Quality of life, care dependency and Paracetamol In advanced Dementia: is paracetamol the panacea to improve quality of life?
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Citation
Dam, P. H. van. (2023, September 6). Quality of life, care dependency and Paracetamol In advanced Dementia: is paracetamol the panacea to improve quality of life?. Retrieved from http://hdl.handle.net/1887.1/item:3638611

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Note: To cite this publication please use the final published version (if applicable).
Chapter 7

General Discussion
The aim of this thesis is to explore the characteristics and quality of life (QoL) of persons with advanced dementia living in long-term care facilities (LTCF) with and without pain medication, the association between QoL, pain and use of pain medication, and to study the effect of paracetamol on QoL, discomfort, pain, neuropsychiatric symptoms, care dependency and daily functioning in persons with advanced dementia living in LTCF. This chapter describes the main findings, the interpretation and critical discussion of findings and methodology, implications for practice and education, and recommendations for future research.

### 7.1 SUMMARY OF MAIN FINDINGS

**Part I – Quality of life and pain medication in dementia**

Part I in this thesis answers questions regarding the difference in characteristics and in QoL between persons with and without pain medication, the association between QoL, pain and use of pain medication (paracetamol, opioids, both paracetamol and opioids, or no pain medication), and the effect of regularly scheduled administration of paracetamol on QoL, discomfort, pain and neuropsychiatric symptoms in persons with advanced dementia living in LTCF.

The differences in characteristics and in QoL between persons with and without pain medication are described in Chapter 2. Cross-sectional data of the Communication, Systematic Assessment and Treatment of Pain, Medication Review, Occupational Therapy, and Safety (COSMOS) study - a multicenter, cluster randomized effectiveness-implementation clinical hybrid trial in 67 Norwegian LTCF clusters - were analyzed. Chapter 2 shows that persons with advanced dementia living in LTCF who used pain medication had 1) more advanced dementia (Functional Assessment Stage 7), 2) pain scores more than twice as high, 3) significantly worse daily functioning, 4) more depressive symptoms, and 5) more neuropsychiatric symptoms, compared with persons who did not use any pain medication. The QoL measured by the QUALIDEM-6D, the short 18-item 6-domain version of the QUALIDEM2,3 specifically for persons with advanced dementia, was significantly lower in persons who used pain medication compared with persons who did not use any pain medication, except for the domain ‘social relationships’.

The association between QoL, pain and use of pain medication (paracetamol, opioids, both paracetamol and opioids, or no pain medication) in persons with advanced dementia living in LTCF was also described in Chapter 2. The cross-sectional data of the COSMOS study showed that the group of persons with advanced dementia living in LTCF with clinically relevant pain (Mobilization-Observation-Behavior-Intensity-Dementia-2 [MOBID-2] total score ≥3) who did not use any pain medication daily had better overall QoL compared with persons who used paracetamol, opioids, or both paracetamol and opioids. In the group that used only paracetamol, the persons who were still in pain had a significantly lower QoL compared with persons with-
out pain. In the other three groups (no pain medication, opioids, and both paracetamol and opioids) no significant differences in overall QoL were seen between persons with and without pain. Because only the paracetamol group showed differences in QoL between persons with and without pain, the association between paracetamol use and QoL was estimated using linear mixed-effects models adjusting for confounding variables and interaction between paracetamol and opioids. No significant association was found between paracetamol use and overall QoL, or between paracetamol use and the 6 domains of the QUALIDEM.

Chapter 3 describes the protocol of the Quality of life and Paracetamol In advanced Dementia (Q-PID) study. This study was a randomized double-blind placebo-controlled crossover trial in 95 persons with advanced dementia living in LTCF across the west of the Netherlands. All participating organizations were members of the University Network for the Care sector South Holland (UNC-ZH). Only persons with low QoL (QUALIDEM-6D ≤70, the median QUALIDEM-6D total score in a general population of persons with dementia living in LTCF in the Netherlands in the STA-OP! study) could participate in the study. Pain was not assessed prior to the study.

The effects of regularly scheduled administration of paracetamol on QoL, discomfort, pain and neuropsychiatric symptoms, as found in the Q-PID study, are described in Chapter 4. After conducting the study, repeated linear mixed models showed that paracetamol, compared to placebo, did not have a positive effect on QoL, discomfort, pain or neuropsychiatric symptoms. However, there were participants who clearly derived benefit from paracetamol during and after the study, according to their nursing staff. Although, on average, baseline pain scores on the Mobilization-Observation-Behaviour-Intensity-Dementia-2 (MOBID-2) pain scale in both treatment groups were lower than the score of ≥ 3 that is considered clinically relevant pain, more than 30% of the total group had a MOBID-2 pain score of ≥ 3 at baseline and did not use any pain medication (as this was an exclusion criterion). Data of the Q-PID study on the QoL revealed significant order – and period effects, which had consequences for the analyses and provided more food for thoughts regarding the design of the study. This subject will be elaborated on in the critical discussion (paragraph 7.2).

Part II – Care dependency, daily functioning, pain medication and QoL

Part II describes the effect of regularly scheduled administration of paracetamol on care dependency and daily functioning, and how care dependent persons with advanced dementia and low QoL living in LTCF are.

After adjusting for period and order effects, and psychotropic medication use, no effect of scheduled administration of paracetamol, compared to placebo, was found on care dependency
and daily functioning in a group of 95 persons with advanced dementia with low QoL living in LTCF. This was shown in the Q-PID study and is described in Chapter 5.

Cross-sectional data of the Q-PID study (baseline) were used to describe how care dependent the participants in the Q-PID study were and which factors were associated with care dependency and daily functioning (Chapter 6). The mean Care Dependency Scale (CDS) score was 37.8 (standard deviation 12.9). Almost 80% of the total group of persons with advanced dementia living in LTCF were completely or to a great extent dependent on care provided by professional caregivers. Most care dependency, i.e., to a great extent or completely care dependent, was seen in learning ability (66.3%), eating and drinking (61.2%) and performing activities (59.3%). The items on which the population was least care dependent, i.e., to a great extent or completely independent, were communication (60.5%), maintaining body posture (58.1%) and mobility (48.8%).

Five variables were associated with care dependency in the univariate linear regression models, as described in Chapter 6: dementia severity (Global Deterioration Scale [GDS] 7), and QUALIDEM-6D domains positive affect, restless/tense behavior, social relationships, and social isolation. The multivariate linear regression model, which consisted of these five variables plus age and sex, showed that dementia severity (GDS 7) and the QUALIDEM-6D domain social relationships were independently associated with care dependency, i.e., the care dependency of persons with very severe dementia (GDS 7) was much higher compared to persons with moderate to severe dementia (GDS 5 and 6), and better social relationships according to the QUALIDEM-6D domain social relationships were associated with less care dependency. Three variables were associated with daily functioning in the univariate linear regression models, i.e., dementia severity (GDS 7), and the QUALIDEM-6D domains positive affect and social relationships. The multivariate regression model was performed with these three variables plus age and sex, and showed that dementia severity (GDS 7) and the QUALIDEM-6D domain social relationships were independently associated with daily functioning - meaning worse daily functioning when having most severe dementia (GDS 7) compared to persons with moderate to severe dementia (GDS 5 and 6) - and better social relationships according to the QUALIDEM-6D domain social relationships was associated with better daily functioning.

7.2 INTERPRETATION AND CRITICAL DISCUSSION OF FINDINGS AND METHODOLOGY

Course and interpretation of QoL in persons with dementia

QoL is determined by many factors and comprises a persons’ values and principles, which are different for each individual. Despite the complexity of QoL, and given the absence of a cure for
dementia, it has become increasingly important to measure QoL as a means of evaluating care and to understand the needs of the person being cared for. The QoL may remain stable over time when measured longitudinally, even when the dementia progresses, as different studies found over a period of 12 to 24 months. This would mean that QoL is generally not expected to change without intervention over the course of 13 weeks, which was the study period in the Q-PID study, in persons with (advanced) dementia. Nevertheless, we found a strong period effect in the second period compared to the first period of the Q-PID study, i.e., the average QoL of all participants was lower in the second period compared to the first study period of six weeks.

**QoL assessment instruments in persons with advanced dementia**

Several studies have reported on the differences in QoL when rated by a proxy (nursing staff and/or relatives) or by a person with dementia himself. When measured by proxy, QoL was rated lower in persons in the most advanced stage of dementia. Moreover, in proxy assessments, QoL was rated lower compared to self-assessment. Agitation, apathy, and caregiver distress were negatively associated factors when rated by proxies, while care dependency, anxiety and depressive symptoms were negatively associated with QoL in self-assessments.

To assess QoL in persons with advanced dementia living in LTCF by nursing staff, the QUALIDEM instrument was chosen throughout the different chapters of this thesis. As a person with advanced dementia is not always able to understand and answer assessment questions, proxy ratings are necessary, but these are subjective because of the proxies’ own values and opinions. The subjective nature of QoL has resulted in a large amount of assessment instruments, which were not all developed and evaluated for use in LTCF. However, to assess and evaluate care in LTCF, the best available option is to measure QoL of the person with dementia being cared for with the existing QoL instruments.

The QUALIDEM, an observational instrument for QoL measured by nursing staff that is based on the adaptation-coping model of Droës, was chosen in the different studies in this thesis. It has the widest set of measurement properties reported with satisfactory test-retest and inter-observer reliability, and content and construct validity, and was therefore the recommended observational instrument for assessing QoL in LTCF residents with dementia by Aspden et al. Also, the usability of different QoL instruments was assessed recently in a systematic review by Hughes et al. Again, the QUALIDEM instrument, together with the QUALID instrument, had the best psychometric evidence, with QUALIDEM having better ratings for most of the assessed items. Moreover, QUALIDEM was rated as the most accessible. Nevertheless, none of the existing assessment instruments for QoL, including QUALIDEM, take into account all the
individual values of the person with dementia, contain appropriate questions or have mixed self and proxy-rated assessments to complement each other.\textsuperscript{18,20}

**Versions of the Dutch QUALIDEM**

To date, the QUALIDEM is used in three versions: the original 37-item version, the shorter 18-item version especially for persons with very advanced dementia\textsuperscript{2}, and an even shorter 8-item version that was established in 2020.\textsuperscript{21} In the different studies of this thesis, we chose to use the 18-item version, since persons with very advanced dementia were included in all our studies and all participants needed to be assessed in the same way to obtain comparable scores. The 8-item version was not yet available when our studies were designed and conducted. However, it comprises some questions that are not applicable to persons with very advanced dementia, so it would not have been useful for evaluation purposes in the population in our studies.

**Calculation of scores of the QUALIDEM instrument**

Originally, the QUALIDEM 18-item instrument consists of 6 domains (care relationship, positive affect, negative affect, restless tense behavior, social relations, and social isolation) that are scored 0 to 3 points per item. Each domain contains a different number of items, so maximum domain scores range from 6 to 12 points. A total score of 0 to 54 can be obtained and higher scores mean higher QoL. As each domain has a different number of items and thus different total scores, the domains could not be easily compared within and between persons. This is why we recalculated each item score to a percentage of the total achievable points for the item. We then had scores between 0 (lowest QoL) to 100 (highest QoL) for each item. Domain scores were calculated by adding up the items scores and dividing this by the number of items in the domain. Subsequently, the QUALIDEM-6D total score was calculated by adding the domain scores and dividing the result by six (number of domains). By recalculating the scores, we improved the comparability of the scores between the participants and between the different domains without weighing. This form of recalculation of the QUALIDEM has already been done successfully in several other studies.\textsuperscript{9,22-24} A first step to improve validity of proxy-rated QoL could be to weigh the different items in the domains of the QUALIDEM, adjusted to which items are perceived, preferably by the person with dementia himself, as affecting QoL most, as was done earlier for caregivers with the CarerQol.\textsuperscript{25} The difficulty here is the inability of a person with advanced dementia to answer these questions, so the weighing would remain (partly) subjective.

**Pain**

**Aspects of pain**

Pain, or ‘an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage’\textsuperscript{26}, is a complex subjective experience that is not always adequately expressed by persons with dementia. According to one of the six key
notes that were added to this definition, vocalization is only one of many behaviors that express pain. When there is an inability to communicate, it does not mean the person does not experience pain. Pain and nociception are different phenomena. Nociception, the neuropathophysiological mechanism of the body that detects a potentially harmful internal or external stimulus, is what triggers pain. However, the latter has other dimensions, as proposed by Loeser. These dimensions include suffering and pain behavior (Fig. 1). It is thus important to recognize all components of pain in a person, i.e., biological, emotional and social, and the suffering and behavior that result from it.

Fig. 1 Loeser’s pain model

Verbal / non verbal expressions such as grimacing, limping or avoid activities that convey to the outside world the patient is in pain

Emotional response triggered by nociception that includes fear, depression, anxiety and hopelessness

An unpleasant sensory and emotional experience associated with tissue damage and emotional activation

Mechanical, chemical and thermal factors irritating nociceptive fibres (injury or tissue damage)


Pain and Quality of Life
Although pain has not been the main topic of the Q-PID study and this thesis, we did look at pain and its association with the use of pain medication and QoL in a population of Norwegian persons with advanced dementia living in LTCF in Chapter 2. When persons were still in pain, despite using pain medication, their QoL tended to be lower than the QoL of persons using pain medication not in pain, but this difference was only significant for paracetamol. This was presumably because of power issues with small groups, with the paracetamol group being the largest.

In our study that was described in Chapter 2 of this thesis, all groups of pain medication users showed higher QoL on average when not in pain, compared to the persons who were still in pain despite using pain medication. This reflects findings in existing literature on the relationship between pain and QoL in persons with dementia. Pain can negatively affect many factors that also affect QoL, i.e., depression, sleep, agitation, daily functioning and care dependency. There is an obvious overlap between pain and QoL, and the two cannot
be regarded separately when taking care of persons with advanced dementia. For this reason, physical well-being and health, which also include pain, are regularly reflected in various models and definitions of quality of life.\(^\text{41-43}\) After researching the literature and practitioner meetings, the UNC-ZH also chose a QoL model that identifies four domains (pillars) that can influence QoL. In this model, ‘pain’ comes under the element of Health, which is part of the domain ‘Functioning’. (fig. 2).

**Fig. 2** Model of Quality of life in persons with dementia chosen by the University Network of the Care sector South Holland (UNC-ZH)

Interventions for pain

*Paracetamol*

As it is known for its antipyretic and analgesic working mechanism, and relatively minor side effects, paracetamol is found on all steps of the World Health Organization (WHO) analgesic ladder; as a sole intervention or together with non-steroidal pain medication (step 1), or as an adjuvant to opioids in moderate to strong pain (steps 2 and 3).\(^\text{44,45}\) Although it is the most widely used painkiller, the mechanism of action of paracetamol is still partly unknown.\(^\text{45}\) However, several studies found a positive effect of paracetamol in persons with dementia regardless of being in pain, e.g., on social interaction\(^\text{46}\) and daily functioning\(^\text{47}\). This, together with the knowledge that pain could lead to low QoL, was the impetus for designing the Q-PID study. However, our inclusion criteria significantly differed from those of the studies of Chibnall et al.\(^\text{46}\) and Sandvik et al.\(^\text{47}\): our main two inclusion criteria were having low QoL and using no pain medication regularly, whereas the participants in the study of Sandvik et al. were included based on signifi-
cant neuropsychiatric symptoms (agitation) and they could already be using pain medication at the start of the study. Also, the MOBID-2 pain score was 3.7 on average, which means clinically significant pain at the start of the study, and the pain scores decreased significantly in the first 8 weeks of paracetamol use. In Chapter 2 we saw that pain medication use and pain may be associated with a lower QoL, but QoL was not measured in the study of Sandvik et al. In the Q-PID study, participants did not use any pain medication at the start of the study, so use of pain medication did not affect low QoL. Also, pain scores of the participants of the Q-PID study were, on average, lower than 3 at baseline. If pain scores are higher at baseline, participants are more likely to improve significantly during treatment with pain medication, than when pain scores are already low at baseline. Unlike Chibnall et al. and Sandvik et al. we did not exclude persons with a short life expectancy or other severe illnesses in the Q-PID study. This may have factored into the type and low QoL of persons who participated in the Q-PID study. A subanalysis of the group of persons who were in pain did not provide any additional insights, partly because of the small remaining sample size and the study was not powered for this.

**Effect vs. side effect of pain medication**

During the Q-PID study no side effects directly linked to the use of paracetamol were observed. Although existing literature confirms that paracetamol is generally well tolerated by persons with advanced dementia, the sample sizes were small and the follow-up to find rare adverse events was short, i.e., max. 13 weeks. Opioids seem to have more side effects that may influence QoL, e.g., daytime sedation, agitation, dizziness, but again the available literature is insufficient.

In Chapter 2 we found that persons who used pain medication and were still in pain, i.e., probable undertreatment of pain, had lower QoL than persons who used pain medication and did not have clinically significant pain. There seems to be a close balance between experiencing side effects and being undertreated for pain.

**Analgesic ladder and non-pharmacological interventions**

Whereas acute pain is mostly temporary and resolves when an injury to the body is healed, chronic pain has a longer duration (3-6 months) and can result in more and longer suffering and psychological consequences, which may lead to a lower QoL, as mentioned above. As this suffering and pain behavior can persist, especially in persons with advanced dementia who are not able to express pain adequately, interventions with pain medication alone may not be sufficient for the management of pain as a whole, but only for nociception, i.e., the stimulus that leads to pain. This may be a reason why paracetamol alone did not improve the QoL, discomfort and neuropsychological symptoms in the Q-PID study. Several authors have proposed an adaptation of the 1986 WHO analgesic ladder, that focuses more on QoL by adding a fourth step (non-pharmacological interventions) and a bidirectional approach, i.e., the possibility to treat acute pain with the strongest analgesics as a first step and tone it down as soon as possible when pain relief is attained.
Also, Leung et al. proposed a change of the concept analgesic ladder to an analgesic platform, where non-pharmacological interventions go hand in hand with every step of the ladder (Fig. 3).\textsuperscript{31}

**Fig. 3** Change of concept from the analgesic ladder to the analgesic platform

![Analgesic Platform Diagram](image)

A—Physiotherapy and physical therapy  |  B—Mind-body integration (e.g., yoga, meditation, and religious support)  |  C—Hypnosis and relaxation therapy  |  D—Acupuncture  |  E—Chiropractic  |  F—External rub/lotions  |  G—Other CAM options (Tai chi, Tu Na)  |  H—Muscle relaxants (e.g., cyclobenzaprine, baclofen, and dantrolene)  |  I—Injectable agents (interferon, local anesthetics)  |  J—Interpersonal reinforcement (e.g., support group)  |  K—Anticonvulsants (e.g., gabapentin, pregabalin, and lamotrigine)  |  L—Antidepressants (e.g., tricyclics, SSRI, SSNR)  |  M—Compounds that act synergistically with opioids (e.g., cannabinoids, naltrexone)  |  N—Cognitive behavior therapy and psychological counseling  |  O—Surgical and neurological procedures (e.g., spinal cord stimulation, deep brain stimulation, spinal delivery of opioids, ganglion ablation by phenol or electrofrequency, sympathectomy)

**Care dependency and daily functioning**

The group of persons with advanced dementia we followed for 13 weeks during the Q-PID study was very care dependent at baseline, i.e., almost 80% of the participants were completely or to a great extent dependent on care of others, and this care dependency lasted throughout the study. As discussed in Chapter 4, we found that both care dependency and daily functioning were associated with the most advanced stage of dementia, which is logically explained by the fact that persons in this stage of dementia all need extensive care from others\textsuperscript{52}, and being in need of care is included in the description of stage 7 of the Global Deterioration Scale\textsuperscript{3}. Also, care dependency and daily functioning were associated with social relationships. We did not see any improvement in care dependency and daily functioning, probably because there was low average pain in the overall group, which is known to be an important factor to make care dependency, daily functioning and QoL worse.\textsuperscript{40,53,54} In a group with relatively low pain scores, paracetamol alone may not be a right fit to improve care dependency and daily functioning, whereas other interventions like physiotherapy or exercises may be more successful.\textsuperscript{55-57}
Limitations of research in LTCF in advanced dementia

Proxy assessment
As discussed before, the persons participating in the Q-PID study were unable to independently answer questions about their QoL and psychological and physical functioning, so the questionnaires had to be completed by nursing staff on the unit of the LTCF. The staff work in shifts and under pressure, so any extra work, such as filling out observational questionnaires, can be challenging.

Because nursing staff work in different shifts, we could not always ensure that the same person completed the questionnaires of one resident at all timeframes. This research was conducted in daily clinical practice, and we did not want to introduce any changes during the study, so we did not want to change shifts of caregivers to ensure that the same person completed the questionnaires every time. Despite the fact that the questionnaires we used were extensively tested for completion by different caregivers, there will always be a subjective component to proxy assessments, particularly when measuring QoL, where the background of proxy raters may be an important factor.

Crossover design
The main reason for conducting a crossover study in LTCFs is that it only takes about a quarter of the number of participants to achieve the same power as a parallel study. It is efficient and less costly, because the variation between two measurements in one individual is much lower than between two individuals, and the comparison in the crossover study is made within one group rather than between two groups in a parallel study. However, there are also disadvantages to a crossover study, for example a ‘carry-over’ effect, where one intervention is influenced by the other. To avoid this as much as possible, a wash-out period long enough for the previous intervention to have worn off can be introduced. Usually this means a wash-out period of more than 4 times the duration of action of the intervention. The wash-out period in the Q-PID study was one week, which is considered more than enough, since the duration of action of paracetamol is six hours. Another limitation of a crossover study we encountered is the (natural) change over time that participants can show and that can interfere with the outcome. This ‘period effect’ can be prevented by randomization at the start of the study for the order in which the intervention will be conducted. Although randomization took place in the Q-PID study, we did find a strong ‘period effect’ for QoL and neuropsychiatric symptoms, i.e., better scores in the first study period. When the health situation of a participant deteriorates quickly, which we see regularly in this population of vulnerable older persons with (advanced) dementia, the characteristics of this person can change. This means more variation between two measurements and probably more participants are needed for the study to achieve sufficient power.
Administration of medication

During the Q-PID study, a striking phenomenon occurred, i.e., the study medication was signed off as having been given, however, after the study periods more study medication remained than there should have been according to the medication administration forms. So, compliance in practice was lower than the administration forms showed. To improve compliance, most medications that are administered in LTCF are delivered in special small bags called a ‘baxter’ system. All medication that should be administered at one time is in this bag. For several reasons, already discussed in Chapter 3, the study medication could not be included in this ‘baxter’ system during the Q-PID study. It seems that providing medication outside such a system still causes too much medication non-adherence, which should clearly be addressed during training of nursing staff responsible for administering medication. There will always be medications that are not allowed in the ‘baxter’ system, due to shelf life or supply, so improving medication quality and safety should be a clear point of focus for LTCFs.

7.3 IMPLICATIONS FOR PRACTICE AND EDUCATION

Several implications for practice and education result from the findings of this thesis. We found no effect of paracetamol alone on QoL, pain and care dependency, among other things, that was administered during daily practice to persons with advanced dementia living in LTCF. It seems important to approach individuals with a low QoL from a broad perspective and to combine multiple treatments or interventions to improve multiple factors. Possible ways to address this will be discussed below.

QoL as an individual perspective

Persons with advanced dementia often can no longer adequately articulate what they consider important in life, and they are often no longer concerned with best health, but rather psychological well-being and cognitive functioning as key factors determining their QoL. Also, these factors can vary greatly between individuals and are also influenced by the setting a person lives in. It is therefore important to define personal individual perspectives that are important for QoL early in life and in the stage of dementia, so relatives can follow these in dialogue with professional caregivers. Once care is needed, it is essential that it is arranged as personally as possible, tailored to the person’s own wishes and needs. The activities offered, either in the LTCF or at home, should also be personalized. In addition, it is important to look closely at the person’s living environment and how it can be improved so that the person feels as comfortable as possible, even in the last phase of life.
**Interventions for QoL**

As we found in the Q-PID study, paracetamol alone is not a panacea to improve QoL in persons with advanced dementia, and certainly not when these individuals have relatively little pain. Evidence suggests that improving social relationships and engagement with activities are important factors in improving QoL, as well as anxiety, pain and depression.\(^{65-67}\) This can be accomplished e.g., by offering meaningful individualized activities inside or outside the LTCF, cognitive stimulation and promoting physical activities.\(^{68-70}\) These personalized interventions can be offered by activity coordinators, nursing staff or family and should be embedded in daily practice in LTCFs. Of course, if pain is observed, the above interventions can also be combined with adequate pain medication, starting with paracetamol.

**Interventions targeting pain and neuropsychiatric symptoms**

When pain is observed, a tailored intervention should be used, based on inhibiting nociception by administration of pain medication and providing distraction from the pain by offering activities such as massage, exercise and robotic care, thereby reducing suffering and improving QoL.\(^{71}\) As pain can cause neuropsychiatric symptoms, treating pain can also ameliorate these symptoms and can thereby improve QoL. A stepwise multidisciplinary approach may be beneficial for both pain and neuropsychiatric symptoms and should be considered when pain is observed or neuropsychiatric symptoms occur.\(^{72,73}\) Pain medication should be administered according to current guidelines, taking into account side effects, especially for opioids, and with frequent monitoring of effect and adjusting dosage and frequency accordingly.

**Care dependency and daily functioning**

It may be relevant for clinicians and nursing staff to find out more about the relationship between the different items of care dependency and existent pain, and which specific items of care dependency need special attention, to have points of reference to improve the care for, and thereby the QoL of, persons with advanced dementia. A multi-domain approach by professionals and informal caregivers is essential to reach this goal.

In Chapter 6 we found that care dependency and daily functioning were associated with social relationships as part of QoL. This reinforces the view that it is important to focus on non-pharmacological interventions targeting social relationships and activities, and to teach nursing staff and family most important to maintain and improve QoL and care dependency are their presence and attention for persons with dementia.

**Training nursing staff and family**

First, good education is needed for nursing staff and family on what QoL means and what to look for to potentially improve QoL for a person with dementia. Being present is one of the most important factors, as mentioned above, but at the times they are not there, there are
still opportunities to offer activities to improve QoL. Since nursing staff often have a heavy workload, it is important that they learn how to offer activities requiring little effort in a low-threshold manner. They can even integrate activities in daily care. Second, teaching nursing staff and family to adequately recognize pain is important so that they can seek timely medical attention for pain treatment and look at offering activities that can reduce pain and pain behavior. Finally, more attention should be paid during training and continuing education to administering medication, especially medication outside a unit dose package. Unfortunately, it is still not uncommon for the medication inside and outside the unit dose package to be properly checked against the medication administration list and be given blindly, as we also found during the Q-PID study.

7.4 RECOMMENDATIONS FOR FUTURE RESEARCH

One possibility to achieve an even better and more individualized measurement of QoL, would be to create a weighted QoL measurement instrument, or use a weighing ‘tariff’ in an existing measurement instrument. Research should look at which factors are seen as more and less important for QoL, for example by involving a large group of older persons and asking their opinion on the most important factors for their QoL. Persons with mild dementia and informal caregivers of persons with advanced dementia can also be asked for their opinions on which factors are most important to them for the best QoL. Gathering this information can help create a weighted QoL score that is more individually oriented and can provide more accurate total scores, so that scores can be better compared between individuals, or the effect of an intervention on QoL in an individual at two or more timepoints can be better examined. This type of weighing by computing a ‘tariff’ has been done before, e.g., for measuring the QoL of informal caregivers (CarerQol instrument). This ‘tariff’ was computed to take into account differences in dimensions of Care-related QoL and other factors like background and education to facilitate including informal care in economic evaluations. The latter seems less important in our population with advanced dementia in LTCF, but looking at the best way to weigh the different dimensions of the QUALIDEM-6D to form a total score may be important for individualizing care.

Future research should also focus on combined interventions targeting QoL, pain and care dependency. One of the pillars for these is the use of pharmacological interventions such as pain medication, but the biggest and most important pillars are non-pharmacological interventions, possibly combined with pharmacological treatment. The reinforcing effect of combining non-pharmacological and pharmacological treatments will have to be properly investigated in persons with advanced dementia living in LTCF.
OVERALL CONCLUSION

QoL in persons with advanced dementia is influenced by many factors, such as environment, background and psychological factors such as depression and agitation. This thesis provides evidence that administration of paracetamol or placebo alone is not effective, i.e., no ‘panacea’, for improving QoL, discomfort, pain, neuropsychiatric symptoms, care dependency and daily functioning in persons with advanced dementia living in LTCF. Personalizing interventions and combining pharmacological and non-pharmacological interventions are important, and we recognize that this will be challenging, but not impossible.
REFERENCES


