

Understanding Young-Onset Dementia

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IMPACT PARAGRAPH

The overall aim of this thesis was to obtain a better understanding of young-onset dementia (YOD). More specifically, in part I we aimed to increase our understanding of the epidemiology of YOD, including factors associated with the onset of the disease, the prevalence, and incidence. Furthermore, in part II we aimed to gain a better understanding of the presentation of people with YOD in the General Practice (GP) years before diagnosis, and we investigated factors influencing the initiation of care use after diagnosis as reported by the GP. This impact paragraph describes the scientific and societal impact of the main findings of this thesis.

Main findings

In part I we focused on the epidemiology of YOD. There are well established factors known to increase the risk of late-onset dementia (LOD), but little studies have investigated the association of these factors with YOD. In the large UK Biobank study, we found that several factors were associated with YOD. Alcohol use, higher formal education and lower physical frailty (higher handgrip strength) were associated with lower incidence of YOD, whereas socioeconomic status, Apolipoprotein E-status, alcohol intoxication, social isolation, vitamin D deficiency, high C-reactive protein levels, hearing impairment, orthostatic hypotension, stroke, diabetes, heart disease and depression were associated with an increased risk of YOD.

Furthermore, we conducted systematic reviews on the prevalence and incidence of YOD. Here, we found an age-standardized prevalence of 119/100,000 persons in the age range 30-64 years, and an age-standardized incidence rate of 11/100,000 person-years. Moreover, we found that the method used to identify people with YOD influences the prevalence or incidence estimates. Active dementia screening of a cohort yielded higher incidence rates or prevalence estimates than register linkage to identify people with YOD. The systematic reviews also identified knowledge gaps to address in future research. These included prevalence and incidence in the younger age bands (30 to 45 years), prevalence and incidence in low-income countries and prevalence and incidence of different subtypes of dementia.

In part II we used GP records to investigate the presentation and care use of people with YOD in a primary care setting in the Netherlands. First, we investigated the presentation of persons with YOD at the general practice up to five years before diagnosis and compared this with an age- and sex-matched control group. We found that cognitive symptoms

were more common already five years before diagnosis, affective symptoms were more common four years before diagnosis, social symptoms three years before diagnosis, behavioral symptoms two years before diagnosis, and a decline in functionality one year before diagnosis. Then, we investigated the care use after diagnosis as described in the GP written notes. Results showed 72% of the persons with YOD were assigned a case manager, most already in the first year after diagnosis. Of the persons with a case manager, a lower percentage was admitted to a care home during follow-up of the study compared to persons without a case manager. Day care was initiated in 42.7% of the persons with YOD, and 44% was admitted to a care home. Main reasons for the use of these care facilities were to relieve caregiver burden, behavioral problems or an unsafe or worrisome situation at home. The start of care was sometimes delayed due to reluctance of the persons with YOD or their caregivers.

Scientific impact

The results from this thesis may be useful for researchers in several ways. First, the studies performed in part I were innovative and therefore showed new insights and directions for further research on YOD. For example, ours is the first study to investigate risk factors for YOD while correcting for a genetic factor. Results indicated that several modifiable factors are associated with the incidence of YOD, even when corrected for a genetic factor. Researchers could use this insight to further explore opportunities for prevention of YOD, but also for further research on the underlying cause of YOD. Furthermore, it is unclear whether factors are associated with specific subtypes of dementia. For instance, stroke, diabetes and heart disease may be more associated with vascular dementia than Alzheimer's dementia. This could be addressed in future research. The findings from our study should also be validated in other cohort studies, to increase external validation of the factors associated with YOD. Additionally, limitations from our factors, such as self-reported factors (alcohol use) and factors with limited information in the UK Biobank (social isolation, cognitive activity) should be further investigated in future studies.

Furthermore, our systematic reviews analyzed the most accurate prevalence and incidence estimates to date. Researchers can use these estimates to emphasize the importance of research on YOD, but also to conduct or design their research on YOD, for instance when they need to assess the sample size and the subsequent recruitment strategy for their study. Our reviews also indicated several knowledge gaps in the prevalence and incidence of YOD. These knowledge gaps could be used to indicate and design future research directions. Examples of research directions

based on our reviews could be investigating prevalence and incidence in low-income countries or investigating prevalence and incidence of different subtypes of YOD.

The findings described in part II were also relevant for researchers. Our study on the presentation of YOD at the GP showed that persons with YOD indeed present differently already five years before diagnosis. These results are not yet clinically relevant, since we investigated broad symptom categories with symptoms which also occur in other conditions such as depression. However, this result could be used as a basis for future research, where individual symptoms and combinations of symptoms should be investigated, leading to a more detailed patient profile which could be clinically relevant for GPs and improve recognition of YOD.

In part II we also identified factors that influenced the use of post-diagnostic care in persons with YOD. Researchers could address these factors by designing and investigating tailored interventions or investigating ways of improvement of care offering and services for persons with YOD. For example, we found GPs were not always aware of their responsibilities regarding dementia healthcare. Researchers could, together with healthcare professionals, develop educational programs for healthcare professionals and use results of our study to identify important topics for these educational programs.

Societal impact

“Hendriks et al have done a service to the dementia community by collecting and analyzing the dozens of individual studies of YOD. The product, a rationally derived estimate of dementia prevalence across the population aged 30 to 64 years, provides a basis for initiating more efforts to improve methods for timely diagnosis and to address the unique needs of patients with YOD.” – David Knopman, editorial Young-Onset Dementia – New Insights for an Underappreciated Problem, JAMA Neurology 2021

The findings in this thesis are relevant for our society. YOD poses a great burden not only on patients and caregivers, but also on healthcare systems and the general society. Although prevalence and incidence estimates are low, people with YOD are in an active life phase. This affects the general society due to the high economic impact of YOD related to both the loss of employment of productive individuals (both the persons with YOD and their caregivers) and high costs of dementia care. Dementia healthcare is mainly focused on people with LOD, thereby not meeting the needs of people with YOD. Policy makers, healthcare professionals, persons with YOD and caregivers can employ our findings in several different ways.

Policy makers

The findings from our systematic reviews provide a basis for the development of specialized healthcare specifically aimed to meet the needs of persons with YOD. Policy makers can use these accurate measures to increase the post-diagnostic care services for people with YOD. People with YOD and their caregivers express different care needs compared to people with LOD. Examples may be day care activities with more physically active elements, with special attention for feeling useful and engaged in daily life, or support to regain reciprocity between persons with YOD and their families or social contexts.

Healthcare professionals

For healthcare professionals, results from both part I and part II of this thesis are relevant. The prevalence and incidence of YOD provide GPs and specialists who diagnose YOD a better insight in the burden of disease, since the prevalence and incidence can be used to estimate the background risk of YOD for someone presenting symptoms at their practice. It also increases awareness of YOD in healthcare professionals. This could lead to an increased number of GPs adding YOD on their list of differential diagnoses, thereby increasing the chance of a timelier diagnosis. It could also increase awareness of YOD in company doctors, which may lead to an earlier referral to a GP or specialist for diagnostic follow-up.

The results from part II are particularly important for GPs. Our finding that symptom categories are more common in persons with YOD already five years before diagnosis indicates that an earlier recognition of YOD by the GP is possible. Although our results are not clinically feasible yet, they could raise awareness on YOD in GPs, again increasing the number of times a GP adds YOD on their differential diagnoses list. Furthermore, our results on the use of post-diagnostic care could aid GPs to improve care for individuals with YOD, emphasizing the importance of case management for persons with YOD, and the engagement in conversation when persons with YOD or their caregivers are reluctant to start care.

Persons with YOD and their caregivers

Results from this thesis could help increase the quality of life of persons with YOD and their caregivers. Specifically results from part II of this thesis, where the aim was to increase recognition of YOD and identify factors that influence care use could

improve healthcare services for people with YOD. When healthcare professionals and services are better able to meet the needs of persons with YOD and their caregivers, their quality-of-life increases. Furthermore, especially the results from the incidence and prevalence estimates increased the knowledge on the existence of YOD in the general population. Often caregivers feel a lack of understanding from their social surroundings, but an increased awareness of the existence and occurrence of YOD can lead to a better understanding of the general public regarding the problems persons with YOD and their caregivers face. This may lead to better support from the social surrounding of persons with YOD and their caregivers.

Dissemination activities

Our results were communicated to the scientific community through articles published in scientific journals, and by means of oral and poster presentations at international conferences (Alzheimer Europe 2019, 2021 & 2022, Alzheimer Association International Conference 2020 & 2021, International Psychogeriatric Association Conference 2020). We also communicated our results through interviews published in the Alzheimer Europe Magazine, the Alzforum and HealthDay News. Our findings were also published in the first chapter of the Dutch book 'Dementie op Jonge Leeftijd'.

Our research findings were noticed by mainstream media, which provided us the opportunity to share our results with a broad audience. We disseminated our results through radio interviews, on national radio (Spraakmakers, NPO radio 1) and regional radio (L1 radio), and through an interview on national television (Op1, NPO 1). These opportunities allowed us to raise awareness for YOD and emphasize the need for better recognition both among healthcare professionals and the general public.

Dissemination also included sharing results with healthcare professionals or other researchers through presentations at the Kenniscentrum Dementie op Jonge Leeftijd and a free webinar organized for everyone interested in YOD. Furthermore, we provided an educational video of our research findings on VuMedi, a free platform for peer-to-peer physician learning. Lastly, we distributed newsletters to researchers, clinicians and other interested parties. All together, these endeavors allowed us to increase the societal and scientific impact of this thesis and to increase awareness of YOD within the general public.