CHAPTER 8

GENERAL DISCUSSION
Aim

The general aims of this thesis were; 1) to study the criterion validity of an Attention-Deficit/Hyperactivity Disorder (ADHD) screener, that was developed for younger adults, in older adults, 2) to determine the prevalence of ADHD in older adults, 3) to examine the stability of ADHD symptoms during the life course, and 4) to study physical and mental health of older adults with ADHD.

Before we started our study little was known about ADHD in older adults. Only very recently the first scientific papers have been published. Therefore, the diagnostics and treatment of ADHD in older adults are mainly based on what is known from younger adults and children, whereas it might be expected that due to aging and increasing somatic comorbidity the diagnostics and treatment of ADHD in older adults may need its own clinical guidelines.

To study ADHD in a representative sample of older adults we used a large population-based cohort in the Netherlands (The Longitudinal Aging Study Amsterdam (LASA)) in which we first screened for ADHD, and subsequently performed a diagnostic interview. The findings of our studies will be summarized and evaluated in this chapter. In addition methodological considerations, implications for the clinical practice, and ideas for future research will be presented.

Summary of main findings

To identify ADHD in older adults a validated screener may be helpful. A screener is an efficient way to determine whether a more expensive diagnostic interview is desirable or not. However, no such screener is available for older adults. Chapter 2 reports about the reliability and criterion validity of an ADHD screener that was originally designed for younger adults. The screener was tested against a semi-structured diagnostic interview (Diagnostic Interview for ADHD in Adults, second edition (DIVA 2.0)). In the first phase 1494 respondents (60 – 94 years) from LASA were assessed with the ADHD screener. Scores on the screener were stratified into three levels: a high scoring group, most likely to have ADHD (score 3 – 9); a moderate scoring group (score 1 – 2) and randomly selected low scoring group (score 0). This way 231 respondents were selected and participated in the diagnostic interview.

The results showed that the screener had an acceptable internal consistency (Cronbach’s α: 0.71) and validity (area under the curve: 0.82) and had a moderate reliability (intraclass correlation coefficient (ICC): 0.56). The optimal cut-off for older adults was found at 2 (sensitivity: 0.80; specificity: 0.77; positive predictive value (PPV): 0.13; negative
predictive value: 0.99). Despite its only moderate ICC, the ADHD screener has proven to show good sensitivity and predictive value in our population-based sample of older adults. Therefore we concluded that it is valid and useful instrument for screening ADHD in older adults.

Since little is known about the prevalence of ADHD among older adults the prevalence of ADHD diagnosis in The Netherlands was estimated (Chapter 3). Our prevalence rates were weighted according to sex and age to be able to generalize our findings to the general older population in The Netherlands. The prevalence of ADHD was calculated using DSM-IV criteria. According to those criteria a syndromic diagnosis of adult ADHD required six symptoms of either inattention and/or hyperactivity-impulsivity during the six months prior to the interview (DSM-IV criterion A) and during childhood. Because these criteria were probably too strict for older adults, we also computed a symptomatic ADHD-diagnosis, which required four symptoms of either inattention and/or hyperactivity-impulsivity during the 6 months prior to the interview and six symptoms of either inattention and/or hyperactivity-impulsivity during childhood.

The estimated prevalence rate of syndromatic ADHD in older adults was 2.8%; for symptomatic ADHD the rate was 4.2%. This correlates roughly with 95000 older adults aged 60 – 94 years in The Netherlands who have syndromatic ADHD, and 145000 older adults who have symptomatic ADHD. Although both age groups were diagnosed with ADHD, younger older adults (60 – 70 years) reported significantly more ADHD symptoms than older adults (71 – 94 years). Results from this study demonstrate that ADHD does not fade or disappear in adulthood. It also shows that it is an important topic to investigate further.

Chapter 4 describes the lifetime stability of ADHD symptoms into old age. A recent study showed the persistence of self-reported childhood ADHD symptoms over the lifespan in older adults. However, in this study no ADHD diagnostic information was available and high attrition rates may have confounded the results.

The results of our study however, also suggest continuity of the number of ADHD symptoms present in childhood into old age. The balance of inattentive/hyperactive-impulsive symptoms in older adulthood and in childhood is the same in persons with and without ADHD. This suggests that aging does not influence the presentation of ADHD.

Studies in children and younger adults have shown that ADHD is associated with smoking, alcohol and drug use, unstable eating patterns, sleep disorders, migraine, and high healthcare use and costs. These unhealthy life styles may lead to poor physical
health at a younger age, or early death in persons with ADHD. Chapter 5 describes the results of the study in which we examined the association between ADHD, physical health and lifestyle in older adults. Information on physical health, medication use, and lifestyle characteristics was collected during home visits in Phase 1 of the study. The results showed that the number of ADHD symptoms was positively associated with the presence of chronic nonspecific lung diseases ($B = 2.58, \ p = .02$), cardiovascular diseases ($B = 2.18, \ p = .02$), and number of chronic diseases ($B = 0.69, \ p = .04$) and was negatively associated with self-perceived health ($B = –2.83, \ p = .002$). These associations were not mediated by lifestyle variables. Contrary to expectations, there were no associations between symptoms of ADHD and lifestyle variables in our older adults. The association between ADHD and cardiovascular disease has not been reported before in younger adults with ADHD. Therefore this association may be specific for older adults. A closer inspection of this association showed that those with ADHD more often had a heart disease, cerebrovascular accident, or used more often medication for one of these conditions than those without ADHD.

Extensive research illustrated cognitive deficits in children and younger adults with ADHD.\textsuperscript{41,42} Few studies have focused on the cognitive functioning in older adults, however. In Chapter 6 we investigated the association between ADHD and cognitive functioning in older adults. Cognitive functioning was assessed with the Mini Mental State Examination (MMSE), Raven’s Coloured Progressive Matrices, Auditory Verbal Learning Test, Alphabet Coding Task-15, Stroop Color-word Test, Trail Making Task, Word Fluency Test, and Digit Span, covering the cognitive domains of executive functioning, information processing speed, memory and attention/working memory. The results showed that ADHD diagnosis and ADHD severity were only negatively associated with cognitive functioning in the attention/working memory domain, but the effect sizes were small. When adjusting for depression, these associations were no longer significant. It was concluded that the association between ADHD and cognitive performance was mainly explained by depressive symptoms.

Comorbidity between ADHD and depression is high,\textsuperscript{140–142} also in older adults as is shown in a paper from our group.\textsuperscript{121} Thus far it is not well understood why ADHD and depression are so strongly interrelated. A factor that may play a role is an increased risk of experiencing adverse life events in persons with ADHD. In Chapter 7 the role of adverse life events in the association between ADHD and depression was studied. Therefore, six-year follow-up data from LASA were used including the life events ‘relocations’, ‘serious conflicts with others’, ‘financial problems’, and ‘total number of life events’. The results showed that compared to older adults without ADHD, those with ADHD reported having more serious conflicts. The increased risk of depression in older adults with ADHD was partly explained by these serious conflicts. Furthermore, the association between the severity of ADHD-symptoms
and depression was stronger in those who experienced serious conflicts, and those who experienced a larger number of adverse life events. The results suggest that better and earlier treatment of ADHD might prevent the development of depression in the presence of life events associated with ADHD.

In conclusion, the findings of our studies have shown that ADHD is a lifelong disorder, which is associated with physical and mental health problems in older adults.

Methodological considerations
Our study was the first that studied ADHD in a large population-based sample, and only few clinical studies among older adults are available. Because so little was known about ADHD in older adults, we had to deal with several limitations, which will be discussed below.

DSM
Diagnosing ADHD in older adults comes with several limitations. It is unclear whether the DSM criteria for ADHD, which were developed for children and younger adults, are appropriate for older adults. Neither the DSM-IV-TR criteria, nor the DSM-5 criteria have been validated in older adults yet. It may be that the expression of symptoms of ADHD changes with age, which might have led to missing ADHD symptoms that are specific for older adults, leading to an underestimation of the prevalence of ADHD in this group. In addition, some ADHD-symptoms that are important in childhood may no longer be relevant in adulthood, since life demands of older adults are significantly different compared to the life demands of children. For this reason, in the DSM-5 the diagnostic criteria for ADHD in adults have been slightly changed compared to the DSM-IV-TR and the cut-off is set at six or more symptoms present in childhood and five or more symptoms present in adulthood. In our studies the cut-off for ADHD was set at four or more symptoms present six month prior to the interview and 6 or more symptoms present in childhood. At the time of our studies the DSM-5 criteria were not yet published, therefore the cut-off used in our studies is based on Kooij et al. They found a clinical relevant rise in impairments in persons with 4 or more current symptoms of ADHD. Whether the DSM-5 criteria are adequate for older adults or that a lower cut-off may be more adequate remains to be determined.

DIVA
The semi-structured diagnostic interview DIVA 2.0 has been developed to operationalize the DSM-IV-TR criteria for ADHD in adults. For our study, the DIVA 2.0 was modified into a fully structured interview. This was necessary because lay interviewers performed the diagnostic interview. However, it is unknown what the effect of this may have been on the results.
Previous studies have shown that fully structured interviews do very well in some disorders, such as anxiety disorder and depression, but tend to underestimate the prevalence of others, such as bipolar disorder. So, it is not clear whether this has led to an over- or underestimation of the prevalence of ADHD in older adults in our study.

RECOLLECTION OF CHILDHOOD SYMPTOMS
With respect to the ADHD diagnoses we had to use retrospective data. However, the recollection of childhood symptoms by older adults may be a problem due to several reasons. Firstly, since childhood was on average 55 years ago, the recollection of the presence or absence of symptoms can be considered less than ideal. It has been shown that older-olds rate fewer childhood ADHD symptoms and also rate their memory worse than younger-olds. Secondly, qualified informants were not available, which means that the ADHD diagnosis relied solely on the respondents’ recollection of childhood symptoms. Although results of studies that examined the validity of retrospectively diagnosing childhood ADHD differ, it is reported that most studies show an underestimation of childhood symptoms. Since we did not find the expected and well-established change in the balance of inattentive/hyperactive-impulsive symptoms in Chapter 4 it is very likely that the childhood symptoms are (relatively more frequently) subject to recall bias.

Studying ADHD and the development of ADHD symptoms over time should preferably be conducted in a clinical sample of persons with the disorder in a prospective design starting at childhood. That way ADHD can be diagnosed early in life and the development of the disorder and its consequences can be follow-up throughout lifespan. At the moment such a sample of ADHD patients that reached old age is not available yet.

LASA
The analyses were carried out in the sixth cycle of LASA 16 years after the baseline measurement. An inevitable problem in studies like LASA is the loss to follow-up of respondents. For the largest part attrition in the LASA cohort can be attributed to mortality, and to a lesser extend to refusal and physical health or cognitive problems. Attrition due to mortality does not necessarily influence the representativeness of the sample since this is a characteristic of older populations. However, attrition due to physical health or cognitive problems is selective, and might influence the representativeness of the sample. Conversely, attrition due to refusal was associated with better health. As very little is known about the determinants of ADHD in older people, it is difficult to estimate the effect of any selective loss of respondents. The result of the studies should therefore be interpreted with some caution.
ADHD-SAMPLE

Even though we used a relatively large cohort of older people, the number of older adults with ADHD was limited. As a result the power in the statistical analyses to uncover clinically relevant associations was modest when we only included the ADHD diagnosis as a variable. By also including the number of ADHD symptoms as a variable in our statistical analyses we have tried to overcome this power issue.

Strengths of the study

This is one of the first studies to report data on ADHD in older adults. An important strength of the study is that we were able to use a wide range of data from LASA, a population-based, representative cohort of older adult, which made it possible to study physical and mental health in older adults with ADHD. We were also able to study and diagnose ADHD in a relatively large sample of older adults, which had never been done before. Therefore, despite the limitations we think that our study contributed importantly to the knowledge about ADHD in older adults.

Implications for clinical practice

ADHD is a lifelong disorder. However, due to the lack of knowledge about ADHD in this age group clinicians are often unaware that someone may have ADHD. Although the consequences of ADHD may be less interfering with daily functioning in older adults as compared to younger ones, because life demands have changed, it may still have considerable impact on the quality of life. Since older adults with ADHD run a relatively high risk to develop other mental health problems, or physical health problems, as shown in Chapter 5, it is important to consider ADHD in older adults when applicable. The ADHD screener described in Chapter 2 could be administered to get an indication of possible ADHD. For those that screen positive at a cut-point of 2 a diagnostic interview using DIVA 2.0 may be performed.

The DIVA 2.0 has not yet been validated, and since it is based on the DSM criteria the cut-off of 5 out of 9 for diagnosing current ADHD symptoms (according to DSM-5 criteria) might be too strict for older adults. It may be considered to use a lower cut-off in older adults because some of the criteria might not apply to older adults.

In treating older adults with ADHD, it is important to take the physical health of these adults into account. We observed that ADHD in older adults is associated with chronic nonspecific lung disease and cardiovascular disease. In addition, as we observed that having serious
conflicts with others partly explained the relation between ADHD and depression, putting more emphasis on conflict handling during treatment could reduce the chance of developing (symptoms of) depression.

Future research
A growing scientific interest in ADHD in older adults can be witnessed; the number of scientific papers on this subject is growing steadily. Still there is a wide range of subjects that needs further exploration.

SCREENING FOR AND DIAGNOSING ADHD
Since neither valid diagnostic criteria nor valid diagnostic instruments for ADHD in older adults are available, priority should be given to establishing age appropriate criteria for this age-group and adapting existing diagnostic instruments to be used in older adults. Furthermore, because full diagnostic assessment of ADHD is only rarely carried out in geriatric psychiatry, a brief, validated and easy to use screener should be further developed for this population.

SAMPLE AND REPLICATION
As mentioned before, the development of ADHD symptoms over time and its consequences may be best studied in a clinical sample of persons with ADHD in a prospective design until old age. These studies should focus on replicating the results described in this thesis in such a sample to improve our understanding of ADHD over the lifespan.

PHYSICAL HEALTH
The association between ADHD and cardiovascular disease has not yet been described before in younger adults. Future studies should focus on replicating this finding and whether this higher prevalence of cardiovascular disease is specific for older adults or that also younger adults with ADHD are prone to developing cardiovascular diseases early on.

MENTAL HEALTH
Although we did not find an association between ADHD and cognitive performance, it should be studied whether ADHD is associated with cognitive decline, and more specifically with mild cognitive impairment and dementia. Especially since higher levels of preceding ADHD symptoms have been found in dementia with Lewy body patients.46
Conclusions

This thesis shows that ADHD is a lifelong disorder, which is still poorly understood. Our study was the first that studied ADHD in a large epidemiological sample of older adults. Our findings increase the knowledge about ADHD in older adults, and have shown that the disorder is associated with negative outcomes. It may be the starting point for more studies on this topic.