Supplemental 1: Quality assessment

Quality criteria for studies that described costs of interventions. Adapted from Stuhldreher et al (2013).

Criterion	Description
Scope	
Study objective	The objective(s) of the study was (were) defined.
Inclusion and exclusion criteria	Clear and objective inclusion and exclusion criteria were defined.
Disease and diagnostic criteria	The disease and its objective diagnostic criteria (ICD, DSM or valid disease-specific instruments) that were used to identify eligible patients were reported.
Non-depressed comparison group	The study included a non-depressed control group in order to calculate excess costs.
Calculation of costs	
Currency	The currency in which the costs were calculated was reported in the text or was uncontroversial.
Reference year	All costs were valued at the price level of a stated base year (and inflated if necessary).
Perspective	The costs were analysed from the perspective of a patient, a payer or the society, the characteristics of the respective perspective were incorporated and the perspective was reported.
Costs incorporated from at least two major categories	The study estimated costs from the utilization of different kinds of health care services, but at least of two of the categories inpatient, outpatient, medication or indirect services, in order to consider at best all costs that accrue from the disease under study.
Data source	The source of information on healthcare utilization or costs was reported.
Valuation of costs	If data on healthcare utilization was collected, the source of unit costs was reported, in case cost data were used these reflected actual charges.
Study design and analysis	
Missing data, imputation method	The proportion of missing data was reported and the way it was dealt with (e.g. imputation method) was described.
Sensitivity analyses	Relevant parameters were varied in univariate and/or probabilistic sensitivity analyses in order to test the robustness of the results.
Presentation of results	
Sample size (subgroup)	The sample size of each group was reported.
Demographics	The characteristics of the sample were described; at least age and gender were reported.
Arithmetic mean costs	The cost estimates were presented as arithmetic means.
Standard deviations	Standard deviations of cost estimates were reported as a measure of variability or could be obtained by reported standard errors or confidence intervals.
Discussion	
Results discussed with respect to other studies	The results were discussed in relation to other studies on the same topic, if any.
Limitations discussed	The limitations regarding in particular the calculation of costs were discussed in detail.

Reference	**Arnow et al 2009[a]**	**Bosmans et al 2010**	**Brillemann et al 2013**	**Carstensen et al 2012**	**Carta et al 2003**	**Chiu et al 2017**	**Choi et al 2014[b]**	**Druss et al 2000**	**Gameroff et al 2006**	**Garis et al 2002**	**Greenberg et al 2015**	**Hamre et al 2010**	**Hsieh et al 2017**	**McTernan et al 2013**	**Shvartzman et al 2005**	**Simon et al 1995**	**Stamm et al 2010**	**Thomas et al 2005**	**Trivedi et al 2004**	**Woo et al 2011**	**Alexandre et al 2016**	**Bock et al 2014**	**Bock et al 2016**	**Callahan et al 1994**	**Callahan et al 1997**	**Fischer et al 2002**	**Katon et al 2003**	**Ludvigsson et al 2018**	**Luppa et al 2013**	**Prina et al 2014**	**Vasiliadis et al 2013**
Subgroup[c]	**1**																				**2**										
Study objective	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Inclusion and exclusion criteria	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Disease and diagnostic criteria	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Non-depressed comparison group	✓	✓	✓	X	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Currency	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Reference year	X	✓	✓	✓	X	✓	✓	✓	X	✓	✓	✓	✓	✓	X	X	✓	✓	✓	X	✓	✓	✓	X	X	✓	X	✓	✓	X	✓
Perspective	X	X	X	X	X	X	X	✓	✓	X	✓	✓	X	X	X	X	✓	X	✓	X	X	✓	✓	X	X	X	X	X	✓	X	✓
Costs incorporated from at least 2 major categories	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X	✓	✓	✓	✓	✓	X	✓	✓	✓	X	X	X	✓	✓	✓	X	✓
Data source	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Valuation of costs	✓	✓	✓	✓	X	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Missing data, imputation method	X	X	✓	X	X	✓	✓	X	X	X	X	✓	✓	X	✓	X	X	X	X	✓	✓	✓	✓	X	X	X	X	✓	✓	X	✓
Sensitivity analyses	X	X	X	X	✓	X	X	X	X	X	✓	✓	✓	X	X	X	X	X	X	X	✓	✓	✓	X	✓	X	X	✓	X	X	X
Sample size (subgroup)	✓	✓	✓	✓	X	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Demographics	✓	✓	✓	✓	X	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Arithmetic mean costs	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Standard deviations	✓	✓	✓	X	✓	✓	✓	X	✓	✓	✓	✓	✓	X	✓	✓	✓	X	X	✓	✓	✓	✓	✓	X	X	✓	✓	✓	✓	✓
Results discussed with respect to other studies	✓	✓	✓	✓	✓	✓	✓	X	✓	X	X	✓	✓	✓	✓	✓	✓	✓	X	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Limitations discussed	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X	✓	X	✓	✓	✓	X	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Rate of criteria each study fulfilled (%)	**78 %**	**83%**	**83%**	**72%**	**67%**	**89%**	**89%**	**78%**	**83%**	**78%**	**89%**	**100 %**	**89%**	**72%**	**78%**	**72%**	**89%**	**78%**	**61%**	**78%**	**94%**	**100 %**	**100 %**	**72%**	**72%**	**72%**	**78%**	**94%**	**94%**	**72%**	**94%**

Reference	Guevara et al 2003	Wright et al 2016	Adam et al 2017	Dagher et al 2012	Edoka et al 2011	Egede et al 2002	Engel et al 1996	Finkelstein et al 2003	Frasure-Smith et al 2000	Gilmer et al 2005	Morgan et al 2008	Petrou et al 2003	Rayner et al 2016	Rosenzweig et al 2002	Rutledge et al 2009	Sullivan et al 2002	Williams et al 2005	Rate of studies that fulfilled the respective criterion (%)
Subgroup[c]	**3**		**4**															
Study objective	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	**100%**
Inclusion and exclusion criteria	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X	**98%**
Disease and diagnostic criteria	✓	✓	✓	✓	✓	✓	✓	✓	✓	X	✓	✓	✓	X	✓	X	✓	**91%**
Non-depressed comparison group	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	**98%**
Currency	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X	**98%**
Reference year	✓	✓	X	✓	✓	✓	X	✓	X	✓	✓	✓	✓	X	✓	✓	X	**69%**
Perspective	✓	✓	X	X	✓	✓	X	X	X	✓	X	✓	X	X	X	✓	X	**35%**
Costs incorporated from at least 2 major categories	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	**88%**
Data source	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	**100%**
Valuation of costs	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X	**96%**
Missing data, imputation method	X	X	X	X	✓	X	X	X	X	✓	✓	X	X	X	X	X	X	**33%**
Sensitivity analyses	✓	✓	X	X	X	X	X	X	X	X	X	✓	X	X	✓	X	X	**27%**
Sample size (subgroup)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	**96%**
Demographics	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	**96%**
Arithmetic mean costs	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	**100%**
Standard deviations	X	✓	✓	✓	✓	X	✓	X	✓	✓	✓	X	✓	✓	✓	✓	✓	**79%**
Results discussed with respect to other studies	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X	**90%**
Limitations discussed	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X	**92%**
Rate of criteria each study fulfilled (%)	**89%**	**94%**	**78 %**	**83%**	**94%**	**83%**	**78%**	**78%**	**78%**	**89%**	**89%**	**89%**	**83%**	**72%**	**89%**	**83%**	**50 %**	**82%**

[a] Reports also data for depression as comorbidity.
[b] Reports also data for depressed and non-depressed in old age.
[c] 1= Depressed and non-depressed in adults; 2= Depressed and non-depressed in old age; 3= Depressed and non-depressed in adolescents; 4= Depression as comorbidity

Supplemental 2: Mean annual costs in 2017 US$-PPP (SD)

Reference	Direct costs												Indirect costs	
	Total direct costs		Inpatient treatment		Emergency treatment		Outpatient treatment		Medication		Others		Total indirect costs	
	D	ND	D	ND	D	ND	D	ND	D	ND	D	ND	D	ND
Depressed and non-depressed in adults														
Arnow et al 2009	**7,663** (10,068)	**5,024** (10,081)	**2,642** (6,349)	**1,573** (6,395)	**331** (438)	**165** (451)	**2,928** (–)	**1,943** (–)	**1,032** (1,705)	**713** (1,730)				
Bosmans et al 2010	**1,455** (1,169)	**335** (545)					**946** (–)	**192** (–)	**239** (365)	**12** (121)	**300** (–)	**132** (–)		
Brilleman et al 2013	**455** (725)	**227** (524)					**213** (245)	**111** (161)	**198** (569)	**87** (423)	**43** (118)	**30** (101)		
Carstensen et al 2012	**2,243** (–)	**668** (–)	**1,558** (–)	**435** (–)			**347** (–)	**110** (–)	**338** (–)	**123** (–)				
Carta et al 2003	**4,885** (2,674)	**1,012** (536)												
Chiu et al 2017	**2,969** (7,985)	**2,845** (10,715)	**1,067** (4,641)	**991** (5,598)	**124** (233)	**104** (532)	**894** (1,292)	**831** (3,470)			**884** (3,675)	**920** (4,002)		
Choi et al 2014	**9,256** (26,153)	**4,631** (15,767)	**2,685** (17,962)	**1,283** (9,674)	**333** (1,641)	**188** (1,083)	**3,173** (–)	**2,108** (–)	**2,732** (6,701)	**901** (2,944)	**333** (–)	**150** (–)		
Druss et al 2000	**5,496** (–)	**1,527** (–)											**2,024** (–)	**552** (–)
Gameroff et al 2006	**27,208** (156,885)	**9,034** (65,983)												
Garis et al 2002	**8,855** (13,769)	**984** (1,905)	**5,743** (–)	**370** (–)			**442** (–)	**233** (–)	**682** (–)	**103** (–)	**1,745** (–)	**164** (–)		
Greenberg et al 2015	**11,081** (21,833)	**4,688** (12,380)	**2,461** (14,877)	**1,167** (8,051)	**443** (1,741)	**190** (936)	**4,654** (10,473)	**2,190** (6,404)	**2,964** (5,322)	**989** (3,510)	**559** (3,946)	**153** (1,613)	**4,360** (7,895)	**1,444** (3,077)
Hamre et al 2010	**7,902** (15,203)	**3,972** (7,663)	**5,357** (14,844)	**2,203** (6,840)			**1,888** (–)	**1,283** (–)	**657** (–)	**485** (–)			**3,157** (7,491)	**1,921** (6,040)
Hsieh et al 2017	**950** (2,239)	**483** (1,938)												
McTernan et al 2013													**8,450** (–)	**6,650** (–)
Shvartzman et al 2005	**1,256** (4,707)	**656** (2,510)	**1,486** (4,026)	**176** (1,517)			**490** (2,090)	**303** (1,461)	**232** (815)	**175** (677)				
Simon et al 1995	**7,417** (12,501)	**4,142** (10,172)	**2,011** (–)	**1,296** (–)	**105** (447)	**47** (264)	**2,886** (–)	**1,485** (–)	**997** (1,115)	**409** (690)	**540** (935)	**377** (660)		
Stamm et al 2010	**6,500** (12,313)	**1,748** (1,749)	**3,136** (8,207)	**1,033** (6,022)					**694** (1,323)	**345** (848)				
Thomas et al 2005	**10,368** (–)	**4,443** (–)							**2,195** (–)	**672** (–)				
Trivedi et al 2004	**10,410** (–)	**2,429** (–)											**371** (–)	**218** (–)
Woo et al 2011													**21,873** (16,757)	**9,499** (7,400)
Depressed and non-depressed in old age														
Alexandre et al 2016	**18,913** (21,860)	**8,796** (13,048)												
Bock et al 2014	**23,135** (29,514)	**8,910** (17,812)	**6,036** (13,262)	**2,767** (11,165)			**2,116** (–)	**1,525** (–)	**2,721** (2,900)	**1,551** (1,994)	**12,262** (–)	**3,068** (–)		
Bock et al 2016	**13,573** (21,165)	**7,285** (14,132)	**4,914** (13,630)	**2,188** (8,090)			**2,016** (1,652)	**1,484** (1,308)	**1,991** (1,747)	**1,329** (1,540)	**4,653** (12,379)	**2,283** (9,666)		
Callahan et al 1994							**2,818** (3,028)	**1,750** (2,187)						
Callahan et al 1997											**2,448** (–)	**1,990** (–)		
Choi et al 2014	**20,271** (17,410)	**10,396** (16,944)	**9,167** (12,064)	**3,992** (12,774)	**324** (1,553)	**168** (659)	**4,653** (–)	**3,053** (–)	**4,538** (7,177)	**2,377** (4,126)	**1,589** (–)	**806** (–)		
Fischer et al 2002							**10,367** (–)	**7,154** (–)						
Katon et al 2003	**9,162** (14,906)	**5,751** (15,230)	**2,181** (8,681)	**1,366** (10,815)	**171** (315)	**103** (640)	**4,159** (–)	**2,766** (–)	**1,413** (–)	**792** (–)	**1,236** (–)	**724** (–)		
Ludvigsson et al 2018	**11,304** (12,380)	**8,588** (8,198)	**4,567** (5,481)	**3,677** (5,274)			**7,405** (–)	**5,139** (–)	**1,354** (832)	**1,205** (1,497)	**10,619** (–)	**7,617** (–)		

Reference	Direct costs												Indirect costs	
	Total direct costs		Inpatient treatment		Emergency treatment		Outpatient treatment		Medication		Others		Total indirect costs	
	D	ND	D	ND	D	ND	D	ND	D	ND	D	ND	D	ND
Luppa et al 2008	**7,962** (10,134)	**5,542** (8,894)	**3,171** (8,681)	**1,961** (5,609)			**585** (589)	**871** (3,168)	**2,142** (2,065)	**1,545** (3,111)	**2,065** (–)	**1,165** (–)		
Prina et al 2014			**8,043** (15,255)	**3,886** (9,776)										
Vasiliadis et al 2013	**3,008** (5,293)	**2,650** (5,049)	**563** (2,002)	**446** (2,184)			**981** (2,063)	**819** (1,855)	**1,115** (1,441)	**1,074** (1,636)	**348** (775)	**312** (582)		
Depressed and non-depressed in adolescents														
Guevara et al 2003	**3,993** (–)	**1,110** (–)	**1,274** (–)	**245** (–)										
Wright et al 2016	**5,348** (11,037)	**2,480** (8,019)	**1,135** (6,709)	**351** (4,735)	**667** (2,991)	**153** (843)	**4,213** (6,122)	**2,318** (4,768)	**548** (1,068)	**295** (1,301)	**205** (334)	**114** (501)		
Depression as comorbidity														
Adam et al 2017	**31,457** (57,500)	**19,812** (37,398)	**23,287** (54,984)	**11,414** (34,199)	**823** (2,093)	**1,069** (2,706)	**7,347** (7,104)	**7,328** (9,979)						
Arnow et al 2009	**9,748** (10,102)	**6,131** (10,196)	**2,717** (6,352)	**1,694** (6,391)	**353** (432)	**211** (454)	**3,271** (–)	**2,392** (–)	**1,856** (1,729)	**1,078** (1,737)				
Dagher et al 2012	**6,320** (20,845)	**2,206** (8,253)	**3,667** (20,414)	**481** (6,026)	**509** (1,247)	**80** (402)	**2,145** (–)	**1,644** (–)						
Edoka et al 2011	**737** (973)	**499** (1,191)	**266** (–)	**262** (–)			**472** (–)	**236** (–)						
Egede et al 2002	**17,902** (–)	**13,254** (–)	**13,957** (–)	**10,587** (–)	**485** (–)	**530** (–)	**1,274** (–)	**922** (–)	**1,927** (–)	**922** (–)	**260** (–)	**292** (–)		
Engel et al 1996											**4,948** (11,334)	**3,520** (6,692)		
Finkelstein et al 2003	**35,107** (–)	**14,339** (–)												
Frasure-Smith et al 2000	**4,764** (7,215)	**3,769** (6,880)	**786** (–)	**682** (–)	**191** (289)	**128** (223)	**661** (468)	**541** (381)						
Gilmer et al 2005	**14,521** (18,103)	**9,816** (10,421)												
Morgan et al 2008	**6,875** (11,988)	**5,031** (6,760)												
Petrou et al 2002	**1,888** (–)	**1,416** (–)	**715** (–)	**648** (–)			**1,173** (–)	**768** (–)						
Rayner et al 2016	**4,305** (10,444)	**2,636** (5,309)	**1,566** (9,589)	**595** (4,095)	**241** (657)	**147** (508)	**2,499** (–)	**1,902** (–)						
Rosenzweig et al 2002	**11,862** (18,730)	**7,110** (11,255)							**3,618** (2,329)	**2,625** (2,491)				
Rutledge et al 2009	**11,436** (–)	**8,861** (–)							**3,401** (1,605)	**2,808** (1,611)				
Sullivan et al 2002	**18,885** (13,586)	**15,667** (13,779)	**10,537** (10,670)	**9,791** (11,785)			**8,780** (4,401)	**5,881** (3,953)						
Williams et al 2005	**21,370** (22,784)	**25,329** (38,438)	**2,855** (15,163)	**3,579** (28,161)	**690** (–)	**306** (–)	**2,234** (–)	**2,067** (–)	**8,876** (9,293)	**11,835** (9,557)	**6,576** (–)	**5,495** (–)		

Supplemental 3: Forest plots of direct cost categories

Figure S3(1): Meta-analysis: Forest plot of outpatient excess costs

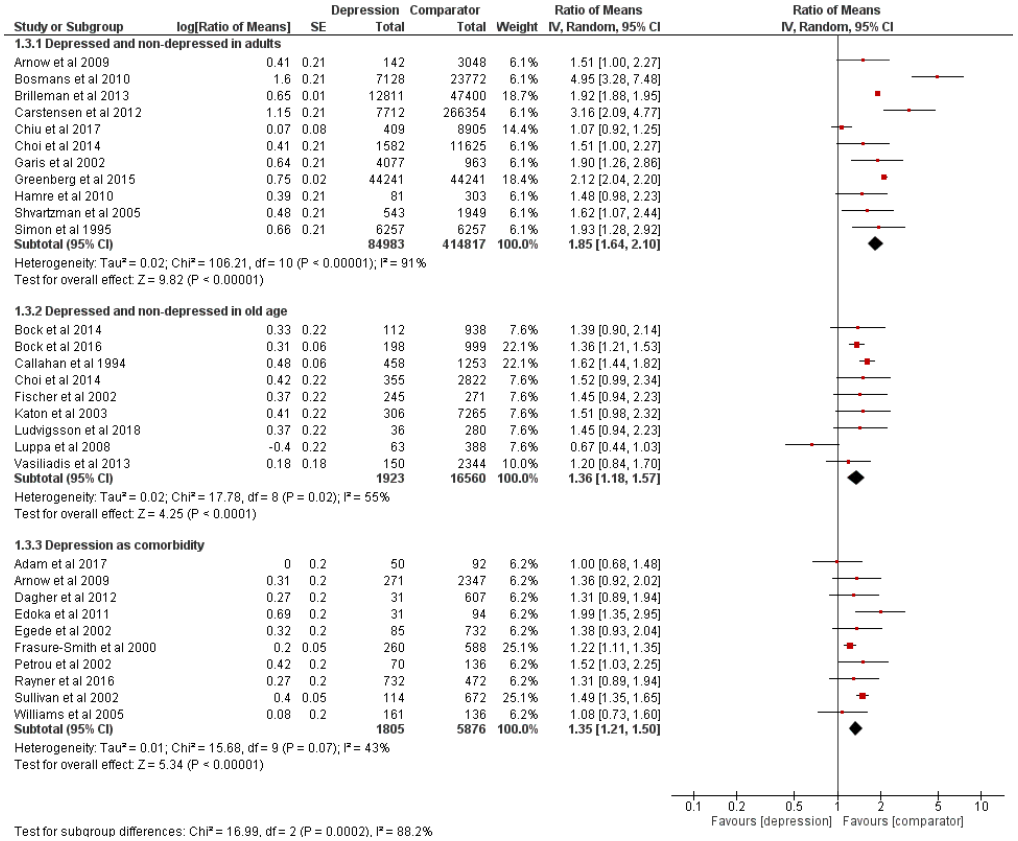


Figure S3(2): Meta-analysis: Forest plot of inpatient excess costs

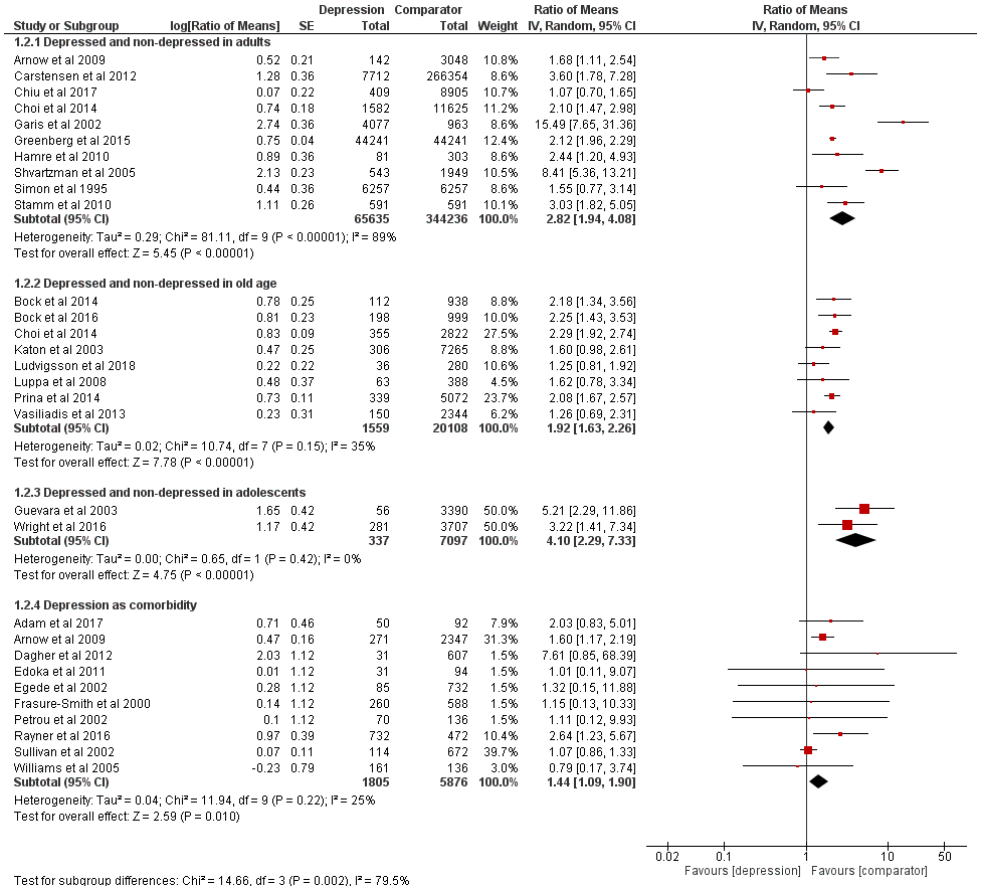
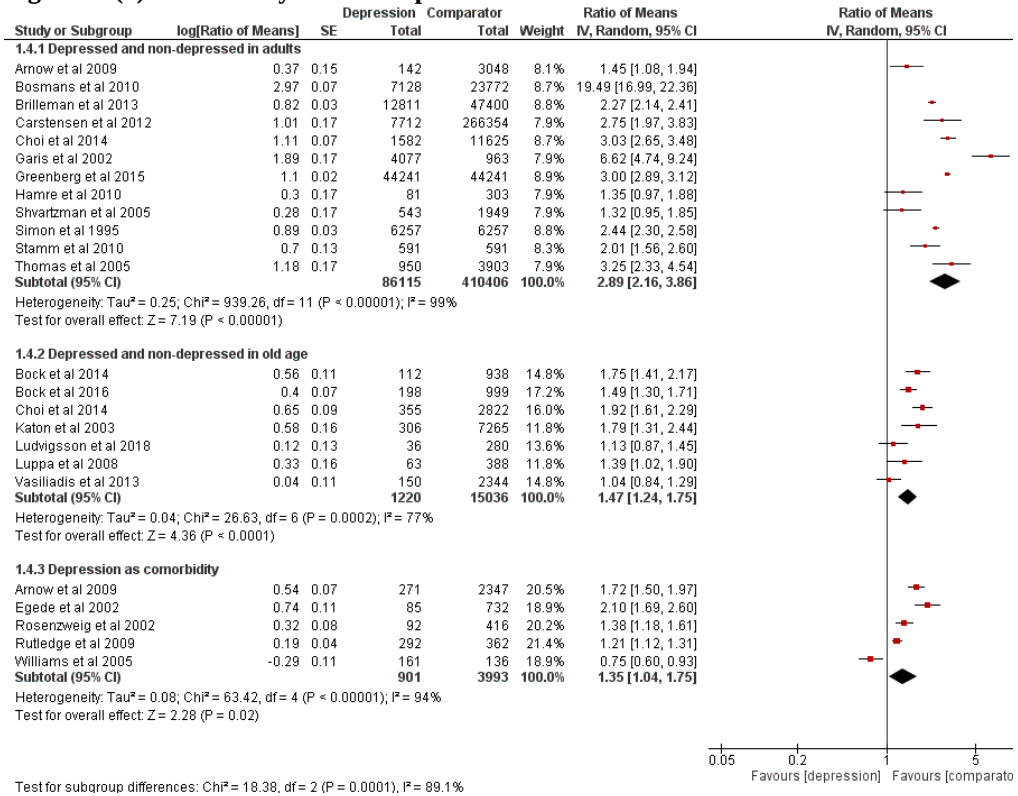


Figure S3(3): Meta-analysis: Forest plot of medication excess costs



Study or Subgroup	log[Ratio of Means]	SE	Depression Total	Comparator Total	Weight	Ratio of Means IV, Random, 95% CI
1.4.1 Depressed and non-depressed in adults						
Arnow et al 2009	0.37	0.15	142	3048	8.1%	1.45 [1.08, 1.94]
Bosmans et al 2010	2.97	0.07	7128	23772	8.7%	19.49 [16.99, 22.36]
Brilleman et al 2013	0.82	0.03	12811	47400	8.8%	2.27 [2.14, 2.41]
Carstensen et al 2012	1.01	0.17	7712	266354	7.9%	2.75 [1.97, 3.83]
Choi et al 2014	1.11	0.07	1582	11625	8.7%	3.03 [2.65, 3.48]
Garis et al 2002	1.89	0.17	4077	963	7.9%	6.62 [4.74, 9.24]
Greenberg et al 2015	1.1	0.02	44241	44241	8.9%	3.00 [2.89, 3.12]
Hamre et al 2010	0.3	0.17	81	303	7.9%	1.35 [0.97, 1.88]
Shvartzman et al 2005	0.28	0.17	543	1949	7.9%	1.32 [0.95, 1.85]
Simon et al 1995	0.89	0.03	6257	6257	8.8%	2.44 [2.30, 2.58]
Stamm et al 2010	0.7	0.13	591	591	8.3%	2.01 [1.56, 2.60]
Thomas et al 2005	1.18	0.17	950	3903	7.9%	3.25 [2.33, 4.54]
Subtotal (95% CI)			**86115**	**410406**	**100.0%**	**2.89 [2.16, 3.86]**
Heterogeneity: Tau² = 0.25; Chi² = 939.26, df = 11 (P < 0.00001); I² = 99%						
Test for overall effect: Z = 7.19 (P < 0.00001)						
1.4.2 Depressed and non-depressed in old age						
Bock et al 2014	0.56	0.11	112	938	14.8%	1.75 [1.41, 2.17]
Bock et al 2016	0.4	0.07	198	999	17.2%	1.49 [1.30, 1.71]
Choi et al 2014	0.65	0.09	355	2822	16.0%	1.92 [1.61, 2.29]
Katon et al 2003	0.58	0.16	306	7265	11.8%	1.79 [1.31, 2.44]
Ludvigsson et al 2018	0.12	0.13	36	280	13.6%	1.13 [0.87, 1.45]
Luppa et al 2008	0.33	0.16	63	388	11.8%	1.39 [1.02, 1.90]
Vasiliadis et al 2013	0.04	0.11	150	2344	14.8%	1.04 [0.84, 1.29]
Subtotal (95% CI)			**1220**	**15036**	**100.0%**	**1.47 [1.24, 1.75]**
Heterogeneity: Tau² = 0.04; Chi² = 26.63, df = 6 (P = 0.0002); I² = 77%						
Test for overall effect: Z = 4.36 (P < 0.0001)						
1.4.3 Depression as comorbidity						
Arnow et al 2009	0.54	0.07	271	2347	20.5%	1.72 [1.50, 1.97]
Egede et al 2002	0.74	0.11	85	732	18.9%	2.10 [1.69, 2.60]
Rosenzweig et al 2002	0.32	0.08	92	416	20.2%	1.38 [1.18, 1.61]
Rutledge et al 2009	0.19	0.04	292	362	21.4%	1.21 [1.12, 1.31]
Williams et al 2005	-0.29	0.11	161	136	18.9%	0.75 [0.60, 0.93]
Subtotal (95% CI)			**901**	**3993**	**100.0%**	**1.35 [1.04, 1.75]**
Heterogeneity: Tau² = 0.08; Chi² = 63.42, df = 4 (P < 0.00001); I² = 94%						
Test for overall effect: Z = 2.28 (P = 0.02)						

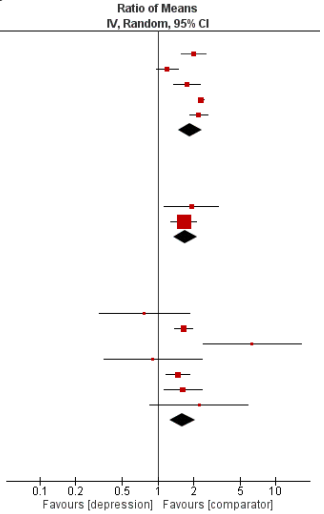
Ratio of Means IV, Random, 95% CI

0.05 0.2 1 5

Favours [depression] Favours [comparato

Test for subgroup differences: Chi² = 18.38, df = 2 (P = 0.0001), I² = 89.1%

Figure S3(4): Meta-analysis: Forest plot of emergency excess costs



Study or Subgroup	log[Ratio of Means]	SE	Depression Total	Comparator Total	Weight	Ratio of Means IV, Random, 95% CI
1.5.1 Depressed and non-depressed in adults						
Arnow et al 2009	0.7	0.12	142	3048	18.8%	2.01 [1.59, 2.55]
Chiu et al 2017	0.18	0.11	409	8905	19.4%	1.20 [0.97, 1.49]
Choi et al 2014	0.57	0.13	1582	11625	18.2%	1.77 [1.37, 2.28]
Greenberg et al 2015	0.85	0.03	44241	44241	23.0%	2.34 [2.21, 2.48]
Simon et al 1995	0.8	0.09	6257	6257	20.6%	2.23 [1.87, 2.65]
Subtotal (95% CI)			**52631**	**74076**	**100.0%**	**1.88 [1.49, 2.37]**
Heterogeneity: Tau² = 0.06; Chi² = 38.19, df = 4 (P < 0.00001); I² = 90%						
Test for overall effect: Z = 5.33 (P < 0.00001)						
1.5.2 Depressed and non-depressed in old age						
Choi et al 2014	0.66	0.27	355	2822	18.8%	1.93 [1.14, 3.28]
Katon et al 2003	0.51	0.13	306	7265	81.2%	1.67 [1.29, 2.15]
Subtotal (95% CI)			**661**	**10087**	**100.0%**	**1.71 [1.36, 2.16]**
Heterogeneity: Tau² = 0.00; Chi² = 0.25, df = 1 (P = 0.62); I² = 0%						
Test for overall effect: Z = 4.60 (P < 0.00001)						
1.5.3 Depression as comorbidity						
Adam et al 2017	-0.26	0.45	50	92	6.5%	0.77 [0.32, 1.86]
Arnow et al 2009	0.51	0.09	271	2347	30.0%	1.67 [1.40, 1.99]
Dagher et al 2012	1.85	0.49	31	607	5.7%	6.36 [2.43, 16.62]
Egede et al 2002	-0.09	0.49	85	732	5.7%	0.91 [0.35, 2.39]
Frasure-Smith et al 2000	0.4	0.12	260	588	26.8%	1.49 [1.18, 1.89]
Rayner et al 2016	0.49	0.19	732	472	19.7%	1.63 [1.12, 2.37]
Williams et al 2005	0.81	0.49	161	136	5.7%	2.25 [0.86, 5.87]
Subtotal (95% CI)			**1590**	**4974**	**100.0%**	**1.62 [1.27, 2.08]**
Heterogeneity: Tau² = 0.05; Chi² = 12.89, df = 6 (P = 0.04); I² = 53%						
Test for overall effect: Z = 3.82 (P = 0.0001)						

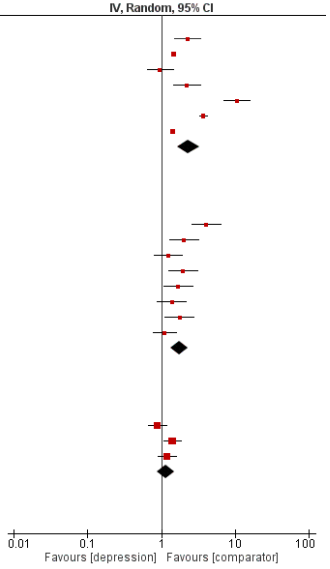
Ratio of Means IV, Random, 95% CI

0.1 0.2 0.5 1 2 5 10

Favours [depression] Favours [comparator]

Test for subgroup differences: Chi² = 0.73, df = 2 (P = 0.69), I² = 0%

Figure S3(5): Meta-analysis: Forest plot of other direct excess costs



Study or Subgroup	log[Ratio of Means]	SE	Depression Total	Comparator Total	Weight	Ratio of Means IV, Random, 95% CI
1.6.1 Depressed and non-depressed in adults						
Bosmans et al 2010	0.82	0.21	7128	23772	13.0%	2.27 [1.50, 3.43]
Brilleman et al 2013	0.39	0.03	12811	47400	16.1%	1.48 [1.39, 1.57]
Chiu et al 2017	-0.04	0.21	409	8905	13.0%	0.96 [0.64, 1.45]
Choi et al 2014	0.8	0.21	1582	11625	13.0%	2.23 [1.47, 3.36]
Garis et al 2002	2.36	0.21	4077	963	13.0%	10.59 [7.02, 15.98]
Greenberg et al 2015	1.3	0.06	44241	44241	15.8%	3.67 [3.26, 4.13]
Simon et al 1995	0.36	0.03	6257	6257	16.1%	1.43 [1.35, 1.52]
Subtotal (95% CI)			**76505**	**143163**	**100.0%**	**2.31 [1.65, 3.24]**
Heterogeneity: Tau² = 0.18; Chi² = 302.37, df = 6 (P < 0.00001); I² = 98%						
Test for overall effect: Z = 4.86 (P < 0.00001)						
1.6.2 Depressed and non-depressed in old age						
Bock et al 2014	1.39	0.23	112	938	12.3%	4.01 [2.56, 6.30]
Bock et al 2016	0.71	0.23	198	999	12.3%	2.03 [1.30, 3.19]
Callahan et al 1997	0.21	0.23	612	3155	12.3%	1.23 [0.79, 1.94]
Choi et al 2014	0.68	0.23	355	2822	12.3%	1.97 [1.26, 3.10]
Katon et al 2003	0.53	0.23	306	7265	12.3%	1.70 [1.08, 2.67]
Ludvigsson et al 2018	0.33	0.23	36	280	12.3%	1.39 [0.89, 2.18]
Luppa et al 2008	0.57	0.23	63	388	12.3%	1.77 [1.13, 2.78]
Vasiliadis et al 2013	0.11	0.19	150	2344	13.7%	1.12 [0.77, 1.62]
Subtotal (95% CI)			**1832**	**18191**	**100.0%**	**1.75 [1.32, 2.31]**
Heterogeneity: Tau² = 0.11; Chi² = 22.61, df = 7 (P = 0.002); I² = 69%						
Test for overall effect: Z = 3.93 (P < 0.0001)						
1.6.3 Depression as comorbidity						
Egede et al 2002	-0.12	0.14	85	732	33.3%	0.89 [0.67, 1.17]
Engel et al 1996	0.34	0.14	394	664	33.3%	1.40 [1.07, 1.85]
Williams et al 2005	0.18	0.14	161	136	33.3%	1.20 [0.91, 1.58]
Subtotal (95% CI)			**640**	**1532**	**100.0%**	**1.14 [0.88, 1.49]**
Heterogeneity: Tau² = 0.03; Chi² = 5.56, df = 2 (P = 0.06); I² = 64%						
Test for overall effect: Z = 0.99 (P = 0.32)						

Ratio of Means IV, Random, 95% CI

0.01 0.1 1 10 100

Favours [depression] Favours [comparator]

Test for subgroup differences: Chi² = 11.19, df = 2 (P = 0.004), I² = 82.1%

Supplemental 4: Sensitivity Analysis

Analysis (1): Exclusion of outliers

Excess cost category	Subgroup	Outliers	Ratio of Means with outliers	Ratio of Means without outliers
Total direct costs	**1**	Chiu et al 2017 Garis et al 2002	RoM = 2.58 [2.01, 3.31] I^2 = 99% Test for overall effect: Z = 7.41 (P < 0.00001)	RoM = 2.49 [1.92, 3.23] I^2 = 99% Test for overall effect: Z = 6.91 (P < 0.00001)
Inpatient costs	**1**	Chiu et al 2017 Garis et al 2002	RoM = 2.82 [1.94, 4.08] I^2 = 89% Z = 5.45 (P < 0.00001)	RoM = 2.66 [1.90, 3.72] I^2 = 83% Z = 5.72 (P < 0.00001)
	4	Dagher et al 2012	RoM =1.44 [1.09, 1.90] I^2 = 25% Z = 2.59 (P = 0.010)	RoM = 1.35 [1.08, 1.70] I^2 = 16% Z = 2.59 (P = 0.010)
Outpatient costs	**1**	Bosmans et al Chiu et al 2017 Garis et al 2002	RoM = 1.85 [1.64, 2.10] I^2 = 91% Z = 9.82 (P < 0.00001)	RoM = 1.95 [1.78, 2.14] I^2 = 77% Z = 14.34 (P < 0.00001)
	2	Luppa et al 2008	RoM = 1.36 [1.18, 1.57] I^2 = 55% Z = 4.25 (P < 0.0001)	RoM = 1.47 [1.36, 1.58] I^2 = 0% Z = 10.42 (P < 0.00001)
Medication costs	**1**	Bosmans et al Garis et al 2002	RoM = 2.89 [2.16, 3.86] I^2 = 99% Z = 7.19 (P < 0.00001)	RoM = 2.26 [1.97, 2.59] I^2 = 93% Z = 11.70 (P < 0.00001)
	4	Williams et al 2005	RoM =1.35 [1.04, 1.75] I^2 = 94% Z = 2.28 (P = 0.02)	RoM = 1.55 [1.22, 1.95] I^2 = 91% Z = 3.67 (P = 0.0002)
Emergency costs	**1**	Chiu et al 2017	RoM = 1.88 [1.49, 2.37] I^2 = 90% Z = 5.33 (P < 0.00001)	RoM = 2.17 [1.94, 2.43] I^2 = 47% Z = 13.51 (P < 0.00001)
	4	Dagher et al 2012	RoM = 1.62 [1.27, 2.08] I^2 = 53% Z = 3.82 (P = 0.0001)	RoM = 1.57 [1.37, 1.80] I^2 = 4% Z = 6.46 (P < 0.00001)
Other costs	**1**	Chiu et al 2017 Garis 2002	RoM = 2.31 [1.65, 3.24] I^2 = 98% Z = 4.86 (P < 0.00001)	RoM = 2.08 [1.53, 2.82] I^2 = 98% Z = 4.69 (P < 0.00001)

Analysis (2): Exclusion of studies in German language

Excess cost category	Subgroup	German language studies	Ratio of Means with German language studies	Ratio of Means without German language studies
Total direct costs	**1**	Stamm et al 2010	RoM = 2.58 [2.01, 3.31] I^2 = 99% Test for overall effect: Z = 7.41 (P < 0.00001)	RoM = 2.51 [1.94, 3.26] I^2 = 99% Test for overall effect: Z = 6.92 (P < 0.00001)
Inpatient costs	**1**	Stamm et al 2010	RoM = 2.82 [1.94, 4.08] I^2 = 89% Z = 5.45 (P < 0.00001)	RoM = 2.80 [1.86, 4.21] I^2 = 89% Z = 4.94 (P < 0.00001)
Medication costs	**1**	Stamm et al 2010	RoM = 2.89 [2.16, 3.86] I^2 = 99% Z = 7.19 (P < 0.00001)	RoM = 2.98 [2.20, 4.05] I^2 = 99% Z = 7.05 (P < 0.00001)

Subgroups:
1= Depressed and non-depressed in adults
2= Depressed and non-depressed in old age
3= Depressed and non-depressed in adolescents
4= Depression as comorbidity