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Review article

Prevalence of attention-deficit/hyperactivity disorder in older adults: A systematic review and meta-analysis



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ABSTRACT

Keywords: Attention-deficit/hyperactivity disorder Prevalence Older adults Systematic review Meta-analysis There is a significant knowledge gap in research on Attention-Deficit/Hyperactivity Disorder (ADHD) in older adults. Via a systematic review and meta-analysis, we aimed to investigate the prevalence of ADHD in older adults, considering different assessment methods. We searched five electronic databases up to June 26, 2020. We identified 20 relevant studies with 32 datasets providing a total sample size of 20,999,871 individuals (41,420 individuals with ADHD). The pooled prevalence estimates differed significantly across assessment methods: 2.18 % (95 % CI = 1.51, 3.16) based on research diagnosis via validated scales, 0.23 % (0.12, 0.43) relying on clinical ADHD diagnosis, and 0.09 % (0.06, 0.15) based on ADHD treatment rates. Heterogeneity was significant across studies for all assessment methods. There is a considerable number of older adults with elevated levels of ADHD symptoms as determined via validated scales, and the prevalence of treated ADHD is less than half of the prevalence of clinically diagnosed ADHD. This highlights the need for increased awareness of ADHD clinical diagnosis and treatment in older adults.

1. Introduction

Attention-Deficit/Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder associated with multiple psychiatric and physical disorders that can persist into adulthood (Goodman et al., 2016; Nigg, 2013; Torgersen et al., 2016). Based on pooled estimates from metaanalyses, ADHD affects 5.3 % (95 % CI = 5.0, 5.6) (Polanczyk et al., 2007) to 7.2 % (95 % CI = 6.7, 7.8) (Thomas et al., 2015) of children and adolescents, and 2.5 % (95 % CI = 2.1, 3.1) of adults across the world (Simon et al., 2009). Findings on the prevalence of ADHD in older adults have not been properly synthesized, although available data suggest a growing number of people aged 50 years and older in need for health-care related to ADHD (Goodman et al., 2016; Nigg, 2013; Torgersen et al., 2016). A rigorous understanding of prevalence estimates of ADHD in older adults can provide relevant information to clinicians in order to adjust clinical assessment procedures and treatment to this population.

To our knowledge, only one systematic review focusing on the ADHD prevalence in adults older than 50 has been conducted thus far (Torgersen et al., 2016). In that systematic review, published in 2016, Torgersen and colleagues (Torgersen et al., 2016) identified only four studies assessing the prevalence of ADHD in older adults. Across the included studies, the prevalence estimates ranged from 1.0 % to 6.2 %. This seminal study can be extended in three important ways. First, by conducting a meta-analytic synthesis, which was beyond the scope of the study. Second, as the authors of that review did not restrict the agerange to older adults alone, it is of interest to estimate the pooled prevalence in this specific age group only. Third, the review by Torgersen et al. (2016) only included studies based on research diagnosis in community samples assessing ADHD symptoms/syndrome using validated scales. Hence, there is a need to synthesize data from prevalence studies using clinical diagnoses and prescribed treatment to identify ADHD cases. Of note, previous systematic reviews and metaanalyses of ADHD prevalence in children, adolescents and young adults

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(Polanczyk et al., 2007; Thomas et al., 2015; Simon et al., 2009; Polanczyk et al., 2014; Willcutt, 2012), have shown that prevalence estimates are highly heterogeneous mostly due to methodological differences of included studies. None of these systematic reviews explored potential differences in the prevalence estimates between studies based on treatment seeking individuals and studies based on research diagnosis using validated scales in community samples.

We aimed to fill these gaps by conducting a meta-analysis of prevalence estimates from pertinent studies in what we define "older adults" (i.e., 50 years old and above) based on a systematic search in a broad range of databases. Additionally, the current study aimed to complement, with data in older adults, the evidence from previous systematic reviews (Torgersen et al., 2016) and meta-analyses in children, adolescents or younger adults (Polanczyk et al., 2007; Thomas et al., 2015; Simon et al., 2009; Polanczyk et al., 2014; Willcutt, 2012), with ADHD, by exploring potential differences between ADHD prevalence estimates based on different assessment methods. Separate prevalence estimates of ADHD research diagnosis, clinical diagnosis and treatment may provide valuable information on potential over- or under-diagnosing and/or over- or under-treatment of ADHD in older adults.

2. Methods

We followed the guidance of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement (Liberati et al., 2009). The protocol for this systematic review was registered in PROSPERO (CRD42019135062).

2.1. Search strategy

The search strategy was developed with the support of librarians at the Medical Library, Örebro University, Sweden. The systematic literature search was conducted in the following electronic databases: Pubmed/MEDLINE, PsycINFO, Web of Science and EMBASE, using search terms (with adequate adjustments for each database) in relation to "Attention-Deficit/Hyperactivity Disorder", and "Aging", from inception until June 6, 2019. An updated search was conducted between June 22 and 26, 2020. Detailed search syntax and strategies are available in Appendix 1 (in Supplementary material). There were no restrictions with regard to language/year of publication/type of document; full-text published articles or conference proceedings. We also hand-searched reference lists of relevant full-text articles and textbooks (Appendix 2 (in Supplementary material)), and contacted experts in the field (Appendix 8 (in Supplementary material)) to identify potentially additional relevant articles.

2.2. Selection criteria

We included observational cohort and cross-sectional studies, focusing on participants aged 50 and older with ADHD with any of the following: a) research diagnosis of ADHD, i.e., meeting the threshold/ cut-off levels on an ADHD validated scales based on the DSM (III, IV, IV-TR or 5) criteria; b) clinical diagnosis according to ICD (9 or 10) or DSM (III, IV, IV-TR or 5) as reported in registers/medical files or self-reported medical history; c) presence of pharmacological (medications recommended in pharmacological treatment of ADHD) (National Guideline Centre (UK), 2018), and/or non-pharmacological treatment (e.g. psychoeducation or psychotherapy) for ADHD, as reported in registers/medical files or self-reported prescription.

The age cut-off \geq 50 was chosen as previous studies have shown that there is a growing number of people aged 50 or older who are being diagnosed with ADHD for the first time (Goodman et al., 2016; Torgersen et al., 2016). If a study did not report on the separate prevalence in this age group, we contacted the authors in order to gather relevant data.

We excluded studies conducted in samples non-representative of the general population and studies that assessed childhood symptoms only, without addressing the presence of adult ADHD symptoms.

2.3. Data extraction (selection and coding)

References to studies identified in both electronic and manual search were managed in EndNote X9. After deletion of duplicates, titles/abstracts were screened by one author (MD), and full-texts articles were independently screened by two authors (MD and CS). A senior author (HL) was consulted in order to reach a consensus, when needed.

Two authors (MD and CS) independently extracted data. In case of disagreement, a third author checked the data (HL). The following data were extracted: first author and year of publication; year of data collection; country; age range; number of individuals with ADHD; sample size; and assessment method (research diagnosis/clinical diagnosis/ treatment). We contacted authors to gather relevant unreported data (Appendix 5 (in Supplementary material)). Prevalence estimates from the same study based on different countries were considered as separate data sets. In case of overlapping study samples, the study that was published earlier and/or the study that was the most pertinent to our criteria, was included. If the prevalence estimate was not reported or could not be calculated based on data from the paper or could not be gathered from the authors, a study was excluded from the meta-analysis. We also contacted authors of studies with reported adjusted/ weighted prevalence estimates in order to get crude prevalence estimates.

2.4. Study quality appraisal

Two reviewers (MD and CS) independently assessed the risk of bias/ study quality of each included study with the adjusted Joanna Briggs Institute Critical Appraisal Checklist for Studies Reporting Prevalence Data (Munn et al., 2014). In case of disagreement, a third reviewer (HL) arbitrated. We assigned a numerical score (0–9) to each study based on a number of fulfilled criteria, and considered a score over five as satisfactory. Studies with a potential high risk of bias and/or low quality were not excluded from the meta-analysis, but potential limitations in this regard were further addressed in the discussion section of the report.

Publication bias was not addressed since the results of studies reporting prevalence estimates should not affect the decision whether a study would be published.

2.5. Statistical analysis

The meta-analysis of included studies was conducted using the software Comprehensive Meta Analysis V3 (https://www.meta-analysis.com). We applied the random-effects model for meta-analyses, in order to allow the true population prevalence to vary between studies due to expected heterogeneity across studies. The pooled prevalence estimates were obtained using the inverse variance method (i.e., the variance in the random model includes both within- and between-study variance) (Borenstein et al., 2011). We used the Cochran Q test, I² index and confidence intervals to assess heterogeneity of results (Higgins et al., 2003). Values of the I² index higher than 75 % were considered high (Higgins et al., 2003).

We conducted subgroup analysis to test for statistically significant differences between the three assessment methods, with the mixed model method, which applies the random-effects model to combine studies within subgroups, and the fixed-effects model to combine subgroups.

We performed four sensitivity analyses to investigate the robustness of our findings:

1) Excluding studies that reported on the prevalence of ADHD research

diagnosis based on assessing only the current ADHD symptoms. The underlying rationale was that such studies might be biased by misclassification of ADHD with other mental health problems (Gentile et al., 2006; Moffitt et al., 2015);

- Excluding studies with self-reported medical history of ADHD diagnosis or pharmacological ADHD treatment, to retain only studies with the most rigorous diagnostic process;
- 3) Limited to studies conducted in regions other than North America within all three assessment methods, as previous studies indicate that the administrative prevalence estimates of ADHD might be higher in North America compared to other regions, probably due to different clinical practices (Anderson, 1996; Timimi and Taylor, 2004);
- 4) Limited to studies that included younger participants (i.e. 45-49 years old) within all three assessment methods.

3. Results

3.1. Description of included articles

A total of 9784 references were screened, 132 full-text papers assessed for eligibility, and 20 studies with 32 data sets were included in the meta-analysis (Fig. 1). Table 1 presents the descriptive data for all studies included in the meta-analysis. The studies were published between 2005 and 2019, and the data were collected in the period between 1997 and 2015. Total sample size across studies included 20,999,871 participants, with 41,420 individuals presenting with ADHD research diagnosis, clinical diagnosis or treatment. A list of references not included in the meta-analysis after the full-text review, with reasons for exclusion, is presented in the Appendix 3 (in Supplementary material). We did not identify any relevant unpublished studies or studies published in languages other than English. We excluded studies that did not provide crude prevalence estimates in the published report or upon e-mail request to the corresponding author.

We identified nine studies based on a research diagnosis of ADHD (45 % of the included studies), reporting individual 14 data sets with 32,766 participants and 701 individuals presenting with a research diagnosis of ADHD. Five studies assessed both the presence of current ADHD symptoms and the persistence of childhood symptoms. Four studies assessed only the presence of current symptoms, without confirming the childhood symptoms. Five studies used the Adult ADHD self-report scale screener version 1.1 (ASRS) (Kessler et al., 2005) for assessment of current ADHD symptoms, but the applied cut-off score was not consistent across studies. Three studies applied a cut-off of 14 using a continuous scale with a possible range of 0–24 (Das et al., 2014; Jacob et al., 2018; Vingilis et al., 2015). Two studies applied a cut-off of minimum four out of six symptoms present (a more strict cut-off) (Park et al., 2011; Wynchank et al., 2018). Park and colleagues (Park et al., 2011), in addition to the ASRS, confirmed the presence of at least one childhood symptom.

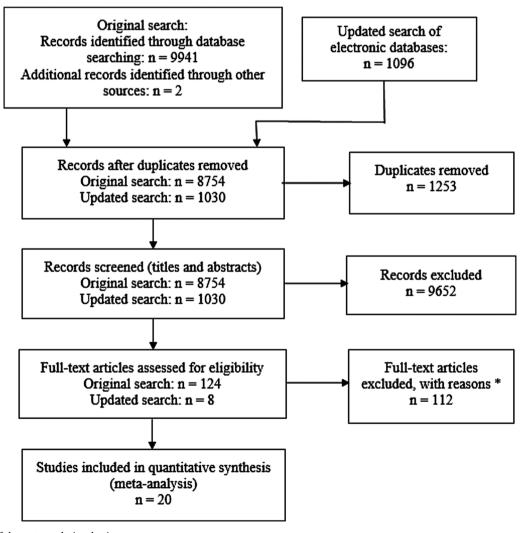


Fig. 1. Flow-chart of the meta-analysis selection process.

^{*} Reasons for exclusion of full-text articles are provided in the Appendix 3 (in Supplementary material).

Fi	First author(year)	Population/Study design	Year of data collection	Female/male (%)	Country	Age range	Age range Events (N)		Sample size (N) Prevalence (%) 95 % CI	Study quality score (0 – 9)
Re 1 (B	Research diagnosis (Bernardi et al., 2012)	NESARC, 2004–2005/Cross-sectional	2004–2005	41.3/58.7	SU	≥65 47 64	33	6704 11.005	0.49 (0.35–0.69) ^{a,d}	8
5 2	(Das et al., 2014)	PATH through life/Longitudinal	2009	52.4/47.6	Australia	43-04 68-72 48 53	34	1536 1536 1007	2.14 (1.50-2.42) 2.21 (1.59-3.08) d 6.13 (7.14 7.20) d	8
9 3	(De Zwaan et al., 2012)	Representative sample/Cross-sectional	2009	55.1/44.9	Germany	40-32 55-64 45-54	11/ 14	1907 396 418	0.13 (J.14-7.30) 3.53 (2.10-5.88) ^{a,d} 4 55 (7 07-7 07) ^{a,d}	7
900	(Guldberg-Kjär et al., 2013)	Hässleholm, south Sweden/Cross- sectional	2004	52.7/47.3	Sweden	65-80	19 16	1599	1.00 (0.61–1.63) ^a	8
15	(Jacob et al., 2018)	Adult Psychiatric Morbidity Survey 2007/Cross- sectional	2006-2007	51.4/48.6	UK	≥60	43	1963	2.19 (1.63–2.94) ^a	7
6 (K	(Kooij et al., 2005)	Nijmegen Health Area Study-2 (NHA-2)/Cross- sectional	1997–1998	55.3/44.7	The Netherlands	60–75	6	395	2.28 (1.19–4.32) ^b	7
6	(Park et al., 2011)	Korean epidemiologic catchment area study stud (KECA)/Cross-sectional	2006–2007	49.5/50.5	Korea	50-59	14	1036	$1.35 (0.80 - 2.27)^{a}$	6
2	(Vingilis et al., 2015)	Centre for Addiction andMental HealthMonitor /Cross-sectional	2011-2012	47.6/52.4	Canada	≥65 47 64	4	670 1 277	0.60 (0.22–1.58) ^{a,d}	ω
2	(Www.hank.at.al 2018)	NEMESIS-2 /Cross-sectional	2013-2015	50 9740 8	The Netherlands	45-64 58-70	49 20	1375 1594	3.56 (2.70–4.68) ^{a.d} 1 82 (1 27–2 61) ^{a.d}	α
				2. 1		48-57	63	1178	5.35 (4.20–6.79) ^{a,d}	5
<u>5</u>	Clinical diagnosis (Adler et al., 2019)	National Health and Wellness Survey	2013	54.5/45.5	SU	≥50	125	11,661	$1.07 \ (0.90-1.28)^{a}$	9
. 8	(Bachmann et al., 2017)	Health insurance company, AOK	2014	50.1/49.9	Germany	50-69	7332	5,982,881	0.12 (0.12–0.13) ^b	8
8 B	(Bogdan and Reeves, 2018)	National Health Interview Survey	2012	55.2/44.8	NS	> 50	207	13,446	$1.54 (1.34 - 1.76)^{a}$	9
9	(Chen et al., 2018)	Swedish National Patient register	2013	43.7/56.3	Sweden	55-64 45-54	2681 8007	1,096,007 1,215,426	0.24 (0.24–0.25) ^d 0.66 (0.64–0.67) ^d	7
۲,	(Knight et al., 2014)	Kaiser Permanent Southern California	2009	52.2/47.8	US California	≥50	1272	1,072,554	$0.12 (0.11 - 0.13)^{c}$	7
E i	(Polyzoi et al., 2018)	Swedish National Patient register	2011	44.8/55.2	Sweden	≥ 65 21	142	1,798,034	0.01 (0.01-0.01)	~ 1
2	(Zhu et al., 2018)	Medicaid database	0107	60.T/39.9	ns	ec≤ 46–55	352 1003	219,333 296,954	0.16 (0.14–0.18) 0.34 (0.32–0.36) ^{b,d}	~
Ŧ,	Treatment									
9	(Castle et al., 2007)	Commercially insured	2005	51.5/48.5	SU	≥65 45–64	828 5655	413,987 807,901	0.20 (0.19–0.21) ^{a,d} 0.70 (0.68–0.72)	ø
E	(Huang et al., 2014)	National Health Insurance Research Database (NHIRD)	2005	NA	Taiwan	≥49	ы	264,550	0.002 (0.000–0.004) ^a	8
E	(Karlstad et al., 2016)	Prescription registry	2012	NA	Denmark Finland	45-64	3498 432	1,487,727 $1,440,000$	$0.24 \ (0.23-0.24)^{c,d} \\ 0.03 \ (0.03-0.03)^{c,d}$	8
					Iceland Norway		544 2303	78,271 1,244,444	$0.69 (0.64-0.76)^{c,d}$ $0.19 (0.18-0.19)^{c,d}$	
3	(McCarthy et al., 2012)	Health Improvement Network (THIN)	2008	51.1/48.9	Sweden UK	< 45	0311 22	2,423,929	0.26 (0.25-0.27) ====================================	a

Table 1

Additionally, seven studies (35 % of the included studies), with nine data sets, based on clinical diagnosis of ADHD, were included in the analysis with 11,706,296 participants and 21,121 individuals with clinical diagnosis of ADHD. These studies were based on registry data (e.g. health insurance databases and population-based patient registries), and in two cases (Adler et al., 2019; Bogdan and Reeves, 2018), on self-reported medical history of ADHD.

Finally, we identified four studies (20 % of the included studies), which reported the prevalence of ADHD treatment drawn from different population-based registries with 9,260,809 participants and 19,598 individuals who received ADHD treatment. These studies contributed with nine data sets. One study in this group included different types of treatment (Huang et al., 2014), including psychological and pharma-cological treatment, while other studies investigated the prevalence of pharmacological ADHD treatment only.

Although diverse geographical regions were represented in the analysis, the majority of studies, 10 out of 20 (50 %), were conducted in Europe, seven (35 %) from North America, two (10 %) from Asia, and one (5 %) from other regions (Australia) (Table 1).

Some of the studies provided data sets with a slightly lower age cutoff. For research diagnosis, three data-sets imposed a lower age cut-off at 48 (Das et al., 2014; Wynchank et al., 2018) and two data-sets at 45 years (Bernardi et al., 2012; De Zwaan et al., 2012); for clinical diagnosis, two data-sets imposed an age cut-off at 45 years (Chen et al., 2018; Zhu et al., 2018); and for ADHD treatment, seven data-sets imposed the lower age cut-off at 45 (Castle et al., 2007; Karlstad et al., 2016; McCarthy et al., 2012).

All selected studies showed satisfactory levels of study quality with summary scores over five (Table 1). The item-by-item assessment is provided in the Appendix 7 (in Supplementary material).

3.2. Main meta-analyses and sub-group analyses

We conducted three main meta-analyses that provided pooled prevalence estimates for each assessment method (Table 2). Using the random-effects model, the estimated pooled prevalence was 2.18 % (95 % CI = 1.51, 3.16), for ADHD research diagnosis based on validated scales. The corresponding estimated pooled prevalence was 0.23 % for clinical diagnosis (0.12, 0.43), and 0.09 for ADHD treatment (0.06, 0.15). Across all levels of the analysis, heterogeneity (Cochran Q test) was significant with the I² values higher than 75 % (Moffitt et al., 2015) (Table 2).

Subgroup analysis showed a significant difference in pooled prevalence estimates between the studies based on research diagnosis, clinical diagnosis and treatment, with Q (2) = 108.74, P < 0.0001. Direct comparisons of the prevalence between the different ADHD outcome measures revealed statistically significant differences between the prevalence provided in studies using research diagnosis of ADHD versus studies using either clinical diagnosis or treatment, with Q (1) = 35.52, P < 0.0001, and Q (1) = 99.40, P < 0.0001, respectively. The subgroup analysis also revealed a statistically significant difference in the prevalence estimated in studies using clinically diagnosed ADHD versus treated ADHD, with Q (1) = 4.80, P < 0.0001.

As shown in Table 2, the pooled prevalence estimates varied across the sensitivity analyses for all assessment methods, but with overlapping confidence interval before and after exclusions. The I² values decreased slightly after conducting sensitivity analyses, although heterogeneity remained significant.

4. Discussion

To our knowledge, the present study is the first to assess the prevalence of ADHD in older adults via a comprehensive systematic review and meta-analysis. Additionally, this is the first systematic review and meta-analysis of the prevalence of ADHD that took into consideration potential differences between studies investigating ADHD prevalence according to the method to establish the diagnosis. Our systematic search of the literature identified 20 studies, reporting 32 data-sets for the meta-analysis. Our findings indicate a notable prevalence gap with significantly higher estimates for ADHD research diagnosis compared to the prevalence of individuals with clinical diagnosis or based on the rates of treatment prescriptions.

Our pooled prevalence estimates of ADHD research diagnosis from the main analysis and sensitivity analyses ranged from 1.49 % to 2.18 %. These estimates are lower than previously identified pooled prevalence estimates based on validated scales: 2.5 % (95 % CI = 2.1, 3.1) in adults with the mean age of 34, (Simon et al., 2009) and 5.0 % (95 % CI = 4.1, 6.2) in young adults (Willcutt, 2012). This is consistent with the well-established effect of age on the prevalence of ADHD (Fayyad et al., 2007; Faraone et al., 2006).

Our findings suggest that a considerable number of older adults reported elevated levels of ADHD symptoms. However, methodological aspects need to be considered when interpreting the gap between the pooled prevalence estimates based on different assessment methods. The estimates from studies based on research diagnosis may overestimate the prevalence of ADHD in older adults. Previous research in children and adolescents has identified higher prevalence estimates based on research diagnosis via DSM-validated scales, compared to the prevalence based on the ICD-9 or ICD-10 diagnostic criteria (Polanczyk et al., 2007; Polanczyk et al., 2014), commonly used in register-based studies. Additionally, five out of nine studies based on research diagnosis included in the present review were based on ADHD screeners, which cover ADHD symptoms present in the last six months and may misdiagnose the condition with other mental health problems or neurological conditions with a similar clinical presentation (Gentile et al., 2006). Indeed, after excluding these studies, the magnitude of the

Table 2

Summary of results in main meta-analyses and sensitivity analyses.

Type of analysis	N of data sets	Pooled prevalence estimate (%)	95 % CI	Heterogeneity	
				Q	I ² (%)
Research diagnosis-all	14	2.18	1.51-3.16	273.05*	95.24
1. Limited to the symptoms present both in childhood and adulthood	7	1.75	1.01-3.03	93.77*	93.60
2. Limited to geographical regions other than North America	10	2.66	1.78-3.97	121.78*	92.61
3. Limited to age cut off ≥ 50	9	1.49	0.96-2.30	72.36*	88.94
Clinical diagnosis-all	9	0.23	0.12-0.43	14643.63*	99.94
1. Limited to registries	7	0.14	0.07-0.29	13769.97*	99.96
2. Limited to geographical regions other than North America	4	0.11	0.04-0.32	12752.78*	99.98
3. Limited to age cut off ≥ 50	7	0.19	0.11-0.32	3834.47*	99.84
Treatment-all	9	0.09	0.06-0.15	8399.43*	99.90
1. Limited to geographical regions other than North America	7	0.06	0.04-0.10	3280.56*	99.82
2. Limited to age cut off ≥ 50	2	0.02	0.00-1.88	108.10*	99.07

* P < 0.0001.

prevalence estimates from studies assessing both childhood and current symptoms decreased, although with overlapping confidence intervals. As problems with attention, anterograde memory and executive functions are common in ADHD and age related cognitive impairment, such as Mild cognitive impairment (MCI) or prodromal dementia (Goodman et al., 2016; Pollak, 2012), a careful differential diagnosis of ADHD should consider the childhood onset of current symptoms and their life long persistence (Goodman et al., 2016; Pollak, 2012). Included studies with prevalence estimates based on clinical diagnosis, treatment and research diagnosis with a confirmed childhood history of ADHD likely ruled out dementia or other mental health disorder as potential causes of current cognitive symptoms. Among studies that used ADHD screeners without confirming history of childhood symptoms, only one study (Das et al., 2014) controlled for probable dementia by excluding individuals with the Mini Mental State Examination (MMSE) score 23 or less. Thus, screening assessment tools for ADHD should only be used as a first step of a more comprehensive clinical ADHD assessment. Future research conducted in community samples should address whether individuals with elevated levels of ADHD symptoms severity meet established diagnostic criteria by applying more comprehensive assessment tools, including the assessment of childhood symptoms. Moreover, future studies should investigate potential reasons behind elevated levels of ADHD symptoms reported via validated scales, such as misclassification with another mental-health or neurological condition (Gentile et al., 2006), or age-inappropriate clinical assessment procedures (Lensing et al., 2015; Brod et al., 2012).

Our results also suggest that clinicians, to some extent, might fail to recognize and properly treat ADHD symptoms in older adults. Clinical presentation of ADHD may change with age, with inattentive symptoms becoming more prevalent than hyperactivity and impulsivity (Lensing et al., 2015; Brod et al., 2012). Additionally, some older adults who do not meet official clinical criteria for an ADHD diagnosis may experience distressing symptoms and may be in need for care (Goodman et al., 2016). Thus, mental health care providers should be aware that symptoms of ADHD persist across the life span in a substantial number of individuals with ADHD.

With the exception of one study that included both pharmacological and non-pharmacological treatment (Huang et al., 2014), studies included in the present review only considered pharmacological treatment. We found that the prevalence of ADHD treatment in older adults is less than half of the prevalence of clinically diagnosed ADHD. It is difficult to interpret whether these differences reflect under- or overtreatment, because precise estimates of the proportion of individuals receiving ADHD treatment is lacking. Previous research is mixed and the percentage of diagnosed individuals who receive pharmacological treatment varies substantially for studies of adults (25-80 %) (Bernardi et al., 2012; Polyzoi et al., 2018) as well as older adults (28-88 %) Polyzoi et al., 2018; Pollak, 2012). Older adults have been reported to have similar benefits from pharmacological treatment as younger adults (Lensing et al., 2015; Manor et al., 2011), however, clinicians may lack awareness on the benefits and proper drug dosage in this age group (Goodman et al., 2016(Lensing et al., 2015). Additionally, older patients and/or their medical care providers may have concerns regarding potential ADHD medication side effects due to older age, comorbid psychiatric and somatic disorders (in particular cardiovascular conditions), and interactions with other medications (Goodman et al., 2016; Lensing et al., 2015; Brod et al., 2012; Herrmann et al., 2008). Thus, adequate pharmacological and psychological treatment in this population should be carefully considered.

We included only studies that provided crude prevalence estimates in the published report or upon request. Prevalence estimates weighted to represent general population were not included in the present metaanalysis but they offer important insights into the topic. A large study from India reported an adjusted prevalence of diagnosed ADHD of 0.22 % or lower for individuals aged 50 and older (Sagar et al., 2020). This finding is in line with our pooled prevalence estimate based on clinical diagnosis. A longitudinal study from the Netherlands (Michielsen et al., 2012), reported an adjusted prevalence of 2.8 % (95 % CI = 0.86, 4.64) in adults aged 60 and older, after a two-phase procedure of screening and a diagnostic interview of current and childhood symptoms. A study from Brazil (Polanczyk et al., 2010) provided an adjusted prevalence of 6.1 % (4.50, 8.30) for adults older than 44 years of age based on an ADHD screener. These prevalence estimates are similar to or higher than our pooled prevalence based on research diagnosis and suggest a more pronounced prevalence of older adults with ADHD symptoms when taking into account population distribution of different socio-economic variables.

4.1. Limitations and future lines of research

All included studies showed a satisfactory level of study quality. This is particularly the case with registry-based studies, applied in large national-based samples, which provide a reliable estimate of the prevalence. The unequal female-to-male distribution observed in eight out of 20 included studies is a potential source of bias as we were unable to provide sex-stratified ADHD prevalence estimates. Additionally, the majority of included studies (13 out of 20) did not provide prevalence estimates in older adults stratified by sex. Such differences have been thoroughly investigated in younger age (Brod et al., 2012; Willcutt and Pennington, 2000). Thus, future research of ADHD should consider potential differences in the prevalence of ADHD between female and male participants in older age.

Significant heterogeneity across studies has previously been identified in systematic reviews and meta-analyses of ADHD prevalence in children and adults, mostly due to methodological differences (Polanczyk et al., 2007; Simon et al., 2009; Willcutt, 2012). The current study observed a substantial heterogeneity, despite pooling separate prevalence estimates for different assessment methods and conducting sensitivity analyses to address other potential sources of heterogeneity. Due to the lack of relevant data (i.e. mean age and SD) and relatively small number of studies per assessment method for ADHD clinical diagnosis (nine data-sets) and treatment (nine data-sets), we could not conduct more detailed sub-group analyses (e.g. for age and geographical region). A minimum of 10 studies per regressor is necessary for the meta-regression analysis, as recommended in the Cochrane handbook (p 284) (Deeks et al., 2011). More high-quality research, based on large samples and from regions other than Europe and North America, is needed to obtain more robust evidence regarding the prevalence of ADHD in older adults.

Another limitation in studies of ADHD in older adults is the use of retrospective reporting of childhood symptoms and recall bias, and a potential underestimation of the prevalence (Simon et al., 2009). Furthermore, self-report as the only source of information in studies with a research diagnosis of adult ADHD is a limitation given that previous research has shown an underestimation of symptoms severity by self-report in young adults compared to reports of parents/teachers (Barkley et al., 2002). In order to somewhat mitigate the effects of recall bias and self-report, future studies of ADHD in older adults should aim to include relevant information from family members.

In conclusion, our findings indicate a substantial gap between the prevalence estimates of older adults with elevated ADHD symptoms assessed via validated scales in community samples and prevalence estimates based on ADHD clinical diagnosis and treatment. Furthermore, our results suggest that the prevalence of treated individuals is less than half of the prevalence of individuals with clinical diagnosis for ADHD. This study also highlights that ADHD is scarcely studied among older adults and that much more research is needed on the topic, in particular research that addresses the effects of different assessment methods, sex and age on the prevalence of ADHD after 50 years of age.

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Declaration of Competing Interest

SC declares honoraria and reimbursement for travel and accommodation expenses for lectures from the following non-profit associations: Association for Child and Adolescent Central Health (ACAMH), Canadian ADHD Alliance Resource (CADDRA), British Association of Pharmacology (BAP), and from Healthcare Convention for educational activity on ADHD.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.neubiorev.2020.07. 042.

References

- Adler, L.A., Faraone, S.V., Sarocco, P., Atkins, N., Khachatryan, A., 2019. Establishing US norms for the Adult ADHD Self-Report Scale (ASRS-v1.1) and characterising symptom burden among adults with self-reported ADHD. Int. J. Clin. Pract. 73https://doi.org/10.1111/jicp.13260. e13260-e.
- Anderson, J.C., 1996. Is childhood hyperactivity the product of western culture? Lancet 348, 73–74.
- Bachmann, C.J., Philipsen, A., Hoffmann, F., 2017. ADHD in Germany: trends in diagnosis and pharmacotherapy. Arztebl. Int. 114, 141–148. https://doi.org/10.3238/arztebl. 2017.0141.
- Barkley, R.A., Fischer, M., Smallish, L., Fletcher, K., 2002. The persistence of attentiondeficit/hyperactivity disorder into young adulthood as a function of reporting source and definition of disorder. J. Abnorm. Psychol. 111, 279. https://doi.org/10.1037/ 0021-843X.111.2.279.
- Bernardi, S., Faraone, S.V., Cortese, S., Kerridge, B.T., Pallanti, S., Wang, S., et al., 2012. The lifetime impact of attention deficit hyperactivity disorder: results from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). Psychol. Med. 42, 875–887. https://doi.org/10.1017/S003329171100153X.
- Bogdan, A.R., Reeves, K.W., 2018. Sleep duration in relation to attention deficit hyperactivity disorder in American adults. Behav. Sleep Med. 16, 235–243. https://doi. org/10.1080/15402002.2016.1188391.
- Borenstein, M., Hedges, L.V., Higgins, J.P., Rothstein, H.R., 2011. Introduction to Metaanalysis. John Wiley & Sons, Chichester, West Sussex, pp. 69–74.
 Brod, M., Schmitt, E., Goodwin, M., et al., 2012. ADHD burden of illness in older adults: a
- Brod, M., Schmitt, E., Goodwin, M., et al., 2012. ADHD burden of illness in older adults: a life course perspective. Qual. Life Res. 21, 795–799. https://doi.org/10.1007/ s11136-011-9981-9.
- Castle, L., Aubert, R.E., Verbrugge, R.R., Khalid, M., Epstein, R.S., 2007. Trends in medication treatment for ADHD. J. Atten. Disord. 10, 335–342 https://doi.org/ 10.1177%2F1087054707299597.
- Chen, Q., Hartman, C.A., Haavik, J., Harro, J., Klungsøyr, K., Hegvik, T.A., et al., 2018. Common psychiatric and metabolic comorbidity of adult attention-deficit/hyperactivity disorder: a population-based cross-sectional study. PLoS One 13. https://doi. org/10.1371/journal.pone.0204516.
- Das, D., Cherbuin, N., Easteal, S., Anstey, K.J., 2014. Attention Deficit/Hyperactivity Disorder symptoms and cognitive abilities in the late-life cohort of the PATH through life study. PLoS One 9, e86552. https://doi.org/10.1371/journal.pone.0086552.
- De Zwaan, M., Gruß, B., Müller, A., Graap, H., Martin, A., Glaesmer, H., et al., 2012. The estimated prevalence and correlates of adult ADHD in a German community sample. Eur. Arch. Psychiatry Clin. Neurosci. 262, 79–86. https://doi.org/10.1007/s00406-

011-0211-9.

- Deeks, J.J., Higgins, J.P., Altman, D.G., 2011. Analysing data and undertaking metaanalyses. In: Higgins, J.P., Green, S. (Eds.), Meta-Regression. Cochrane Handbook for Systematic Reviews of Interventions. John Wiley & Sons, Chichester, West Sussex 284 p.
- Faraone, S.V., Biederman, J., Mick, E., 2006. The age-dependent decline of attention deficit hyperactivity disorder: a meta-analysis of follow-up studies. Psychol. Med. 36, 159–165. https://doi.org/10.1017/S003329170500471X.
- Fayyad, J., De Graaf, R., Kessler, R., Alonso, J., Angermeyer, M., Demyttenaere, K., et al., 2007. Cross-national prevalence and correlates of adult attention-deficit hyperactivity disorder. Br. J. Psychiatry 190, 402–409. https://doi.org/10.1192/bjp.bp. 106.034389.

Gentile, J.P., Atiq, R., Gillig, P.M., 2006. Adult ADHD: diagnosis, differential diagnosis, and medication management. Psychiatry 3, 25.

- Goodman, D.W., Mitchell, S., Rhodewalt, L., Surman, C.B., 2016. Clinical presentation, diagnosis and treatment of attention-deficit hyperactivity disorder (ADHD) in older adults: a review of the evidence and its implications for clinical care. Drugs Aging 33, 27–36. https://doi.org/10.1007/s40266-015-0327-0.
- Guldberg-Kjär, T., Sehlin, S., Johansson, B., 2013. ADHD symptoms across the lifespan in a population-based Swedish sample aged 65 to 80. Int. Psychogeriatr. 25, 667–675. https://doi.org/10.1017/S1041610212002050.
- Herrmann, N., Rothenburg, L.S., Black, S.E., Ryan, M., Liu, B.A., Busto, U.E., et al., 2008. Methylphenidate for the treatment of apathy in Alzheimer disease: prediction of response using dextroamphetamine challenge. J. Clin. Psychopharmacol. 28, 296–301. https://doi.org/10.1097/JCP.0b013e318172b479.
- Higgins, J.P., Thompson, S.G., Deeks, J.J., Altman, D.G., 2003. Measuring inconsistency in meta-analyses. BMJ (Online) 327, 557–560. https://doi.org/10.1136/bmj.327. 7414.557.
- Huang, C.L., Chu, C.C., Cheng, T.J., Weng, S.F., 2014. Epidemiology of treated attentiondeficit/hyperactivity disorder (ADHD) across the lifespan in Taiwan: a nationwide population-based longitudinal study. PLoS One 9, e95014. https://doi.org/10.1371/ journal.pone.0095014.
- Jacob, L., Haro, J.M., Koyanagi, A., 2018. Attention deficit hyperactivity disorder symptoms and disordered eating in the English general population. Int. J. Eat. Disord. 51, 942–952. https://doi.org/10.1002/eat.22934.
- Karlstad, Ø, Zoëga, H., Furu, K., Bahmanyar, S., Martikainen, J.E., Kieler, H., et al., 2016. Use of drugs for ADHD among adults-a multinational study among 15.8 million adults in the Nordic countries. Eur. J. Clinl. Pharmacol. 72, 1507–1514. https://doi.org/10. 1007/s00228-016-2125-y.
- Kessler, R.C., Adler, L., Ames, M., Demler, O., Faraone, S., Hiripi, E., et al., 2005. The World Health Organization adult ADHD self-report scale (ASRS): a short screening scale for use in the general population. Psychol. Med. 35, 245–256. https://doi.org/ 10.1017/S0033291704002892.
- Knight, T.K., Kawatkar, A., Hodgkins, P., Moss, R., Chu, L.H., Sikirica, V., et al., 2014. Prevalence and incidence of adult attention deficit/hyperactivity disorder in a large managed care population. Curr. Med. Res. Opin. 30, 1291–1299. https://doi.org/10. 1185/03007995.2014.901940.
- Kooij, J.J.S., Buitelaar, J.K., van den Oord, E.J., Furer, J.W., Rijnders, C.A.T., Hodiamont, P.P.G., 2005. Internal and external validity of attention-deficit hyperactivity disorder in a population-based sample of adults. Psychol. Med. 35, 817–827. https://doi.org/ 10.1017/S003329170400337X.
- Lensing, M.B., Zeiner, P., Sandvik, L., Opjordsmoen, S., 2015. Psychopharmacological treatment of ADHD in adults aged 50+: an empirical study. J. Atten. Disord. 19, 380–389 https://doi.org/10.1177%2F1087054714527342.
- Liberati, A., Altman, D.G., Tetzlaff, J., Mulrow, C., Gøtzsche, P.C., Ioannidis, J.P., et al., 2009. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. PLoS Med. 6, e1000100.
- Manor, I., Rozen, S., Zemishlani, Z., Weizman, A., Zalsman, G., 2011. When does it end? Attention-deficit/hyperactivity disorder in the middle aged and older populations. Clin. Neuropharmacol. 34, 148–154. https://doi.org/10.1097/WNF. 0b013e3182206dc1.
- McCarthy, S., Wilton, L., Murray, M.L., Hodgkins, P., Asherson, P., Wong, I.C.K., 2012. The epidemiology of pharmacologically treated attention deficit hyperactivity disorder (ADHD) in children, adolescents and adults in UK primary care. BMC Pediatr. 12, 78. https://doi.org/10.1186/1471-2431-12-78.
- Michielsen, M., Semeijn, E., Comijs, H.C., van de Ven, P., Beekman, A.T., Deeg, D.J., et al., 2012. Prevalence of attention-deficit hyperactivity disorder in older adults in the Netherlands. Br. J. Psychiatry 201, 298–305. https://doi.org/10.1192/bjp.bp.111. 101196.
- Moffitt, T.E., Houts, R., Asherson, P., Belsky, D.W., Corcoran, D.L., Hammerle, M., et al., 2015. Is adult ADHD a childhood-onset neurodevelopmental disorder? Evidence from a four-decade longitudinal cohort study. Am. J. Psychiatry 172, 967–977. https://doi. org/10.1176/appi.ajp.2015.14101266.
- Munn, Z., Moola, S., Riitano, D., Lisy, K., 2014. The development of a critical appraisal tool for use in systematic reviews addressing questions of prevalence. Int. J. Health Policy Manag. 3, 123. https://doi.org/10.15171/ijhpm.2014.71.
- National Guideline Centre (UK), 2018. Attention Deficit Hyperactivity Disorder: Diagnosis and Management. 2018 Mar. (NICE Guideline, No. 87.) F, Evidence review for combined pharmacological and non-pharmacological treatments review. Available from: National Institute for Health and Care Excellence (UK), London. https://www.ncbi.nlm.nih.gov/books/NBK542670/.
- Nigg, J.T., 2013. Attention-deficit/hyperactivity disorder and adverse health outcomes. Clin. Psychol. Rev. 33, 215–228. https://doi.org/10.1016/j.cpr.2012.11.005.
- Park, S., Cho, M.J., Chang, S.M., Jeon, H.J., Cho, S.J., Kim, B.S., et al., 2011. Prevalence, correlates, and comorbidities of adult ADHD symptoms in Korea: Results of the

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Korean epidemiologic catchment area study. Psychiatry Res. 186, 378–383. https://doi.org/10.1016/j.psychres.2010.07.047.

- Polanczyk, G., De Lima, M.S., Horta, B.L., Biederman, J., Rohde, L.A., 2007. The worldwide prevalence of ADHD: a systematic review and metaregression analysis. Am. J. Psychiatry 164, 942–948.
- Polanczyk, G., Laranjeira, R., Zaleski, M., Pinsky, I., Caetano, R., Rohde, L.A., 2010. ADHD in a representative sample of the Brazilian population: estimated prevalence and comparative adequacy of criteria between adolescents and adults according to the item response theory. Int. J. Methods Psychiatr. Res. 19, 177–184. https://doi. org/10.1002/mpr.319.
- Polanczyk, G.V., Willcutt, E.G., Salum, G.A., Kieling, C., Rohde, L.A., 2014. ADHD prevalence estimates across three decades: an updated systematic review and meta-regression analysis. Int. J. Epidemiol. 43, 434–442. https://doi.org/10.1093/ije/ dvt261.
- Pollak, J., 2012. Distinguishing between adult ADHD and mild cognitive impairment. Curr. Psychiatr. 11, 48–50.
- Polyzoi, M., Ahnemark, E., Medin, E., Ginsberg, Y., 2018. Estimated prevalence and incidence of diagnosed ADHD and health care utilization in adults in Sweden - a longitudinal population-based register study. Neuropsych. Dis. Treat. 14, 1149–1161. https://doi.org/10.2147/NDT.S155838.
- Sagar, R., Dandona, R., Gururaj, G., Dhaliwal, R.S., Singh, A., Ferrari, A., et al., 2020. The burden of mental disorders across the states of India: the global burden of disease study 1990–2017. Lancet Psychiatry 7, 148–161. https://doi.org/10.1016/S2215-0366(19)30475-4.
- Simon, V., Czobor, P., Balint, S., Meszaros, A., Bitter, I., 2009. Prevalence and correlates of adult attention-deficit hyperactivity disorder: meta-analysis. Br. J. Psychiatry 194,

204-211. https://doi.org/10.1192/bjp.bp.107.048827.

- Thomas, R., Sanders, S., Doust, J., Beller, E., Glasziou, P., 2015. Prevalence of attentiondeficit/hyperactivity disorder: a systematic review and meta-analysis. Pediatrics 135, e994–e1001. https://doi.org/10.1542/peds.2014-3482.
- Timimi, S., Taylor, E., 2004. ADHD is best understood as a cultural construct. Br. J. Psychiatry 184, 8–9. https://doi.org/10.1192/bjp.184.1.8.
- Torgersen, T., Gjervan, B., Lensing, M.B., Rasmussen, K., 2016. Optimal management of ADHD in older adults. Neuropsychiatr. Dis. Treat. 12, 79–87.
- Vingilis, E., Erickson, P.G., Toplak, M.E., Kolla, N.J., Mann, R.E., Seeley, J., et al., 2015. Attention deficit hyperactivity disorder symptoms, comorbidities, substance use, and social outcomes among men and women in a Canadian sample. Biomed. Res. Int. 2015, 982072. https://doi.org/10.1155/2015/982072.
- Willcutt, E.G., 2012. The prevalence of DSM-IV attention-deficit/hyperactivity disorder: a meta-analytic review. Neurotherapeutics 9, 490–499. https://doi.org/10.1007/ s13311-012-0135-8.
- Willcutt, E.G., Pennington, B.F., 2000. Comorbidity of reading disability and attentiondeficit/hyperactivity disorder: differences by gender and subtype. JLD 33, 179–191 https://doi.org/10.1177%2F002221940003300206.
- Wynchank, D., Have, M., Bijlenga, D., Penninx, B.W., Beekman, A.T., Lamers, F., et al., 2018. The association between insomnia and sleep duration in adults with attentiondeficit hyperactivity disorder: results from a general population study. J. Dent. Sleep Med. 14, 349–357. https://doi.org/10.5664/jcsm.6976.
- Zhu, Y., Liu, W., Li, Y., Wang, X., Winterstein, A.G., 2018. Prevalence of ADHD in publicly insured adults. J. Atten. Disord. 22, 182–190 https://doi.org/ 10.1177%2F1087054717698815.