



## Research paper

## Societal burden of adolescent depression, an overview and cost-of-illness study

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## ABSTRACT

**Background:** Depression in adolescents is a serious problem to society because of the high prevalence rate, the high subjective burden of illness and negative (economic) consequences. Information regarding the economic burden of adolescent depression is scarce. The goal of this study is twofold. First, an overview of the literature on prevalence, burden of disease, and costs related to adult and adolescent depression is given. Second, a prevalence-based cost-of-illness study is being conducted.

**Methods:** In this study a cost-of-illness study using a societal perspective was conducted using data of 56 clinically depressed Dutch adolescents aged 12–21. Bottom-up acquired costs were measured by means of cost questionnaires.

**Results:** The calculations showed that clinically depressed adolescents referred to treatment cost the Dutch society €37.7 million a year. The calculated costs were higher when a more recent prevalence rate was used in a secondary analysis.

**Limitations:** Limitations of this study are that only older Dutch prevalence rates were available, a relatively small sample size was used and no long term costs could be calculated.

**Conclusion:** Even though the sample size is small, the calculated costs are indicative for the societal costs of adolescents with depression. Cost-effective prevention and intervention methods seem warranted to reduce these enormous costs.

## 1. Introduction

Depression in adolescents is a huge humanistic and societal problem because of the high prevalence rate and high burden of the illness, which could reflect in high societal costs. There are only a few studies that have roughly estimated these costs from national registrations but until now costs related to adolescent depression have not been calculated from a societal perspective using individual patient data. The aim of this article is twofold. First, an overview is given on the prevalence, burden of disease, and estimated costs related to adolescent depression, the latter which is preceded by a short introduction on cost-of-illness studies. Since there is a lack of studies in adolescents, studies with adult populations are presented as well. Second, a cost of illness study was conducted to estimate costs of clinical depressed adolescents. Prevalence rates from the overview were used to perform this cost-of-illness study.

## 2. Overview

## 2.1. Prevalence

Worldwide estimations suggest that 350 million people of all ages suffer from depression (WHO, 2000). The mean estimated lifetime prevalence was 14.6% in high-income and 11.1% in low-middle income countries. The life time prevalence rate in the Dutch adult population (18 to 65 year olds) is 18.7% indicating that approximately 1 out of 5 people suffer at least once from a depressive disorder during their life (de Graaf et al., 2010). Prevalence rates for adolescent depression vary across different studies and countries from 1.3 to 18.2% (Costello et al., 2006). Costello et al. (2006) estimated an overall prevalence rate of 5.6% for youth aged 13 to 18 years old, based on 26 studies worldwide. In a report of the Substance Abuse and Mental Health Services Administration National it was found that at least 1 in 10 (11.4%) adolescents aged 12 to 17 had a major depressive disorder in the past year

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in the United States (Lipardi, Hughes & Williams, 2016). The Dutch prevalence rate of depressive disorders among youth aged 13 to 17 years old is 2.8% (Verhulst et al., 1997). The year prevalence rate in older youth (18 to 24 years old) is 9% percent (de Graaf et al., 2010). These two latter prevalence rates were used in primary analyses of this study.

The prevalence rates increase substantially when subclinical depressive symptoms are taken into account. In the general Dutch population, more than half (53.2%) of the adults report feelings of depression (Kessler & Bromet, 2013). In a Dutch population of adolescents aged 13 to 17 years old, 21.4% report depressive symptoms in a random week. So 1 out of 5 adolescents reported depressive complaints (Kramer, 2000). Subclinical depressive symptoms are often chronic and pose a risk factor for the development of a clinical depressive disorder in adolescence or adulthood (Smit et al., 2003).

## 2.2. Burden of disease

Besides the high prevalence rates, depression is also high in the ranking of burden of disease. Depression is the second leading cause of global disability (Years Lived with Disability; YLDs) and the eleventh leading cause of global burden of disease (Disability Adjusted Life Year; DALYs) in 2010. Major Depressive disorders accounted for 8.2% of YLDs and 2.5% of DALYs (Ferrari et al., 2013). The WHO (2008) stated that depression is in third place of leading causes of burden of disease (65.5 million DALYs) for all ages worldwide and even first place in middle- and high-income countries. In the Netherlands, depressive disorders are in second place of diseases that have the highest burden of disease (DALYs) in 15 to 65 year olds (145,100 DALYs) and in eighth place in 0 to 14 years old (3,200 DALYs) in 2011 (Hoeymans et al., 2011). To conclude, depression is one of the most leading disabling conditions worldwide because of the subjective burden of the disease on the client.

The high burden of disease is also obvious from reduced participation at work due to depressive symptoms. Depression is the main contributor to the number of disability days (386.6 million days a year) (Merikangas et al., 2007). Another study found that depression is related to 27.2 additional days of absence (absenteeism) and poorer functioning (presenteeism) due to depression and 65.5 additional days due to dysthymic disorder a year. Extrapolating this to the US civilian labor force, a total of 225.0 million workdays are lost per year due to depression (Kessler et al., 2006). In the Netherlands, depressive disorders are also the main cause of absence and explain 8.2% of the absence days of the working population. The mean number of days of absence of people suffering from depression is 35.3 days, which is 22.8 additional days of absence compared to people without a depressive disorder. People with a depressive disorder also have poorer quantitative (31.4 days) and qualitative (16.7 days) functioning at work, which is an 21.4 days extra loss compared to people without depression. In total, 56.3 days are lost (29.8 additional days) (de Graaf et al., 2011). It is known that depression in adolescents is often associated with more learning problems, worse school performance and more school absenteeism than adolescents without depression (Birmaher et al., 2007). One study involving adolescents at risk for depression due to maternal depression found that a depressive disorder at the age of 15 is associated with increased impairment in work and household responsibilities at age 20, even when controlling for depression at age 20 (Keenan-Miller et al., 2007). However, the exact number of days of productivity loss or school absenteeism in depressed adolescents is unknown.

A depressed adolescent also often has social problems, a higher risk of juridical problems, more negative life-events, physical complaints, and teen pregnancies (Birmaher et al., 2007). These negative consequences can cause an increase in school absenteeism and burden of disease and even avert the adolescent from finishing their education or start secondary education. This in turn, results in decreased future chances in their working career. Due to the high risk of suicide (Ryan, 2005), the chance of premature death is also higher.

Approximately 60% of depressed adolescents report suicidal thoughts and 30% has committed a suicide attempt (Birmaher et al., 2007). Next to suicide, there is another reason for premature death in depressed individuals. It seems that depressed people often exhibit an unhealthy lifestyle and are less compliant to medical treatments for physical complaints, increasing the chance of premature death. The chance of premature death is 1.65 times higher in depressed adults than non-depressed adults (Cuijpers & Smit, 2002). However, these costs have never been examined.

## 2.3. Costs

Societal costs can be measured by means of a cost-of-illness study. The purpose of a cost-of-illness study is to translate the burden on society of a particular disease or condition into monetary costs. All costs associated with the illness are identified and measured, including health care costs, patient and family costs and costs occurring in other sectors. Results of this cost-of-illness study can be used to gain insight in how much is being spent on depression in youth, both on a family and societal level, and how much potentially can be saved if an effective treatment is offered. It also helps setting priorities for health care efficiency research (Rice & Miller, 1995). In the current study, both direct and indirect societal costs will be measured from a prevalence-based perspective and using a bottom-up approach. Using a prevalence-based perspective, the costs associated with a specific illness are identified for a specific period that matches the prevalence of that specific illness (the number of people with that illness in a specific time frame). Usually, costs are based on a time-frame of one year, with the year prevalence rate. In a bottom-up approach data are obtained at patient level by means of registrations or self-report measures such as retrospective cost questionnaires, retrospective cost interviews or prospective cost diaries (Sleed et al., 2005). The bottom-up approach provides detailed information on resource use that is likely to vary from patient to patient and is difficult to extract from existing data sources based on aggregated data, the latter which are used in a top-down approach. Another advantage of the bottom-up approach is that costs outside the health care sector, such as costs due to school absence, productivity loss of parents, etc. can be estimated as well.

Productivity loss can be caused by absenteeism and presenteeism. Especially in depressed people, absenteeism and presenteeism is high resulting in high costs on a societal level. For example, \$36.6 billion salary-equivalent lost productivity per year was associated with depression in the US (Kessler et al., 2006). In the systematic review of Luppá et al. (2007) it was found that in bottom-up cost-of-illness studies, costs related to lost productivity ranged between \$52 (Russia) and \$913 (Spain) per year. In top-down studies, indirect morbidity costs (lost productivity) ranged between \$94.14 (USA) and \$8355.19 (South Australia) and mortality costs were \$108.88 (Sweden) to \$866.42 (USA). The authors concluded that the average annual morbidity costs were between \$2000 to \$3700 and between \$200 to \$400 for mortality costs. Greenberg et al. (2003) estimated that 62% (51.5 billion) of the costs in the US were related to productivity loss. Another study also estimated this number at 31 billion per year (Stewart et al., 2003). In the Netherlands, costs due to productivity loss in depressed adults were estimated to be 953 million euro a year (Romijn et al., 2008). Another Dutch study found that the majority of the costs (85%, 1.8 billion) of depression in adults are due to productivity loss (work absence). The remaining 15% are health care costs. In this study, the annual costs of depression in 18 to 65 year olds are estimated to be 311 million euro (Smit et al., 2006). Other research has confirmed the high indirect costs (De Graaf et al., 2011). It is unknown, how high these costs related to school absence (as an indicator of productivity loss) are in adolescents.

On top of costs related to productivity loss, treatment costs should be considered as well. Given the high subjective burden of disease, high productivity loss and the negative consequences of depression, the majority of depressed individuals seeks help. In the US, 56% of

depressed adults receive treatment (Kessler et al., 2008). In the Netherlands, this percentage was 58.5% (de Graaf et al., 2010). Accordingly, international research shows that depressed adults have a high level of mental health care consumption. As a consequence, the yearly costs of the American health care of depressed adults are significantly higher (\$4246) than health care costs of adults without a depressive disorder (\$2371) (Simon et al., 1995). A systematic review of Luppá et al. (2007) of 24 cost-of-illness studies on depression in adults performed in the USA ( $n = 12$ ), Europe ( $n = 10$ ), Australia ( $n = 1$ ) and Multi-national ( $n = 1$ ) showed that health care costs vary considerably. Bottom-up studies revealed that costs related to diagnostics and treatment in health care ranged from \$1345 (Germany) to \$2746 (Germany) per year. Total annual health care costs (including comorbidity) ranged from \$152 (Russia) to \$7659 (USA). Compared to non-depressed adults, the excess (additional) costs in health care were between \$1000 and \$2500 (without outliers). Top down (prevalence-based) studies showed that direct costs per case (depression related) were between \$244.09 (UK) to \$2488.52 (South Australia) per year. The authors concluded that the average annual costs per case ranged from \$1000 to \$2500 for direct costs. The huge variation in costs could be explained by the study sample (different levels of severity), age, different health care financing and provision, and publication year. In the Netherlands, the annual treatment costs per year for depressed adults are estimated to be 660 million euro (Romijn et al., 2008) and 966 million euro (Slobbe et al., 2011).

Studies examining costs associated with health care consumption in depressed youth are scarce. A study involving adolescents at risk for depression due to maternal depression found that a depressive disorder at the age of 15 is associated with increased health care utilization at age 20 (Keenan-Miller et al., 2007). A Dutch study found that merely 3.5% of 4 to 18 year old children with a mental disorder (including depression) had been referred yearly to mental health care for treatment (Verhulst & Van der Ende, 1997). According to an estimation of Smit et al. (2006), 3% of the 660 million euro's health care costs in the Netherlands is spent on children and adolescents aged 0 to 19 years old (approximately 20 million euro). The largest amount is spent on young adults between 15 and 19 years old (over 16 million euro). However, these estimations were made using a top-down method, in which existing (national) registrations were used. A bottom-up cost-of-illness study to estimate costs of clinical depressed adolescents at a societal and family level has not yet been performed.

### 3. Method

#### 3.1. Participants

In this cost-of-illness study, the baseline data of a large randomized controlled trial were used. In this RCT the cost-effectiveness of an individual CBT was compared to Treatment as Usual (Stikkelbroek et al., 2013). In total, 56 families with a clinically depressed adolescent were included in this sub-study. The inclusion criteria were: (1) a primary diagnosis of Major Depressive Disorder or Dysthymic disorder based on the semi-structured interview the K-SADS (Kaufman et al., 1997), (2) age 12 to 21 years, and (3) referred to one of the participating mental health care institutions. The exclusion criteria were (1) acute suicide risk (2) substance abuse, pervasive developmental disorder, or bipolar disorder and (3) not fluent in Dutch, Turkish, Arabic or Berber language. This subpopulation included 49 girls (87.5%) and 7 boys (12.5%) with a age range of 12 to 21 years ( $M = 16.2$ ,  $SD = 2.07$ ). Most families had the Dutch nationality (96%), one adolescent was from Iran and one from Angola. Adolescent's highest educational level was primary school (1.8%), low level (30.3%), middle level (16.1%), high level (44.8%) and 7.1% was missing. Adolescents included in this sub-study were comparable to adolescents whose parents did not fill out the cost questionnaires and were excluded ( $n = 32$ ), based on gender,  $\chi^2 = 1.84$ ,  $p > .10$  and age, ethnicity, educational level, severity of the

depression, comorbidity and frequency of previous health care, all  $F$ 's  $< 2.52$ ,  $p > 0.10$ . Written informed consent was obtained by both the adolescent and the parent(s). The study design was approved by the independent Medical Ethical Committee of Utrecht Medical Centre at Utrecht University, number 10/446. The trial was registered with the Dutch Trial register (NTR) number 2676.

#### 3.2. Cost questionnaire

A cost questionnaire was used that was based on a cost-of-illness study in anxious children (Bodden et al., 2008) and was adapted such that all costs related to adolescent depression which are relevant to society were captured. Cost questionnaires were completed retrospectively by one of the parents or the adolescent (if the adolescent was 18 years or older) and covered a period of three months, prior to treatment. Parents or the adolescent reported on four categories of resource use. One, direct health care costs included visits to health care professionals (e.g. psychologist, psychiatrist, etc.), alternative care (e.g. reiki, reflexology, etc.), day treatment, general practitioner, outpatient consultations at the hospital, medical examinations (e.g. blood and urine test), medication with a prescription (e.g. antidepressants and sleep medication), medication without a prescription (e.g. painkillers), and hospitalisation. Two, direct non-health care costs were costs related to professional (formal) care (e.g. paid house help, children's day care) and informal care (persons near the family, such as relatives, friends, or neighbors, take over some domestic or babysit tasks). Indirect costs included productivity losses due to absence of work by the parents, loss of household activities or voluntary work, loss of leisure time, absence from school of the child, and costs of substance abuse. The last category is "out-of-pocket" costs which are actual expenses made by the family (and are therefore paid 'out of the pocket'), and include for example transportation costs, parking costs, and own monetary contributions for health care services which are not fully reimbursed by health insurance companies. The cost questionnaire also assessed for which family member the resource use was applicable (child, sibling, mother or father), as well as the reason for the resource use by that family member. The reported reasons were grouped into (1) due to depression, (2) due to psychological problems, (3) due to behavioral problems, (4) due to physical problems and (5) other reasons. For the main analysis, only resources used related to the depression of the adolescent were used. Both a family (costs per family with a depressed adolescent) and societal perspective (costs for society as a whole) were used. For the secondary analyses, the remaining four reasons were also included. The cost questionnaire had good discriminant validity in a study with anxious children (Bodden et al., 2008).

#### 3.3. Unit prices

The volumes of the resources used from the cost questionnaires (e.g. number of visits to psychologist) were multiplied by the unit price of each resource (e.g. the unit price of a psychologist). Costs were calculated for 2009 (€ 1 = \$1.33, January 2009). Unit prices consist of personnel, material and capacity costs, as well as costs of housing and overhead. Most unit prices were obtained by using standardized unit prices from the Dutch guideline (Hakkaart-van Roijen et al., 2010). However, medication prices were calculated per person and were based on the Daily Defined Dosage (DDD), which indicates the mean medication usage per person a day with a "claw back" reduction of 6.82% and value added tax (VAT 6%) obtained from the Medication database from the Dutch Care Institute (<https://www.medicijnkosten.nl>). In this database, both low (minimum) and high (maximum) cost prices are calculated. In the main analysis, the lowest medication prices were used, in the secondary analyses, the highest. The unit price of informal care, loss of leisure time, voluntary work and domestic activities was based on a 'shadow price' as stated in the Dutch guideline (Hakkaart-van Roijen et al., 2010). To determine the unit prices associated with

absence from school, actual annual tuition, which consists of a contribution by parents and a state-subsidy per child was divided by the total annual hours at school according to the standard, resulting in a price per hour of school absence (Bodden et al., 2008). Productivity costs of the parents due to absence from paid work were calculated by means of the friction cost method (Hakkaart-van Roijen et al., 2010). This method assumes that productivity loss is usually restricted to a specific period (usually 3 months), afterwards the sick employee is replaced.

### 3.4. Cost-of-illness

As mentioned, the volume of the resources used from the cost questionnaires was multiplied by the unit price of each resource, resulting in the costs (Hakkaart-van Roijen et al., 2010). The costs per family over a period of three months were extrapolated to a period of 1 year (i.e. multiplied by 4) under the assumption that data obtained with the cost diaries were representative for that period. The annual costs per family were then multiplied by a weighted Dutch prevalence rate which was based on earlier prevalence studies on depressive disorders. This weighted average was calculated by determining the percentage of 13 to 17 year olds (80%) and the percentage of 18 to 21 year olds (20%) in our sample and multiplying these with prevalence rates of depressive disorders found in earlier studies respectively 2.8% (Verhulst et al., 1997) and 9% (De Graaf et al., 2010). This resulted in a multiplying factor of 4%. Subsequently, this prevalence rate (4%) was multiplied by the percentage of children with a mental disorder that are referred to mental health care (3.5%) (Verhulst & van der Ende, 1997). As a result, the total annual societal cost-of-illness of families of clinically depressed adolescents referred for treatment could be calculated. Secondary analyses were done using an international and more recent prevalence rate for 13 to 17 year olds, which is 5.6% (Costello et al., 2006).

### 3.5. Statistical analysis

Missing items in the cost questionnaires were handled with the Missing Value Analysis of SPSS based on the regression models. To investigate whether data were normally distributed, a Kolmogorov-Smirnov test was performed. Due to highly skewed cost distributions, bootstrap simulations were conducted in order to get insight in the uncertainty surrounding the calculated costs. The bootstrap method estimates the sampling distribution of a statistic through 1000 simulations, based on sampling with replacement from the original data (Briggs et al., 1997).

## 4. Results

All resources used and costs made related to the depressive disorder of the adolescent, were summed and averaged for the reported 3 months and were extrapolated to a year (see Table 1). The mean costs per family with a clinically depressed adolescent amounted to €14,795.03. Costs were not normally distributed, Kolmogorov-Smirnov = 0.31,  $p < .01$  and were skewed to the left. Only 4 families reported no costs due to the depression of the adolescent. The remaining families varied in costs between €107.80 to €129,261.21. The majority of families (71.4%) had costs below €10,000 a year related to the depression of the adolescent. The highest costs were related to institutionalized treatment (41% of total costs), mental health care (26%), school absence (10%) and productivity loss of the parents (9%).

The total number of Dutch children aged 13 to 21 years old in 2013 was 1,819,851 (Central Bureau of Statistics; CBS, 2015). Multiplying this figure by 4% resulted in 72,794 Dutch children suffering from a depressive disorder. Again, this figure was multiplied by 3.5% because this study included referred adolescents. This culminated in a year prevalence of 2548 clinically referred depressed adolescents. Hence, the

**Table 1**

Mean total resource use, subtotal and total societal costs per family related to the depressive disorder of the adolescent using a bottom-up approach.

|  | Total costs per family (3 months) | Total costs per family a year |
|--|-----------------------------------|-------------------------------|
| Direct health care costs                   | <i>M (SD)</i>                     | <i>M (SD)</i>                 |
| Mental health care professional            | 959.02 (1066.18)                  | 3836.07 (4264.73)             |
| Day/part-time treatment                    | 257.16 (1515.20)                  | 1028.64 (6060.81)             |
| G.P  | 23.50 (44.04)                     | 94.00 (176.15)                |
| Hospital/policlinic visit                  | 10.54 (40.73)                     | 42.14 (162.91)                |
| Medical examination                        | 0.44 (3.30)                       | 1.76 (13.20)                  |
| Medication                                 | 12.60 (21.81)                     | 50.44 (87.26)                 |
| Institutionalized treatment                | 1506.98 (5278.09)                 | 6027.86 (21,112.37)           |
| <i>Subtotal</i>                            | <i>2770.23 (6271.14)</i>          | <i>11,080.91(25,084.57)</i>   |
| <i>Bootstrapped subtotal</i>               | <i>2827.95 (832.15)</i>           | <i>10,999.56 (3268.68)</i>    |
| Direct non-health care costs               |                                   |                               |
| Professional help at home                  | 22.93 (127.45)                    | 91.71 (509.82)                |
| Informal care                              | 44.20 (181.08)                    | 176.79 (724.32)               |
| <i>Subtotal</i>                            | <i>67.13 (286.91)</i>             | <i>268.50 (1147.63)</i>       |
| <i>Bootstrapped subtotal</i>               | <i>67.65 (39.40)</i>              | <i>262.92 (148.62)</i>        |
| Indirect costs                             |                                   |                               |
| School absence                             | 376.01 (626.22)                   | 1504.03 (2504.90)             |
| Paid work                                  | 347.64 (864.34)                   | 1390.57 (3457.36)             |
| Loss of leisure time/unpaid work           | 75.22 (229.11)                    | 300.89 (916.44)               |
| Substance use                              | 9.04 (40.33)                      | 36.17 (161.33)                |
| <i>Subtotal</i>                            | <i>807.92 (1273.18)</i>           | <i>3231.67 (5092.74)</i>      |
| <i>Bootstrapped subtotal</i>               | <i>803.09 (161.13)</i>            | <i>3253.36 (683.65)</i>       |
| Out-of-pocket costs                        |                                   |                               |
| Own contribution alternative treatment     | 0.71 (5.35)                       | 2.86 (21.38)                  |
| Own contribution medication not prescribed | 1.77 (4.42)                       | 7.10 (17.66)                  |
| Own contribution other costs               | 12.65 (43.07)                     | 50.61 (172.30)                |
| Own contribution (transport etc.)          | 38.35 (110.14)                    | 153.39 (440.55)               |
| <i>Subtotal</i>                            | <i>53.49 (114.29)</i>             | <i>213.95 (457.14)</i>        |
| <i>Bootstrapped subtotal</i>               | <i>53.57 (15.55)</i>              | <i>215.14 (60.46)</i>         |
| <b>Total costs</b>                         | <b>3698.76 (6825.89)</b>          | <b>14,795.03 (27,303.57)</b>  |
| <i>Bootstrapped total costs</i>            | <i>3697.90 (903.84)</i>           | <i>14,701.54 (3614.42)</i>    |

annual societal cost-of-illness accumulated to €37,697,736.44 for families of clinically depressed adolescents aged 12 to 21 referred for treatment in the Netherlands. This implies that clinically depressed adolescents cost the Dutch society annually more than 37 million euros.

Three secondary analyses were performed.

First, besides costs related to the depression of the adolescent, costs related to other mental problems, behaviour problems and physical problems were assessed. The annual societal costs in a family with a depressed adolescent, including all costs, were €19,386.72. Costs for the entire group of clinically depressed adolescents accumulated to €49,397,362.56. The total costs of all reasons were highest for depression related problems of the adolescent (76% of the total costs), followed by psychological problems (18%), physical problems (4%) and behavior problems (2%), see Table 2.

Second, all calculations were repeated using the highest unit prices for medication. The total medication costs were merely €7.34 per 3 months ( $m = 19.94$ ,  $sd = 31.83$ ), that is €29.33 a year ( $m = 79.77$ ,  $sd = 127.32$ ), more compared to the lowest unit price for prescribed medication.

Third, the analyses were done based on an international and more recent prevalence rate (5.6%). Again, a weighted average was used namely 80% of 13 to 17 year olds and 20% of 18 to 21 year olds. The overall international year prevalence rate of depressive disorders among adolescents (13 to 17 year olds) was found to be 5.6% (Costello et al., 2006). In 18 to 24 years old, the same prevalence rate of 9% was used (De Graaf et al., 2010). This resulted in a multiplying

**Table 2**  
Subtotal and total annual costs per family ( $n = 56$ ) related to adolescent depression, psychological, behavioural and physical problems.

|  | Reason depression<br><i>M (SD)</i> | Reason psychological<br><i>M (SD)</i> | Reason behavioural<br><i>M (SD)</i> | Reason physical<br><i>M (SD)</i> |
|--|------------------------------------|---------------------------------------|-------------------------------------|----------------------------------|
| Direct health care costs                   |                                    |                                       |                                     |                                  |
| Mental health care professional            | 3836.07 (4264.73)                  | 200.71 (748.27)                       | 173.79 (1187.92)                    | 44.00 (329.27)                   |
| Day/part-time treatment                    | 1028.64 (6060.81)                  | 0.00 (0.00)                           | 0.00 (0.00)                         | 0.00 (0.00)                      |
| G.P  | 94.00 (176.15)                     | 112.00 (120.82)                       | 21.50 (45.30)                       | 63.50 (137.22)                   |
| Hospital/policlinic visit                  | 42.14 (162.91)                     | 0.00 (0.00)                           | 0.00 (0.00)                         | 195.79 (542.54)                  |
| Medical examination                        | 1.76 (13.20)                       | 0.00 (0.00)                           | 0.00 (0.00)                         | 74.86 (241.72)                   |
| Medication                                 | 50.44 (87.26 low)                  | 32.17 (57.59)                         | 75.35 (191.61)                      | 38.17 (72.31)                    |
| Institutionalized treatment                | 6027.86 (21,112.37)                | 2485.71 (13,033.04)                   | 0.00 (0.00)                         | 48.96 (271.12)                   |
| <i>Subtotal</i>                            | <i>11,080.91(25,084.57)</i>        | <i>2830.60 (12,999.69)</i>            | <i>270.64 (1203.50)</i>             | <i>465.28(1094.32)</i>           |
| <i>Bootstrapped subtotal</i>               | <i>10,999.56 (3268.68)</i>         | <i>2929.30 (1682.80)</i>              | <i>272.35 (159.93)</i>              | <i>466.75(140.06)</i>            |
| Direct non-health care costs               |                                    |                                       |                                     |                                  |
| Professional help at home                  | 91.71 (509.82)                     | 0.00(0.00)                            | 0.00 (0.00)                         | 0.00 (0.00)                      |
| Informal care                              | 176.79 (724.32)                    | 4.46 (33.41)                          | 22.32 (167.04)                      | 0.00 (0.00)                      |
| <i>Subtotal</i>                            | <i>268.50 (1147.63)</i>            | <i>4.46 (33.41)</i>                   | <i>22.32 (167.04)</i>               | <i>0.00 (0.00)</i>               |
| <i>Bootstrapped subtotal</i>               | <i>262.92 (148.62)</i>             | <i>4.32 (4.38)</i>                    | <i>22.54 (21.88)</i>                | <i>0.00 (0.00)</i>               |
| Indirect costs                             |                                    |                                       |                                     |                                  |
| School absence                             | 1504.03 (2504.90)                  | 137.85 (702.51)                       | 0.00 (0.00)                         | 202.59 (899.77)                  |
| Paid work                                  | 1390.57 (3457.36)                  | 302.34 (1240.53)                      | 8.58 (64.19)                        | 0.00 (0.00)                      |
| Loss of leisure time/unpaid work           | 300.89 (916.44)                    | 37.50 (202.32)                        | 0.00 (0.00)                         | 0.00 (0.00)                      |
| Substance use                              | 36.17 (161.33)                     | 130.56 (793.46)                       | 0.00 (0.00)                         | 0.00 (0.00)                      |
| <i>Subtotal</i>                            | <i>3231.67 (5092.74)</i>           | <i>608.25 (1614.40)</i>               | <i>8.58 (64.19)</i>                 | <i>202.59(899.77)</i>            |
| <i>Bootstrapped subtotal</i>               | <i>3253.36 (683.65)</i>            | <i>617.36 (214.82)</i>                | <i>8.77 (8.14)</i>                  | <i>208.41(123.63)</i>            |
| Out-of-pocket costs                        |                                    |                                       |                                     |                                  |
| Own contribution alternative treatment     | 2.86 (21.38)                       | 0.00 (0.00)                           | 0.00 (0.00)                         | 5.00 (28.60)                     |
| Own contribution medication not prescribed | 7.10 (17.66)                       | 5.75 (40.11)                          | 0.00 (0.00)                         | 6.68 (26.86)                     |
| Own contribution other costs               | 50.61 (172.30)                     | 14.29 (106.90)                        | 14.29 (106.90)                      | 61.71 (323.58)                   |
| Own contribution (transport etc.)          | 153.39 (440.55)                    | 13.04 (48.35)                         | 42.36 (281.12)                      | 15.86 (50.81)                    |
| <i>Subtotal</i>                            | <i>213.95 (457.14)</i>             | <i>33.07 (153.93)</i>                 | <i>56.64 (387.71)</i>               | <i>89.26 (326.33)</i>            |
| <i>Bootstrapped subtotal</i>               | <i>215.14 (60.46)</i>              | <i>32.16 (20.25)</i>                  | <i>56.90 (52.44)</i>                | <i>89.04 (43.42)</i>             |
| <b>Total costs</b>                         | <b>14,795.03 (27,303.57)</b>       | <b>3476.38 (13,328.41)</b>            | <b>358.18 (1343.47)</b>             | <b>757.13 (1543.79)</b>          |
| <i>Bootstrapped total costs</i>            | <i>14,701.54 (3614.42)</i>         | <i>3441.03 (1838.89)</i>              | <i>361.45 (178.57)</i>              | <i>762.19 (203.06)</i>           |

factor of 6.3%. Calculations of this higher prevalence rate showed the following results; there were 114.650 adolescents with a depressive disorder, of whom 3.5% were referred to a mental health care facility (4013 adolescents). This was multiplied by the annual costs and led to a total of €59,369,074.06. With a more recent (but international) prevalence rate, the annual societal costs for depressed adolescents were more than 1.5 times as high compared to the main analysis namely €59.4 million.

## 5. Discussion

To the authors' knowledge, this is the first cost-of-illness study carried out in a sample of clinically depressed adolescents. The aim of this study was to measure the magnitude of the annual societal cost-of-illness in families with a clinically depressed adolescent aged 12 to 21 years old, by means of a prevalence-based bottom-up approach using retrospective cost questionnaires.

The main finding is that clinically referred adolescents cost our society annually almost €38 million. Using a more recent, international prevalence rate, the costs even augmented to €59 million a year. There is no previous research that has collected data related to indirect health care costs and school absence, therefore total costs cannot be compared. There is one previous study that estimated health care costs using a top-down approach (with registrations). They found that approximately €20 million is spent on health care costs children and adolescents with a depressive disorder in the Netherlands (Smit et al., 2006). However in this top-down approach, the estimation was based on registrations and was limited to health care costs. A bottom-up cost-of-illness approach is considered to be more precise and reliable (Hakkaart-van Roijen et al., 2010) although it carries a danger of selection bias. Comparing our health care costs and those of Smit et al. (2006), ours are substantially higher namely 28 million. A comparable bottom-up cost-of-illness study using the same design in a sample of children with a clinical anxiety

disorder (8 to 18 years old) showed that the annual societal costs for a family were about €20 million (Bodden et al., 2008). The prevalence rate for anxiety disorders in children is 9.7%, which is almost 2.5 times as high compared to that of depressive disorders in children and adolescents. However, the annual societal costs for depressed adolescents are almost twice as high. So despite the fact that depression is less frequently present in children and adolescents than anxiety, the society pays more for depressed adolescents. Also, the burden of disease (DALY's) for depression is higher than that of anxiety. This might suggest that depression is a more complex disorder that needs more care.

On a family level, this study showed that the costs per family with a clinically referred depressed adolescent are €14,641 euro. This is five times as high as the costs that a family spends on a clinically referred anxious child or adolescent (€2748 euro) (Bodden et al., 2008). In the same study, the total annual costs for families from the general population were assessed as well and were found to be €148. The annual social costs of families with a clinically anxious child or adolescent were 21 times as high. However, the annual societal costs of families with a clinically depressed adolescent were astonishingly higher, namely 99 times as high. Similar results have been found in adult studies (18 to 65 year olds). In adults, the annual costs per individual with affective disorders were higher (€5,009) than for anxiety disorders (€3587). However, using a societal perspective and based on prevalence rates, costs for anxiety disorders in adults were higher (€405 million) than those of affective disorders (€311 million) (Smit et al., 2006). This difference in costs was partially due to the difference in prevalence rate, which was 6.2% for depression and 11.3% for anxiety.

There are some cost-of-illness studies performed with children and adolescents with other psychopathology. The total annual costs per family in a sample of ten children (aged 4 to 10) with behavioral problems were €22,272 (Knapper al. 1999), €8781 in a sample of children (aged 3 to 8 years) with anti-social behavior (Romeo et al., 2006) and €51,844 in a sample of children with autism (Järbrink et al., 2003).

However the prevalence rate of conduct disorder (2.6%, Verhulst et al., 1997) and autism spectrum disorders (0.22% to 0.25% van der Gaag et al., 1996) is lower than that of depression (2.8% and 9%). Consequently, the *relative societal costs* (multiplying prevalence rate by costs) for depression will probably be higher. Comparisons should be made with caution given the differences in design, unit prices in the countries where the studies were performed and the year of baseline. We can conclude that costs for clinically depressed adolescent are tremendously and are probably higher than for other psychological disorders.

In accordance with these studies (Knapp et al., 1999; Romeo et al., 2006; Järbrink et al., 2003), our study showed that a large proportion of costs (9%) could be assigned to productivity loss of the parents. Another relevant cost driver was school absence (10% of the total costs in our study), which was similar to the cost-of-illness study in anxious children. In Dutch research using an adult sample, costs related to the productivity loss were much higher namely 85% (Smit et al., 2006). Other research with depressed adults has confirmed these high indirect costs (1.8 billion a year) (De Graaf et al., 2011). The costs related to school absence in depressed adolescents are indeed much lower than those related to productivity loss in depressed adults. However, it should be mentioned that depressive disorder with adolescent-onset is often chronic. Around 34 to 69% of depressed adolescents develop a new depressive disorder within one to five years (Kennard et al., 2008). So the costs we measured were just the tip of the iceberg and possible future productivity losses were not taken into account. This is called the accumulation of human capital (Eisenberg et al., 2009). This indicates that depressed children or adolescents develop less knowledge, skills and competences during their lives due to their depression and the absence from school and work. A recent study assessed the global functioning of adolescents, 3.5 years after their participation in a randomized controlled trial comparing fluoxetine, CBT, combination treatment (fluoxetine + CBT), or placebo. Adolescents assigned to the placebo condition, adolescents with multiple comorbidity and adolescents with depressive relapse showed relatively poorer global functioning after 3.5 years (Peters et al., 2016). In line, depressed adults are more likely to lose their job than the average employee, (Lerner et al., 2004). Since, we only included depressed adolescents aged 12 to 21 years old and no adults, we have no information on the long term costs associated with the transition into adulthood. An incidence-based study including people of all ages should be conducted to investigate costs throughout the lifespan of a depressed person. These incidence-based costs are far more higher than the €38 million which was found in our (prevalence-based) study.

The most relevant cost driver were costs related to treatment and hospitalization, which is in line with adult studies (Luppa et al., 2007). This is probably due to the high burden of illness, which causes the adolescent to seek treatment more rapidly. Looking solely at treatment costs for a depressed adolescent, the annual costs were €27,754,268.36 for society. Other studies with adult samples show the same high treatment costs namely €966 million a year (Slobbe et al., 2011).

The enormous costs of clinically referred depressed adolescents raises the question whether these costs could be reduced with evidence-based prevention or intervention programs. Perhaps the €38 million could be reduced by giving adolescents an effective preventive intervention at an early stage. Also effective interventions could be important to reduce these costs. For example, a recent study showed that achieving developmental milestones (such as college and employment) become more likely over time after the adolescent received treatment for early-onset depression. Also global functioning improved over time (Peters et al., 2016), reducing costs. However, cost-effectiveness studies have to shed more light on this matter.

This study has some limitations. First, only older Dutch prevalence rates were available. Therefore, a secondary analysis was performed using a more recent, though international, prevalence rate. Second, a relatively small sample size was used in this study which increases the uncertainty of the estimated results. Third, since a prevalence-based

method was used no long term costs could be calculated. An incidence-based study should be conducted to measure costs related to depression across the life span.

In conclusion, this cost-of-illness study shows that the annual societal costs of families with a clinically depressed adolescent are tremendous and amount to almost €38 million in The Netherlands. These costs are likely to be higher than those of other psychological disorders. Given the small sample size this is an indication of the actual costs. More cost-of-illness studies with larger sample sizes are necessary to test the reliability of these estimated costs. Combined with the high burden of disease, the need for cost-effective prevention and intervention programs seems warranted.

### Conflict of interest

We warrant that the material contained in the manuscript represents original work, has not been published elsewhere, and is not under consideration for publication elsewhere.

My co-authors and I do not have any interests that might be interpreted as influencing the research, and APA ethical standards were followed in the conduct of the study. We have no declarations of interest. We confirm full responsibility for reported research and participation in concept and design; analysis and interpretation; drafting and revising of the manuscript.

### Contributors

DB is responsible for data collection, data analysis, and for reporting the study results. YS was also responsible for data collection. CD supervised the data analysis. YS and CD read the manuscript and provided suggestions for improvement. DB is and grant applicant. All authors have read and approved the final manuscript. My co-authors have agreed to submission of the manuscript in this form. I have assumed responsibility for keeping my co-authors informed of our progress through the editorial review process, the content of the reviews, and any revisions made.

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### Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.jad.2018.06.015](https://doi.org/10.1016/j.jad.2018.06.015).

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