

Research Article

Long-term Effects of Attention Deficit Hyperactivity Disorder (ADHD) on Social and Health Care Outcomes

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<u>ABSTRACT</u>

Introduction: Research on the effects of treatment for Attention Deficit Hyperactivity Disorder (ADHD) on long-term educational and social outcomes are limited. We aimed to evaluate long-term outcomes in patients diagnosed with ADHD and the possible effects of early diagnosis in childhood (<18 years of age) compared with diagnosis in adulthood (18 years-30 years of age), as well as whether pharmacologic treatment for ADHD is associated with improved socioeconomic outcomes in adulthood.

Methods: We included patients diagnosed with ADHD and patients collecting ADHD medication in the period 1995-2016 using national registry data. Eligible patients were <30 years of age or had reached the age of 30 in the period 2005-2016 (minimum 10-year observation period). We applied a case-control design, matching patients with ADHD 1:4 with the general population based on age, sex, and municipality at index year.

Results: Patients with ADHD had poorer somatic and psychiatric health and lower social status at the age of 30 years compared with controls. An early diagnosis of ADHD (<18 years) had a positive effect on employment; a later diagnosis (18 years-30 years) was associated with increased psychiatric comorbidities, alcohol and drug abuse, and lower employment rates. We did not find an association between adherence to ADHD medication and having completed education at age 30. Adherence to ADHD medication appeared to have a negative effect on employment status at age 30, but this was confounded by psychiatric comorbidity severity.

Conclusions: Patients with ADHD experienced substantial socioeconomic difficulties impacting their daily lives, as demonstrated by increased direct health care costs, high rates of psychiatric comorbidities and co-medication use. We showed that stronger adherence to ADHD medication was associated with negative long-term effects on education and employment; however, psychiatric comorbidities were the main driver affecting the social outcomes.

Keywords: Attention deficit hyperactivity disorder; Education; Employment; Health care costs; Psychiatric comorbidity

INTRODUCTION

Attention Deficit Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder that affects 2%-3% of children, predominantly males [1,2]. ADHD is characterized by hyperactivity, impulsivity and/or inattention and has a complex etiology of genetic and environmental factors [3]. Onset of ADHD is often in childhood or adolescence. The early age at onset of the disorder, and its effects across multiple domains affecting patient quality of life, cause substantial intellectual, educational,

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personal, social, familial, and societal burdens. In many cases ADHD is a life-long disorder, the influence of the diagnosis on educational and social prognosis is considerable. The disease is frequently related to significant comorbidities and mortality, and approximately persists into adulthood [4-11]. Patients diagnosed with ADHD often face significant social stigma, psychosocial adversities, and reduced working abilities, which can have a substantial socioeconomic impact on both individual and societal levels [12-18]. ADHD also affects caregivers and families [19]. Diagnosing ADHD is often complicated and calls for specialized units systematically identifying symptoms. Treatment includes both pharmacologic and non-pharmacologic management [15,20-25]. Patients with ADHD have significantly higher levels of social problems, increased risk of involvement in crime, comorbid psychiatric disorders, and family problems than the general population [6,26,27]. Several studies have evaluated the short-term consequences associated with ADHD; however, no systematic data exist regarding the total socioeconomic costs of ADHD for patients and families, and the longterm effects of treatment. Limited knowledge on adherence to ADHD treatment and the effects of early versus late diagnosis, as well as the effect of comorbidities exists. Further research on the psychiatric and health comorbidities related to ADHD and whether pharmacologic treatment can improve the educational and professional outcomes of patients with ADHD is warranted. In this study we aim to evaluate the long-term social and health outcomes of patients with ADHD by analysing socioeconomic factors such as education, employment, income, marital status, and health care costs. We also aim to evaluate the effect of ADHD treatment, patient outcomes for early (<18 years) vs late (18 years-30 years) ADHD diagnosis, and the presence of psychiatric comorbidities.

MATERIALS AND METHODS

In Denmark, national registry data are available for all Danes regarding contact with public and private hospitals, general specialist practice in the last years, and information on all prescription medication, social transfers, labour market income and employment status. All Danes are registered using a unique identification number (Central Personal Registration (CPR) number), which can be used to link data across the national databases. Patient contact with the hospital system is recorded in the Danish National Patient Registry (NPR) at the time of contact and includes the primary diagnosis [28]. The NPR is a time-based national database that includes data from all inpatient and outpatient contacts, meaning that the data extracted are representative of the population in Denmark who has received a specific diagnosis in public and private hospitals. Furthermore, all contact with the primary sector (general and specialist practices) and medication use are recorded in the National Health Security and the Register of Pharmaceutical Sales databases, respectively. The population in this study included Danes aged <30 years who during the period 1995-2016 had received an ADHD diagnosis (ICD-10: F90x, F98.8C) and/or been treated with methylphenidate or other centrally acting drugs (ATC: N06BA02, N06BA04, N06BA09, N06BA12), defined as at least two prescriptions within 12 months. As the ICD-10 has been used since 1994 and the use of prescription medication is registered in Denmark since 1995, we defined the inclusion period from 1995 to 2016 (latest data available) (Figure 1).

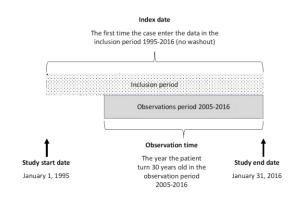


Figure1: Study timelines

This case-control study matched patients with ADHD or patients who received treatment for ADHD and the general population 1:4, respectively. Cases were matched on age, sex, and municipality at index year. Analysis of the long-term effects of ADHD on social and health care outcomes requires that patients with ADHD have reached adulthood. Therefore, we analysed outcomes for patients with ADHD the year they reached 30 years of age and the 10 year period before (21 years-30 years of age). Patients were excluded if they were diagnosed with a sleep disorder (narcolepsy [DG474] or hypersomnia [DG471]) in the period 1995-2016, had not reached 30 years of age in the period 2005-2016, were diagnosed with ADHD or first received ADHD medication after age 30, or were younger than 12 years in 1995.

Socioeconomic Status at Age 30

The labour market affiliation status was based on Statistics Denmark's information about the most important source of income or employment for the person in the year. Income from employment and public transfer payments was calculated for the year the ADHD cases and controls reached age 30, based on data from the Danish national income registry from Statistics Denmark. The reported income was predicted based on estimates from a regression model for cases and controls, to adjust for social background (parents' education) [29-32].

Health Care Cost at Age 30

Health care costs regarding hospitalization (inpatient) and outpatient visits were calculated using information on contacts and tariffs from the NPR. Data on the use and costs of prescription drugs were obtained from the Register of Pharmaceutical Sales databases. The primary health care costs of consultations with general practitioners and other specialists were obtained from the National Health Security registry. The reported health care costs were also based on a prediction to adjust for social background. Health care costs were divided into psychiatric and somatic costs. Psychiatric costs were divided into: Inpatient admissions, outpatient services, psychologist-primary health care sector, psychiatrist-primary health care sector and medication-psychiatric. Furthermore, psychiatric medication costs were subdivided into: ADHD medication (only case), antipsychotics (N05A), anxiolytics (N05B), hypnotics (N05C) and antidepressants (N06A). Income and costs were converted from Danish crone (DKR) to Euro (€) and the 2016 price index was used (exchange rate 7.45 DKR).

Psychiatric Comorbidity

The presence of psychiatric comorbidities was based on psychiatric diagnoses (ICD-10 F0-F9, WHO chapter V-Mental and behavioural disorders) excluding ADHD, and usage of psychiatric medication excluding ADHD medication. Concomitant medication was based on ATC codes and data from the Danish Medicine Agency database. Patients collecting medication of one of the following ATC codes at least twice in one year in the 10-year period before the age of 31 years were included: Antipsychotics (N05A), anxiolytics (N05B), hypnotics (N05C) or antidepressants (N06A). Patients with comorbidities were divided into one of four comorbidity groups: Severe psychiatric comorbidity included patients admitted to a psychiatric hospital with a mental and behavioural disorder based on ICD-10 diagnosis (F0-F9); moderate psychiatric comorbidity included outpatients who contacted a psychiatric hospital with a mental and behavioural disorder based on ICD-10 diagnosis (F0-F9); mild psychiatric comorbidity included patients with no secondary psychiatric contact but who collected the same type of psychiatric medication (excluding ADHD); and no psychiatric comorbidity included patients with no secondary psychiatric contact or who did not collect other psychiatric medications.

Substance Use Disorder

Substance abuse was based on psychiatric diagnosis for abuse F1 (ICD-10) and/or treatment for drug abuse in the 10-year period from the age of 21 years-30 years old. Medications for the treatment of substance abuse included methadone (N07BC02), buprenorphine (N07BC01, N07BC51), medication for alcohol dependence (disulfiram [N07BB01]), acamprosate (N07BB03), naltrexone (N07BB04), and nalmefene (N07BB05). Substance abuse was included as a binary variable (yes or no).

ADHD Treatment Adherence and Socioeconomic Outcomes in Adulthood

Correlation between ADHD treatment (adherence with ADHD medication) and socioeconomic outcomes in adulthood was investigated in the ADHD cohort. The socioeconomic outcomes were education status (completion of vocational or college education by the age of 30) and status of labour market affiliation ('employed/under education' or 'not employed' by the age of 30) at the age of 30. Adherence to ADHD medication was determined for each patient over the 10 year period prior to the age of 30 years (from 21 years to 30 years old). For each year, the number of defined daily doses (DDDs) was identified (yearly DDD/365 days) and treatment adherence set as 70%. Therefore, each year had a yes or no outcome for each patient, depending on whether they reached 70% adherence. Patients who had adherence=0 were also included, meaning they did not collect any medication that year. Thus, patients who, for instance, started ADHD treatment at age 26 and were 70% compliant until the age of 30 years had 5 years of adherence in the 10 year period analysed (21 years-30 years).

Statistical Methods

A conditional logistic regression model (nested case-control design) was used to estimate the differences in education level, labour market affiliation status and spouse/partner status for case versus control. A dummy variable for the 'parent education (1)' (vocational or college) versus 'no parent education (0)' (primary or secondary school only) was used in the models to adjust for social background, based on the parent with the highest attained education level. In cases when parent education was unknown, a dummy for 'education unknown (1)' versus 'no parent education (0)' was included. For income and health care-cost analysis, a 2-step model with a Probit model and a Poisson model was used, also controlling for parents' education. The estimates were used to predict income and health care cost for cases and controls when parents had no education. The p-values from the model were reported but the estimates were not reported. To analyse the relationship between ADHD treatment adherence and socioeconomic outcomes in adulthood we used a logistic regression model only including ADHD cases and estimated the odds ratio for a socioeconomic outcome in relation to ADHD treatment adherence in the 10 year period from age 21 years-30 years. In this model we adjusted for parent's education, psychiatric comorbidity, substance abuse and time since index. Time since index was included to adjust for the time the patient could have received treatment for ADHD. All statistical analyses were performed using SAS 9.4 TS Level 1M5 (SAS, Inc., Cary, NC, USA).

RESULTS

The study included 4,897 patients aged <30 years diagnosed with ADHD or collecting ADHD medication in the period 1995-2016 and who also reached the age of 30 years during 2005-2016 (Figure 2).

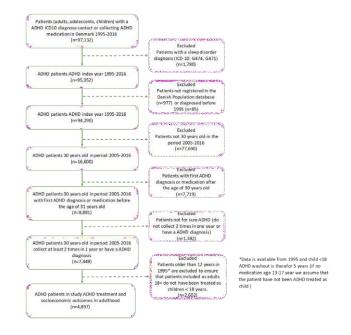


Figure 2: Flow chart showing patient identification and eligibility

The demographics and educational distribution of ADHD cases and matched controls is shown in **Table 1**. Most patients with an ADHD diagnosis were male and had parents with lower education levels. At age 30, people with ADHD were more likely to be living alone and have a lower education level and were less likely to be employed compared to the general population, even when adjusting for social background (P<0.0001 for each) (**Table 2**).

Table 1: Patient demographics and educational status

-	ADHD	Control	P-value*
Number, n	n=4,897	n=18,931	
	n (%)	n (%)	
	S	ex	
Female	1821 (37.2)	7043 (37.2)	Matched
Male	3076 (62.8)	11888 (62.8)	
	Backç	ground	
Denmark	4657 (95.1)	16793 (88.7)	<0.0001
Western countries	99 (2)	485 (2.6)	
Non-western countries	136 (2.8)	1653 (8.7)	
	Parents highest a	ttained education**	
No education	1159 (23.7)	3277 (17.3)	<0.0001
Vocational	2144 (43.8)	8217 (43.4)	
College short (KVU)	182 (3.7)	917 (4.8)	
College medium (MVU)	929 (19)	4012 (21.2)	
College Master/PhD (LVU)	294 (6)	1470 (7.8)	
Unknown	189 (3.9)	1038 (5.5)	

Table 2: Education level, employment and spous e status at the age of 30 years

-	ADHD	Control	P-value*	ADHD Odds Ratio	P-value
Number, n	n=4,897	n=18,931	-	-	-
	n (%)	n (%)	-	OR (95% CI)	-
		Spouse status a	at the age of 30		
Living alone	3090 (63.1)	8695 (45.9)	<0.0001	Ref	-
larried or cohabiting	1807 (36.9)	10236 (54.1)	-	0.4 (0.4;0.4)	<0.0001
		Highest attained educ	ation at the age of 30)	
Primary	2663 (54.4)	3905 (20.6)	<0.0001	Ref	
Secondary	428 (8.7)	1616 (8.5)	-	0.3 (0.3;0.4)	<0.0001
Vocational	1146 (23.4)	6567 (34.7)	-	0.2 (0.2;0.3)	<0.0001
College short (KVU)	82 (1.7)	914 (4.8)	-	0.1 (0.1;0.1)	<0.0001
College medium (MVU)	320 (6.5)	3480 (18.4)	-	0.1 (0.1;0.1)	<0.0001
College Master/PhD (LVU)	83 (1.7)	2152 (11.4)	-	0 (0.0;0.1)	<0.0001
Unknown	175 (3.6)	297 (1.6)	-	1 (0.8;1.2)	0.6949
		Labor market status at	the age of 30 (SES)*	*	
Employed	1739 (35.5)	14058 (74.3)	<0.0001	Ref	-
Education	430 (8.8)	1494 (7.9)	-	2.4 (2.1;2.7)	<0.0001
Unemployment benefit	106 (2.2)	465 (2.5)	-	1.9 (1.6;2.4)	<0.0001
Sick leave or other leave	160 (3.3)	470 (2.5)	-	3 (2.4;3.6)	<0.0001
Social security	1658 (33.9)	1215 (6.4)	-	12.3 (11.1;13.5)	<0.0001
Disability pension	601 (12.3)	603 (3.2)	-	9.1 (8.0;10,4)	<0.0001
Other	203 (4.1)	626 (3.3)	-	3 (2.5;3.6)	<0.0001

"Based on Socio13 Statistic Denmark. Socio13 status is, as a general rule, based on information about the most important source of income or employment for the person in the year Total wage income from employment and unemployment benefits was 28,251 Euros (95% CI: 25,639; 31,007) in the ADHD cohort, which was significantly lower than the 36,254 Euros in the control group (95% CI: 35,258; 37,269. P<0.0001) (**Table 3**). For the ADHD cohort, unemployment benefits were lower than in the control group (P<0.0001). Income from public transfer was significantly higher in the ADHD cohort, at 16,260 Euros (95% CI: 14,604; 18,039), compared with the control group at 6,064 Euros (95% CI: 5,589; 6,571; P<0.0001). Direct and indirect somatic and psychiatric health care costs, including all cost domains of psychiatric medication (ADHD medication, antipsychotics, antidepressants, hypnotics), were significantly higher among ADHD patients versus controls (P<0.0001) (Table 3).

Table3: Predicted income and health care cost per person in the year they reach age 30 for patients with ADHD and controls who have parents with no education (2016 price index)*

-	ADHD (95% CI)	Control (95% CI)	P-value
		education	
Number, n	n=1,159	n=3,277	-
Income	€ 10000 (0 514 14 000)		-
Wage income-employment	10300 (9,514;11,098)	28975 (28,525,29,410)	<0.0001
	•	ansfer payments	
Unemployment benefit	875 (743;1,022)	1134 (1,060;1,211)	<0.0001
Sick pay (public funded)	1056 (880;1,256)	998 (919;1,083)	<0.0001
Social security	9690 (9,106;10,266)	2505 (2,350;2,666)	<0.0001
Disability pension	4640 (3,875;5,495)	1427 (1,260;1,610)	<0.0001
come public transfer payments total	16260 (14,604;18,039)	6064 (5,589;6,571)	<0.0001
	Other public tra	nsfer payments	
Housing benefits	880 (807;955)	406 (381;432)	<0.0001
Child benefits	810 (713;914)	809 (763;857)	<0.0001
Income total	28251 (25,639;31,007)	36254 (35,258;37,269)	<0.0001
Health care cost	€	€	-
	Total health care cost (s	omatic and psychiatric)	
Inpatient admissions	763 (657;879)	549 (507;594)	<0.0001
Outpatient services	698 (654;741)	560 (539;581)	<0.0001
Primary health sector	439 (432;445)	236 (233;239)	<0.0001
Medication (prescription)	878 (857;898)	108 (105;111)	<0.0001
tal health care cost (somatic and psychiatric)	2778 (2,601;2,964)	1454 (1,385;1,525)	<0.0001
	Somatic hea	Ith care cost	
Inpatient admissions-somatic	751 (646;867)	543 (501;588)	<0.0001
Outpatient services	695 (651;738)	559 (528;579)	<0.0001
rimary not psychiatrist and psy- chologist	307 (302;311)	224 (221;226)	<0.0001
Medication not ADHD and other psychiatric medication**	160 (153;166)	83 (81;85)	<0.0001
Total somatic health care cost	1912 (1,752;2,082)	1408 (1,340;1,479)	<0.0001
	Psychiatric he	ealth care cost	
Inpatient admissions-Psychiatric not ADHD	12 (5;30)	6 (4;11)	<0.0001
utpatient services-Psychiatric not ADHD	3 (1;7)	1 (1;2)	<0.0001
sychologist-Primary health sector	12 (8;18)	9 (8;11)	0.5278
Psychiatrist-Primary health sector	121 (95;151)	5 (4;7)	<0.0001
, ,		psychiatric	
DHD medication (mean cost)***	629		-
Antipsychotics (N05A)	61 (51;72)	14 (12;16)	<0.0001
Anxiolytics (N05B)	5 (4;8)	1 (1;1)	<0.0001
Hypnotics (N05C)	6 (4;8)	1 (1;1)	< 0.0001
Antidepressants (N06A)	30 (26;34)	4 (4;5)	<0.0001
Total psychiatric health care cost	879 (821;908)	42 (33;55)	<0.0001

²-step Probit+Poisson used to predicat the income and the health care cost for cases and controls adjusting for parents' education "Other psychiatric medication: Antipsychotics (N05A), Anxiolytics (N05B), Hypnotics (N05C), Antidepressants (N06A) Presence of mild, moderate, or severe psychiatric comorbidities and alcohol or drug abuse was significantly higher in the ADHD cohort versus the general population (OR: 11.5 [95% CI: 10.5; 12.5], 9.4 [95% CI: 8.1; 11.0], 14.7 [95% CI: 12.9; 16.8], 5.5 [95% CI: 5.0; 6.1], respectively; P<0.0001 for all) (Table 4).

Table 4: Psychiatric comorbidity and alcohol/drug abuse over the 10-year period (21-30 years old)

-	ADHD	Control	ADHD Odds Ratio	P-value
Number, n	n=4,897 n=18,931		-	-
-	n (%)	n (%)	OR (95% CI)	-
		Psychiatric comorbidity*		
No psychiatric comorbidity	1345 (27.5)	15156 (80.1)	Ref	-
Mild psychiatric comor- bidity	2446 (49.9)	2625 (13.9)	11.5 (10.5;12.5)	<0.0001
Moderate psychiatric comorbidity	377 (7.7)	517 (2.7)	9.4 (8.1;11.0)	<0.0001
Severe psychiatric comor- bidity	729 (14.9)	633 (3.3)	14.7 (12.9;16.8)	<0.0001
		Alcohol or drug abuse**		
Alcohol or drug abuse	1014 (20.7)	891 (4.7)	5.5 (5.0;6.1)	<0.0001

'Psychiatric comorbidity is in the 10-year period from 21-30 years of age grouped and ranked as:

-Severe psychiatric comorbidity (admitted to a psychiatric hospital other than for ADHD diagnosis)

-Moderate psychiatric comorbidity (outpatient contact to a psychiatric hospital other than for ADHD diagnosis)

-Mild psychiatric comorbidity (no secondary contact but collected the same type of psychiatric medication [not ADHD] at least twice in one year) -No psychiatric comorbidity

**Alcohol or drug abuse: F1 diagnosis for mental and behavioural disorders due to psychoactive substance use and/or medication abuse:

-Methadone (N07BC02)

-Buprenorphine (N07BC01, N07BC51)

-Medication alcohol dependence

-Disulfiram (N07BB01)

-Acamprosate (N07BB03)

-Naltrexone (N07BB04) -Nalmefene (N07BB05)

The age at which patients were diagnosed with ADHD is shown in Figure 3. Both patients with early and later diagnosis or treatment initiation for ADHD (index age <18) were mostly males (87.1% and 60.3%). Patients with an earlier (i.e., childhood or adolescence) diagnosis or initiation of treatment for ADHD were more likely to have vocational education and those with later diagnosis or initiation of treatment were more likely to have a college education (P<0.0001). The share of patients with no education compared to education (vocational or college) were not significantly higher for patients with an earlier (i.e., childhood or adolescence) diagnosis or initiation of treatment for ADHD (chi-square binomial test p=0.4). Additionally, patients in the early ADHD diagnosis group had higher employment rates at the age of 30 than those diagnosed later (47.6% versus 34.3%; P<0.0001). Overall, the patients with an early ADHD diagnosis, 16.4% and 24.9% were on social security or disability pension by the age of 30, respectively, compared with 35.6% and 11.0% of patients with a later ADHD diagnosis, respectively. More patients who were diagnosed with ADHD at an early age did not have psychiatric comorbidities than those diagnosed later (52.8% versus 24.9%; P<0.0001). Early versus late diagnosis or treatment for ADHD had no effect on whether patients completed vocational or college training by the age of 30 when adjusted for parent education, substance abuse and presence of psychiatric comorbidities. Patients with an early diagnosis or early treatment initiation for ADHD were more likely to be employed or in education at age 30 than patients with later diagnosis or later treatment initiation (OR: 1.43 [95% CI: 1.17; 1.73]; P=0.0004), even when adjusted for parent education and substance abuse (OR: 1.35 [95% CI: 1.10; 1.64];

P=0.0033); however, when also adjusting for psychiatric comorbidities this difference was no longer significant.

Figure 4 shows number of years the patients over the 10 year period between the age of 21 to 30 have been adherent to ADHD medication (defined as 70% adherence). Patients with index year later than their 21st year were included as non-adherent in the period before their ADHD index year. Nearly 50% of the patients had no years between the age of 21 to 30 where they were adherent to ADHD medication, 27.4% were adherent 1-2 years in period and only < 1% were adherent all 10 years between the age of 21 to 30. Years with adherence to ADHD treatment between the age 21 to 30 had no effect on whether patients had completed a vocational or college education at age 30 when tested in a logistic model adjusted for parent education, presence of psychiatric comorbidities, substance abuse and time since ADHD diagnosis (OR: 1.00 [95% CI: 0.97, 1.03]; P=0.9448). Table 4 shows that psychiatric comorbidities by itself had a significant negative effect on completed education that increased with severity (for mild psychiatric comorbidity, OR: 0.69 [95% CI: 0.60; 0.80]; P<0.0001, and for severe psychiatric comorbidity, OR: 0.49 [95% CI: 0.38; 0.62]; P<0.0001). Parent education significantly increased the odds of had completed an education at age 30 (OR: 2.08 [95% CI: 1.78; 2.43]; P<0.0001). ADHD treatment adherence had a significant negative effect on employment status at age 30 when adjusted for parent education, presence of psychiatric comorbidities, substance abuse and time since ADHD diagnosis (OR: 0.96 [95% CI: 0.94; 0.99]; P=0.0101). Similar to completing education, the presence of a psychiatric comorbidity significantly decreased the odds of patients being employed/in education at the age

of 30 (for mild psychiatric comorbidity, OR: 0.40 [95% CI: 0.34; 0.46]; P<0.0001, and for severe psychiatric comorbidity, OR: 0.22 [95% CI: 0.17; 0.27]; P<0.0001). Parent education significantly increased the odds of being employed/in education at age 30 (OR: 1.93 [95% CI: 1.67; 2.23]; P<0.0001).

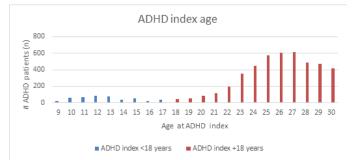


Figure 3: Age at ADHD diagnosis in patients with index <18 years old and 18-30 years old

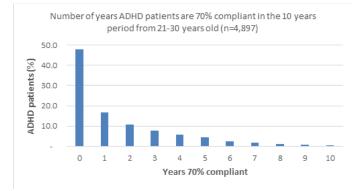


Figure 4: Adherence to ADHD treatment over the 10-year period in those aged 21-30 years

DISCUSSION

ADHD was found to be associated with negative long-term effects. Patients with ADHD had at age 30 poorer somatic and psychiatric health outcomes, as well as lower social status as measured by education level, employment, and spouse/ partner status, compared with the general population. These effects depended on the age at ADHD diagnosis, as patients with an early diagnosis (<18 years) generally had a positive socioeconomic outcomes regarding employment at age 30; conversely, patients with a later diagnosis of ADHD (18-30 years old) showed higher levels of psychiatric comorbidities and alcohol and drug abuse. Most of the difference in social outcomes could be attributed to the presence of psychiatric comorbidities, which were more prevalent among patients diagnosed in adulthood than in those diagnosed in childhood or adolescence. Adult ADHD diagnosis and treatment were associated with worse prognosis than childhood/adolescence ADHD which was primarily driven by the high load of psychiatric comorbidities. We showed that ADHD medication treatment (70% adherence) between the age of 21 to 30 had no positive impact on completing an education or being employed at age 30 when adjusting for social background, presence of psychiatric comorbidities, substance abuse and time since ADHD diagnosis. We cannot assess whether ADHD is the cause of the poorer employment outcomes for patients, or whether the social frameworks and conditions are early contributors to the negative social prognoses. We cannot exclude that part of

the elevated presence of comorbidities in the adult diagnosed ADHD is due to lower intervention earlier in life. For children and young patients with special needs, there is a general agreement on the need for multimodal interventions in addition to medication; however, there is little knowledge about which diagnostic procedures and interventions result and combinations hereof in the best long-term outcomes [33]. This is an issue not only in ADHD but other mental, psychiatric, and neurological disorders [25,34]. Ideally, each pharmacologic or cognitive intervention should be tested in randomized prospective studies. Often, short-term outcomes, like behavioural, or psychophysiological measures are assessed; however, analysis of patient outcomes, such as well-being, over a longer period is more difficult [15,23,25]. Despite the availability of new treatments and increased resource utilization in the management of children and young patients with ADHD, there is a lack of systematic evaluation, long-term follow-up, and direct comparisons between interventions.

We found that the use of psychiatric medication was elevated in patients with ADHD, including antipsychotic, antidepressant, and hypnotic drugs. This can be indicative of the complex nature of ADHD and the associated high burden of psychiatric comorbidities, as patients with ADHD often describe depressive symptoms and sleep problems [11,25,35]. The present study demonstrated that psychiatric comorbidities are more common in patients with ADHD diagnoses than in the general population and described some of the impacts of these disorders. This study has several strengths. First, we identified patients with ADHD and other neuropsychiatric diagnoses from public and private hospitals, as well as those who received medication, including the dosage and the frequency of medication use, as defined by DDD. Diagnoses were identified from hospital contacts, but we also included patients treated for ADHD in private psychiatric clinics. We identified the educational levels, employment status, income amounts, and health status of patients with ADHD; as a result, we obtained a thorough estimate of their long-term wellbeing, and used this information to track long-term outcomes of patients with ADHD from childhood to adulthood. Limitations included the lack of access to diagnoses from private practicing psychiatrists, leading to identification of ADHD patients through prescriptions. As a result, a group of patients who were diagnosed but did not receive medical treatment were overlooked (no identified) in this study. We believe that this was a small group. We would expect that this group not treated with ADHD medication would be functionally less affected than the study population, thus potentially biasing the study towards the null hypothesis. A further limitation is that the current study was observational and causal mechanisms cannot be inferred. We cannot specifically predict mechanisms or effects of specific interventions. Moreover, we did not have full information on other non-pharmacologic interventions that patients may have received for ADHD, such as psychological and support classes at home or in school.

CONCLUSION

In conclusion, this study demonstrated that patients with ADHD face substantial long-term negative consequences in education, employment, and health outcomes, including a high burden of psychiatric comorbidities and comedication use. Patients with

ADHD who were diagnosed earlier rather than in adulthood were more likely to be employed or in education at age 30; however, this effect was not significant after adjusting for psychiatric comorbidities. We found no association between adherence to pharmacologic ADHD treatment in adulthood and completion of education. The study suggests the importance of early diagnosis of ADHD to support timely treatment and initiation of multimodal intervention and reduce negative health and social outcomes among patients with ADHD.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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