1	Impaired health-related quality of life, and depressive symptoms in a cohort of healthy
2	adults with symptoms of Attention Deficit/Hyperactivity Disorder
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42

ABSTRACT

43 Background

44 Attention Deficit/Hyperactivity Disorder (ADHD) prevalence has increased in the last 10 45 years, most likely due to increased recognition by clinicians. Even so, an issue with under-46 diagnostics may persist. Historically ADHD has been described as a male-dominant disorder. 47 However, recent evidence shows that ADHD prevalence is similar between the sexes, but that 48 the related impairment or symptomatology might vary. This study estimated the prevalence of 49 undiagnosed ADHD symptoms (pADHD) and explored the sex-stratified symptomatology and 50 associations with self-perceived health-related quality of life (HRQL) and experience of 51 depressive symptoms.

52 Methods

This was done in a unique cohort of 50,937 healthy blood donors—individuals who successfully maintain regular commitments despite potential ADHD symptoms. ADHD symptoms were estimated using Adult ADHD Self-Report Scale (ASRS), health-related quality of life (HRQL) measured using mental and physical component scores (MCS/PCS) estimated based on 12-item Short-Form Health Survey (SF-12) with a higher score indicating better HRQL, and depressive symptoms were measured using Major Depression Inventory (MDI) with higher score indicating more depressive symptoms.

60 **Results**

In total, 3% classified with pADHD (sex ratio 1:1). pADHD was associated with reduced MCS and PCS, and increased MDI score. Males scored on average higher on inattentive symptoms compared to females, whereas females scored on average higher on hyperactive-impulsive

- 64 symptoms. Individuals scoring high on the combined inattentive and hyperactive-impulsive
- 65 ADHD symptom presentation were most likely to be impaired in terms of higher MDI score
- 66 and lower PCS when compared to non-ADHD controls.

67 Conclusions

- 68 In conclusion, ADHD symptoms are common in this seemingly healthy and undiagnosed
- 69 population. Symptom presentations differs between sexes and type of presentation seem to
- 70 impact the association with depressive symptoms and level of reduced HRQL.

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73 Keywords

- ADHD subtype, ADHD presentation, ADHD symptomatology, the Danish Blood Donor
- 75 Study, DBDS, ASRS, MDI, SF12, HRQL, HRQoL, cross-sectional, depression, depressive
- 76 disorder, major depressive disorder

77

MANUSCRIPT

78 **1. Introduction**

79 Attention-Deficit/Hyperactivity Disorder (ADHD) affects between 1.5% and 3.6% of adults in 80 European populations [1–3], representing a significant public health concern. Rather than being 81 a binary condition, ADHD exists on a symptom continuum, with presentations varying across 82 the lifespan as inattentive, hyperactive-impulsive, or combined [4]. The diagnosis requires 83 onset of symptoms before age 12, and that an individual meets distinct deficits in core 84 symptoms of inattention, hyperactivity, and impulsivity for at least six months. The symptoms 85 must be occurring in two or more settings, and must interfere with social or school functioning, 86 and finally, that the symptoms are not explained by another mental disorder [5]. The disorder 87 often continues to impact multiple facets of life into adulthood, including impaired general 88 functioning and well-being [6,7].

89 ADHD symptoms are associated with significant distress due to feelings of depression and 90 isolation, as well as self-esteem issues [6]. Beyond these direct negative impacts, individuals 91 diagnosed with ADHD experience substantial psychosocial impairment due to high lifetime 92 comorbidity rates of 60-80%, including a 45% lifetime prevalence of mood disorders [8,9]. 93 The more pronounced the diagnosed ADHD symptomatology, the more likely affected 94 individuals will experience mental health comorbidity. Research indicates that having three or 95 more psychiatric diagnoses associates with a ten-fold increase in ADHD risk [1]. ADHD 96 particularly impacts physical health through fatigue and energy depletion [6]. Individuals with 97 diagnosed ADHD often experience exhaustion when controlling behavioral traits, as this 98 requires substantial energy. These impacts can create a cycle of physical and mental health 99 challenges that affect overall well-being [6].

100 Historically described as male-dominant, resulting in significant sex-disparity in research, 101 recent evidence shows similar ADHD prevalence between sexes, though impact varies 102 considerably [10]. The findings of Williamson and Johnston [11] suggest significant variation 103 in ADHD comorbidity, psychosocial impairment, and cognitive functioning between sexes, 104 supported by Faheem et al. (2022). Females more often receive diagnosis in adulthood than 105 males, possibly in part due to the disorder being masked by reductions in male hyperactive-106 impulsive symptom expression over time. This sex-based variation in presentation and 107 diagnosis timing highlights the need for more nuanced understanding of ADHD manifestation 108 across populations.

While increased clinical recognition has improved diagnosis rates compared to prior decades, evidence suggests ADHD remains significantly underdiagnosed and undertreated in many European countries, particularly among individuals who have developed effective adaptive strategies [9,10].

In Denmark, ADHD medication use increased 71% in the last decade, especially among those aged 25-44, likely reflecting late diagnoses [13]. This trend suggests a substantial population of adults with unrecognized ADHD who may benefit from identification and support.

Current diagnostic practices may miss individuals who have developed successful coping mechanisms, particularly those who maintain regular employment and social commitments because related impairments may go beyond their abilities to uphold such. These individuals may experience significant symptoms and impairment while appearing to function well in daily life. Understanding this population's experiences and needs requires novel research approaches that look beyond traditional clinical populations.

This study presents such an approach by examining the prevalence of ADHD symptoms in
healthy adult blood donors—individuals who successfully maintain regular commitments

despite potential symptoms. Unlike previous studies focused on clinical cases, our research specifically targets those who may have developed adaptive strategies to mask symptoms and remain undiagnosed. Blood donors represent a distinct study population as they must meet strict health criteria while maintaining regular employment and social commitments, potentially masking underlying ADHD symptoms through developed coping mechanisms.

Building on diagnostic criteria requiring onset before age 12, we hypothesize that undiagnosed and untreated ADHD symptoms are associated with poorer self-rated mental health and increased depressive symptoms later in life. Our study examines this relationship in a population that hasn't sought clinical attention for these symptoms, potentially providing new insights into the long-term impact of undiagnosed ADHD.

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135 **2. Methods**

The questionnaire was administered to 52,771 individuals. After filtering, 50 937 individualswere included in the study (Figure 1).

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2.1 Study population and material

This study utilized data from the Danish Blood Donor Study (DBDS), a national prospective cohort study and biobank established in 2010. The DBDS relies on existing Danish blood bank infrastructure, with donors invited to participate when visiting blood banks. Participants provide informed consent for individual-level information retrieval from Danish registers and complete web-based research questionnaires. Since participants are active blood donors upon inclusion, they meet general health requirements for donation eligibility [14,15].

146 Data collection occurred between May 2015 and May 2018, including self-reported ADHD

147 symptoms, lifestyle factors (height, weight, depression history, smoking status, alcohol habits),

148 and demographic characteristics. Information on redeemed prescriptions and socio-economic

149 characteristics came from Danish registers, including the Prescription Register and Population

150 Register. After filtering, 50,937 individuals were included in the study. In this study the term

151 "sex" refers to the sex the participants were assigned at birth, which was based solely on the

152 visible external anatomy of a newborn.

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2.2.1 Adult ADHD Self-Report Scale (ASRS)

155 The Adult ADHD Self-Report Scale V1.1 (ASRS), commonly used for adult ADHD screening 156 and validated in general population samples [16], serves as a primary screening instrument in 157 Danish clinical guidelines [17]. The scale contains 18 items scored on a five-point Likert scale 158 (never to very often) based on six-month experiences. Nine items represent inattentive

159 symptoms (items 1-4 and 7-11) and nine assess hyperactivity-impulsiveness (items 5-6 and 12-160 18). A total score >37 indicates probable ADHD, while subscale scores >24 identify specific 161 presentations. It is possible to meet the criteria of ADHD (sum score \geq 37) without scoring \geq 24 162 in either or both subscales. For this study, we classified these individuals as Non-specific. The 163 ASRS has been reported to have a good reliability and diagnostic utility among adults with a 164 sensitivity of 0.92, a specificity of 0.69, and positive and negative predictive values of 0.48 and 165 0.97, respectively [18]. Similar psychometric properties were reported among Scandinavian 166 adolescents[19].

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2.2.2 Health-related quality of life (HRQL)

170 The 12-Item Short Form Health Survey (SF-12) assessed health-related quality of life through 171 mental (MCS) and physical (PCS) components, validated across populations and particularly 172 suitable for general population mental health measurement [20]. The scale comprises 12 items 173 addressing four-week health state and health impacts on daily life. Component scores range 0-174 100, with 100 representing optimal health status. Danish population means are 51 for PCS and 175 52.8 for MCS. Categories were defined following Danish Health Authority methodology: 176 lowest 10% classified as "low," highest 65% as "good," and remaining 25% as "moderate" 177 (Steenstrup et al., 2013). The SF-12 measures following eight domains: General health 178 perceptions, limitations in physical activities because of health problems, limitations in 179 social activities because of physical or emotional problems, limitations in usual role 180 activities because of physical health problems, bodily pain, general mental health 181 (psychological distress and well-being), limitations in usual role activities because of 182 emotional problems, and vitality (energy and fatigue).

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185**3.1.3**Major Depression Inventory Scale (MDI)

The Major Depression Inventory Scale (MDI) measured current depression through ten symptoms within the previous two weeks, validated in Danish language [22]. The composite score ranges 0-50, with scores above 20 indicating depression (21 for mild, 26 for moderate, 31 for severe depression). Additional questions assessed previous depression diagnosis and treatment history (medical or other).

191

192 **3.1 Statistics**

193 The ADHD prevalence of ADHD symptoms (potential ADHD/pADHD) and the distribution 194 of the individual characteristics and potential covariates are presented using descriptive 195 statistics. Categorical and dichotomous variables are described in frequencies (n) and 196 percentages (%) for females, males, and the total cohort comparing those with and without 197 probable ADHD assessed according to the predefined full edition cut-off. Initially, the normal 198 distribution of continuous variables was tested by performing a Shapiro-Wilk normality test. 199 Normally distributed variables were described by mean and standard deviation (SD), whereas 200 non-normally distributed variables were described using the median and interquartile range 201 (IOR). Differences in characteristics between pADHD and non-ADHD were investigated by 202 using the Chi-squared test for dichotomous variables, by t-tests for normally distributed 203 variables, and by Mann-Whitney U-tests for non-normally distributed variables. Also, the basic 204 characteristics and frequencies of the specific pADHD presentations are illustrated along with 205 measures of association (Risk Ratio). Difference in sex strata was tested by using Mantel-206 Haenszel, and results are presented as a Risk Ratio (MH RR) or as Female RR/Male RR when 207 the Breslow-Day Test for Homogeneity were significant.

For analyzing the effect of pADHD (ASRS full edition) on the different assumed dependent mental health outcomes, crude multinomial logistic regression models were fitted for each outcome (scores of MDI and MCS, and history of depression).

211 Additional analyses were done to explore which factors impacted this association. For these, 212 multivariate multinominal logistic regression models were computed. We explored the impact 213 of age, history of depression, income level, educational level, employment status, number of 214 children, BMI, alcohol consumption, and smoking status. Further, we included the investigated 215 outcomes (depression, PCS, MCS) as covariates in models where they were not the outcome. 216 The investigated covariates were selected based on previous literature. First, covariates were 217 included in *fully* adjusted multinomial logistic regression analyses. Second, stepwise backward 218 manual variable selection method was applied to the models to identify variables with any kind 219 of impact on the associations between pADHD and MCS, PCS, and depression, respectively. 220 The selected models are referred to as *final* models. Based on a priori knowledge these analyses 221 were stratified by sex. All risk estimates (crude, fully adjusted, and final) are presented. Results 222 are presented as odds ratios (OR) with a 95% confidence interval (CI), reported for each 223 subgroup (sex and ADHD status). Based on the final multinomial logistic regression analyses, 224 indirect effects of each identified assumed mediator were calculated using the *nlcom* command 225 in statistical software Stata. We then determined the total indirect effect by summing the 226 individual indirect effects. The proportion of the total indirect effect attributable to each 227 mediator was calculated to understand the relative contribution of each mediator to the 228 association between ADHD and outcomes MCS and depression, respectively. Subsequently, 229 sex-stratified Cox regression analyses were conducted to assess whether pADHD, and 230 presentations of pADHD, predict later filled prescriptions for anti-depressive medication 231 (ATC: N06A).

232	A test was considered statistically significant if the Bonferroni-corrected p -value <0.05, in
233	multiply comparison analyses. All P values presented have been Bonferroni-corrected.
234	
235	Analyses were performed using the SAS statistical software version 9.4 (SAS Institute, Cary,
236	North Carolina, USA) and using Stata/SE version 18.0 (StataCorp, College Station, TX).
237	
238	3.1 Ethics
239	All participants have signed an informed consent form. Moreover, the study was registered in
240	the Capital Region's research directory (P-2019-99), and in the Scientific Research Ethics
241	Committee system in the Central Denmark Region (1-10-72-95-13).
242	
243	3. Results
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3.1.1 Possible ADHD presentation

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Of the 1 507 individuals who were classified with pADHD, the non-specific presentation wasthe most common (Figure 2).

The average MDI scores varied according to ASRS score in both females and males with the highest MDI score observed for the group of individuals classifying with the combined inattentive and hyperactive-impulsive pADHD presentation. The average MCS only varied significantly according to ASRS score in males where the lowest average MCS was observed for the inattentive pADHD presentation (Table 2).

262 When adjusting for multiple comparison using Bonferroni correction there were no statistically

significant variation in risk of presenting with a specific set of ADHD symptoms depending on

sex. Females with pADHD had a nominally significant 24% lower risk (non-adjusted p = 0.01)

265 of having an inattentive presentation compared to males with pADHD (Table 3).

266

267 **3.2 Depressive symptoms and health-related quality of life**

268 Irrespective of the ASRS scoring method (total score or only using items representing each 269 specific presentation), experiencing pADHD symptoms was associated with a 3.5-5 times 270 higher risk of having a low mental health component score as well as a 2 to 4 times higher risk 271 of having been diagnosed with a depression in the past in both females and males (Table 4). 272 The combined inattentive and hyperactive-impulsive pADHD presentation had the highest 273 prevalence of both former and present depression, reflected in a 17.5 times higher risk (crude 274 RR 17.48, 95%-Cl 11.2-21.5) of co-occurring depressive symptoms compared to the non-275 ADHD group.

Similar propensities regarding lower HRQL and the occurrence of depressive symptoms in
participants with pADHD were observed in the sex-stratified regression analysis (Table 5). The

278	odds for a low MCS score were 13.6 (95% CI: 11.1-16.7) and 12.6 (95% CI:10.5-15.1) times
279	higher in females and males with pADHD symptoms compared to those without. The
280	associations remained statistically significant after adjustments, but the risk estimates were
281	reduced. Similar pattern was observed for the MDI-score.
282	
283	
284	3.3 Mediation tests
285	Number of children, general physical health and previous depression impacted the observed
286	associations for both sexes. In males, it appeared that socioeconomic status had a bigger impact
287	compared to in females.
288	The covariates identified in the model search were included in mediation tests to estimate the
289	proportion of the total indirect effect attributable to each of these.
290	It was observed that 14% of the total association between pADHD and MDI score among
291	females was explained by the pathways going through all the included mediators combined,
292	while 8.9% was explained among males. In both sexes most of the estimated indirect effect
293	between pADHD and MDI score was explained by MCS score (90.4% for females and 93.1%
294	for males), whereas 4.0% was explained by history of depression for females, and 4.9% was
295	explained by registered income level for males.
296	Also, it was observed that 35% of the association between pADHD and MCS score was
297	explained by pathways going through all included mediators in females, while this was 24.4%
298	in males. For this association the main mediator pathway was through MDI score (89.6%% for
299	females and 84.4% for males), whereas 5.9% was explained by history of depression for
300	females, and 8.6% was explained by registered income level for males.

The isolated indirect effects as well as the proportion of the total indirect effect explained byeach of the mediators are displayed in Table 6.

303

304 3.4 ADHD symptoms and subsequent anti-depressive treatment

305 Overall, 1934 participants received a prescription of anti-depressive medication after inclusion 306 date (median number of days after inclusion = 1485, inter quartile range (IOR): 891-1892). In 307 total, 652 (14.9%) of these reported having a previous depression diagnosis. For the cox 308 regression analysis, the date of censoring was set as date of filled prescription, date of death, 309 or December 31st, 2022, whichever came first. Each participant was observed at risk of being 310 prescribed anti-depressive medicine for 5.9 person-years on average (a total of 311,419.75 311 person-years). The hazard of being prescribed anti-depressive medication after the ADHD 312 assessment was increased for those with pADHD compared to those without ADHD symptoms 313 in both sexes. The inattentive and combined presentations were associated with the most 314 increased hazard in both sexes (Table 7).

315 **4. Discussion**

Our study reveals several important findings regarding undiagnosed ADHD in wellfunctioning adults. In this healthy cohort meeting strict blood donation criteria, we found substantial pADHD prevalence (~3%) with significant impacts on health-related quality of life and depression risk. These findings in individuals who successfully navigated life's demands without formal diagnosis suggest ADHD symptoms may persist and impact well-being even in seemingly well-adjusted adults.

The prevalence of pADHD reported here is similar to what has been estimated in populations throughout developed and developing countries. In childhood, ADHD is among the most

common psychiatric disorders with a prevalence rate of 3-5% [9], and 5.9% of youth [10]. A 324 325 2020 systematic review and meta-analysis including older adults reported a prevalence ranging 326 from 1.5% to 2.2% [3]. This is on the lower end compared to estimates reported in a 2017 meta-327 analysis, based on the WHO World Mental Health Surveys across 20 countries, which found 328 an ADHD prevalence of 3.6% in high-income countries [1]. The differences in the prevalence 329 of adult ADHD across studies could suggest variation in the expression of ADHD related to 330 developmental change, cultural differences across populations, and/or due to differences in 331 methodology across studies [23]. Prevalence estimates strongly depend on diagnostic tools 332 used (e.g., ICD-10 vs. DSM-IV or DSM-5), informant type (such as parent/teacher vs. self-333 reports). This could also be speculated to be due to underestimation of the true number of 334 ADHD cases or the occurrence of a late-onset ADHD syndrome [24]. Moreover, our findings 335 support previous evidence of the combined or non-specific presentation of ADHD being the 336 most prevalent (estimated 50%-75% of cases) [25]. However, it has been reported that in adult 337 populations, the inattentive subtype predominates as hyperactive-impulsive symptoms 338 attenuate, often manifesting with functional impairments that may be misinterpreted as mood 339 or anxiety disorders [26].

A key aspect of our study is the examination of ADHD-depression relationships in previously undiagnosed individuals. While the correlation between diagnosed ADHD and Major Depressive Disorder (MDD) is well-documented [27] with lifetime MDD prevalence ranging from 11 to 50% among adults with ADHD [8,28], the impact of undiagnosed ADHD symptoms on depression risk has remained largely unexplored. Our findings reveal that 25% of participants with pADHD reported current depressive symptoms, with increased hazard of antidepressant medication prescription up to 5 years after assessment.

Particularly noteworthy was our finding that approximately 20% of individuals with pADHD
reported prior depression diagnosis while remaining untreated for ADHD. This observation

may suggest a potentially critical gap in clinical practice where ADHD may be the underlying cause of depressive symptoms yet remains unrecognized. This aligns with a previous Danish study [29], that showing common anti-depressive treatment prior to ADHD diagnosis. On the contrary, it is also possible that this (or at least part of it) could be explained by MDD symptoms mimicking ADHD symptoms. Mohr-Jensen et al. (2020) also reported lifetime increase in treatment with anti-depressive drugs in ADHD patients [29].

355 Our study revealed several unexpected findings regarding symptom presentations in this 356 undiagnosed population. Contrary to previous research, we found more males reporting 357 inattentive symptoms and females more frequently reporting hyperactive-impulsive symptoms. 358 This novel finding challenges existing literature and may reflect how ADHD presents 359 differently in individuals who have developed successful coping strategies throughout life 360 without formal diagnosis. However, our finding of similar pADHD prevalence between the 361 sexes support previous findings suggesting that males exhibit higher prevalence in childhood, 362 but that this may be due to underdiagnosis in females, which then narrows the prevalence gap 363 in adulthood [30].

364 Furthermore, present findings suggest that type of ADHD symptom presentation matters in 365 terms of the level of MDD and MCS impact. We found that the non-specific presentation was 366 the most common, and that individuals classifying with the combined inattentive and 367 hyperactive-impulsive presentation experienced the highest burden associated with their 368 experienced ADHD symptoms in terms of highest risk of increased MDI score. Additionally, 369 we observed the highest hazard ratio for later being prescribed anti-depressive medications for 370 those with the inattentive presentation among males, whereas this was the case for the 371 combined presentation among females. This finding may indicate that the impact on depressive 372 symptoms varies dependent on the expression of the experienced ADHD symptomatology. In 373 any case, early diagnosis and initiation of ADHD treatment may reduce future comorbid depressive disorder [31], highlighting the importance of healthcare professionals notmisattributing ADHD as depression.

Moreover, it is relevant to point out that we identified physical health impacts in this otherwise healthy population. Individuals with pADHD were twice as likely to report low physical health compared to those below the ASRS cut-off, regardless of sex. This finding is particularly significant given our study population's general good health status and suggests that even wellcompensated ADHD symptoms may have broader health implications than previously recognized. It is also possible that such impairment could overshadow the ADHD symptoms, thus making it more difficult to obtain appropriate (ADHD) diagnosis and treatment [10,32].

383

4.1 Strengths and limitations

384 The blood donor population represents both a strength and limitation of this study. While the 385 Healthy Donor Effect may limit generalizability [14,33], this population provides unique 386 insights into ADHD manifestation in high-functioning adults who developed effective coping 387 strategies. The cohort's health requirements and regular commitments make our findings 388 particularly relevant for understanding ADHD in well-functioning populations. While our 389 study identifies a subset of participants with elevated ADHD symptoms using the ASRS 390 screening tool, we emphasize that this does not constitute a clinical diagnosis. The ASRS is a 391 validated screening instrument with high sensitivity (0.92) and specificity (0.69), but it cannot 392 replace comprehensive clinical assessment. Our findings should be interpreted as exploring the 393 potential impact of elevated ADHD symptoms in a high-functioning population, rather than 394 definitively identifying undiagnosed ADHD cases. In line with this, it is important to note that 395 even though this study excluded individuals with a history of medically treated ADHD, the 396 exclusion criteria focused on medical ADHD treatment but did not comprehensively assess 397 prior clinical diagnoses and addressed the possibility of individuals with a non-medically 398 treated ADHD diagnosis among participants.

399 Further, the cross-sectional design prevents causal inference, though our longitudinal analysis 400 of anti-depressive medication provides temporal insights. This mixed approach helps balance 401 the limitations of cross-sectional data while offering some perspective on temporal 402 relationships between ADHD symptoms and depression. Self-reported data introduces 403 potential misclassification bias, though validated questionnaires and objective prescription data 404 mitigate this concern. Previous research suggests blood donors have no incentive to falsify 405 information, though adults with ADHD may underreport symptom severity. Our use of 406 multiple data sources helps address these potential limitations. Being unable to account for 407 other psychiatric diagnoses limits our ability to determine whether impairments result from 408 ADHD alone or condition combinations. However, individuals with high psychiatric diagnosis 409 burden likely wouldn't become blood donors initially, providing some natural control for severe 410 psychiatric comorbidity.

411

412 Our findings suggest significant ADHD underdiagnosis among Danish adults, even in well-413 functioning populations. The present study challenges traditional interpretations of the ADHD 414 diagnosis impairment criterion. While participants meet strict blood donation health criteria, 415 our findings reveal significant functional impairments across mental health and quality of life 416 domains. The elevated ADHD symptom scores associated with lower mental component scores 417 and increased depressive symptoms suggest that impairment can be subtle yet substantive, even 418 in seemingly well-functioning adults. This underscores the complexity of ADHD 419 manifestation, where individuals may develop sophisticated compensatory strategies that mask 420 overt functional deficits while still experiencing meaningful internal challenges. Our results 421 highlight that functional impairment should not be narrowly defined by external markers of 422 success, but rather by comprehensive assessments of mental health, personal experience, and 423 quality of life. To sum up, this study highlights the need for increased awareness of late-

424 diagnosed ADHD and suggests current diagnostic practices may need revision to better identify 425 affected individuals who developed effective compensatory strategies. The substantial impacts 426 on mental and physical health, even in this healthy population, emphasize the importance of 427 identifying and addressing ADHD symptoms regardless of apparent life function level. 428 These results may have important implications for clinical practice, suggesting the need for 429 ADHD screening in patients presenting with depression, particularly in well-functioning adults 430 who may have developed coping strategies that mask traditional ADHD presentations. Future 431 research should examine the effectiveness of targeted screening approaches based on sex-432 specific presentation patterns and explore the mechanisms linking ADHD to physical health 433 outcomes in otherwise healthy populations.

434

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441 **Data availability statement**

- 442 Data can be made available upon reasonable request to info@dbds.dk (for more detail please
- 443 see: https://bloddonor.dk/bloddonorstudiet/the-danish-blood-donor-study-eng/)

444 **Conflict of interest statement**

- 445 The authors declare that they have no known competing financial interests or personal
- 446 relationships that could have appeared to influence the work reported in this paper.

447

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561

	Female (n:	24 760)		Male (n	n: 26 177)	
			<i>p</i> - Valu			р-
	pADHD	Non-pADHD	e <0.00	pADHD	Non-pADHD	Value
e (%)	693 (2.8)	24 067 (97.2)	<0.00 1	814 (3.1)	25 363 (96.9)	<0.001
		ASRS score	<0.00	40.0 (38.0-	19.0 (14.0-	
Iedian (IQR)	40.0 (38.0-44.0)	19.0 (14.0-24.0)	<0.00 1	45.0)	24.0)	<0.001
		Age in years				
ledian (IQR)	27.9 (22.93- 38.86)	39.3 (26.8-50.5)	<0.00 1	29.5 (25.3- 38.2)	41.3 (30.1- 51.5)	<0.001
25	269 (38.82)	4527 (18.2)		192 (23.6)	3033 (11.9)	
6-35	196 (28.28)	5489 (22.2)	-0.00	353 (43.4)	6046 (23.8)	
6-45	128 (18.47)	5023 (20.9)	<0.00 1	146 (17.9)	5897 (23.3)	<0.001
6-55	71 (10.25)	5362 (22.3)		97 (11.9)	6063 (23.9)	
55	29 (4.18)	3666 (15.2)		26 (3.2)	4324 (17.1)	
	Perce	eption of health (SF	-12)			
		tal component summ				
ICS score median (IQR)	39.9 (29.4-48.8)	53.2 (47.5-56.7)	<0.00 1	44.8 (34.9- 51.2)	54.7 (49.6- 56.7)	<0.001
ow MCS	337 (48.6)	2675 (11.1)	<0.00 1	278 (34.1)	1715 (6.8)	<0.001
Ioderate MCS	215 (31.0)	6181 (25.7)		305 (37.5)	5778 (22.8)	
Good MCS	127 (18.3)	14626 (60.8)		216 (26.5)	17286 (68.2)	
lissing	14 (2.0)	585 (2.4)		15 (1.8)	584 (2.3)	
	()	cal component sum	narv	- (-)		
		-	0.542	55.6 (51.6-	55.5 (53.2-	
CS score median (IQR)	55.6 (51.1-58.4)	55.5 (53.1-56.9)	6	57.9)	56.8)	0.4838
ow PCS	141 (20.4)	2475 (10.3)		137 (16.8)	2175 (8.6)	
Ioderate PCS	148 (21.4)	5611 (23.3)	<0.00 1	192 (23.6)	6433 (25.4)	<0.001
Good PCS	390 (56.3)	15396 (63.9)	1	470 (57.7)	16171 (63.8)	
lissing	14 (2.0)	585 (2.4)		15 (1.8)	584 (2.3)	
	Presenc	e of depressive syn		120/70		
IDI score median (IQR):	14.0 (9.0-22.0)	4.0 (2.0-7.0)	<0.00 1	12.0 (7.0- 19.0)	4.0 (1.0-7.0)	<0.001
o depressive disorder	476 (68.7)	23068 (95.9)		640 (78.6)	24649 (97.2)	
Aild depressive disorder Aoderate depressive	87 (12.6)	374 (1.6)	<0.00 1	68 (8.4)	257 (1.1)	<0.001
isorder	62 (8.9)	222 (0.9)	1	62 (7.6)	117 (0.5)	
evere depressive disorder	61 (8.8)	143 (0.6)	~0.00	33 (4.1)	68 (0.3)	
resent depressive isorder	210 (30.3)	739 (3.1)	<0.00 1	163 (20.0)	442 (1.7)	<0.001
Aissing	7 (1.1)	260 (1.1)		11 (1.4)	272 (1.1)	
	History	of diagnosed depr				
lo	497 (71.7)	21506 (89.4)	<0.00 1	699 (85.9)	23910 (94.3)	<0.001
es	195 (28.1)	2518 (10.5)	-	114 (14.0)	1406 (5.5)	
<i>fissing</i> Received medical reatment*	-	43 (0.2)		-	47 (0.2)	
cauncill			<0.00			
Self-reported yes	89 (45.6)	1253 (49.8)	1	50 (43.9)	711 (50.6)	<0.001
Self-reported no	106 (54.4)	1262 (50.1)		64 (56.1)	688 (48.9)	

Table 1. Characteristics of the study popula	tion
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<i>Missing</i> Anti-depressive	0	-		0	7 (0.1)	
medication in prescription	89 (12.8)	1,253 (5.9)		50 (6 1)	711 (2.9)	~0.001
register Received other treatment	134 (68.7)	1,233 (3.9)		50 (6.1) 87 (76.3)	711 (2.8) 924 (65.7)	<0.001
No	61 (31.3)	729 (28.9)	<0.00	27 (23.7)	480 (34.1)	<0.001
Missing	0	7 (0.3)	1	0		
111000005		st achieved education	onal level	0		
Compulsory	164 (23.7)	2938 (12.2)		127 (15.6)	2844 (11.2)	
Upper	× ,	()		~ /	()	
secondary/vocational/othe r	222 (32.0)	7430 (30.9)	<0.00	302 (37.1)	11226 (44.3)	<0.001
Diploma/bachelor	214 (30.9)	9636 (40.0)	1	250 (30.7)	7494 (29.6)	<0.001
Master or PhD	92 (13.3)	3891 (16.2)		125 (15.4)	3571 (14.1)	
Missing	-	172 (0.7)		10 (1.2)	288 (0.9)	
	F	Employment status				
Employed	516 (74.5)	20277 (84.3)	<0.00	692 (85.0)	22646 (89.3)	
Unemployed	23 (3.3)	463 (1.9)	<0.00 1	18 (2.2)	436 (1.7)	<0.001
Student/Retired	154 (22.2)	3327 (13.8)		104 (12.8)	2281 (8.9)	
		Income level				
Low	268 (38.7)	5343 (22.2)		196 (24.1)	4256 (16.8)	
Low-medium	192 (30.2)	6223 (25.9)	<0.00	209 (23.6)	3560 (14.4)	<0.001
Medium	103 (14.9)	5432 (22.6)	1	158 (19.4)	4474 (17.6)	
High-medium	74 (10.7)	4406 (18.3)		135 (16.6)	5629 (22.9)	
High	39 (5.6)	2663 (11.1)		133 (16.3)	7444 (29.4)	
0		umber of children		A77 (59 ()	11000 (10 0)	
0	437 (63.1)	13237 (55.0)		477 (58.6)	11869 (46.8)	
1	97 (14.0)	3596 (14.9)	0.002	137 (16.8)	4351 (17.2)	<0.001
2 ≥3	111 (16.0)	4880 (20.3)	9	142 (17.4) 56 (6.9)	5908 (23.3) 2245 (8.0)	-01001
25 Missing	42 (6.1) 6 (0.9)	1584 (6.6) 770 (3.2)		50 (0.9)	2245 (8.9) 990 (3.9)	
missing		Body mass index		-	990 (3.9)	
		Body mass mucx	0.080	25.5 (23.4-	25.5 (22.8-	
Score median (IQR)	24.6 (22.4-28.0)	24.4 (22.2-27.6)	9	27.8)	27.9)	0.2449
Underweight	6 (0.9)	6 (0.9)		-	75 (0.3)	
Normal weight	363 (52.4)	13295 (55.2)		361 (44.4)	11009 (43.4)	
Overweight	206 (29.7)	7025 (29.2)	0.155	333 (40.9)	11050 (43.6)	0 6277
Moderately Obese	88 (12.7)	2455 (10.2)	4	91 (11.2)	2529 (9.9)	0.6377
Severely Obese	16 (2.3)	754 (3.1)		19 (2.3)	527 (2.1)	
Morbidly Obese	11 (1.6)	277 (1.2)		6 (0.7)	140 (0.6)	
Missing	-	90 (0.4)		-	33 (0.1)	
Never/almost never	-	cy of alcohol consu	триоп	200 (17 7)	12955 (54 6)	
Sometimes a month	367 (52.9) 291 (41.9)	15251 (63.4) 8056 (33.5)		388 (47.7) 366 (44.9)	13855 (54.6) 10196 (40.2)	
Sometimes a week	31 (4.5)	375 (1.6)	<0.00	46 (5.7)	999 (3.9)	<0.001
Daily/almost daily	51 (4.5)	13 (0.1)	1	40 (3.7) 5 (0.6)	51 (0.2)	
Missing	-	372 (1.6)		9 (0.0) 9 (1.1)	262 (1.0)	
174 6337FIFE	- Сл	rrent smoking stat	115	> (1.1)	202 (1.0)	
Non-smoker	503 (72.6)	20888 (86.7)		650 (79.9)	22106 (87.2)	<0.001

Smoker	187 (26.9)	3132 (13.0) <0.00	161 (19.8)	3207 (12.6)	
Missing	-	47 (0.2) 1	-	50 (0.2)	

562 563 Note. *n*: number. IQR: Interquartile range. Level of significance: *p*-value < 0.05 (in **bold**). "-": less than five individuals (according to the terms and conditions of Danish legislation (the Danish Act on Processing of Personal Data) tables must contain at least 5 units per cell).

564 pADHD: Possible ADHD; ASRS: WHO Adult ADHD Self-Report Scale. ADHD is considered present with an ASRS full edition score equal to or above 37.

566MDI: Major Depression Inventory Scale. Mild depression = MDI score of 21, moderate depression = MDI score of 26. Severe depression =567MDI score of 31. Present depressive disorder = MDI score equal to or above 21.

568
569SF-12: 12-Item Short Form Health Survey. PCS: Physical Component Summary. MCS: Mental Component Summary. Low = the 10% of
the population scoring the lowest. Good = the 65% of the population scoring the best. Moderate = the remaining 25%.

572 *Items on self-reported depression treatment was only asked to those who reported having a history of diagnosed depressio

Scoring method	ASRS full edition	Inattentive subscale	Hyperactive- impulsive subscale	Combined Inattentive and Hyperactive- Impulsive subscale	Non-specific presentation	
Cut-off	≥37	≥24	≥24	≥24/≥24	≥37	P value
ASRS items	1-18	1-4+7-11	5-6+12-18	1-4+7-11/5-6+12-18	1-18	
ASRS score, median (IQR)	40.0 (38.0-44.0)	43.0 (40.0-47.0)	43.0 (39.0-46.0)	54.0 (51.0-58.0)	39.0 (38.0-40.0)	< 0.001
Female	40.0(38.0-44.0)	44.0 (39.0-47.0)	42.0 (39.0-46.0)	56.0 (52.0-58.0)	39.0 (38.0-41.0)	< 0.001
Male	40.00 (38.0-45.0)	43.0 (39.0-47.0)	43.0 (40.0-47.0)	54.0 (51.0-56.0)	39.0 (38.0-40.0)	
n (%)	1507 (100.0)	289 (19.2)	202 (13.4)	136 (9.0)	880 (58.4)	
Female	693 (48.7)	121 (41.9)	102 (50.5)	58 (42.7)	412 (46.8)	0.22
Male	814 (51.3)	168 (58.1)	100 (49.5)	78 (57.4)	468 (53.2)	0.02
Age in years, <i>n</i> (%)						0.01
≤25	461 (30.6)	103 (35.6)	49 (24.3)	45 (33.1)	264 (30.0)	
26-35	549 (36.4)	102 (35.3)	80 (39.6)	57 (41.9)	310 (35.2)	
36-45	274 (18.2)	48 (16.6)	33 (16.3)	20 (14.7)	173 (19.7)	
46-55	168 (11.2)	32 (11.1)	32 (15.8)	10 (7.4)	94 (10.7)	
>55	55 (3.7)	4 (1.4)	8 (3.9)	4 (2.9)	39 (4.4)	
MDI score median (IQR)						< 0.001
Female	14.0 (9.0-22.0)	16.00 (8.0-24.0)	13.00 (8.0-20.0)	20.00 (11.0-30.0)	14.00 (9.00-21.00)	< 0.001
Male	12.0 (7.0-19.0)	14.00 (9.0-22.0)	11.00 (7.0-17.0)	18.00 (9.0-25.0)	11.00 (7.00-16.00)	0.01
MCS score median (IQR)						< 0.001
Female	39.9 (29.4-48.8)	37.7 (26.1-47.7)	42.9 (33.9-49.9)	35.8 (24.4-50.7)	40.0 (30.2-48.9)	0.11
Male	44.8 (34.9-51.2)	40.2 (32.2-48.1)	48.7 (38.0-54.3)	42.9 (28.7-49.9)	45.7 (37.5-51.3)	< 0.001
PCS score median (IQR)						0.01
Female	55.6 (51.1-58.4)	56.1 (51.1-58.9)	56.8 (52.9-58.8)	54.4 (47.5-59.0)	55.1 (51.0-58.0)	0.14
Male	55.6 (51.6-57.9)	55.2 (50.80-6.8)	56.2 (53.1-58.4)	54.9 (51.3-58.1)	55.5 (51.7-57.8)	0.06

Table 2. Mental and physical health scores (MDI and SF-12) of individuals classified with possible ADHD according to the full ASRS, and the specific ADHD presentations

Note. n: number. IQR: Interquartile range.

P value was estimated using Kruskall-Wallis test

ASRS: WHO Adult ADHD Self-Report Scale ASRS full edition was assessed using questions 1 through 18 score and ADHD is considered present with a score equal to or above 37. Different presentations of ADHD (in participants with full edition score \geq 37) were considered using different blocks (items) of questions from the ASRS:

- The inattentive ADHD subscale was assessed using questions 1 through 4 and 7 through 11 (inattentive symptoms are considered present with a score equal to or above 24)

- The hyperactivity-impulsivity ADHD subscale was assessed using questions 5 through 6 and 12 through 18 (hyperactivity-impulsivity symptoms are considered present with a score equal to or above 24)

- The combined Inattentive and Hyperactive-Impulsive were assessed using questions 1 through 18 (combined symptoms are considered present with a score equal to or above 24 on both subscales)

- The non-specific presentation was assessed using questions 1 through 18 (non-specific symptoms are considered present with a total score above or equal to 37 but below 24 in either subscale)

SF-12: 12-Item Short Form Health Survey. PCS: Physical Component Summary. MCS: Mental Component Summary.

MDI: Major Depression Inventory Scale. MDI score equal to or above 21 = depressive disorder.

Table 3. Risk ratios (RR) and 95% confidence intervals (Cl) of the association between the different presentations and sex among possible ADHD participants

0.6-0.9)	0.0572
0.8-1.3)	1.0
0.6-1.1)	1.0
0.8-1.1)	1.0
((0.6-1.1) (0.8-1.1)

Note. Comparison group: females with possible ADHD vs. males with possible ADHD. A Bonferonni-corrected p-value < 0.05 is considered statistically significant

Scoring method		ASRS	full edition					
Cut-off			≥37					
ASRS items		1-18						
	n (%)	Crude RR (95% Cl)	<i>p</i> -Value	MH RR (95% Cl)	<i>p</i> -Value			
Perception of health (SF-12)								
Low mental health state (MCS)	612 (41.41)	4.6 (4.3-4.9)	<0.01	4.6 (4.3-5.0)	<0.0			
Moderate/Good mental health state (MCS)	866 (58.59)	1.0		1.0				
Low physical health state (PCS) Moderate/Good physical health state	282 (19.08)	1.9 (1.8-2.2)	<0.01	2.0 (1.8-2.2)	<0.0			
(PCS)	1196 (80.92)	1.0		1.0				
Present depressive disorder	252 (25.05)	10 4 (0 2 11 5)	-0.01	10.5 (0.5.11.7)	-0.0			
Yes	373 (25.05)	10.4 (9.3-11.5)	<0.01	10.5 (9.5-11.7)	<0.0			
No	1116 (74.95)	1.0		1.0				
History of diagnosed depression	200 (20 52)		-0.01		-0.0			
Yes	309 (20.53)	2.6 (2.3-2.9)	<0.01	2.6 (2.4-2.9)	<0.0			
No	1196 (79.47)	1.0		1.0				
Scoring method		Inatten	tive subscale					
Cut-off			≥24					
ASRS items	n (%)	Crude RR	4+7-11 <i>p</i> -Value	MH RR	<i>p</i> -Value			
	<i>n</i> (70)	(95% Cl)	p^{-1} and	(95% Cl)	p-value			
Perception of health (SF-12)								
Low mental health state (MCS)	144 (50.70)	5.2 (4.6-5.8)	<0.01	5.2 (4.7-5.9)	<0.0			
Moderate/Good mental health state (MCS)	140 (49.30)	1.0		1.0				
Low physical health state (PCS) Moderate/Good physical health state	58 (20.42)	2.1 (1.6-2.6)	<0.01	2.0 (1.6-2.5)	<0.0			
(PCS)	226 (79.58)	1.0		1.0				
Present depressive disorder								
Yes	96 (33.57)	11.5 (9.7-13.7)	<0.01	11.9 (10.1-14.0)	<0.0			
No	190 (66.43)	1.0		1.0				
History of diagnosed depression								
Yes	68 (22.01)	2.9 (2.3-3.5)	<0.01	3.0 (2.4-3.6)	<0.0			
No	221 (77.90)	1.0		1.0				
Scoring method		Hyperactive-	impulsive subscale					
Cut-off			≥24					
ASRS items	n (%)	5-0 Crude RR (95% Cl)	6+12-18 <i>p</i> -Value	MH RR (95% Cl)	<i>p</i> -Value			

Accepted manuscript: Authors' Copy Table 4. Frequency and associations (RR) of mental and physical health-related quality of life, and depression, respectively with ADHD

Perception of health (SF-12)			_						
Low mental health state (MCS)	72 (36.36)	3.7 (3.1-4)	<0.01	3.5 (2.9-4.2)	<0.01				
Moderate/Good mental health state (MCS)	126 (63.64)	1.0		1.0					
Low physical health state (PCS) Moderate/Good physical health state	30 (15.15)	1.5 (1.1-2.1)	0.062	1.5 (1-1-2-0)	0.073				
(PCS)	168 (84.85)	1.0		1.0					
Present depressive disorder	42 (21 11)	7.0 (5.2.0.2)	-0.01		-0.01				
Yes	42 (21.11)	7.0 (5.3-9.2)	<0.01	6.5 (5.0-8.5)	<0.01				
No	157 (78.89)	1.0		1.0					
History of diagnosed depression	2((17.92)	22(1(20))	-0.01		-0.01				
Yes	36 (17.82)	2.2 (1.6-2.9)	<0.01	2.2 (1.6-2.8)	<0.01				
No	166 (82.18)	1.0		1.0					
Scoring method			Combi	ned Inattentive and Hyp		ve subscale			
Cut-off				≥24/≥					
ASRS items	n (%)	Crude RR (95% Cl)	<i>p</i> -Value	1-4+7-11/5- MH RR (95% Cl)	<i>p</i> -Value	Female RR (95% Cl)	<i>p</i> -Value	Male RR (95% Cl)	<i>p</i> -Value
Perception of health (SF-12)									
Low mental health state (MCS)	63 (46.67)	5.2 (4.3-6.2)	<0.01	4.9 (4.1-5.8)	<0.01				
Moderate/Good mental health state (MCS)	72 (53.33)	1.0		1.0					
Low physical health state (PCS)	33 (24.44)	2.5 (1.9-3.4)	<0.01	2.5 (1.8-3.3)	<0.01				
Moderate/Good physical health state (PCS)	102 (75.56)	1.0		1.0					
Present depressive disorder									
Yes	57 (42.22)	17.48 (11.2-21.5)	<0.01	14.8 (12.0-17.9)	<0.01				
No	78 (57.78)	1.0		1.0					
History of diagnosed depression									
Yes	37 (27.21)	3.4 (2.6-4.5)	<0.01			4.1 (3.1-5.5)	<0.01	2.4 (1.4-4.2)	<0.01
No	99 (72.79)	1.0				1.0		1.0	
Scoring method		Non-speci	fic presentation						
Cut-off			≥37						
ASRS items			1-18						
	n (%)	Crude RR (95% Cl)	<i>p</i> -Value	MH RR (95% Cl)	<i>p</i> -Value				
Perception of health (SF-12)									
Low mental health state (MCS)	333 (54.41)	4.3 (3.9-4.7)	0.01	4.1 (3.8-4.5)	<0.01				
Moderate/Good mental health state (MCS)	528 (8.31)	1.0		1.0					
Low physical health state (PCS) Moderate/Good physical health state	161 (18.70)	1.9 (1.7-2.2)	0.715	1.9 (1.7-2.2)	<0.01				
(PCS)	700 (81.30)	1.0		1.0					
Present depressive disorder									

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Yes	178 (47.72)	8.5 (7.4-9.8)	<0.01	7.4 (6.5-8.5)	<0.01			
No	691 (61.92)	1.0		1.0				
History of diagnosed depression								
Yes	168 (19.13)	2.4 (2.1-2.8)	0.256	2.4 (2.1-2.7)	<0.01			
No	710 (80.87)	1.0		1.0				

Note. Comparison: ADHD (screening positive on the specific subscale) vs. Non-ADHD (ASRS score <37). n: number. p-value (level of significance: Bonferroni-corrected p-value< 0.05 in bold).

Mantel-Haenszel Risk Ratio (MH RR): adjusted for sex, Female/Male RR present sex-stratified estimates when Breslow-Day Test for Homogeneity was significant.

ASRS: WHO Adult ADHD Self-Report Scale. ASRS full edition was assessed using questions 1 through 18 score and ADHD is considered present with a score \geq 37. Different presentations of ADHD were considered using different blocks (items) of questions from the ASRS:

- The inattentive ADHD subscale was assessed using questions 1 through 4 and 7 through 11 (inattentive symptoms are considered present with a score ≥24)

- The hyperactivity-impulsivity ADHD subscale was assessed using questions 5 through 6 and 12 through 18 (hyperactivity-impulsivity symptoms are considered present with a score ≥24)

- The combined Inattentive and Hyperactive-Impulsive were assessed using questions 1 through 18 (combined symptoms are considered present with a score \geq 24 on both subscales)

- The non-specific presentation was assessed using questions 1 through 18 (non-specific symptoms are considered present with a total score above or equal to 37 but below 24 in either subscale)

Present depressive disorder = Major Depression Inventory Scale score ≥ 21 .

SF-12: 12-Item Short Form Health Survey. PCS: Physical Component Summary. MCS: Mental Component Summary. Low = the 10% of the population scoring the lowest. Moderate/Good = the remaining 90%.

	Female (<i>n: 24 760</i>)							Male (<i>n: 26 177</i>)					
Outcome	Crude OR (95% CI)	<i>p-</i> Value	Fully adjusted OR (95% CI)	<i>p</i> - Valu e	Final OR (95% CI)	<i>p</i> - Value	Crude OR (95% CI)	<i>p</i> - Valu e	Fully adjuste d OR (95% CI)	<i>p</i> - Valu e	Final OR (95% CI)	<i>p</i> - Value	
MCS score													
	13.6		5.8		6.9		12.6		5.8				
	(11.1-		(4.6-		(5.5-		(10.5-	< 0.00	(4.7-	<0.00	56.8		
Low MCS	16.7)	< 0.001	7.4)	< 0.001	8.7)	<0.001	15.1)	1	7.3)	1	(5.5-8.4)	< 0.001	
			2.8		3.2				2.9		3.5		
	3.8		(2.1-		(2.6-		4.01	<0.00	(2.4-	<0.00	(2.9-		
Moderate MCS	3.0-4.7)	<0.001	3.6)	<0.001	3.9)	<0.001	(3.5-4.9)	1	3.5)	1	4.2)	<0.001	
Good MCS	1.0		1.0		1.0		1.0		1.0		1.0		
MDI score													
No depressive													
disorder	1.0		1.0		1.0		1.0		1.0		1.0		
			3.3		3.5				2.7		2.9		
Mild depressive	11.3		(2.4-		(2.6-		10.2	< 0.00	(1.9-	<0.00	(2.1-		
disorder	(8.7-14.5)	< 0.001	4.3)	< 0.001	4.6)	<0.001	(7.7-13.5)	1	3.7)	1	4.0)	< 0.001	
Moderate	13.5		3.7		4.1		20.4		5.1				
depressive	(10.0-		(2.6-		(2.9-		(14.9-	< 0.00	(3.6-	< 0.00	5.4		
disorder	18.2)	< 0.001	5.1)	<0.001	5.7)	< 0.001	28.0)	1	7.3)	1	(3.8-7.7)	< 0.001	
Severe	20.7		4.8		5.5		18.7		4.9				
depressive	(15.1-		(3.4-		(3.9-			<0.00	(3.1-	<0.00	5.2		
disorder	28.3)	< 0.001		< 0.001	7.8)	< 0.001	28.5)	1	7.9)	1	(3.3-8.1)	< 0.001	

 Table 5. Association between possible ADHD and mental health characteristics based on

 multinominal logistic regression analyses including possible ADHD as the independent variable

 and the mental health outcomes as dependent variables

Note. Comparison groups: possible ADHD vs. Non-ADHD (with complete data: "n:"). ADHD is considered present with a WHO adult ADHD Self-Report Scale full edition score equal to or above 37. *n*: number. p-value (level of significance: < 0.05 in **bold**).

MDI: Major Depression Inventory Scale. No depressive disorder = MDI score equal to or less than 20. Mild depression = MDI score >21<26, moderate depression = MDI score >26<31. Severe depression = MDI score >31. Present depressive disorder = MDI score equal to or above 21.

SF-12: 12-Item Short Form Health Survey. MCS: Mental Component Summary. Low = the 10% of the population scoring the lowest. Good = the 65% of the population scoring the best. Moderate = the remaining 25%.

Models:

1 2 3

4 5

678910112131415161781920

- 1. Crude: unadjusted
 - 2. Fully adjusted: Adjusted for age (continuous) and all other covariates except the specific outcome in question (history of depression, body mass index (BMI), alcohol consumption ("Sometimes a week" coupled with "Daily/almost daily" due to low prevalence of daily drinkers), smoking status, income level, educational level, employment status, number of children, and mental/physical health wherever this was not included as the dependent variable.

3. Final: Adjusted for age (continuous), and variables that remained statistically associated with the outcome variable at the level of p < 0.05 after backward selection:

- MCS outcome:
 - o Female: number of children, PCS score, MDI score, History of depression, BMI, Smoking status
 - Male: number of children, Employment status, educational level, Income level, PCS score, MDI score, History
 of depression, BMI, Smoking status

MDI outcome:

- Female: number of children, Employment status, MCS score, PCS score, History of depression, Smoking status
- o Male: number of children, Income level, MCS score, PCS score, History of depression, BMI

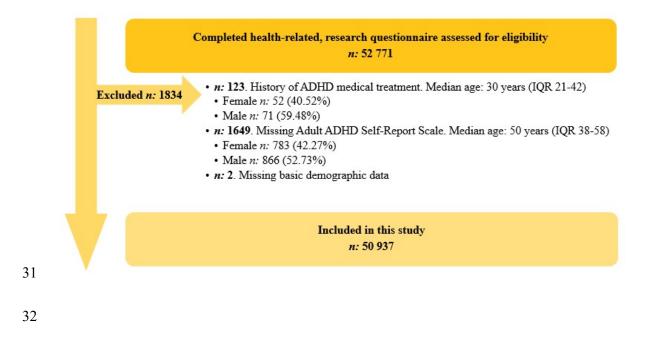
Mediator	Female (<i>n: 24 760</i>)						Male (n: 26 177)					
	MCS score			MDI score			MCS score			MDI score		
	Coef.	P value	%×	Coef.	P value	%×	Coef.	P value	%×	Coef.	P value	%×
Total indirect effect*	-0.347 (-0.3680.326)	< 0.001	35	0.144 (0.134-0.154)	< 0.001	14	-0.244 (-0.2590.228)	< 0.001	24.4	0.089 (0.083-0.095)	<0.001	8.9
Number of children	-0.002 (-0.0040.001)	0.011	0.6	0.001 (0.000-0.002)	0.01	0.7	0.001 (-0.00-0.003)	0.140	0	0.001 (0.000-0.002)	0.005	1.2
PCS score	-0.002 (-0.004-0.000)	0.118	0.5	0.001 (0.000-0.003)	0.023	1.0	-0.006 (-0.0090.004)	< 0.001	2.6	-0.001 (-0.00-0.00)	0.104	0
MCS score				0.130 (0.121-0.139)	< 0.001	90.4				0.083 (0.077-0.089)	< 0.001	93.1
MDI score	-0.311 (-0.3310.291)	< 0.001	89.6				-0.206 (-0.2200.191)	< 0.001	84.4			
History of depression	-0.021 (-0.0260.015)	< 0.001	5.9	0.006 (0.004-0.008)	< 0.001	4.0	-0.007 (-0.0100.004)	< 0.001	3.0	0.001 (0.000-0.002)	0.002	1.4
Body mass index	0.000 (-0.000 - 0.001)	0.905	0	-	-	-	0.000 (-0.000-0.000)	0.883	0	-0.000 (-0.000-0.000)	0.637	0
Smoking status	-0.011 (-0.0150.007)	< 0.001	3.3	0.002 (0.000-0.004)	0.038	1.4	-0.004 (-0.0060.002)	< 0.001	1.5	-	-	-
Employment status	-	-	-	0.003 (0.002-0.004)	< 0.001	2.3	-0.001 (-0.003- 0.000)	0.084	0.5	-	-	-
Income level	-	-	-	-	-	-	-0.211 (-0.0260.016)	< 0.001	8.6	0.004 (0.077-0.089)	< 0.001	4.9

Table 6. Displaying indirect effects explained by each mediator pathway

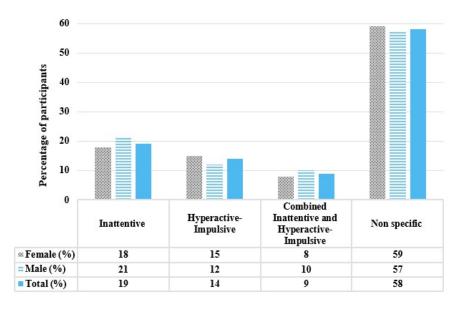
Note. Coef. = coefficient (95% confidence interval) *The total indirect effect explains how much of the association between pADHD and the outcome in question is explained by pathways through the included mediators collectively *Proportion of the total indirect effect explained by the mediator

medication. Cox regression analysis										
	Men (n= 26	177)	Women (n= 24 760)							
ADHD	HR (95% CI)	P value	HR (95% CI)	P value						
symptomatology										
Possible ADHD	3.34 (2.62-4.26)	< 0.01	3.58 (2.91-4.41)	< 0.01						
Hyperactive-impulsive	3.04 (1.51-6.10)	0.012	3.49 (2.06-5.91)	< 0.01						
Inattentive	5.25 (3.47-7.96)	< 0.01	4.79 (3.14-7.31)	< 0.01						
Combined inattentive										
and hyperactive-	3.47 (1.65-7.31)	0.006	6.02 (3.48-10.4)	< 0.01						
impulsive										
Non-specific	2.71 (1.92-3.82)	< 0.01	2.94 (2.20-3.93)	< 0.01						

 Table 7. ADHD symptomatology and risk of subsequently being prescribed anti-depressive medication. Cox regression analysis



33 Figure 2



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