

5. Selection of appropriate preventive treatment

As very old people can differ considerably from one another with respect to their health, and functional and cognitive status, instead of a 'one size fits all' approach a personalized preventive care approach is needed. In addition, it is recommended to incorporate 'lag time to benefit' in the preventive care decisions for older populations.³⁹ Lag time to benefit is defined as the period between an intervention and the moment that improved health outcome is observed.⁴⁰ Incorporating lag time estimates into preventive care for vulnerable older persons will encourage a more explicit consideration of the risks and benefits of prevention.⁴¹

In this thesis, cranberry use for the prevention of clinical UTI showed a positive treatment effect from 2 months of follow-up onward, with a risk reduction of 22% in high UTI-risk residents during the 12-month follow-up (Chapter 5). This level of risk reduction seems to be meaningful in this specific population in which clinical UTI are frequently present.

The CRANBERRY study showed positive effects of cranberry capsule use for UTI in LTCF residents; other benefits of cranberry capsules may also be considered. For example, in daily practice, cranberry use may also reduce antibiotic prescription, including inappropriate prescriptions. In other words prevention with cranberry may lead to even less antibiotic resistance in long-term care. Also, less clinical UTI will lead to a reduction in the burden of UTI symptoms and to less discomfort.

It is important to realize that many preventive measures have not yet been tested in LTCF populations. More research is needed in this specific population to achieve an optimal, personalized and tailored prevention strategy, in which prevention is focused on increased quality of life, minimization of the impact of disease, reduction of the burden of disease in the prevention of complications, comorbidity and disability, and a dignified end-of-life.

Thus, prevention in LTCF needs to be examined in contexts other than the traditional prevention approach which has the prevention of disease and mortality as its ultimate goal. A new framework for preventive care in LTCF needs to be developed which involves both the older person and their informal caregiver(s). Within the individualized preventive care for vulnerable very old persons, the practical feasibility of interventions needs to be taken into account, as well as an effective implementation in daily care which includes education, knowledge and professional development, regulations, and financial considerations.

6. Cost-effectiveness of clinical UTI prevention

Justifying the implementation of new prevention strategies not only requires evaluation of its effectiveness, but also requires economic evaluation. For an economic evaluation in long-term care the impact of clinical UTI on the resident's health is relevant, and the resident's quality of life plays an important role in the societal valuation. The ultimate goal in long-term care is not simply adding 'years to life' but adding 'quality of life to years'. Therefore, the costs and benefits of interventions to prevent clinical UTI in LTCF populations need to be carefully weighed.

The CRANBERRY study shows that it is unlikely that cranberry capsule use will be cost-effective in the investigated dosage, frequency and setting (Chapter 6). However, cranberry capsules can be 'efficient' from the perspective of the individual resident with a high risk of UTI, resulting in a lower incidence of clinical UTI, less impact of UTI on the resident's health (e.g. less disability in ADL, care dependency and less discomfort), and a better quality of life. Also, less antibiotic use and (probably) less antibiotic resistance is likely to lower the costs. The costs attributed to antibiotic resistance were not discounted in the CRANBERRY study.

Economic evaluations usually express the effects of the intervention in the number of life-years gained and in health-related quality of life.⁴² Preferably, a cost-utility analysis is performed for economic evaluations, whereby the effectiveness of the intervention in terms of quality-adjusted life years (QALYs) is expressed in a cost-utility ratio per QALY. This ratio is defined as the amount of money the society is willing to pay to gain one QALY.^{43:44} The CRANBERRY study shows that the health gain in terms of QALYs was small in comparison with the costs. Most of this gain was due to the prevented clinical UTI mortality, i.e. a QALY gain in life expectancy of two weeks (Chapter 6). Although two weeks seems relatively small, in a vulnerable LTCF population with a life expectancy of around 1.5 years after admission to a LTCF, this is relatively large. The six-month mortality rate in LTCF residents with advanced dementia ranges from 18% to 37%,^{45,46} and the overall 2-year mortality rate after institutionalization is 57%.⁴⁷

Usually the QALYs are based on health-related quality of life, measured using the European Quality of Life utility measure (EQ-5D); this is a generic preference-based measure using a health state classification system with five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression).⁴⁸ Although use of the EQ-5D allows to compare economic evaluations internationally, it is less suitable for use in the LTCF setting.⁴⁹⁻⁵¹ Normally, quality of life measurements require the resident's self-assessment of their fulfilment and impairment in daily life;⁵⁰ however, because the most vulnerable people, often with (advanced) dementia, live in LTCF, the proxy (e.g. the responsible nurse, or relative) generally provides the utility measure. However, there is evidence that the rating of quality of life by proxy is influenced by the personal and/or professional characteristics of the proxy, the nature of the relationship, the time spent with the resident, the stage of dementia, and also the caregiver burden.^{49,50} Thus, there is often a discrepancy between the quality of life rating acquired from the residents themselves and that of their proxy, although the viewpoint of the proxy appears to be important when rating the EQ-5D.⁵² Despite that, the responsible nurse is well acquainted with the residents, it is difficult to rate the resident's pain/discomfort and anxiety/depression, especially in residents suffering from dementia. The EQ-5D is too narrowly focused and does not cover the domains relevant to the quality of life of persons with dementia. In the CRANBERRY study the EQ-5D had to be filled in by a professional proxy because 76% of the participants had dementia. A recently developed prototype of the Dementia Quality of life Instrument (DQI) seems more suitable, but has not yet been tested in a large LTCF population.⁴⁹

Another aspect related to economic evaluations in LTCF needs to be addressed, i.e. how do we measure the additional nursing care for LTCF residents who already have continuous care? Until now, there is no standard for measuring the costs of additional nursing care in LTCF residents who are already highly care dependent. Therefore, we calculated the additional nursing costs during the two weeks following a clinical UTI, by estimating the proportion of change on the Care Dependency Scale (Chapter 6).⁵³ Although this method was suitable for our study, additional research is required to validate this method.

In the light of all these difficulties related to economic evaluations in long-term care, there is an urgent need for a more suitable instrument to conduct economic evaluations, because the present methods may never demonstrate cost-effectiveness.

RESEARCH IN LONG-TERM CARE FACILITIES: CHALLENGES AND BARRIERS

The above mentioned substantive and methodological points show that research in LTCF populations is challenging and needs specific knowledge and a specific infrastructure. This section discusses the challenges and barriers to research in LTCF populations.

The proportion of older people is steadily rising worldwide; moreover, they live longer and manage their daily activities for longer than ever before.⁵⁴ However, these people also have a higher risk of higher care dependency, institutionalization and mortality.^{55,56} Admission to a LTCF is usually the result of a complex interaction of problems in many domains, in which care and treatment are insufficient to handle all the needs that the individual resident has. Especially behavioral problems (e.g. wandering, aggression, delusions), as well as depression and anxiety, apathy, resistance to care, functional impairment, incontinence, and informal caregiver burden, are reasons for institutionalization.^{57,58} Therefore, in the future, LTCF will probably admit only the most problematic and vulnerable persons, often with (advanced) dementia. Prevention of loss of quality of life and self-reliance is challenging in this vulnerable population. However, an even greater challenge is to minimize the impact of a disease, and reduce the burden of this disease in the prevention of complications, comorbidity and disability; all this requires specific insight and solid evidence. Therefore, research is needed in LTCF populations to generate specific knowledge that also takes into account implementation of this new knowledge into daily practice.

LTCF residents are often excluded from participation in research, sometimes due to the high prevalence of cognitive impairments (e.g. dementia) and sometimes due to medico-ethical considerations.⁵⁹ Also, difficulty in acquiring informed consent for study participation from representatives is often a reason for not conducting research in this population. In addition, various methodological issues may form a barrier to research in an LTCF population: for example, difficulties in formulating clear research outcomes or clinical endpoints, problems in defining a clear and unambiguous diagnosis of the disease, the high mortality rate in this

population, and the related high level of drop-out during a study. Moreover, some logistic challenges in performing research in LTCF are present, such as obtaining permission from the directors for their organization(s) to participate in the research project and the geographical distance between the participating organizations; often, this distance makes data collection and monitoring of the research project both difficult and costly.

Most research in LTCF is pragmatic and will take place in a 'real world' LTCF population. Therefore, research in LTCF requires a specific infrastructure as well as a considerable effort to enable research in this population. In 2003 the formation of academic nursing home research networks was started in the Netherlands. Currently, in 2014, there are five networks (located in Amsterdam, Groningen, Leiden, Maastricht, and Nijmegen) that have expertise related to performing research in complex care among vulnerable persons living in LTCF. The mission of an academic nursing home research network includes the development of an infrastructure for research.^{60,61} Care professionals collaborate with scientists of a university medical center to develop, implement, and test initiatives to improve quality of care.⁶⁰ Within this structure, university and practice are closely linked. Research outcomes will be directly implemented in daily practice and in the education/training of care professionals; hopefully, all this will serve to improve directly patient care.

CLINICAL IMPACT AND RECOMMENDATIONS FOR FUTURE RESEARCH

Based on the work presented in this thesis, the following conclusions can be drawn:

1. The natural course of care dependency is a dynamic process. LTCF residents can either improve or deteriorate in their care dependency status during their stay in a LTCF. Regular and simple assessment of the care dependency status is important, since this allows nursing staff to become more aware of the variability in the care dependency status of their residents, manage care, anticipate residents' care needs, and provide better tailored care for individual residents. Awareness of the course of care dependency is essential for residents, as well as for their formal and informal caregivers, when considering therapeutic, palliative, and end-of-life care options. Although care dependency can be influenced by individually-tailored interventions, these types of interventions need additional research.

2. In older persons without ADL disability at 86 year of age, clinical infections predict the development of disability in ADL from age 86 years onwards. These infections may be used as a predictor for ADL disability in the oldest-old who are not yet disabled. General practitioners and elderly care physicians should be vigilant when older persons without ADL disability have an infection. Besides treatment, they may start active functional rehabilitation to maintain independence in ADL. Future studies need to address whether the prevention of infections, a quick recovery after infections, and functional rehabilitation, are beneficial in the oldest-

old in the general population to maintain independence in ADL and to avoid adverse health outcomes.

3. Diagnosing clinical UTI is challenging in vulnerable very old persons. Although several guidelines are available to assist physicians in the diagnosis of clinical UTI in this population, there is no unambiguous definition of clinical UTI. The current guidelines are not optimal for clinical decision-making, or for a 100% confirmation of clinical UTI. Additional studies are required to further refine these consensus guidelines and to establish how to optimally diagnose clinical UTI in vulnerable very old persons.

4. It is possible to select vulnerable very old persons at high risk for developing UTI. LTCF residents with long-term catheterization, diabetes mellitus, or at least one UTI in the preceding year, are considered to be at high risk of UTI. It is possible that the use of other criteria would have selected a group with even higher risks or even more preventable UTI. Therefore, prediction rules to select residents at risk for UTI need to be studied to enable a more efficient prediction of the UTI risk in this specific population. In addition, it is recommended to evaluate UTI risk on a regular basis, because the risk for developing UTI can change over time.

5. The use of cranberry capsules (twice daily) is effective in the prevention of clinical UTI in LTCF residents at high risk of UTI. The capsules reduce the incidence of clinical UTI and thereby reduce the days of illness and the negative consequences of UTI, e.g. a reduction of the burden of the symptoms of UTI and less discomfort. The use of the capsules was shown not to be cost-effective; nevertheless, for reasons of effectiveness, it is still recommended to give residents at high risk of UTI preventive treatment with cranberry capsules.

Finally, additional studies are required to investigate whether, for example, clinical UTI prevention with cranberry capsules is effective in providing improvement in care from the perspective of the resident. In this case, the care improvement should focus mainly on quality of life, minimization of the impact of a disease, and a reduction in the burden of this disease in the prevention of complications, comorbidity and disability. To stratify residents and to make a well-considered choice for the indicated preventive interventions, assessment of the impact of the disease on an individual's functional capacity and their ability to maintain independence, is recommended.

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