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	The study estimated costs from the utilization of different kinds of health care services, but
categories	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	The results were discussed in relation to other studies on the same topic, if any.
studies	
Limitations discussed	The limitations regarding in particular the calculation of costs were discussed in detail.

Reference	Arnow et al 2009ª	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	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	Х	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~
Non-depressed comparison group	~	~	~	Х	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~
Currency	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~
Reference year	X	~	~	~	Х	~	~	~	Х	~	~	~	~	~	Х	Х	~	~	~	Х	~	~	~	Х	Х	~	Х	~	~	Х	~
Perspective	Х	Х	Х	Х	Х	Х	Х	~	~	Х	~	~	Х	Х	Х	Х	~	Х	~	Х	Х	~	~	Х	Х	Х	Х	Х	~	Х	~
Costs incorporated from at least 2 major categories	~	~	~	~	~	~	~	~	~	~	~	~	~	Х	~	~	~	~	~	Х	~	~	~	Х	Х	Х	~	~	~	Х	~
Data source	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~
Valuation of costs	~	~	~	~	Х	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~
Missing data, imputation method	Х	Х	~	Х	Х	~	~	Х	Х	Х	Х	~	~	Х	~	Х	Х	Х	Х	~	~	~	~	Х	Х	Х	Х	~	~	Х	~
Sensitivity analyses	Х	Х	Х	Х	~	Х	Х	Х	Х	Х	~	~	~	Х	Х	Х	Х	Х	Х	Х	~	~	~	Х	~	Х	Х	~	X	Х	Х
Sample size (subgroup)	~	~	~	~	Х	~	~	~	~	~	~	~	~	~	~	~	~	~	Х	~	~	~	~	~	~	~	~	~	~	~	~
Demographics	~	~	~	~	Х	~	~	~	~	~	~	~	~	~	~	~	~	~	Х	~	~	~	~	~	~	~	~	~	✓	~	~
Arithmetic mean costs	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	✓	~	~
Standard deviations	~	~	~	Х	~	~	~	Х	~	~	~	~	~	Х	~	\checkmark	~	х	Х	~	~	~	~	~	Х	Х	~	~	~	~	~
Results discussed with respect to other studies	~	~	~	~	~	~	~	X	~	Х	Х	~	~	~	~	~	~	~	Х	~	~	~	~	~	~	~	~	~	~	~	~
Limitations discussed	~	~	~	~	~	~	~	~	~	~	~	~	X	~	Х	~	~	~	Х	~	~	~	~	~	~	~	~	~	~	~	~
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		T	T	T		1	1	4	1		1	1	1	1		
Study objective	~	✓	~	~	✓	✓	~	~	~	~	~	~	~	~	~	~	~	100%
Inclusion and exclusion criteria	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	Х	98%
Disease and diagnostic criteria	~	~	~	~	~	~	~	~	~	Х	~	~	~	Х	~	Х	~	91%
Non-depressed comparison group	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	98%
Currency	~	~	~	~	~	~	\checkmark	~	~	~	~	~	~	~	~	~	Х	98%
Reference year	~	~	Х	~	~	~	Х	~	Х	~	~	~	~	Х	~	~	Х	69%
Perspective	~	~	Х	Х	~	~	Х	Х	Х	~	Х	~	Х	Х	Х	~	Х	35%
Costs incorporated from at least 2 major categories	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	88%
Data source	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	100%
Valuation of costs	~	~	✓	~	~	~	~	~	~	~	~	~	~	~	~	~	Х	96%
Missing data, imputation method	Х	Х	Х	Х	~	X	Х	Х	Х	~	~	Х	Х	Х	Х	Х	Х	33%
Sensitivity analyses	~	~	Х	Х	Х	Х	Х	Х	Х	Х	Х	~	Х	Х	~	Х	Х	27%
Sample size (subgroup)	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	96%
Demographics	~	~	✓	~	~	~	~	~	~	~	~	~	~	~	~	~	~	96%
Arithmetic mean costs	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	100%
Standard deviations	Х	~	~	~	~	Х	~	Х	~	~	~	Х	~	~	~	~	~	79%
Results discussed with respect to other studies	~	✓	✓	✓	✓	~	~	~	~	~	~	~	~	~	~	~	Х	90%
Limitations discussed	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	~	Х	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)

D 4	Direct costs Total direct Inpatient				Emerge	encv	Outpati	ent			0.1		Indirect costs Total indirect		
Reference	costs		treatme	nt	treatme	ent	treatme	nt	Medica	tion	Others		costs		
Depressed and	D Inon don	ND	D	ND	D	ND	D	ND	D	ND	D	ND	D	ND	
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	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	l non-dep	ressed ir	n old age											<u> </u>	
Alexandre et al 2016	18,913 (21,860)	8,796 (13,048	5)												
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 (-)			

	Direct co	osts											Indire	ct costs
Reference	ect	Inpatient			ncy nt	Outpati	ent nt	Medicat	tion	Others		Total i	ndirect	
	D	ND	D	ND	D	ND	D	ND	D	ND	D	ND	D	ND
Luppa et al 2008 Prina et al 2014	7,962 (10,134)	5,542 (8,894)	3,171 (8,681) 8,043 (15,255)	1,961 (5,609) 3,886 (9,776)	-	1.2	585 (589)	871 (3,168)	2,142 (2,065)	1,545 (3,111)	2,065 (-)	1,165 (-)	2	
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	l non-dep	ressed in	adolesce	nts										
Guevara et al 2003 Wright et al 2016	3,993 (-) 5,348 (11,037)	1,110 (-) 2,480 (8,019)	1,274 (-) 1,135 (6,709)	245 (-) 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	comorbid	ity												
Adam et al 2017 Arnow et al 2009	31,457 (57,500) 9,748 (10,102)	19,812 (37,398) 6,131 (10,196)	23,287) (54,984) 2,717) (6,352)	11,414 (34,199) 1,694 (6,391)	823 (2,093) 353 (432)	1,069 (2,706) 211 (454)	7,347 (7,104) 3,271	7,328 (9,979) 2,392 (-)	1,856 (1.729)	1,078 (1,737)				
Dagher et al 2012 Edoka et al	6,320 (20,845) 737	(10,190) 2,206 (8,253) 499	3,667 (20,414) 266	481 (6,026) 262	509 (1,247)	80 (402)	2,145 (-) 472	1,644 (-) 236	(1,727)	(1,757)				
2011 Egede et al 2002 Engel et al 1996	(973) 17,902 (-)	(1,191) 13,254 (-)	(-) 13,957 (-)	(-) 10,587 (-)	485 (-)	530 (-)	(-) 1,274 (-)	(-) 922 (-)	1,927 (-)	922 (-)	260 (-) 4,948 (11,334)	292 (-) 3,520 (6,692)		
et al 2003 Frasure-Smith et al 2000 Gilmer et al 2005 Morgan et al	(-) 4,764 (7,215) 14,521 (18,103) 6 875	(-) 3,769 (6,880) 9,816 (10,421) 5 031	786 (-)	682 (-)	191 (289)	128 (223)	661 (468)	541 (381)						
2008 Petrou et al 2002 Rayner et al 2016	(11,988) 1,888 (-) 4,305 (10,444)	(6,760) 1,416 (-) 2,636 (5,309)	715 (-) 1,566 (9,589)	648 (-) 595 (4.095)	241 (657)	147 (508)	1,173 (-) 2,499 (-)	768 (-) 1,902 (-)						
Rosenzweig et al 2002 Rutledge et al 2009	(10,111) 11,862 (18,730) 11,436 (-) 18,885	7,110 (11,255) 8,861 (-)	10.537	0 701	(001)	(200)	8 780	5 891	3,618 (2,329) 3,401 (1,605)	2,625 (2,491) 2,808 (1,611)				
2002 Williams et al 2005	(13,586) 21,370 (22,784)	(13,779) 25,329 (38,438)	10,557 (10,670) 2,855)(15,163)	(11,785) 3,579 (28,161)	690 (-)	306 (-)	(4,401) 2,234 (-)	(3,953) 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

	D	enression (omparator	Ratio of Means	Ratio of Means		Depression	Comparator	Ratio of Means	Ratio of Means
Study or Subgroup	Ion(Ratio of Means) SE	Total	Total Weight I	V Random 95% CL	IV Bandom 95% Cl	Study or Subgroup	log[Ratio of Means] SF Total	Total Weight	IV. Random, 95% Cl	IV. Random, 95% Cl
1.3.1 Depressed and non	depressed in adults	Total	rotai moight i	, randon, oo // or		1.2.1 Depressed and non	1-depressed in adults		,	,
Arnow et al 2009	0.41 0.21	142	3048 61%	1 51 [1 00 2 27]		Arnow et al 2009	0.52 0.21 142	3048 10.8%	1.68 [1.11, 2.54]	
Bosmans et al 2010	16 0.21	7128	23772 61%	4 95 [3 28 7 48]		Carstensen et al 2012	1.28 0.36 7712	266354 8.6%	3.60 [1.78, 7.28]	
Brilleman et al 2013	0.65 0.01	12811	47400 187%	1 92 [1 88 1 95]		Chiu et al 2017	0.07 0.22 409	8905 10.7%	1.07 [0.70, 1.65]	_ _
Carstensen et al 2012	1 15 0 21	7712	266354 6196	3 16 [2 09 4 77]		Choi et al 2014	0.74 0.18 1582	11625 11.2%	2.10 [1.47, 2.98]	
Chiu et al 2017	0.07 0.08	409	8905 144%	1 07 0 92 1 25	_ _ _	Garis et al 2002	2.74 0.36 4077	963 8.6%	15.49 [7.65, 31.36]	
Choi et al 2014	0.41 0.21	1582	11625 61%	1.51 [1.00, 2.27]	_ _	Greenberg et al 2015	0.75 0.04 44241	44241 12.4%	2.12 [1.96, 2.29]	•
Garis et al 2002	0.64 0.21	4077	963 61%	1 90 [1 26 2 86]		Hamre et al 2010	0.89 0.36 81	303 8.6%	2.44 [1.20, 4.93]	
Greenberg et al 2015	0.75 0.02	44241	44741 184%	2 1 2 [2 04 2 20]		Shvartzman et al 2005	2.13 0.23 543	1949 10.5%	8.41 [5.36, 13.21]	
Hamre et al 2010	0.13 0.02	81	303 61%	1 48 [0 98 2 23]	.	Simon et al 1995	0.44 0.36 6257	6257 8.6%	1.55 [0.77, 3.14]	
Shvartzman et al 2005	0.48 0.21	543	1949 61%	1.62 [1.07, 2.44]	_ 	Stamm et al 2010	1.11 0.26 591	591 10.1%	3.03 [1.82, 5.05]	
Simon et al 1995	0.66 0.21	6257	6257 61%	1 03 [1 28 2 02]		Subtotal (95% CI)	65635	344236 100.0%	2.82 [1.94, 4.08]	•
Subtotal (95% CI)	0.00 0.21	84983	414817 100.0%	1.85 [1.64, 2.10]	•	Heterogeneity: Tau ² = 0.2	9; Chi² = 81.11, df = 9 (P < 0.00001); l² = 899	6		
Heterogeneity Tau ² = 0.02	Chi¥=10621 df=10 (P≤00	0001): 17 = 919	×.		· ·	Test for overall effect: Z =	5.45 (P < 0.00001)			
Test for overall effect 7 - 1	2,011 = 100.21, ut = 10 (1 × 0.0	0001),1 = 31	<i>,</i> 0			4.9.9.0				
restion overall ellect 2 = .	5.62 (1 4 6.66661)					1.2.2 Depressed and non	1-depressed in old age			
1.3.2 Depressed and non	-depressed in old age					Bock et al 2014	0.78 0.25 112	938 8.8%	2.18 [1.34, 3.56]	
Bock et al 2014	033 022	112	039 7 6%	1 30 m 00 2 1 /1		BOCK et al 2016	0.81 0.23 198	999 10.0%	2.25 [1.43, 3.53]	
Bock et al 2014	0.31 0.06	198	000 771%	1 36 [1 21 1 53]	+	Criticite at 2014	0.83 0.09 300	2822 27.5%	2.29 [1.92, 2.74]	
Callahan et al 1994	0.31 0.00	458	1253 22.1%	1.62 [1.44, 1.82]	+	Katori et al 2003	0.47 0.25 300	7200 8.8%	1.00 [0.98, 2.01]	
Choi et al 2014	0.42 0.22	366	7200 22.1%	1.62 [1.44, 1.02]		Luppo et al 2000	0.22 0.22 30	200 10.070	1.20 [0.01, 1.92]	-
Fischer et al 2002	0.37 0.22	245	271 7.6%	1 45 [0.00, 2.04]	.	Dripp of al 2000	0.40 0.37 03	507 9.370	2.00 [1.67, 2.54]	+
Katon et al 2002	0.31 0.22	306	7265 7.6%	1.51 [0.98, 2.32]		Vaciliadic at al 2014	0.73 0.11 338	2344 62%	2.00 [1.07, 2.37]	
Ludvigsson et al 2018	0.37 0.22	36	280 7.6%	1 45 [0 94 2 23]	.	Subtotal (95% CI)	1559	20108 100.0%	1.92 [1.63, 2.26]	•
Lunna et al 2008	-0.4 0.22	63	388 7.6%	0.67 [0.44 1.03]		Heterogeneity: Tau ² = 0.0	2' Chi ² = 10 74 df = 7 (P = 0 15): I ² = 35%			•
Vasiliadis et al 2013	0.18 0.18	150	2344 10.0%	1 20 [0.84 1 70]	_ 	Test for overall effect: Z =	7.78 (P < 0.00001)			
Subtotal (95% CI)	0.10 0.10	1923	16560 100.0%	1.36 [1.18, 1.57]	•					
Heterogeneity Tau ² = 0.01	$2 \text{ Chi}^2 = 17.78 \text{ df} = 8 (P = 0.02)^2$	I ² = 55%			•	1.2.3 Depressed and non	1-depressed in adolescents			
Test for overall effect 7 = 4	1 25 (P < 0 0001)	1 - 00 10				Guevara et al 2003	1.65 0.42 56	3390 50.0%	5.21 [2.29, 11.86]	
						Wright et al 2016	1.17 0.42 281	3707 50.0%	3.22 [1.41, 7.34]	∎
1.3.3 Depression as com	orbidity					Subtotal (95% CI)	337	7097 100.0%	4.10 [2.29, 7.33]	•
Adam et al 2017	0 02	50	92 6.2%	1 00 0 68 1 48		Heterogeneity: Tau ² = 0.0	10; Chi ² = 0.65, df = 1 (P = 0.42); I ² = 0%			
Arnow et al 2009	0.31 0.2	271	2347 6.2%	1 36 [0.92, 2.02]	_	Test for overall effect: Z =	4.75 (P < 0.00001)			
Danher et al 2012	0.27 0.2	31	607 6.2%	1 31 [0 89 1 94]						
Edoka et al 2011	0.69 0.2	31	94 6.2%	1 99 [1 35 2 95]		1.2.4 Depression as com	norbidity			
Errede et al 2002	0.32 0.2	85	732 6.2%	1 38 [0 93 2 04]	_	Adam et al 2017	0.71 0.46 50	92 7.9%	2.03 [0.83, 5.01]	
Erasure-Smith et al 2000	0.2 0.05	260	588 25.1%	1 22 [1 11 1 35]	+	Arnow et al 2009	0.47 0.16 271	2347 31.3%	1.60 [1.17, 2.19]	
Petrou et al 2002	0.42 0.2	70	136 6.2%	1.52 [1.03, 2.25]	_ _	Dagher et al 2012	2.03 1.12 31	607 1.5%	7.61 [0.85, 68.39]	
Ravner et al 2016	0.27 0.2	732	472 6.2%	1 31 [0 89, 1 94]	_	Edoka et al 2011	0.01 1.12 31	94 1.5%	1.01 [0.11, 9.07]	
Sullivan et al 2002	0.4 0.05	114	672 251%	1 49 [1 35 1 65]	-	Egede et al 2002	0.28 1.12 85	732 1.5%	1.32 [0.15, 11.88]	
Williams et al 2005	0.08 0.2	161	136 6.2%	1.08 [0.73, 1.60]	-	Frasure-Smith et al 2000	0.14 1.12 260	588 1.5%	1.15 [0.13, 10.33]	
Subtotal (95% CI)	0.00 0.2	1805	5876 100.0%	1.35 [1.21, 1.50]	•	Petrou et al 2002	0.1 1.12 70	136 1.5%	1.11 [0.12, 9.93]	
Heterogeneity Tau ² = 0.01	1° Chi ² = 15.68 df = 9 (P = 0.07) ^o	1 ² = 43%			•	Rayner et al 2016	0.97 0.39 7.32	4/2 10.4%	2.64 [1.23, 5.67]	
Test for overall effect 7 = 4	5 34 (P < 0.00001)					Sullivan et al 2002	0.07 0.11 114	072 39.770	0.70 [0.60, 1.33]	
						Subtotal (95% CI)	-0.23 0.79 161	5876 100.0%	1 44 [1 09 1 90]	· · · · · · · · · · · · · · · · · · ·
						Heterogeneity Tau ² - 0.0	14° Chi ² = 11.94 df = 9 (P = 0.22); 12° - 25%	3010 130.07		•
					0.1 0.2 0.5 1 2 5 10	Test for overall effect: 7 -	2 59 (P = 0.010)			
Test for subgroup differen	ces: Chi ² = 16.99. df = 2.(P = 0.0	1002), I ² = 88 3	7%		Favours [depression] Favours [comparator]	restion overall ellett. Z =	2.00 () = 0.010)			
										-1
										U.U2 U.1 1 10 50
										Favours (depression) Favours (comparator)

Test for subgroup differences: Chi² = 14.66, df = 3 (P = 0.002), I² = 79.5%

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

0 ()	·		Depression Comparator		Ratio of Means	Ratio of Means
Study or Subgroup	log[Ratio of Means]	SE	Total Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.4.1 Depressed and no	n-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: Tau ² = 0.2	!5; Chi ² = 939.26, df = 1	1 (P <	< 0.00001); I ² = 99%			
Test for overall effect: Z =	7.19 (P < 0.00001)					
1.4.2 Depressed and no	n-depressed in old age	9				
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: Tau ² = 0.0	14; Chi ² = 26.63, df = 6	(P = 0	.0002); I ² = 77%			
Test for overall effect: Z =	4.36 (P < 0.0001)					
1.4.3 Depression as con	norbidity					
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: Tau ² = 0.0	18; Chi² = 63.42, df = 4	(P < 0	.00001); I² = 94%			
Test for overall effect: Z =	2.28 (P = 0.02)					
					-	105 0.2 1 5
		_			č	Favours (depression) Favours (comparate
Tect for subaroun differe	neae: ∩hi≩ – 19 39. df –	- 2 (P -	- 0 0001\ P≥- 90 1%			

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

8			Depression	Commenter		Datia of Maana	Datis of Manua
Study or Subgroup	log(Datio of Moane)	¢E	Depression	Comparator	Moight	Kauo ol means	Ratio of means
study of Subgroup	n doproceod in adulte	30	TUtal	TUtal	weight	IV, Rahuolii, 95% Ci	IV, Kalluolli, 95% CI
1.5.1 Depressed and not	n-uepresseu in auuns	0.40	140	2040	10.00	2 04 14 50 2 551	
Amow et al 2009 Obiu et al 2007	0.7	0.12	142	3040	10.070	2.01 [1.09, 2.00]	
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)			52031	74076	100.0%	1.88 [1.49, 2.57]	-
Heterogeneity: Tau* = 0.0	J6; Chi*= 38.19, df= 4 (F	< 0.0	0001); F= 90%	6			
Test for overall effect: Z =	5.33 (P < 0.00001)						
1.5.2 Depressed and no	n-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: Tau ² = 0.0	0; Chi ² = 0.25, df = 1 (P :	0.62); I ² = 0%				
Test for overall effect: Z =	4.60 (P < 0.00001)						
1.5.3 Depression as con	norbidity						
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]	
Ravner et al 2016	0.49	0.19	732	472	19.7%	1.63 11.12 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: Tau ² = 0.0)5; Chi² = 12.89, df = 6 (F	= 0.0	4); I² = 53%				
Test for overall effect: Z =	3.82 (P = 0.0001)						
						-	0.1 0.2 0.5 1 2 5 10
							Favours (depression) Favours (comparator)
Fact for cubaroun diffora	nana: Chit = 0.70 dt = 0	/m = 0	R = 0.00				

Test for subgroup differences: Chi# = 0.73, df = 2 (P = 0.69), I# = 0%

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

)		Depression	Comparator		Ratio of Means	Ratio of Means
Study or Subgroup	log[Ratio of Means]	SE	Total	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.6.1 Depressed and no	on-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: Tau ² = 0.	18; Chi ² = 302.37, df =	6 (P =	: 0.00001); I ² = !	98%			
Test for overall effect: Z:	= 4.86 (P < 0.00001)						
1.6.2 Depressed and no	on-depressed in old ag	е					
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: Tau ² = 0.	11; Chi ² = 22.61, df = 7	(P = 1	0.002); I² = 69%	5			
Test for overall effect: Z	= 3.93 (P < 0.0001)						
1.6.3 Depression as co	morbidity						
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: Tau ² = 0.	.03; Chi² = 5.56, df = 2 (P = 0.	.06); I² = 64%				
Test for overall effect: Z	= 0.99 (P = 0.32)						
							++
							0.01 0.1 1 10 100
		0.00					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] P = 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] P = 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] P = 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] P = 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] P = 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] P = 98% Z = 4.69 (P < 0.00001)



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] l 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:

2= Depressed and non-depressed in old age 4= Depression as comorbidity

1= Depressed and non-depressed in adults3= Depressed and non-depressed in adolescents