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Societal costs of subclinical depressive symptoms in Dutch adolescents: a cost-of-illness study

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Background: Subclinical depressive symptoms are highly prevalent among adolescents and are associated with negative consequences, which may pose an economic burden for society. We conducted a prevalence-based cost-of-illness study using a societal perspective to investigate the cost-of-illness of subclinical depressive symptoms among adolescents. **Methods:** Using a bottom-up approach, cost questionnaires were assessed to measure costs from 237 Dutch families with an adolescent aged 11–18 with subclinical depressive symptoms (of which 34 met the criteria of a depressive disorder). The study is registered in the Dutch Trial Register (Trial NL5584/NTR6176; www.trialregister.nl/trial/5584). **Results:** Our calculations show that adolescents with subclinical depressive symptoms cost the Dutch society more than €42 million annually, expressed in costs related to depressive symptoms. Secondary analyses were performed to test the reliability and stability of the costs. When costs related to psychological problems were considered, the annual costs amounted to €67 million. The total societal costs related to physical problems amounted to approximately €126 million. All costs combined (depressive, psychological, behavioural and physical problems and other reasons) amounted to a €243 million. Total costs were highest for physical-related problems of the adolescent (52% of the total costs), followed by psychological (28%), depressive (17%) and behavioural problems (1%). Using an international prevalence rate, societal costs related to depressive symptoms resulted in €54 million a year. **Conclusions:** Cost-effective prevention programmes seem warranted given the high societal costs and risk of future costs as subclinical depressive symptoms could be a precursor of clinical depression later in life. **Keywords:** Adolescence; depression; economic evaluation.

Introduction

Depressive disorders are very common among adolescents, and seem to increase in the last three decades. A study focusing on adolescents between 12 and 17 years old found that in 2005, the year prevalence rate of a major depressive disorder (MDD) was 8.7%, while in 2017, this rate was 13.2%, which is an increase of 52% (Twenge, Cooper, Joiner, Duffy, & Binau, 2019). This is just the tip of the iceberg, as prevalence rates increase even more when subclinical depressive symptoms are assessed. An international literature review found prevalence rates ranging from 5.3% (year prevalence) to 29.2% (point prevalence) for subclinical depressive symptoms among adolescents under the age of 18 years (Carrellas, Biederman, & Uchida, 2017). In the Dutch population of adolescents aged 13–17 years, the year prevalence of MDD has been estimated at 3.8% (Meijer, Smit, Schoemaker, & Cuijpers, 2006) and 21.4% reported depressive symptoms in a random week (Kramer, 2000). In our overarching study, wherein we screened 8,603 adolescents on depressive symptoms, a comparable result was found namely 23.4% of the adolescents had an elevated

level of depressive symptoms (percentile score >75 on Children's Depression Inventory-2; CDI-2; Bodden, Braet, & Stikkelbroek, 2016) (Van den Heuvel et al., in press). These results indicate that approximately one out of five Dutch adolescents suffers from subclinical depressive symptoms.

Depressive disorders are often associated with school absenteeism (Finning et al., 2019), poor academic functioning, social problems, legal problems, family conflicts, exposure to negative life-events, physical illness, teen pregnancies, substance use, obesity and suicide (e.g. Birmaher & Brent, 2007; Thapar, Collishaw, Pine, & Thapar, 2012). Besides, depressive disorders tend to be chronic and recurrence is high. In a longitudinal study, a recurrence rate of 75.2% after 20 years was found (Fombonne, Wostear, Cooper, Harrington, & Rutter, 2001). Also long-term consequences of adolescent depression have been found in a meta-analysis, including failure to complete secondary school and unemployment (Clayborne, Varin, & Colman, 2019). Subsequently, depressive disorders are among one of the highest burdens of disease in young people (World Health Organisation, 2020) and causes high healthcare utilization, resulting in high societal costs (Bodden, Stikkelbroek, & Dirksen, 2018). But also subclinical depressive symptoms are associated with

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severe consequences such as comorbid psychiatric disorders, impairment in school, with peers and at home and a high rate of suicidality (Carrellas et al., 2017) and they often pose a risk factor for the development of a clinical depressive disorder later in life (Smit, Bohlmeijer, & Cuijpers, 2003). However, it is unknown whether this population poses a societal burden in terms of monetary costs as well. Therefore, the aim of this study was to perform a cost-of-illness study of subclinical depressive symptoms among adolescents.

There are only a few cost-of-illness studies that have estimated costs related to adolescent depression. A recent meta-analysis that focused on excess costs related to clinical depression found two cost-of-illness studies using a comparison group design (König, König, & Konnopka, 2020). The total direct excess costs (inpatient, emergency and outpatient treatment, medication and other direct healthcare costs) per year for depressed adolescents compared with nondepressed adolescents ranged from \$2,868 to \$2,883, showing that direct healthcare costs were 179% higher in depressed adolescents. In one of two studies by Guevara, Mandell, Rostain, Zhao, and Hadley (2003), healthcare costs for youth (2–18 years old) with behavioural disorders (emotional and disruptive disorders) (\$1,492) were similar to those of children with physical disorders (\$1,245), which were both significantly higher than costs for children without disorders (\$834). Zooming in on behavioural disorders, healthcare costs related to emotional disorders (anxiety and depression) were twice as high (\$2,152) compared with costs related to disruptive disorders (conduct disorder (CD), oppositional deviant disorder (ODD) and attention deficit hyperactivity disorder (ADHD)) (\$1,027). The costs for children aged 2–18 years old with a depressive disorder amounted to \$2,555. A similar study by Mandell, Guevara, Rostain, and Hadley (2003, not included in the meta-analysis), found that the presence of any psychiatric disorder (adjustment disorder, CD, ODD, ADHD, depression) was associated with increased healthcare costs compared with no diagnosis and that depression and CD were associated with the highest total costs. The second study in the meta-analysis by Wright et al. (2016) included adolescents aged 13–17 years old in primary care that were screened for depressive symptoms using a self-report questionnaire. The healthcare costs for adolescents who screened positive for depression were more than twice as high (\$5,083) compared with adolescents who screened negative (\$2,357). They also found an association between an increase in costs and an increase in severity of depressive symptoms; there was a 49% increase in healthcare costs for adolescents with mild depressive symptoms and a 247% increase in healthcare costs for adolescents with moderate-to-severe depressive symptoms compared with adolescents who screened negative for depression.

Most cost-of-illness studies, including the ones included in the meta-analysis, only calculated direct healthcare costs, not taking into account indirect costs such as productivity loss or school absence. Besides, cost-of-illness studies often use a so-called top-down approach in which the cost estimation is based on registrations. A bottom-up cost-of-illness approach is considered to be more precise and reliable, because data are collected at patient level (Hakkaart-van Roijen, Van der Linden, Bouwmans, Kanters, & Tan, 2015). In 2018, we conducted a cost-of-illness study using a societal perspective to estimate both direct and indirect costs of clinically depressed adolescents aged 12–21. Bottom-up acquired costs were measured by means of cost-questionnaires. Our calculations showed that clinically depressed adolescents referred to treatment cost the Dutch society €37.7 million a year, with the annual costs per family being €14,795 (Bodden et al., 2018). Our study also showed the importance of including indirect costs, because a large proportion of costs was due to productivity loss of the parents (9% of total costs) and school absence (10% of total costs).

Given the high prevalence of subclinical depressive symptoms and the similar adverse consequences as depressive disorders, societal costs might be tremendous as well. No study has estimated both direct and indirect costs using a bottom-up approach in adolescents with subclinical depressive symptoms yet. Therefore, the aim of this cost-of-illness study was to estimate costs of subclinical depressive symptoms in adolescents aged 11–18 years old. In this study, both direct and indirect societal costs were measured from a prevalence-based perspective and using a bottom-up approach in order to translate the societal burden of subclinical depressive symptoms into monetary costs.

Methods

Procedure and participants

In this cost-of-illness study, we used the baseline data of a cluster-randomized prevention microtrial with four parallel conditions that investigated the relative (cost)effectiveness of four Cognitive Behavioural Therapy (CBT)-components (cognitive restructuring, behavioural activation, problem solving and relaxation) and four different sequences of these components (Van den Heuvel, Bodden, Moerbeek, Smit, & Engels, 2019).

The inclusion criteria were: (a) age 10–20 years, (b) sufficient knowledge of the Dutch language and (c) an elevated level of depressive symptoms at screening (percentile score >75 on CDI-2). The exclusion criteria were (a) absence of adolescents' consent (and parental consent for adolescents aged younger than 16), (b) receiving treatment for mood- or anxiety-related problems and (c) acute suicide risk. Furthermore, to be included in the cost-of-illness study, a completed cost-questionnaire at baseline had to be available. In total, 237 adolescents (aged 11–18 years) and their parent(s) were eligible to participate. As it turns out, 14.3% ($n = 34$) of these adolescents met the criteria of a depressive disorder (MDD or

persistent depressive disorder) based on the Kiddie-Schedule for Affective Disorders and Schizophrenia, present and lifetime version (K-SADS-PL; Kaufman et al., 1997; Reichart, Wals, & Hillegers, 2000). Therefore, the sample was divided in two groups, namely (a) adolescents with elevated depressive symptoms (CDI-2 score >75 percentile) not meeting the DSM criteria for a depressive disorder, called the subclinical depression group ($n = 203$) and (b) adolescents with elevated depressive symptoms meeting the diagnostic criteria of a depressive disorder (based on the K-SADS), called the clinical depression group ($n = 34$). Demographic characteristics for the total sample of adolescents and the two subgroups separately are displayed in Table 1. The subgroups did not differ in terms of gender, $\chi^2 = 0.3$, $p > .05$, age, $F = 1.5$, $p > .05$, ethnicity, $\chi^2 = 2.5$, $p > .05$ and educational level, $\chi^2 = 1.0$, $p > .05$. For the main analyses, only the subclinical depression sample was used as the aim of this study was to examine the cost-of-illness of adolescents with subclinical depressive symptoms.

Of the parents in the subclinical depression group, 135 (66.5%) were mothers and 68 (33.5%) fathers, with a mean age of 47.3 years ($SD = 4.7$, range 35–71). In the clinical depression group, 28 (82.4%) were mothers and 6 (17.6%) fathers, with a mean age of 46.7 years ($SD = 4.9$, range 37–58). The subgroups did not differ in terms of gender, $\chi^2 = 3.4$, $p > .05$ and age, $F = 0.4$, $p > .05$. Parents were predominantly biological parents (96%) and the remaining foster- and step parents. Most families had the Dutch nationality (98%).

Adolescents were screened for depressive symptoms at school. When they had elevated levels of depressive symptoms, these adolescents and their parents were approached for the overarching research examining the effectiveness of an indicated prevention programme. Written informed consent was obtained by the adolescents and their parent(s) for their own participation. When adolescents were younger than 16 years old, their parents also provided informed consent for their child. More information about the procedure can be found in Van den Heuvel et al. (in press). The study was approved by the Medical Ethics Committee CMO Region Utrecht in The Netherlands (NL59152.041.16) and registered in the Dutch Trial Register (Trial NL5584/NTR6176).

Table 1 Baseline demographic variables of adolescents for the total sample and subclinical and clinical depression group

Variable	Total ($n = 237$) M (SD)	Subclinical depression group ($n = 203$) M (SD)	Clinical depression group ($n = 34$) M (SD)
Age (years)	13.69 (1.44)	13.65 (1.42)	13.97 (1.53)
	n (%)	n (%)	n (%)
Gender			
Girls	129 (54.4)	109 (53.7)	20 (58.8)
Boys	108 (45.6)	94 (46.3)	14 (41.2)
Ethnicity			
Dutch	223 (94.1)	193 (95.1)	30 (88.2)
Other	14 (5.9)	10 (4.9)	4 (11.8)
Education level			
Low	14 (5.9)	11 (5.4)	3 (8.8)
Moderate	98 (41.4)	86 (42.4)	12 (35.3)
High	125 (52.7)	106 (52.2)	19 (55.9)

Low: prevocational secondary education (in Dutch: vmbo-basis/kader/gl), moderate: higher general secondary education (in Dutch: vmbo-tl, vmbo-tl/havo, havo), high: preuniversity education (in Dutch: havo/vwo, vwo).

Cost-questionnaire

We used the same cost-questionnaire as in the cost-of-illness study in clinically referred depressed adolescents (Bodden et al., 2018). A copy of the cost-questionnaire has been added in Appendix S1. The cost-questionnaire was completed retrospectively and covered a period of three months. For the purpose of this cost-of-illness study, we used the questionnaire filled out prior to the intervention. The assessment took place in the winter (December–March) between 2017 and 2019. Questionnaires were filled out by one of the parents; if both parents filled out the questionnaire, we merged the information of both questionnaires into a mean score. The cost-questionnaire consists of instructions, an example and 15 resources which cover all societal costs relevant for adolescents with depressive symptoms. The 15 resources can be divided into four categories of resource use; direct healthcare costs, direct nonhealthcare costs, indirect costs and out-of-pocket costs. Direct healthcare costs are costs related to visits to healthcare professionals (e.g. psychologist, psychiatrist), alternative care (e.g. reiki, reflexology), (partial) day treatment, general practitioner, outpatient consultations at the hospital, medical examinations (e.g. blood and urine test), medication with a prescription (e.g. antidepressants, sleep medication), medication without a prescription (e.g. painkillers) and hospitalization at a hospital or mental health care facility. Direct nonhealthcare costs are costs related to professional (formal) care (e.g. paid house help, after school care, homework counselling) and informal care (persons near the family, such as relatives or friends taking over some domestic tasks or stays with the adolescent or siblings in absence of the parents). Indirect costs are costs related to productivity losses due to absence of work (both adolescent and parent), loss of household activities or voluntary work by the parents, loss of leisure time by the parents and adolescent school absence. The so-called out-of-pocket costs are costs including 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 healthcare services and medication, which are not fully reimbursed by health insurance companies.

Also, on a family level, the parent(s) reported for whom the resource use was applicable (adolescent, sibling, mother or father) and the reason for the resource use by that family member (for example; a mother reporting her child's visit to general practitioner, because he/she felt down and could not sleep). The reasons can be categorized into due to (a) depressive symptoms, (b) (other) psychological problems, (c) behavioural problems, (d) physical problems and (f) other reasons. For the cost-of-illness analysis, only resource use related to the depressive symptoms of the adolescent were included. Costs were calculated at family level (costs per family with an adolescent with subclinical depressive symptoms) and at a societal level (costs for society as a whole) per 3 months and per year. In a previous study investigating the cost-effectiveness of children with anxiety disorders, this cost-questionnaire has shown good discriminant validity (Bodden, Dirksen, & Bögels, 2008).

Costs

Costs were calculated by multiplying the frequency of resource use obtained in the cost-questionnaire (e.g. total visits to GP) by the unit price of that specific resource (e.g. the cost price of a GP visit). Cost prices were determined by using standardized unit prices from Dutch guidelines (Drost, Paulus, Ruwaard, & Evers, 2014; Hakkaart-van Roijen et al., 2015). The reference year was 2017 (€1 = \$1.06, January 2017), the start of study inclusion. Unit prices consist of personnel, material and capacity costs, as well as costs of housing and overhead. Medication prices were calculated per person and were based

on the Daily Defined Dosage (DDD; 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 (2020). In this database, both a low (minimum) and high (maximum) cost price is calculated. In the all analysis, the low medication prices were used. Unit prices of alternative care and medication without a prescription were based on the filled out own contribution in the cost-questionnaire. If own contribution was missing, actual costs of alternative care and medication were calculated based on the mean costs displayed on multiple internet sites.

Unit prices of informal care, loss of leisure time, volunteer work and household activities were determined by the 'shadow price' as stated in the Dutch guidelines (€14 per hour; Hakkaart-van Roijen et al., 2015). To determine the unit prices associated with absence from school, standardized unit prices from a Dutch guideline were used (€8.30 per hour; Drost et al., 2014). Productivity costs of parents because of absence of paid work were calculated by means of the friction costs method (women €31.60, men €37.90; Hakkaart-van Roijen et al., 2015). The same method was used in previous cost-of-illness studies (Bodden et al., 2008, 2018).

Cost-of-illness

Costs were estimated by multiplying the reported unit prices by the unit prices of each resource. These 3-months costs per family were extrapolated to a period of one year by multiplying the costs by four, under the assumption that data obtained in the cost-questionnaires were representative for that period. The Dutch prevalence rate of subclinical depressive symptoms among adolescents was calculated from the sample of our overarching study. In the overarching study, 2,009 out of 8,603 adolescents were identified as having elevated levels of depressive symptoms (23.4%). However, 44 of those 2009 (2.2%) adolescents were excluded from this study, because they already received treatment for their suicidal or depressive symptoms, resulting in 1,965 adolescents with elevated levels of depressive symptoms without being in treatment (Van den Heuvel et al., in press). Dividing the 1,965 adolescents by 8,603 results in a percentage of 22.8%, which was used as a prevalence rate for adolescents with subclinical depressive symptoms. The annual costs per family were then multiplied by this prevalence rate (22.8%). As a result, the total annual societal cost-of-illness of Dutch families of adolescents with subclinical depressive symptoms could be calculated.

Analyses

Missing items (2%) in the cost-questionnaires were handled with the Missing Value Analysis of SPSS based on regression models (single imputation). Kolmogorov–Smirnov tests were performed to investigate whether data were normally distributed. Since cost distributions were highly skewed, 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 1,000 simulations, based on sampling with replacement from the original data (Briggs, Wonderling, & Mooney, 1997). Secondary analyses were done to test the robustness of the findings. First, costs related to psychological problems were calculated given the fact that parents sometimes describe depressive symptoms as stress symptoms or other psychological complaints, while these costs can partially be attributed to depressive symptoms. Second, physical complaints such as headache and stomach ache often co-occur with depressive symptoms (Birmaher et al., 2007), which might cause more medical care and could also partially be explained by depressive symptoms. Therefore, costs related to physical complaints

were calculated as well. Third, all costs related to depressive, psychological, behavioural and physical problems and other reasons related to the adolescent were calculated. Fourth, the cost-of-illness analysis was repeated with an international prevalence rate of 29.2% for subclinical depressive symptoms among adolescents under the age of 18 (Carrellas et al., 2017). Fifth, as we identified a subgroup of adolescents with subclinical levels of depressive symptoms but also meeting a depressive disorder, we estimated the costs of this subgroup ($n = 34$) as well, using the Dutch prevalence rate of 3.8% (Meijer et al., 2006). In order to provide an insight in the possible differences in the annual costs per family between the subclinical and clinical depression group, an ANOVA was used.

Results

Cost-of-illness of subclinical depressive symptoms

All care consumption used and costs made within the family related to the subclinical depressive symptoms of the adolescent were summed up and averaged over the reported 3-month period. The average costs per family with an adolescent with subclinical depressive symptoms were €32.53 ($SD = 165.08$). These costs were extrapolated to a year and amounted to €130.13 per family a year. Costs were not normally distributed, $D(203) = .48$, $p < .001$ and ranged between €0 to €5,883.84. Only 20 out of 203 families (10%) reported costs related to depressive symptoms. The majority of those 20 families had costs related to school absence (36%), mental health care (24%), homework counselling (21%), loss of leisure time/volunteer work of the parents (12%) and visits to the GP (6%).

The total number of Dutch adolescents in the age of 12–18 years old was 1,432,307 in 2017 (Central Bureau for Statistics (CBS), 2020). This number was multiplied by our prevalence rate of subclinical depressive symptoms which was 22.8% and resulted in an estimate of 326,566 adolescents with subclinical depressive symptoms. Hence, the annual societal cost-of-illness could be calculated by multiplying the number of adolescents with subclinical depressive symptoms (326,566) by the annual costs per family (€130.13), which resulted in €42,496,033.58. This implies that adolescents with subclinical depressive symptoms cost the Dutch society annually approximately €42 million. All costs of the subclinical depression group can be found in Table 2.

Secondary analyses

Psychological problems. The average costs per family with an adolescent with subclinical depressive symptoms related to psychological problems were €51.47 ($SD = 173.32$), which is annually €205.86 per family. Costs were not normally distributed, $D(203) = .39$, $p < .001$ and ranged between €0 to €5,774.80. The total societal costs a year summed up to €67,226,876.76. This implies that adolescents with subclinical depressive symptoms

Table 2 Subtotal and total 3-months costs (in Euros) per family with an adolescent with subclinical depressive symptoms ($n = 203$) related to depressive, psychological, behavioural and physical problems of the adolescent, including total annual costs per family and for society

	Total <i>M (SD)</i>	Reason depression <i>M (SD)</i>	Reason psychological <i>M (SD)</i>	Reason behavioural <i>M (SD)</i>	Reason physical <i>M (SD)</i>
Direct healthcare costs					
Mental healthcare professional	30.72 (126.77)	7.85 (48.37)	21.51 (112.95)	1.35 (11.32)	0.00 (0.00)
Alternative healthcare professional	5.94 (37.68)	0.00 (0.00)	1.96 (19.04)	0.00 (0.00)	3.98 (30.28)
General practitioner	11.21 (27.49)	1.96 (9.81)	2.37 (11.61)	0.25 (3.51)	6.64 (23.01)
Hospital/policlinic visit	5.44 (26.42)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	5.44 (26.42)
Medical examination	2.39 (12.82)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	2.39 (12.82)
Medication prescribed (low price)	3.42 (16.13)	0.00 (0.00)	2.16 (12.44)	0.33 (4.75)	0.93 (8.30)
Medication prescribed (high price)	5.43 (27.88)	0.00 (0.00)	3.68 (23.22)	0.33 (4.75)	1.42 (14.46)
Direct non-healthcare costs					
Informal care	1.24 (15.83)	0.00 (0.00)	1.10 (15.72)	0.00 (0.00)	0.00 (0.00)
Homework counselling	10.38 (110.03)	6.92 (98.61)	2.13 (30.32)	0.00 (0.00)	0.00 (0.00)
Indirect costs					
School absence	87.29 (179.46)	11.61 (95.60)	0.41 (4.80)	0.00 (0.00)	74.33 (157.99)
Paid work	3.19 (10.71)	0.16 (2.22)	1.45 (7.45)	0.00 (0.00)	1.25 (6.16)
Loss of leisure time/unpaid work	4.93 (40.86)	4.03 (40.48)	0.14 (1.97)	0.28 (3.93)	0.07 (0.98)
Out-of-pocket costs					
Own contribution mental health care	0.34 (4.91)	0.00 (0.00)	0.34 (4.91)	0.00 (0.00)	0.00 (0.00)
Own contribution alternative health care	3.00 (20.25)	0.00 (0.00)	1.33 (13.81)	0.00 (0.00)	1.67 (14.96)
Own contribution medication	0.57 (6.30)	0.00 (0.00)	0.57 (6.30)	0.00 (0.00)	0.00 (0.00)
Medication not prescribed (low price)	2.46 (22.45)	0.00 (0.00)	2.45 (22.45)	0.00 (0.00)	0.01 (0.11)
Medication not prescribed (high price)	4.57 (31.75)	0.00 (0.00)	4.52 (31.75)	0.00 (0.00)	0.05 (0.65)
Own contribution medication not prescribed	0.27 (2.73)	0.00 (0.00)	0.12 (1.75)	0.00 (0.00)	0.15 (2.11)
Own costs homework counselling	13.42 (106.71)	0.00 (0.00)	13.42 (106.71)	0.00 (0.00)	0.00 (0.00)
Total 3-months costs per family					
Low medication price	168.62 (306.94)	32.53 (165.08)	35.68 (129.51)	2.21 (16.91)	95.03 (174.50)
High medication price	172.75 (309.93)	32.53 (165.08)	39.27 (136.62)	2.21 (16.91)	95.57 (174.91)
Own contribution	17.61 (108.38)	0.00 (0.00)	15.79 (107.60)	0.00 (0.00)	1.82 (15.09)
Low medication price + own contribution	186.23 (339.53)	32.53 (165.08)	51.47 (173.32)	2.21 (16.91)	96.86 (176.15)
Bootstrapped	185.51 (24.09)	32.22 (11.97)	51.54 (11.94)	2.24 (1.19)	96.57 (12.48)
Total annual costs ^a					
Per family	744.93 (1358.11)	130.13 (660.32)	205.86 (693.29)	8.84 (67.64)	387.43 (704.59)
Societal costs	243,268,810.38	42,496,033.58	67,226,876.76	2,886,843.44	126,521,465.38

Total is all problems and other reasons.

^a4 × 3-months costs per family low medication price + own contribution (non-bootstrapped).

cost our society yearly around €67 million because of costs related to psychological problems.

Physical problems. The average costs per family with an adolescent with subclinical depressive symptoms related to physical problems were €96.86 ($SD = 176.15$), which is annually €387.43 per family. Costs were not normally distributed, $D(203) = .29$, $p < .001$ and ranged between €0 to €5,423.84. The calculated total societal costs a year were €126,521,465.38, implying that adolescents with subclinical depressive symptoms cost our society yearly approximately €126 million because of costs related to physical problems.

All costs. All costs related to depressive, psychological, behavioural and physical problems and other reasons for a 3-month period were summed up and amounted to €186.23 ($SD = 339.53$) per family with an adolescent with subclinical

depressive symptoms, which is annually €744.93. Costs were not normally distributed, $D(203) = .29$, $p < .001$ and ranged between €0 to €11,164.96. Multiplying these costs with the amount of adolescents with subclinical depressive symptoms (326,566) led to total annual societal costs of €243,268,810.38. This suggest that adolescents with subclinical depressive symptoms cost the Dutch society yearly around €243 million because of depressive, psychological, behavioural and physical problems and other reasons. The total costs were highest for physical related problems (52% of the total costs), followed by psychological (28%), depressive (17%) and behavioural problems (1%).

Cost-of-illness using an international prevalence rate. The cost-of-illness analysis was repeated using an international prevalence rate of 29.2% for subclinical depressive symptoms (Carrellas et al., 2017). This prevalence rate was multiplied by the

total number of Dutch adolescents in the age of 12–18 years old (1,432,307; CBS, 2020). This resulted in 418,234 adolescents with subclinical depressive symptoms. This number was multiplied by the annual costs related to depressive problems per family (€130.13). Hence, the annual cost-of-illness resulted in €54,424,790.42. This indicates that when an international prevalence rate was used, the annual societal costs for adolescents with subclinical depressive symptoms are 1.28 times higher compared with the main analysis in which the Dutch prevalence rate was used.

Cost-of-illness of adolescents with a clinical depressive disorder. Since we identified a subgroup of adolescents meeting the diagnostic criteria of a depressive disorder, we calculated costs separately for this subgroup. The average costs per family with an adolescent with a clinical depressive disorder were €123.76 ($SD = 240.76$), which is €495.04 per family annually. Costs were not normally distributed, $D(34) = .31$, $p < .001$ and ranged between €0 to €4,200.00. The total number of Dutch adolescents in 2017 (1,432,307) was multiplied by the prevalence rate of adolescents with clinical depressive disorder of 3.8% (Meijer et al., 2006) and resulted in an estimate of 54,428 adolescents with a clinical depressive disorder (meeting the DSM criteria). The annual societal costs resulted in €26,944,037.12. This implies that adolescents with a clinical depressive disorder cost the Dutch society annually approximately €27 million. All costs of the clinical depression group can be found in Table 3.

ANOVA analysis showed a significant difference in the costs of adolescents with subclinical depressive symptoms and adolescents with a depressive disorder, $F(1, 235) = 7.68$, $p = .006$. Annual costs per family of the depressive disorder group were 3.8 times as high as compared with the costs of families of an adolescent with subclinical depressive symptoms (€495.04/€130.13). However, from a societal point of view, costs of subclinical depressive symptoms are 1.5 times higher (€42 million) than costs of clinical depressive disorders (€27 million), since the prevalence rate of subclinical depressive symptoms is higher (22.8% vs. 3.8%).

Discussion

The goal of this bottom-up cost-of-illness study was to calculate the annual societal costs related to depressive symptoms in families of adolescents aged 11–18 years with subclinical depressive symptoms. The main results show that adolescents with subclinical depressive symptoms cost the Dutch society yearly more than €42 million, when considering costs related to depressive symptoms. When all costs are included, that is costs related to depressive, psychological, behavioural and physical problems

and other reasons, the total annual societal costs amounted to €243 million.

We estimated that the annual societal costs related to depressive symptoms were €42,496,033.58 for families with an adolescent with subclinical depressive symptoms. The average costs per family a year were €130.13, which is lower than those found in US studies from Guevera et al. (2003) and Wright et al. (2016), respectively \$2,555 and \$5,083 (in 2017 euros €2,410 and €4,795). The difference in costs can be explained by the differences in healthcare system and expenditures between the United States and the Netherlands. For example, the healthcare costs per capita are \$11,072 in the United States compared with \$5,496 in the Netherlands (Organisation for Economic Co-operation & Development, 2020). Also, in the United States, the healthcare prices are higher (Anderson, Hussey, & Petrosyan, 2019). The difference in costs could also be explained by the severity of the depressive symptoms. In the Guevera study, only adolescents with depressive disorders and in the Wright study, adolescents screened positive for depression were included. This assumes that the severity of depressive disorders is associated with higher costs. Indeed, secondary analyses revealed a significant difference in costs between adolescents with subclinical depressive symptoms and adolescents meeting the criteria of a depressive disorder. The annual costs per family of adolescents with a depressive disorder was 3.8 times as high as the costs of adolescents with subclinical depressive symptoms (€495.04 vs. €130.13). Also, in a similar cost-of-illness study, annual costs per family with a clinically referred depressed adolescent were €14,795 (Bodden et al., 2018). Compared with the annual costs per family with an adolescent with subclinical depressive symptoms, costs for a clinically referred depressed adolescent are almost 114 times as high. This indicates that more severe depressive symptoms are associated with higher costs; the cost per family being the lowest for subclinical depressive symptoms, increasing when the adolescent has a depressive disorder and being the highest for clinically referred depressed adolescents. This is in line with Wright et al. (2016) who also found a positive association between costs and severity of depressive symptoms.

So, the costs per family of an adolescent with subclinical depressive symptoms might seem lower. However, the Dutch prevalence rate of subclinical depressive symptoms (22.8%) is six times as high compared with the Dutch prevalence rate of depressive disorders (3.8%) resulting in higher societal costs, respectively €42,496,033.58 vs. €26,944,037.12. This indicates that societal costs related to subclinical depressive symptoms are 1.6 times higher than societal costs related to depressive disorders. Also, the societal costs for subclinical depressive symptoms (€42,496,033.58) are 1.1 times

Table 3 Subtotal and total 3-months costs (in Euros) per family with an adolescent meeting the criteria of a depressive disorder ($n = 34$) related to depressive, psychological, behavioural and physical problems of the adolescent, including total annual costs per family and for society

	Total <i>M (SD)</i>	Reason depression <i>M (SD)</i>	Reason psychological <i>M (SD)</i>	Reason behavioural <i>M (SD)</i>	Reason physical <i>M (SD)</i>
Direct healthcare costs					
Mental healthcare professional	264.48 (599.29)	77.60 (226.57)	181.32 (577.86)	5.56 (32.39)	0.00 (0.00)
Alternative healthcare professional	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)
General practitioner	13.65 (26.28)	4.41 (14.99)	0.00 (0.00)	0.00 (0.00)	9.24 (23.45)
Hospital/policlinic visit	18.56 (78.02)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	18.56 (78.02)
Medical examination	17.40 (70.01)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	17.40 (70.01)
Medication prescribed (low price)	9.15 (25.72)	0.00 (0.00)	7.71 (24.91)	0.00 (0.00)	1.44 (7.30)
Medication prescribed (high price)	12.16 (32.38)	0.00 (0.00)	10.72 (31.50)	0.00 (0.00)	1.44 (7.30)
Direct non-healthcare costs					
Informal care	2.88 (9.61)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)
Homework counselling	41.32 (240.95)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)
Indirect costs					
School absence	89.84 (124.15)	38.33 (91.17)	8.79 (25.19)	0.00 (0.00)	37.59 (105.92)
Paid work	5.76 (14.85)	1.95 (7.93)	0.00 (0.00)	1.02 (5.96)	2.79 (11.97)
Loss of leisure time/unpaid work	4.94 (20.06)	0.00 (0.00)	0.00 (0.00)	2.47 (14.41)	0.00 (0.00)
Out-of-pocket costs					
Own contribution mental health care	2.00 (9.03)	1.47 (8.57)	0.53 (3.09)	0.00 (0.00)	0.00 (0.00)
Own contribution alternative health care	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)
Own contribution medication	4.50 (18.72)	0.00 (0.00)	4.50 (18.72)	0.00 (0.00)	0.00 (0.00)
Medication not prescribed (low price)	0.03 (0.17)	0.00 (0.00)	0.03 (0.17)	0.00 (0.00)	0.00 (0.00)
Medication not prescribed (high price)	0.03 (0.17)	0.00 (0.00)	0.03 (0.17)	0.00 (0.00)	0.00 (0.00)
Own contribution medication not prescribed	1.15 (5.33)	0.00 (0.00)	1.15 (5.33)	0.00 (0.00)	0.00 (0.00)
Own costs homework counselling	41.74 (171.58)	0.00 (0.00)	0.00 (0.00)	24.09 (140.46)	0.00 (0.00)
Total 3-months costs per family					
Low medication price	468.01 (841.51)	122.29 (240.18)	197.85 (586.97)	9.05 (35.31)	87.02 (253.33)
High medication price	471.01 (847.17)	122.29 (240.18)	200.86 (593.10)	9.05 (35.31)	87.02 (253.33)
Own contribution	49.38 (171.20)	1.47 (8.57)	6.18 (21.75)	24.09 (140.46)	0.00 (0.00)
Low medication price + own contribution	517.39 (876.58)	123.76 (240.76)	204.02 (589.29)	33.14 (157.15)	87.02 (253.33)
Bootstrapped	518.54 (111.48)	124.20 (32.16)	203.39 (80.03)	33.10 (20.90)	86.89 (34.11)
Total annual costs ^a					
Per family	2069.55 (3506.31)	495.04 (963.02)	816.09 (2357.15)	132.54 (628.60)	348.08 (1013.31)
Societal costs	112,641,467.40	26,944,037.12	44,418,146.52	7,213,887.12	18,945,298.24

Total is all problems and other reasons.

^a4 × 3-months costs per family low medication price + own contribution (non-bootstrapped).

higher compared with the societal costs of adolescents who are clinically referred for their depressive disorder (€37,697,736.44). The societal costs increased even more when the cost-of-illness analysis was repeated with an international prevalence rate (29.2%, Carrellas et al., 2017) in secondary analysis. Then the total annual societal costs related to subclinical depressive symptoms were estimated to be €54,424,790.42. Moreover, given the fact that adolescents with subclinical depressive symptoms have a high risk of developing a clinical depressive disorder later in life (Smit et al., 2003), costs of subclinical depressive symptoms could be even

larger when future costs are taken into account. In a review of cost-of-illness studies on adult depression, annual direct costs per case ranged from \$244.09 to \$2,488.51 and indirect costs per case ranged from \$94.14 to \$5,360.99, combined total costs ranged from \$338.23 to \$7,849.50 (Luppa, Heinrich, Angermeyer, König, & Riedel-Heller, 2007). So, future costs of depressive symptoms could rise immensely when depressive symptoms turn into depressive disorders.

The tremendous costs of adolescents with subclinical depressive symptoms warrants effective prevention programmes. A part of €42 million a

year could be saved by offering adolescents with subclinical depressive symptoms an effective intervention (selective or indicated prevention). Cost-effectiveness studies should be conducted to shed more light on this issue. In our study, the most relevant cost drivers were costs related to school absence (36%), mental health care (24%), homework counselling (21%), loss of leisure time/volunteer work of parents (12%) and visits to the GP (6%). So, although these adolescents don't have a clinical depressive disorder, they do seek help and the depressive symptoms interfere with school and parents' life.

We calculated costs related to psychological problems, physical problems and all problems in secondary analyses. The total annual costs for families with an adolescent with depressive symptoms related to psychological problems resulted in €67,226,876.76, which is 1.6 times as high as the costs related to depressive symptoms. Since our sample consisted of adolescents with subclinical depressive symptoms, parents might not be able to differentiate well between depressive and psychological problems or could consider them to be the same. Only when parents mentioned depressive symptoms, did we classify them as reason depressive symptoms. Sleep problems and concentration problems were classified as psychological problems, because we did not know whether these were symptoms of depression, another disorder or mildly present. Besides, comorbid problems are often associated with depressive symptoms (Angold & Costello, 2001). Therefore, it is more likely that the exact total costs related to depressive symptoms could be in the range of 42–67 million.

The total annual costs related to physical problems amounted to €126,521,465.38. Physical symptoms such as weight gain or loss, decrease or increase in appetite, fatigue or loss of energy are criteria of the depressive disorder listed in the DSM-V (American Psychiatric Association, 2013). Also other physical complaints such as headaches and stomach aches often co-occur with depressive symptoms, especially among children and adolescents (Birmaher et al., 2007; Masi, Favilla, Millepiedi, & Mucci, 2000; Romero-Acosta et al., 2013). Many adolescents tend to express emotional problems through psychical problems, because they experience difficulties in expressing their feelings and have low emotional awareness (Stewart, 2003). Because of these physical problems, adolescents with subclinical depressive symptoms might stay home more often and refuse to go to school but also seek more medical care, increasing societal costs.

When all costs were taken into account (depressive, psychological, behavioural and physical problems and other reasons), the total annual costs amounted to €243,268,810.38. Costs were highest for physical related problems (52%), followed by psychological (28%), depressive (17%) and

behavioural (1%). This stresses the importance of adequate screening for depressive symptoms as depressive symptoms might be expressed in a different way.

The strength of this study is that this is one of the first studies estimating cost-of-illness of subclinical depressive symptoms among adolescents. Usually cost-of-illness of psychiatric disorders are estimated. However, the prevalence rate of subclinical levels is higher, suggesting more societal impact. Besides, very few cost-of-illness studies estimate indirect costs (Luppa et al., 2007). In our study, both direct and indirect costs including school absenteeism were estimated. Also, not only costs related to depressive symptoms but also costs related to psychological, behavioural and physical problems were estimated and a bottom-up approach was used, increasing the reliability of the findings.

This study also has some limitations. First, no recent Dutch prevalence rate of subclinical depressive symptoms was found. So, we used the prevalence rate of our overarching study, which was comparable to the prevalence rate of Kramer (2000). However, this study was not designed as a prevalence study. Second, the estimates in this study may be biased because this cost-of-illness study was part of a prevention trial, which limits generalizability to the Dutch population of adolescents with subclinical depressive symptoms. Participation in a trial demonstrates motivation to reduce depressive symptoms. These families may also be more willing to incur costs, suggesting a selection bias. Also, our sample was not representative of the full population of Dutch adolescents in terms of age, ethnicity and school level, as mainly young, highly educated adolescents with a Dutch ethnicity participated. Third, the 3-months costs per family were extrapolated to a one-year period by multiplying the costs by four, under the assumption that the data obtained in the cost questionnaires were representative of that period. However, this could be inaccurate since most questionnaires were completed in winter. Costs per year might have been overestimated due to seasonality of symptoms and costs. Fourth, we did not calculate long term costs. Since adolescents with subclinical depressive disorders have a high risk of developing a depressive disorder, it could be assumed that the costs related to adolescents with a clinical depression and referred to treatment (€37.7 million) could partially be an estimation for future costs.

Conclusion

This cost-of-illness study shows that the annual societal costs of Dutch families with an adolescent with subclinical depressive symptoms are enormous and are estimated to be more than €42 million. Given the high risk of future costs related to clinical depression, the high prevalence rate and the high

burden of disease, the need for cost-effective prevention programmes seems warranted.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article:

Appendix S1. Cost questionnaire.

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Key points

- Societal costs related to adolescent subclinical depressive symptoms are unknown.
- Adolescent subclinical depressive symptoms cost the Dutch society €42 million a year.
- All costs combined (related to depressive, psychological, behavioural and physical problems and other reasons) amounted to €243 million a year.
- Total costs were highest for physical related problems (52%) followed by psychological (28%), depressive (17%) and behavioural problems (1%).
- The magnitude of costs and risk of future costs, warrants cost-effective depression prevention programs for adolescents with subclinical depressive symptoms.

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