The treatment costs of ADHD

A framework for future economic evaluations

Second year master thesis

Johan Eberhard & Erik Simonsson
2016-06-02

Department of Economics
Supervisor: Ulf Gerdtham

Abstract

Attention Deficit Hyperactivity Disorder (ADHD) is one of the most common neurobehavioral problems among both children and adults. Around 5% of the children and 3-4% of the adults suffers from the condition in Sweden. In general, diagnosed children achieve poorer results on standardized tests, receive lower grades and are more prone to dropout of school. Adults tend to struggle with work-performance, have lower socioeconomic status, and also finding it tougher with handling social bonds. Occasionally psychological intervention is enough for treating the condition; nevertheless, in general there is an additional need of pharmacological treatment. The ADHD-related drug use and ADHD-prevalence has increased considerably since the year 2006 in Sweden, yet no study fully investigating the associated costs has so far been conducted. In consideration to this, the aim of this thesis is to investigate the direct costs related to ADHD in Sweden. The results can be of assistance when performing economic evaluations of the costs and benefits of treating ADHD, as well as when performing health economic simulation modelling. These are some of the most common policy tools when it comes to determining the interventions regarding health policies.

Longitudinal panel data between 2006-2013, based on four linked registers of the total Swedish population diagnosed with ADHD, is used in order to investigate the direct costs. The four registers enable us to investigate subgroups and cost patterns over time in a more comprehensive way than what have been possible in previous studies. The main results are that the predicted marginal cost for an individual diagnosed with ADHD is 11,344 SEK per year and drug costs followed by outpatient procedure costs are the largest cost drivers. Over a ten-year period, the costs peak at the first year of follow-up, i.e. the year of diagnosis, and thereafter decrease gradually. Furthermore, individuals diagnosed with regular ADHD, or more than one diagnoses, and individuals aged 40-59 years bear the highest costs. Finally, the predicted marginal cost of having a comorbidity related to ADHD is 1,771 SEK per individual and year. The results suggest that there are large costs associated with being diagnosed with ADHD, and that further research and policy interventions are important in order to increase efficiency.

Keywords: *ADHD, two-part model, register panel data, direct costs, Sweden*

Acknowledgements

To begin with we want to thank Lundbeck for letting us conduct this project. Especially Linus Jönsson for his invaluable support and guidance through out the whole process. Last, but not least, we want to thank our supervisor, Ulf Gerdtham, for his advices and assistance in making this thesis possible.

Any errors are our own.

Glossary of abbreviations

ADHD	Attention Deficit Hyperactivity
ADD	Attention Deficit Disorder
AR	Autoregressive
ATC	Anatomic Therapeutic Chemical Classification System
CEA	Cost-Effectiveness Analysis
COI	Cost-of-Illness
DRG	Diagnosis Related Group
GEE	Generalized Estimating Equation
GLM	Generalized Linear Model
ICD	International Statistical Classification of Diseases and Related Health Problems
QUALY	Quality Adjusted Life Year
SEK	Swedish Kronor
TPM	Two-Part Model

Table of contents

List of tables

List of graphs

1. Introduction

Attention Deficit Hyperactivity Disorder (ADHD) is one of the most common neurobehavioral problems among both children and adults. Around 5% of the children and 3-4% of the adults suffers from the condition in Sweden. Hence, both children and adults suffering from ADHD are facing various difficulties due to the disorder. (Hjärnfonden, 2015).

ADHD is a heritable chronic neurobehavioral disorder that is defined by hyperactivity, inattention and impulsivity. Individuals suffering from the condition tend to be more impulsive and finding it harder to process new information. In general, diagnosed children achieve poorer results on standardized tests, receive lower grades and are more prone to dropout of school. Adults tend to struggle with work-performance, have lower socioeconomic status, and also finding it tougher with handling social bonds. Furthermore, impulsiveness also raises the probability of being involved in accidents, such as traffic accidents, or criminal activities and more substance abuse than non-ADHD diagnosed individuals. Psychological interventions and behavioural therapy is sometimes enough in order to treat the issues that follows an ADHD-diagnosis. However, in many cases there is an additional need of pharmacological treatment in order to treat the main symptoms. (Clarberg, 2015). Finally, ADHD-individuals tend have one or more comorbidities, i.e. mental disorders, implying further challenges for these individuals. (Sharma & Couture, 2014).

The number of studies on the economic impact of ADHD performed in a European setting is limited, still the economic and social burden in Europe is believed to be substantial, see Le et.al. (2013). Since the amount of studies is limited in Europe, it should come as no surprize that the number of studies in Sweden is even more limited. Yet, the prevalence of ADHD-related drug usage has increased significantly between 2006 and 2011 in Sweden, from approximately one individual per thousand citizens in 2006 to seven individuals per thousand citizens in 2011 (Nepi, 2012). The increased drug use and research from other countries, especially the United States, suggest that the topic and its associated costs are highly relevant for investigation also in Sweden.

From the perspective of health economics, costs are divided into three subgroups, i.e. direct, indirect and intangible costs. Direct costs include consumption of resources, which are a direct consequence of the state or disease, for example medical treatment or care. Indirect costs are costs associated with indirect causes that originate from the state or disease, for example inability to work or accidents related to the condition. Intangible costs consist of more abstract costs, for example the fact that an individual feel better or worse due to being treated, i.e. Quality Adjusted Life Year (QUALY) (Byford et. al, 2000).

The main purpose in this thesis is to examine the direct costs associated with being diagnosed with ADHD in Sweden. Estimating the direct cost can aid health economic modelling with determining the long-term economic impact of interventions from treating a condition. Consequently, the results can be of assistance when performing economic evaluations of the costs and benefits from treating ADHD, i.e cost-effectiveness analysis, health economic simulation modelling and cost-of-illness studies. Cost-effectiveness analysis and simulation models are two of the most common policy tools for determining interventions regarding health policies. In the extension interventions can make it possible to reduce future costs and increase efficiency. Furthermore, it is important to know what type of individuals and during what time in the individual's life a policy should be targeted in order to make appropriate and cost effective interventions. (Byford et. al, 2000). Additionally, it is also of relevance to examine the impact of comorbidities on costs since patients may experience multiple complications which for example increases the complexity of treatment and health care costs (Valderas et. al, 2009). From knowing when costs are at its peak, and which sub groups that are the largest cost drivers, researchers can further investigate the reason for the differences, making it possible for policy setters to target the most exposed individuals. This translates into the following research questions:

- *What is the (expected) direct costs of treatment for an individual diagnosed with ADHD?*
- *How does the cost pattern evolve after being diagnosed?*
- *How do the costs differ depending on the age and gender of the individual?*
- *How does the cost of being diagnosed differ depending on which ADHD diagnosis the individual receives?*
- *Are there any incremental costs associated with having comorbidities after being diagnosed with ADHD?*

To answer these questions, we use longitudinal panel data between 2006-2013 based on four linked registers of the total Swedish population diagnosed with ADHD. Two of the registers are from the Swedish National Patient Register and contains data on all inpatient visits from 1987-2013 and all outpatient visits from 2001-2013. These two registers contain Diagnosis Related Group (DRG) codes, which are matched with average costs gathered from the Swedish Association of Local Authorities and Regions. Furthermore, the registers contain International Statistical Classification of Diseases and Related Health Problems (ICD) codes which enables each ADHD treatment episode to be matched with the corresponding cost. The third register is the National Prescription Drug Register where all drug prescriptions from 2006-2015 and the associated costs for all individuals are registered. The drug register contains Anatomic Therapeutic Chemical Classification System codes (ATC) which makes it possible to trace which drug costs that are related to ADHD. The final register contains information on whether individuals have died during the study period, the register is called the National Cause of Death Statistics. Finally, since all Swedish citizens have their own personal identification number it is possible to match the registers over both individual and time.

As far as we know, no similar study using registers linked together has been conducted, either in Sweden or elsewhere. Since all individuals in our dataset have ADHD, and only costs related to ADHD are considered, we assume the costs to be incremental costs due to ADHD. Furthermore, using the four registers enables us to investigate subgroups and cost patterns over time in a more comprehensive way than what have been possible in previous studies. For example, there is to our knowledge no existing study investigating the costs related to different diagnoses of ADHD. We hope that this study will shed light on the cost associated with ADHD and that the results could serve as a foundation for future economic evaluations and modelling since the direct costs are an important input in such analysis. In the extension, this can lead to a more effective management of ADHD and efficient policy recommendations. In order to predict the costs a Two-Part Model is used, along with a Generalized Estimating Equation model as a robustness check.

The main results found are that the predicted marginal cost for an individual with an ADHD diagnosis is 11,344 SEK per year, of which drug cost and outpatient care are the biggest cost drivers. Over a ten-year period, the costs peak at the first year of follow-up, i.e. the year of diagnosis, and thereafter decrease gradually. Furthermore, individuals diagnosed with regular

ADHD, or more than one diagnoses, and individuals aged 40-59 years bear the highest costs. Finally, the predicted marginal cost of having a comorbidity related to ADHD is 1,771 SEK per individual and year.

The thesis will begin by briefly introducing some theoretical framework and application areas relevant for our results. Thereafter, we present previous research applicable to our field of study and research questions. In section 4, we present the registers and how they are used to construct the dataset. Subsequently, the methodology of the thesis is introduced before revealing the results. Finally, we end the thesis with a discussion and a conclusion of what our result entail for the subject, future research and policy interventions.[1]

[1] For additional information about ADHD, see Appendix 10.1

2. Theoretical Framework and Applications

One of the aims of this study is to provide estimates of the direct costs associated with an ADHD diagnosis. These estimates are thereafter possible to apply in future Cost-Effectiveness Analysis (CEA), economic simulation models and Cost-of-Illness (COI) studies. In order to make the reader understand the relevance of this paper we in this section briefly explain the main principles of cost-effective analysis, economic simulation models and cost-of-illness studies, and most importantly how our findings can be applied in these models.

2.1 Cost-Effective Analysis and Simulation Models

In cost-effectiveness analysis one examines the effects, E_i, where i identifies a specific treatment program, and costs, C_i, by expressing the relationship in terms of the amount of costs per unit of effect, i.e. C_i/E_i. In contrast to cost-benefit analysis, where all related costs always should be included, which costs to include is not always crystal clear in cost-effectiveness analysis. For example, some may argue that indirect costs, paid by patients should not be included, this since one requirement in Cost-Effectiveness Analysis is a fixed budget constraint. The costs supplied in this paper are the direct costs, i.e. drug treatment costs, inpatient care and outpatient care costs, which in the case of an Cost-Effectiveness Analysis therefore all are relevant. The second step is to define the effect that is relevant to examine in relation to the costs. An effect is defined as the consequence due to an illness when there is no intervention. In order to perform a Cost-Effectiveness Analysis it is vital to be able to ascertain that it really does exist an effect. In the case of ADHD, it has been shown that there are many different effects on individuals, such as poorer work performance, higher risk for criminality and drug abuse. Hence, performing an Cost-Effectiveness Analysis on ADHD treatment, one could for example examine how drug treatment, inpatient care treatment and outpatient care treatment of ADHD affect the social loss in terms of income for individuals. In that case, one would begin by calculate the average cost-effectiveness ratio for the different treatment programs and rank them from lowest to highest. (Brent, 2014). In summary, in order to perform a Cost-Effectiveness Analysis one needs to know both the costs and effects of the subject of interest in order to decide on if a treatment is effective, or what treatment that is most effective. The purpose of this paper is to provide the estimates of the costs, in order for future research to also examine the effects, such as cost of drug abuse or social loss**.**

Concerning simulation models it is a useful instrument in order to evaluate long-term impacts of interventions in different policy areas. Health care is a very complex area since decisions and choices by individuals are dynamic, i.e. it can change over time. Consequently, dynamic simulations concerning long-term outcomes that are based on current predictions is a useful policy tool. Nevertheless, in order to perform proper simulations, there is a need of comprehensive and relevant inputs, e.g. the direct costs estimated in this thesis. (Marshall et.al. 2015).

2.2 Cost-of-Illness Studies

Cost-of-illness studies are a common concept in health economics and are used to examine the economic impact of a specific disease or health problem in society. Determining the cost of an illness or disease is useful due to many reasons. First of all, it provides information on how much society is spending on different treatments. Furthermore, it makes it possible to estimate how costs are allocated between e.g. different individuals and healthcare sectors, and which factors that are cost-driving. This kind of information is additionally useful since it can be used as foundation for future cost-effectiveness analyses, simulation models and also provide material recognising areas of inefficiency, that policy makers might have to prioritize. (Byford et.al., 2000) (Ament & Evers, 1993).

When it comes to cost of illness studies there are three types of relevant costs, namely direct, indirect and intangible costs (Drummond et.al., 2013). Direct costs can be estimated on behalf of the individuals out of pocket expenses, the health care system expenses or on a societal level, i.e. aggregating the individual level cost and the healthcare sector cost (Byford & Raferty, 1998). In this paper focus will lie on the direct costs on a societal level, yet the cost of comorbidities related to ADHD will be estimated as well, which is an indirect cost. The advantage with concentrating on a societal level is the fact that it enables policy setters to evaluate an alternative resource use, and simulate if efficiency is improved when changing costs between sectors (Byford et.al., 2000). Furthermore, management of ADHD requires information on the annual average healthcare costs related to a lot of different incidents, e.g.

inpatient episodes, outpatient episodes or drug costs. The results from this paper could therefore serve as an input in long-term economic modelling and simulations. Which in turn can help to improve the long-term management of ADHD, be of help in resource planning and enlighten where there is potential for cost savings. Finally, health economic modelling and simulations will also be dependant on what subgroups that are the largest cost drivers, results which also will be provided within this study. (Saramago et.al., 2012).

3. Previous Research

Research devoted to the consequences of ADHD is a quite well explored area in the US, however the scope of European studies is smaller, and in Sweden no study, to our knowledge, has so far investigated the subject. The studies that are presented in this section are the ones we deem to be most relevant for our purpose. They are picked based on a selection criterion that they mainly investigate the incremental drug and treatment costs from being diagnosed with ADHD. In addition to this, some studies explore the indirect costs in order to estimate the full cost of the illness, see for example Secnik et.al. (2005). Firstly, a section with the previous research in an U.S. context is provided, and secondly a section of previous research in a European setting. Lastly, a table summing up the previous research is provided.

3.1 U.S-based studies

Swensen et.al (2003) investigate the direct and indirect costs for children aged 0-18 who suffer from ADHD in the U.S. As an indicator for the indirect costs the incremental cost for families with a ADHD diagnosed child is used. The sample consists of more than 100,000 individuals of which 1,308 have at least one ADHD claim in the time period 1996-1998. The ADHD-diagnosed individuals are matched to with the rest of the sample. T-tests and a Generalized Estimating Equation are used to examine the incremental costs for ADHD-diagnosed individuals. The authors find that the average costs for children with ADHD is $1,574 compared to an average cost of $541 for the matched control. Furthermore, the average cost for a family with an ADHD diagnosed child (direct plus indirect costs) is $2,728 while it is $1,440 for the matched control. Moreover, the authors conclude that ADHD carries a substantial financial burden due to the cost of medical care as well as work loss, both for the diagnosed individuals and their families.

In an article by Guevara et. al (2001), the authors examine the impact from ADHD on utilization and cost of health care. Their objective is similarly to Swensen et. al to explore the differences in health care utilization costs for children positively and negatively diagnosed with ADHD. They use a Two-Part Model, first estimating the probability of any cost with a logistic regression and then a Generalized Linear Model to estimate the incremental cost. Further all dependant variables are logged in order to reduce skewness. Children in the age 3-

17 in 1997 are included in the study, and the inclusion criteria for being in the ADHD cohort is that a child has been diagnosed with ADHD or received prescription of an ADHD stimulant. The controls are randomly selected based on age and gender. 2,992 children are identified as treated and they indeed incur considerable higher average costs than those not treated, $1,465 compared to $690. Furthermore, they estimate the incremental costs for children with just ADHD to be $375 and $812 for those with comorbidities. Nevertheless, it should be noted that the non-ADHD diagnosed cohort in this paper consist of individuals that have had a hospital visit for other reasons

A slightly different objective is presented in Ray et. al (2006). The main purpose of their study is to examine the excess costs before and after the initial diagnosis of ADHD, important to note is that the author's does not include patient out of pocket costs. Also Ray et. al run a Generalized Linear Model with an autoregressive covariance structure and ADHD related cost as dependant variables. 3,122 children between 2-10 years old in 1996-2004 that has been diagnosed with ADHD is identified and compared to 15,899 children without ADHD. In the analysis they compare the costs two years before and two years after the initial diagnosis. They find that children with ADHD has $488 higher costs two years before diagnosis, $678 more in the year before. In the year after diagnosis the costs are $1,328 higher and $1,040 higher two years after the diagnosis. An interesting feature with this article comes from the fact that they compare costs before and after diagnosis in order to capture the incremental cost.

Secnik et.al. (2005) examine the prevalence of comorbidities, resource use, direct medical costs, and costs associated with missed work for adults diagnosed with ADHD. The authors match an ADHD cohort (2,252 individuals) with a non-ADHD cohort (2,252 individuals), based upon age, gender, metropolitan statistical area and type of insurance coverage. The statistical method used to investigate the cost difference between the cohorts is analysis of covariances, which is a General Linear Model. The costs are logged and the smearing estimator is used in order to re-transform the results. The study takes place between 1999-2001. The results suggest that ADHD individuals are significantly more likely to have a comorbid diagnosis of asthma, anxiety, bipolar disorder, depression, drug/alcohol abuse, antisocial disorder or oppositional disorder. When the authors control for the impacts of comorbidities they find that ADHD-individuals have significantly higher outpatient costs

($3,009 vs. $1,492), inpatient costs, ($1,259 vs. $514) prescription drug costs ($1,673 vs. $1,008), and total medical costs.

Burd et. al (2003) estimates the prevalence and costs of ADHD treatment for children 0-21 years of age in North Dakota 1996-1997. They find that the prevalence of ADHD is 3.9 % and that it peaks at 10.3% when the individuals are 10 years old. The annual cost of care for children with ADHD is 5.1 million dollars. Furthermore, they find that the mean annual cost of care is 31% higher for children with ADHD, they also find that inpatient costs are 60% higher and outpatient costs are 148% higher for subjects with ADHD. One further interesting feature with their study is that male children with ADHD have lower costs than female, however in the control group there is no difference. It should be noted that Burd et.al. do not have data on medical costs, only inpatient and outpatient treatment costs.

Doshi et.al (2012) reviews studies that has been performed on the incremental costs of ADHD for both children and adults. They base their paper on 19 studies between 1990-2011, the inclusion criterion is that individual costs from ADHD-patients compared to a control group are reported. Their results suggest that the incremental national annual costs of ADHD are between $143-266 billions. The largest share of these costs are linked to the adult population, mainly due to productivity and income losses. Concerning children, the most significant cost driver is health care and education i.e. ADHD-diagnosed children require more resources, in addition large costs are also borne by the families of the ADHD-diagnosed individuals.

3.2 European-based studies

So far the we have mostly reviewed studies in the US, the main reason is that the number of studies in Europe are limited. One exception is Braun et. al (2013) who analyse the costs of treating ADHD-patients from the perspective of a major German health insurance fund. Approximately 6.3 million insured customers are available out of which 30,764 fulfilled the ADHD criteria. The population of study included all individuals with at least one inpatient or outpatient ADHD-diagnosis for two different quarters in 2008. Similar to the previous mentioned articles the costs for ADHD patients are matched and compared to a control group. In the study all ages are analysed, however also cost differences for subgroups depending on age are examined. The authors find that the reimbursement for insurers without ADHD is much smaller than for those with ADHD, the incremental costs for ADHD diagnosed individuals are €2,902 on average per patient. Furthermore, they find that the incremental cost for pharmaceuticals is €359 if having ADHD. Concerning the subgroups, the findings suggest that costs increases with age for inpatient and outpatient care as well as pharmaceuticals.

One further study that takes place in Europe is conducted by De Ridder & De Graeve (2006). The authors aim at quantify the economic and social burden borne by families that have a child with ADHD in Belgium. A second objective is to evaluate the costs for the public health system associated with a child who has ADHD. Questionnaires was randomly sent out to adults (parents) who are members of the Flemish ADHD society. The parents were asked to fill in their record of utilization of health care, social care as well as other non-medical resources for their ADHD child and his/her sibling. The model used is a Generalized Linear Model with a log link and gamma distribution in order to account for the skewness of the data. The authors conclude that ADHD affects the school results for the child and also the productivity of the parent. Further they find that children with ADHD are more likely to use health care and that a child with ADHD has a probability of visiting a general practitioner of 60.3%, compared to 37.4% if not having ADHD. In addition, ADHD children visits specialists and the emergency more often. Compared to their sibling an ADHD-diagnosed child in general incur medical costs for his/her parents that are five times higher (€588.33 compared to €91.5). Additionally, they find that public costs are twice as high (€779 vs €371). Obviously, ADHD does not only incur costs directly related to the condition, but also indirect costs in the form of lower productivity both for the child and his/her family.

Le et.al. (2013) state that the economic and social burden from ADHD in Europe is substantial, still there is a lack of studies that actually investigates the costs. Their purpose is to review the evidence from different studies and quantify the economic burden from ADHD in a European setting, using the Netherlands as a reference case. The study population used is children and adolescents due to a lack of studies investigating the costs for adults. By conducting a systematic literature search the authors extracted data on costs related to ADHD from seven articles. This data is further used to estimate the annual national ADHD-related costs by also examining the prevalence rate of ADHD. The authors conclude that the societal ADHD-related costs are around €1 billion per year for a society with around 16 million inhabitants. This result can be compared to the paper by Doshi et.al, who perform a similar analysis in an American setting and finds that the national annual costs incurred by ADHD to be between 143-266 billion dollars. Reasons for the great difference is probably that the prevalence of ADHD is much higher in the US than in the Netherlands. Further there are more cost of illness studies in the US than in Europe, implying that more cost drivers that are related to the condition might have been identified, additionally they also identified the costs associated with adult patients as well. Most importantly the US has a much larger population than the 16 million inhabitants that are considered in the case of the Netherlands.

In conclusion, these studies reveal that there are significant incremental costs associated with ADHD. In the U.S. the subject is quite well explored, in Europe, however, the number of studies are few, and in Sweden no research has been conducted. Furthermore, no study, to our knowledge, has investigated the ADHD related costs with a sample consisting of all diagnosed individuals within a country over a longer time-period. This implies that there are no exact estimates on the cost of ADHD in the previous literature. It should also be pointed out that no study has explored the cost distribution in a way that is as comprehensive as is performed in this study, e.g. examining the cost depending on ADHD diagnosis, age and gender. Overall, this stresses the importance of estimating the ADHD related cost for an individual as well as the total societal cost in a Swedish setting in order for policy setters to increase efficiency of the ADHD management and make informed interventions.

Table 1: Previous research summary

Study	Purpose	Location	Method	Conclusion/Findings
Swensen et.al	Investigate the direct and indirect costs for children aged 0-18 who suffer from ADHD.	U.S.	Matching to a control group without ADHD, using t-tests and a GEE model to estimate the incremental costs of those diagnosed with ADHD. The sample consists of over 100, 000 individuals.	The average cost of children with ADHD is $1574 compared to average cost of $541 of the matched control.
Guevara et.al (2001)	Examine the impact from ADHD on utilization and cost of health care on children.	U.S	Matching to a control group of children without ADHD. Two-part model is used, with a Logit and GLM specification. Sample of 2992 children	Individulas with ADHD incur much higher medical costs compared to those without, $1464 compared to $690. In addition they find that the children with just ADHD has incremental costs of $375, while those with comprbidities have $812.
Ray et.al (2006)	Explore the excess costs before and after initial diagnosis of ADHD for children aged 2-10 years.	U.S.	ADHD sample of 3122 individuals matched to sample of 15,899 individuals without ADHD. Using a GLM model with autoregressive covariance structure.	The year after diagnosis the incremental cost of for children with ADHD are $1328 and two years after $1040.
Secnik et.al (2005)	Examine the prevalence of comorbidities, resource use, direct medical costs, and costs associated with missed work for adults diagnosed with ADHD	U.S.	Matched ADHD cohort of 2252 individuals with non-ADHD of 2252 individuals. The statistical method is a analysis of covariances, which is a general linear model	They find that ADHD-individuals have significantly higher outpatient costs ($3009 vs. $1492), inpatient costs ($1259 vs. $514) , prescription drug costs ($1673 vs. $1008), and total medical costs.
Burd et.al (2003)	Estimate the prevalence and costs for children 0-21 years old.	North Dakota, U.S.	Comparasions of mean with a control group.	The prevalence of ADHD is 3,9 % and peaks at the age of 10, 10,3%. The annual cost of care for children with ADHD is 5.1 million dollars. Further they find that the mean annual cost of care is 31% higher for children with ADHD
Doshi et.al (2012)	Investigate the the incremental costs from ADHD both for children and adults.	U.S	Meta analysis. The paper is based on 19 studies between 1990-2011, the inclusion criteria is that individual costs for ADHD patients compared to a control-group are reported.	Their results suggests that the incremental national annual costs for ADHD are between $143-266 billions. The largest share of these costs are linked to the adult population, mainly due to productivity and income losses.
Braun et.al (2013)	Analyse the costs of treating ADHD patients from the perspective of a major German health insurance fund.	Germany	Approximately 6.3 million insured customers are available out of which 30,764 fulfilled the ADHD criteria. The costs for ADHD patients are matched and compared to a control group (all ages).	The incremental costs for ADHD diagnosed individuals are €2,902 on average per patient. Further they find that the incremental costs for pharmaceuticals are €359 if having ADHD
De Ridder & De Graeve (2006)	They aim at quantifying the economic and social burden borne by families that have a children with ADHD in Belgium, They also investigate the public health costs associateed with a child diagnosed ADHD	Belgium	Questionnaires was randomly sent out to adults (parents) who are members of Flemish ADHD society. The model used is a generalized linear model with a log link and gamma distribution	Compared to their sibling an ADHD-diagnosed child in general incur medical costs for his/her parents that are five times higher (€588.33 compared to €91.5). Additionally they find that public costs are twice as high (€779 vs €371)
Le et.al (2013)	Their purpose is to review the evidence from different studies and quantify the economic burden from ADHD in a European setting, using the Netherlands as a reference case	Netherlands	3000 randomly selected households. The study population used is children and adolescents due to a lack of studies investigating the costs for adults. By conducting a systematic literature search the authors extracted data on costs related to ADHD from seven articles	The authors conclude that the societal ADHD-related costs are around €1 billion per year for a society with around 16 million inhabitant

4. Data

This section begins by a brief review over the Swedish data registers used. Furthermore, the procedure of the creation of the longitudinal panel dataset used in this study is presented. Thereafter, the construction of the dependent and independent variables is explained. Finally, some descriptive statistics are presented.

4.1 Data Registers

The dataset used in the study is based on four linked registers from the Swedish national registers of total Swedish population diagnosed with ADHD. In Sweden each individual has its own unique personal identification number, which is used in for example the healthcare system. These identification numbers have been replaced with study identification numbers by the National Board of Health and Welfare and the personal identification number has not been saved, implying that the data is anonymized. The study identification number makes it possible to identify and link individuals over time to various activities between the registers, in this particular case activities associated with the health care system. Since the registers contains data for the entire Swedish population, all individuals diagnosed with ADHD in inpatient care since 1987 or outpatient care since 2001 will be in the study, thereby little or possibly no selection bias should be present.

Two of the registers are from the Swedish National Patient Register, containing data on all inpatient visits between 1987 and 2013 and all outpatient visits between 2001 and 2013. Each individual has his or her first ADHD diagnosis as index date, consequently appearing for the first time in the dataset at that point. After that date, all inpatient or outpatient care contacts are reported in the dataset, along with main diagnosis, other diagnoses, date of inpatient/outpatient visit, gender and age. The diagnoses are reported in International Statistical Classification of Diseases and Related Health Problems (ICD) 9 and 10 codes, see for example table 2 section 4.3.2. Furthermore, in order to link an inpatient or outpatient episode to a treatment cost, Diagnosis Related Group (DRG) codes are used. These represents specific treatments and are reported for every inpatient and outpatient episode in the registers. This makes it possible to link average treatment costs, reported by the Swedish Association of Local Authorities and Regions, to each individual.

The third register comes from the National Prescription Drug Register and reports all drug prescriptions since 2006, its associated costs and the prescription date of the drug for all individuals. Furthermore, it contains Anatomic Therapeutic Chemical classification system (ATC) codes, which states what specific drug that has been prescribed. This enables drugs associated with ADHD and comorbidities to be linked to specific costs. The fourth register, The National Cause of Death Statistics, contains information on which individuals that have died during the study period and for those individuals the end of follow-up is their date of death. For all other individuals, the end of follow-up is the 31th of December 2013, since that is the last date of data on inpatient and outpatient care.

4.2 Dataset construction

Since all individuals have their own personal study identification number it is possible to match the registers over both individual and time. All events in the registers are reported on date level, however for the analysis they are collapsed to year level in order to estimate the yearly costs. In order to merge and collapse the registers efficiently the first step is to create an index variable equal to one for the first observation for each individual, i.e. the date at which an individual got his or her first ADHD main diagnosis. Thereafter, the registers are collapsed on year and quarters, e.g. 2006q1, and by individual and quarter the datasets are filled in order to have a panel dataset without gaps in time. Since the registers includes all hospital visits, drug prescriptions etc. for each individual the newly created observations are treated as zero observations for that specific quarter. i.e. zero cost, zero drug prescriptions etc. For example, if individual one is diagnosed in 2008q1 but have neither drug costs, inpatient visit nor outpatient visit in 2008q2 or 2008q3 they will be filled out as zero cost observations for this individual.

Collapsing the dataset on quarters enables the estimation of yearly costs to be more specific. Hence, after being collapsed on quarters a time variable reporting the number of quarters since the first diagnosis is generated for each individual. Thereafter, the datasets are collapsed on every fourth quarter to get the exact yearly data for each individual. In this way, for example, an individual who has been diagnosed in the fourth quarter of 2006 will not only have one quarter of costs representing the costs in the first year. Instead the first, second and third quarter of 2007 also will be accounted for, and so on.

After being collapsed on yearly basis the registers are merged on identification number and year. Important to mention is also that observations before 2006 and after 2013 are dropped since the period 2006-2013 is the only period that all datasets cover. This implies that the maximum number of observations for one specific individual could be 8. However, since each individual first observation is recorded at the year of receiving a diagnosis, most individuals will not have 8 observations, e.g. if being diagnosed in 2009q1 the individual will have 5 observations. Furthermore, some individuals have been diagnosed before 2006, but through the creation of the year variable they are still in the dataset, but their costs before 2006 are not observed. In order to limit the study, and due to lack of observations as the year variable increases we choose to focus on the first ten years after an ADHD diagnosis. The final dataset contains 97,183 individuals and 388,768 observations, with a mean of 4 observations per individual.

4.3 Variable construction

4.3.1 Dependent variables

In this thesis five dependant variables will be used. These are the direct ADHD-related cost of drug treatment, outpatient care, inpatient care, the direct total cost of ADHD and finally the indirect total cost from ADHD-related comorbidities. The costs variables are based on the aggregated cost of public expenses and patient out-of-pocket expenses. Below a description of the construction of these variables is presented.

The cost of drug treatment is calculated per individual and year from 2006-2013, or from the point the individual got diagnosed with ADHD after 2006. In order to match which costs that are relevant to include, we use the ATC codes reported in the register for each drug prescription. The ATC codes are identification codes classifying each drug depending on application and chemical substance, it enables specific costs to be linked to drugs prescriptions related to ADHD or a comorbidity.[2][3]

---

[2] A list of relevant ATC-codes can be found in Appendix 10.3, table 12.

[3] All drug costs are converted into 2016 year's prices.

Inpatient and outpatient treatment costs, i.e. the costs of treating individuals in inpatient or outpatient care, are used as dependent variables. These costs are calculated for every visit in inpatient and/or outpatient care related to a main diagnosis of ADHD, furthermore the comorbidity costs are calculated for every visit related to a comorbidity diagnosis. As the dataset contains every individual's inpatient and outpatient visit since his or her first ADHD diagnosis we use the ICD-9 and 10 codes, reported in the registers, to link inpatient and outpatient episodes to ADHD and comorbidity diagnosis. For each of those visits we thereafter calculate the costs using DRG codes, reported for every inpatient and outpatient episode. A DRG code represents which kind of treatment that has been given to an individual at a specific health care contact and diagnosis. In order to link each DRG code to a cost we use the average cost per DRG code in 2014. The average costs are recovered in the Cost per Patient database, supplied by Swedish Association of Local Authorities and Regions (SKL A, 2015). The average costs per DRG code are based on statistics from 48 Swedish Hospitals, of which all supply inpatient care and 44 outpatient care, in 2014 (SKL B, 2015). Since the reported average costs are in 2014 year's prices, they are converted to 2016 year's prices for the data analysis (SCB A, 2016).[4]

The fourth dependent variable used is total cost per individual, i.e. the sum of drug treatment cost, inpatient cost and outpatient cost per individual and year. This in order to see the overall effect of an ADHD diagnosis. Regarding the fifth dependent variable, total comorbidity costs, it is only examined from a total cost perspective due to a low number of observations with costs greater than zero.

4.3.2 Independent variables

Since all individuals in the dataset have ADHD, one purpose of this paper is to investigate how costs differ depending on what specific ADHD diagnosis an individual has. The interest in examining the costs for all types of diagnoses is that it will help to decompose the ADHD costs not only for ADHD in general, but also for every specific type. This makes it possible to find out where the biggest cost drivers are and thereby revealing where treatment interventions are most important. In the regression analysis a categorical variable indicating which type of ADHD diagnosis an individual has, or if he or she has more than one diagnosis, is used. This in order to also be able to see how the costs differ for individuals suffering from

[4] The DRG codes related to ADHD and relevant comorbidities, its average costs and type of treatment are reported in the Appendix 10.3, table 13.

more than one diagnosis. The categorical variable is created by using the ICD-10 codes reported for each individual at inpatient and outpatient episodes in the dataset. The included diagnoses and their ICD-10 codes can be observed in table 2 below.

Table 2: ICD-10 codes and ADHD diagnoses

ICD-10	Diagnosis
F90.0	Distrurbance of Activity and Attention
F90.0A	Deficits in Attention, Motor control, and Perception (DAMP)
F90.0B	Attention Deficit Hyperactivity Disorder (ADHD)
F90.0C	Attention Deficit Disorder (ADD)
F90.0X	ADD, unspecified type
F90.1	Hyperkinetic Conduct Disorder
F90.8	Other Hyperkinetic Disorders
F90.9	ADHD, unspecified type

Source: Socialstyrelcen C (2016)

In the analysis categorical variables indicating gender type and age group are also used. The age groups are in the spans 0-9 years, 10-19 years, 20-29 years, 30-39 years, 40-59 years and 60≤ years. This distribution is used in order to keep the individuals within the groups as even and homogeneous as possible. The year variable is also categorical, and indicates the number of years since the first ADHD diagnosis. Additionally, it could be argued to be desirable to include control variables such as income and other socioeconomic background statistics. However, since the linked registers does not include such variables it is not possible to control for.

In order to control for comorbidities, we use a dummy variable equal to one every year after an individual has received a comorbidity diagnosis. So if the individual received a comorbidity diagnosis the second year after an ADHD diagnosis, the comorbidity dummy takes the value one for year 2 and the subsequent years. The comorbidities are, as the ADHD diagnoses, reported in ICD-9 and ICD-10 codes in the registers, and the comorbidities that are controlled for are anxiety, depression, bipolar disorder and schizophrenia.[5] In table 3 below all independent categorical variables and their levels can be observed.

[5] A table of comorbidity ICD-codes can be found in Appendix 10.3, table 13.

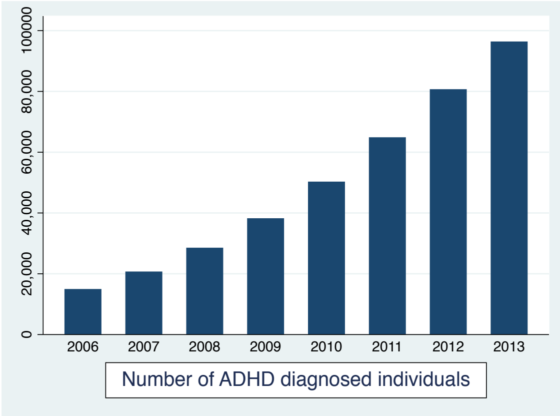
Table 3: Independent categorical variables and levels

Variable	Categories
Age groups	0-9 10-19 20-29 30-39 40-59 60≤
Gender	Male Female
Diagnosis	Distrurbance of Activity and Attention Deficits in Attention, Motor control, and Perception (DAMP) Attention Deficit Hyperactivity Disorder (ADHD) Activity Deficit Disorder (ADD) ADD, unspecified type Hyperkinetic Conduct Disorder Other Hyperkinetic Disorders ADHD, unspecified type 1< diagnosis
Year of diagnosis	1st year of diagnosis 2nd year of diagnosis 3rd year of diagnosis 4th year of diagnosis 5th year of diagnosis 6th year of diagnosis 7th year of diagnosis 8th year of diagnosis 9th year of diagnosis 10th year of diagnosis
Comorbidity	No Yes

4.4 Descriptive Statistics

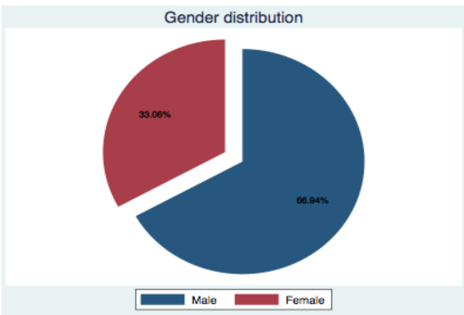
In the tables and graphs below some descriptive statistics are presented. In contrast to the empirical analysis the descriptive statistics does not use year since diagnosis as time variable. Instead, the yearly trend between 2006 and 2013 is shown in order to shed light on the development of ADHD related costs and prevalence during this time period.

As can be seen in graph 1, the total number of individuals diagnosed with ADHD has increased drastically during the time period. Furthermore, the growth seems to be increasing exponentially. This implies, that in the empirical analysis many individuals will only be observed for a short time span before the end of follow-up.

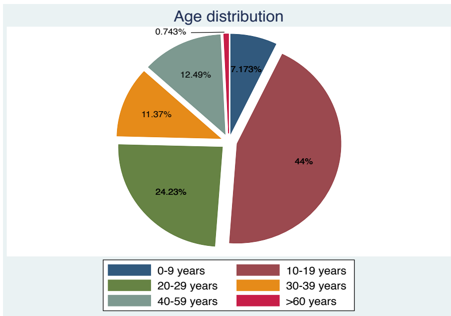


Graph 1: Total number of ADHD diagnosed individuals per year

In graph 2 and 3 we can see the gender and age distribution from the population under study. Concerning gender around two thirds of the ADHD diagnosed individuals in Sweden are men, which is indeed quite remarkable and well worth noting. From the second graph the age distribution of the diagnosed individuals can be seen. Most strikingly is that 44% of the individuals are between 10-19 years, further it should be noted that the number of diagnosed individuals over 60 years are very low.

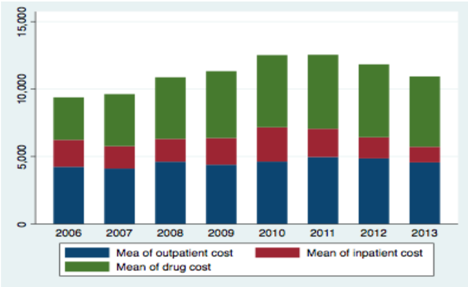


Graph 2: Gender distribution

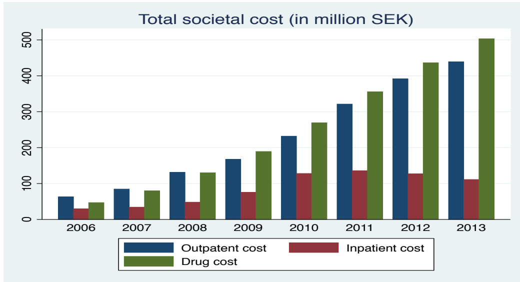


Graph 3: Age distribution

In graph 4 the development of ADHD related drug costs, outpatient costs and inpatient costs can be seen. Evidently, the mean total ADHD related direct costs ranges from slightly below 10,000 SEK to around 12,000 SEK per year, with a peak in 2011. It should be noted that the mean of drug and outpatient costs stand for the largest share of the total mean cost. The same cost distribution can also be observed in graph 5, where the total societal cost is illustrated. The total societal drug cost stretches from 47 million SEK in 2006 to 500 million SEK in 2013. Regarding the total societal outpatient cost, it ranges between 63 million SEK in 2006 and 439 million SEK in 2013. The total societal inpatient cost ranges between 30 million SEK in 2006 and 136 million SEK in 2011. Finally, it should be noted that the mean cost is relatively constant over time, while the total sum cost increases from one year to the next, probably because the number of ADHD diagnosed individuals increase, see graph 1.

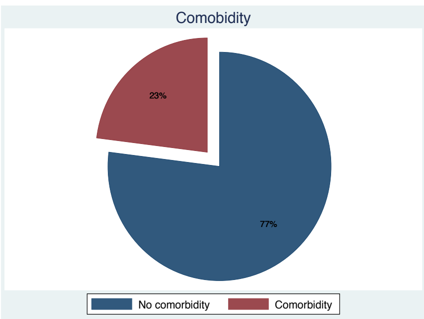


Graph 4: Mean ADHD cost (outpatient/inpatient/drugs)

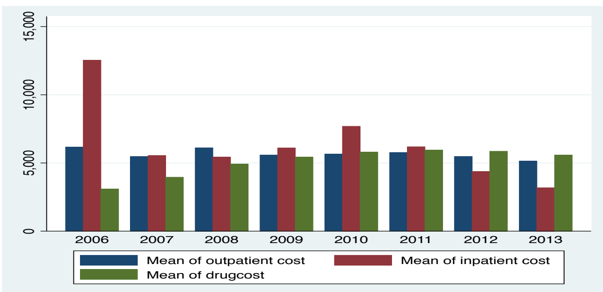


Graph 5: Societal ADHD cost (outpatient/inpatient/drugs)

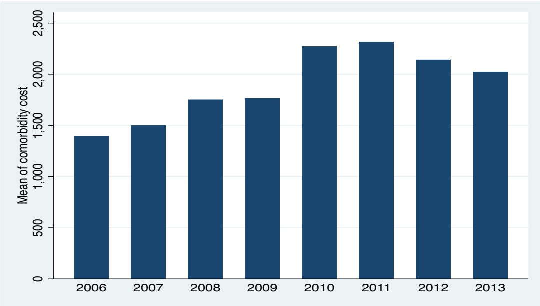
In graph 6 the share of individuals in the population that have one or more comorbidities is displayed. Around 23% of the individuals have comorbidities, this is relevant since estimating the comorbidity costs is one of the main purposes of this thesis. Graph 7 illustrates the mean of ADHD related medical, outpatient and inpatient costs for individuals having one or more comorbidities. Graph 7 can be compared to graph 4 where the ADHD mean cost for the entire sample can be seen. The ADHD related drug costs are significantly higher for these individuals than for the entire sample. It is also evident that the mean inpatient costs for individuals having one comorbidity is far greater than for the entire sample, also the mean outpatient costs appear higher, yet not as evidently. The mean cost of having a comorbidity is showed in graph 8. The mean cost is gradually increasing from slightly below 1,500 SEK in 2006 to somewhere between 1,500 and 2,000 SEK in 2011. After 2011 the trend reverses again and the mean costs are around 1,500 SEK in 2013. Lastly, graph 9 illustrates the distribution of the diagnoses. The most prevalent diagnoses are regular ADHD, Disturbancy of Activity and Attention and if the individuals has more than one diagnosis.



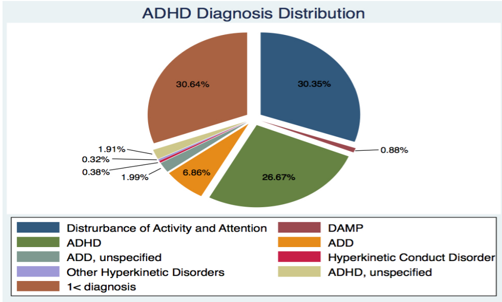
Graph 6: Comorbidity distribution



Graph 7: Mean ADHD cost, conditional comorbidity



Graph 8: Mean ADHD comorbidity cost



Graph 9: ADHD Diagnosis Distribution

Table 4: Descriptive statistics

Variable		Mean	Std. Dev.	Min	Max	Observations
ADHD Drug cost	overall	4954.95	7369.516	0	388266	N = 388768
	between		6063.146	0	203564.5	n = 97183
	within		4022.404	-193509.5	189656.5	T-bar = 4.00037
ADHD Inpatient cost	overall	1737.548	20070.88	0	2320710	N = 388768
	between		13731.02	0	795672	n = 97183
	within		16042.76	-683424.5	1526776	T-bar = 4.00037
ADHD Outpatient cost	overall	4671.673	7205.687	0	262062	N = 388768
	between		5638.629	0	169915.7	n = 97183
	within		5284.706	-85485.99	183177.7	T-bar = 4.00037
ADHD Aggregated cost	overall	11364.17	23894.11	0	2334516	N = 388768
	between		17091.16	0	811884.8	n = 97183
	within		17967.65	-690010.6	1533995	T-bar = 4.00037
Comorbidity cost	overall	1745.731	13983.81	0	1489318	N = 388768
	between		8955.127	0	615504	n = 97183
	within		10569.02	-481997.5	1283624	T-bar = 4.00037
ADHD visits inpatient care	overall	.0245082	.2399116	0	42	N = 388768
	between		.1634954	0	14.4	n = 97183
	within		.1866464	-12.37549	27.62451	T-bar = 4.00037
ADHD visits outpatient care	overall	1.258069	1.912712	0	69	N = 388768
	between		1.490286	0	44.66667	n = 97183
	within		1.407347	-22.4086	48.25807	T-bar = 4.00037
Comorbidity visits inpatient care	overall	.0091906	.1714824	0	20	N = 388768
	between		.1108815	0	10	n = 97183
	within		.1300375	-5.990809	17.00919	T-bar = 4.00037
Comorbidity visits outpatient care	overall	.1705567	.8962921	0	67	N = 388768
	between		.7157598	0	33.5	n = 97183
	within		.6237042	-33.32944	35.54556	T-bar = 4.00037
Gender (1=male, 2=female)	overall	1.333569	.4714884	1	2	N = 388768
	between		.4794557	1	2	n = 97183
	within		0	1.333569	1.333569	T-bar = 4.00037
Age group (1=0-9, 2=10-19, 3=20-29, 4=30-39, 5=40-59, 6=60≤.)	overall	2.839902	1.165157	1	6	N = 388768
	between		1.17114	1	6	n = 97183
	within		.283285	1.951013	3.728791	T-bar = 4.00037
Number of years after diagnosis	overall	3.588824	2.385315	1	10	N = 388768
	between		1.68763	1	10	n = 97183
	within		1.657742	-.4111758	7.588824	T-bar = 4.00037
Year	overall	2010.757	2.017688	2006	2013	N = 388768
	between		1.212977	2006	2013	n = 97183
	within		1.677159	2007.257	2014.257	T-bar = 4.00037

Table 4 shows the descriptive statistics in numbers. Mainly this table give some accurate values for the graphs and figures above. The mean of ADHD drug, outpatient, inpatient and total costs is in order 4,954 SEK 4,671 SEK, 1,737 SEK and 11,364 SEK. Also the mean annual comorbidity cost is presented, it is 1,745 SEK. The four variables ADHD visits inpatient care, ADHD visits outpatient care, comorbidity visits inpatient care and comorbidity visits outpatient care indicates the mean number of inpatient and outpatient visits for a given year for all observations in the sample. As can be seen the mean number of visits for inpatient visits are much smaller than the mean number of visits for outpatient visits both when it comes to ADHD and comorbidities. This is a quite logical finding since an inpatient procedure is more comprehensive than an outpatient procedure. In addition to the above mentioned the maximum value for some of the variables should be noted. The mean outpatient cost is higher than the mean of inpatient care cost; however, the maximum value of inpatient cost is, not surprisingly, much higher. Further it is worth noting that the maximum drug costs for comorbidities is very high compared to the mean, probably this can be explained by the fact that only a small number of individuals have comorbidities and possibly even fewer take medicals for them.

5. Empirical Methodology

In order to investigate the medical costs associated with being diagnosed with ADHD various econometric techniques will be used to account for the special structure of our data. Based on similar cost of illness studies and econometric textbooks a Two-Part Model (TPM) is primarily used, see for for example Guevara et.al (2001) and Gerdtham et.al (2009). In addition, results from a Generalized Estimating Equation (GEE) model will be presented in order to robustness test the results from the Two-Part Model. Both methods are used when the data not are independently and identically distributed[6].

5.1 The Two-Part Model

The main reason for using a Two-Part Model is that the dependant variable used, cost, is a mixed discrete-continuous variable, implying that it takes values greater or equal to zero, and that it frequently takes a value equal to zero. When having data, which is distributed with a mass point at zero a model with only one index point might have its limitations. Using, a Two-Part Model helps to account for this. The idea of the Two-Part Model is that one fit the probability of observing a positive versus zero outcome using a binary choice model, i.e. Probit or Logit. Based on personal characteristics, the probability of incurring a cost is fitted. Conditional on having a positive cost, a regression model is then used to estimate the cost. (The Stata journal, 2015). In the case of this study it is obvious that a lot of individuals will have years with zero drug cost, zero outpatient costs, zero inpatient costs, and possibly all of the three. The Two-Part Model accounts for this by permitting the zeroes and non-zeroes to be generated by different densities, which is not plausible with for example an Ordinary Least Squares regression. (The Stata journal, 2015). In equation 1 the model specification can be seen, C is the cost variable and X is a vector of independent variables. The first part of the model, a logit-model, estimate the log odds ratio of incurring a cost, depending on the independent variables (see equation 2). The second part of the specified model performs a Generalized Linear Model (GLM) estimation, i.e. a nonlinear transformation of the linear index function. This is done in order to allow for a more flexible distribution of the error terms and is commonly used when analysing the special characteristics of health care

[6] See Appendix 10.5 for distribution plots

expenditures (Jones, 2010) (see equation 3). In this case we suspect that the distribution of the cost variable also is skewed when only allowing positive costs. As can be seen in equation 3 the natural logarithm of the cost is used in the GLM regression, which is used in order to deal with the skewness of the distribution and heteroscedasticity (The Stata journal, 2015). Further a gamma distribution is assumed since it is suitable when variables with positive scale values that are skewed towards large values. Moreover, after examining the data, using the AIC and BIC[7] criterion to decide the gamma distribution is deemed to be appropriate. The dependant variables (C) is the either the ADHD associated medical costs, outpatient costs, inpatient costs, total ADHD cost or total comorbidity costs. The independent variables are the four categorical variables i.e. diagnosis, age group, gender and years since first diagnosis.

Equation 1: $E(C|X) = \Pr(C > 0|X) * E(Ln(C)|C > 0, X)$

Equation 2: $\Pr(C|X) = \frac{e^{\propto+\beta X}}{1+e^{\propto+\beta X}}$

Equation 3: $Ln(\widehat{C}) = \phi(X\hat{\beta}) * e^{X\hat{\delta}}$

We then predict yearly costs and transform the logarithmic values from the Two-Part Model, see equation 4. The same procedure is then used in order to predict the marginal impact from the independent variables.

Equation 4: $E(\hat{C}|\hat{X}) = \Pr(\hat{C} > 0|X) * E(Ln(\hat{C})|C > 0, X)$

Since all independent variables are categorical variables we treat those variables as factor variables. This makes it possible to estimate the margins for every level of the categorical variables, e.g. estimate the predicted marginal cost for both males and females, and not only be able to compare the incremental cost of being female in relation to being male. In the Two-Part Model regression output, the coefficients are, however, reported in relation to the base-level. This since the categorical variables specifies their first level as a base-level. For the diagnosis categorical variable this is undesirable since every individual do have some of the diagnosis, hence we want to keep all levels of the diagnosis variable in the model. To overcome this, we specify the diagnosis variable to be treated as if it has no base. In order for the diagnosis variable to not suffer from collinearity we also drop the constant from the

[7] See Appendix 10.6, table 16, for AIC and BIC values

regression model. This does not have any effect on the predicted marginal costs, but it enables us to observe the Two-Part Model regression results for all the different ADHD diagnoses. (Stata User's Guide, 2013) (Higbee, 2015).

5.2 Generalized estimating equations

In order to robustness check the results from the Two-Part Model a General Estimated Equation model is estimated. The General Estimated Equation model is, similarly to the Two-Part Model, commonly used in the field of health economics since it also can deal with costs that are not independently and identically distributed. The General Estimated Equation model uses a variance function which is calculated from the observed mean, i.e. instead of dealing with probabilities as the Two-Part Model, robust standard errors are derived from the observed data. The model can be specified in several different ways, it can account and adjust for clustering within sample observations, time, different correlation matrixes, different distributions and different link functions. If specifying the model correctly the model can be shown to estimate consistently. (Ballinger, 2004). In accordance to what was the case in the Two-Part Model a log link function and a gamma distribution is used. Further in an attempt to account for the longitudinal structure within groups a first order autoregressive (AR1) covariance matrix is used. In order to account for the panel structure of the data the model was specified to account for the individuals and time since diagnosis. It should be noted that since using an AR(1) structure individuals with only one observations are dropped out of the sample.

6. Results

In this part the results from the empirical estimation, i.e. the Two-Part Model will be presented. Focus will lie providing material to answer the research questions, i.e. what the direct costs of being diagnosed with ADHD is per individual, how the cost pattern evolves over time after being diagnosed and how the costs differ between different diagnoses, age groups and gender. We will also predict the incremental costs associated with having one or more comorbidities. Finally, we will specify an example of how the cost pattern develops for a male individual aged in-between 40-59 years and suffering from the most cost-driving diagnosis. In addition to the Two-Part Model predictions we also supply predictions using a Generalized Estimating Equations model as a robustness check[8].

6.1 Estimation results

6.1.1 Two-Part Model regression results

Table 5 presents the regression results from the Two-Part Model. In the first column for all dependent variables we can see the estimates from the logistic regression, which estimates the log odds ratio of incurring a positive cost based on the specified variables. The second columns provide the log coefficients from the GLM regression conditional on the value in the logistical regression. It should be noted that the GLM coefficients are difficult to interpret at this stage since they are logged.

In the nine first rows the categorical variable indicating what diagnosis an individual has received can be seen. In addition, gender, year fixed effects, age group fixed and comorbidity are used as independent categorical variables. The first year (the year of being diagnosed) after diagnosis, male in the gender variable, and the age group 0-9 years old indicates the base level for each categorical variable, and are therefore not included. The interpretation of the log-odds ratio from the categorical variables with a base level cannot directly be converted into probabilities. Instead, they are interpreted as an increased or decreased log-odds ratio in comparison to their base level. Consequently, a positive log odds ratio on the age group 40-59

[8] The GEE regression results can be found in Appendix 10.2, table 11.

years of age implies that compared to the base level, i.e. individuals aged 0-9 years, they have a higher log odds ratio and thereby probability of incurring a cost.

As can be seen in column 1 and column 2 most of the variables are highly significant regressed on drug costs. Being a female seems to increase the log odds ratio of having a drug cost compared to the base level (men), yet having a positive effect on the estimated costs conditional on actually having a cost. The log odds ratio for the age groups increases for the age group 10-19, while decreasing for the other groups. The coefficients on almost all diagnoses are positive in both column 1 and 2, implying that they have a probability over 50% of incurring a cost[9] and also have an incremental effect on the costs conditional on having a cost[10]. The only exceptions are other hyperkinetic disorders whose log odds ratio is insignificant and unspecified ADD which has a negative significant log odds ratio and therefore has a probability smaller than 50% of incurring a cost. To be noted is that compared to the base level year (year of diagnosis) the log odds ratio of incurring a cost decreases all the forthcoming years. Moreover, we can observe that having a comorbidity has a negative and significant log odds ratio on having an ADHD drug cost. In general, also the GLM estimates are significant implying that conditional on incurring a cost all the significant independent variables has a positive effect.

[9] See Appendix 10.4, table 15 for transformation of log-odds ratios to probabilities

[10] Diagnosis categorical variable has no base level

Table 5: Two-Part Model Estimation results

	1	2	3	4	5	6	7	8	9	10
VARIABLES	ADHD Drug Cost	ADHD Drug Cost	ADHD Inpatient Cost	ADHD Inpatient Cost	ADHD Outpatient Cost	ADHD Outpatient Cost	ADHD Total Cost	ADHD Total Cost	Comorbidity Total Cost	Comorbidity Total Cost
	Logistic	GLM	Logistic	GLM	Logistic	GLM	Logistic	GLM	Logistic	GLM
Distrurbance of Activity and Attention	1.068***	8.762***	-6.192***	11.14***	3.028***	9.250***	4.205***	9.604***	-2.904***	7.496***
	(0.0177)	(0.00725)	(0.154)	(0.104)	(0.0248)	(0.00697)	(0.0359)	(0.00775)	(0.0320)	(0.0555)
Deficits in Attention, Motor control, and Perception (DAMP)	0.151***	8.711***	-6.749***	11.05***	2.163***	9.102***	3.366***	9.407***	-3.055***	7.659***
	(0.0461)	(0.0264)	(0.327)	(0.213)	(0.0573)	(0.0407)	(0.0566)	(0.0344)	(0.0617)	(0.143)
Attention Deficit Hyperactivity Disorder (ADHD)	1.526***	8.811***	-5.966***	11.19***	3.459***	9.184***	4.674***	9.664***	-3.063***	7.374***
	(0.0176)	(0.00688)	(0.153)	(0.104)	(0.0248)	(0.00652)	(0.0356)	(0.00723)	(0.0319)	(0.0558)
Attention Deficit Disorder (ADD)	1.166***	8.562***	-6.645***	11.17***	3.245***	9.167***	4.312***	9.447***	-2.978***	7.147***
	(0.0216)	(0.00945)	(0.165)	(0.130)	(0.0281)	(0.00900)	(0.0383)	(0.0118)	(0.0351)	(0.0618)
ADD, unspecified type	-0.136***	8.506***	-6.801***	11.09***	2.093***	9.009***	2.969***	9.240***	-3.273***	7.224***
	(0.0302)	(0.0205)	(0.209)	(0.164)	(0.0342)	(0.0177)	(0.0434)	(0.0219)	(0.0444)	(0.0861)
Hyperkinetic Conduct Disorder	0.202***	8.771***	-5.746***	10.82***	1.847***	9.072***	3.253***	9.481***	-2.671***	7.599***
	(0.0625)	(0.0398)	(0.281)	(0.114)	(0.0839)	(0.0472)	(0.0754)	(0.0435)	(0.0814)	(0.119)
Other Hyperkinetic Disorders	-0.0108	8.740***	-6.157***	11.10***	2.132***	8.979***	3.026***	9.420***	-2.716***	7.169***
	(0.0680)	(0.0522)	(0.339)	(0.200)	(0.0840)	(0.0498)	(0.0817)	(0.0552)	(0.0808)	(0.117)
ADHD, unspecified type	1.033***	8.724***	-6.080***	11.32***	2.733***	9.210***	4.138***	9.583***	-2.730***	7.819***
	(0.0296)	(0.0161)	(0.181)	(0.185)	(0.0369)	(0.0165)	(0.0454)	(0.0252)	(0.0432)	(0.0771)
1< diagnoses	2.164***	8.804***	-4.964***	11.31***	4.459***	9.414***	5.598***	9.916***	-2.661***	7.507***
	(0.0186)	(0.00735)	(0.152)	(0.104)	(0.0256)	(0.00689)	(0.0364)	(0.00820)	(0.0324)	(0.0560)
Female	0.109***	-0.0864***	0.0158	0.0918***	0.0690***	0.0289***	0.112***	-0.0104*	0.464***	-0.173***
	(0.00775)	(0.00394)	(0.0267)	(0.0286)	(0.00846)	(0.00401)	(0.00888)	(0.00625)	(0.00892)	(0.0165)
10-19 years of age	0.103***	0.0209***	1.847***	0.105	-0.130***	-0.0864***	-0.101***	0.0371***	1.048***	0.148***
	(0.0167)	(0.00670)	(0.153)	(0.105)	(0.0193)	(0.00648)	(0.0223)	(0.00676)	(0.0321)	(0.0555)
20-29 years of age	-0.660***	0.0935***	2.735***	0.314***	-0.595***	-0.0560***	-0.796***	0.180***	1.826***	0.500***
	(0.0175)	(0.00788)	(0.154)	(0.105)	(0.0202)	(0.00750)	(0.0230)	(0.0103)	(0.0327)	(0.0554)
30-39 years of age	-0.184***	0.410***	2.759***	0.288***	-0.319***	0.0814***	-0.299***	0.376***	2.399***	0.639***
	(0.0190)	(0.00865)	(0.155)	(0.105)	(0.0217)	(0.00854)	(0.0247)	(0.0108)	(0.0333)	(0.0558)
40-59 years of age	-0.0680***	0.526***	2.556***	0.296***	-0.270***	0.0969***	-0.190***	0.410***	2.436***	0.580***
	(0.0189)	(0.00849)	(0.155)	(0.106)	(0.0214)	(0.00848)	(0.0244)	(0.0104)	(0.0331)	(0.0558)
60≤ years of age	-0.397***	0.428***	1.914***	0.296	-0.474***	0.151***	-0.542***	0.315***	2.611***	0.194**
	(0.0413)	(0.0240)	(0.229)	(0.209)	(0.0455)	(0.0299)	(0.0464)	(0.0343)	(0.0528)	(0.0761)
2nd year of diagnosis	-0.660***	0.136***	-1.120***	-0.0550	-3.159***	-0.264***	-3.323***	-0.270***	-0.354***	-0.0229
	(0.0116)	(0.00512)	(0.0366)	(0.0393)	(0.0183)	(0.00520)	(0.0290)	(0.00751)	(0.0125)	(0.0233)
3rd year of diagnosis	-1.022***	0.172***	-1.424***	-0.119***	-3.545***	-0.360***	-3.753***	-0.338***	-0.547***	-0.0809***
	(0.0121)	(0.00574)	(0.0415)	(0.0436)	(0.0189)	(0.00599)	(0.0291)	(0.00842)	(0.0139)	(0.0250)
4th year of diagnosis	-1.271***	0.184***	-1.635***	-0.0551	-3.832***	-0.412***	-4.052***	-0.374***	-0.688***	-0.0637**
	(0.0130)	(0.00643)	(0.0474)	(0.0583)	(0.0197)	(0.00689)	(0.0295)	(0.0105)	(0.0157)	(0.0276)
5th year of diagnosis	-1.483***	0.184***	-1.810***	-0.0568	-4.069***	-0.463***	-4.305***	-0.417***	-0.791***	-0.0695**
	(0.0140)	(0.00736)	(0.0550)	(0.0601)	(0.0207)	(0.00787)	(0.0300)	(0.0112)	(0.0179)	(0.0335)
6th year of diagnosis	-1.638***	0.180***	-1.846***	-0.0264	-4.228***	-0.486***	-4.468***	-0.440***	-0.854***	-0.0392
	(0.0155)	(0.00835)	(0.0616)	(0.0616)	(0.0219)	(0.00931)	(0.0307)	(0.0131)	(0.0203)	(0.0368)
7th year of diagnosis	-1.771***	0.162***	-2.019***	-0.0435	-4.399***	-0.495***	-4.629***	-0.482***	-0.890***	-0.00694
	(0.0175)	(0.00999)	(0.0771)	(0.0809)	(0.0238)	(0.0118)	(0.0318)	(0.0158)	(0.0234)	(0.0427)
8th year of diagnosis	-1.912***	0.168***	-1.918***	-0.0474	-4.534***	-0.486***	-4.787***	-0.462***	-0.888***	0.132**
	(0.0200)	(0.0118)	(0.0864)	(0.0812)	(0.0262)	(0.0141)	(0.0332)	(0.0195)	(0.0269)	(0.0576)
9th year of diagnosis	-2.057***	0.158***	-1.876***	0.104	-4.677***	-0.513***	-4.935***	-0.463***	-0.903***	0.237***
	(0.0231)	(0.0141)	(0.0974)	(0.117)	(0.0293)	(0.0189)	(0.0350)	(0.0266)	(0.0304)	(0.0714)
10th year of diagnosis	-2.129***	0.146***	-2.016***	0.0933	-4.785***	-0.504***	-5.041***	-0.475***	-0.984***	0.228***
	(0.0265)	(0.0176)	(0.116)	(0.122)	(0.0329)	(0.0204)	(0.0372)	(0.0329)	(0.0346)	(0.0769)
Comorbidity	-0.0605***	0.00362	1.142***	0.0787***	0.00921	0.171***	0.0322***	0.294***	2.288***	1.606***
	(0.0104)	(0.00584)	(0.0286)	(0.0290)	(0.0110)	(0.00614)	(0.0115)	(0.0105)	(0.0113)	(0.0170)
Observations	388,768	229,123	388,768	6,560	388,768	205,580	388,768	268,713	388,768	98,792

Robust standard errors in parentheses

*** p<0.01, ** p<0.05, * p<0.1

In column 3 and 4 the same procedure is done, yet having inpatient costs as the dependant variable. All of the diagnosis coefficients are approximately minus 6 and significant in the logistic regression, implying that the probability of incurring an inpatient cost is less than 1%. Further, there is no significant log odds ratio for being a female, while ageing is significant and higher for all groups in comparison to the base level. Furthermore, the log odds ratio of incurring an inpatient cost is decreasing as we move away from the year of being diagnosed, except during year 8 and 9. In the GLM regression we can see that most of these year variables not are significant, this can probably be explained by the small number of observations in this part of the regression. It should be noted that some of the coefficients from the GLM regression is negative, however this is a log regression implying that these coefficients will become positive values when transforming the coefficients back to real values. Regarding the comorbidity variable, it is significant and positive in both the logistic regression and the GLM, implying higher inpatient costs if suffering from a comorbidity.

Column 5 and 6 presents the same results with outpatient costs as the dependant variable. All the diagnosis categories are significant and positive in both the logistic and GLM regression, with a log-odds ratio around 2-3 implying a very high probability of incurring an outpatient cost. Being a female increases the log odds ratio of incurring an outpatient cost, while all age groups have lower log odds ratio of incurring a cost compared to the base level. In accordance with the log odds ratio of incurring drug costs, the log odds ratio of incurring an outpatient costs decreases when moving further away from the date of the diagnosis. Finally, all coefficients in the GLM regression are significant.

Column 7 and 8 provides the total estimates, meaning that all costs have been aggregated into one variable. The log-odds ratio coefficients for all diagnosis are very high and significant, indicating an almost 100 % probability of incurring a cost. Being female seem to increase the log odds ratio of incurring a cost. Furthermore, the log odds ratio decreases for all age groups in relationship to the base level. Moreover, the log odds ratio of incurring a cost seems to decrease the further away from the date of the diagnosis they get. Lastly, having a comorbidity increases the log odds ratio of having an ADHD related cost.

The results from column 9 and 10 are total cost estimates (drug cost, inpatient costs, outpatient costs) for ADHD related comorbidities. All the diagnoses have significant log-odds ratios around minus 2.5-3, which translates to a low probability of incurring a comorbidity cos. The pattern that females have a higher log odds ratio of incurring a cost are equivalent to what was the case for the direct ADHD related costs. In addition, the log odds ratio of incurring a comorbidity cost are greater for all age groups than it is for those who are 0-9 years old. Further the log odds ratio of incurring a comorbidity cost decreases the subsequent years after being diagnosed, yet, many of the year coefficients are insignificant in the GLM estimation. Finally, it should be noted that having a comorbidity obviously increases the log odds ratio of having a comorbidity cost.

In summary, most variables in the Two-Part Model estimation are significant, independently of which diagnosis, gender, age, years since diagnosis that is considered, or if the individual has a comorbidity. Still, it seems to be different sub-groups that are cost driving depending on what costs that are regarded. In general, it is difficult to interpret the coefficients from the GLM estimation at this stage since they have not been transformed back to real values. In the next section the probabilities from the Logistic regression and coefficients from GLM regression will be multiplied and transformed back from log values, making it possible to predict the sub-group costs and total costs.

6.1.2 Predicted Marginal Effects

Table 6: Predicted marginal costs

	1	2	3	4	5	6	7
	TPM	TPM	TPM	TPM	TPM	GEE	GEE
VARIABLES	ADHD Drug Cost	ADHD Inpatient Cost	ADHD Outpatient Cost	ADHD Total Cost	Comorbidity Total Cost	ADHD Total Cost	Comorbidity Total Cost
Margin	4,954***	1,738***	4,667***	11,344***	1,771***	11,123***	1,678***
	(11.42)	(32.00)	(10.26)	(36.55)	(22.08)	(53.39)	(33.74)
Observations	388,768	388,768	388,768	388,768	388,768	372,633	372,633

Standard errors in parentheses

*** p<0.01, ** p<0.05, * p<0.1

In table 6 the predicted marginal costs per year can be seen. Column 1-4, displays the overall Two-Part Model predicted marginal drug cost, inpatient cost, outpatient cost and total cost of ADHD. The results suggest that of the three cost drivers it is the drug treatment that has the highest predicted marginal cost per year, 4,954 SEK, while inpatient care has the lowest, 1,738 SEK, and outpatient a predicted marginal cost of 4,667 SEK per year. This is interesting since we know that an inpatient episode has very high costs. Although, as shown in the logistic regression, table 5 column3, the probability of being treated in inpatient care is very low. Our findings suggest that the predicted marginal total cost per year of an individual suffering from ADHD is 11,344 SEK. Column 5 shows the Two-Part Model predicted marginal cost per year of having a comorbidity and is equal to 1,771 SEK. Finally, the Generalized Estimating Equations-predictions can be observed in column 6-7[11]. The predicted marginal total ADHD cost is estimated to 11,123 SEK per year. Noteworthy, is that the Two-

[11] Only the predicted total cost per year of ADHD is shown in the Generalized Estimating Equations case, since it is only used as a robustness check.

Part Model predicted margin has a lower standard error (36.55) than the Generalized Estimating Equations predicted margins (53.39). The Generalized Estimating Equations predicted marginal comorbidity cost is lower, 1,678 SEK per year, than when using the Two-Part Model. However, as in the case of ADHD total costs, the standard error is lower when using the Two-Part Model (22.08) in comparison to the Generalized Estimating Equations (33.74).[12]

Table:7 Predicted marginal cost, per year after ADHD diagnosis

	1	2	3	4	5	6	7
	TPM	TPM	TPM	TPM	TPM	GEE	GEE
VARIABLES	ADHD Drug Cost	ADHD Inpatient Cost	ADHD Outpatient Cost	ADHD Total Cost	Comorbidity Total Cost	ADHD Total Cost	Comorbidity Total Cost
1st year of diagnosis	5,833***	4,863***	10,300***	20,167***	2,013***	23,890***	2,805***
	(22.59)	(144.2)	(31.70)	(109.0)	(33.75)	(168.6)	(115.0)
2nd year of diagnosis	5,646***	1,733***	4,523***	11,825***	1,821***	12,228***	2,219***
	(26.82)	(76.11)	(24.77)	(78.14)	(36.56)	(88.21)	(85.96)
3rd year of diagnosis	5,164***	1,268***	3,474***	9,942***	1,657***	9,724***	1,829***
	(29.61)	(64.88)	(23.43)	(76.64)	(37.00)	(79.02)	(69.50)
4th year of diagnosis	4,716***	1,120***	2,847***	8,713***	1,633***	8,285***	1,721***
	(32.26)	(74.94)	(23.27)	(86.56)	(41.39)	(84.09)	(66.84)
5th year of diagnosis	4,283***	945.3***	2,363***	7,604***	1,592***	7,129***	1,521***
	(35.49)	(69.97)	(23.38)	(85.48)	(51.22)	(82.71)	(64.80)
6th year of diagnosis	3,945***	944.6***	2,097***	6,980***	1,623***	6,378***	1,472***
	(39.07)	(74.97)	(25.32)	(96.14)	(57.87)	(89.58)	(70.33)
7th year of diagnosis	3,613***	771.7***	1,864***	6,227***	1,666***	5,608***	1,436***
	(44.48)	(81.98)	(29.14)	(108.0)	(69.01)	(100.2)	(79.72)
8th year of diagnosis	3,363***	816.9***	1,714***	5,840***	1,923***	5,152***	1,563***
	(50.86)	(91.12)	(32.70)	(120.9)	(108.8)	(113.0)	(103.5)
9th year of diagnosis	3,057***	978.4***	1,513***	5,462***	2,134***	4,648***	1,614***
	(56.94)	(146.4)	(38.39)	(169.0)	(153.8)	(133.5)	(122.8)
10th year of diagnosis	2,888***	832.4***	1,415***	5,116***	2,054***	4,248***	1,550***
	(66.55)	(136.6)	(40.61)	(190.7)	(158.3)	(156.5)	(153.0)
Observations	388,768	388,768	388,768	388,768	388,768	372,633	372,633

Standard errors in parentheses
*** $p<0.01$, ** $p<0.05$, * $p<0.1$

Since one of the aims of this thesis is to examine the cost pattern for an ADHD-diagnosed individual evolves over time, these predictions are presented in table 7. Column 1-3 displays the Two-Part Model predicted marginal cost of drug treatment, inpatient and outpatient care, while column 4 shows the total predicted marginal cost of ADHD. All predictions are significant at the one percent level. The predicted marginal total cost is decreasing through the whole period, yet the pace is diminishing. This development is also true if only observing the predicted marginal drug cost, column 1. Still the decrease is not as significant between year one and two as for the other cost drivers. Regarding column 2 and 3 there is a very high, in

[12] The GEE has fewer observations due to an AR(1) structure.

comparison to following years, predicted marginal inpatient and outpatient cost in year one. However, that might be explained by the fact that it is the year when individuals receive their diagnosis, hence every individual has been visiting outpatient and/or inpatient care in year one and therefore all individuals will have a cost. This also explains the relatively large decrease in predicted marginal cost, for both inpatient and outpatient care, between year 1 and year 2. In column 5 the Two-Part Model predicted marginal costs of comorbidities over the ten years can be observed. Year one represents the first year of receiving an ADHD diagnosis. Examining the results, we can observe that the costs vary depending on in which year after diagnosis an individual receives a comorbidity. The maximum predicted marginal cost is in year nine, 2,134 SEK.

The over time predicted ADHD costs since the year of being diagnosed estimated with the Generalized Estimating Equations model can be seen in column 6. The Generalized Estimating Equations predicts the costs to be a bit higher than the Two-Part Model predicts during the first years, while the opposite relationship can be seen during the later years. However, importantly is that the cost-pattern, i.e. decreasing costs, is the same. It should be noted that the standard errors in the Generalized Estimating Equations is greater than for the Two-Part Model the first years after diagnosis, while the opposite relationship occurs towards the end of follow up. A reason might be that the data has a more autoregressive structure further away from the index date, which the Generalized Estimating Equations model is better at accounting for than the Two-Part Model. In column 7 the Generalized Estimating Equation predictions for comorbidity costs can be seen.

Table 8: Predicted marginal costs, depending on diagnosis

	1	2	3	4	5	6	7
	TPM	TPM	TPM	TPM	TPM	GEE	GEE
VARIABLES	ADHD Drug Cost	ADHD Inpatient Cost	ADHD Outpatient Cost	ADHD Total Cost	Comorbidity Total Cost	ADHD Total Cost	Comorbidity Total Cost
Distrurbance of Activity and Attention	4,078***	932.5***	3,788***	8,796***	1,808***	8,194***	2,006***
	(18.70)	(37.44)	(17.94)	(47.68)	(29.45)	(73.01)	(81.06)
Deficits in Attention, Motor control, and Perception (DAMP)	2,352***	468.7***	2,477***	5,670***	2,016***	4,418***	1,604***
	(88.41)	(163.3)	(108.3)	(218.5)	(270.2)	(331.8)	(376.5)
Attention Deficit Hyperactivity Disorder (ADHD)	5,171***	1,244***	4,062***	10,515***	1,512***	10,178***	1,481***
	(22.24)	(48.01)	(16.30)	(56.71)	(31.84)	(84.10)	(65.89)
Attention Deficit Disorder (ADD)	3,483***	660.7***	3,764***	7,831***	1,243***	7,462***	1,232***
	(31.43)	(67.03)	(30.34)	(84.67)	(39.09)	(112.4)	(68.35)
ADD, unspecified type	1,577***	533.2***	2,223***	4,291***	1,200***	4,083***	986.3***
	(42.29)	(103.4)	(42.42)	(102.4)	(83.47)	(156.8)	(84.53)
Hyperkinetic Conduct Disorder	2,581***	1,032***	2,168***	5,909***	2,170***	4,850***	2,417***
	(141.3)	(243.6)	(117.0)	(287.5)	(240.4)	(440.4)	(779.1)
Other Hyperkinetic Disorders	2,175***	873.5***	2,157***	5,100***	1,390***	4,101***	1,588***
	(148.3)	(299.3)	(120.8)	(298.0)	(148.4)	(431.3)	(296.6)
ADHD, unspecified type	3,862***	1,284***	3,315***	8,431***	2,651***	7,874***	2,353***
	(73.07)	(234.1)	(60.41)	(213.3)	(161.2)	(284.0)	(282.3)
1< diagnosis	6,260***	3,967***	6,734***	16,407***	1,985***	17,688***	2,173***
	(22.44)	(105.7)	(23.47)	(93.93)	(33.13)	(150.9)	(83.40)
Observations	388,768	388,768	388,768	388,768	388,768	372,633	372,633

Standard errors in parentheses

*** p<0.01, ** p<0.05, * p<0.1

Knowledge concerning what types of ADHD that are the largest cost drivers, can aid decision makers, enabling them to make cost efficient policies in the future. Therefore, column 1-4 in table 8 presents the Two-Part Model predicted marginal costs depending on which diagnosis an individual has received, and if he or she has received more than one diagnosis. In column 4 we can observe the total predicted marginal ADHD treatment cost. As can be seen, an individual with more than one diagnosis has much higher cost than if he or she only has one diagnosis. If only considering the different diagnosis, one can observe that the diagnoses that have the highest predicted marginal total costs are ADHD (both regular and unspecified), ADD and Disturbance of Activity and Attention. Most interesting is that regular ADHD have a much higher predicted marginal cost than the other diagnoses, i.e. 10,515 SEK per year. This is also the case for predicted marginal drug cost, 5,171 SEK per year, and outpatient cost, 4,062 SEK per year concerning ADHD. Nevertheless, the predicted marginal inpatient cost for unspecified ADHD is the highest, 1,284 SEK per year. Concerning column 5, the Two-Part Model predictions of comorbidity costs, depending on diagnosis, are observable. Interesting to point out is that unspecified ADHD is the largest comorbidity cost driver, and having more than one diagnosis. The Generalized Estimating Equations model, column 6, predicts costs roughly similar to the Two-Part Model, foremost the cost pattern is the comparable, even though some of the predicted marginal costs differs slightly. In column 7 it can be seen that the Generalized Estimating Equations model prediction of comorbidity costs differs slightly from the predictions of the Two-Part Model. However, the standard errors are larger.

Table 9: Predicted marginal cost, depending on age group and gender

	1	2	3	4	5	6	7	8	9	10	11	12	13	14
	TPM	TPM	TPM	TPM	TPM	TPM	TPM	TPM	TPM	TPM	GEE	GEE	GEE	GEE
VARIABLES	ADHD Drug Cost	ADHD Inpatient Cost	ADHD Outpatient Cost	ADHD Total Cost	Comorbidity Total Cost	ADHD Drug Cost	ADHD Inpatient Cost	ADHD Outpatient Cost	ADHD Total Cost	Comorbidity Total Cost	ADHD Total Cost	Comorbidity Total Cost	ADHD Total Cost	Comorbidity Total Cost
0-9 years of age	4,480***	109.9***	5,105***	9,880***	400.1***						9,612***	386.3***		
	(50.58)	(20.62)	(52.98)	(111.1)	(23.81)						(96.54)	(30.03)		
10-19 years of age	4,730***	824.3***	4,537***	10,158***	892.3***						10,530***	854.1***		
	(30.63)	(42.11)	(27.74)	(80.05)	(16.35)						(63.06)	(36.02)		
20-29 years of age	3,693***	2,920***	4,165***	10,543***	1,820***						9,294***	1,668***		
	(21.83)	(96.04)	(21.63)	(94.41)	(33.37)						(109.2)	(66.77)		
30-39 years of age	6,122***	3,010***	5,193***	14,315***	2,583***						13,350***	2,575***		
	(51.60)	(148.8)	(44.08)	(166.4)	(48.24)						(196.0)	(117.1)		
40-59 years of age	6,940***	2,371***	5,264***	14,732***	2,466***						14,676***	2,859***		
	(119.1)	(268.1)	(90.59)	(333.5)	(46.74)						(204.2)	(118.4)		
60≤ years of age	5,362***	1,194***	5,113***	12,034***	1,773***						12,411***	2,528***		
	(234.5)	(417.4)	(244.2)	(685.2)	(99.91)						(681.1)	(250.5)		
Male						5,040***	1,572***	4,564***	11,187***	1,801***			11,021***	1,711***
						(14.39)	(37.86)	(12.61)	(42.56)	(27.73)			(66.80)	(67.83)
Female						4,797***	1,985***	4,857***	11,638***	1,775***			11,301***	2,081***
						(18.45)	(56.89)	(18.06)	(65.32)	(25.78)			(96.32)	(72.44)
Observations	388,768	388,768	388,768	388,768	388,768	388,768	388,768	388,768	388,768	388,768	372,633	372,633	372,633	372,633

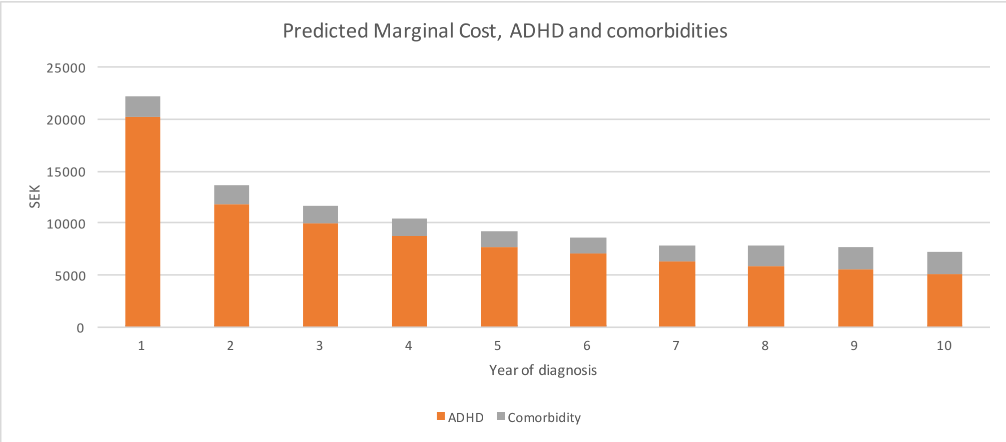
Standard errors in parentheses

*** p<0.01, ** p<0.05, * p<0.1

Table 9 shows the predicted costs depending on age and gender. Most striking in column 1, where the predicted drug cost is presented, is that individuals 40-59 years incur a lot higher cost, 6,940 SEK per year, than the other age groups. It should also be noted that the costs seem to be lowest for individuals in the age group 20-29 years, 3,693 SEK per year. In column 2 the inpatient costs are presented, the youngest group has the lowest inpatient costs and after this costs increase with each age group until we get to the two oldest groups where the development of the coefficients suddenly reverses and decrease again. The cost range goes between 109 SEK per year (0-9 years old) to 3,010 SEK per year (30-39 years old). Concerning the outpatient cost there is no pattern as evident as for the inpatient costs. The youngest age group has very high costs, 5,105 SEK per year, yet the individuals aged 40-59 years has the highest predicted average cost, 5,264 SEK per year. Similarly, to what was the case with the drug costs, the individuals between 20-29 years of age has the lowest cost, 4,165 SEK per year. In column 4 the total costs can be seen. The three older age groups have significantly higher costs than the three younger. Especially individuals aged 30-39 and 40-59 have particularly high total costs, 14, 315 and 14, 732 SEK per year. These two groups are also largest comorbidity cost bearers, see column 5.

Column 6-10 displays the predicted marginal yearly drug cost, inpatient cost, outpatient cost, total cost and comorbidity cost, conditional on being a male or female. Regarding drug costs comorbidity costs, column 6 and 10, the predicted marginal cost is higher for males than females. However, inpatient and outpatient costs are predicted to be higher for females than males. This also is the case if we examine the predicted marginal total cost in column 9, where we can see that the costs for females are higher on the total level.

Column 11-12 presents the, per age group, total predicted costs and comorbidity costs using the Generalized Estimating Equations model. The cost pattern of ADHD costs is unchanged, except for a quite lower predicted marginal cost in the Generalized Estimating Equations for individuals 20-29 years old. The predicted comorbidity cost pattern is also similar, yet the age group 40-59 years incurs the highest costs. Furthermore, column 13-14 presents the Generalized Estimating Equations predictions depending on being a male or female, as before the results are for total ADHD costs are similar to Two-Part Model estimates. In contrast, the predictions for comorbidity costs in the Generalized Estimating Equations model is reversed, i.e. females bear the highest cost. Nevertheless, as before, the standard errors in the Generalized Estimating Equations model predictions are larger.



Graph 10: Total predicted marginal ADHD and comorbidity cost (TPM)

Graph 10 above presents the Two-Part Model predicted marginal cost of ADHD and comorbidities stacked over time. Evidently, the ADHD related costs decreases over time while the comorbidity costs increase during the last years of the ten-year period. This leads to that the predicted cost of ADHD flattens out, if the individual has a comorbidity.

Table 10: Predicted margins for a male in the age group 40-59 yea

	1	2	3
	ADHD	>1 diagnosis	Comorbidity
1st year of diagnosis	23,130***	37,634***	15,472***
	(829.8)	(1,617)	(1,339)
2nd year of diagnosis	13,447***	27,250***	11,741***
	(604.6)	(1,220)	(1,260)
3rd year of diagnosis	12,155***	21,737***	10,730***
	(591.7)	(779.4)	(1,163)
4th year of diagnosis	11,042***	21,000***	8,777***
	(701.3)	(999.3)	(762.7)
5th year of diagnosis	9,790***	18,972***	10,495***
	(859.5)	(1,029)	(1,467)
Observations	6,841	8,766	6,791

Standard errors in parentheses

*** p<0.01, ** p<0.05, * p<0.1

Finally, as an experiment and an attempt to illustrate how the findings above can be combined into comparing a two specific cases, a prediction of the costs for a male aged 40-59 years is presented in table 10. The reason for choosing this age group is that the results suggest that this the age group that incur the highest costs. The gender male is chosen due to the fact that they represent 67% of the sample. We choose to compare the diagnosis which is the largest cost driver, i.e. regular ADHD, with if the individual suffers from more than one diagnosis during five years after being diagnosed. Strikingly is that the costs for if the individual has more than one diagnosis is very high, see column 2. For the first four years the years the cost is larger than 20,000 SEK. It can also be seen that the cost of being diagnosed with regular ADHD, column 1, for a male aged 40-59 years is higher for the four first years after being diagnosed than what the predicted marginal cost is, see table 8, column 4, row 3. Moreover, column 3 provides the comorbidity costs for the individual, yet considering all ADHD diagnoses. The reason for including all diagnoses is that the number of observations would have been too low if only regarding one specific diagnosis. Compared to the results in table 7, column 5, the costs for a male aged 40-59 years are many times larger than the average.

In summary, the predictions exhibit some interesting patterns. Firstly, it could be observed that costs decrease over time. Secondly, the deviations in costs depending on diagnosis are quite large. Thirdly, some age groups tend to incur significantly higher mean costs than others. Fourthly, the incremental costs for individuals with a comorbidity is substantially higher than if not having one. Finally, a male aged 40-59 years diagnosed with either regular ADHD or more than one diagnosis incur a lot higher costs than the average. Regarding the robustness of the results, we can see that over time, the cost pattern is in general the same using both models. Nevertheless, the standard errors of the predicted margins are in general lower using the Two-Part Model estimation. Due to the fact that the two model predictions are similar, and that the standard errors are smaller in the Two-Part Model, our further discussion will focus on the predictions from the Two-Part Model.

7. Discussion

In this part the results from the predictions will be discussed in more detail and compared to the previous studies presented in section 3[13]. Furthermore, we will provide answers to our research questions, highlight the importance of our findings, and discuss how the results can be applied. Finally, some limitations of the study and how they might affect the results will also be discussed.

7.1 Result comparisons

In accordance with most studies we find substantial cost increases for individuals with an ADHD diagnosis. Since none of the studies reviewed estimates the cost for the population as a whole it is somewhat difficult to directly compare our results with those. Additionally, some of these studies only investigate inpatient and outpatient costs or the cost from drug use, implying that we ought to expect costs that are higher. However, due to the two facts that we have divided the costs into inpatient, outpatient and drug costs, and into different sub-groups some comparison will be possible. For example, De Ridder & De Graeve (2006) investigates the incremental medical costs for children with an ADHD diagnosis compared to a sibling, in Belgium. They find that the ADHD diagnosed sibling incurs 5,000 SEK higher costs. This is comparable to the results in table 9 in which we can see that the ADHD related drug costs for children aged 0-9 years is 4,480 SEK and for children aged 10-19 years 4,730 SEK in this thesis. Hence, the results in a Belgium setting are similar to ours in Sweden. Swensen et.al. (2003) who examine the direct costs from ADHD for children 0-18 years old find that the average direct cost for these children are 15,378 SEK compared to 5,286 SEK for the matched control. In order to make their findings comparable to ours, we must assume that 5,286 SEK is an average cost that is non-ADHD related and assume that the incremental part of the cost is related to ADHD, i.e. 10,092 SEK[14]. The incremental costs can then be compared with our predictions in table 9. The estimated total ADHD costs from our estimation is 9,880 SEK, for children 0-9 years, and 10,158 SEK, for children/adolescents 10-19 years, implying that the predicted results from this paper is in line with theirs.

[13] All prices in the previous studies have been converted to Swedish SEK 2016 years' prices (Ekonomifakta, 2016) (SCB A, 2016)
[14] 15,378-5286 = 10,092 SEK

Results similar to Swensen et.al is found by Ray et.al (2006). Ray et.al. estimate the incremental costs of being diagnosed with ADHD to be 10,332 SEK the first year after diagnosis, and 8,091 SEK two years after being diagnosed. This is the same pattern as is found in this thesis, however our estimated costs are higher, 20,167 SEK during the first year and 11,825 SEK the second year after diagnosis. An explanation for the different results in this paper compared to Ray et.al. might be that they do not consider patient out of pocket costs. However, in our thesis both public expenses and patient out of pocket costs are considered. Moreover, Braun et.al. (2013) find that the incremental reimbursements for an ADHD diagnosed individual, from an insurance perspective, is on average 24,783 SEK per patient and 3,066 SEK for pharmaceuticals. An explanation for the costs in their paper being much higher than the costs found in this thesis could be that not all costs are directly related to ADHD in contrast to what is the case in this thesis. For example, costs related to comorbidities and non-ADHD related costs for inpatient and outpatient episodes could be a part of the reimbursement, and so can indirect costs. None of which are included in our thesis. Nevertheless, in accordance to the findings in our study, they find that inpatient and outpatient costs as well as drug costs increase with age.

Secnik et.al. (2005), find large incremental costs for individuals with ADHD and at least one comorbidity. For outpatient care, inpatient care and ADHD related drug prescription the incremental costs are in order, 12,669 SEK, 5,908 SEK and 5,655 SEK, and the predicted total cost is 24,192 SEK. This can, however, not be compared to the results in table 6 where the marginal cost in our paper is presented. There is one main reason for this, Secnik et.al. only observe individuals at one point in time, the year of ADHD diagnosis. This implies that their results should be compared to the results in the first row of table 7, where the predicted costs at the year of diagnosis can be observed. Since Secnik et.al. also consider comorbidity costs, the predicted cost of those should be included for an applicable comparison. The predicted cost in our thesis is 20,167 SEK for ADHD in the year of diagnosis and 2,013 SEK for comorbidities. This adds up to 22,180 SEK, consequently the results in this thesis are almost equivalent.

Guevara et.al. (2001) predict the incremental cost of having an ADHD diagnosis for children aged 3-17 years, compared to the costs of a non ADHD cohort, to be 3,540 SEK. This is lower than the predicted cost in this thesis. If additionally to ADHD, an individual has mental health disorder, i.e. a comorbidity, they predict the incremental cost to be 7,665 SEK. Thus, the incremental cost of comorbidities is 4,125 SEK[15]. In comparison, the results in our thesis suggests that the incremental cost of comorbidities are considerably lower for the corresponding age groups, 400 SEK for children 0-9 years and 892 SEK for children 10-19 years old. There are several reasons for why the results differ, both concerning ADHD and comorbidity costs. First of all, the non-ADHD diagnosed cohort in the paper by Guevara et.al. consist of individuals that have had a hospital visit for other reasons. This implies that the health costs of these individuals are not representative for the whole population. Secondly, the data used in the study by Guevara et.al. is cross-sectional data from 1997, while we use panel data from 2006-2013. Thirdly, Guevara et.al. includes a larger number of mental disorders as comorbidities than in this paper. Finally, Guevara et.al. have a slightly different inclusion criterion than is the case in our thesis. Guevara et.al. include individuals either diagnosed with ADHD or a drug prescription for ADHD stimulants, while we only include individuals that have been diagnosed with ADHD.

Overall the results from our thesis show that the direct costs of an ADHD diagnosis in Sweden are somewhat similar to what has been found in other countries and during other time periods. The advantage with this thesis is, most importantly, that it is based on four linked registers enabling all ADHD diagnosed individuals in Sweden between 2006-2013 to be examined. This implies that the study population is greater and more representative than in all other studies, which cannot be emphasised enough. This also entails that the predictions in this study are more accurate. More time periods and age groups are included than in most other studies enabling us to observe the cost pattern, both over time and subgroups. This enables further predictions of future prevalence and costs to be more applicable. It should also be noted that most other studies use a control group in order to estimate the incremental ADHD cost, while this is not the case in this study, instead costs that are strictly related to ADHD are the only ones being evaluated.

7.2 Answering the research questions

The main purpose of this paper is to investigate and estimate the average direct costs that are related to being diagnosed with ADHD. It is also of interest to explore how the costs pattern develops over time since the year of diagnosis since this could help setting appropriate policy.

[15] 7,665-3,530 = 4,125 SEK

For example, knowing that costs tend to peak during the first year after diagnosis could open up for more extensive research concerning why the costs are greatest at this point and in the extension lead to policies that can reduce costs in the future. Due to the same reason it is also of interest to identify what type of ADHD diagnosis, which age groups and whether males or females are the biggest cost drivers. In an attempt to also investigate some of the indirect costs related to ADHD, also comorbidity costs associated with ADHD is examined. Knowledge concerning the ADHD related costs are vital and one of the cornerstones in order to be able to estimate a cost effectiveness analysis, health economic simulation models and the cost of illness, see section 2. The results from this paper can serve as an input in all these models. This will make it possible to determine the degree of morbidity and the long-term costs associated with ADHD. We therefore believe that the results in the extension can guide policy into more efficient resource allocation and enlighten where there are potential for cost savings.

The predicted average cost per year from being diagnosed with ADHD can be seen in table 6, for drug prescriptions it is 4,954 SEK, inpatient care 1,738 SEK and outpatient care 4,667 SEK, while the total predicted average cost is 11,344 SEK per. Moreover, the total societal cost from ADHD can be seen in graph 5, evidently the costs has increased drastically over time, and it is approximately 1 billion SEK in year 2013. This can be compared to the findings by Le et al. (2013) who estimate that the total societal cost for a country with 16 million inhabitants is approximately 1 billion Euro, nevertheless they account for indirect costs as well, which partly can explain the difference along with that Sweden has a smaller population. These are costs that further stress the importance of intervention or at least more comprehensive research.

How the costs differ depending on what type of diagnosis an individual has can be viewed in table 8. By observing the total predicted marginal cost per year, there are four diagnoses that tend to incur higher costs than the others. These are ADHD diagnosis, 10,515 SEK, disturbance of activity and attention, 8,796 SEK, unspecified ADHD, 8,431 SEK, and ADD, 7,831 SEK. Furthermore, the predicted marginal cost if suffering from more than one diagnosis is considerably larger, 16,407 SEK. In contrast, individuals diagnosed with for example unspecified ADD, incur costs only half of the amount, 4291 SEK, compared to individuals diagnosed with the four diagnoses mentioned above. Observing graph 9, see section 4.4, the distribution of different diagnosis can be found. The conclusion from observing the graph is that three of the four most common diagnoses, ADHD (26.67 %), Disturbance of Activity and Attention (30.35 %) and ADD (6.86 %), also bear the largest costs. Furthermore, 30.64 % of the individuals have sometime during the study period more than one diagnosis. Accordingly, researchers should aim at investigating why this is, and policymakers should focus on mitigating the costs from individuals suffering from these diagnoses.

In table 7 it can be seen that the costs peak at the year of diagnosis and then steadily decreases for the entire period. However, the standard errors increase after year seven, making these predictions less reliable. It should be noted that most of the individuals in the dataset do not have observations for years 7-10, which explain the higher standard errors. Further it should be stated that the predicted cost in year one is a lot higher than for the subsequent years, particularly on behalf of inpatient and outpatient costs. Most certainly, this is due to the fact that all individuals have an inpatient or outpatient episode in year one since that is the year the receive a diagnosis. Thus, the probability of incurring either an inpatient or outpatient cost larger than zero will be equal to one in year one. It should be highlighted that he predicted drug costs does also decrease between year one and two, but not as steep as the inpatient and outpatient costs. This implies that drug treatment is a more constant cost driver, and more likely to occur during the subsequent years in relation to outpatient and inpatient care episodes.

The predicted costs depending on age, see table 9, reveals that individuals aged 40-59 years, which represent around 13% of the sample, see graph 3 in section 4.4, incur the highest costs. Above all, their drug costs are significantly higher than for other age groups. This is noteworthy since many of the previous studies tend to focus on children and adolescents. Our findings emphasize that also the adult population is a large cost bearer in the context of ADHD, and that it is something that seem to have been overlooked previously. Concerning female and male direct costs they are approximately the same. Males have slightly higher drug costs while females have somewhat higher outpatient and inpatient costs. This implies that there is no reason on only focusing future investigations on only one gender. On the contrary, men are more likely of receiving an ADHD diagnosis, see distribution in graph 1, implying that men bear a greater societal cost.

Regarding the incremental cost of comorbidities our results suggests that the cost decreases during the first six years after ADHD diagnosis, and thereafter start to increase. It should also be noted that the combined cost of both ADHD and comorbidities decreases throughout the entire period, see graph 10. Yet, the increasing cost of comorbidities towards the end of the follow up period makes the combined cost to not decrease in the same manner as when only reporting the ADHD related costs. As a consequence of this, it is evident that also investigating the comorbidities related to ADHD is of importance since it is a contributing factor to the associated costs. Not investigating comorbidities can for example lead Cost-Effectiveness Analysis models to be miscalculated.

As an experiment, in order to illustrate a more specific case, we combine the most significant cost drivers for a male individual, i.e. being 40-59 years old and suffering from regular ADHD or more than one diagnosis, during the first five years after diagnosis. The costs incurred, see table 10, are considerably higher than the suggested average costs for the whole population over the first five years. The same relationship can be seen considering the comorbidity cost for the specific individual examined. Hence, the importance of investigating the cost patterns for different sub-groups is once again highlighted.

The results mentioned above should be translated into areas where policy interventions are of great importance. These interventions should be based on simulation models and cost-effectiveness analysis. In conclusion it can be said that the predicted marginal costs of having an ADHD diagnosis is 11,344 SEK per year and individual. Considering the large number of people with ADHD in Sweden, see graph 1, this is a large societal cost that if possible should be reduced. Further, it is the first years after being diagnosed that individuals bear the highest costs. As described there are some sub-groups that incur a larger part of these costs. These are individuals diagnosed with Disturbance of Activity and Attention, ADHD (both regular and unspecified) or with more than one diagnosis and individuals in the age group 40-59 years old. As a consequence, when policy is set, these are the individuals one primarily should target in order to reduce the costs the society has to bear due to ADHD.

7.3 Limitations

There are some limitations that should be considered. First of all, the data contains no information about patients that are lost to follow-up due to emigration. However, the impact of this is probably to be small since the amount of affected individuals is about 0.5 % of the overall population per year during the period (SCB B, 2015). Furthermore, the data set does not contain diagnosis of ADHD in primary care. This leads to that some individuals suffering from ADHD will not be identified in case of not having a diagnosis at an inpatient or outpatient contact. Also, patients might therefore have had ADHD treatment in primary care when they are diagnosed at an inpatient or outpatient contact.

Moreover, there is the risk of omitted variable bias, i.e. some important variable affecting the cost of ADHD is not included in the model leading to over- or underestimations of the included independent variables. Variables that arguably could be included in the model are for example socioeconomic-related factors, such as education as in the paper by Doshi et.al. (2012), or income. However, the dataset used in this thesis is based on the Swedish national registers and therefore there is no possibility to include such factors. Hence, there is a risk for estimates in the regression models to be biased. Further, it should also be considered that individuals might not have problems due to ADHD during the whole time period. It could be argued that these individuals then should be picked out from the dataset. Although no register indicating this is available and on top of this it can be argued that less severe symptoms comes as a reaction to treatment. Thereby not changing the fact that the individual has a diagnosis. Finally, the fact that most individuals have a mean follow up period of 3.59 years implies that the number of observations when the time since diagnosis increases will be less accurate.

8. Conclusion

Attention Deficit Hyperactivity Disorder is today one of the most common neurobehavioral problems. In the U.S. the area is quite well explored, however, the number of studies in a European setting is limited. Yet, the economic and social burden is believed to be substantial. In Sweden no study has, to our knowledge, been conducted on the direct costs associated with ADHD. Therefore, the aim of this thesis is to examine the direct treatment costs of ADHD in Sweden, and the indirect costs associated with comorbidities. Furthermore, we examine how the cost pattern evolves over time after being diagnosed, how the costs differ depending on age and gender, and lastly which type of ADHD diagnosis that induces the highest cost.

In order to perform the analysis longitudinal panel dataset between 2006-2013 based on four linked registers of the total Swedish population diagnosed with ADHD were used. The registers, which were supplied by the National Board of Health and Welfare, most importantly contained data on inpatient and outpatient visits, and drug prescriptions costs. Moreover, costs associated with inpatient and outpatient care were collected from the Swedish Association of Local Authorities and Regions. A Two-Part Model, along with a GEE-model was used to carry through the analysis.

Our main results suggest that the predicted marginal cost of treatment for an ADHD diagnosed individual is 11,344 SEK per year, and that drug treatment is the largest cost driver. Over a ten-year period after diagnosis there is a decreasing cost pattern, especially from year one to year two. Furthermore, individuals diagnosed with more than one ADHD diagnosis and aged between 40-59 years incur the highest costs. Finally, the marginal incremental cost of having a comorbidity is 1,771 SEK per year.

These estimates could aid future economic evaluations and health economic modelling regarding the economic impact of ADHD. They are important determinants in for example cost-effectiveness analysis and economic simulation models, which are some of the most common policy tool for determining interventions regarding health policies. Hence, the results are therefore mainly of interest to policy makers and health economic researchers since they in the extension can develop policies in order to increase efficiency and reduce costs. The results imply that there are large costs associated with being diagnosed with ADHD, and that further research and policy interventions are important in order to increase efficiency. Further research should aim at investigating the indirect costs, in terms of social loss. This would enable more comprehensive cost-effectiveness analysis and cost-of-illness studies. In addition, productivity gains from treating individuals diagnosed with ADHD should be examined, making it possible to evaluate the net-benefit of different treatments.

9. Reference list

Ament, A, & Evers, S. (1993). Cost of illness studies in health care: a comparison of two cases. *Health Policy*, *26(1): 29-42.*

Ballinger, G.A. 2004. Using Generalized Estimating Equations for Longitudinal Data Analysis. *Organizational Research Methods, 7(2): 127-150*

Belotti, F, Deb, P, Manning, W.G, Norton, E. C. 2015. twopm: Two-Part Models. *The Stata Journal, 15(1): 3–20*

Brownell M, Chartier M, Santos R, Ekuma O, Au W, Sarkar J, MacWilliam L, Burland E, Koseva I, Guenette W. 2012. How are Manitoba's Children Doing?. Winniepeg, MB: Manitoba Centre for Health Policy, 2012.

Braun, S, Zeidler, J, Linder, R, Engel, S, Verheyen, F Greiner, W. 2013. Treatment cost of attention deficit hyperactivity disorder in Germany. *European Journal of Health Economics, 14(6): 939-945*

Brent, R. 2014. *Cost-Benefit Analysis and Health Care Evaluations.* (2. ed.). [Electronic resource] Edward Elgar.

Burd, L, Klug, MG, Coumbe, MJ, Kerbeshian, J. 2003. Children and adolescents with attention deficit-hyperactivity disorder: 1. Prevalence and cost of care. *Journal of Child Neurol, 18(8):555-61.*

Byford, S. & Raftery, J. 1998. Perspectives in economic evaluation. *British Medical Journal*, *316(7143), 1529-30.*

Byford S., Torgerson D.J., Raftery J. 2000. Cost of illness studies. *British Medical Journal 2000; 320:1335.*

Clarberg A. 2015: "ADHD hos vuxna". Report from Netdoktorpro.se. Available at: http://www.netdoktorpro.se/psykiatri/medicinska-oversikter/adhd-hos-vuxna_0/ (2015-05-21)

Consumer Health Choices, 2012. "Evaluation Prescription Drugs Used to Treat: Attention Deficit Hyperactivity Disorder (ADHD)". Report by *Consumer Health Choices.* Available at: http://consumerhealthchoices.org/wp-content/uploads/2012/08/BBD-ADHD-Full.pdf (2016-05-25)

De Ridder, A De Graeve, D. 2006. Healthcare Use, Social Burden and Costs of Children With and Without ADHD in Flanders, Belgium. *Clinical drug investigation, 26(2):75-90*

Doshi, J, Hodkins, P, Kahle, J, Sikirica, V, Cangelosi, M, Setyawan, J, Erder, H, Neumann, P. (2012). Economic Impact of Childhood and Adult Attention-Deficit/Hyperactivity Disorder in the United States. *Journal of the American Academy of Child & Adolescent Psychiatry,* 51(10): 990–1002.

Drummond, MF., Sculpher, MJ., Torrance, GW., O'Brien, BJ., & Stoddart, GL. (2005). Methods for the Economic Evaluation of Health Care Programmes (3. uppl.). New York: Oxford University Press.

Ekonomifakta, 2016. "Växelkursutveckling". Available at: http://www.ekonomifakta.se/Fakta/Ekonomi/Finansiell-utveckling/Vaxelkursutveckling/ (2016-05-21)

Gerdtham, U.G, Clarke, P, Hayes, A, Gudbjornsdottir, S. 2009. Estimating the Cost of Diabetes Melitus-Related Events from Inpatients Admissions in Sweden Using Administrative Hospitalization Data, *Pharmaeconimics, 27(1):81-90.*

Ginsberg, Y., Hirvikoski, T., & Lindefors, N. (2010). Attention Deficit Hyperactivity Disorder (ADHD) among longer-term prison inmates is a prevalent, persistent and disabling disorder. *British Medical Journal Psychiatry*. 2010; 10:112.

Guevara, J, Lozano, P, Wickizer, T, Mell, L, Gephart, H. 2001. Utilization and Cost of Health Care for Children with Attention-deficit/Hyperactivity Disorder. *Pediatrics,* 108(1): 71-78.

Higbee K. 2015. "How do I keep all levels of my categorical variable in my model?" *StataCorp.* Available at: http://www.stata.com/support/faqs/statistics/keep-all-levels-of-variable/ (2016-05-21)

Hjärnfonden 2015. "Vad är ADHD och ADD?". Available at: http://www.hjarnfonden.se/om-hjarnan/diagnoser/adhd/?gclid=CJrCiPzW48wCFasMcwodOR8NCQ (2016-05-21)

Jones, A.M. 2010. Models for Health Care. *Working paper*, available at:https://www.york.ac.uk/media/economics/documents/herc/wp/10_01.pdf

Le, H, Hodgkins, P, Postma, M, Kahle, J, Sikirica, V, Setyawan, J, Haim, M, Doshi, J. 2014. Economic impact of childhood/adolescent ADHD in a European setting: the Netherlands as a reference case. *Eur Child Adolesc Psychiatry.; 23(7): 587–598.*

Lichtenstein, P., Halldner, L., Zetterrqvist, J., Sjolander, A., Serlachius, E., Fazel, S., Långström, N., Larsson, H. 2012. Medication for attention deficit-hyperactivity disorder and criminality. *The New England Journal of Medicine.* 2012; 367(21): 2006-2014.

Läkemedelsverket. 2016. "Läkemedel vid adhd - behandlingsrekommendation". Report by *The Medical Products Agency - Sweden.* Available at: https://lakemedelsverket.se/upload/halso-och-sjukvard/behandlingsrekommendationer/Lakemedel_%20vid_adhd_behandlingsrekommendation.pdf (2016-05-21)

Marshall, D. A, Burgos-Liz, L, Ijzerman, J. M, Osgood, D. N, Padula, V. W, Higashi, K. M, Wong, K. P, Pasupathy, S. K, Crown, W. 2015. Applying Dynamic Simulation Modeling Methods in Health Care Delivery Research – The SIMULATE Checklist: Report of the ISPOR Simulation Modeling Emerging Good Practices Task Force. *Value in Health*, 18(1): 5-16

NEPI 2012. "Läkemedel vid ADHD m.m. i Sverige 2006-2011". Report by *Stiftelsen Nätverk för läkemedelsepidemiologi.* Available at: http://www.nepi.net/res/dokument/NEPI-rapport-ADHD-slutlig-220dpi.pdf (2016-05-21)

Ray, GT, Levine, P, Croen, LA, Bokhari, FA, Hu, TW, Habel, LA. 2006. Attention-deficit/hyperactivity disorder in children: excess costs before and after initial diagnosis and treatment cost differences by ethnicity. *Archives of Pediatrics and Adolescents Medicine,* 160(10):1063-1069

Saramago, P, Manca, A, Sutton J. A. 2012. Deriving Input Parameters for Cost-Effectiveness Modelling: Taxonomy of Data Types and Approaches to Their Statistical Synthesis. *Value in Health, 15(): 639-649*

SCB A 2016. "Prisomräknaren". Supplied by *Statistics Sweden.* Available at: http://www.sverigeisiffror.scb.se/hitta-statistik/sverige-i-siffror/prisomraknaren/ (2016-05-21)

SCB B 2015. "FRÅN MASSUTVANDRING TILL REKORDINVANDRING". Supplied by *Statistics Sweden.* Available at: http://www.sverigeisiffror.scb.se/hitta-statistik/sverige-i-siffror/manniskorna-i-sverige/in-och-utvandring/#8e548002-18b4-4923-b98d-24ed6045e6bb (2016-05-25)

Secnik, K, Swensen, A, Lage, MJ. 2005. Comorbidities and costs of adult patients diagnosed with attention-deficit hyperactivity disorder. *Pharmaeconomics*, 23(1):93-102.

Sharma A. & Couture J., 2014. A Review of the Pathophysiology, Etiology, and Treatment of Attention-Deficit Hyperactivity Disorder (ADHD). *Annals of Pharmacotherapy* 2014, Vol. 48(2): 209–225.

SKL A. 2015. Cost per Patient Database. Supplied by: *Swedish Association of Local Authorities and Regions.* Available at: https://stat.skl.se/kpp/index.htm (2016-05-21)

SKL B. 2015. “Medverkande sjukhus”. Supplied by *Swedish Association of Local Authorities and Regions.* Avaialble at: http://skl.se/ekonomijuridikstatistik/statistik/kostnadperpatientkpp/databaskpp/medverkandesjukhus.1056.html (2016-05-21)

Socialstyrelsen A. 2002. “ADHD hos barn och vuxna”. Report by The National Board of Health and Welfare. Available at: http://www.socialstyrelsen.se/lists/artikelkatalog/attachments/10942/2002-110-16_200211017.pdf (2016-05-21)

Socialstyrelsen B. 2015. “Läkemdelsbehandling av adhd hos barn och vuxna”. Report by *The National Board of Health and Welfare*. Available at: http://www.socialstyrelsen.se/Lists/Artikelkatalog/Attachments/19805/2015-4-14.pdf (2016-05-21).

Socialstyrelsen C (2016). ICD-10 Codes. Available at: http://www.socialstyrelsen.se/SiteCollectionDocuments/fordj2016.pdf (2016-05-22)

Socialstyrelsen D (1987). ICD-9 Codes. Available at: http://www.socialstyrelsen.se/klassificeringochkoder/Documents/KLASS87.pdf (2016-05-22)

Stata User’s Guide. 2013. “Working with categorical data and factor variables”. *Stata Press*. Chapter 25: 451-368. Avialable at: http://www.stata.com/manuals13/u.pdf (2016-05-25.

Swensen, A, Birnbaum, H, Claxtton, A, Greenberg, P, Marynchenko, M, Secnik, K. (2003). Attention-Defecit/Hyperactivity Disorder: Increased Costs for Patients and Their Families. *Journal of the American Academy of Child & Adolescent Psychiatry*, 42(12): 1415-1423

UCLA 2016. “FAQ: How do I interpret odds ratios in logistic regression?”. *UCLA: Statistical Consulting Group.* Available at: http://www.ats.ucla.edu/stat/mult_pkg/faq/general/odds_ratio.htm (2016-05-22)

Valderas, J.M., Starfield B., *Sibbald* B., Salisbury C., Roland M. 2009. *Annals of Family Medicine.* 2009 July: 7(4): 357-363.

Vårdguiden. 2013. “Adhd”. Available at: http://www.1177.se/Skane/Fakta-och-rad/Sjukdomar/Adhd/ (2016-05-21)

10. Appendix

10.1 Background of ADHD

To provide the readers with some background of how ADHD has developed and affects individuals this section gives a brief presentation of the main characteristics of ADHD, the treatment patterns, and the main implication and comorbidities of the disorder.

10.1.1 Attention Deficit Hyperactivity Disorder

ADHD is one of the most common neurobehavioral problems among both children and adults. The most common characteristics of the condition are lack of attention, ability to concentrate, over activity and impulsivity. Up until the 1980's it was called Minimal Brain Damage (MBD) and researchers believed that it disappeared when individuals came into adulthood. However, today it has been shown that ADHD is a lifelong condition, which limits individuals in terms of e.g. difficulties with social interactions and constrained ability to learn. Under childhood, non-diagnosed individuals might have a well functioning and structured environment, but when for example moving out, beginning a higher education and/or their first work the difficulties might be more problematic. (Clarberg, 2015). Still, to what extent it limits individuals differs, some people are only partly limited by the condition, while others may have to depend on others for their entire life. (Socialstyrelsen A, 2002).

ADHD is mainly developed due to that the brain neurotransmitters, primarily dopamine and norepinephrine, do not work efficient. Dopamine increases individuals' ability of perception and concentration, while norepinephrine regulates e.g. behavioural and cognitive functions. Furthermore, research has shown that ADHD is hereditary, especially since the condition can be developed by a lack of structure and a high degree of stress. Children, who has one or two parents suffering from ADHD has a higher risk of being raised in a dysfunctional environment, and thus they have a higher risk of developing ADHD. (Clarberg, 2015). This makes it even more important to be able to treat the condition in an early age, but at the same time the condition is very difficult to diagnose. In many cases individuals might have concentration difficulties or similar but not to the degree that an ADHD diagnosis can be made. So far no clear diagnostic marker exists, making it difficult to make sure individuals are getting the proper treatment. In Sweden there are two different guidelines that should be followed by physicians, the first is the American Diagnostic and Statistical Manual of Mental Disorder (DSM) or the manual from WHO, International Classification of Diseases, tenth edition (ICD-10). In order for an individual to be diagnosed a number of criteria concerning attention difficulties, hyperactivity and impulsivity must be met. (Socialstyrelsen A, 2002).

For some individuals, psychological interventions and behavioural therapy is enough to treat the issues that follows an ADHD-diagnosis. However, in many cases there is an additional need of pharmacological treatment as well in order to treat the main symptoms of ADHD. (Socialstyrelsen B, 2015). The drugs used to treat ADHD are central nervous system stimulant medication which affect the levels of dopamine and norepinephrine in the brain. This leads to better concentration levels and a lower impulsive behaviour. (Vårdguiden, 2013). In Sweden, methylphenidate is the most common pharmaceutical substances used to treat ADHD and both the prevalence and incidence has had a substantial increase since 2006. (Läkemdelsverket, 2016). Other pharmaceutical substances used for treatment of ADHD are amfethamine, dexamfetamine, lisdexamfetamine and atomoxetine, and are all centrally acting sympathomimetic substances, belonging to the ATC-group *N06BA*.

10.1.2 Comorbidities and other impacts

With ADHD there is a risk of developing comorbidities with other psychological conditions, also the risk of ending up in criminality or drug abuse is also higher (Clarberg, 2015). For example, studies among long term convicted interns, and interns convicted for violent and sexual assault, in Swedish prisons show that around 40 %meet the criteria for an ADHD diagnosis (Ginsberg et.al. 2010). However, if an individual is undergoing drug treatment there is a 32 %lower risk of committing a crime, in relationship to when not taking any medicine (Lichtenstein et. al. 2012). The main reason for that individuals suffering from ADHD ends up in criminality is the high presence of spite behaviour and conductive disorder in the childhood which, if enduring to adulthood, develops to antisocial personality disorder which increases the risk for aggressive traffic behaviour, crime etc. (Clarberg, 2015).

As mentioned, comorbidities that are commonly related to ADHD are depressive conditions, such as emotional instability, mainly caused by not being able to handle a stressful environment. Furthermore, anxiety and borderline personality disorder is common among ADHD-diagnosed individuals, however it is difficult to make a distinction between the two conditions since they have very similar criterias. (Clarberg, 2015).

10.2 GEE estimation results

Table 11: GEE estimation results

	1	2
	GEE	GEE
VARIABLES	Total ADHD Costs	Total Comorbidity Costs
10-19 years of age	0.0912***	0.793***
	(0.0101)	(0.0682)
20-29 years of age	-0.0336**	1.463***
	(0.0152)	(0.0744)
30-39 years of age	0.328***	1.897***
	(0.0179)	(0.0801)
40-59 years of age	0.423***	2.002***
	(0.0175)	(0.0779)
60≤ years of age	0.256***	1.879***
	(0.0562)	(0.119)
Distrurbance of Activity and Attention	9.534***	4.942***
	(0.0120)	(0.0676)
Deficits in Attention, Motor control, and Perception (DAMP)	8.916***	4.718***
	(0.0755)	(0.237)
Attention Deficit Hyperactivity Disorder (ADHD)	9.750***	4.638***
	(0.0114)	(0.0689)
Attention Deficit Disorder (ADD)	9.440***	4.454***
	(0.0179)	(0.0782)
ADD, unspecified type	8.837***	4.232***
	(0.0387)	(0.0957)
Hyperkinetic Conduct Disorder	9.009***	5.128***
	(0.0911)	(0.326)
Other Hyperkinetic Disorders	8.841***	4.708***
	(0.105)	(0.192)
ADHD, unspecified type	9.494***	5.101***
	(0.0362)	(0.128)
1< diagnosis	10.30***	5.021***
	(0.0125)	(0.0691)
Female	0.0251**	0.196***
	(0.0108)	(0.0321)
2nd year after diagnosis	-0.670***	-0.234***
	(0.00735)	(0.0184)
3rd year after diagnosis	-0.899***	-0.428***
	(0.00920)	(0.0249)
4th year after diagnosis	-1.059***	-0.489***
	(0.0112)	(0.0327)
5th year after diagnosis	-1.209***	-0.612***
	(0.0129)	(0.0384)
6th year after diagnosis	-1.321***	-0.645***
	(0.0155)	(0.0478)
7th year after diagnosis	-1.449***	-0.670***
	(0.0190)	(0.0574)
8th year after diagnosis	-1.534***	-0.585***
	(0.0229)	(0.0672)
9th year after diagnosis	-1.637***	-0.553***
	(0.0292)	(0.0721)
10th year after diagnosis	-1.727***	-0.593***
	(0.0373)	(0.0967)
Comorbidity	0.288***	3.004***
	(0.0169)	(0.0581)
Observations	372,633	372,633
Number of individuals	81,048	81,048

Robust standard errors in parentheses
*** p<0.01, ** p<0.05, * p<0.1

10.3 ATC-codes, DRG-codes and ICD-codes

Table 12: ATC-codes

ADHD drugs and ATC-codes	
ATC-code	
N06BA01	Mixed Salt Amphetamine
N06BA02	Dextroamphetamine Sulfate
N06BA04	Methylphenidate Hydrochloride
N06BA05	Pemoline
N06BA07	Modafinil
N06BA09	Atooxetine Hydrochloride
N06BA12	Lisdexamfetamine
Comorbidity drugs and ATC-codes	
Antipsychotic drugs	
ATC-code	
N05AA01-07	Phenothiazines with aliphatic side-chian
N05AB01-10	Phenothiazines with piperazine structure
N05AC01-04	Phenothiazines with piperidinestructure
N05AD01-09	Butyrophenone derivatives
N05AE01-05	Indole derivatives
N05AF01-05	Thioxanthene derivatives
N05AG01-03	Diphenylbutylpiperidone derivatives
N05AH01-06	Diazepines, oxazepines, thiazepines and oxepines
N05AL01-07	Benzamides
N05AX07-08, 10-14	Other antipsychotics
Antidepressant drugs	
ATC-code	
N06AB02-10	Selective serotonin reuptak inhibitors
N06AA01-19, 21, 23	Non-selective monoamine reuptake inhibitors
N06AX16-17, 21.23	Other antidepressants

Source: Brownell (2012)

Table 13: ICD-codes comorbidities

ICD-10	ICD-9	Diagnosis
F40-F41 F32.0-F32.3	300.00-300.02 296.2-296.3	Anxiety
F32.8-F32.9 F33.0-F33.4 F33.8-F33.9	300.4 311	Depression
F31	296.0, 296.4-296.8	Bipolar Disorder
F20	295	Schizophrenia

Source: Socialstyrelsen C (2016), Socialstyrelsen D(1987)

Table 14: DRG-codes

		DRG-code	Treatment	Average cost
ADHD	Outpatient	T990/8800	Medical appoinment for mental health diseases and drug addiction	3798 SEK
		T99X/880P	Medical group appointment for mental health diseases and drug addiction	4613 SEK
	Inpatient	T41N/431B	Neuropsychiatric conditions	55255 SEK
		T49N/432C	Unspecified Mental disorders	27354 SEK
		T58N/432M	Psychiatric care 29-90 days	235600 SEK
		T59N/432N	Psychiatric care >90 days	615504 SEK
Comorbidities	Outpatient	T990/8800	Medical appoinment for mental health diseases and drug addiction	3798 SEK
		T99X/880P	Medical group appointment for mental health diseases and drug addiction	4613 SEK
	Inpatient	T10N/426A	Bipolar disorder <60 days	33841 SEK
		T11N/426B	Bipolar disorder >59 days	44602 SEK
		T12N/426C	Mood disorder <60 days	29188 SEK
		T13N/426D	Mood disorder >59 days	44564 SEK
		T18N/427D	Somatoform/Dissociative disorder	37759 SEK
		T30N/430A	Schizophrenia <30 days	48811 SEK
		T31N/430B	Schizophrenia 30-59 days	44581 SEK
		T32N/430C	Schizophrenia >59 days	37030 SEK
		T41N/431B	Neuropsychiatric conditions	55255 SEK
		T49N/432C	Unspecified Mental disorders	27354 SEK
		T58N/432M	Psychiatric care 29-90 days	235600 SEK
		T59N/432N	Psychiatric care >90 days	615504 SEK

Source: SKL A (2015)

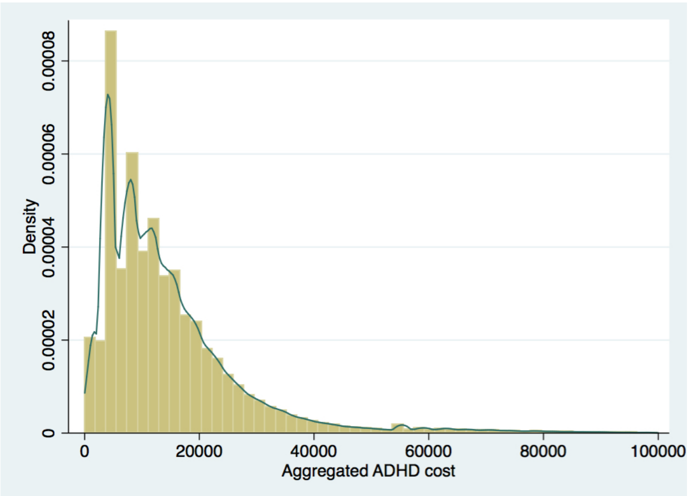
10.4 Log-odds ratio to probability

Table 15: Log-odds ratio to probability

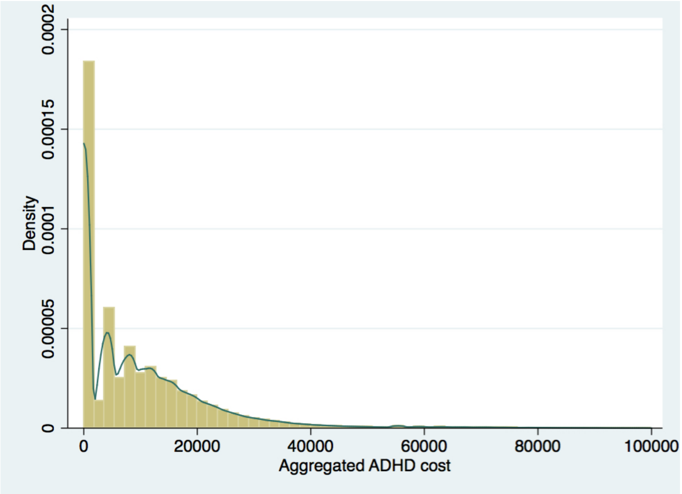
p	odds	logodds
.001	.001001	-6.906755
.01	.010101	-4.59512
.15	.1764706	-1.734601
.2	.25	-1.386294
.25	.3333333	-1.098612
.3	.4285714	-.8472978
.35	.5384616	-.6190392
.4	.6666667	-.4054651
.45	.8181818	-.2006707
.5	1	0
.55	1.222222	.2006707
.6	1.5	.4054651
.65	1.857143	.6190392
.7	2.333333	.8472978
.75	3	1.098612
.8	4	1.386294
.85	5.666667	1.734601
.9	9	2.197225
.999	999	6.906755
.9999	9999	9.21024

Source: UCLA (2016)

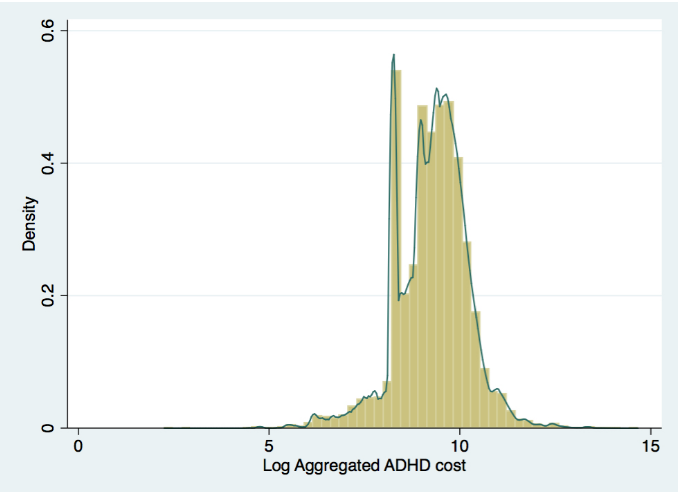
10.5 Density plots



Graph 11: Density plot Total ADHD cost, conditional on not equal to zero and lower than 100,000 SEK.



Graph 12: Density plot Total ADHD cost, conditional on lower than 100,000 SEK.



Graph 13: Density plot: Log Total ADHD cost

10.6 AIC and BIC values

Table 16: AIC and BIC values

Distribution:	Gamma	Poisson	Inverse-Gaussian	Gaussian
AIC	21.34	15032.5	29.65	23.23
BIC	-3,145,280	4.03e+09	-3,358,950	1.93e+14