# Resource Use and Health Care Costs of Newly Medicated Adults with Attention Deficit Hyperactivity Disorder: A Retrospective Cohort Study

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**Abstract**

**Purpose:** To investigate the use of health care resources and costs of first-time pharmacologically treated adults with attention deficit hyperactivity disorder (ADHD) compared with a control group of non-pharmacologically treated ADHD patients.

**Methods:** A Retrospective cohort study including all adult ADHD patients in Central Denmark Region and North Denmark Region using prescribed ADHD medicine (ATC-code: N06BA04 (methylphenidates) and N06BA09 (atomoxetine)). Study period was 2007-2011. Controls were defined as the pre-index therapy year for patients with an index therapy date in 2009. Costs covered pharmaceuticals, hospital in-house and ambulatory visits and outpatient visits (general practitioner, neurologists, psychiatrist and psychologists). Two Ordinary Least Square (OLS) regression with fixed effects were made. One model was applied to estimate adjusted mean costs before and after initiation of medical treatment of ADHD and one model to explain the cost of patients with different comorbidities and treatments.

**Results:** The OLS regression model show a rise of 9.8% of adjusted mean cost per patient to DKK 39,790 first post-index therapy year. The second post-index therapy year mean cost per patient fell with 21.8% to DKK 29,003. Both post-index therapy years were compared with the pre-index therapy year mean cost of DKK 36.070.

**Conclusion:** Adjusted overall health care costs were raised first post-index therapy year but lowered the second post-index therapy year for the medicated group indicating a lowering effect of ADHD medical treatment on overall healthcare costs after one year of treatment.

## Introduction

Attention deficit hyperactivity disorder (ADHD) is one of the leading causes of psychiatric illness worldwide, affecting approximately 5% of children.[1] For many years, ADHD was a child diagnosis but recent years' longitudinal cohort studies have found that ADHD persists through adolescence into adulthood in 60% of patients.[2] The three main clinical symptoms of ADHD include: hyperactivity, inattention and impulsivity.[3] Additionally ADHD patients have reduced executive function, i.e. patients have poor time management, low organizational planning and reduced complex problem solving capacity.[4,5] Altogether, ADHD impairs the patients, which is revealed in poor school/work performance, low educational level and low socioeconomic status.[6-8]

Patients with ADHD have in 65-89% of cases one or multiple co-occurring psychiatric disorders throughout their life.[9] This presents as substance abuse-, mono- or bipolar-, anxiety-, sleep-, personality- or eating disorders.[9-12]

When considering treatment of adults with ADHD, a combination of pharmacological and psychotherapy has proven the best treatment combination.[13-15] In Denmark stimulant therapy (methylphenidate) is considered first-line pharmacological therapy, and non-stimulant

(atomoxetine) is second-line therapy.[16] Methylphenidates show a reduction in core ADHD symptoms in 70-85% of the patients, while atomoxetine also shows a reduction in symptoms.[17,18] Both treatments have proven cost-effective for children with ADHD.[19-22]

ADHD patients consume an enormous amount of the health care services, seen from a socioeconomic view.[23,24] Adults with ADHD have significantly higher use of health care resources and costs when compared to non-ADHD adults.[25] This is also the case for ADHD patient families, which have significantly higher use of health care resources and costs when compared to non-ADHD families.[26] Moreover, ADHD adults have a risk-seeking behaviour, which elevates the risk of traffic- or work accidents contributing to the resource use of ADHD patients.[27-29] Additionally, adults with ADHD have high productivity loss due to low work performance, contributing to the overall societal cost, which is considerably higher than the overall societal cost of non-ADHD adults.[7,8,30]

In the past years a rise in prescriptions on ADHD medicine to adult ADHD patients were seen in Denmark. This raised concerns in the Central Denmark Region due to the higher costs to prescription co-payments and other related health care costs to the growing group of adult ADHD patients.

Little is known about the pharmacological treatment effects on resource use for adult ADHD patients. Thus, the purpose of this study was to investigate the use of health care resources before and after first-time pharmacologically treated adults with ADHD compared with a control group of non-pharmacologically treated ADHD patients.

## Methods

### Data

The retrospective study was based on data of health resource and demographic data, from The North Denmark Region and Central Denmark Region covering approximately 1.8 million citizens altogether. Patient health care resource use included data from:

1. Outpatient data were defined as visits to the psychologists, neurologists, psychiatrists and general practitioners, all with a private practice.
2. Inpatient data included all hospital registrations within the two regions, both in and out ambulatory hospital visits and hospitalizations as well as procedure codes and ICD-10 codes for diagnoses.
3. Pharmaceutical prescriptions covering all pharmaceuticals picked up by the patient at pharmacies in the regions along with item number of the drug. The pharmaceutical costs did not include patient co-payments, co-insurance or deductibles.

All data included cost, registration dates and identification number of ward or prescription filler and person identification number (CPR-number), which are a unique person specific number all citizens in Denmark are given when born. This allows for patient specific data gathering across national databases.

### Patient Selection

The overall study sample included all men and

women living in the two regions. Patients were identified and included if they met the following criteria:

1. Adults aged 18 to 60 years with at least one pharmacy claim of methylphenidate National drug codes (ATC-code): N06BA04 covering either short- or long-acting formulations) or one claim for atomoxetine (ATC-code: N06BA09).
2. Therapy start was initiated in the period 01.01.2008-12.31.2009.
3. No pharmacy claim on methylphenidate or atomoxetine 2007 until therapy start.
4. All patients with a pharmacy claim on dex-amphetamines (ATC code: N06BA02) were excluded due to low prescription rates.

After identification of patients, all use of health resources was gathered from databases one year prior to therapy index date and to two years after the therapy index date. Therapy index date was the date where the patient claimed his/her first prescription for methylphenidate or atomoxetine at a Danish pharmacy.

**Cost Data**

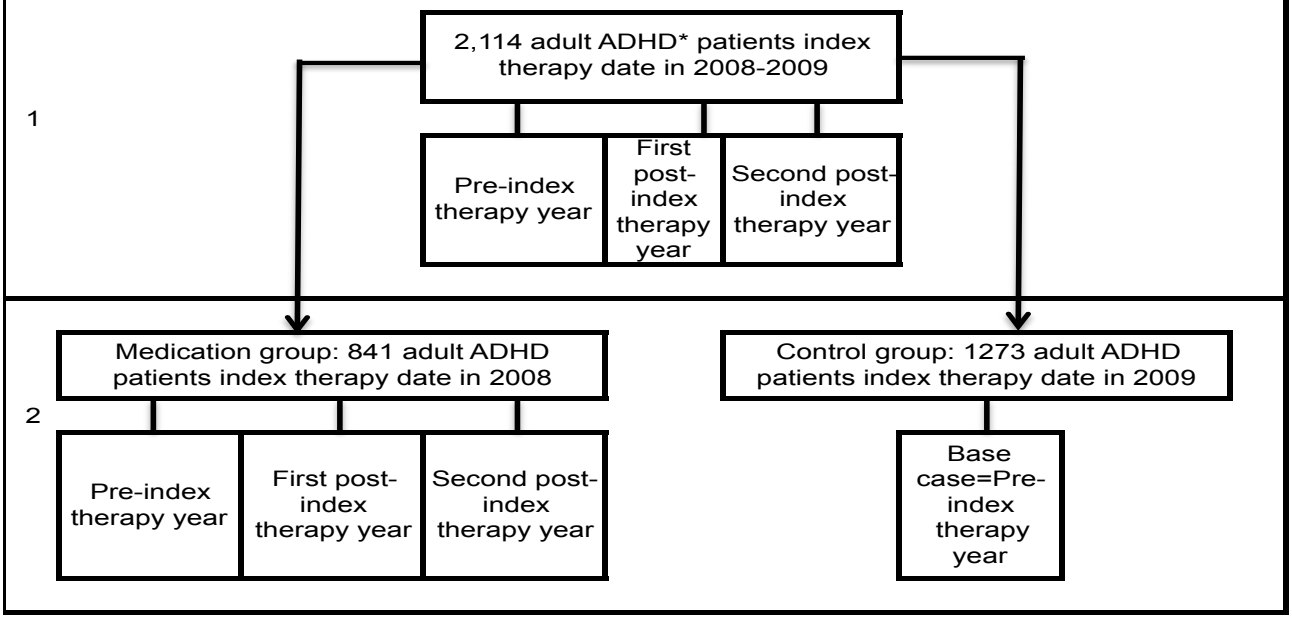
The perspective of the cost estimation was seen from a health care perspective. Consequently, cost only included transfers made from the two regions to hospitals, private practitioners and pharmacy claim co-payments. Inpatient costs included co-payments up to DKK 7.954 per patient from municipalities in the two regions. Inpatient admission periods with an admission date prior to the pre-index therapy year, were included if the discharge date was in the pre-index therapy year. Admissions with an admission date in the post-index therapy years and a discharge date not in the post-index therapy period were also included. Inpatient costs were converted by DRG price index.

All general practitioners and specialists have a general agreement specific for their speciality, specifying the services the regions will pay for. Each service has a registration code, which was used to convert all outpatient service prices into 2012 prices. Out of date registration, codes were converted to 2012 prices by a price index for registration codes in the primary sector in Denmark. Pharmaceutical costs were calculated as 75% of retail price, to adjust for patient co-payments included in the retail price. All prices were delivered in 2012 prices except pharmaceuticals with market item numbers from 01.01.2007-12.31.2011 indicating that the pharmaceutical was out of production. Here, the different prices for these item numbers were converted to the same 2012 by the pharmaceutical price index from Denmark.

**Study Design and Analyses**

The study included two Ordinary Least Square (OLS) linear regression models with fixed effects. The patient groupings in the different OLS regression models are shown in a flow diagram in Figure 1. The first OLS regression model predicted the pre-index therapy year and the two post-index therapy years overall healthcare cost of patients with an index therapy date in 2008 (medication group), when controlling for age group (0 if 18-30 years, 1 if 31-60 years), gender, region and control group. The control group included the pre-index therapy year for patients with a therapy

Figure 1: Grouping of the 2,114 patients in the two regression analysis and in the comparison between the medicated group and the control group




1: Adult ADHD patients, from 2008-2009, pre-index therapy year, first post-index therapy year and second post-index therapy year were used in the ordinary least square regression model with fixed effects.

2: Adult ADHD patients, from 2008, pre-index therapy year, first post-index therapy year and second post-index therapy year were used as medicated group and compared to the pre-index therapy year for adult ADHD patients, from 2009, grouped as the control group in the second OLS regression model

* Attention Deficit Hyperactivity Disorder (ADHD)

index date in 2009. Additionally unadjusted comparisons with independent T-tests were made between the medication group three years and the control group pre-index therapy year.

The second OLS linear regression model were based on all patients, with an index therapy date in 2008 and 2009, pre-index therapy year and two post-index therapy years. The dependent variable were overall yearly patient cost. Independent variables were divided into three groups. The first group was patient characteristics and incorporated the following dummy variables: gender (1 if woman, 0 if man), age group (0 if 18-30 years, 1 if 31-60 years), region (0 if Central Denmark Region, 1 if North Denmark Region), first post-index year (0 if pre-index therapy year, 1 if first post-index therapy year and 0 if second post-index therapy year), second post-index year (0 if pre-index therapy year, 0 if first post-index therapy year and 1 if second post-index therapy year). The second group was medical treatment dummy variables including: atomoxetine treatment (0 if methylphenidate only, 1 if atomoxetine only and 0 if mixed therapy), mixed pharmacological treatment (0 if methylphenidate only, 0 if atomoxetine only and 1 if mixed therapy), over 61 defined daily doses (DDD) first post-index therapy year (0 if <60 DDD, 1 if >60 DDD) and over 61 DDD second post-index therapy year (0 if <60 DDD, 1 if >60 DDD). The last group incorporated inpatient admission data dummy variables: admission with a obsessive-compulsive disorder diagnosis (OCD) (ICD-10

Table 1: Characteristics of the included patients N= 2,114

| | Number (%) if not stated otherwise | | |
|---|---|---|---|
| | All patients N=2,114 | Control group N=1,200 | Medication group N=841 |
| Male | 1,200 (56.8%) | 705 (55.4%) | 495 (58.9%) |
| Female | 914 (43.2%) | 568 (44.6%) | 346 (41.1%) |
| Age mean (median) | 32.1 (31.0) | 32.2 (31.0) | 31.8 (31.0) |
| Age group 18-30 years and (31-60 years) | 1,023 (48.4%) and 1,091 (51.6%) | 607 (47.7%) and 666 (52.3%) | 416 (49.5%) and 425 (50.5%) |
| Methylphenidate therapy | 1,726 (83.3%) | - | 731 (86.9%) |
| Atomoxetine therapy | 136 (6.4%) | - | 50 (5.9%) |
| Mixed therapy* | 217 (10.3%) | - | 60 (71.%) |
| Central Denmark Region patients | 1,764 (83.3%) | 1,082 (85%) | 682 (81.1%) |
| North Denmark Region patients | 350 (16.6%) | 191 (15%) | 159 (18.9%) |
| Admission with a OCD** diagnosis | 26 (1.2%) | 14 (1.1%) | 12 (1.4%) |
| Admission with a mental diagnosis do to substance abuse disorder | 330 (15.5%) | 196 (15.4%) | 134 (15.9%) |
| Admission with a affective disorder diagnosis | 317 (15%) | 197 (15.5%) | 120 (14.3%) |
| Admission with a ADHD*** diagnosis | 666 (31.5%) | 392 (30.8%) | 274 (32.6%) |
| Overall cost pre-index therapy year DKK mean [SD] (median; range) | 48,730 [105,365] (18,614; 383.56-1,341,870) | 49,271 [105,391] (18,609; 409,10-1,341,870) | 47,911 [105,386] (18,646; 383.56-1,085,566) |
| Overall cost first year post-index therapy DKK mean [SD] (median; range) | 39,337 [79,300] (19,928; 478.55-1,353,540) | - | 38,563 [82,819] (18.962; 478.55-1,353,540) |
| Overall cost second year post-index therapy DKK mean [SD] (median; range) | 37,176 [97,190] (16,255; 383.56-2,235,630) | - | 36,888 [91,110] (15,306; 383.56-1,379,710) |

* Patients were treated with both methylphenidate and atomoxetine

** Obsessive Compulsive Disorder (OCD)

*** Attention Deficit Hyperactivity Disorder (ADHD)

F42.X)[31] (0 if not having admission, 1 if having admission), admission with a mental disorder due to psychoactive substance abuse diagnosis (ICD-10 F10.X-F19.X)[31] (0 if not having admission, 1 if having admission), admission with a ADHD diagnosis (ICD-10 F90.X)[31] (0 if not having admission, 1 if having admission), admission with a affective disorder diagnosis (ICD-10 F30.X-F39.X)[31] (0 if not having admission, 1 if having admission), all other inpatient admission registrations not including the above-mentioned diagnosis (0 if not having admission, 1 if having admission).

The model were used to explain the yearly cost of a patient with different admissions due to comorbidities and medication use, thus the reference person in the regression models was the pre-index therapy year cost of a man, aged 18-30 years, living in the Central Denmark Region, without any admissions due to a mental diagnoses and other hospital registrations.

Both dependent variables in the two OLS linear regression models were LN transformed because of the skewed cost data. The Duan smearing method was used to correct the independent variables outputs, which are underestimated when back transformed with the exponential function, due to the LN transformation[32].

All data were analysed using Microsoft Excel (version 14.1.3, Microsoft Corporation) and IBM SPSS Statistics (Version 19, IBM Company).

## Results

### Patients' Characteristics

The study included 2,114 (1,200 men; 914 females) patients, of which 1,200 (705 men; 568 females) were grouped as the control group and 841 (495 men; 346 females) were grouped

Table 2: Three Years Cost and Utilization Comparisons Between Medication and Control Group

| Mean [SD] | Control group (N=1273) | Medication group (N=841) | | | P-values** | | |
|---|---|---|---|---|---|---|---|
| | Base year* (A) | Pre-index therapy year (B) | First post-index therapy year (C) | Second post index therapy year (D) | A vs. B | A vs. C | A vs. D |
| Inpatient cost (DDK) | 41,717 [103,242] | 40,528 [102,414] | 21,881 [79,956] | 22,989 [88,305] | - | < 0.001 | < 0.001 |
| Hospital cost without psychiatric hospitals | 16,528 [56,861] | 18,248 [72,802] | 14,075 [64,756] | 13,526 [66,031] | - | - | - |
| Psychiatric hospital cost | 25,189 [84,460] | 22,279 [66,238] | 7,805 [39,975] | 9,463 [55,661] | - | < 0.001 | < 0.001 |
| Emergency room Visits | 0.23 [0.65] | 0.37 [1.12] | 0.22 [0.87] | 0.15 [0.53] | <0.05 | - | <0.05 |
| Emergency room visits cost | 209 [672] | 388 [1,300] | 203 [808] | 146 [531] | <0.05 | - | <0.05 |
| Outpatient cost | 4,512 [3,718] | 4,323[3762] | 4,371 [4,029] | 3,461 [3,503] | - | - | < 0.001 |
| General practitioners claims registered | 22.98 [31] | 23.53 [33] | 22.95 [31] | 20.85 [25] | - | - | - |
| General practitioners visit claims*** | 6.76 [6.03] | 6.73 [7.10] | 6.01 [6.94] | 5.62 [5.78] | - | < 0.05 | < 0.05 |
| General practitioners telephone claims | 7.02 [8.51] | 7.80 [9.36] | 9.04 [10.91] | 7.99 [9.78] | <0.05 | < 0.05 | < 0.05 |
| General practitioners cost | 2,390 [1,987] | 2,315 [2,221] | 2,102 [1,882] | 1,991 [1,598] | - | < 0.05 | < 0.001 |
| Private psychiatric specialist cost | 1,847 [2,230] | 1,823 [2,958] | 2,126 [3,435] | 1,238 [2,668] | - | < 0.05 | < 0.05 |
| Overall cost without psychiatric hospitals | 24,082 [56,998] | 25,632 [75,621] | 30,758 [67,395] | 27,425 [68,693] | - | < 0.05 | - |
| Overall cost without psychiatric hospitals and ADHD medicine | 24,082 [56,998] | 25,632 [75,621] | 21,765 [66,055] | 20,215 [67,999] | - | - | - |
| Overall cost | 49,271 [105,391] | 47,912 [105,386] | 38,563 [82,819] | 36,888 [91,130] | - | < 0.05 | < 0.05 |

* Base year (A) represents pre-index therapy year for the patients starting ADHD medication in 2009 = The control group
** Independent Sample T-test for equality of means and Levene's Test were used for equality of variances. A space marked with - means no significance detected
*** Based on 0101 code, which represents a normal visit to the general practitioners.

as the medication group. In Central Denmark Region lived 1,764 (83.4%) patients and 350 (16.6%) lived in North Denmark Region. All other patients' characteristics are shown in Table 1.

**Resource Use Analyses**

The resource use and cost comparisons between the pre-index therapy year, the first post-index therapy year and the second post-index therapy year for the medicated group, and the pre-index therapy year for the control group are shown in Table 2.

Medicated patients had no significant difference in general practitioner claim registrations (E-mail, visits, laboratory registrations, etc.) when compared to control group. Registration visits to the doctor significantly decreased (P-value < 0.05) both post-index therapy years, first post-index therapy year mean number of visits [SD] 6.01 [6.94] and second year post-index therapy 5.62 [5.78], respectively, as compared to the control group 6.78 [6.03]. Medicated patients had significantly higher telephone registration claims for all three years when compared to the control group (P-values < 0.05) (Table 2).

Few patients from both groups used neurologist and psychologist, which was not analysed.

Mean visits per patient to the emergency wards at hospitals were significantly higher (P-value < 0.05) for the pre-index therapy year 0.37 [1.12] visits as compared to the control group 0.23 [0.65] visits per patient. Mean visits per patient

the second post-index therapy year 0.15 [0.53] were significantly lower (P-value < 0.05) as compared to the control group (Table 2).

**Cost Analyses**

Overall cost (inpatient, outpatient and all pharmaceuticals) for the pre-index therapy year DKK 47,912 [105,386], first post-index therapy year DKK 38, 563 [82,819] and second post- index therapy year DKK 36,888 [91,130], were significantly (P-value < 0.05) lower for both post-index therapy years as compared to the control group DKK 49,471 [105,391], but not significantly different to the pre-index year, which are shown in Table 2.

Overall cost without psychiatric registrations showed a significant (P-value <0.05) increase in cost for the first post-index therapy year DKK 30,758 [67,395] as compared to the control group DKK 24,082 [56,998]. When analysing the overall costs without psychiatric registration and ADHD prescription claims, no significant difference was observed.

For the inpatient costs both post-index therapy years DKK 21,881 [79,956] first year and DKK 22,989 [88,305] second year, were significantly lower (P-value < 0,001) as compared to the control group DKK 41,981 [101,515].

For the psychiatric hospital costs, both post-index therapy years DKK 7,805 [39,975] first year and DKK 9,463 [55,661] second year were significantly reduced (P-value <0.001) by more than 50% compared to the control group DKK 25,189 [84,460]. Somatic hospital use did not show any significant reductions. Cost by claims registered at an emergency ward was lowered significantly (P-value < 0,001) in second post-index therapy year DKK 146 [531] as compared to the control group DKK 209 [672].

Outpatient costs were significantly lowered (P-value < 0.001) the second post-index therapy year DKK 3,461 [3,503] as compared to the control group DKK 4,512 [3,718]. Of the outpatient costs general practitioners accounted for DKK 2,316 [2,221], DKK 2,101 [1,863] and DKK 1,991 [1,600], which were significantly lower (P-values < 0.05) for both post-index therapy years as compared to control group DKK 2,361 [2,001], but not significantly different to the pre-index therapy year. Private psychiatrist costs showed an increase (P-value < 0.05) of cost in the first post-index therapy year DKK 2,122 [3,435] as compared to the control group DKK 1,817 [2,915], but showed lower costs in the second post-index therapy year DKK 1,237 [2,699](P-value < 0,001).

**Ordinary Least Square Regression with Fixed Effects: The Prediction Model**

The main results of the study are shown in

**Table 3: Fixed effects OLS linear regression predicting the overall healthcare cost for the pre-index therapy year and the two post-index therapy for the patients with index therapy date in 2008, when controlling for age group, gender, region and control group**

| Parameter* | Estimate** | Std. Error | 95% Confidence Interval | |
|---|---|---|---|---|
| | | | Lower Bound | Upper Bound |
| Pre-index therapy year | 9.601207 | 0.056433 | 9.49055 | 9.711863 |
| First post-index therapy year | 0.098175 | 0.049044 | 0.001984 | 0.194366 |
| Second post-index therapy year | -0.21805 | 0.049049 | -0.31425 | -0.121849 |

* Parameters were adjusted for age group, gender, region and control group

** All estimates were significant (P-value <0.05)

**Table 4: Fixed effects OLS linear regression with dummy variables representing all 2,114 patients yearly cost**

| Parameter | Estimate* | Std. Error | 95% Confidence Interval | |
|---|---|---|---|---|
| | | | Lower Bound | Upper Bound |
| Pre-index therapy year** | 7.894689 | 0.082384 | 7.733134 | 8.056244 |
| First post-index therapy year | 0.101572 | 0.030368 | 0.042035 | 0.161109 |
| Second post-index therapy year | -0.246271 | 0.03037 | -0.305812 | -0.18673 |
| North Denmark Region | -0.170176 | 0.047162 | -0.262666 | -0.077686 |
| Over 61 DDD*** first post-index therapy year | 0.330463 | 0.068252 | 0.196614 | 0.464312 |
| Over 61 DDD second post-index therapy year | 0.604591 | 0.039259 | 0.5276 | 0.681582 |
| Admission with a affective disorder diagnosis | 1.236927 | 0.068776 | 1.102051 | 1.371804 |
| Admission with a mental disorder do to substance abuse diagnosis | 0.566678 | 0.049242 | 0.47011 | 0.663246 |
| Admission with a OCD**** diagnosis | 0.591831 | 0.156536 | 0.284849 | 0.898813 |
| Admission with a ADHD**** diagnosis | 0.376754 | 0.039771 | 0.298759 | 0.454749 |
| Admission with all other inpatient registrations****** | 0.744207 | 0.05352 | 0.63925 | 0.849164 |
| Atomoxetine treatment | 0.180702 | 0.075388 | 0.03286 | 0.328544 |
| Mixed pharmacological treatment******* | 0.213042 | 0.054293 | 0.106567 | 0.319516 |
| Over 31 years old | 0.262997 | 0.0347 | 0.194947 | 0.331047 |
| Female patient | 0.277626 | 0.035716 | 0.207583 | 0.347669 |

* All estimates were significant (P-value <0.05)

** Pre-index therapy year represents base case patient, which was a male at the age of 18-30, with no mental illness diagnosis, living in Central Denmark Region, receiving no ADHD pharmaceuticals

*** Defined Daily Doses (DDD)

**** Obsessive Compulsive Disorder (OCD)

***** Attention Deficit Hyperactivity Disorder (ADHD)

****** All other inpatient registrations that not included in the registrations from Mental disorder do to substance abuse disorder, OCD diagnosis, Affective disorder diagnosis and ADHD diagnosis

******* Patients were treated with both methylphenidate and atomoxetine

Table 3 where the overall adjusted yearly cost (mean) of the medicated group were predicted, when controlled for age group, region, gender and control group. The adjusted mean cost per patient pre-index therapy year was DKK 36,070. First post-index therapy year cost per patient was raised with 9.8% to DKK 39,790. The second post-index therapy year adjusted mean cost per patient fell with 21.8% to DKK 29,003 compared to pre-index therapy year. A Duan smear factor of 2.44 was multiplied to the back transformed costs. All parameter estimates were significant (P-value<0.05).

**Ordinary Least Square Regression with Fixed Effects: The Explanation Model**

Table 4 represents the result of the fixed effects OLS linear model, explaining the yearly cost of a patient with different attributes. The dependent variable "overall yearly patient cost" was LN transformed and all independent variables were significant (P-value <0.05). The pre-index therapy year mean cost of a male patient, between 18-30 years of age, living in Central Denmark Region and with no mental diagnosis, was DKK 6,439. For the corresponding female with same characteristics as mentioned above, the mean cost was DKK 8,501. In the first post-index therapy year a 10% increase in health care cost, not including any of the other independent variables, were observed. Second post-index therapy year showed a 25% reduction in health care cost not including any of the other independent variables.

Treatment with more than 61 DDD of methylphenidate raised the cost with 33% first post-index therapy year and by 60% second post-index therapy year.
The most expensive treatment regimen was the mixed pharmacological treatment with a 21% increase in costs as compared to treatment with methylphenidate.
The most expensive diagnosis was the affective disorder diagnosis with a 124% increase in costs as compared to no disorders.
Patients from North Denmark Region were on average 17% less costly than patients from Central Denmark Region. A Duan smear factor of 2.40 was multiplied to the back transformed costs.

## Discussion

The study investigated the effect of ADHD medicine treatment on newly medicated adult patients on their resource use and health care cost, because of rises in ADHD medicine prescriptions and their related costs to the regions of Denmark. The main results from the prediction OLS regression model controlling for age group, gender, region and control group, shows that the first post-index therapy year cost DKK 39,790. The second post-index therapy year cost per patient fell with 21.8% to DKK 29,003 compared with pre-index therapy year cost DKK 36.070. Unadjusted mean [SD] overall health care cost DKK 38,563 [82,819] and DKK 36,888 [91,130] and inpatient cost DKK 21,881 [79,756] and DKK 22,989 [88,305] in both years post-index therapy date were lowered significantly (p-values $< 0.05$), when comparing patients to the control group. A drop in psychiatric hospital costs by over 50% and a smaller drop in somatic hospital costs caused lowering of inpatient costs, which absorbed the rise in costs to pharmacological ADHD treatments. This may be due to five patients representing an overall cost $> 1{,}000{,}000$ DKK in the control group and only four patients in the medicated group. When comparing unadjusted overall costs without psychiatric hospital claims and ADHD prescriptions, there was no significant difference observed between years, indicating that ADHD treatment does not increase other health care costs significantly.
To the author's knowledge, it is the first time that the effect of treatment on adult ADHD patient' use of health care resources and costs pre- and post-index therapy date has been shown. Wu et al.[33] carried out a similar study but focused on specific drug formulations cost six months post-index therapy start. Able et al.[34] used an undiagnosed ADHD patient cohort as a control group, but focused on the impairment and functional level. Other articles have compared adult ADHD patients' resource use with non-ADHD patients' or compared with other groups with a chronic illness, concluding that adult ADHD patients were significantly more costly than non-ADHD patients[23,25,26] but were not as costly compared to patients with diabetes or depression[35].
Studies have shown that different formulations of methylphenidate is the least expensive treatment compared to atomoxetine and mixed amphetamine salts in children ADHD patients[19,21]. The explanation OLS regression model from this study showed the same,

however in adult ADHD patients, which was also shown in another study with adult ADHD patients receiving pharmacological treatment.[33]

**Limitations**

The article was a retrospective study based on patient claims data. Therefore, it was not possible to control for the ADHD severity. The study only controlled for selected co-morbid psychiatric disorders.

Only 666 out of 2,114 patients had an ADHD diagnosis (ICD-10 F90.X), because they had received treatment at a psychiatric hospital. It was not possible to retrieve diagnostic codes from outpatient psychiatrists and neurologists.

The perspective of the study only included health care costs associated with payments made from the Central Denmark Region and North Denmark Region. A societal perspective may have captured other effects of ADHD treatment like higher educational level[34], higher socio economic status[34], a lowering of accidents at work or when driving[27,28] and a better quality of life[34]. Further there might be potential lowering of government payments in social service benefits due to employment rather than unemployment, reduced loss in production[29] and reduced costs to criminality[30]

This study only used the overall formulations of methylphenidate and atomoxetine. Therefore, there might have been a difference in overall treatment costs if long- and short-acting formulations of methylphenidate had been taken into account. Other drug formulations like amphetamine-salts were not included in the study due to their limited use as a treatment option in Denmark.

The study used all patient registrations one year pre- and two years post-index therapy start. No attempts to differentiate between ADHD specific registrations and non-ADHD registrations were done. This could potentially overestimate the real costs associated with ADHD.

Finally, the number of patients with a co-morbid mental illness may be underestimated, because diagnostic codes only were found in patients, who had been admitted to a psychiatric hospital in the study period.

## Conclusion

Adjusted overall health care costs were raised first post-index therapy year but lowered the second post-index therapy year for the medicated group indicating a lowering effect of ADHD medical treatment on overall healthcare costs after one year of treatment.

## Acknowledgements

The author would like to thank Jens Jørgen Jeppesen, Central Region Denmark, and Ole Schou Rasmussen, North Region Denmark, for their work with the data gathering process. Furthermore the author would like to thank Central Denmark Region and North Denmark Region for their cooperation in the process of making the study.

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