functional baseline variables on five selected outcome variables. Three selected outcome variables showed a significant effect in the RCT i.e. severity of multiple psychiatric symptoms of the psychogeriatric patient, general burden and competence of the caregiver. Memory and self-care of the patient were two important background outcome variables. The prognostic potentialities were applied to long term (after six months follow-up). In addition, as the number of outcome variables equaled five, we have explored opportunities for building models to optimize decision making, in which the performances of MEAN AVERAGE, MINIMAX- , and MAXIMIN-decision rules were compared.

2. Material and methods

2.1 Patients

The psychogeriatric patients were recruited from the urban region of Nieuwe Waterweg Noord (NWN), near Rotterdam in the Netherlands (approx. 180.000 inhabitants). The patients were referred from an (ambulant) mental health service (5.4%), a general hospital (13.8%), a memory clinic (6%) and general practitioners or primary healthcare services (75.1%). Before inclusion, all referred patients underwent a comprehensive geriatric assessment. The initial inclusion criteria were a DSM IV classification for dementia, amnestic disorders or other cognitive disorders. Additional inclusion criteria were: 1) age: ≥ 65 years; 2) cognitive functioning: MMSE ≥ 18 and ≤ 27 as well as Barthel Index (BI) ≥ 5 and ≤ 19; 3) psychiatric symptoms: Neuropsychiatric Inventory (NPI) 3 or more symptoms, and 4) informed consent. The exclusion criteria were: 1) delirium; 2) life-threatening somatic co-morbidity; 3) active coercive admission regime (according to psychiatric legislation), and 4) insufficient command of the Dutch language.

2.2 Design

The study was an open RCT, with a parallel group design and was performed from 2001 until 2006. Patients who met the inclusion criteria were randomly and blindly assigned to either IRR or usual care (UC), with a randomization algorithm. In the first half of the study the assignment was in a ratio of 1 (IRR): 2 (UC). However, due to the limited number of eligible patients, time restrictions and financial limitations, in the second half of the study the ratio was reversed to 2 (IRR): 1 (UC). We finally included 168 patients (81 IRR and 87 UC). Patient's "Multiple Psychiatric Symptoms" was the primary outcome variable. In view of clinically relevant background information about the effects of IRR, 'burden' for the caregiver, 'cognitive functioning', 'quality of life' of the patient, and 'nursing home admission' were selected as secondary outcome variables. The assessments

were carried out simultaneously in both groups of the study at two measurement points: T1 (within two weeks after inclusion) and T3 (follow-up, six months after the end of the intervention). Furthermore, data were gathered by trained co-workers who were not members of the intervention team. The study protocol was approved by the Medical Ethics Committee of the Erasmus University Medical Centre.

2.3   Intervention

IRR (duration 13 weeks, clinical admission to a separate 15-bed specialized unit of a psychiatric skilled nursing home) comprised-supplementary to usual multidisciplinary nursing home care and psychotropic drugs treatment integrative psychotherapeutic interventions on MPS of the psychogeriatric patient as well as family therapy of the caregiver system. The psychotherapeutic interventions were based on a problem solving theoretical framework. [31] A more extensive description of IRR programme is published elsewhere. [31, 32]

Usual care (UC) consisted of a relatively high level of multidisciplinary nursing home care provided in the following settings: at home (25.3%), at home with mental healthcare (out-reaching) or psycho-geriatric day care/treatment (15.7%), in a home of assisted living (7.2%) and in a nursing home (51.8%).

The UC was provided by different types of core multidisciplinary teams, each with a different theoretical framework, mostly emotion-oriented.

2.4   Assessments

To be able to answer the objectives of this study we have used the following instruments out of a larger set of assessments.

Multiple Psychiatric Symptoms (MPS) of the patient were assessed by means of the Neuropsychiatric Inventory (NPI 12 item version; 'NPI-symptoms' 0 to 12; 'NPI-sum-severity': 0 to 144; 0 = no symptoms at all). [44, 45] The NPI was administered to the caregiver. General burden of the caregiver was assessed by the Caregiver Burden (CB: 0 to 100; 0 = optimal) [46], while the Caregiver Competence List (CCL: 28 to 112; 112 = optimal) assessed the competence of the caregiver. [47] For 'Cognitive functioning' of the patient, memory was measured by the Mini Mental State Examination (MMSE: 0 to 30; 30 = normal) [48] and self care by the Barthel Index (BI: 0 to 20; 20 = normal). [49] To assess the risk for being placed in a nursing home the Global Deterioration Scale (GDS: 1 to 7; 1 = normal) was used. [50] For registration of somatic co-morbidity the ICD-10 was used. Furthermore, the DSM IV disorders (axes I and II) were classified by a research psychiatrist. Finally, the following demographic data were collected from patient and caregiver: gender, age, marital status, family relationship, domicile and education level.

2.5   Statistical analyses

First of all, the means of continuous data and percentages of categorical data as measures of central tendency of the biographic characteristics as well as all baseline variables were estimated. Following Cummings, improvement was defined as a difference of a half sd or more of the baseline value, corresponding to > 30 % improvement. [33-36] For long term effects the selected five outcome variables were dichotomized into beneficial (coded 1) versus non-beneficial (coded 0). The non-beneficial effects comprised dropouts as well.

To identify the prognostic potentialities of the diagnostic variables (i.e., vascular dementia, Alzheimer dementia and personality disorder) and of the 'functional' variables, (i.e., MMSE, Barthel-index (BI) and number of NPI-symptoms), both assessed at baseline, in predicting improvement on the five dichotomized outcome variables individually, the method of logistic regression analysis was applied. The analysis strategy ran in three steps: 1. the diagnostic and the functional variables were individually entered into the logistic model; 2. the prognostic potentialities of the joint diagnostic as well as the joint functional variables were estimated; and, finally, 3. the prognostic potentialities of the diagnostic and the joint functional variables simultaneously were estimated. In case of the latter strategy the candidate-variables had to meet the following criteria: P-value for entering model <0.20 and P-value for removal >0.25. The very reason for this selection strategy was that we would prevent the risk of multicollinearity. In all analyses the intervention (UC coded 0, IRR coded 1) was entered into the model. Also gender, (centered) age and somatic co-morbidity were consistently entered into the model, although these estimates will not be presented. The analyses were executed for long term (six months follow-up; T1–T3).

Subsequently, by means of the prognostic formulae derived from the foregoing logistic analyses, for each patient the probability was estimated that (s)he would benefit from IRR and UC, respectively. So, for each patient five probabilities of having benefit from IRR and an equal number of probabilities of having benefit from UC were estimated.

As a measure of performance of the individual prognostic variable the odds ratio (OR) was used, including as a measure of precision the standard error of OR (95% confidence intervals). OR based on the logistic analysis indicates the change of odds of the probability that the patient is improved to the probability that the patient is not improved by one-unit change on the prognostic variable.

Variance explained. The performances of the biographic and baseline characteristics as predictor variables for the five outcome variables were derived from Nagelkerke R^2 [50] which quantifies the proportion of explained variation in the logistic regression model. Nagelkerke R^2 is a modification of the Cox and Snell R^2 in that the maximum value of 1.00 can be achieved. [51]

Double cross-validation. The very real question in prediction is not how well the logistic regression determined for the sample works but rather how well it works in the population. One of the strategies to be followed is that of double-cross-validation. This strategy runs as follows: in IRR and UC, randomly fifty percent

of the patients is assigned to subsample A and a similar percentage to B. Once the subsample A was the training sample and, as a consequence, the subsample B was validation sample, and once, reversed, subsample B was the training sample and, as a consequence, subsample A was the validation sample. The regression weights were estimated in the training samples and the prediction of validation subsample was based on the regression weights of the training sample. In IRR and UC the means of the posterior probabilities of the validation samples were averaged. These means were compared to that of the overall predictability: the closer the corresponding values the more stable the solutions, and, the less the shrinkage.

To optimize medical decision making in a complex context a decision model was developed for long term benefit. From literature we selected three decision methods of optimally assigning patients. [40 - 43] These decision methods are described briefly as follows: First, the highest MEAN AVERAGE calculated over the posterior probability of benefit. Secondly, the MINIMAX or 'Regret'-method, assigns the patient to the Intervention of which the loss of benefit on any outcome variable is lowest. The third decision rule was 'MAXIMIN'-criterion implying that the intervention with the best score on the worst possible outcome was assigned to the patient. The decision rules were applied to all patients in this study. The statistical analyses were performed with SPSS, version 15.

3.   Results

3.1   Characteristics of the study sample

The flow-chart (Figure 1) shows that, of the 336 eligible patients, 168 (50%) consented to participate. The non-participants did not differ significantly from the participants with regard to the inclusion criteria. The 168 patients were randomly assigned to either IRR (N=81) or UC (N=87). The differences between the two study groups in the number of drop-outs – the majority caused by death - were insignificant at all measurement points. Moreover, the drop-outs did not differ significantly with regard to any baseline assessment or length of time participating in the programme (Cox regression analysis: HR 1.21; P<0.54). With respect to biographical data, there were no significant differences between the two groups (Table 1). Mean somatic co-morbidity in the IRR group was significantly higher (IRR 5.6 [sd 2.6] ; UC 4.5 [sd 2.4] ; p<0.01). In our analyses we controlled for somatic co-morbidity. A mean GDS score 4.2 (sd 0.8) suggested that the study sample consisted of psycho-geriatric patients with mild cognitive impairment who were at risk for admission to a nursing home [50]. At T1 (Table 2) there were no significant mean differences between the IRR group and the UC group.

3.2 Predictability of improvement by the individual diagnosis and functional variables assessed at baseline

Only the main findings are presented. For detailed information one is referred to Table 3, in which for every analysis the baseline value of the OR together with the OR of the intervention are presented. All analyses were adjusted for gender, age and somatic co-morbidity.

Long term prediction of improvement on NPI-sum-severity of psychogeriatric patients.
First of all, intervention (IRR) appeared to be significant when it was entered into the logistic model with any individual diagnostic and functional variable, except for the baseline value of the corresponding outcome variable and number of NPI-symptoms at baseline. The significant ORs for Intervention varied from 2.11 to 2.42. When Alzheimer dementia together with Intervention was entered into the logistic model, also this diagnostic variable was positively associated with improvement on NPI-sum-severity. The same holds true for the baseline values of NPI-sum-severity (OR 1.06) and number of NPI-symptoms (OR 1.59).

Long term prediction of improvement on general burden of caregiver
The pattern of the predictability of improvement on general burden of caregiver was quite similar to the predictability of NPI-sum-severity, albeit with a minor difference with respect to BI. Intervention (IRR) appeared to be significant, with ORs varying from 2.20 to 2.42. Combined with the individual baseline variable, IRR had beneficial effect on improvement of general burden of caregiver.

Long term prediction of improvement on competence of caregiver
The quality of the predictability on competence of caregiver lies above those of NPI-sum- severity and general burden of the caregiver. It didn't matter which variable was entered into the logistic model with Intervention, IRR turned out to be beneficial. The ORs for Intervention ranged from 2.97 to 3.28. Moreover, the baseline values of CCL (OR 1.03) and the number of NPI-symptoms (OR 1.24) were significantly related to improvement when they were analysed together with Intervention.

Long term prediction of improvement on MMSE
In sharp contrast to the results of predictability of improvement on the three foregoing outcome variables, neither individual baseline variable together with Intervention was of statistical significance in predicting improvement on MMSE. Phrased otherwise, improvement on MMSE could be predicted by neither diagnosis nor functional variable, both assessed at baseline, along with Intervention. There was, however, a minor difference compared to foregoing improvement, in that the ORs for Intervention were a bit below 1.00, albeit statistically insignificant.

Long term prediction of improvement on Barthel-Index (BI)
In line with the findings regarding improvement on MMSE, none of the individual baseline variables together with Intervention was of significance in predicting improvement on BI. Furthermore, the analysis did not show any significant effect of Intervention; the ORs were a bit above 1.00, though insignificant

Long term effects summarized, when Intervention was analysed with the individual diagnosis and functional variables IRR appeared of significance with respect to improvement on NPI-sum-severity of the patient, on general burden of the caregiver as well as to improvement on competence of the caregiver.

Predictability of improvement by both joint diagnosis and joint functional variables
It has to be stated a priori that throughout the analyses gender, age and somatic co-morbidity were entered into the logistic regression model. On two outcome variables (NPI-sum-severity and general burden) only the corresponding baseline value was significant with low ORs. On competence the OR of the corresponding baseline value was significant and below one. In contrast intervention showed relatively high significant ORs (3.34 and 3.10). On MMSE and BI only baseline value of BI was significant on BI improvement with respect of joint functional variables.

Efficient selection of diagnostic and functional variables
From the baseline assessments of outcome variables and both the diagnostic and functional variables only the most powerful variables were selected for predicting improvement on the dichotomised outcome variables in long term. It has to be noted that gender, age, somatic co-morbidity and type of intervention were entered into the logistic regression models throughout the analyses. First of all, the qualities of the variables enabling predicting the NPI-sum-severity of psychogeriatric patients who suffer from cognitive impairment or dementia were substantial (R^2 0.39) . Also competence of the caregiver (R^2 0.23) could be substantially predicted. The qualities of the predictor variables for the other outcome variables were moderate (See Table 4).

Efficient predictability of NPI-sum-severity of psychogeriatric patients
Table 5 shows that Alzheimer dementia (OR 3.01) appeared to be the most important predictor variable, at great distance followed by the baseline assessment of NPI-sum-severity (OR 1.04). Although statistical insignificant, personality disorder was of prognostic value (OR 2.34). The same applies to Intervention i.c. participating in IRR (OR 2.15).

Efficient predictability of general burden of caregiver
Furthermore, Table 5 shows that Intervention i.c. participating in IRR was of significant prognostic value (OR 2.29) together with general burden of caregiver assessed at baseline (OR 1.02).

Efficient predictability of competence of caregiver.
In long term, IRR appeared to have significant large predictive qualities (OR 3.34). The baseline value of competence was also significant but with a level below 1 (OR 0.96).

Efficient predictability of MMSE.
No significant diagnostic or functional variables could be identified.

Efficient predictability of Barthel-Index (BI).
No significant diagnostic or functional variables could be identified, with the exception of baseline value of BI with OR 0.85.

Robustness of the predictions
To get insight into the stability of the findings in IRR and UC we have compared the mean of the posterior probabilities based on the logistic regression models of the two interventions. IRR and UC with those of the double cross-validation, in long term (see Table 6). Before cross-validation the mean predicted probabilities of improvement were highest on NPI-sum-severity of the patient according to the caregiver (IRR: 0.46; UC: 0.28). General burden of caregiver in IRR showed a mean value of 0.32 while that of UC with 0.16 was moderate. In IRR competence of caregiver had a value of 0.36; in UC 0.16. The performances on MMSE and BI have to be considered low. Although generally the mean posterior probabilities changed a bit after double-cross validation, yet the findings may be qualified as stable at a low level (For more detailed information see Table 6).

Towards decision making
First of all, for the five outcome variables the predicted proportion of improved patients in UC and IRR are presented in Table 6. IRR typically performed better on NPI-sum-severity of the patient, both general burden and competence of the caregiver. When in long term the 'highest average'-decision rule on the five outcome variables would be applied, then the patient should be assigned to IRR (0.23); in UC the proportion improved patients equalled 0.16. This means that the performance in IRR on improvement was 30.4% better than in UC. Also, when the 'MINIMAX'-decision rule was applied, due to the substantial regret of UC on improvement of NPI-sum-severity of the patient and general burden of the caregiver the patient should be assigned to IRR. The 'highest regret' was lowest for the patients in IRR, i.e. 0.02 on MMSE, while that was in UC 0.20 on competence. Similarly, applying the 'MAXIMIN'-decision rule the patient should be assigned to IRR, as MMSE equalled 0.09 and BI in UC 0.07.

4.   Discussion

Predictability of improvement

Irrespective the effectiveness of randomized controlled trials, prognostic modeling may be promising. [52 - 56] In this clinical-empirical exploration in long term (six months follow-up after the end of intervention) prognostic modeling of five clinically relevant outcome variables, i.e. improvement on severity of multiple psychiatric symptoms, general burden of the caregiver, competence of the caregiver, and cognitive functioning (memory and self-care) was feasible. The performance of the prognostic models was moderate. On average, the changes in severity of psychiatric function disorders of psychogeriatric patients and both general burden and competence of caregivers could be predicted nicely. Apart from corresponding baseline value and participation in IRR, dementia of the Alzheimer type showed significant positive prognostic qualities. On cognitive functioning (both memory and self-care) the prognostic models performed less well. Apart from BI at baseline, no significant variables could be identified. An important implication for the inclusion of psychogeriatric patients for IRR is that the scores on MMSE and BI, within the limits of the inclusion criteria in this RCT, are of relatively low clinical importance. This result confirms the findings of the effect modification study. [57] Patients with lower as well as higher scores on MMSE and BI may be included in future studies. Furthermore, improvement of interventions on cognitive dysfunctions is another important issue, e.g. by enriching the IRR programme with specific cognitive training programmes in combination with prescription of cognitive enhancers like rivastigmine, galantamine or memantine. Nevertheless, due to the fact that a discernible percentage of variance was unexplained, it is of clinical interest to identify additional determinants. Literature shows that in general, the kind and quality of the patient-caregiver relationship is likely of importance. [58, 59] If the caregiver is the spouse of the patient, then the quality of premorbid relationship would be of value. [60, 61] In addition, the personality structure might be of relevance. Of greatest importance is whether the caregiver can be characterised by stress tolerance, feelings of empathy and ability to give and ask social support. [62] Furthermore, the structure of motives, to be distinguished by rational versus irrational motives, might be decisive. [63] All these characteristics might be determinants of improvement on relevant outcome variables. More research on this is cogently needed.

What is more, is that the ingredients of intervention might be of prognostic value. Depending on the kind and severity of multiple psychiatric function disorders, personality disorders, type of cognitive disfunctioning, along with specific somatic co-morbidity, certain ingredients of the interventions rather than the whole intervention programme might be of prognostic value. Also, the identification of these ingredients as well as the evaluation of new supplementary interventions on cognitive functioning, preferably integrated with the psychosocial determinants, deserve a consecutive, large scale multi-centre study. [32, 64, 65] After all, in case of identification of the most effective therapeutic components in combination with the availability of a powerful prognostic, the effectiveness of IRR could be enhanced.

Optimal decision making
From micro viewpoint (i.e. patient level) as well as meso (hospital) and macro (society) viewpoints it is highly desired that medical decision making will be optimized. [40 - 43] To that end, we have contributed to optimizing decision making by utilising prognostic information. In this paper we have restricted decision making by using three decision rules, i.e. highest mean average-rule, 'MINIMAX'-rule (regret method) and the 'MAXIMIN'-rule. Applying these decision rules on the improvement on five outcome variables resulted into IRR as indicated. In literature many more decision rules are described, e.g. MAXIMAX (assign the patient to the intervention with the highest performance on any outcome variable), and Pessimism-Optimism criterion. [66] The latter criterion implies that the score of the highest and lowest outcome value will be averaged, and assign the patient to the intervention with the highest average; the weighing may deviate from fifty-fifty. Anyway, the application of these rules also indicated IRR as preferred intervention. To all probability, the optimal combination of clinically relevant rules is the royal road to optimal decision making in the near future. For purposes of implementation the strategy of optimal decision making is more than justified, stronger it underlines evidence based medicine. More research on decision making would be welcome.

Strengths of the clinical-empirical study
To our knowledge, this study is one of the first studies having addressed the development of multidimensional prognostic models for an integrative psychotherapeutic nursing home programme to reduce multiple psychiatric symptoms of psychogeriatric patients who suffer from cognitive impairment or dementia and burden of the caregiver in combination with clinically relevant decision rules. Particularly, on psychiatric symptoms of the patient as well as competence of the caregiver prognostic modeling showed a moderately performance, despite the fact that the sample size was pretty small. Another strength of this study was that it was well designed and conducted, according to the strict methodology of randomized controlled trials.

Limitations of the clinical-empirical study
First of all, there was no a priori hypothesis; the modelling was of a post-hoc nature. Furthermore, for prognostic purposes, the sample size of the study is one of the major drawbacks. Robust prognostic modeling requires undeniably larger sample sizes. [55, 64] Despite the fact that in this study the sample size was insufficient, the findings are promising, also after internal cross-validation. External cross-validation would be of importance depending on generalisation across time and/of settings.

As administering a comprehensive diagnostic set by qualified professionals in combination with a series of questionnaires is time-consuming and costly, it is highly recommended for clinical practice to develop a feasible set of instruments. Therefore, it is of interest to compress and to ease data sampling. [56, 65, 67, 68]

In conclusion, prognostic modeling, specifically of positive change on severity of multiple psychiatric function disorders of psychogeriatric patients who suffer from cognitive impairment or dementia and on both general burden and competence of caregivers was feasible. The inclusion of a broader range of psychogeriatric patients i.e. lower or higher scores on MMSE and BI, in combination with specific interventions to enhance cognitive functioning, seems justified. Applying three decision rules, all resulted in IRR as indicated intervention. Although the performances of the prognostic models found was considered moderate, this strategy is promising. Therefore, designing and conducting a study tailored to timely identifying psychogeriatric patients who likely benefit from an cognitively enriched IRR programme is recommended, preferably in a large scale multi-centred blinded study comprising a sufficient sample size.

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┌─────────────────────────────────────────────────────────────┐
│   Not randomized                   n = 168                   │
│   Refusal of referral/treatment    n = 152                   │
│   Refusal of participation          n = 9                    │
│   Reasons unknown                   n = 7                    │
└─────────────────────────────────────────────────────────────┘
                              │
                              ▼
                    ┌─────────────────────┐
                    │   Randomization     │
                    │   n = 168           │
                    └─────────────────────┘
```

IRR	UC
Intervention as allocated **(n=81)** Did not receive standard Intervention as allocated n = 1	Intervention as allocated **(n=87)** Did not receive experimental Intervention as allocated n = 1
Time 1: available: n = 78 death: n = 2 refusal: n = 1 loss: n = 0 total drop out: n = 3 4 %	**Time 1:** available: n = 83 [1] death: n = 4 refusal: n = 0 loss: n = 0 total drop out: n = 4 5 %
Time 2: available: n = 69 death: n = 10 refusal: n = 1 loss: n = 1 total drop out: n = 12 15 %	**Time 2:** available: n = 77 [2] death: n = 9 refusal: n = 0 loss: n = 1 total drop out: n = 10 12 %
Time 3: available: n = 54 death: n = 24 refusal: n = 2 loss: n = 1 total drop out: n = 27 33 %	**Time 3:** available: n = 64 [3] death: n = 23 refusal: n = 0 loss: n = 0 total drop out: n = 23 26 %

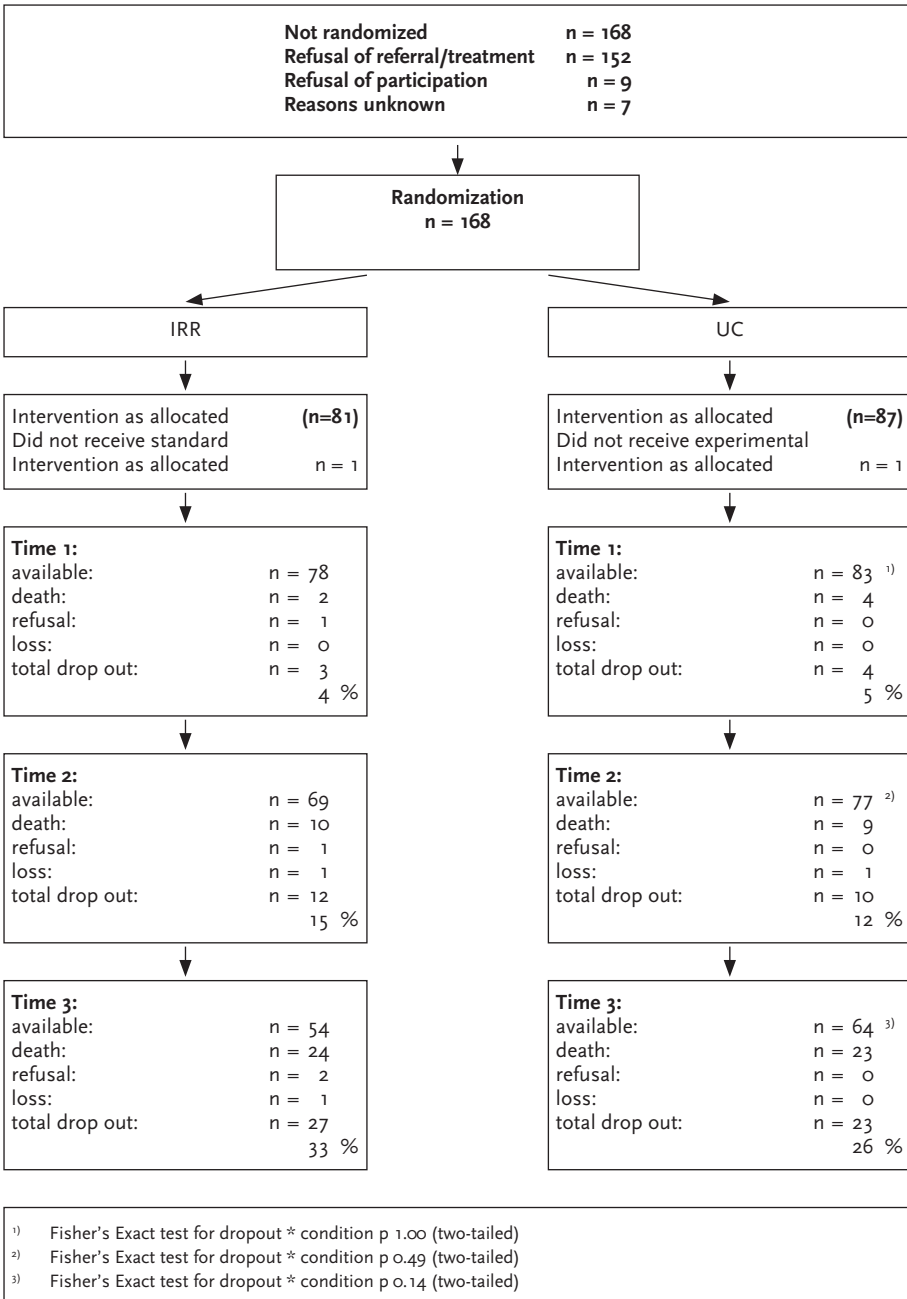|	
[1]	Fisher's Exact test for dropout * condition p 1.00 (two-tailed)
[2]	Fisher's Exact test for dropout * condition p 0.49 (two-tailed)
[3]	Fisher's Exact test for dropout * condition p 0.14 (two-tailed)

Figure 2. Flow chart discribing progress of patients through randomized controlled trial

Table 1. General details of participants, distinguished by intervention

	IRR	UC	
	n=81	n=87	p-value
Patient characteristics			
gender (females)	66.7%	62.1%	0.63[1]
age (in years), mean (sd)	79.8 (6.1)	81.5 (7.1)	0.10[2]
marital status: alone	77.8%	80.5%	0.71[1]
educational level: low	67.5%	68.7%	0.90[1]
domicile: at home	76.5%	66.7%	0.17[1]
primary caregiver: spouse	17.3%	13.8%	0.33[1]
DSM-IV dementia, (axis-I), count (%)			
dementia of the Alzheimer's type	18.5%	17.2%	0.84[1]
vascular dementia	23.5%	25.3%	0.86
dementia due to other conditions	16.0%	19.5%	0.69
amnestic/cognitive disorders	32.1%	31.0%	1.00
other	6.2%	2.3%	0.26
DSM-IV personality disorders (axis-II), count (%)	16.0%	9.2%	0.24
GDS-deterioration, mean (sd)	4.2 (0.7)	4.3 (0.9)	0,62[2]
somatic co-morbidity (ICD-10), mean (sd)	5.6 (2.6)	4.5 (2.4)	0.01[2]
Caregiver characteristics			
gender (females)	70.5%	61.7%	0.32[1]
age (in years), mean (sd)	58.6 (11.9)	58.9 (12.0)	0.86[2]
marital status: living together	91.4%	94.8%	0.52[1]
educational level: low	4.3%	2.6%	0.39[1]

[1] Fisher's Exact Test (twotailed)
[2] t-Test (twotailed)

Table 2. Level of outcome across time (T1 - T3) distinguished by intervention

	range	high score = (+/-) *)	T1 (baseline measurement)										T3 (six months follow-up)			
			IRR			UC			Mean diff.	UC-IRR 95% CI		IRR		UC	
			n	mean	sd	n	mean	sd				n	mean	n	mean
Psychiatric function disorders patient (by caregiver)															
NPI-symptoms	0 to 12	(-)	72	5.92	2.35	76	5.23	2.16	-0.68	-1.41	0.05	49	3.49	51	3.84
NPI-sum-severity	0 to 144	(-)	72	35.90	21.84	76	29.68	20.12	-6.22	-13.05	0.62	49	15.84	51	18.61
Caregiver burden															
Caregiver burden (CB)	0 to 100	(-)	72	52.47	25.65	77	46.69	27.66	-5.79	-14.42	2.85	42	28.81	50	44.90
Competence (CCL)	28 to 112	(+)	72	84.62	14.24	77	86.58	14.46	1.96	-2.69	6.6	49	96.35	50	91.78
Cognitive functioning patient															
MMSE	0 to 30	(+)	76	20.04	4.50	82	20.58	3.84	0.54	-0.77	1.85	51	19.46	60	19.50
Barthel Index (BI)	0 to 20	(+)	77	15.39	3.77	80	14.71	3.55	-0.68	-1.83	0.48	54	12.38	63	13.24

*) + = high score is beneficial, - = high score is unfavourable

Table 3. Predictability of dichotomised improvement on five outcome variables by individual diagnosis variables and functional baseline variables, along with Intervention, in long term [*)]

	T3 (six months follow-up)					
	corresponding variable			intervention		
predictor variables	OR	95% CI		OR	95% CI	
NPI sum-severity of patient						
baseline outcome	**1.06**	1.03	1.08	2.08	0.94	4.62
vascular dementia	0.89	0.38	1.79	**2.18**	1.11	4.26
dementia of the Alzheimer's type	**3.43**	1.45	8.10	**2.14**	1.08	4.26
DSM-IV personality disorders	2.51	0.96	6.53	**2.11**	1.07	4.15
MMSE at baseline	1.00	0.92	1.08	**2.42**	1.21	4.84
BI at baseline	1.01	0.92	1.11	**2.20**	1.10	4.41
NPI at baseline	**1.59**	1.31	1.92	2.07	0.95	4.49
general burden of caregiver						
baseline outcome	**1.02**	1.00	1.04	2.10	0.95	4.66
vascular dementia	0.87	0.36	2.09	**2.25**	1.05	4.83
dementia of the Alzheimer's type	2.00	0.80	4.98	**2.20**	1.02	4.75
DSM-IV personality disorders	0.40	0.11	1.48	**2.38**	1.10	5.13
MMSE at baseline	1.01	0.92	1.11	**2.42**	1.11	5.27
BI at baseline	1.04	0.94	1.15	2.17	0.99	4.75
NPI at baseline	1.11	0.94	1.32	2.14	0.97	4.71
competence of caregiver						
baseline outcome	**1.03**	1.01	1.05	**3.03**	1.34	6.84
vascular dementia	1.81	0.80	4.11	**3.20**	1.48	6.91
dementia of the Alzheimer's type	2.02	0.82	4.96	**3.03**	1.41	6.55
DSM-IV personality disorders	0.56	0.17	1.81	**3.19**	1.48	6.89
MMSE at baseline	0.95	0.87	1.04	**3.28**	1.50	7.19
BI at baseline	1.03	0.93	1.14	**3.11**	1.41	6.83
NPI at baseline	**1.24**	1.04	1.48	**2.97**	1.33	6.63
mmse of patient						
baseline outcome	0.98	0.95	1.01	0.62	0.20	1.90
vascular dementia	0.66	0.18	2.51	0.62	0.21	1.82
dementia of the Alzheimer's type	2.84	0.90	8.97	0.59	0.20	1.77
DSM-IV personality disorders	1.76	0.43	7.16	0.59	0.20	1.77
MMSE at baseline	0.93	0.82	1.05	0.58	0.19	1.78
BI at baseline	1.04	0.90	1.20	0.59	0.20	1.77
NPI at baseline	0.88	0.70	1.12	0.60	0.20	1.83

predictor variables	T3 (six months follow-up)					
	corresponding variable			intervention		
	OR	95% CI		OR	95% CI	
	barthel-index of patient					
baseline outcome	0.98	0.95	1.02	1.01	0.29	3.55
vascular dementia	1.72	0.52	5.73	1.35	0.43	4.29
dementia of the Alzheimer's type	mc[1]	mc	mc	1.33	0.42	4.19
DSM-IV personality disorders	1.07	0.21	5.29	1.32	0.42	4.19
MMSE at baseline	1.08	0.94	1.25	1.45	0.45	4.62
BI at baseline	0.89	0.78	1.02	1.54	0.47	5.03
NPI at baseline	0.91	0.70	1.20	0.98	0.28	3.45

[*] all analyses were adjusted for gender, centered age and somatic co-morbidity
[1] due to multicollinearity the pertinent variable eliminated

Table 4. Predictability of dichotomised improvement on five outcome variables by joint diagnosis varia-
bles and joint functional variables respectively, along with intervention, in long term *)

	T3 (six months follow-up)			Nagelkerke
	OR	95% CI		R squared
NPI-sum severity				
intervention	2.04	0.91	4.58	0.36
NPI-sum-severity at baseline	**1.06**	1.03	1.08	
vascular dementia	0.71	0.26	1.98	
dementia of the Alzheimer's type	2.25	0.79	6.36	
personality disorders	2.02	0.61	6.67	
intercept	0.04			
intervention	2.20	0.95	5.06	0.35
NPI-sum-severity at baseline	**1.04**	1.01	1.08	
MMSE at baseline	1.04	0.94	1.16	
BI at baseline	1.00	0.90	1.12	
NPI at baseline	1.17	0.86	1.58	
intercept	0.01			
General burden				
intervention	2.22	0.98	5.01	0.16
general burden at baseline	**1.02**	1.01	1.04	
vascular dementia	0.65	0.24	1.76	
dementia of the Alzheimer's type	1.52	0.56	4.12	
personality disorders	0.29	0.07	1.23	
intercept	0.06			
intervention	2.16	0.94	4.96	0.13
general burden at baseline	**1.02**	1.00	1.04	
MMSE at baseline	1.03	0.93	1.14	
BI at baseline	1.03	0.92	1.15	
NPI at baseline	1.05	0.88	1.26	
intercept	0.02			
Competence caregiver				
intervention	**3.34**	1.46	7.65	0.20
Competence at baseline	**0.96**	0.93	0.99	
vascular dementia	2.02	0.79	5.20	
dementia of the Alzheimer's type	2.03	0.74	5.55	
personality disorders	0.62	0.17	2.28	
intercept	4.02			

	T3 (six months follow-up)			Nagelkerke
	OR	95% CI		R squared
intervention	**3.10**	1.31	7.30	0.21
Competence at baseline	**0.96**	0.85	0.99	
MMSE at baseline	0.94	0.85	1.05	
BI at baseline	1.05	0.94	1.18	
NPI at baseline	1.15	0.96	1.39	
intercept	2.47			
MMSE				
intervention	0.52	0.17	1.66	0.12
MMSE at baseline	0.94	0.82	1.07	
vascular dementia	0.94	0.21	4.00	
dementia of the Alzheimer's type	2.30	0.65	8.06	
personality disorders	1.43	0.33	6.27	
intercept	0.15			
intervention	0.52	0.16	1.66	0.13
MMSE at baseline	0.89	0.77	1.03	
BI at baseline	1.06	0.91	1.24	
NPI at baseline	0.86	0.67	1.09	
intercept	0.63			
Barthel Index (BI)				
intervention	1.52	0.46	4.97	0.07
BI at baseline	0.89	0.77	1.02	
vascular dementia	1.86	0.51	6.81	
dementia of the Alzheimer's type	mc[1]	mc[1]	mc[1]	
personality disorders	1.47	0.27	8.02	
intercept	0.50			
intervention	1.20	0.33	4.44	0.08
MMSE at baseline	1.09	0.93	1.27	
BI at baseline	**0.86**	0.74	1.00	
NPI at baseline	0.93	0.70	1.23	
intercept	0.04			

[*] age patient-65 years
[1] due to multicollinearity the pertinent variable eliminated

Table 5. Predictability of dichotomised improvement on five outcome variables by diagnosis variables and functional variables all together, along with intervention, in long term[*)]

	T3 (six months follow-up)		
	OR	95% CI	
NPI-sum-severity			
intervention	2.15	0.93	4.97
NPI-sum-severity at baseline	**1.04**	1.03	1.08
vascular dementia			
dementia of the Alzheimer's type	**3.01**	1.04	8.74
personality disorders	2.34	0.69	7.91
MMSE at baseline	1.08	0.97	1.19
BI at baseline			
NPI at baseline	1.24	0.90	1.69
intercept	0.00		
R2=0.39			
General burden			
intervention	**2.29**	1.01	5.19
general burden at baseline	**1.02**	1.00	1.04
vascular dementia			
dementia of the Alzheimer's type	0.34	0.09	1.34
personality disorders			
MMSE at baseline			
BI at baseline			
NPI at baseline			
intercept	0.07		
R2=0.15			
Competence caregiver			
intervention	**3.34**	1.43	7.93
Competence at baseline	**0.96**	0.93	0.99
vascular dementia	2.19	0.84	5.70
dementia of the Alzheimer's type	1.84	0.67	5.08
personality disorders			
MMSE at baseline			
BI at baseline			
NPI at baseline	1.15	0.95	1.39
intercept	1.20		
R2=0.23			

	T3 (six months follow-up)		
	OR	**95% CI**	
		MMSE	
intervention	0.56	0.15	1.62
vascular dementia			
dementia of the Alzheimer's type	2.34	0.71	7.80
personality disorders			
MMSE at baseline	0.92	0.80	1.06
BI at baseline			
NPI at baseline	0.84	0.66	1.08
intercept	0.85		
	R2=0.15		
		Barthel Index (BI)	
intervention	1.19	0.32	4.50
NPI-sum-severity at baseline			
vascular dementia	2.79	0.73	10.68
dementia of the Alzheimer's type			
personality disorders			
MMSE at baseline	1.11	0.95	1.31
BI at baseline	**0.85**	0.73	1.00
NPI at baseline			
intercept	0.04		
	R2=0.11		

[*]   age patient-65 years

Economic evaluation of an integrative psychotherapeutic nursing home programme to reduce multiple psychiatric symptoms of psychogeriatric patients and caregiver burden;

A randomized controlled trial[1]

1.   Introduction

In psychogeriatric patients who suffer from cognitive impairment or dementia, there is an 80% prevalence of two or more psychiatric symptoms, e.g. depression, anxiety, paranoia, aggression. [1-5] Multiple psychiatric symptoms (MPS) have many related negative secondary effects. For the patients there are negative effects on cognitive functioning, quality of life and they predict admission to a nursing home. Furthermore, MPS are a burden for the caregiver. [3, 6-12] Moreover, these MPS are number one among the top three problems experienced by dementia patients and their caregivers. [13] In usual nursing home care, psychotropic drugs are widely used to treat the MPS of psychogeriatric patients despite of their limited effects and potentially harmful side-effects e.g. (a)typical antipsychotics. [2,5,14,15] There is a lack of integrative psychotherapeutic programmes, even though reports in the literature indicate that for individual psychiatric symptoms, e.g. depression and anxiety, as well as caregiver burden, psychotherapeutic treatment may be effective in both nursing home and primary care settings. [16-19, 20-24] However, psychotherapeutic interventions focussing on the MPS of psychogeriatric patients who suffer from cognitive impairment or dementia are complex, due to their multiplicity in combination with cognitive disorders, somatic co-morbidity, and social problems (e.g. relationships, loneliness) [25, 26]. Furthermore, integrative psychotherapeutic programmes in nursing homes have never been evaluated in large-scale comprehensive studies. [10, 16, 27-30] For these reasons, we developed a unique integrative psychotherapeutic nursing home programme: integrative reactivation and rehabilitation (IRR). [31] The performed RCT was designed to test the effectiveness of IRR to reduce MPS in psychogeriatric patients who suffer from cognitive impairment or dementia, and burden of the caregiver. The primary analyses regarded the mean differences between IRR and the control group (usual care) on continuous data of the primary and secondary outcome variables. The results of this analysis are published elsewhere. [32]

From the perspective of the caregivers, the IRR had a significant and moderate to large surplus effect (up to 34%) in reducing the MPS of psychogeriatric patients who suffer from cognitive impairment of dementia in both short term and the long term. In fact, at the six-month follow-up there was a total reduction in MPS up to 46% in number and 61% in severity. Furthermore, with regard to secondary outcome variables, on caregiver burden and competence the IRR had a large positive surplus effect (up to 36%) at the end of the treatment. During the follow-up the surplus effect even increased to a reduction of 50%, while usual care had hardly any effect at all. Irrespective of beneficial clinical effects it is important to take into account the economic aspects, i.e. an economic evaluation. [33-36] In this paper we report the results of an economic evaluation of a RCT in which IRR was compared to usual multidisciplinary nursing home care. The two objectives of this economic evaluation were to assess the cost-utility of IRR as well as the cost-effectiveness on six outcome variables of IRR compared to usual care (UC).

2.   Materials and methods

2.1   Patients

The psychogeriatric patients were recruited from the urban region of Nieuwe Waterweg Noord (NWN), near Rotterdam in the Netherlands (approximately 180.000 inhabitants). The patients were referred from an (ambulant) mental health service (5.4%), a general hospital (13.8%), a memory clinic (6%) and general practitioners or primary healthcare services (75.1%). Before inclusion, all referred patients underwent a comprehensive geriatric assessment. The initial inclusion criteria were a DSM IV classification of dementia, amnestic disorders or other cognitive disorders. Additional inclusion criteria were: 1) age: $\geq$65 years; 2) cognitive functioning: MMSE $\geq$18 and $\leq$27 as well as Barthel Index (BI) $\geq$5 and $\leq$19; 3) psychiatric symptoms: Neuropsychiatric Inventory (NPI) 3 or more symptoms, and 4) informed consent. The exclusion criteria were: 1) delirium; 2) life-threatening somatic co-morbidity; 3) active coercive admission regime (according to psychiatric legislation), and 4) insufficient command of the Dutch language.

2.2   Design

The economic evaluation was embedded in an open RCT, with a parallel group design and which was performed from 2001 until 2006. The patients who met the selection criteria, were asked to participate in the RCT. If the participant or his caregiver signed a written informed consent, he was randomly assigned to either IRR (experimental intervention) or usual care (UC). By the inclusion committee randomization was carried out block wise (i.e. three subjects per block.) In the first half of the study the patients were assigned in a ratio 1 (IRR): 2 (UC). Due to limited numbers of eligible patients and time restrictions of the study, in the second half the assignment ratio was reversed to 2 (IRR): 1 (UC). In total, the study included 168 patients, 81 assigned to IRR and 87 to UC (1). In the original study, 'multiple psychiatric symptoms of the patient' was the primary outcome variable for effectiveness. In view of clinically relevant background information of the effect of IRR, 'Burden' of the caregiver, 'Cognitive functioning' and 'Quality of life' of the patient were selected as secondary outcome variables. For economic evaluation the data of direct medical costs of the patient were collected. The outcome variables were simultaneously assessed in both arms at two moments: T1 (within two weeks after intake) and T3 (follow-up; six months after the end of intervention), but measurements of the costs were conducted every 8 weeks from the moment of inclusion (TO) over the preceding last four weeks. Blinding of the two trained co-workers collecting the outcome variables was not feasible as they had to visit the patients as well as their caregivers and knew their intervention history. This study was approved by the Medical Ethical Committee of the Erasmus University Medical Centre.

2.3   Intervention

The IRR programme had a duration of 13 weeks with clinical admission to a separate 15-bed specialized unit of a psychiatric skilled nursing home. In addition to usual multidisciplinary nursing home care, including psychotropic drugs treatment, the IRR consisted of integrative psychotherapeutic interventions for MPS of the psychogeriatric patient and family therapy for the caregiver. The psychotherapeutic interventions were based on a problem solving theoretical framework. [21] A more extensive description of IRR programme has been published elsewhere. [31, 32]

Usual care (UC) consisted of a relatively high level of multidisciplinary nursing home care provided in the following settings: at home (25.3%), at home with mental healthcare (out-reaching) or psycho-geriatric day care/treatment (15.7%), in a home of assisted living (7.2%) and in a nursing home (51.8%).

The UC was provided by different types of core multidisciplinary teams, each with a different theoretical framework, mostly emotion-oriented.

2.4   Assessments

To answer the two objectives of the economic evaluation we have used two sets of instruments. One for the patient and caregiver and one for the economic aspects. For the patient and caregiver we used the following instruments out of a larger set of assessments. MPS of the patient (the primary outcome variable) was assessed by means of the Neuropsychiatric Inventory (NPI 12 item version: *'NPI-sum-severity'*: 0 to 144; 0 = no severity symptoms at all). [37, 38] NPI was administrated to the caregiver. Of the secondary outcome variables, General burden of the caregiver was assessed with Caregiver Burden (CB: 0 to 100; 0 = optimal) [39], and Caregiver Competence List (CCL: 28 to 112; 112 = optimal) assessed the competence of the caregiver. [40] For Cognitive functioning of the patient, memory was measured by the Mini Mental State Examination (MMSE: 0 to 30; 30 = normal) [41] and self care by Barthel Index (BI: 0 to 20; 20 = normal). [42] To assess the risk for being placed in a nursing home the Global Deterioration Scale (GDS: 1-7; 1 is normal) was used. [43] For somatic comorbidity ICD-10 was used. Furthermore, the DSM IV disorders (axes I and II) were classified by a research psychiatrist. Finally, the following demographic data were collected from patient and caregiver: gender, age, marital status, family relation, domicile, education level, income level and job employment.

For the economic evaluation (CUA) we used the following instruments. Quality of life was assessed with EQ5D (−0.59 to 1.0; 1.0 = optimal) completed by the patient [44]. The EQ5D is a validated tool for measuring general health–related quality of life. EQ5D consists of five items (mobility, self-care, usual activities, pain/discomfort and anxiety/depression), each having the rating of 'no problems', 'some problems' and 'extreme problems'. The health descriptions can be linked directly to empirical valuations of the general public, which allows utilities to be computed. [45] We used TiC-P to collect data on direct medical costs from the patients. [46] The TiC-P measures medical resource utilisation by asking the number of contacts over the

preceding last four weeks with different (medical and psychological) health care providers e.g. general practitioner, psychiatrist, medical specialist, physiotherapist, day care/hospital and nursing home length of stay. The number of days admitted to the nursing home was collected directly from the participating centres. Unit prices for all nursing home days were estimated based on information of the financial department of Argos Zorggroep. Data on the direct (e.g. medical staff, nursing staff) and indirect costs (e.g. overhead, housing) of 2004 was used to calculate the unit costs per day for IRR and UC. Other health care utilisation was valued by the reference unit prices. [47] Unit prices of health care services for 2004 were adjusted to prices of 2005 by using the consumer price index (www.cbs.nl). Subsequently, the number of medical contacts was multiplied by the corresponding unit costs to estimate the costs. All costs were estimated for the year 2005 and are presented in Euros. The patient mean utility scores were estimated by applying the area-under-the curve method (AUC), which is implemented by summing the areas of the geometrical shapes obtained by linearly interpolating between utility scores over the study period. [48] The costs and utility scores of patients who died were valued zero if one died in the first 4 weeks of a measurement period and in the consecutive measurement periods. If a patient died in the last 4 weeks of a measurement period we valued the costs and utility scores as missing or the available costs of the measurement period in which the person died, and zero in the consecutive periods.

2.5   Statistical analyses

The economic evaluation was based on all relevant costs due to medical resource utilisation by the patients (direct medical costs). The direct medical costs of caregivers were not available. In order to account statistically for missingness, we used in the cost-utility analysis the technique of multiple imputation. This is a technique in which each missing value is replaced by $m>1$ simulated values. [49 – 51] After the multiple imputations are generated, the m versions of the complete data were individually analysed by standard statistical methods for complete data. Subsequently, the results of the m analyses were combined including the uncertainty as a result of missing data. [52 – 54] For the proportions of missing information in the current study, m=10 was found to be sufficiently large to stabilise the outcomes in terms of the standard errors for all analyses. [54] The overall mean costs are calculated as the mean of the mean costs in each dataset. The overall associated variance is found by combining the variance within the datasets with the variance between the datasets. [54] We used the Monte Carlo Markov Chain (MCMC) approach to impute the missing values. This MCMC approach assumes the underlying distribution to be multivariate normal, although it was shown in a large simulation study that even with skewed data this approach often performs well. [55] Multiple imputation gives valid results if data are missing completely at random (MCAR), and if data are at random (MAR). MAR assumes that missingness de-

pends only on observed variables. The cost-utility was evaluated by relating the difference in direct medical costs per patient receiving either IRR or UC to the difference in terms of Quality Adjusted Life Years gained (QALY), which yielded a cost per QALY estimate. The endpoint of the cost utility analysis was 40 weeks. In addition, to estimate cost-effectiveness of IRR we tested the mean differences between the two interventions (i.c. IRR and UC) on the primary outcome variable (NPI), on four selected secondary clinical outcome variables and on the EQ5D. We used a complete cases (CC) approach, excluding patients who had missing data before the endpoint. Specifically, in case of a relatively high number of drop outs in both arms of the study and no significant differences between drop outs on relevant baseline and outcome measures or on time participating in the programme, results of a CC analysis may present a more accurate estimation of the clinical effect of IRR. The very reason is that only patients and caregivers who fully participated in IRR programme, could completely benefit of the offered interventions. The cost-effectiveness analysis spanned an interval from the start of intervention (T1) until the endpoint at 40 weeks. We compared differences in total medical costs combined with mean differences in effects in terms of Incremental Cost-Effectiveness Ratio (ICER). [56] For estimation of the participation interval of dropouts (time in days participating in the study) a Cox-regression analysis was performed. The 95% confidence intervals (CI) were presented when relevant. All significance testing was fixed at P<0.05 (two-tailed). The data were analysed according to the intention to treat (ITT)-principle. The statistical analyses were performed with the software programmes SPSS, version 15, and SAS, version 8.2

3. Results

3.1 Characteristics of the study sample

The flow-chart (Figure 1) shows that of the 336 eligible 168 (50%) consented to participate in the RCT. The non-participants did not differ significantly from the participants on the inclusion criteria. The 168 patients were randomly assigned to either IRR (N = 81) or UC (N = 87). The differences between the two study groups in number of dropouts – the majority caused by death - were insignificant at all measurement points. Moreover, the dropouts did not differ significantly with regard to any baseline assessment or on length of time participating in the programme (Cox regression analysis: HR 1.21; P<0.54). With respect to biographical data there were no significant differences between the two groups (Table 1). Mean somatic co-morbidity in the IRR group was significantly higher (IRR 5.6; UC 4.5;P<0.01). A mean GDS-score 4.2 (sd 0.8) suggested that the study sample consisted of psychogeriatric patients with mild cognitive impairment or dementia who were at risk for permanent admission to a nursing home. [57]

At T1 (Table 2) there were no significant mean differences between the IRR group and the UC group. Specifically, the mean sum-severity of NPI-symptoms of the patient (IRR 35.90 and UC 29.68) did not differ significantly.

3.2   Cost utility analysis

The results of the cost and QALY analyses are presented as mean values (including 95% CI). At baseline (week 8), data of TiC-P and EQ5D were available for 96% (n=161) of the subjects. At 40 weeks follow-up, these data were available for 38% (n=63) of the participants. Table 3 presents the results of mean costs per patient and mean QALY analysis after applying multiple imputation (MI). At 40 weeks the direct medical costs in IRR were significantly higher (€ 4.572,--) than those in UC (95 % CI: 364.24 to 8797.76). This implies € 53,-- extra per IRR-treatment day (in total: on average 90 days treatment duration). At the same time the number of QALYs of the patients was non-significantly 0.02 lower in IRR (95% CI:-0.10 to 0.05).

3.3   Cost effectiveness analysis

In Table 4, the costs for the individual cost-factors, based on the CC approach, are presented. This table shows that the highest costs had to be ascribed to nursing home costs. The mean nursing home costs per patient (including the costs of IRR) after 40 weeks were non-significantly higher in IRR than in UC. However, the costs of home care and day care were significantly lower in IRR at 40 weeks. In Table 5 the cost-effectiveness after 40 weeks i.e. estimated ICER is presented. IRR was significantly more effective on the primary outcome variable NPI-sum-severity of the patient. and the secondary outcome variables caregiver burden and caregiver competence; on EQ5D of the patient the difference was non-significant. Regarding medical costs, for NPI-sum-severity of the patient, the net-result equalled to about € 320.--, implying that for one more point improvement on this outcome variable in IRR the costs were € 320.-- (mean difference 10 points). The least expensive was improvement on general burden of the caregiver, with almost € 130.-- for one point more improvement in IRR compared to UC (mean difference 25 points). Clearly more expensive was improving on competence of the caregiver in IRR compared to UC. The net-costs were € 540.-- (mean difference 6 points). The net-costs of improvement on EQ5D of the patient were high, namely about € 80,000.-- for one point improvement (mean difference 0.04 points). As IRR performed (non-significantly) less well on the other secondary outcome variables (MMSE and BI) than UC, it did not make sense to estimate their net-costs.

4.   Discussion

The objective of this study was an economic evaluation of IRR on cost-utility as well as on cost-effectiveness. Therefore, the cost-utility (QALYs) and cost-effectiveness (ICERs) of IRR were estimated by comparing this intervention to usual care at six month follow-up after the end of intervention i.e. 40 weeks. The cost-utility analysis suggests the amount of QALYs for psychogeriatric patients did not differ significantly between IRR and Usual Care while the costs were significantly lower in UC. It has to be noted that the changes on the underlying EQ5D-scores (number and mean) were very small in both study groups. Looking at total medical costs, IRR was more expensive, if these estimations were statistically adjusted for dropout; about € 53.-- per day, for 90 days € 4.572.--. In contrast, the effectiveness analysis (ICERs) showed that significant improvement of patients and caregivers participating in IRR on general burden was least expensive; about € 130.-- per point. Improvement on severity of multiple psychiatric symptoms took a middle position with about € 320.-- per point. One point improvement on competence costed € 540.--. Improvement on EQ5D was non-significant higher in IRR, but was most expensive; about € 80,000.-- per point. The findings of the ICER are clinically relevant results because MPS of patients and caregiver burden are the two as most problematic experienced phenomena in dementia care. [13, 58] However, cost-effectiveness results can not be easily compared to cost-effectiveness results of other health care interventions, because there are no reference values of costs per effect unit for the different clinical outcome measures. Hence, this type of information (ICERs) is of less value in health care policy decision making than QALYs. When we compared in a post-hoc analysis the costs of patients who improved on the primary outcome variable NPI-sum severity we found that in both groups the improved patients were significantly more cost-expensive than the non-improved. Improving seemed inextricably related to more medical costs. In IRR, significantly more patients improved and as a consequence they were responsible for most of the higher total medical costs in IRR (not presented). An explanation may be that improved patients lived longer. In a foregoing study we found that patients discharged after IRR at home or to a residential home with restricted support had a 3.2 time higher probability of survival than the patients who were discharged to a nursing home. [59]

Remarkable and problematic is the difference in results between QALYs and ICERs found in this study. The ICERs of clinically relevant outcomes i.e. severity of psychiatric symptoms of psychogeriatric patients, caregiver burden and competence were clearly in favour of IRR, with relatively large numbers of improved patients ($\geq$ 0.5 sd). [33–36] At the same time, the numbers needed to treat (NNT) for NPI of IRR were relatively low i.e. four. For comparison the NNT of donezepil = 10, memantine NNT = 3 - 8, and cognitive behaviour therapy NNT = 5 - 10. [60, 61] In contrast, the QALYs of patients were almost equal between IRR and usual care. In the cost-effectiveness analysis, the mean difference on EQ5D between the interventions was just small (0.04), with relatively small numbers of clinically relevant ($\geq$ 0.5 sd) improved patients (not presented). [33–36, 62, 63] This means that for psychiatric patients suffering from multiple psychogeriatric symptoms the EQ5D turned

out to be relatively irresponsive to change. This corresponds with the findings of Ballard and Katona, [64 – 66], who showed that clinically relevant improvement on BPSD had just small effects on regular quality of life measurements. [64 – 66] Completing of EQ5D by proxy i.e. the caregiver may enhance the performance. All in all this means a drawback in comparing the effects of different interventions in a cost-utility study in psychogeriatrics. [67] Further research is urgently needed on the discrepancy between the results on clinically relevant instruments and EQ5D. [66, 68 – 73] The same holds true for the higher costs of improved patients irrespective of type of intervention.

The strength of this study on economic evaluation of the RCT was that it was based on a relatively large sample size of patients. [20] Furthermore, the benefit of full participation could be estimated as the relatively high percentage of dropouts did not differ significantly on the observed variables. The majority of dropouts could be ascribed to death of geriatric patients, being not significantly different in IRR and UC. The phenomenon of high dropout percentages is well known in geriatric research. [2, 5, 14 - 19] Basically, it reflects the vulnerability of the psychogeriatric patients suffering from MPS. In addition, the relatively irresponsiveness of the patient's EQ5D compared to the significant beneficial change on the severity of MPS corresponds with results reported in literature. [64, 65, 67, 69, 72, 73]

Furthermore, this RCT was, according to our knowledge, one of the first comprehensive studies in a nursing home setting, with a relative large sample size that addressed integrative psychotherapeutic treatment of psychogeriatric patients and their caregivers.

What were the limitations of this study? First of all, RCT was not blinded. In a clinical study like this, blinding is not feasible. As the research co-workers had to visit the patients and caregivers personally, they knew the intervention history of the patients. Although we trained the research co-workers in proper administering the assessment instruments, it is not precluded that information bias emerged. Whether bias emerged in favour of IRR, is difficult to demonstrate. As the assessments at baseline showed just minor differences between IRR and usual care, excepted for somatic co-morbidity, the information bias at baseline seems to be limited. However, future studies have to be performed to strengthen the evidence, preferably as blinded RCTs. Another weakness was that only direct medical costs of patients were available; so other costs, specifically informal care at home were excluded. This may lead to an underestimation of costs at home, especially in usual care. In addition, in nursing home costs also food, social activities and the like are incorporated, resulting in an overestimation of nursing home costs, especially in IRR. Another relatively large limitation was the missing of cost-data of the caregiver. The more so, taking into account the significant beneficial effects of IRR on burden and competence of the caregiver which may have lowered their medical consumption. This means that the result of the economic evaluation was probably an underestimation of IRR. Furthermore, the study ended at 40 weeks. On the longrun, the trend in cost-effectiveness of IRR versus UC looked more favourable in IRR, specifically for caregivers.

Regarding generalization of the findings of this RCT, it is important to keep in mind that 50% of the eligible patients refused to participate. Relatively many of these patients lived with a spouse. The core motive for refraining participation was fear to be admitted in case of assignment to IRR. However, a post-hoc prognostic analysis showed that living together did not have prognostic quality, with respect to improvement on the primary outcome variable. In IRR the beneficial long term effects on multiple psychiatric symptoms of the patient and on the burden as well as the competence of caregiver are in line with those in literature of psychotherapeutic interventions on individual MPS. [17-19, 72-80] It is expected that by identifying the less effective therapeutic components and, consequently, by making them more effective or leaving them out, the beneficial effects of IRR will enlarge. To identify and, by consequence, to select the psychogeriatric patients and their caregivers with a relatively high likelihood to improve is another opportunity to enlarge the beneficial effects of IRR. To optimize medical decision making, the construction of a prognostic instrument identifying the vulnerable psychogeriatric patient along with his caregiver is clinically relevant.

5.   Conclusion

On QALYs, no significant differences were found, while total medical costs of psychogeriatric patients in IRR were significantly higher. In contrast, fully participating patients and their caregivers improved in IRR significantly more on mean scores of the primary outcome variable severity of multiple psychiatric symptoms of the patient and of the secondary outcome variables general caregiver burden and competence of the caregiver, with ICERs varying from € 130.-- to € 540.--. The large discrepancy between QALYs and ICERs due to the relative irrisponsiveness of EQ5D to clinically relevant change, found in this study on psychogeriatric patients may mean a drawback in cost-utility studies in psychogeriatrics. It demands further research on validation of EQ5D in intervention studies with psychogeriatric patients. Considering all available evidence, the surplus costs of IRR are considered acceptable when the beneficial effects were taken into account on the high societal costs of suffering from multiple psychiatric symptoms of psychogeriatric patients and high burden of caregivers. To optimize the cost-utility and cost-effectiveness of IRR, the construction of a tool enabling to identify suitable psychogeriatric patients and caregivers for IRR is of high economical and clinical interest. Such a tool would contribute to optimize medical decision making based on an economical evaluation. Future studies have to be performed to strenghten the evidence, preferably as blinded RCTs.

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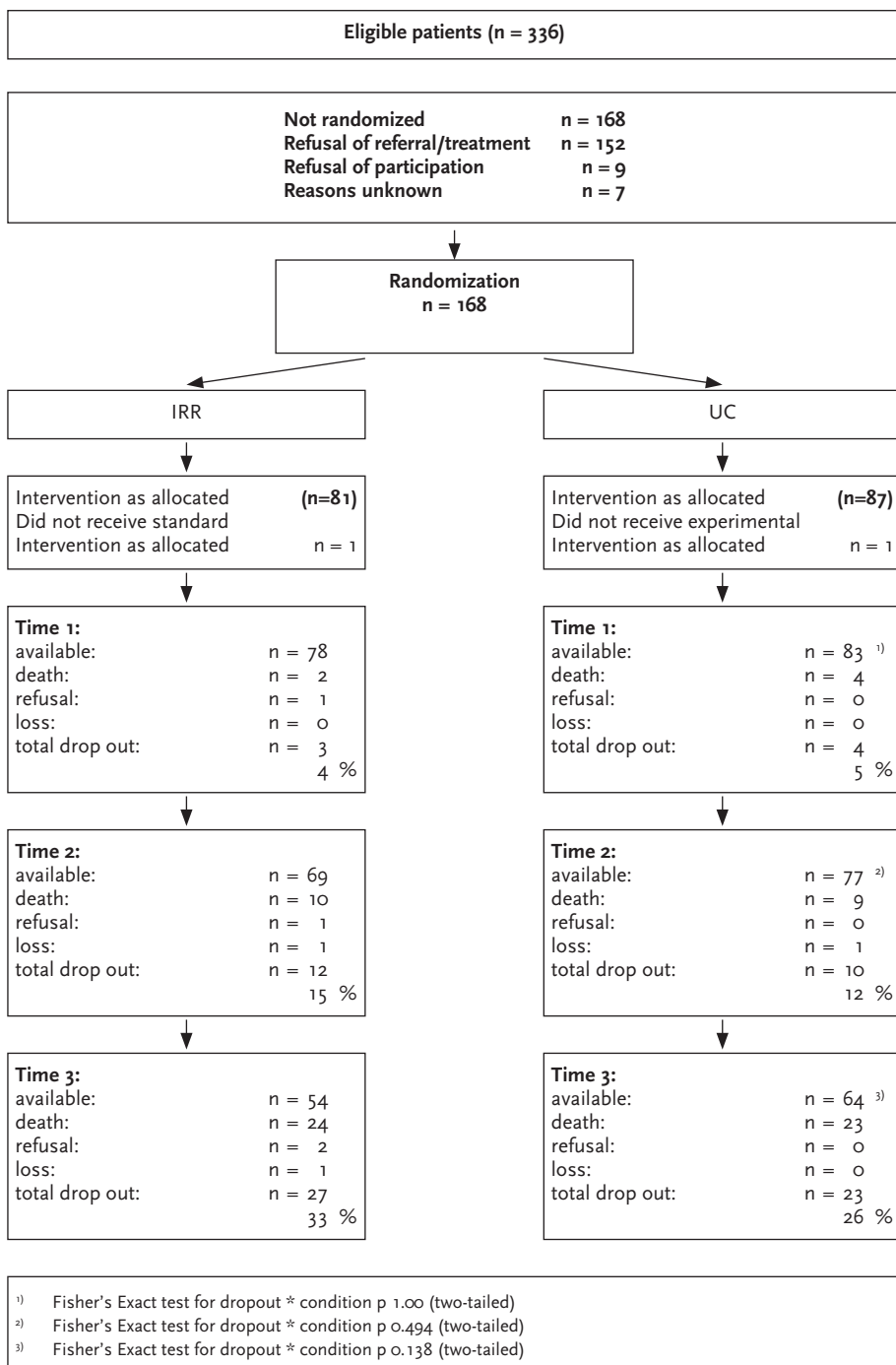
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Eligible patients (n = 336)

</div>

Not randomized	n = 168
Refusal of referral/treatment	n = 152
Refusal of participation	n = 9
Reasons unknown	n = 7

Randomization
n = 168

IRR	UC

Intervention as allocated **(n=81)**	Intervention as allocated **(n=87)**
Did not receive standard	Did not receive experimental
Intervention as allocated n = 1	Intervention as allocated n = 1

Time 1:		**Time 1:**	
available:	n = 78	available:	n = 83 [1]
death:	n = 2	death:	n = 4
refusal:	n = 1	refusal:	n = 0
loss:	n = 0	loss:	n = 0
total drop out:	n = 3	total drop out:	n = 4
	4 %		5 %

Time 2:		**Time 2:**	
available:	n = 69	available:	n = 77 [2]
death:	n = 10	death:	n = 9
refusal:	n = 1	refusal:	n = 0
loss:	n = 1	loss:	n = 1
total drop out:	n = 12	total drop out:	n = 10
	15 %		12 %

Time 3:		**Time 3:**	
available:	n = 54	available:	n = 64 [3]
death:	n = 24	death:	n = 23
refusal:	n = 2	refusal:	n = 0
loss:	n = 1	loss:	n = 0
total drop out:	n = 27	total drop out:	n = 23
	33 %		26 %

[1]   Fisher's Exact test for dropout * condition p 1.00 (two-tailed)
[2]   Fisher's Exact test for dropout * condition p 0.494 (two-tailed)
[3]   Fisher's Exact test for dropout * condition p 0.138 (two-tailed)

Figure 1. Flow chart discribing progress of patients through randomized controlled trial

Table 1. General details of participants, distinguished by intervention

	IRR	UC	
	n=81	n=87	p-value
Patient characteristics			
gender (females)	66.7%	62.1%	0.63[1]
age (in years), mean (sd)	79.8 (6.1)	81.5 (7.1)	0.10[2]
marital status: alone	77.8%	80.5%	0.71[1]
educational level: low	67.5%	68.7%	0.90[1]
domicile: at home	76.5%	66.7%	0.17[1]
primary caregiver: spouse	17.3%	13.8%	0.33[3]
DSM-IV dementia, (axis-I), count (%)			
dementia of the Alzheimer's type	18.5%	17.2%	0.84[1]
vascular dementia	23.5%	25.3%	0.86
dementia due to other conditions	16.0%	19.5%	0.69
amnestic/cognitive disorders	32.1%	31.0%	1.00
other	6.2%	2.3%	0.26
DSM-IV personality disorders (axis-II), count (%)	16.0%	9.2%	0.24
GDS-deterioration, mean (sd)	4.2 (0.7)	4.3 (0.9)	0,62[2]
somatic co-morbidity (ICD-10), mean (sd)	5.6 (2.6)	4.5 (2.4)	0.01[2]
Caregiver characteristics			
gender (females)	70.5%	61.7%	0.32[1]
age (in years), mean (sd)	58.6 (11.9)	58.9 (12.0)	0.86[2]
marital status: living together	91.4%	94.8%	0.52[1]
educational level: low	4.3%	2.6%	0.39[1]

[1] Fisher's Exact Test (twotailed)
[2] t-Test (twotailed)
[3] Pearson Chi-square (twotailed)

Table 2. Level of outcome across time (T1 - T3) distinguished by intervention

	range	high score = (+/-) *)	T1 (baseline measurement)							UC-IRR		T3 (six months follow-up)			
			IRR			UC			mean diff.	95% CI		IRR		UC	
			n	mean	sd	n	mean	sd				n	mean	n	mean
Psychiatric function disorders patient (by caregiver)															
NPI-sum-severity	0 to 144	(-)	72	35.90	21.84	76	29.68	20.12	-6.22	-13.05	0.62	49	15.84	51	18.61
Caregiver burden															
Caregiver burden (CB)	0 to 100	(-)	72	52.47	25.65	77	46.69	27.66	-5.79	-14.42	2.85	42	28.81	50	44.90
Competence (CCL)	28 to 112	(+)	72	84.62	14.24	77	86.58	14.46	1.96	-2.69	6.6	49	96.35	50	91.78
Cognitive functioning patient															
MMSE	0 to 30	(+)	76	20.04	4.50	82	20.58	3.84	0.54	-0.77	1.85	51	19.46	60	19.50
Barthel Index (BI)	0 to 20	(+)	77	15.39	3.77	80	14.71	3.55	-0.68	-1.83	0.48	54	12.38	63	13.24
Quality of life patient															
EQ5D	-0.59 to 1.00	(+)	77	0.54	0.34	80	0.58	0.29	0.04	-0.06	0.14	45	0.62	62	0.55

*) + = high score is beneficial, - = high score is unfavourable

Table 3. Mean costs (€) and QALY after 40 weeks, distinguished by Intervention; Multiple imputation (MI)

	IRR[1]			UC[2]			IRR-UC		
	mean	95% CI		mean	95% CI		mean	95% CI	
week 40									
QALY	0.37	0.31	0.43	0.39	0.35	0.43	-0.02	-0.10	0.06
direct costs	42979.00	39650.92	46307.08	36299.00	33082.64	39515.36	4572.00	346.24	8797.76

[1]   Integrative Reactivation and Rehabilitation
[2]   Usual care

Table 4. Mean costs (€) after 40 weeks for the individual outcome variables, distinguished by Intervention; Complete case analysis (CC)

	mean IRR[1]	95% CI		mean UC[2]	95% CI		mean IRR-UC	95% CI	
week 40									
Home care	21.05	-20.21	62.31	2895.01	921.53	4868.49	-2873.96	-4847.88	-900.04
Day care	0.00	0.00	0.00	2279.18	433.60	4124.76	-2279.18	-4124.76	-433.60
Hospital	964.74	27.66	1901.82	420.34	-49.61	890.29	544.40	-503.93	1592.73
Nursing home (incl. IRR)	27675.61	22724.36	32626.86	20123.51	14231.46	26015.56	7552.10	-144.08	15248.28
Service home	4902.63	2371.74	7433.52	4033.14	1624.22	6442.06	869.49	-2624.56	4363.54
Other care	149.16	64.68	233.64	757.05	138.89	1375.21	-607.89	-1231.80	16.02

[1]   Integrative Reactivation and Rehabilitation
[2]   Usual care

Table 5. Costeffectiveness after 40 weeks; distinguished by Intervention; ICER-approach

	high score =(+/-) *)	COSTS		EFFECTS						ICER
		Costs IRR	Costs UC	IRR	UC	Costs IRR-UC	p-value	Effects IRR-UC	p-value	Costs/ effects
WEEK 40										
NPI-sum-severity	(-)	33713.19	30508.23	21.78	11.86	3204.95	0.37	9.92	0.04	323.08
Caregiver burden (CB)	(-)	33713.19	30508.23	24.76	0.00	3204.95	0.37	24.76	0.00	129.44
Caregiver competence (CCL)	(+)	33713.19	30508.23	10.35	4.42	3204.95	0.37	5.93	0.01	540.46
MMSE	(+)	33713.19	30508.23	-1.25	-1.07	3204.95	0.37	-0.18	0.82	--
Barthel-Index (BI)	(+)	33713.19	30508.23	-3.61	-2.06	3204.95	0.37	-1.55	0.07	--
EQ5D patient	(+)	33713.19	30508.23	0.00	-0.04	3204.95	0.37	0.04	0.47	80123.85

*)   + = high score is beneficial, - = high score is unfavourable

General discussion

1. Introduction

The objective of the work described in this thesis was first to design and secondly to test the effects of Integrative Reactivation and Rehabilitation (IRR). In this chapter the most important results of the research comprising this dissertation will be summarized by addressing the research objectives of both three explorative observational studies and one RCT study concerning the integrative psychotherapeutic nursing home programme of IRR. IRR consists of interventions to reduce multiple psychiatric symptoms of psychogeriatric patients who suffer from cognitive impairment or dementia as well as the burden of the caregiver. Methodological issues of the studies are discussed. Furthermore, implications of the results for professionals, managers and policymakers will be described. Finally, opportunities to improve IRR are explored.

2. Summary of relevant results

In chapter two a case study was presented. The case study illustrated the need and feasibility of integrative psychotherapeutic interventions based on problem-solving principles and focussed on psychiatric symptoms of psychogeriatric patients and on burden of caregivers.

In the following three chapters the results of the explorative observational studies are presented addressing three research objectives, i.e.:

1. to identify prognostic characteristics for the probability of discharge of psychogeriatric patients with psychiatric function disorders, in order to optimize patient selection for the reactivation programme (chapter two).
2. to estimate the life expectancy of patients having participated in a psychogeriatric reactivation programme as well as to identify prognostic characteristics for survival after discharge (chapter three).
3. to estimate the prevalence and co-occurrences of psychiatric function disorders in psychogeriatric patients suffering from cognitive function disorders at referral to clinical as well as non-clinical (transmural) psychogeriatric programmes (chapter four).

In chapter three, (title 'Psychogeriatric Reactivation in an Psychiatric-Skilled Nursing Home; a Clinical-Empirical Exploration') the results showed that 16 characteristics of psychogeriatric patients and caregivers, belonging to four dimensions i.e. Cognitive function disorders, Psychiatric function disorders, Caregiver system and Somatic co-morbidity had potential prognostic qualities for probability of discharge after participation in IRR programme [1].

In chapter four, (title 'Life Expectancy Following Psychogeriatric Reactivation') a preliminary prognostic model for survival after participation in IRR programme was presented. Six characteristics of the psychogeriatric patient as well as the caregiver – distributed over the same four dimensions i.e. cognitive function disor-

ders, psychiatric function disorders, caregiver system and somatic co-morbidity - were relevant factors in the prognostic model. This model performed relatively well; about 30% of the variance was explained. Another clinically relevant finding was that the prognosis of psychogeriatric patients who suffer from delirium was bad. So, we decided to exclude patients suffering from delirium from participation in the RCT.

In chapter five (title 'Prevalence of Psychiatric Function Disorders in Psychogeriatric Patients at Referral to Nursing Home Care – the Relation to Cognition, Activities of Daily Living and General Details') the prevalence and co-occurrences of psychiatric function disorders in psychogeriatric patients who suffered from cognitive function disorders are presented. The psychiatric function disorders were measured by the neuro-psychiatric inventory (NPI) at the moment of intake, and administered to the caregiver.

The prevalence of NPI-symptoms was high, in that about 90% of the referred psychogeriatric patients, still living at home, had one or more NPI-symptom, about 80% two or more. These percentages of psychogeriatric out-patients were higher than those of patients within nursing homes; in the latter setting about 70% patients suffer from one or more NPI-symptoms. The most important NPI-symptoms were depression, apathy, anxiety and agitation/aggression. Clinically relevant was the finding that NPI-symptoms constituted a dimension on their own, different from cognitive function disorders as measured by MMSE (memory) and BI (self care). We argued that the NPI-symptoms could be/might be considered as an expression of psychiatric pathology. In a replication study (attached as a supplement to this dissertation) we identified the same dimensional structure in a population of patients at the moment of referral to a memory clinic [2].

In the RCT study we addressed the following five research objectives:
1. To test in terms of mean differences the effectiveness of IRR compared to usual multidisciplinary nursing home care (UC) to reduce multiple psychiatric symptoms in psychogeriatric patients and caregiver burden (chapter six).
2. To identify and estimate, whether beneficial long term effects of IRR on severity of multiple psychiatric symptoms of psychogeriatric patients and general burden of caregivers were modified by level of cognitive function disorders and/or type of dementia (chapter seven).
3. To evaluate long term benefit of IRR compared to UC in terms of percentages of clinically relevant improved psychogeriatric patients and caregivers and numbers needed to treat (chapter eight).
4. To identify prognostic factors for a favourable long term effect of IRR for psychogeriatric patients and caregivers on five selected outcome variables as well as to explore the performances of three decision rules (chapter nine).
5. To assess cost-utility as well as cost-effectiveness on six selected outcome variables of IRR compared to usual care (chapter ten).

In chapter six (title 'Integrative Psychotherapeutic Nursing Home Programme to reduce Multiple Psychiatric Symptoms of Psychogeriatric Patients and Caregiver Burden; a Randomized Controlled Trial), from the perspective of the caregiver the results showed that, at the end of the integrative psychotherapeutic nursing home programme, IRR had a significant and moderate to large beneficial surplus effect in curtailing the number and severity of multiple psychiatric symptoms (MPS) of the psychogeriatric patients who suffer from cognitive impairment or dementia. Comparted with UC, the patients in the IRR programme had up to 34% more reduction in their symptoms. Furthermore, IRR had a specific beneficial effect on hyperactivity. In addition, IRR had a large surplus beneficial effect on burden and the reported competence of the caregivers. Compared to UC, the caregivers in the IRR programme had up to 36% surplus beneficial effects. At six months follow-up, the surplus effect on multiple psychiatric symptoms of the patient remained. At this time, the effect on the burden of the caregiver appears to have increased: in the IRR condition burden had reduced up to 50%, while in UC there were no changes in the reported burden.

In chapter seven (title 'Effect Modification of Integrative Psychotherapeutic Nursing Home Programme to reduce Multiple Psychiatric Symptoms of Psychogeriatric Patients and Caregiver Burden; a Randomized Controlled Trial) it turned out that neither cognitive functioning (MMSE and BI-score) nor the type of dementia (vascular and Alzheimer) modified the effects of IRR. This means, that the surplus effect of IRR versus UC was beneficial for a wide group of psychogeriatric patients and caregivers who suffer from the two as most problematic experienced items in dementia care i.e. psychiatric symptoms and caregiver burden. Maybe, a broader range of patients i.e. (psycho)geriatric patients suffering from a lower level of cognitive functioning (MMSE $\geq$ 12 instead of $\geq$ 18) and/or different types of cognitive disorder (CVA or a post-crash syndrome) can also benefit from the IRR programme.

In chapter eight (title 'Benefit of Integrative Psychotherapeutic Nursing Home Programme to reduce Multiple Psychiatric Symptoms of Psychogeriatric Patients and Caregiver Burden after Six Months Follow-Up; a Randomized Controlled Trial') the results show that at the end of six months follow-up in IRR a significant and clinically relevant percentage (40%) of the psychogeriatric patients with hyperactivity improved and a small number needed to be treated (NNT: four). In addition, the same applies to the percentage (36%) of caregivers who improved on competence (NNT: five). Overall, at six months follow-up, for patients and caregivers who fully completed the IRR programme the likelihood to improve on multiple psychiatric symptoms, on caregiver burden as well as competence, was considerably higher in IRR than in usual care. For psychogeriatric patients the ORs varied from 2.80 to 3.46 and up to 76% patients improved. The ORs for caregivers varied from 2.40 to 4.18 and up to 71% caregivers improved.

Regarding prognostics (chapter nine: title 'To Identify Prognostic Factors for a Favourable Long-Term Outcome of Psychogeriatric Patients and Caregivers Following an Integrative Psychotherapeutic Nursing Home Programme to reduce Multiple Psychiatric Symptoms of Psychogeriatric Patients and Caregiver Burden; a Clinical-Empirical Study') it turned out that prognostic modelling for the chance of improvement on five outcome variables was feasible i.e. on severity of multiple psychiatric symptoms of the psychogeriatric patients, on burden and competence of the caregiver, and on cognitive function disorders (memory and self-care). More specifically, on severity of multiple psychiatric symptoms of the patients and on competence of the caregiver the performance of the prognostic models was substantial, albeit on burden of caregiver and on cognitive function disorders (memory and self-care) the performance was low. The inclusion of a broader range of psychogeriatric patients i.e. lower or higher scores on MMSE or BI, in combination with specific interventions to enhance cognitive functioning seems justified.

From the perspective of optimizing medical decision making, we explored the performance of three decision rules. The first decision rule (highest Mean Average-rule) is aimed to calculate the average percentage improvement in either intervention. The second rule concerns to minimize the maximum possible loss ('MINIMAX'-rule); this latter rule attempts to avoid the risk of missing benefit by comparing the highest difference between the interventions on each score over all outcome variables; than choose for the intervention with the lowest loss of benefit. The third decision rule concerns the 'MAXIMIN'-rule which implies that the patient will be assigned to the intervention with the lowest level of avoidable risk by comparing the difference between the interventions of the lowest score on all outcome variables. Applying these three rules on the expected improvement at six months of follow-up resulted all three into IRR as indicated as best treatment.

In chapter ten (title 'Economic Evaluation of Integrative Psychotherapeutic Nursing Home Programme to reduce Multiple Psychiatric Symptoms of Psychogeriatric Patients and Caregiver Burden; a Randomized Controlled Trial') we have undertaken an economic evaluation of IRR programme based on all relevant costs due to medical resource utilisation at 40 weeks. However, non-medical costs and costs of caregivers were not included in the analyses. Regarding cost-utility on QALYs no significant differences were found, while total medical costs of patients in IRR were significantly higher. It has to be noted that, in case of surplus costs of IRR, a probable discount due to non-medical costs as well as to diminished caregiver costs was not taken into account. With respect to cost-effectiveness, patients and their caregivers who fully participated in the programme improved in IRR significantly more on mean scores i.e., on severity of multiple psychiatric symptoms of the psychogeriatric patient, on general burden of the caregiver, and on competence of the caregiver, with ICERS varying from € 130.-- to € 540.--. The large discrepancy between QALYs and ICERs, as well as to the relatively irresponsiveness of EQ5D to clinically relevant change, found in this study on psychogeriatric patients who suffer from cognitive impairment or dementia, may mean a drawback in cost-utility

studies in psychogeriatrics. It demands further research on the validation and value of EQ5D in psychogeriatric studies. Another issue for further research is, that we found that irrespective of type of intervention the improved patients were responsible for higher medical costs. A reason may be that they lived longer (see chapter 4). All in all, the surplus costs of IRR are considered acceptable when the beneficial effects were taken into account on the high societal costs of suffering from multiple psychiatric symptoms of psychogeratric patients and high burden of caregivers. To optimize the cost-utility and the cost-effectiveness of IRR, the construction of a tool enabling to identify suitable psychogeriatric patients and caregivers for IRR is of highly clinical interest. Such a tool contributes to optimize medical decision making on an economic evaluation.

3. Methodological issues

In this paragraph the strengths and limitations of respectively the case study, explorative-observational, and RCT studies will be discussed. The major strength of the case study was the detailed information about the content and feasibility of the reactivation process. It illustrated the potential beneficial effect of a multi-disciplinary and integrative psychotherapeutic nursing home programme, based on a person-oriented and problem-solving theoretical framework. [3] In the explorative, observational studies the clinical and scientific relevance of a multidimensional approach comprising the dimensions 'Cognitive function disorders', 'Psychiatric function disorders', 'Caregivers system' and 'somatic co-morbidity' nicely emerged from the results. [4, 5] In addition, the observational studies showed that psychogeriatric patients who suffered from delirium may not benefit from IRR. Furthermore, it became clear that most psychogeriatric patients suffer from multiple psychiatric symptoms. [6 - 9] In the explorative, observational studies the sample size of available patient data and participating patients and caregivers was relatively high. The positive findings of the explorative studies warranted to carry out an RCT. In our RCT the sample size of participating patients and caregivers was relatively large compared to other intervention studies. [3, 10 - 13] According to our knowledge this RCT is one of the first that addressed the effectiveness of multidisciplinary and integrative psychotherapeutic treatment in a nursing home setting. Multidisciplinary care including psychotropic drugs treatment is available in many nursing homes, especially in the Netherlands. [7, 14] However, the results of this RCT underline the surplus value of psychotherapeutic know-how – based on problem-solving principles - in treatment and care of psychogeriatric patients suffering from multiple psychiatric symptoms and their caregivers.[15] An important question is which ingredients of IRR were of relevance for the results? In literature the following ingredients are pointed out as crucial factors for beneficial effects in (psycho)geriatrics: Person-oriented, problem-solving based, integrative psychotherapeutic technique combining treatment of patient and caregiver, multidisciplinary approach, optimistic attitude, and methodological rigor. [3, 10, 12, 13,

[16 – 21] We think that the IRR programme comprises these crucial ingredients. More attention can be paid to the cognitive aspects, by enriching the IRR programme with explicit cognitive (memory, orientation and self-care) training and support interventions in combination with – if appropriate – the prescription of cognitive enhancers. Furthermore, a broader range of (psycho)geriatric patients may benefit of this second generation of IRR. At last, an improved version of the computerized treatment plan and the GAS-score system would facilitate the performance of the IRR programme by the professionals. Many psychogeriatric patients as well as their caregivers will benefit if cure and care programmes like IRR become available. Moreover, the effect modification study showed that neither type of dementia nor level of cognitive function disorders (MMSE ≥ 18 and BI ≥ 5) had any modification effect on the results regarding severity of multiple psychiatric symptoms of patients as well as general burden of caregivers.

The clinical relevance of the effects of IRR found in the RCT is high, which becomes obvious by considering the top three of experienced problems in dementia in the Netherlands, i.e. psychiatric symptoms, burden of caregiver, and admission to a nursing home. [7, 8, 22 – 27] Moreover, psychotherapeutic know-how should become an integrative part of the education programmes of various involved disciplines. The part of the dissertation that focussed on long term benefit, showed that participating fully in the IRR programme enlarged the likelihood to improve for both patients and caregivers. This underlines the need to study possible means to improve non-participation and dropout/withdrawal in psychogeriatric research. This is even more important as it is known that for this group of elderly patients, even in longitudinal observational studies without intervention, the percentage of dropout is generally very high (up to 40%). [14, 28 - 30] Basically, it reflects the vulnerability of psychogeriatric patients on the verge of admission to a nursing home. In this study, dropout-patients of both arms did not significantly differ in number, baseline outcome values or in participation period. So, selective dropout between both arms of the RCT is unlikely. The gain in results of IRR compared to UC, when focussing on patients and caregivers who fully participated demonstrated the efficacy of IRR. The strength of the prognostic part of the dissertation was that the identified models were relatively stable despite the small sample size for this type of study. Moreover, the models showed a substantial performance for severity of multiple psychiatric function disorders of the psychogeriatric patient and competence of the caregiver. Applying the three selected decision rules was another strength of this prognostic part of the dissertation; all three pointed to the same direction and resulted in IRR as first choice. For economic evaluation, the direct medical costs of the patients could be calculated. The influence of dropout on the results and the consequences of different statistical strategies could be shown by comparing different outcome methods, i.e. QALY as well as an ICER (incremental cost effectiveness ratio) outcome approach. In the ICER-results patients and caregivers on IRR showed a discernibly higher likelihood of improvement on clinically relevant outcomes (i.e. psychiatric symptoms, caregiver burden and competence) against higher costs.

Limitations

Which were the limitations of this dissertation i.e. case study, explorative, observational and RCT studies? The single case study (or N=1 study) is conducted without a comparison between pre-/post treatment options. So, it only provides some common sense and clinical logics about the relevance of an IRR programme. However, it is an important first step to enable in the long run to design and conduct a RCT. Drawback of the observational studies was lack of proving effect and causal associations. Despite of that, it can reveal important aspects or induce hypotheses to test in a RCT or design or controlled study.

Regarding the RCT, a point of discussion is generalization of the results. About 50% of the eligible psychogeriatric patients and caregivers refused to participate in the study. Comparatively many of these refusing patients lived with a spouse. The core motive for refraining participation was fear of clinical admission in case of assignment to IRR. Fear of admission to a nursing home is number three of the top three of experienced problems in dementia care in the Netherlands. [22] Therefore, it is of importance to develop a short preliminary (outreaching) programme focussed to diminish the fear for admission. Furthermore, the follow-up period was six months. The beneficial effects for the patients remained and for the caregivers increased. However, it is an important question whether the effects will remain over a longer period of time. Furter research is needed.

Another limitation of the RCT was that the research co-workers were not blinded for type of intervention. They had to visit the patients and caregivers personally, so they knew the intervention history of the involved patients. In a clinical study like this blinding was not feasible. Other sources of observer bias or lack of inter-rater reliability were minimized by training the co-workers carefully in properly administering the assessment instruments.

In sum however, the question is relevant whether overall bias distorted the results of this RCT. At baseline there was only one significant difference (somatic co-morbidity) between both arms. Even between dropouts there were no significant differences. Moreover, in the RRM-analyses, adjusting for baseline value and dropouts, the results were in line with the unadjusted Cohen's-d analyses. All in all, in our view it is unlikely that the results of the RCT were biased, but an effect of unblinded assessment cannot be excluded.

With respect to the results on the primary outcome variable using the NPI (mean differences, RRs [including NNTs] and ORs) the clinical relevance of the findings can be presented in continuous data as well as dichotomous data. There is a lot of discussion about the issue of the magnitude of an effect to be regarded as clinically relevant.[31, 32] De Vet and Norman advise a half of a standard deviation as a minimally clinically relevant change in health care studies. However, there is not much literature available about the minimal clinically relevant change in NPI scores, apart from the articles of Cummings himself.[33, 34] More research is needed on this issue. However, the surplus effect of IRR found in the RCT was relatively large with respect to mean differences as well as percentages of patients and caregivers who improved 30% and over.

Another issue that needs to be discussed is the differences in scores between the NPI administered to the nurse of a nursing team compared with those to the caregiver. The trend of both scores was the same and the Pearson correlation was significant and increasing over time (at T3 r= 0.48; df=93; p=< 0.001). How can the difference in NPI-score be explained? First of all, the caregivers formed a stationary group from the moment of inclusion until end of treatment and six months follow-up. In addition to the information they received from the nursing team, caregivers also have supplementary information, because they have more long lasting individual contacts with the patient. In general, according to literature their opinion corresponds more with needs, thoughts and feelings of the patient [35-38] In contrast, the data of the nursing team were discontinuous in both arms; the researchers had to ask different nurses of a nursing team for NPI-data. So the question is to whom the NPI has to be administered to collect adequate data about the multiple psychiatric symptoms of the patient. To the nursing team, the caregiver or both? This is an important issue to address in future research projects. [3, 35-38] However, the caregiver NPI showed to be very responsive to changes in number as well as severity of psychiatric symptoms. In any case, we recommend always to collect also data from the caregivers.

In both study groups, on the EQ5D just small changes could be estimated. Moreover, in both groups, relatively small numbers of psychogeriatric patients as well as caregivers improved on the EQ5D. The EQ5D instrument showed a relatively low responsiveness, compared to the clinically important instruments i.e. NPI, CB and CCL. The low responsiveness of EQ5D in this RCT did put a constraint to the cost-utility analysis in terms of QALYs. This finding confirms the results found in literature about the relation between quality of life measures and measures of psychiatric symptoms like NPI; specifically by Ballard, Katona and Wimo. An adapted ('proxy'?) measurement instrument which can be used for cost-utility research in psychogeriatric patients is urgently needed. [38-41] Another limitation of the cost-utility and cost-effectiveness study was that costs included only direct medical costs of the patient. Other patients costs, all caregiver costs, and any profits were note taken into account. The development of a more comprehensive approach is recommended. In sum, the strength of the evidence and recommendations of this RCT can be evaluated as moderately strong according to the GRADE approach (Grading of Recommendations Assessment, Development and Evaluation) of the Cochrane Collaboration and taking into account the above mentioned limitations.[42, 43]

4. Implications for professionals, managers and policymakers

Looking for the implications of the findings of the dissertation for professionals, we advise to address the implementation of psychotherapeutic know-how in usual psychogeriatric care and in education programmes of professionals e.g. nursing,

physician, psychologist, physiotherapist, occupational therapist, social worker and so on. There is no need to do more, but rather to do different things i.e. person-oriented and psychotherapeutic problem-solving based interventions. Furthermore, research on the optimal implementation strategy for implementation of IRR is of relevance to enable a widespread application of IRR. In addition, it is of clinical relevance to develop a second, cognitively enriched generation of IRR, including a prognostic tool to optimize the interventions to reduce multiple psychiatric symptoms in general as well as more specific psychiatric symptoms of psychogeriatric patients and burden of the caregiver. As stressed by the outcome of the National Dementia Programme in the Netherlands, there is a high level of suffering on both the psychiatric aspects of the patient as well as burden of the caregiver. The latter suffers from high levels of disabilities and loss of well-being; up to 80%. [15] Regarding professionals, to have access to psychotherapeutic strategies, based on a problem-solving theoretical framework as well as a person-oriented approach will enable them to optimize their skills in order to get better results. [3, 10] This will make it more attractive to become a professional worker in this particular domain, which is of great socio-economical importance looking at demographic developments.

With respect to research like the ZonMw programmes, especially the National Programme for the Elderly (NPO), an important implication is to address the development of responsive quality of life instruments, which correspond with other clinically relevant outcome measures. The issue of the appropriate measurement of quality of life of (psycho)geriatric patients, suitable for the evaluation of the cost-utility of interventions (QALYs), should be solved and deserves high priority. Furthermore, the problem from whom the patient data of the multiple psychiatric symptoms have to be derived from (the psychogeriatric patient him-/herself, the nursing team and/or caregiver), urgently needs to be solved. In addition, the development of a comprehensive economic model, including all relevant costs and profits, to evaluate intervention programmes from an economical perspective is another important item for future ZonMw research programmes. From an international perspective and according to the evidence available from this RCT and literature reviews, intervention studies of multiple psychogeriatric symptoms in psychiatric patients preferably should comprise integrative psychotherapeutic interventions as part of the index interventions or as part of the control interventions; even so in pharmaceutical studies.

For both managers and policymakers it is interesting that, in general, improvement either in usual nursing home care or in IRR was more cost expensive than non-improvement. As in the worst case scenario IRR was just about € 53.-- more expensive than usual care, which is about half the costs of a CVA-unit (€ 102.--) the implementation of IRR should be facilitated e.g. by adaptation of the financial package linked to the weight of care; called in the Netherlands "ZZPs". Especially ZZP-9, which is now predominantly directed on somatic rehabilitation, should

be made suitable for rehabilitation and revalidation of multiple psychiatric symptoms of psychogeriatric patients as well as on burden of the caregiver. Within this context, it is of relevance to join the promising development to position the "Geriatric Revalidation" outside the AWBZ.

With respect to ZZPs it is also important to realise that an actual ZZP-classification of a psychogeriatric patient not automatically fits the needs and demands for psychotherapeutic care and treatment to relieve the suffering of the patient and the caregiver. Patients with a wide range of ZZPs were eligible for IRR according to the inclusion criteria. Moreover, the correlation between ZZP-7 (active psychiatric disorder) and actual NPI scores was minor. We recommend to registrate and manage this discrepancy, in order to clarify the consequences for daily practice as well as governmental care politics. As the next step the development of a specific, evidence based prognostic tool, is a feasible goal. In our opinion, policy makers have to decrease the current gap between the economic-oriented ZZP-classification system and the robust clinical assessment instruments, used for inclusion of patients in tailor made treatment and care programmes. We recommend managers and policy makers to focus on the content and methodological aspects of psychotherapeutic treatment and care of psychogeriatric patients and their caregivers, in order to integrate them with the usual financial and management control topics. Finally, specific attention is needed for improving the quality of care in chronic nursing home care with respect to the treatment of multiple psychiatric symptoms of psychogeriatric patients, though in the RCT usual care – mostly emotion-oriented - showed already a mean 30% reduction of the complaints. More reduction in chronic nursing home care seems possible by applying (partial) techniques of IRR. E.g. in nursing home care we successfully introduced the concept of 'behaviour consultant nurse', who is educated to perform the nurse-diagnostic and psychotherapeutic interventions derived from the IRR programme. Furthermore, the burden of caregivers can be considerably reduced by using the different family therapy techniques of IRR. Of course, these developments need further scientific evaluation.

5.   Recommendations for improvement of IRR

What are the possibilities to enhance the beneficial effects of IRR?

Based on the studies we performed we concluded that effects of IRR are already beneficial, but still can be improved. First of all, a preliminary programme should be developed to diminish the fear for admission. Another recommendation is to develop a powerful prognostic logarithm to optimize clinical decision making to admit psychogeriatric patients and caregivers with a high chance to profit from IRR. With respect to the IRR-programme itself, more attention is needed for cognitively enriched interventions, differentiation between short and long duration of IRR, especially regarding personality disorders and development of more specific interventions protocols to common psychiatric symptoms like depression, anxi-

ety and apathy are important issues. Moreover, a more comprehensive outpatient follow-up programme is needed to enhance the treatment results. In addition, a large scaled blinded RCT should be designed and conducted with a broader study sample. The objectives to identify the most important therapeutic elements of a second generation of IRR and on the other hand to construct robust prognosticum in order to compress the IRR programme into a less complex intervention for a specific target group of cognitive impaired patients. As a consequence, IRR may become more cost effective.

6.   General conclusion

In this dissertation the development and testing of a psychotherapeutic nursing home programme (IRR) to reduce multiple psychiatric symptoms of psychogeriatric patients who suffer from cognitive impairment or dementia and caregiver burden is evaluated. In general, from the perspective of the caregiver the surplus effects of IRR were significant of a moderate to large size. After six months follow-up the effects on the psychogeriatric patients were stable and on the caregiver even enlarged. From the perspective of the nursing team, the results were insignificant, though pointed to the same direction and were significantly and increasingly correlated over time. The extra costs of IRR were acceptable and the numbers needed to treat were low (four to five) compared to donepezil (=10) and to memantine (=3-8). Moreover, the favourable effects were not modified by type of dementia or level of cognitive functioning. However, because of the methodological issues the results have to be interpreted cautiously. According the GRADE approach the strength of the recommendations can be evaluated as moderately strong. The findings presented in this dissertation may inspire to further scientific research to reduce multiple psychiatric symptoms of psychogeriatric patients who suffer from cognitive impairment or dementia, and burden of the caregivers. In order to relieve the suffering of psychogeriatric patients and their caregivers, professionals, researchers, managers and policy makers have to address the implementation barriers for psychotherapeutic treatment inside and outside nursing homes e.g. integrative psychotherapeutic training programmes, quality of life research, person-oriented and content-oriented management and modification of the ZZP-classification system.

As 80% of psychogeriatric patients suffer from multiple psychiatric symptoms and 70-80% of caregivers are moderately to heavily overburdened, the implementation of integrative psychotherapeutic treatment based on a problem-solving theoretical framework as well as a person-oriented approach is urgent. Future studies have to be performed to strengthen the evidence, preferably as blinded RCTs with a long follow-up period.

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Supplement 1

Integratieve reactivering en rehabilitatie (IRR)

Een revalidatieprogramma voor kwetsbare ouderen, lijdend aan multipele psychiatrische functiestoornissen, en hun mantelzorgers

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INLEIDING

De laatste jaren is duidelijk geworden – vooral door het internationaal toenemend gebruik van de Neuro-Psychiatric Inventory van Cummings[1] – dat 70 tot 90% van patiënten lijdend aan dementie één of meer psychiatrische functiestoornissen (PFS'en) heeft. Voor CVA-patiënten ligt dit rond de 65%. Opvallend hierbij is het fenomeen van multipsychopathologie; het merendeel van de patiënten lijdt aan multipele PFS'en. Hoge prevalentie hebben depressie, angst, achterdocht, agitatie en agressie.[2,3] Bekend is dat PFS'en een negatief effect hebben op het cognitief functioneren, de kwaliteit van leven en overlevingsduur van de patiënt. Bovendien zijn PFS'en belastend voor de mantelzorger. Daarnaast zijn PFS'en belangrijke voorspellers van opname in een verpleeghuis.[4-7] Uit onderzoek van het Nivel in het kader van het Landelijk Dementie Programma bleek dat stemmings- en gedragsproblemen en belasting van de mantelzorg de top twee vormden van ervaren problematiek bij dementie.[8] Verder heeft dit onderzoek aangetoond dat bij dementie 20% van de mantelzorgers zich erg belast tot ziek voelt en 58% matig belast.[9] Wat betreft de behandeling van PFS'en is van belang vast te stellen dat het gebruik van psychofarmaca, bijvoorbeeld (a)typische antipsychotica, veel voorkomt, ondanks de potentiële schadelijke bijwerkingen.[2,10-13] Positief is dat er een toename is van het aantal bewezen effectieve psychosociale interventies dat gericht is op verbetering van psychiatrische symptomen van kwetsbare ouderen en/of vermindering van de belasting van de mantelzorger.[14-16] De onderzochte psychosociale interventies hebben echter gemeen dat ze niet of beperkt integratief van aard zijn. De interventie richt zich bijvoorbeeld op één deelaspect van de zorg, zoals voeding of depressie, of er is sprake van één interventie zoals snoezelen. Meer in het bijzonder in de psychogeriatrie zijn er aanwijzingen dat psychotherapeutische interventies, mits rekening wordt gehouden met het niveau van cognitief functioneren van de patiënt, effectief zijn.[1,17,18] Echter, als gevolg van somatische comorbiditeit, cognitieve problematiek en sociale problemen (relatieproblemen en eenzaamheid) blijft de toepassing van psychotherapeutische interventies bij

kwetsbare ouderen een complexe zaak. Een multidisciplinaire en integratieve behandeling gericht op multipele PFS'en van kwetsbare ouderen en de belasting van de mantelzorger is derhalve gewenst.[16,17,19,20] Dit is ook een door de NVVA-richtlijn ondersteund beleid.[21]

Wij ontwikkelden en onderzochten in een Randomized Controlled Trial (RCT) een dergelijk multidisciplinair en integratief behandelprogramma, genaamd Integratieve Reactivering en Rehabilitatie (IRR). IRR is een klinisch programma met een duur van ± drie maanden. De multidisciplinaire interventies binnen IRR richten zich primair op de multipele PFS'en van patiënten en de belasting van de mantelzorgers. Bij IRR ligt de nadruk op de psychotherapeutische/psychiatrische invalshoek. IRR is een persoonsgericht programma bestemd voor zowel psychogeriatrische patiënten met lichte tot matige cognitieve stoornissen, die lijden aan PFS'en, als voor hun mantelzorgers. Het doel van dit artikel is zowel de behandeling van multipele PFS'en bij revalidatie van kwetsbare ouderen te beschrijven als de systeemtherapeutische begeleiding van hun mantelzorgers. Hierbij wordt gefocust op de ontwikkelde methodiek van IRR; aan de hand van casuïstiek wordt een vertaling gemaakt naar de praktijk.

WAARUIT BESTAAT IRR?

Het IRR-programma biedt een klinische opname op een unit met ±20 bedden. IRR heeft een gemiddelde duur van ±13 weken. Het programma is gebaseerd op integratieve psychotherapeutische interventies die multidisciplinair worden toegepast. De interventies zijn gericht op de multipele PFS'en van de patiënt in combinatie met systeemtherapie gericht op de belasting van de mantelzorger. Het IRR-proces kent drie fases:

1. observatie, beoordeling en behandeling van overheersende PFS'en en somatische comorbiditeit,
2. bereiken, herwinnen of stabiliseren van controle over de

Samenvatting

Psychiatrische functiestoornissen (PFS'en) hebben een hoge prevalentie bij kwetsbare ouderen en komen vaak in combinatie voor. PFS'en hebben een grote negatieve impact op zowel patiënt als mantelzorger. Een multidisciplinair revalidatieprogramma voor kwetsbare ouderen gericht op multipele PFS'en is gewenst. Integratieve reactivering en rehabilitatie (IRR), oorspronkelijk ontwikkeld voor de psychogeriatrie, is een dergelijk persoonsgericht programma. IRR omvat een drie maanden durende klinisch programma, gebaseerd op integratieve psychotherapeutische interventies, die multidisciplinair worden toegepast, gericht op zowel de patiënt als de mantelzorger. Een casus illustreert de werkwijze van IRR. Implementatie wordt aanbevolen evenals het meer bekwamen van professionals op het gebied van psychiatrie, psychotherapie en psychofarmaca.

Summary

Multiple psychiatric function disorders (PFDs) have a high prevalence among frail elderly. Moreover, PFDs have a large negative impact on patients as well as the caregivers.
A multidisciplinairy rehabilitation programme for frail elderly focused on multiple PFDs is needed. Integrative reactivation and rehabilitation (IRR), developed in psychogeriatrics, is such a person-oriented programme. A description is given about the IRR methodology. IRR is a clinical programme applying an integrative psychiatric/psychotherapeutic perspective to both patient and caregiver, executed by a multidisciplinary team. A case history illustrates the presented methodology. Implementation is recommended as well as the incorporation of psychiatric, psycho-therapeutic and pharmaco-therapeutic know-how into the education programmes of involved professionals.

PFS'en van de patiënt en de problematiek van de mantelzorger. Daarmee het verbeteren van het welzijn van beiden, en ten slotte

3. training van patiënt en mantelzorger gericht op het ontslag.

In alle drie de fasen wordt aandacht besteed aan het optimaliseren van het cognitief functioneren en aan de somatische comorbiditeit. Bij IRR worden mogelijke functionele stoornissen van patiënt en mantelzorger systematisch geordend naar zes dimensies:

1. emotie (waaronder depressie, angst, agressie, paranoïdie),
2. persoonlijkheid (interpersoonlijk gedrag, waaronder kenmerken van narcisme, borderline, afhankelijkheid, theatraliteit),
3. levensgebeurtenissen (waaronder traumatische gebeurtenissen zoals oorlog, incest, mishandeling, overlijden van een echtgeno(o)t(e) en/of kind),

4. psychosociaal functioneren (waaronder relatieproblemen met de echtgeno(o)t(e), kinderen, verlies van sociale activiteiten of hobby's, zorgafhankelijkheid, leven in een groep),
5. cognitief functioneren (waaronder geheugen, oriëntatie, zelfzorg/ADL), en
6. somatische functiestoornissen (waaronder mobiliteit, vallen, lichamelijke conditie, polyfarmacie, intercurrente infecties, CVA, hartfalen, voedingsdeficiënties, cachexie).

Bij aanvang van het programma wordt van de patiënt en diens systeem een analyse gemaakt van relevante problemen en mogelijkheden met behulp van een functionele assessmentlijst (FAL; zie www.verpleeghuisartsen.nl). De FAL is opgebouwd uit de genoemde zes dimensies en bevat naast biografische gegevens de meest voorkomende functiestoornissen. Deze assessment wordt uitgevoerd door de arts en psycholoog tezamen. Op basis hiervan en van verder aanvullend onderzoek en observatie worden multidisciplinair de relevante functionele problemen (van patiënt en mantelzorger) geformuleerd, waarop het IRR-programma zich zal richten. Vervolgens wordt in overleg met de patiënt en diens mantelzorger een individueel, persoonsgericht interventieplan opgesteld.[22]

Casus

Mevrouw B., 83 jaar, is aangemeld voor IRR. Enkele maanden geleden is haar toegewijde echtgenoot vrij plotseling overleden. Sindsdien is mevrouw toenemend passief en verwaarloost zij zichzelf. Haar enig kind (zoon) woont in Duitsland. Hij en zijn vrouw komen regelmatig naar Nederland, maar hun zorg schiet tekort, ook al wordt deze aangevuld met thuiszorg. Mevrouw B. eet en drinkt matig, ligt veel op bed, komt af en toe verward over en valt enkele keren. Kortom, de zorgproblemen stapelen zich thuis op.
Mevrouw B. is na veel aarzeling bereid een multidisciplinaire, poliklinische screening te ondergaan. Hieruit komt het advies tot een tijdelijke opname voor revalidatie (IRR), om op te knappen en haar zoon te ontlasten. Mevrouw stemt hiermee in, want zo is het ook geen doen, maar ze had liever gezien dat haar zoon en schoondochter bij haar introkken. Na opname blijkt mevrouw op de afdeling veel in bed te liggen, voortdurend lichamelijke klachten te uiten en te klagen over de zorg. Zij eist een eigen kamer en wil direct bij alles geholpen worden. Opvallend is dat mevrouw met bijna geen woord rept over het recente overlijden van haar echtgenoot. Eten en drinken gaan matig en 's nachts is mevrouw vaak wakker. In afwachting van het multidisciplinaire interventieplan wordt besloten mevrouw B. een begeleidingsbenadering door de verpleging te geven, gericht op het (voorlopig) accepteren van het gedrag en minimaliseren van negatieve gevolgen. Verder krijgt zij een eigen kamer en de nachtrust wordt geregeleerd met zopiclon. Hierdoor ontstaat de nodige rust en ruimte om een relatie op te bouwen. De FAL-assessment wordt door de arts en psycholoog uitgevoerd.

Binnen IRR zijn verschillende psychotherapeutische interventies beschikbaar, die integratief (gecombineerd vanuit verschillende therapeutische scholen) en multidisciplinair worden toegepast.[23] Alle interventies zijn discipline overstijgend geformuleerd en vervolgens schriftelijk uitgewerkt in protocollaire richtlijnen voor iedere discipline.

De volgende negen typen interventies zijn voorhanden:

1. consultatie (bijv. diagnostiek en advies),
2. inzicht geven in door het verleden bepaald gedrag (bijv. counseling, life review, interpersoonlijke therapie),
3. inzicht geven in door het heden bepaald gedrag (bijv. counseling, cognitieve gedragstherapie),
4. structuur bieden (bijv. gedragstherapie gebaseerd op conditionering)
5. begeleiding (bijv. accepteren van gedrag en minimaliseren negatieve effecten),
6. regressieve benadering (bijv. tijdelijk accepteren van regressief gedrag, tegemoetkomend aan de behoeften van de patiënt),
7. rehabilitatie (bijv. stimuleren van de patiënt en/of mantelzorger doelen te formuleren en te behalen in het kader van ontslag),
8. psycho-educatie (bijv. patiënt en/of mantelzorger informeren/instrueren over de omgang met specifieke psychiatrische stoornissen), en
9. systeemtherapie van de mantelzorg (bijv. construeren van een genogram, verkennen en veranderen van mantelzorgrollen binnen het systeem).

De interventies worden overwegend uitgevoerd in een groep en wanneer nodig individueel. Indien noodzakelijk worden er gericht psychofarmaca voorgeschreven. De duur van een interventie is tussen de 4 tot 12 weken met een intensiteit die varieert van minimaal 1 tot maximaal 7 keer per week. Na multidisciplinaire consultatie schrijft de verpleeghuisarts gespecialiseerd in psychiatrische behandeling de overeengekomen interventies, inclusief farmacotherapie, voor. Het IRR-team bestaat uit een team van verzorgenden/verpleegkundigen, een verpleeghuisarts, een gezondheidszorgpsycholoog/systeemtherapeut, een maatschappelijk werker, een muziektherapeut, een psychomotore therapeut, een creatief therapeut, een fysiotherapeut, een ergotherapeut, een logopedist, een diëtist, een activiteitenbegeleider/sociaal pedagogisch hulpverlener en een beperkt aantal vrijwilligers. Alle disciplines zijn getraind -- met name in de psychiatrische aspecten -- om systematisch het IRR-programma toe te passen.

Vervolg casus
Op basis van de FAL-assessment en de multidisciplinaire onderzoeken/observaties worden bij mevrouw B. een aantal thema's geselecteerd ten behoeve van het persoonsgerichte interventieplan, dat vervolgens met mevrouw en haar zorgwaarnemer (zoon) besproken wordt. Het plan bevat een negental thema's. De belangrijkste worden hieronder nader beschreven.

Op de somatische dimensie worden de thema's gewicht, eten/drinken en mobiliteit (vallen) geselecteerd met interventie door verpleging, fysiotherapie en verpleeghuisarts. Wat betreft emotionele beleving blijkt er sprake te zijn van manisch-depressieve kenmerken (mede op basis van de heteroanamnese) met nu een depressieve fase. Verder heeft mevrouw B. last van somatisatie; zij uit in een lange reeks van lichamelijke ongemakken, die zoals later zal blijken, staan voor spanning en verdriet gerelateerd aan het overlijden van haar man. Gestart wordt met begeleiding door de verpleging, structuur door psychomotore therapeut, groepstherapie met structuur (gegeven

door creatief therapeut met psycholoog samen) en inzichtgevende therapie (counseling) door de verpleeghuisarts. Tevens wordt citalopram geadviseerd, hetgeen patiënte aanvankelijk afwijst. Later in de behandeling stemt ze er alsnog mee in. In verband met de somatisatiekenmerken wordt hier nog fysiotherapie aan toegevoegd, waarbij ondersteuning en uitleg gegeven wordt over de betekenis van de lichaamssensaties bij lichamelijk belastende oefeningen. Op de dimensie persoonlijkheid worden dominante en egocentrische kenmerken benoemd. Hiervoor wordt een zogenoemde 'all-good' benadering (structuur) afgesproken, waarbij grote nadruk ligt op bekrachtigen van positief gedrag, met als doel het zelfbeeld van patiënte te herstellen; conflicten en begrenzingen worden zo veel mogelijk vermeden. Voor de zoon en schoondochter wordt systeemtherapie afgesproken, gericht op het omgaan met de ziekte van mevrouw B., waarvan belangrijke kenmerken al voor het overlijden van haar echtgenoot zichtbaar waren (info uit heteroanamnese). Deze werden echter door de echtgenoot opgevangen/gemaskeerd. Verder wordt, in overleg met mevrouw B., een positief activiteitenplan door de activiteitenbegeleider opgesteld.

In de wekelijkse interdisciplinaire patiëntenbespreking wordt de voortgang van de patiënt/mantelzorger in het programma bijgehouden. Hierbij wordt gebruikgemaakt van een gestandaardiseerde methode van Goal Attainment Scaling (GAS). Dit betreft een 7-puntsschaal; de scores variëren van 1-2 (volledig functioneel afhankelijk), 3-4 (regelmatig functioneel afhankelijk), 5 (geen hulp, alleen begeleiding), 6 (functioneel onafhankelijk met aanpassing) tot 7 (onafhankelijk).[24] Zie Figuur 1 en 2. Bij het benoemen van een functioneel probleem (thema) wordt multidisciplinair tegelijkertijd een start GAS-score geschat in combinatie met een doel GAS-score. Deze doelscore ligt meestal 1 à 2 punten hoger dan de startscore. Tijdens elke wekelijkse patiëntenbespreking wordt een tussentijdse GAS-score geschat en aan het eind van het programma de eindscore. Deze methode maakt het mogelijk de ontwikkeling van patiënt en systeem per benoemd functioneel probleem per week te volgen en zo nodig het interventieplan bij te stellen. Alle genoemde instrumenten en overzichten/plannen zijn computerondersteund beschikbaar.

Niveaus Functionele Autonomie

7. Volledige onafhankelijkheid — GEEN HELPER
6. Aangepaste onafhankelijkheid (m.n.hulpmiddelen)

Aangepaste afhankelijkheid — HELPER

5. Toezicht / stimulering
4. Minimale hulp (subject = 75% - 100%)
3. Matige hulp (subject = 50% - 75%)

Volledige afhankelijkheid

2. Maximale hulp (subject - 25% - 50%)
1. Totale hulp (subject = 0% - 25%)
Metingen: M1 — EERSTE METING
M2 — DOEL
M3 — TWEEDE METING
M4 — EINDMETING

Figuur 1. Gestandaardiseerde GAS-score
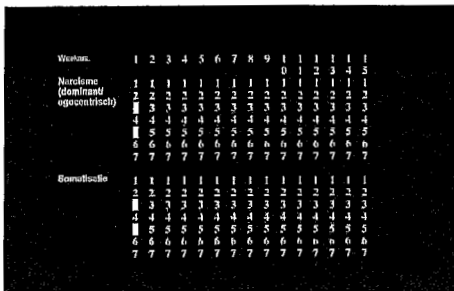
Figuur 2. GAS-beloop

Vervolg casus

De GAS-scores van de psychiatrische problemen van mevrouw B. bij opname worden door het team ingeschat op niveau 2; als doelscore wordt 4 à 5 aangegeven. Voor het systeem komt de begin GAS-score uit op 4 en de doelscore op 6 à 7. Op basis hiervan wordt ingeschat dat mevrouw B. bij voldoende herstel geschikt lijkt voor een verzorgingshuis (basiszorg of een meerzorgafdeling psychiatrie). De gekozen thema's zijn herkenbaar en er is instemming met het interventieplan. Bij de systeemtherapeut heeft de schoondochter inmiddels aangegeven, omdat mevrouw B. nauwelijks opknapt en slecht eet en drinkt – dat zij desnoods wel permanent uit Duitsland naar Nederland wil komen. Haar echtgenoot schrikt hier zichtbaar van en pleit ervoor om het nog een periode aan te zien. Aanvankelijk reageert mevrouw B. nauwelijks op de behandeling, wel wordt het contact langzaam positiever zowel met de verpleging als op het spreekuur van de verpleeghuisarts. Patiënte laat zich overtuigen om citalopram in te nemen. Voor dit middel is gekozen vanwege het lage risico op bijwerkingen. Eten en drinken gaan beter en mevrouw komt vaker haar kamer uit; af en toe geniet ze van de positieve activiteiten. De GAS-scores lopen op naar niveau 3. Mevrouw B. wordt wel drukker en maakt hierbij een eufore indruk. Besloten wordt een stemmingstabilisator (natriumvalproaat) aan de medicatie toe te voegen. Geleidelijk, bij een oplopende dosering wordt mevrouw B. rustiger. Het lukt nu ook met haar over haar gedrag en gevoelens te praten. Een doorbraak is dat zij in het spreekuur spontaan aangeeft dat al die lichamelijke klachten die ze uit, staan voor haar verdriet over het overlijden van haar echtgenoot. Deze betekenisgeving wordt door de betrokken disciplines verder met haar uitgewerkt. Na verloop van tijd onderneemt ze ook met haar zoon en schoondochter activiteiten buiten de instelling. Op het moment dat de GAS-scores van de patiënt de doelscore benaderen wordt de derde/laatste fase van IRR gestart. De patiënt wordt functioneel getest door de ergotherapeut met behulp van de Assessment of Motor and Process Skills (AMPS).[25] Met behulp van dit internationaal geijkte instrument kan men het vermogen om zelfstandig zorgtaken te verrichten analyseren, rekening houdend met complexiteit van de opdracht en omgevingsfactoren. Deze test geeft hierbij inzicht in het vermogen tot procesmatig handelen. Met patiënt en mantelzorger wordt een rehabilitatieplan opgesteld gericht op de ontslagbestemming. Oriënterende bezoeken aan een zorgcentrum of geleidelijk op te voeren dagen/nachten naar huis worden geregeld. Met de mantelzorger(s) wordt nadrukkelijk gesproken over hoe de toekomst eruit kan zien en wat hun rol hierbij kan zijn. Bij het feitelijk ontslag, al dan niet na een wachtperiode wordt relevante informatie uitgewisseld met de hulpverleners van de ontslagbestemming.

Mevrouw B. gaat kijken in een zorgcentrum waar ook aanvullend enige psychiatrische begeleiding door de GGZ beschikbaar is. Zij vindt het een goed huis met een mooie kamer en stemt in met deze bestemming. De AMPS heeft inmiddels uitgewezen dat zorgcentrumzorg met psychiatrische begeleiding het best passend is voor mevrouw B. mede gelet op haar sociale kwetsbaarheid (mantelzorg ver weg wonend). Binnen de systeemtherapie is de positieve ontwikkeling doorgesproken, maar ook de verwachtingen over de toekomst. Wat te doen bij terugval, nieuwe aandoening, enzovoort. De zoon en zijn echtgenote zijn het erover eens dat zij niet terug naar Nederland zullen komen in dergelijke situaties en vooral op de beschikbare hulpverlening willen vertrouwen. Ook mevrouw B. geeft niet meer aan dat zij eigenlijk vindt dat haar zoon/schoondochter voor haar zouden moeten zorgen; nee, het is goed zo. Mevrouw B. houdt zich goed aan het rehabilitatieplan en kan binnenkort met ontslag.

DISCUSSIE

Revalidatie van kwetsbare ouderen lijdend aan multipele PFS'en in combinatie met aanpak van mantelzorgproblematiek is klinisch relevant en uitvoerbaar. Integratieve reactivering en rehabilitatie (IRR) is hiervoor een geschikt en beschikbaar programma. In een RCT is de effectiviteit van IRR vergeleken met gebruikelijke zorg. Gelet op de hoge prevalentie van multipele PFS'en bij kwetsbare ouderen, is bij gebleken effectiviteit brede beschikbaarheid binnen de verpleeghuiszorg wenselijk. De vraag dient zich hierbij aan of IRR betaalbaar is. Onderzoek naar de kosten-effectiviteit van IRR geeft aan dat de overall meerkosten geschat worden op maximaal € 50,- per dag per patiënt gedurende drie maanden. Dit is ongeveer de helft van de kosten voor CVA-revalidatie. Dit lijkt een maatschappelijk aanvaardbaar bedrag. Het lijkt gerechtvaardigd meer algemeen te concluderen dat het belangrijk is dat professionals en management werkzaam in de zorg voor kwetsbare ouderen zich nadrukkelijk meer bekwamen in kennis en kunde op het gebied van psychiatrie en psychotherapie in combinatie met doelgericht gebruik van psychofarmaca. Hierbij is het aan te bevelen apart aandacht te geven aan het belang van systeemtherapie voor de mantelzorg. Hetzelfde geldt voor de opleidingen van professionals. Een belangrijke vraag bij implementatie van IRR is wat de beste implementatiemethode is. Scholing alleen lijkt onvoldoende. Onderzoek hiernaar is aangewezen. Onze onderzoeksgroep heeft hiertoe een onderzoeksvoorstel geformuleerd. ∎

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Redactionele kanttekeningen bij het artikel 'Integratieve reactivering en rehabilitatie (IRR), een revalidatieprogramma voor kwetsbare ouderen, lijdend aan multipele psychiatrische functiestoornissen, en hun mantelzorgers'

Op de eerste versie van het artikel kwam uitvoerige kritiek van een vijftal referenten van zowel binnen als buiten de redactie. Binnen de redactie heerste er ook na beoordeling van derde en laatste versie van het artikel nog steeds verschil van mening over het al dan niet plaatsen van het artikel in het tijdschrift. De doorslag om wel tot publicatie over te gaan wordt gegeven door het feit dat Bakker en Van der Lee voor het toetsen van de effectiviteit van hun revalidatieprogramma via een RCT in de praktijk een door ZonMw gesubsidieerd onderzoek hebben uitgevoerd en tevens dat een aantal verpleeghuizen inmiddels de bereidheid heeft getoond om aan een implementatieonderzoek deel te nemen.

Samenvattend komt onze kritiek neer op het volgende:
- Het multidisciplinaire en integratieve karakter van het behandelprogramma staat blijkbaar centraal, maar de reden daarvan wordt met de gerefereerde literatuur onvoldoende wetenschappelijk onderbouwd.
- De IRR is in vergelijking met 'reguliere' psychogeriatrische zorg een ingewikkelde mix van diverse nogal uiteenlopende onderzoeks- en behandelingsinterventies met een groot aantal betrokken disciplines. Er wordt onvoldoende duidelijk beschreven wat ieders afzonderlijke bijdrage is, zowel inhoudelijk als qua geïnvesteerde tijd. De indruk wordt gewekt dat qua tijd en aandacht er aanzienlijk meer beschikbaar is dan in de 'reguliere' psychogeriatrische zorg mogelijk is. Het lijkt erop alsof met de IRR diverse verschillende interventies tegelijkertijd plaatsvinden, die binnen dit programma niet op hun eigenlijke en afzonderlijke werkzaamheid beoordeeld worden. Alleen de mogelijke uitkomst van de mix aan interventies is beoordeelbaar. Daarmee is de vraag of met het onderzoek wel de inhoud van de IRR als revalidatieprogramma beoordeeld wordt of dat het de (extra) geïnvesteerde tijd en aandacht los van de inhoud van het geboden betreft. En daarmee staat voor ons de wetenschappelijke kwaliteit van het programma nog steeds onvoldoende vast en dus ter discussie.
- Onder de kop 'discussie' van het artikel wordt aangegeven dat de meerkosten van IRR op maximaal 50 euro per oudere per dag geschat worden. Dat komt voor een traject van 3 maanden neer op maximaal 4550 euro per deelnemende oudere, hetgeen bij aangetoonde werkzaamheid een alleszins acceptabel bedrag lijkt. Nadere onderbouwing van deze kostenraming wordt echter niet gegeven. Als het wel klopt zullen – om de IRR geïmplementeerd te krijgen – wetenschappelijk degelijk onderbouwde en overtuigende resultaten van de IRR in vergelijking met andere psychogeriatrische begeleidings- en behandelingsmogelijkheden gepresenteerd moeten kunnen worden. Binnen de huidige ZZP-structuur lijkt toepassing van dit programma op financiële gronden niet of nauwelijks haalbaar.

De redactie

Supplement 2

De relatie van psychiatrische functiestoornissen met cognitie, activiteiten dagelijks leven (ADL) en biografische gegevens

Een replicatie-onderzoek op een polikliniek voor cognitieve functiestoornissen

T.J.E.M. Bakker[a], H.J. Duivenvoorden[b], J. van der Lee[c], M.W. Ribbe[d]

Psychiatric function disorders: association with cognitive function, activities of daily living and biographical data

Background: The prevalence of non-cognitive, psychiatric function disorders (PFD) in psychogeriatric patients, staying in a nursing home is high; it varies from 70 to 80%.

It has a negative impact on the quality of life and life-expectancy. It affects caregiver distress and is an important predictor of permanent admission to an institution. In addition the PFD has predictive potentialities for discharge from reactivation programmes and survival. Although there is a relationship between PFD (measured by NPI) and cognitive function disorders it has to be stated explicitly that from psychiatric point of view these two entities have to be distinguished. This distinction, already been studied by this research group, needed to be replicated in another population.

Objective is to estimate 1) to which degree the prevalence of PFD in psychogeriatric patients, referred to a policlinics for cognitive function disorders (Index condition), differs from community dwelling psychogeriatric patients at referral to clinical and transmural nursing home programmes (Reference condition); 2) to which degree PFD is associated with both cognitive function disorders, activities of daily living for the two conditions; 3) to which degree PFD is associated with relevant general details of the patient, particularly gender, age and marital status, for the two conditions.

Methods: In the Index condition particated patients aged ≥ 65 years suffering from cognitive function disorders (N=70) who were referred to a policlinic for cognitive function disorders who were suspected to suffer from psychiatric function disorders. For 35 patients of them complete data on NPI, MMSE en Barthel Index (BI) were available. In the Reference condition participated patients (age ≥ 65), who were referred to clinical and transmural nursing home programmes and who suffered from cognitive function disorders (MMSE ≤ 29) (N=487). For 385 patients of them all data on NPI, MMSE and BI were available.

Results: Of all patients 92% suffered from at least one NPI symptom; 82% from two or more. Depression, Apathy, Anxiety and Irritability had high prevalences in the two samples. Application of logistic regression analysis for the prediction of total as well as individual NPI-symptoms showed that the

prognostic potentialities of MMSE, BI and biographic data were very limited ($R^2 = 0.11$; max.). The non-metric princal component analysis and confirmatory factor analysis of NPI, MMSE and BI for the two samples, showed that MMSE and BI loaded highly on the dimension 'Cognition' and NPI on the dimension 'Psychiatric function disorders'. The dimensional structure of the two samples did not show significant differences.

Conclusion: The dimensional structure of the Index condition highly corresponded to the Reference condition; that is to say that the PFD appeared to be relatively independent of cognition and ADL. High prevalences of PFD (NPI), the broad variance of NPI-symptoms and the limited prognostic importance of MMSE, BI and general details for total NPI-score as well as individual NPI-symptoms were confirmed in both conditions. The dimension 'Psychiatric function disorder' was relative independent of the dimension 'Cognition'. As a result it is of clinical interest – in case of referral to clinical and transmural programmes – to distinguish the psychiatric dimension from the cognitive dimension.

Samenvatting

Probleemstelling: Psychiatrische functiestoornissen (PFS) hebben een negatief effect op de kwaliteit van leven van psychogeriatrische patiënten, op hun levensduur en op het mantelzorgsysteem. Ook zijn PFS voorspellers voor zowel permanente opname als voor de kans op ontslag. De prevalentie van PFS bij psychogeriatrische patiënten in een verpleeghuis ligt tussen 70 en 80%. In een eerder onderzoek werden relatief zwakke relaties gevonden tussen PFS en cognitieve functiestoornissen, zelfzorg-problemen en biografische gegevens. Dit onderzoek wordt hier gerepliceerd. De prevalentie van PFS is onderzocht bij psychogeriatrische patiënten die zich aanmeldden voor onderzoek op een polikliniek voor cognitieve functie-stoornissen.

Onderzoek en methode: In de Indexconditie participeerden 70 patiënten (leeftijd ≥ 65) met klachten over cognitief functioneren die verwezen werden naar een polikliniek voor cognitieve functiestoornissen in de regio Nieuwe Waterweg Noord en van wie vermoed werd dat zij leden aan aanmerkelijke psychiatrische functiestoornissen. Van 35 patiënten waren volledige data op NPI, MMSE en Barthel Index (BI) beschikbaar. In de Referentieconditie participeerden 487 patiënten (leeftijd ≥ 65) uit de regio Nieuwe Waterweg Noord, verwezen voor trans- of intramurale verpleeghuiszorg en van wie vermoed werd dat zij leden aan cognitieve functiestoornissen (MMSE ≤ 29). Van 385 patiënten waren alle data beschikbaar op NPI, MMSE en BI.

Resultaten: Van de patiënten had 92% minimaal 1 symptoom score of meer op de NPI; 82% had twee of meer symptomen. De NPI-symptomen Depressie, Apathie, Angst en Prikkelbaarheid toonden een hoge prevalentie in beide steekproeven. Logistische regressieanalyse liet zien dat MMSE, BI en biografische gegevens een geringe voorspellende waarde hadden voor zowel de totale NPI-score als voor afzonderlijke NPI-symptomen (R^2=0,11; max). Een niet-metrische principale componentenanalyse en een confirmatieve factoranalyse toonden aan dat de relaties tussen NPI, MMSE en BI in de twee steekproeven niet significant verschilden. MMSE en BI correleerden in de twee steekproeven met de dimensie 'Cognitie', en NPI met de dimensie 'Psychiatrische functiestoornis'.

Conclusie: In de Indexconditie (N=35) werden de bevindingen uit de Referentieconditie (N=385) bevestigd. Dit betrof de hoogte van de frequentie van PFS (NPI), de brede spreiding over de NPI-symptomen; de minimale

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prognostische rol van MMSE, BI en biografische gegevens voor zowel de totale NPI-score als de individuele NPI-symptomen. De PFS vormden ook in de Indexconditie een dimensie op zich. Met name bij verwijzing en indicatiestelling voor behandeling en zorg is het van belang een onderscheid te maken tussen de psychiatrische en de cognitieve dimensie.

Inleiding

Psychiatrische functiestoornissen spelen een belangrijke rol in de psychogeriatrie; veelal in het kader van dementie. Naast de voor dementie kenmerkende cognitieve functiestoornissen hebben psychiatrische functiestoornissen een negatief effect op de kwaliteit van leven van de psychogeriatrische patiënten en hun levensduur. Bovendien belasten zij ook het mantelzorgsysteem.[1-6] Verder zijn psychiatrische functiestoornissen voorspellers voor relatief vroege permanente opname in een instelling (veelal verpleeghuis) maar ook voor de kans op ontslag en de overlevingsduur in het kader van psychogeriatrische interventieprogramma's.[7-11] Voor het onderzoek van psychiatrische functiestoornissen (verder te noemen PFS) bij psychogeriatrische patiënten ontwikkelde Cummings et al. een valide en betrouwbaar meetinstrument, de Neuro-Psychiatric Inventory (NPI).[12] Dit instrument is reeds in vele studies gebruikt.[13-19] De Nederlandse versie is ontwikkeld en gevalideerd door Kat et al.[20]

Literatuuronderzoek laat zien dat de prevalenties van non-cognitieve, psychiatrische functiestoornissen (PFS) bij psychogeriatrische patiënten verblijvend in een verpleeghuis of zorgcentum fluctueren tussen 70% en 80%.[21-24] Aalten et al. rapporteerden dat van de patiënten die een geheugenpolikliniek bezochten, 90% aan PFS leed.[25] Bakker et al. vonden bij patiënten die zich voor verpleeghuiszorg aanmeldden (intra- of transmuraal) een percentage van 92.[13] De relatie tussen PFS - gemeten met de NPI - en de voor de psychogeriatrie kenmerkende cognitieve functiestoornissen en de eraan gerelateerde stoornissen in het verrichten van de activiteiten van het dagelijks leven (ADL) is evenwel niet zonder meer duidelijk.[13,16,26] Hetzelfde geldt voor de relatie tot relevante biografische gegevens zoals geslacht, leeftijd en burgerlijke staat. Bakker et al. vonden met betrekking tot deze gegevens maximaal een verklaarde variantie van 12% in een steekproef van patiënten die zich had aangemeld voor intra- of transmurale verpleeghuiszorg, in dit onderzoek verder de

Referentieconditie genoemd.[13] Een in het kader van dat onderzoek uitgevoerde structuuranalyse liet twee dimensies zien. Een 'cognitieve' dimensie, waarmee cognitieve functiestoornissen en ADL correleerden en een psychiatrische dimensie waarmee de NPI correleerde. Hiermee werd 83% van de variantie verklaard. De belangrijkste conclusie was dat de PFS relatief los staan van de cognitieve functiestoornissen en ADL en als zodanig dienen te worden onderscheiden en te worden behandeld vanuit het psychiatrisch perspectief.[13] Replicatie van dit onderzoek is van klinisch belang om meer zekerheid te verkrijgen over de geldigheid van de bevindingen.

Daartoe werd een Indexconditie onderzocht, waarin een verwante populatie participeerde, nl. patiënten in een beginfase van cognitieve functiestoornissen, die zich hadden aangemeld bij een Polikliniek voor Cognitieve Functiestoornissen (PCF), afdeling Neurologie Vlietland Ziekenhuis, locatie Vlaardingen.

Binnen het replicatieonderzoek werden de volgende onderzoeksvragen geformuleerd:
- In hoeverre verschilt de prevalentie van de psychiatrische functiestoornissen (PFS) bij psychogeriatrische patiënten die zich aanmelden voor onderzoek op de Polikliniek voor Cognitieve Functiestoornissen (de Indexconditie; N=35) met de Referentieconditie (N=385).
- In hoeverre zijn de PFS gerelateerd aan zowel de cognitieve functiestoornissen als de ADL in de twee onderscheiden steekproeven.
- In hoeverre is PFS gerelateerd aan relevante algemene patiëntkenmerken met name geslacht, leeftijd en burgerlijke staat in de twee onderscheiden steekproeven.

Verwacht wordt dat de gevonden relaties in de Indexconditie (N= 35) in hoge mate overeenkomen met de relaties gevonden in de Referentieconditie (N= 385).

Onderzoek en methode

In de Indexconditie participeerden patiënten (leeftijd ≥ 65) met klachten over cognitief functioneren (N=70) uit de regio Nieuwe Waterweg Noord (NWN) die verwezen werden naar de Polikliniek voor cognitieve functiestoornissen en van wie na een triage vermoed werd dat zij leden aan aanmerkelijke psychiatrische functiestoornissen (N=46). Van de 46 patiënten die aan de selectiecriteria voldeden waren van 35 patiënten de data beschikbaar op de NPI, Mini Mental State Examination (MMSE) en Barthel-index (BI). De patiënten werden verwezen door Riagg, huisarts of neuroloog.

In de Referentieconditie participeerden patiënten (leeftijd ≥ 65) uit de regio Nieuwe Waterweg Noord die verwezen werden naar transmurale en intramurale verpleeghuiszorg en van wie vermoed werd dat zij leden aan cognitieve functiestoornissen (MMSE ≤ 29) (N=487). Van de 487 patiënten die aan de selectiecriteria voldeden

waren er 385 patiënten van wie de data beschikbaar waren op de NPI, MMSE en BI.

Design

De designs van de twee steekproeven waren van een prospectief observationeel karakter. Het onderzoek werd uitgevoerd in de regio Nieuwe Waterweg Noord, vlakbij Rotterdam. Deze regio telt ongeveer 180.000 inwoners; 16% van hen is 65 jaar of ouder.

In de Indexconditie (N=35) liep de observatieperiode van september 2002 tot september 2003. De metingen werden uitgevoerd als onderdeel van het onderzoeksprotocol van de Polikliniek Cognitieve Functiestoornissen in het Vlietland Ziekenhuis afdeling Neurologie te Vlaardingen. In de PCF participeren het Vlietland Ziekenhuis, de Riagg RNW en Argos Zorggroep. In de Referentieconditie (N=385) liep de observatieperiode van juni 2001 tot oktober 2002. De metingen werden uitgevoerd als onderdeel van de aanmeldingsprocedure voor enige vorm van verpleeghuiszorg. De Referentieconditie maakte deel uit van een grotere studie betreffende een RCT met een parallelle groepsdesign naar de (kosten-)effectiviteit van psychogeriatrische reactivering.[13]

Assessment

In beide studies werden de volgende biografische gegevens van de patiënt vastgelegd: geslacht (vrouw code 1, man code 0), leeftijd (jaren), burgerlijke staat (samenwonend, code 1; alleen, code 0). De cognitieve functionele status van de patiënt werd gemeten met de MMSE, range 0-30; 30 is normaal.[27] De activiteiten van het dagelijks leven (ADL) werden gemeten met de BI range 0-20; 20 is normaal.[28] Zowel MMSE als BI zijn gerenommeerde meetinstrumenten in de psychogeriatrie. Voor het meten van de PFS is de NPI gebruikt, range 0-12; 0 is afwezigheid van symptomen.[12] Op elke NPI symptoom scoorde de patiënt een 1 wanneer hij/zij dat gedrag minimaal eenmaal per week gedurende de laatste vier weken had vertoond. In beide studies waren de professionals getraind in het toepassen van de meetinstrumenten.

Statistische analyses

Voor de categorale data werd het percentage gebruikt als maat voor centrale tendentie, terwijl voor de continue data het gemiddelde werd berekend. De standaarddeviatie werd gebruikt als maat voor de spreiding van de continue data. Gedichotomiseerde variabelen werden getoetst met de Fisher's Exact test. Een t-test voor twee onafhankelijke steekproeven werd toegepast voor continue data, cq. voor als continue beschouwde data. Mann-Whitney U-test voor ongepaarde steekproeven werd gebruikt voor het toetsen van verschillen tussen twee onafhanke-

lijke groepen op continue data. Indien meer dan één voorspeller en/of confounder variabele werd gebruikt, werd de multiple lineaire regressieanalyse toegepast in geval van continue uitkomstvariabelen en een logistische regressieanalyse in geval van binaire uitkomstvariabelen.

In geval van de methode van multipele lineaire regressieanalyse werd de gestandaardiseerde regressiecoëfficiënt van de individuele variabele gebruikt als maat van relatieve importantie, terwijl ook de ongestandaardiseerde regressiecoëfficiënt wordt vermeld. In geval van logistische regressieanalyse werd de odds-ratio van de individuele variabele gebruikt als maat van relatieve importantie. De 95% betrouwbaarheidsintervallen van zowel de ongestandaardiseerde regressiecoëfficiënten en de odds-ratio's van de individuele voorspellervariabelen worden vermeld ten einde zicht te krijgen op de onbetrouwbaarheidsmarges.

De gekwadrateerde multipele correlatiecoëfficiënt (R^2) en de Nagelkerke R^2 [29] zijn statistische maten, gebruikt om de mate van variantie verklaard door de lineaire respectievelijk logistische modellen te kwantificeren. Beide maten voor R^2 variëren theoretisch tussen 0,0 (hoegenaamd geen enkel voorspellend vermogen) en 1,00 (perfect voorspellend vermogen). Alle statistische toetsingen werden gedaan op 0,05 (tweezijdig).

De structuur van de interrelaties van MMSE, BI en NPI werden onderzocht met behulp van de methode van niet-metrische principale componentenanalyse. Het computeralgoritme is genaamd 'PRINCALS'.[30-32] Deze methode maakt het ook mogelijk om de verschillen (van categorieën) van determinanten te kwantificeren en te visualiseren. Het totaalpercentage verklaarde variantie werd beschouwd als de algehele maat van de adequaatheid van het model. De componentladingen van de individuele variabelen zijn indicatief voor de mate waarin zij adequaat in de structuur worden gerepresenteerd.

Vervolgens is getoetst of de tweedimensionale factorstructuren met elkaar overeenkomen, daargelaten de random fluctuatie die immer optreedt. Daartoe werd gebruik gemaakt van de volgende performance maten: 1. X^2-toets (inclusief p-waarden), deze p-waarden dienen bij voorkeur niet significant te zijn, 2. Confirmatory Fit Index (CFI, idealiter: 1,0), 3. Tucker-Lewis Index (TLI, idealiter: 1,0) en 4. wortel uit gemiddelde kwadraten van de residuals (SRMR) hoe dichter bij 0,00 hoe beter.

Resultaten

Kenmerken van beide steekproeven

Van de 35 patiënten van de Indexconditie was 45,7% vrouw en 54,3% man (Tabel 1). De gemiddelde leeftijd van de vrouwen was 75,3 en van de mannen 74,6 (P = 0,90). Van de vrouwen leefde

Tabel 1	Biografische gegevens, MMSE, NPI and Barthel-index, onderscheiden naar geslacht in index-conditie (n = 35).				
	indexconditie (n = 35)				
	mannen (n = 19)	*vrouwen (n = 16)*	*totaal*	*toetsings-grootheid*	*P-waarden (tweezijdig)*
leeftijd (in jaren) gemiddelde (s)	74,6 (9,6)	75,3 (8,1)	74,9 (8,8)	z = -0,13	0,91[1]
burgerlijke staat samenwonend (%)	77,8	62,5	71,4		0,46[2]
NPI (0-12) gemiddelde (s)	5,4 (2,7)	6,8 (2,7)	6,0 (2,7)	z = -1,60	0,12[1]
> 1 score	100,0	100,0	100,0		1,00[2]
> 2 scores	94,7	100,0	97,1		1,00[2]
MMSE (0-30) gemiddelde (s)	21,8 (5,4)	20,4 (5,6)	21,2 (5,5)	z = 0,63	0,55[1]
Barthel-index (0-20) gemiddelde (s)	18,5 (3,7)	18,6 (1,9)	18,5 (3,0)	z = - 1,43	0,23[1]

[1] Mann-Whitney U-test voor ongepaarde steekproeven; p-waarden (exact; tweezijdig)
[2] Fisher's exact (df = 1); tweezijdig

Tabel 2	Biografische gegevens, MMSE, NPI en Barthel-index, onderscheiden naar geslacht in referentieconditie (n = 385).				
	referentieconditie (n = 385)				
	mannen (n = 124)	*vrouwen (n = 261)*	*totaal*	*toetsings grootheid*	*P-waarden (tweezijdig)*
leeftijd (in jaren) gemiddelde (s)	79,7 (7,5)	82,5 (6,6)	81,6 (7,0)	z = -3,43	0,001[1]
burgerlijke staat samenwonend (%)	65,8	27,1	39,7		0,001[2]
NPI (0-12) gemiddelde (s)	3,5 (2,2)	3,7 (2,4)	3,6 (2,3)	z =-0,47	0,64[1]
> 1 score	92,3	90,3	91,7		0,56[2]
> 2 scores	80,8	83,1	81,6		0,67[2]
MMSE (0-30) gemiddelde (s)	18,4 (6,3)	17,0 (5,7)	17,4 (5,9)	z = 0,74	0,003[1]
Barthel-Index (0-20) gemiddelde (s)	15,1 (4,6)	13,7 (5,5)	14,8 (5,3)	z = 2,16	0,03[1]

[1] Mann-Whitney U-test voor ongepaarde steekproeven; tweezijdig.
[2] Fisher's exact (df = 1); tweezijdig.

62,5% samen, van de mannen 77,8% (P = 0,46). Wat betreft MMSE en BI was er geen significant verschil tussen vrouwen en mannen. (P = 0,55, resp. P = 0,23). Ook op de NPI was er geen significant geslachtsverschil (P = 0,12). Tabel 1 laat verder zien dat van de patiënten 100% minimaal één symptoom op de NPI had; 97,1% had twee of meer symptomen. De symptomen Depressie (77,1%), Angst (77,1%), Prikkelbaarheid (65,7%), Doelloos repetitief gedrag (62,9%) en Apathie (57,1%) toonden een hoge prevalentie (Tabel 3). Slechts op één NPI symptoom was er sprake van een significant verschil tussen vrouwen en mannen, namelijk eetgedragveranderingen (P < 0,05). Nachtelijke onrust was marginaal significant (P = 0,07); relatief veel vrouwen hadden eetgedragsveranderingen en nachtelijke onrust (niet weergegeven).

Van de 385 patiënten van de Referentieconditie was 67,8% vrouw en 32,2% man (Tabel 2). De gemiddelde leeftijd van de vrouwen was 82,5 en

van de mannen 79,7. Van de vrouw leeft 27,1% samen, van de mannen 65,8% (P= 0,001). Wat betreft MMSE was er een significant verschil tussen vrouwen en mannen (p=0,003); dit gold eveneens voor BI (P= 0,03). Op de NPI was er geen significant geslachtsverschil. Tabel 2 laat zien dat 91,7% van de patiënten minimaal één symptoom op de NPI had; 81,6% had twee of meer symptomen.

De NPI-symptomen Depressie (43,9%), Apathie (43,1%), Angst (41,6%) en Prikkelbaarheid (36,9%) toonden een hoge prevalentie (Tabel 3). Op vier individuele NPI symptomen was er sprake van een significant verschil tussen mannen en vrouwen, te weten Wanen, Hallucinaties, Agressie en Angst (bij vrouwen vaker dan bij mannen) (niet weergegeven).

Bij de patiënten uit de Indexconditie (PCF) was er sprake van een hoger percentage psychiatrische functiestoornissen (100% 1 of meer; 97,1% 2 of meer bij een gemiddelde van 6 symptomen)

Tabel 3	Vergelijking index- en referentieconditie op MMSE, Barthel-index en NPI-symptomen.			
	indexconditie n = 35	referentieconditie n = 385	toetsingsgroot-heid	p-waarde
totaal scores [1]				
MMSE	21,17	17,54	t = 3,75	0,001[1]
Barthel-Index	18,51	14,17	t = 7,56	0,000
NPI-score	6,03	3,63	t = 5,04	0,000
NPI-symptomen [2]	%	%		
wanen	45,7	22,6		0,01[2]
hallucinaties	28,6	21,6		0,41
agitatie/agressie	45,7	31,2		0,19
depressie	77,1	43,9		0,001
angst	77,1	41,6		0,001
euforie	14,3	3,9		0,03
apathie	57,1	43,1		0,29
ontremd gedrag	54,3	17,7		0,001
prikkelbaarheid	65,7	36,9		0,004
doelloos repetitief gedrag	62,9	22,1		0,001
nacht. onrust	31,8	23,6		0,42
eetgedragverandering	42,9	36,1		0,59

[1] t-toets voor ongepaarde steekproeven; tweezijdig
[2] Fisher's exact (df = 1); tweezijdig

dan bij de Referentieconditie. In de Index-
conditie hadden alle patiënten minstens één
symptoom op de NPI, terwijl dit in de
Referentieconditie voor 91,7% gold. Dit verschil
in NPI-score was marginaal significant (p=0,10).
In geval van minstens twee symptomen op de
NPI bleken de twee condities significant van el-
kaar te verschillen (p =0,02), resp. 97,1% en 81,6%
(Zie Tabellen 1 en 2). Wat betreft de NPI totaal-
score (zie Tabel 3) was er eveneens sprake van een
significant verschil (6,03 resp. 3,63; p=0,000); ten
nadele van de Indexconditie. Op MMSE en BI
scoorde de Indexconditie significant hoger dan
de Referentieconditie (resp. p=0,001 en p=0,000);
ten gunste van de Indexconditie. Verder waren
op 7 van de 12 NPI-symptomen de percentages
significant hoger (ongunstiger) in de index-
conditie. De gevonden hoge prevalenties van
PFS zijn geheel in lijn met de literatuur.[5,20,23-25]

Prognostiek van de totale NPI-score van beide steekproeven

Allereerst werd, om de prognostische relaties
van de MMSE en BI tot de NPI te verkennen, de
totale score van de NPI van de twee steekproeven
gezamenlijk in één regressiemodel ingevoerd;
gecombineerd met de algemene kenmerken ge-
slacht en leeftijd. Om de verschillen tussen de
twee steekproeven te toetsen werden tevens het
type conditie en de interactie van type conditie

met geslacht en leeftijd in het model ingevoerd
(Tabel 4). De drie significante variabelen in het
model waren leeftijd (p < 0,03), MMSE (p < 0,00)
en type conditie (P < 0,00). De verklaarde varian-
tie van het model was laag (R^2 = 0,08).

Prognostiek van de afzonderlijke NPI symptomen van beide steekproeven

Om de prognostische relaties van MMSE en BI
tot de individuele NPI symptomen te analyseren
werden afzonderlijke regressieanalyses met de
data van beide steekproeven gezamenlijk uitge-
voerd voor elk NPI symptoom apart (Tabel 5).
Dit werd tevens gedaan voor de biografische ge-
gevens van de patiënt. Om de verschillen tussen
de twee steekproeven te toetsen werden tevens
het type conditie en de interactie van het type
conditie met geslacht en leeftijd als co-
variabelen in het model ingevoerd. In verband
met de overzichtelijkheid wordt alleen de Nagel-
kerke R^2 als maat voor de verklaarde variantie
van het model gepresenteerd (Tabel 5). De ver-
klaarde varanties waren laag; van 0,01 minimaal
tot 0,11 maximaal. Verder bleek dat bij niet één
NPI symptoom de toegevoegde interactie ter-
men significante waarden bereikten. Dit bete-
kent dat er tussen de twee steekproeven geen
significante verschillen waren in de prognostiek
van de individuele NPI-symptomen.

Tabel 4	Regressieanalyse van totale NPI-score op MMSE, Barthel-index en biografische gegevens, groepseffecten en effectmodificatie.			
	B'	p-waarde	95% betrouwbaarheidsinterval	
geslacht [3]	0,14	0,60	-0,37	0,65
leeftijd	-0,02	0,03	0,03	-0,00
MMSE	-0,07	0,00	-0,11	-0,02
Barthel-index	0,01	0,77	-0,04	0,05
type conditie [4]	2,40	0,00	1,11	3,62
type conditie x geslacht	1,10	0,20	-0,55	2,71
type conditie x leeftijd	0,06	0,22	-0,03	0,15
R-Squared (change)[2] = 0.08				

[1] ongestandaardiseerde regressiecoëfficiënten
[2] verklaarde variantie van de variabelen gezamenlijk
[3] geslacht gecodeerd als: man = 0 en vrouw = 1
[4] type conditie: referentieconditie = 0 (n = 385) en indexconditie = 1 (n = 35)

Tabel 5	Prevalentie van NPI-symptomen in twee groepen patiënten; index- vs. referentieconditie, invloed van geslacht, leeftijd, MMSE, BI en groep.				
	index conditie n = 35	referentie conditie n = 385	$R^{2\,1}$	$R^{2\,2}$	$R^{2\,3}$
NPI-symptomen	%	%			
wanen	45,7	22,6	0,07	0,09	0,09
hallucinaties	28,6	21,6	0,09	0,09	0,10
agitatie/agressie	45,7	31,2	0,04	0,04	0,04
depressie	77,1	43,9	0,01	0,05	0,06
angst	77,1	41,6	0,04	0,09	0,09
euforie	14,3	3,9	0,04	0,08	0,09
apathie	57,1	43,1	0,03	0,03	0,03
ontremd gedrag	54,3	17,7	0,03	0,09	0,09
prikkelbaarheid	65,7	36,9	0,02	0,04	0,04
doelloos repetitief gedrag	62,9	22,1	0,03	0,10	0,11
nacht. onrust	31,8	23,6	0,03	0,04	0,05
eetgedragverandering	42,9	36,1	0,01	0,02	0,03

[1] Nagelkerke R^2 (verklaarde variantie); covariabelen: geslacht, leeftijd, MMSE en BI

[2] Nagelkerke R^2 (verklaarde variantie); covariabelen: geslacht, leeftijd, MMSE, BI en type conditie

[3] Nagelkerke R^2 (verklaarde variantie); covariabelen: geslacht, leeftijd, type conditie, geslacht x type conditie en leeftijd x type conditie

Niet-metrische principale componentenanalyse

Aangezien de data van de variabelen niet van duidelijk metrisch niveau zijn en het bovendien niet uitgesloten is dat er sprake is van non-lineaire samenhang tussen de variabelen, is gekozen voor de niet-metrische benadering van de Principale Componenten Analyse[30-32].

Om inzicht te krijgen in de structuur van de relaties tussen NPI, MMSE en BI werd voor de twee steekproeven een niet-metrische principale componentenanalyse uitgevoerd (Figuren 1A en 1B). MMSE en BI correleerden in de twee steekproeven met 'Cognitie' (Dimensie 1) en NPI met 'Psychiatrische functiestoornis' (Dimensie 2). De modelfit was goed, blijkend uit de verklaarde variantie van 83% in de Referentieconditie (N= 385) en 78% in de Indexconditie (N= 35). Om te toetsen of de structuur van de Indexconditie (N= 35) overeenkwam met die van de Referentieconditie (N= 385) werd een toetsende analyse uitgevoerd. X^2-toets voor modelfit leverde een waarde op van 4,62 (df=3) en de erbij behorende p-waarde was 0,20. CFI bedroeg 0,97 en TLI 0,93; SRMR was gelijk aan 0,03. De conclusie lijkt gerechtvaardigd dat de tweedimensionale factorstructuur van de Referentieconditie niet significant verschilde van de Indexconditie; de structuren van de twee condities kwamen vrijwel overeen.
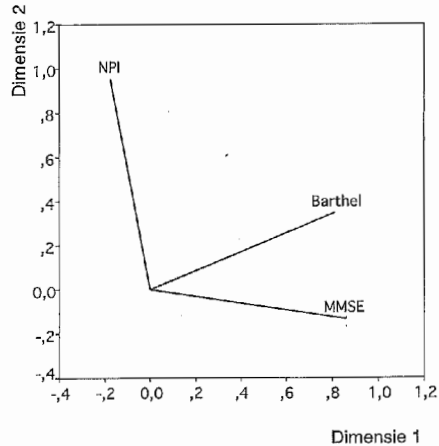
Discussie

Het prognostisch model voor de steekproeven tezamen voor de total NPI-score bevatte drie significante variabelen (leeftijd, MMSE en type conditie), maar de verklaarde variantie was laag (R^2 = 0,08). Ook voor de individuele prognostische modellen van de NPI-symptomen werden slechts lage verklarende varanties gevonden (Nagelkerke R^2: min. 0,01, max 0,11). Hierbij had geen van de interactie termen betreffende type conditie noch gecombineerd met leeftijd noch met geslacht een significante waarde. Qua prognostische modellering voor de NPI score als totaal noch voor individuele NPI-symptomen was er sprake van significante verschillen tussen de twee steekproeven, hoewel de hoogte van de scores op NPI, MMSE en BI duidelijk verschilden.
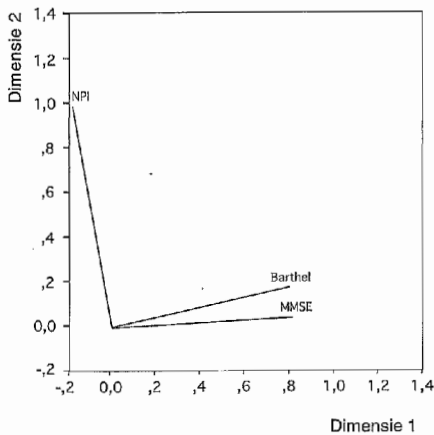
De gepresenteerde patroonanalyses bevestigden deze bevindingen met verklaarde varianties van 78% en 83%. De NPI vormde een dimensie op zichzelf.

Tussen de Indexconditie (N=35) betreffende polikliniekpatiënten en de Referentieconditie (N=385) betreffende patiënten aangemeld voor intra-/transmurale verpleeghuiszorg was er sprake van wezenlijke verschillen. De scores op de NPI waren in de Indexconditie hoger dan in de Referentieconditie. Verder waren de patiënten jonger, waren er meer mannen; de patiënten waren cognitief beter. Hetzelfde gold voor de zelfzorg. Ondanks deze verschillen en de beperkte omvang van de steekproef van de Indexconditie (N=35) werd dezelfde structuur aangetroffen tussen de NPI en de MMSE, BI. De psychiatrische functiestoornissen, gemeten met de NPI vormden ook hier een dimensie op zichzelf; ADL en MMSE vormden tezamen een cognitieve dimensie. Deze bevinding lijkt van groot belang voor de inrichting van de psychogeriatrische behandeling en zorg. Immers de PFS komen vaak voor en hebben een grote impact op de kwaliteit van leven van de patiënt zelf; ze bepalen het opnamerisico en de overlevingsduur. Verder belasten zij de mantelzorger in hoge mate.[1-3,6-8,16,25,33] In andere studies zijn ook aanwijzingen te vinden voor dit onderscheid tussen PFS en cognitieve kenmerken en biografische gegevens. Tran et al. vonden dat de NPI-symptomen meer bijdroegen aan stress bij mantelzorgers en professionals, terwijl de cognitieve status geen significante voorspeller voor stress was.[26] Wood et al. vonden eenzelfde relatie tussen de ernst van de gedragsproblemen en stress bij mantelzorgers, maar niet voor cognitieve status en evenmin geslacht.[19] Ook Aalten et al. (2005b) vonden geen significante prognostische relaties tussen het beloop van neuropsychiatrische symptomen (gemeten met NPI) en leeftijd, geslacht en sociaal economische status.[15] Alleen tussen psychose, een half jaar na baseline gemeten en milde cognitieve stoornissen (MMSE > 20) werd een significant verband gevonden. In de studie wordt de verklaarde variantie niet gegeven. Overigens, alle studies geven hoge prevalentiepercentages van het hebben en/of ontwikkelen van PFS bij psychogeriatrische patiënten lijdend aan cognitieve functiestoornissen, veelal in het kader van een vorm van dementie. De resultaten van onze studie (vergelijkings- en Indexconditie) onderbouwen de conclusies van de IPA European Regional meeting in Geneve (2003), namelijk dat na jaren van relatieve verwaarlozing de psychiatrische aspecten van de psychogeriatrie meer wetenschappelijke aandacht behoeven, niet alleen wat betreft diagnostiek maar ook wat betreft psycho-therapeutische mogelijkheden. Naast belevingsgerichte zorg, warme zorg, kleinschalig wonen en ondersteuning van mantelzorgers is er een dringende behoefte aan psychiatrische/ psychotherapeutische methodiek, toegesneden op de PFS van psychogeriatrische patiënten.[34] Alle professionals in intra-/transmurale settings behoren in de psychiatrische/psychotherapeutische methodiek opgeleid te zijn/ worden. Immers, literatuurstudie laat zien dat in verpleeghuizen alleen al zo'n 50% van de voorgeschreven psychofarmaca niet in overeenstemming is met de actuele psychiatrische beelden.[21,23,35] Daarnaast is de werkzaamheid van psychofarmaca omstreden in de psychogeriatrie; er worden namelijk veel bijwerkingen geconstateerd, ook bij de nieuwe 'atypische' antipsychotica. Psychotherapeutische interventies zijn meer dan welkom. Verder lijkt ook de rol van de mantelzorger – hoe deze zelf gewend is om te gaan met de gedragsproblemen van de patiënt – van forse invloed op een mogelijke op-

name.[16] In de literatuur bestaan indicaties voor positieve effecten van aangepaste vormen van psychotherapeutische interventies, met name voor depressie en angst.[9-11,33,36-39] In de uitgevoerde randomized controlled trial (RCT) naar (kosten-)effectiviteit van psychogeriatrische reactivering is het interventieprogramma met name toegesneden op de PFS vanuit een psychiatrisch/ psychotherapeutisch perspectief.

Conclusies

De validering van een eerder uitgevoerde studie (Referentieconditie) door middel van een vervolgonderzoek onder poliklinische patiënten (Indexconditie) was op de belangrijkste punten positief. Bevestigd werden de hoogte van de frequentie van PFS zoals gemeten met de NPI; een brede spreiding over de NPI-symptomen; een minimale prognostische rol van MMSE; BI en biografische gegevens zowel voor de totale NPI-score als individuele NPI-symptomen. De PFS vormden een dimensie ('Psychiatrische functiestoornis') op zichzelf. Hetzelfde gold voor cognitie en ADL 'cognitie' tezamen. In geval van verwijzing, i.c. indicatiestelling en behandeling/ zorg is het derhalve van belang te denken en te handelen in termen van dimensies i.p.v. categorieën nl. de psychiatrische en de cognitieve dimensies. De relatieve onafhankelijkheid van PFS van de cognitieve functiestoornissen en de hoge frequentie van voorkomen evenals de grote impact van PFS op de patiënt zelf alsmede op de mantelzorger geven hoge urgentie aan de ontwikkeling van en het onderzoek naar psychiatrische/psychotherapeutische en psychofarmacologische interventies toegesneden op de psychogeriatrie.

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