Handling, and judging risk of bias associated with missing participant data in meta-analyses of binary and continuous outcomes

Elie Akl, Shanil Ebrahim, Gordon Guyatt

1866 AUB American University of Beirut الجامعة الأميركية في بيروت

STANFORD SCHOOL OF MEDICINE

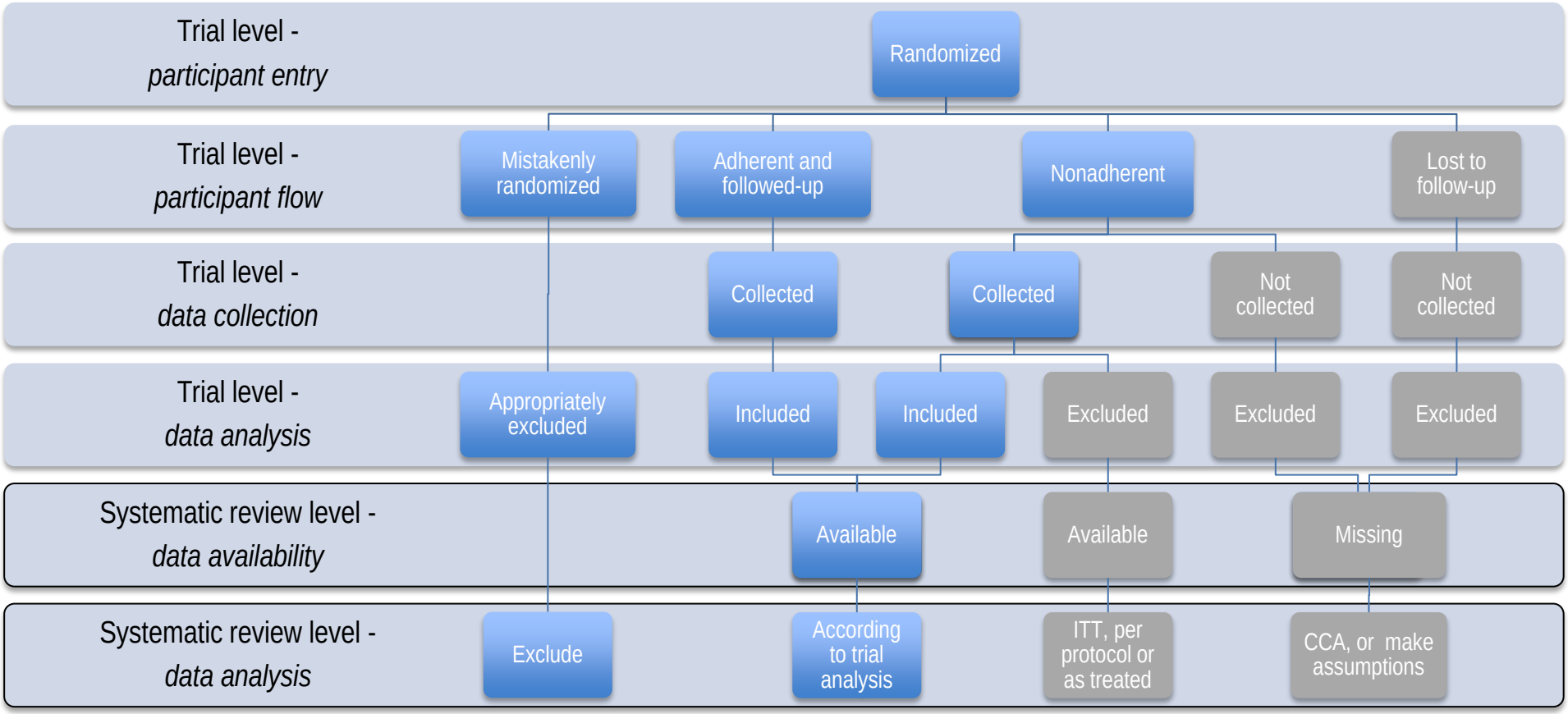
McMaster University

- No conflicts of interest to declare

- This work has been partly funded by the Methods Innovation Fund (MIF)

Objective

- To develop guidance for systematic review authors on how to handle, and judge risk of bias associated with missing participant data in meta-analyses of binary and continuous outcomes

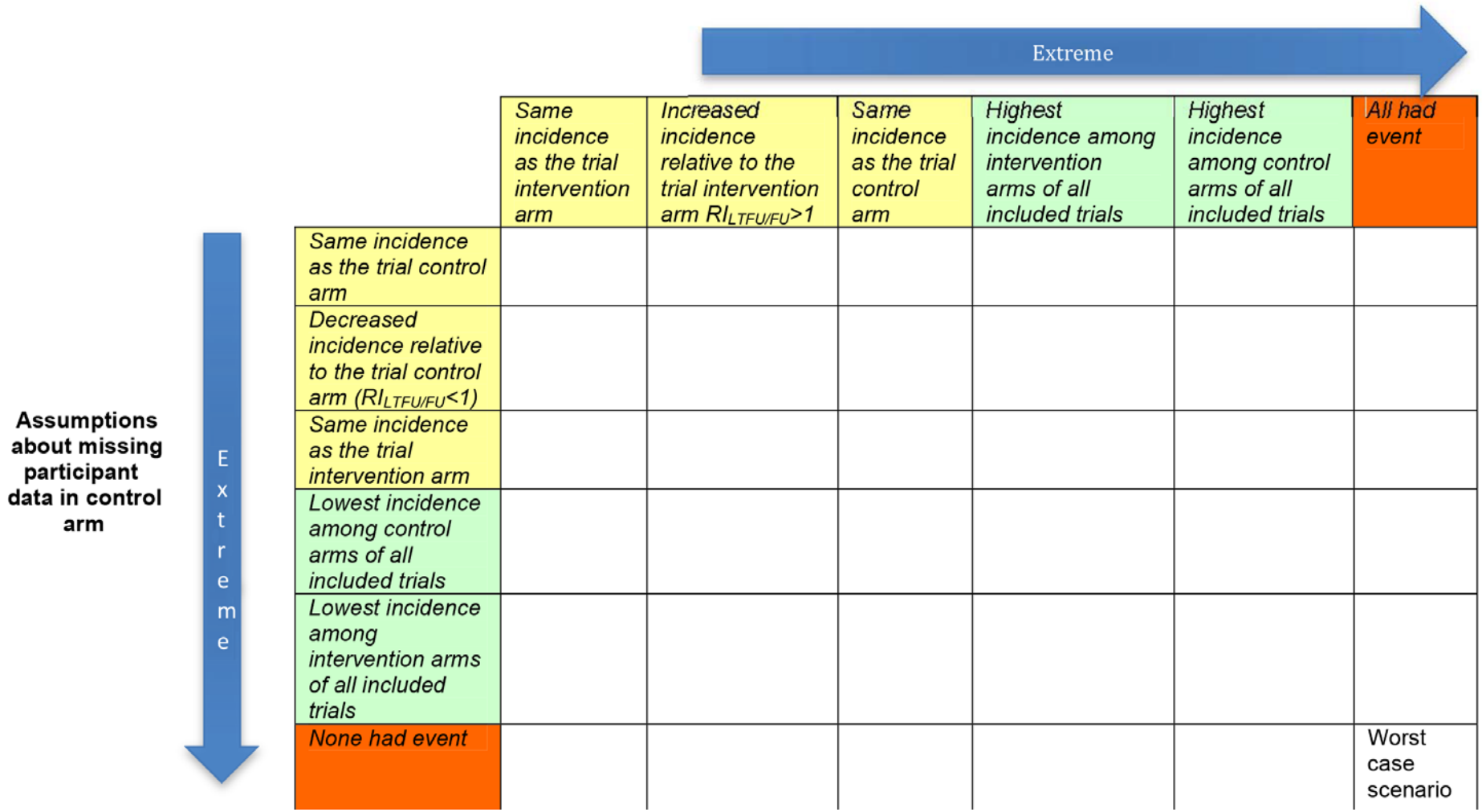

Trial level -
participant entry
Randomized
Trial level -
participant flow
Mistakenly randomized
Adherent and followed-up
Nonadherent
Lost to follow-up
Trial level -
data collection
Collected
Collected
Not collected
Not collected
Trial level -
data analysis
Appropriately excluded
Included
Included
Excluded
Excluded
Excluded
Systematic review level -
data availability
Available
Available
Missing
Systematic review level -
data analysis
Exclude
According to trial analysis
ITT, per protocol or as treated
CCA, or make assumptions

Proposal to handle MPD

- For the primary analysis: exclude participants with missing data (complete case analysis)

- To assess the risk of bias, and when the primary analysis suggests important effect, we suggest sensitivity meta-analyses making different assumptions about the outcome of participants with missing data

Akl et al. PLoS One. 2013;8(2):e57132


Extreme
Assumptions about missing participant data in control arm
Extreme
Same incidence as the trial intervention arm
Increased incidence relative to the trial intervention arm $RI_{LTFU/FU}>1$
Same incidence as the trial control arm
Highest incidence among intervention arms of all included trials
Highest incidence among control arms of all included trials
All had event
Same incidence as the trial control arm
Decreased incidence relative to the trial control arm ($RI_{LTFU/FU}<1$)
Same incidence as the trial intervention arm
Lowest incidence among control arms of all included trials
Lowest incidence among intervention arms of all included trials
None had event
Worst case scenario

Judging RoB dichotomous MPD

- Results robust to a worst case scenario → missing data does not represent a risk of bias

- Results not robust to worst case scenario → test progressively more extreme assumptions culminating in a "worst plausible case”

- Important changes in results with such sensitivity analyses suggest serious RoB

Example

- Meta-analysis assessing effects of probiotics for prevention clostridium difficile-associated diarrhea

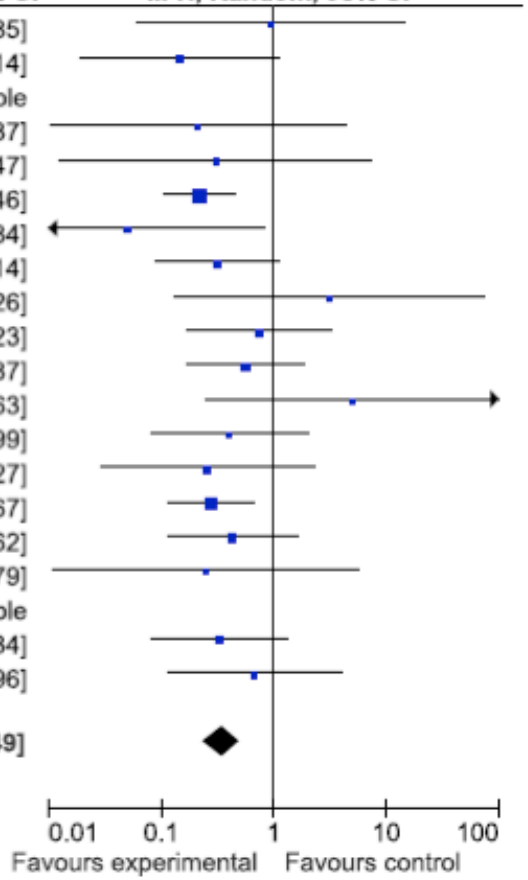
Neumann et al. Ann Intern Med. 2012 May 15;156(10)

Complete case analysis

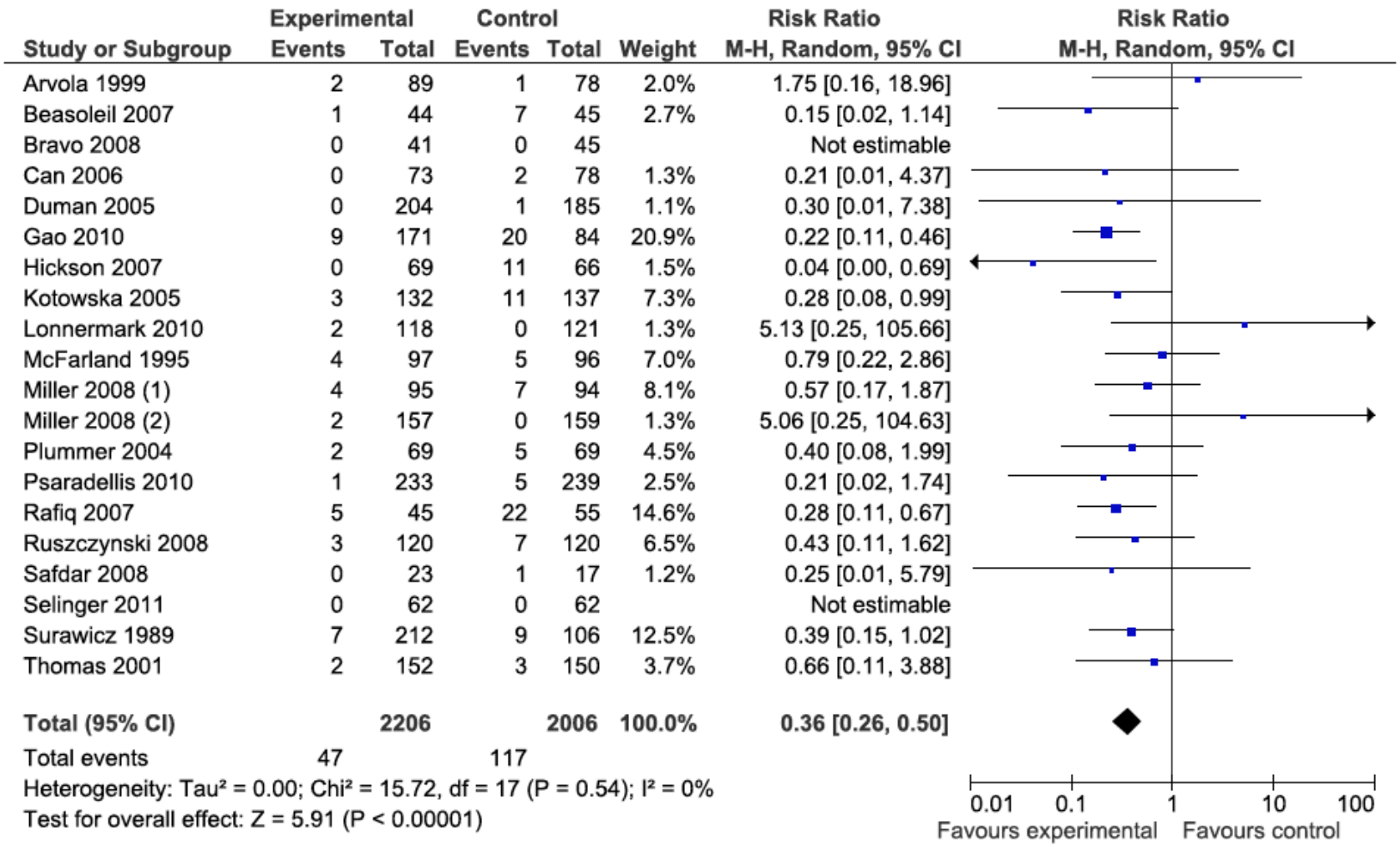
Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Arvola 1999	1	61	1	58	1.7%	0.95 [0.06, 14.85]
Beasoleil 2007	1	44	7	45	3.0%	0.15 [0.02, 1.14]
Bravo 2008	0	41	0	45		Not estimable
Can 2006	0	73	2	78	1.4%	0.21 [0.01, 4.37]
Duman 2005	0	196	1	180	1.2%	0.31 [0.01, 7.47]
Gao 2010	9	171	20	84	23.0%	0.22 [0.11, 0.46]
Hickson 2007	0	56	9	53	1.6%	0.05 [0.00, 0.84]
Kotowska 2005	3	119	10	127	7.9%	0.32 [0.09, 1.14]
Lonnermark 2010	1	80	0	83	1.3%	3.11 [0.13, 75.26]
McFarland 1995	3	97	4	96	5.9%	0.74 [0.17, 3.23]
Miller 2008 (1)	4	95	7	94	8.9%	0.57 [0.17, 1.87]
Miller 2008 (2)	2	157	0	159	1.4%	5.06 [0.25, 104.63]
Plummer 2004	2	69	5	69	4.9%	0.40 [0.08, 1.99]
Psaradellis 2010	1	216	4	221	2.7%	0.26 [0.03, 2.27]
Rafiq 2007	5	45	22	55	16.1%	0.28 [0.11, 0.67]
Ruszczynski 2008	3	120	7	120	7.2%	0.43 [0.11, 1.62]
Safdar 2008	0	23	1	17	1.3%	0.25 [0.01, 5.79]
Selinger 2011	0	62	0	62		Not estimable
Surawicz 1989	3	116	5	64	6.5%	0.33 [0.08, 1.34]
Thomas 2001	2	133	3	134	4.0%	0.67 [0.11, 3.96]
Total (95% CI)		**1974**		**1844**	**100.0%**	**0.34 [0.24, 0.49]**
Total events	40		108			

Heterogeneity: Tau² = 0.00; Chi² = 12.09, df = 17 (P = 0.79); I² = 0%

Test for overall effect: Z = 5.87 (P < 0.00001)



Event rate: 1.5:1



Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Arvola 1999	2	89	1	78	2.0%	1.75 [0.16, 18.96]
Beasoleil 2007	1	44	7	45	2.7%	0.15 [0.02, 1.14]
Bravo 2008	0	41	0	45		Not estimable
Can 2006	0	73	2	78	1.3%	0.21 [0.01, 4.37]
Duman 2005	0	204	1	185	1.1%	0.30 [0.01, 7.38]
Gao 2010	9	171	20	84	20.9%	0.22 [0.11, 0.46]
Hickson 2007	0	69	11	66	1.5%	0.04 [0.00, 0.69]
Kotowska 2005	3	132	11	137	7.3%	0.28 [0.08, 0.99]
Lonnermark 2010	2	118	0	121	1.3%	5.13 [0.25, 105.66]
McFarland 1995	4	97	5	96	7.0%	0.79 [0.22, 2.86]
Miller 2008 (1)	4	95	7	94	8.1%	0.57 [0.17, 1.87]
Miller 2008 (2)	2	157	0	159	1.3%	5.06 [0.25, 104.63]
Plummer 2004	2	69	5	69	4.5%	0.40 [0.08, 1.99]
Psaradellis 2010	1	233	5	239	2.5%	0.21 [0.02, 1.74]
Rafiq 2007	5	45	22	55	14.6%	0.28 [0.11, 0.67]
Ruszczynski 2008	3	120	7	120	6.5%	0.43 [0.11, 1.62]
Safdar 2008	0	23	1	17	1.2%	0.25 [0.01, 5.79]
Selinger 2011	0	62	0	62		Not estimable
Surawicz 1989	7	212	9	106	12.5%	0.39 [0.15, 1.02]
Thomas 2001	2	152	3	150	3.7%	0.66 [0.11, 3.88]
Total (95% CI)		**2206**		**2006**	**100.0%**	**0.36 [0.26, 0.50]**
Total events	47		117			

Heterogeneity: Tau² = 0.00; Chi² = 15.72, df = 17 (P = 0.54); I² = 0%

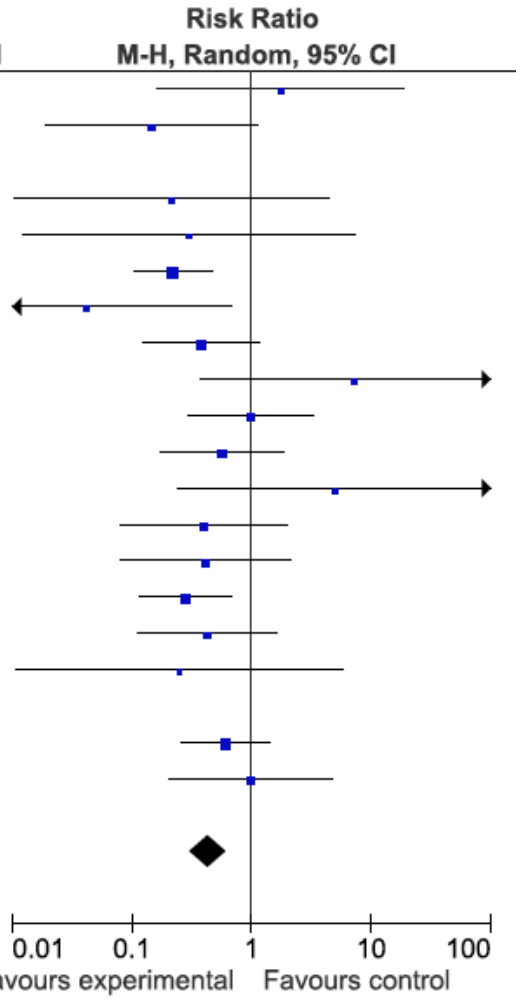
Test for overall effect: Z = 5.91 (P < 0.00001)

Event rate: 3:1

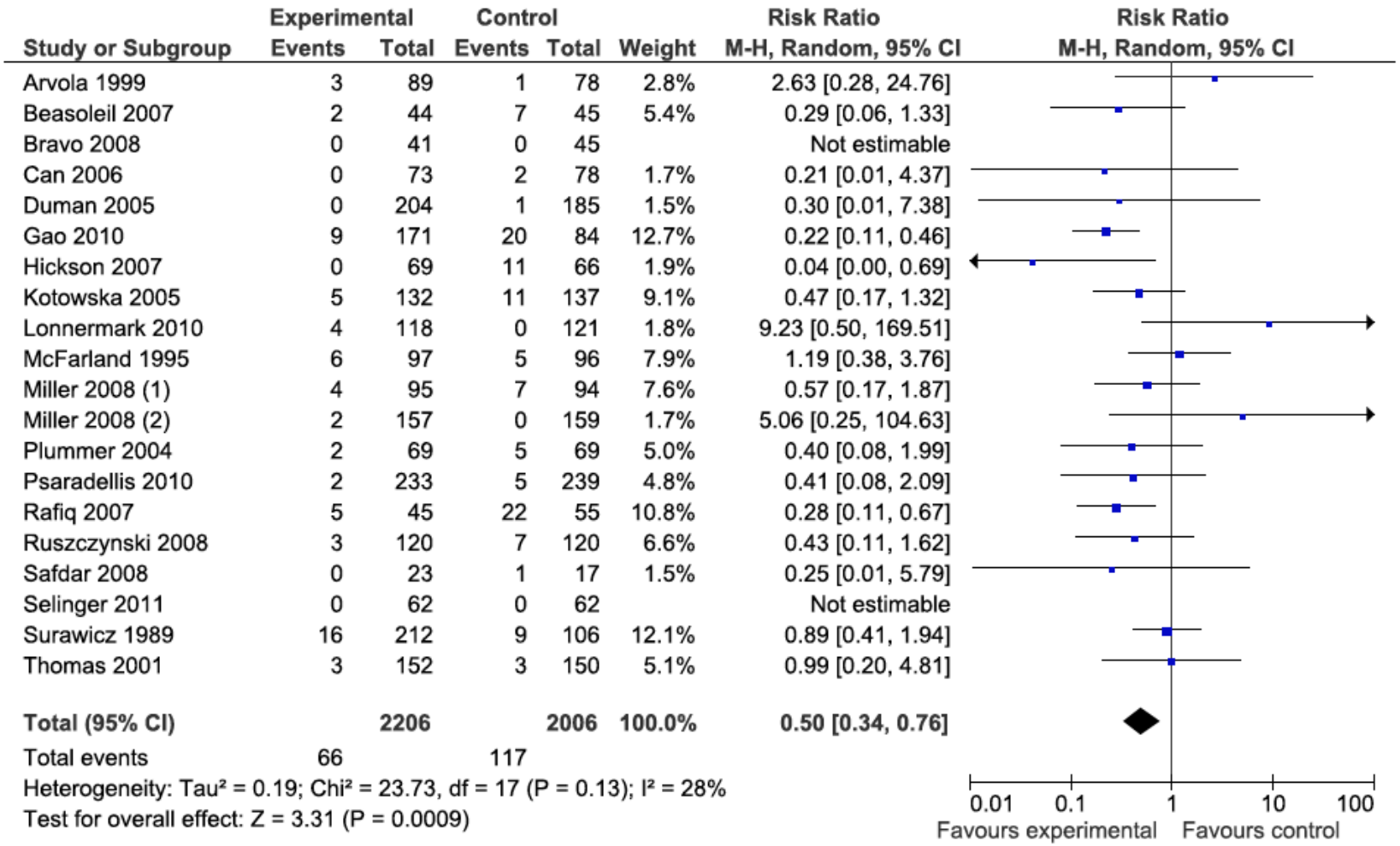
Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Arvola 1999	2	89	1	78	2.2%	1.75 [0.16, 18.96]
Beasoleil 2007	1	44	7	45	2.9%	0.15 [0.02, 1.14]
Bravo 2008	0	41	0	45		Not estimable
Can 2006	0	73	2	78	1.4%	0.21 [0.01, 4.37]
Duman 2005	0	204	1	185	1.3%	0.30 [0.01, 7.38]
Gao 2010	9	171	20	84	16.1%	0.22 [0.11, 0.46]
Hickson 2007	0	69	11	66	1.6%	0.04 [0.00, 0.69]
Kotowska 2005	4	132	11	137	8.7%	0.38 [0.12, 1.16]
Lonnermark 2010	3	118	0	121	1.5%	7.18 [0.37, 137.44]
McFarland 1995	5	97	5	96	7.6%	0.99 [0.30, 3.31]
Miller 2008 (1)	4	95	7	94	7.8%	0.57 [0.17, 1.87]
Miller 2008 (2)	2	157	0	159	1.4%	5.06 [0.25, 104.63]
Plummer 2004	2	69	5	69	4.6%	0.40 [0.08, 1.99]
Psaradellis 2010	2	233	5	239	4.5%	0.41 [0.08, 2.09]
Rafiq 2007	5	45	22	55	12.5%	0.28 [0.11, 0.67]
Ruszczynski 2008	3	120	7	120	6.5%	0.43 [0.11, 1.62]
Safdar 2008	0	23	1	17	1.3%	0.25 [0.01, 5.79]
Selinger 2011	0	62	0	62		Not estimable
Surawicz 1989	11	212	9	106	13.3%	0.61 [0.26, 1.43]
Thomas 2001	3	152	3	150	4.7%	0.99 [0.20, 4.81]
Total (95% CI)		**2206**		**2006**	**100.0%**	**0.43 [0.30, 0.62]**
Total events	56		117			

Heterogeneity: Tau² = 0.07; Chi² = 19.28, df = 17 (P = 0.31); I² = 12%

Test for overall effect: Z = 4.50 (P < 0.00001)



Event rate: 5:1



Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Arvola 1999	3	89	1	78	2.8%	2.63 [0.28, 24.76]
Beasoleil 2007	2	44	7	45	5.4%	0.29 [0.06, 1.33]
Bravo 2008	0	41	0	45		Not estimable
Can 2006	0	73	2	78	1.7%	0.21 [0.01, 4.37]
Duman 2005	0	204	1	185	1.5%	0.30 [0.01, 7.38]
Gao 2010	9	171	20	84	12.7%	0.22 [0.11, 0.46]
Hickson 2007	0	69	11	66	1.9%	0.04 [0.00, 0.69]
Kotowska 2005	5	132	11	137	9.1%	0.47 [0.17, 1.32]
Lonnermark 2010	4	118	0	121	1.8%	9.23 [0.50, 169.51]
McFarland 1995	6	97	5	96	7.9%	1.19 [0.38, 3.76]
Miller 2008 (1)	4	95	7	94	7.6%	0.57 [0.17, 1.87]
Miller 2008 (2)	2	157	0	159	1.7%	5.06 [0.25, 104.63]
Plummer 2004	2	69	5	69	5.0%	0.40 [0.08, 1.99]
Psaradellis 2010	2	233	5	239	4.8%	0.41 [0.08, 2.09]
Rafiq 2007	5	45	22	55	10.8%	0.28 [0.11, 0.67]
Ruszczynski 2008	3	120	7	120	6.6%	0.43 [0.11, 1.62]
Safdar 2008	0	23	1	17	1.5%	0.25 [0.01, 5.79]
Selinger 2011	0	62	0	62		Not estimable
Surawicz 1989	16	212	9	106	12.1%	0.89 [0.41, 1.94]
Thomas 2001	3	152	3	150	5.1%	0.99 [0.20, 4.81]
Total (95% CI)		**2206**		**2006**	**100.0%**	**0.50 [0.34, 0.76]**
Total events	66		117			

Heterogeneity: Tau² = 0.19; Chi² = 23.73, df = 17 (P = 0.13); I² = 28%

Test for overall effect: Z = 3.31 (P = 0.0009)

Handling continuous MPD

- Strategies to combine imputations for participants with missing data with those with complete data
- Progressively more stringent strategies to challenge estimates

Ebrahim et al. J Clin Epidemiol. 2013 Sep;66(9):1014-1021.e1

Imputing effect & precision

Measure of effect

5 sources of data reflecting real observed mean scores in participants followed-up in individual trials in a meta-analysis:

- Ranging from:
    - Best mean score among intervention arms
    - Worst mean score among control arms

Measure of precision

- Median SD (plausible)

Imputation strategies

- Developed **4** progressively more stringent imputation strategies for participants with missing data in both arms

		Assumptions about the means of participants in INTERVENTION		
		C: Mean score from the control arm of the same trial	*D: Worst mean among intervention arms*	*E: Worst mean among control arms*
Assumptions about the means of participants in CONTROL	*A: Best mean among intervention arms*			4 Intervention: Worst mean among control arms Control: Best mean among intervention arms
	B: Best mean among the control arms		2 Intervention: Worst mean among intervention arms Control: Best mean among control arms	3 Intervention: Worst mean among control arms Control: Best mean among control arms
	C: Mean score from the control arm of the same trial	1 Intervention and control: Mean score from the control arm of the same trial		

Combining observed & imputed data

3-step method for each strategy:

[1] Combine observed means and SDs of those with available data with imputed means and SDs for those with missing data

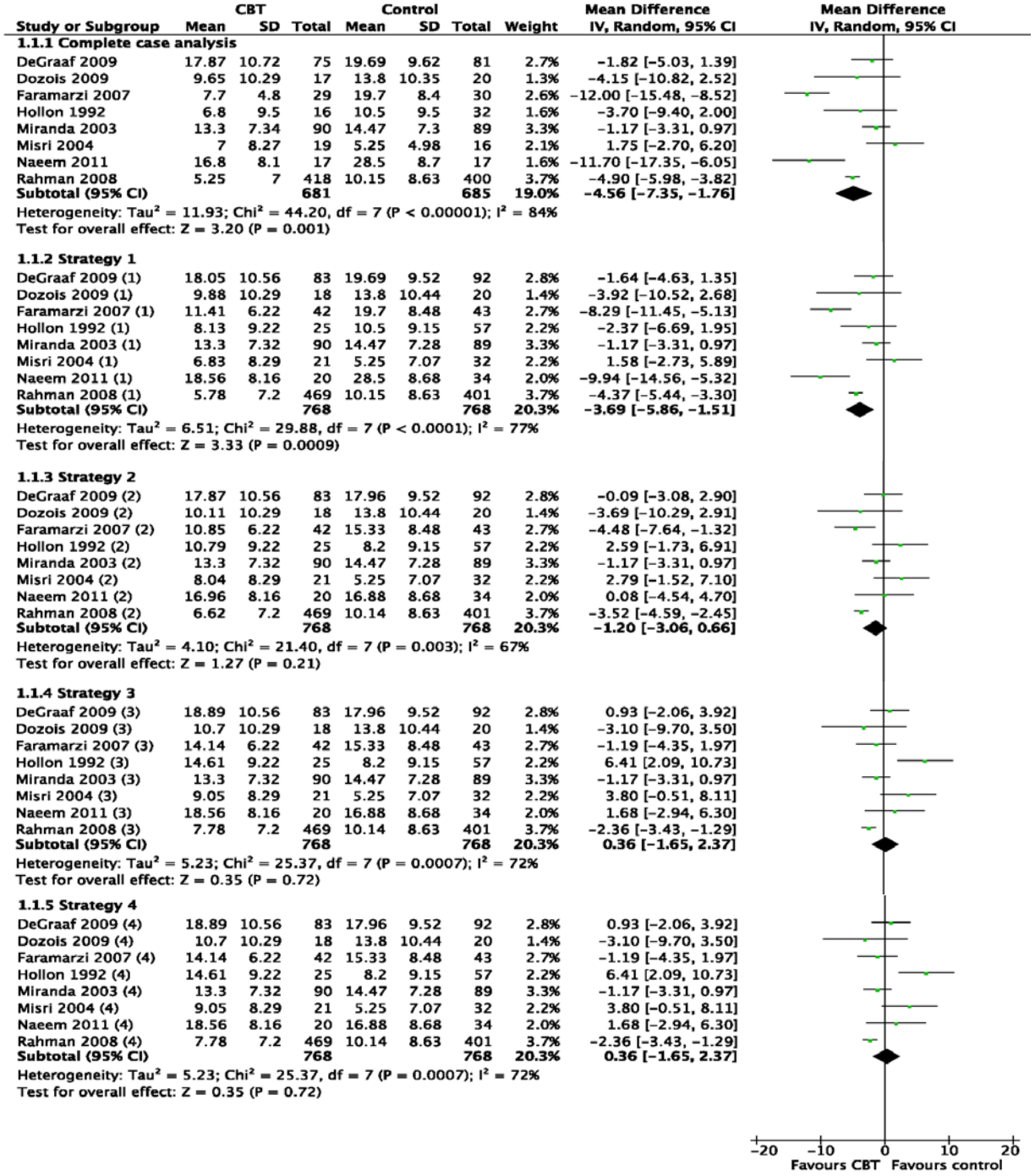
[2] Use pooled estimates to calculate treatment effect per study

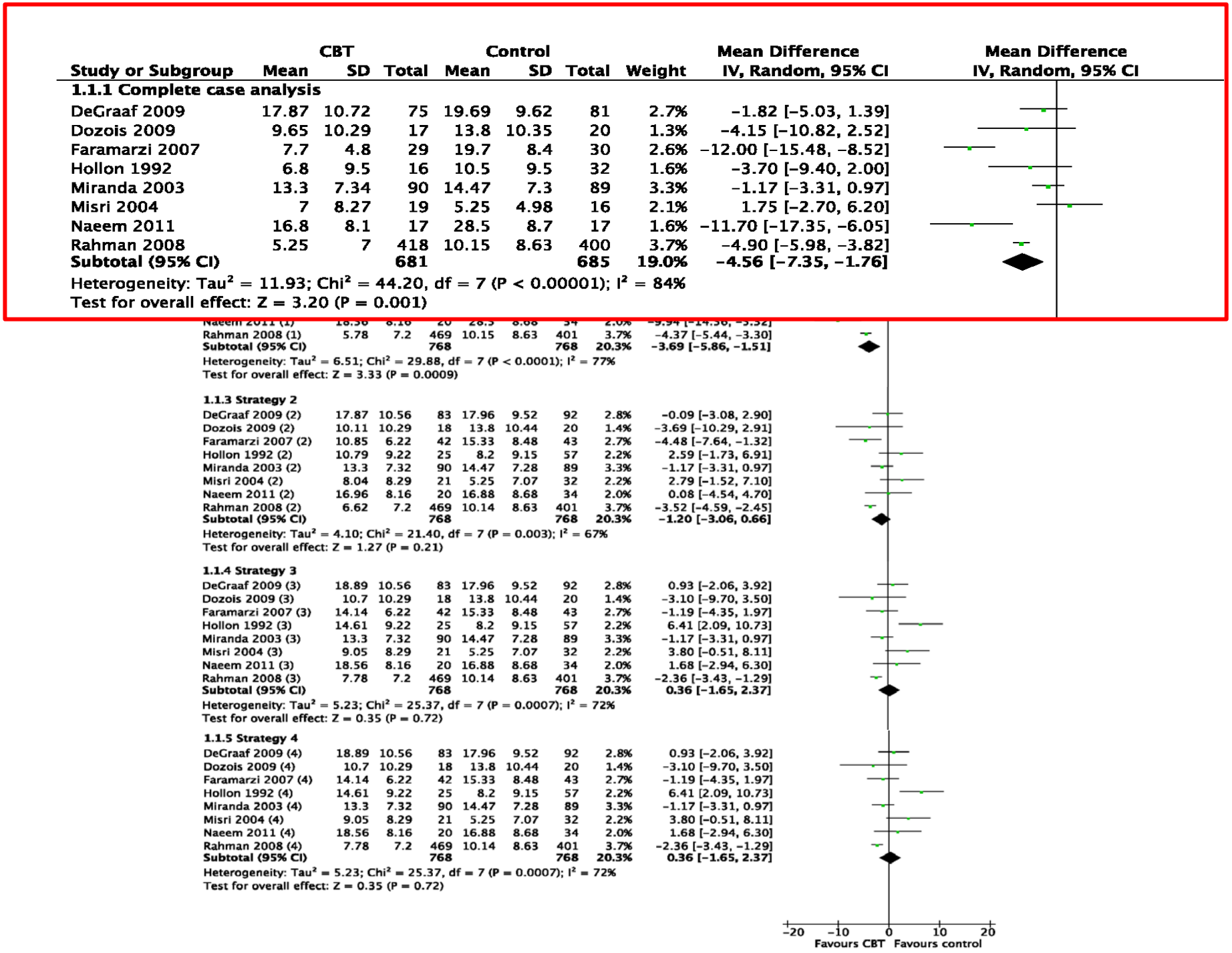
[3] Perform a standard random-effects meta-analysis to pool

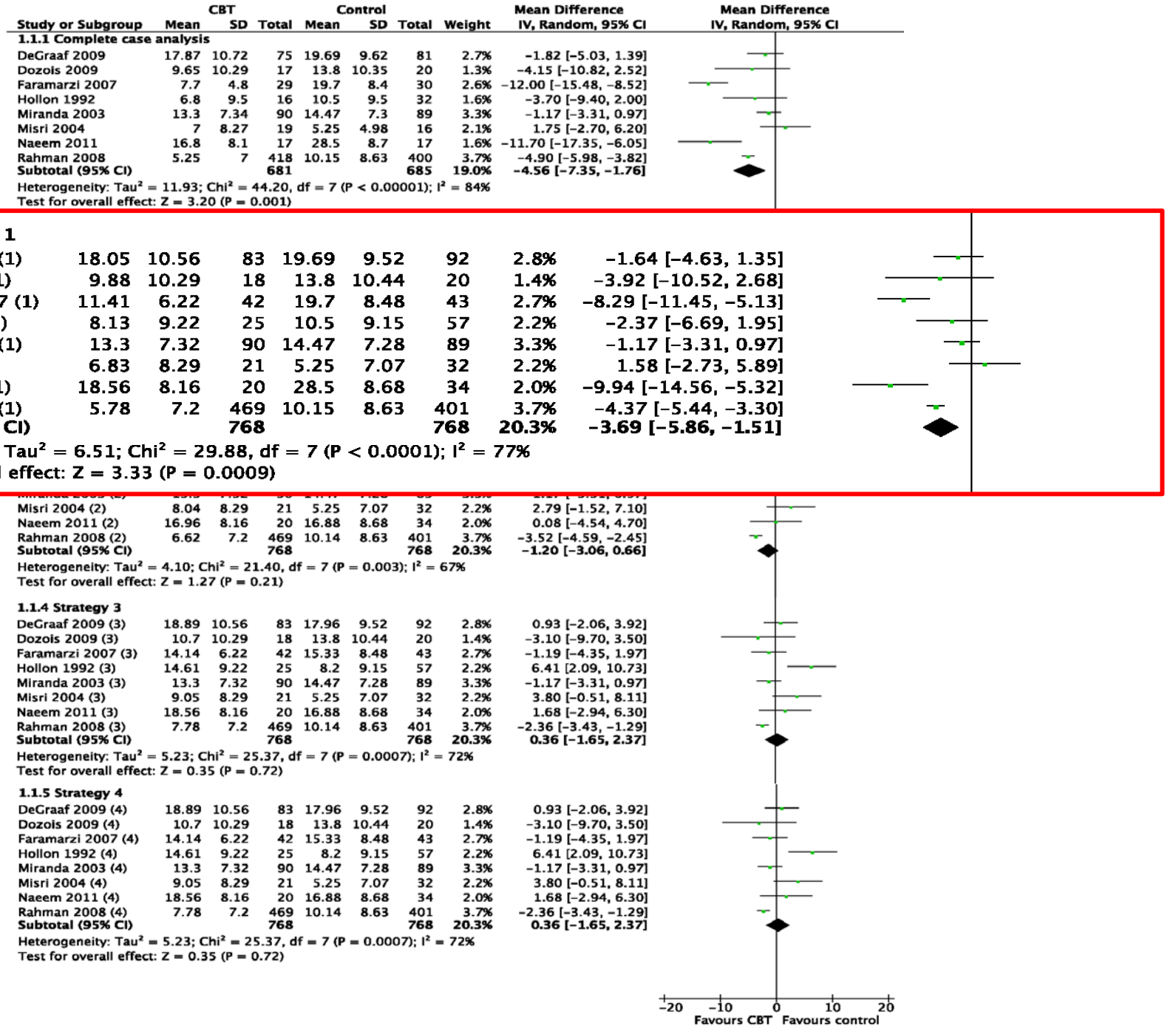
Application of approach: 1

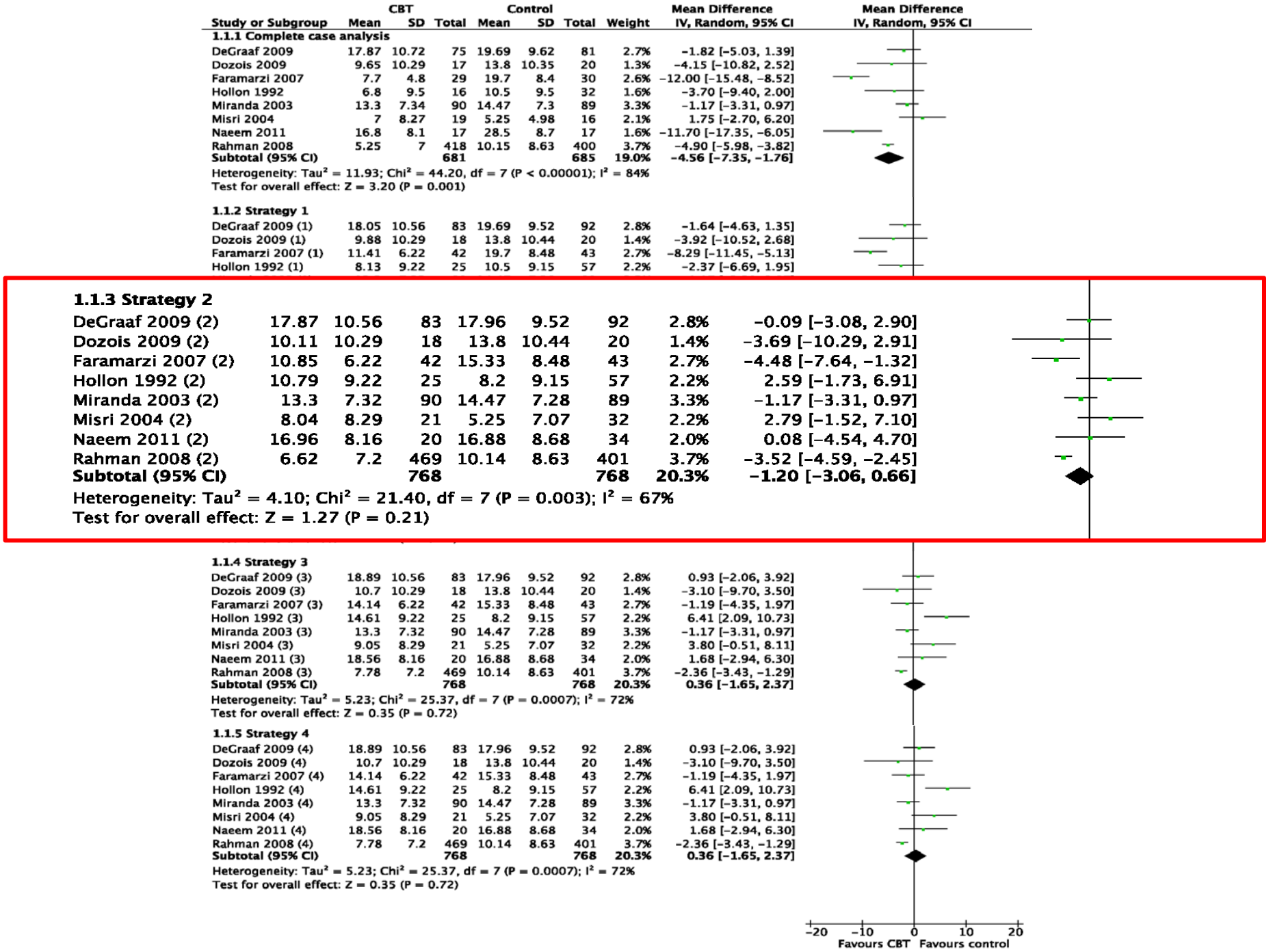
- Cognitive behavioural therapy (CBT) versus minimal or no treatment for depression in patients receiving disability benefits
- 8 RCTs: Beck Depression Inventory
- Median missing participant data rate = 21% (range 0 to 41%)

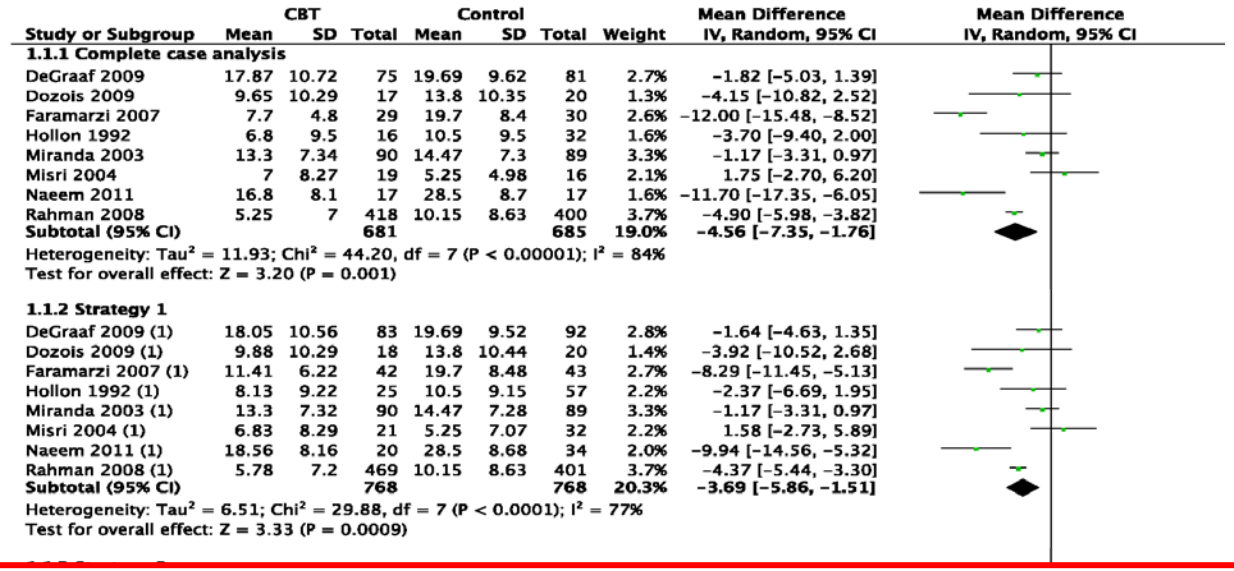
Ebrahim et al. PLoS One. 2012;7(11):e50202


CBT
Control
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
1.1.1 Complete case analysis
DeGraaf 2009 17.87 10.72 75 19.69 9.62 81 2.7% -1.82 [-5.03, 1.39]
Dozois 2009 9.65 10.29 17 13.8 10.35 20 1.3% -4.15 [-10.82, 2.52]
Faramarzi 2007 7.7 4.8 29 19.7 8.4 30 2.6% -12.00 [-15.48, -8.52]
Hollon 1992 6.8 9.5 16 10.5 9.5 32 1.6% -3.70 [-9.40, 2.00]
Miranda 2003 13.3 7.34 90 14.47 7.3 89 3.3% -1.17 [-3.31, 0.97]
Misri 2004 7 8.27 19 5.25 4.98 16 2.1% 1.75 [-2.70, 6.20]
Naeem 2011 16.8 8.1 17 28.5 8.7 17 1.6% -11.70 [-17.35, -6.05]
Rahman 2008 5.25 7 418 10.15 8.63 400 3.7% -4.90 [-5.98, -3.82]
Subtotal (95% CI) 681 685 19.0% -4.56 [-7.35, -1.76]
Heterogeneity: Tau² = 11.93; Chi² = 44.20, df = 7 (P < 0.00001); I² = 84%
Test for overall effect: Z = 3.20 (P = 0.001)
1.1.2 Strategy 1
DeGraaf 2009 (1) 18.05 10.56 83 19.69 9.52 92 2.8% -1.64 [-4.63, 1.35]
Dozois 2009 (1) 9.88 10.29 18 13.8 10.44 20 1.4% -3.92 [-10.52, 2.68]
Faramarzi 2007 (1) 11.41 6.22 42 19.7 8.48 43 2.7% -8.29 [-11.45, -5.13]
Hollon 1992 (1) 8.13 9.22 25 10.5 9.15 57 2.2% -2.37 [-6.69, 1.95]
Miranda 2003 (1) 13.3 7.32 90 14.47 7.28 89 3.3% -1.17 [-3.31, 0.97]
Misri 2004 (1) 6.83 8.29 21 5.25 7.07 32 2.2% 1.58 [-2.73, 5.89]
Naeem 2011 (1) 18.56 8.16 20 28.5 8.68 34 2.0% -9.94 [-14.56, -5.32]
Rahman 2008 (1) 5.78 7.2 469 10.15 8.63 401 3.7% -4.37 [-5.44, -3.30]
Subtotal (95% CI) 768 768 20.3% -3.69 [-5.86, -1.51]
Heterogeneity: Tau² = 6.51; Chi² = 29.88, df = 7 (P < 0.0001); I² = 77%
Test for overall effect: Z = 3.33 (P = 0.0009)
1.1.3 Strategy 2
DeGraaf 2009 (2) 17.87 10.56 83 17.96 9.52 92 2.8% -0.09 [-3.08, 2.90]
Dozois 2009 (2) 10.11 10.29 18 13.8 10.44 20 1.4% -3.69 [-10.29, 2.91]
Faramarzi 2007 (2) 10.85 6.22 42 15.33 8.48 43 2.7% -4.48 [-7.64, -1.32]
Hollon 1992 (2) 10.79 9.22 25 8.2 9.15 57 2.2% 2.59 [-1.73, 6.91]
Miranda 2003 (2) 13.3 7.32 90 14.47 7.28 89 3.3% -1.17 [-3.31, 0.97]
Misri 2004 (2) 8.04 8.29 21 5.25 7.07 32 2.2% 2.79 [-1.52, 7.10]
Naeem 2011 (2) 16.96 8.16 20 16.88 8.68 34 2.0% 0.08 [-4.54, 4.70]
Rahman 2008 (2) 6.62 7.2 469 10.14 8.63 401 3.7% -3.52 [-4.59, -2.45]
Subtotal (95% CI) 768 768 20.3% -1.20 [-3.06, 0.66]
Heterogeneity: Tau² = 4.10; Chi² = 21.40, df = 7 (P = 0.003); I² = 67%
Test for overall effect: Z = 1.27 (P = 0.21)
1.1.4 Strategy 3
DeGraaf 2009 (3) 18.89 10.56 83 17.96 9.52 92 2.8% 0.93 [-2.06, 3.92]
Dozois 2009 (3) 10.7 10.29 18 13.8 10.44 20 1.4% -3.10 [-9.70, 3.50]
Faramarzi 2007 (3) 14.14 6.22 42 15.33 8.48 43 2.7% -1.19 [-4.35, 1.97]
Hollon 1992 (3) 14.61 9.22 25 8.2 9.15 57 2.2% 6.41 [2.09, 10.73]
Miranda 2003 (3) 13.3 7.32 90 14.47 7.28 89 3.3% -1.17 [-3.31, 0.97]
Misri 2004 (3) 9.05 8.29 21 5.25 7.07 32 2.2% 3.80 [-0.51, 8.11]
Naeem 2011 (3) 18.56 8.16 20 16.88 8.68 34 2.0% 1.68 [-2.94, 6.30]
Rahman 2008 (3) 7.78 7.2 469 10.14 8.63 401 3.7% -2.36 [-3.43, -1.29]
Subtotal (95% CI) 768 768 20.3% 0.36 [-1.65, 2.37]
Heterogeneity: Tau² = 5.23; Chi² = 25.37, df = 7 (P = 0.0007); I² = 72%
Test for overall effect: Z = 0.35 (P = 0.72)
1.1.5 Strategy 4
DeGraaf 2009 (4) 18.89 10.56 83 17.96 9.52 92 2.8% 0.93 [-2.06, 3.92]
Dozois 2009 (4) 10.7 10.29 18 13.8 10.44 20 1.4% -3.10 [-9.70, 3.50]
Faramarzi 2007 (4) 14.14 6.22 42 15.33 8.48 43 2.7% -1.19 [-4.35, 1.97]
Hollon 1992 (4) 14.61 9.22 25 8.2 9.15 57 2.2% 6.41 [2.09, 10.73]
Miranda 2003 (4) 13.3 7.32 90 14.47 7.28 89 3.3% -1.17 [-3.31, 0.97]
Misri 2004 (4) 9.05 8.29 21 5.25 7.07 32 2.2% 3.80 [-0.51, 8.11]
Naeem 2011 (4) 18.56 8.16 20 16.88 8.68 34 2.0% 1.68 [-2.94, 6.30]
Rahman 2008 (4) 7.78 7.2 469 10.14 8.63 401 3.7% -2.36 [-3.43, -1.29]
Subtotal (95% CI) 768 768 20.3% 0.36 [-1.65, 2.37]
Heterogeneity: Tau² = 5.23; Chi² = 25.37, df = 7 (P = 0.0007); I² = 72%
Test for overall effect: Z = 0.35 (P = 0.72)
-20 -10 0 10 20
Favours CBT Favours control


CBT
Control
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
1.1.1 Complete case analysis
DeGraaf 2009 17.87 10.72 75 19.69 9.62 81 2.7% −1.82 [−5.03, 1.39]
Dozois 2009 9.65 10.29 17 13.8 10.35 20 1.3% −4.15 [−10.82, 2.52]
Faramarzi 2007 7.7 4.8 29 19.7 8.4 30 2.6% −12.00 [−15.48, −8.52]
Hollon 1992 6.8 9.5 16 10.5 9.5 32 1.6% −3.70 [−9.40, 2.00]
Miranda 2003 13.3 7.34 90 14.47 7.3 89 3.3% −1.17 [−3.31, 0.97]
Misri 2004 7 8.27 19 5.25 4.98 16 2.1% 1.75 [−2.70, 6.20]
Naeem 2011 16.8 8.1 17 28.5 8.7 17 1.6% −11.70 [−17.35, −6.05]
Rahman 2008 5.25 7 418 10.15 8.63 400 3.7% −4.90 [−5.98, −3.82]
Subtotal (95% CI) 681 685 19.0% −4.56 [−7.35, −1.76]
Heterogeneity: Tau² = 11.93; Chi² = 44.20, df = 7 (P < 0.00001); I² = 84%
Test for overall effect: Z = 3.20 (P = 0.001)
Naeem 2011 (1) 18.56 8.16 20 28.5 8.68 34 2.0% −9.94 [−14.56, −5.32]
Rahman 2008 (1) 5.78 7.2 469 10.15 8.63 401 3.7% −4.37 [−5.44, −3.30]
Subtotal (95% CI) 768 768 20.3% −3.69 [−5.86, −1.51]
Heterogeneity: Tau² = 6.51; Chi² = 29.88, df = 7 (P < 0.0001); I² = 77%
Test for overall effect: Z = 3.33 (P = 0.0009)
1.1.3 Strategy 2
DeGraaf 2009 (2) 17.87 10.56 83 17.96 9.52 92 2.8% −0.09 [−3.08, 2.90]
Dozois 2009 (2) 10.11 10.29 18 13.8 10.44 20 1.4% −3.69 [−10.29, 2.91]
Faramarzi 2007 (2) 10.85 6.22 42 15.33 8.48 43 2.7% −4.48 [−7.64, −1.32]
Hollon 1992 (2) 10.79 9.22 25 8.2 9.15 57 2.2% 2.59 [−1.73, 6.91]
Miranda 2003 (2) 13.3 7.32 90 14.47 7.28 89 3.3% −1.17 [−3.31, 0.97]
Misri 2004 (2) 8.04 8.29 21 5.25 7.07 32 2.2% 2.79 [−1.52, 7.10]
Naeem 2011 (2) 16.96 8.16 20 16.88 8.68 34 2.0% 0.08 [−4.54, 4.70]
Rahman 2008 (2) 6.62 7.2 469 10.14 8.63 401 3.7% −3.52 [−4.59, −2.45]
Subtotal (95% CI) 768 768 20.3% −1.20 [−3.06, 0.66]
Heterogeneity: Tau² = 4.10; Chi² = 21.40, df = 7 (P = 0.003); I² = 67%
Test for overall effect: Z = 1.27 (P = 0.21)
1.1.4 Strategy 3
DeGraaf 2009 (3) 18.89 10.56 83 17.96 9.52 92 2.8% 0.93 [−2.06, 3.92]
Dozois 2009 (3) 10.7 10.29 18 13.8 10.44 20 1.4% −3.10 [−9.70, 3.50]
Faramarzi 2007 (3) 14.14 6.22 42 15.33 8.48 43 2.7% −1.19 [−4.35, 1.97]
Hollon 1992 (3) 14.61 9.22 25 8.2 9.15 57 2.2% 6.41 [2.09, 10.73]
Miranda 2003 (3) 13.3 7.32 90 14.47 7.28 89 3.3% −1.17 [−3.31, 0.97]
Misri 2004 (3) 9.05 8.29 21 5.25 7.07 32 2.2% 3.80 [−0.51, 8.11]
Naeem 2011 (3) 18.56 8.16 20 16.88 8.68 34 2.0% 1.68 [−2.94, 6.30]
Rahman 2008 (3) 7.78 7.2 469 10.14 8.63 401 3.7% −2.36 [−3.43, −1.29]
Subtotal (95% CI) 768 768 20.3% 0.36 [−1.65, 2.37]
Heterogeneity: Tau² = 5.23; Chi² = 25.37, df = 7 (P = 0.0007); I² = 72%
Test for overall effect: Z = 0.35 (P = 0.72)
1.1.5 Strategy 4
DeGraaf 2009 (4) 18.89 10.56 83 17.96 9.52 92 2.8% 0.93 [−2.06, 3.92]
Dozois 2009 (4) 10.7 10.29 18 13.8 10.44 20 1.4% −3.10 [−9.70, 3.50]
Faramarzi 2007 (4) 14.14 6.22 42 15.33 8.48 43 2.7% −1.19 [−4.35, 1.97]
Hollon 1992 (4) 14.61 9.22 25 8.2 9.15 57 2.2% 6.41 [2.09, 10.73]
Miranda 2003 (4) 13.3 7.32 90 14.47 7.28 89 3.3% −1.17 [−3.31, 0.97]
Misri 2004 (4) 9.05 8.29 21 5.25 7.07 32 2.2% 3.80 [−0.51, 8.11]
Naeem 2011 (4) 18.56 8.16 20 16.88 8.68 34 2.0% 1.68 [−2.94, 6.30]
Rahman 2008 (4) 7.78 7.2 469 10.14 8.63 401 3.7% −2.36 [−3.43, −1.29]
Subtotal (95% CI) 768 768 20.3% 0.36 [−1.65, 2.37]
Heterogeneity: Tau² = 5.23; Chi² = 25.37, df = 7 (P = 0.0007); I² = 72%
Test for overall effect: Z = 0.35 (P = 0.72)
−20 −10 0 10 20
Favours CBT Favours control


CBT
Control
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
1.1.1 Complete case analysis
DeGraaf 2009 17.87 10.72 75 19.69 9.62 81 2.7% -1.82 [-5.03, 1.39]
Dozois 2009 9.65 10.29 17 13.8 10.35 20 1.3% -4.15 [-10.82, 2.52]
Faramarzi 2007 7.7 4.8 29 19.7 8.4 30 2.6% -12.00 [-15.48, -8.52]
Hollon 1992 6.8 9.5 16 10.5 9.5 32 1.6% -3.70 [-9.40, 2.00]
Miranda 2003 13.3 7.34 90 14.47 7.3 89 3.3% -1.17 [-3.31, 0.97]
Misri 2004 7 8.27 19 5.25 4.98 16 2.1% 1.75 [-2.70, 6.20]
Naeem 2011 16.8 8.1 17 28.5 8.7 17 1.6% -11.70 [-17.35, -6.05]
Rahman 2008 5.25 7 418 10.15 8.63 400 3.7% -4.90 [-5.98, -3.82]
Subtotal (95% CI) 681 685 19.0% -4.56 [-7.35, -1.76]
Heterogeneity: Tau² = 11.93; Chi² = 44.20, df = 7 (P < 0.00001); I² = 84%
Test for overall effect: Z = 3.20 (P = 0.001)
1.1.2 Strategy 1
DeGraaf 2009 (1) 18.05 10.56 83 19.69 9.52 92 2.8% -1.64 [-4.63, 1.35]
Dozois 2009 (1) 9.88 10.29 18 13.8 10.44 20 1.4% -3.92 [-10.52, 2.68]
Faramarzi 2007 (1) 11.41 6.22 42 19.7 8.48 43 2.7% -8.29 [-11.45, -5.13]
Hollon 1992 (1) 8.13 9.22 25 10.5 9.15 57 2.2% -2.37 [-6.69, 1.95]
Miranda 2003 (1) 13.3 7.32 90 14.47 7.28 89 3.3% -1.17 [-3.31, 0.97]
Misri 2004 (1) 6.83 8.29 21 5.25 7.07 32 2.2% 1.58 [-2.73, 5.89]
Naeem 2011 (1) 18.56 8.16 20 28.5 8.68 34 2.0% -9.94 [-14.56, -5.32]
Rahman 2008 (1) 5.78 7.2 469 10.15 8.63 401 3.7% -4.37 [-5.44, -3.30]
Subtotal (95% CI) 768 768 20.3% -3.69 [-5.86, -1.51]
Heterogeneity: Tau² = 6.51; Chi² = 29.88, df = 7 (P < 0.0001); I² = 77%
Test for overall effect: Z = 3.33 (P = 0.0009)
Misri 2004 (2) 8.04 8.29 21 5.25 7.07 32 2.2% 2.79 [-1.52, 7.10]
Naeem 2011 (2) 16.96 8.16 20 16.88 8.68 34 2.0% 0.08 [-4.54, 4.70]
Rahman 2008 (2) 6.62 7.2 469 10.14 8.63 401 3.7% -3.52 [-4.59, -2.45]
Subtotal (95% CI) 768 768 20.3% -1.20 [-3.06, 0.66]
Heterogeneity: Tau² = 4.10; Chi² = 21.40, df = 7 (P = 0.003); I² = 67%
Test for overall effect: Z = 1.27 (P = 0.21)
1.1.4 Strategy 3
DeGraaf 2009 (3) 18.89 10.56 83 17.96 9.52 92 2.8% 0.93 [-2.06, 3.92]
Dozois 2009 (3) 10.7 10.29 18 13.8 10.44 20 1.4% -3.10 [-9.70, 3.50]
Faramarzi 2007 (3) 14.14 6.22 42 15.33 8.48 43 2.7% -1.19 [-4.35, 1.97]
Hollon 1992 (3) 14.61 9.22 25 8.2 9.15 57 2.2% 6.41 [2.09, 10.73]
Miranda 2003 (3) 13.3 7.32 90 14.47 7.28 89 3.3% -1.17 [-3.31, 0.97]
Misri 2004 (3) 9.05 8.29 21 5.25 7.07 32 2.2% 3.80 [-0.51, 8.11]
Naeem 2011 (3) 18.56 8.16 20 16.88 8.68 34 2.0% 1.68 [-2.94, 6.30]
Rahman 2008 (3) 7.78 7.2 469 10.14 8.63 401 3.7% -2.36 [-3.43, -1.29]
Subtotal (95% CI) 768 768 20.3% 0.36 [-1.65, 2.37]
Heterogeneity: Tau² = 5.23; Chi² = 25.37, df = 7 (P = 0.0007); I² = 72%
Test for overall effect: Z = 0.35 (P = 0.72)
1.1.5 Strategy 4
DeGraaf 2009 (4) 18.89 10.56 83 17.96 9.52 92 2.8% 0.93 [-2.06, 3.92]
Dozois 2009 (4) 10.7 10.29 18 13.8 10.44 20 1.4% -3.10 [-9.70, 3.50]
Faramarzi 2007 (4) 14.14 6.22 42 15.33 8.48 43 2.7% -1.19 [-4.35, 1.97]
Hollon 1992 (4) 14.61 9.22 25 8.2 9.15 57 2.2% 6.41 [2.09, 10.73]
Miranda 2003 (4) 13.3 7.32 90 14.47 7.28 89 3.3% -1.17 [-3.31, 0.97]
Misri 2004 (4) 9.05 8.29 21 5.25 7.07 32 2.2% 3.80 [-0.51, 8.11]
Naeem 2011 (4) 18.56 8.16 20 16.88 8.68 34 2.0% 1.68 [-2.94, 6.30]
Rahman 2008 (4) 7.78 7.2 469 10.14 8.63 401 3.7% -2.36 [-3.43, -1.29]
Subtotal (95% CI) 768 768 20.3% 0.36 [-1.65, 2.37]
Heterogeneity: Tau² = 5.23; Chi² = 25.37, df = 7 (P = 0.0007); I² = 72%
Test for overall effect: Z = 0.35 (P = 0.72)
-20 -10 0 10 20
Favours CBT Favours control


CBT
Control
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
1.1.1 Complete case analysis
DeGraaf 2009 17.87 10.72 75 19.69 9.62 81 2.7% -1.82 [-5.03, 1.39]
Dozois 2009 9.65 10.29 17 13.8 10.35 20 1.3% -4.15 [-10.82, 2.52]
Faramarzi 2007 7.7 4.8 29 19.7 8.4 30 2.6% -12.00 [-15.48, -8.52]
Hollon 1992 6.8 9.5 16 10.5 9.5 32 1.6% -3.70 [-9.40, 2.00]
Miranda 2003 13.3 7.34 90 14.47 7.3 89 3.3% -1.17 [-3.31, 0.97]
Misri 2004 7 8.27 19 5.25 4.98 16 2.1% 1.75 [-2.70, 6.20]
Naeem 2011 16.8 8.1 17 28.5 8.7 17 1.6% -11.70 [-17.35, -6.05]
Rahman 2008 5.25 7 418 10.15 8.63 400 3.7% -4.90 [-5.98, -3.82]
Subtotal (95% CI) 681 685 19.0% -4.56 [-7.35, -1.76]
Heterogeneity: Tau² = 11.93; Chi² = 44.20, df = 7 (P < 0.00001); I² = 84%
Test for overall effect: Z = 3.20 (P = 0.001)
1.1.2 Strategy 1
DeGraaf 2009 (1) 18.05 10.56 83 19.69 9.52 92 2.8% -1.64 [-4.63, 1.35]
Dozois 2009 (1) 9.88 10.29 18 13.8 10.44 20 1.4% -3.92 [-10.52, 2.68]
Faramarzi 2007 (1) 11.41 6.22 42 19.7 8.48 43 2.7% -8.29 [-11.45, -5.13]
Hollon 1992 (1) 8.13 9.22 25 10.5 9.15 57 2.2% -2.37 [-6.69, 1.95]
1.1.3 Strategy 2
DeGraaf 2009 (2) 17.87 10.56 83 17.96 9.52 92 2.8% -0.09 [-3.08, 2.90]
Dozois 2009 (2) 10.11 10.29 18 13.8 10.44 20 1.4% -3.69 [-10.29, 2.91]
Faramarzi 2007 (2) 10.85 6.22 42 15.33 8.48 43 2.7% -4.48 [-7.64, -1.32]
Hollon 1992 (2) 10.79 9.22 25 8.2 9.15 57 2.2% 2.59 [-1.73, 6.91]
Miranda 2003 (2) 13.3 7.32 90 14.47 7.28 89 3.3% -1.17 [-3.31, 0.97]
Misri 2004 (2) 8.04 8.29 21 5.25 7.07 32 2.2% 2.79 [-1.52, 7.10]
Naeem 2011 (2) 16.96 8.16 20 16.88 8.68 34 2.0% 0.08 [-4.54, 4.70]
Rahman 2008 (2) 6.62 7.2 469 10.14 8.63 401 3.7% -3.52 [-4.59, -2.45]
Subtotal (95% CI) 768 768 20.3% -1.20 [-3.06, 0.66]
Heterogeneity: Tau² = 4.10; Chi² = 21.40, df = 7 (P = 0.003); I² = 67%
Test for overall effect: Z = 1.27 (P = 0.21)
1.1.4 Strategy 3
DeGraaf 2009 (3) 18.89 10.56 83 17.96 9.52 92 2.8% 0.93 [-2.06, 3.92]
Dozois 2009 (3) 10.7 10.29 18 13.8 10.44 20 1.4% -3.10 [-9.70, 3.50]
Faramarzi 2007 (3) 14.14 6.22 42 15.33 8.48 43 2.7% -1.19 [-4.35, 1.97]
Hollon 1992 (3) 14.61 9.22 25 8.2 9.15 57 2.2% 6.41 [2.09, 10.73]
Miranda 2003 (3) 13.3 7.32 90 14.47 7.28 89 3.3% -1.17 [-3.31, 0.97]
Misri 2004 (3) 9.05 8.29 21 5.25 7.07 32 2.2% 3.80 [-0.51, 8.11]
Naeem 2011 (3) 18.56 8.16 20 16.88 8.68 34 2.0% 1.68 [-2.94, 6.30]
Rahman 2008 (3) 7.78 7.2 469 10.14 8.63 401 3.7% -2.36 [-3.43, -1.29]
Subtotal (95% CI) 768 768 20.3% 0.36 [-1.65, 2.37]
Heterogeneity: Tau² = 5.23; Chi² = 25.37, df = 7 (P = 0.0007); I² = 72%
Test for overall effect: Z = 0.35 (P = 0.72)
1.1.5 Strategy 4
DeGraaf 2009 (4) 18.89 10.56 83 17.96 9.52 92 2.8% 0.93 [-2.06, 3.92]
Dozois 2009 (4) 10.7 10.29 18 13.8 10.44 20 1.4% -3.10 [-9.70, 3.50]
Faramarzi 2007 (4) 14.14 6.22 42 15.33 8.48 43 2.7% -1.19 [-4.35, 1.97]
Hollon 1992 (4) 14.61 9.22 25 8.2 9.15 57 2.2% 6.41 [2.09, 10.73]
Miranda 2003 (4) 13.3 7.32 90 14.47 7.28 89 3.3% -1.17 [-3.31, 0.97]
Misri 2004 (4) 9.05 8.29 21 5.25 7.07 32 2.2% 3.80 [-0.51, 8.11]
Naeem 2011 (4) 18.56 8.16 20 16.88 8.68 34 2.0% 1.68 [-2.94, 6.30]
Rahman 2008 (4) 7.78 7.2 469 10.14 8.63 401 3.7% -2.36 [-3.43, -1.29]
Subtotal (95% CI) 768 768 20.3% 0.36 [-1.65, 2.37]
Heterogeneity: Tau² = 5.23; Chi² = 25.37, df = 7 (P = 0.0007); I² = 72%
Test for overall effect: Z = 0.35 (P = 0.72)
-20 -10 0 10 20
Favours CBT Favours control



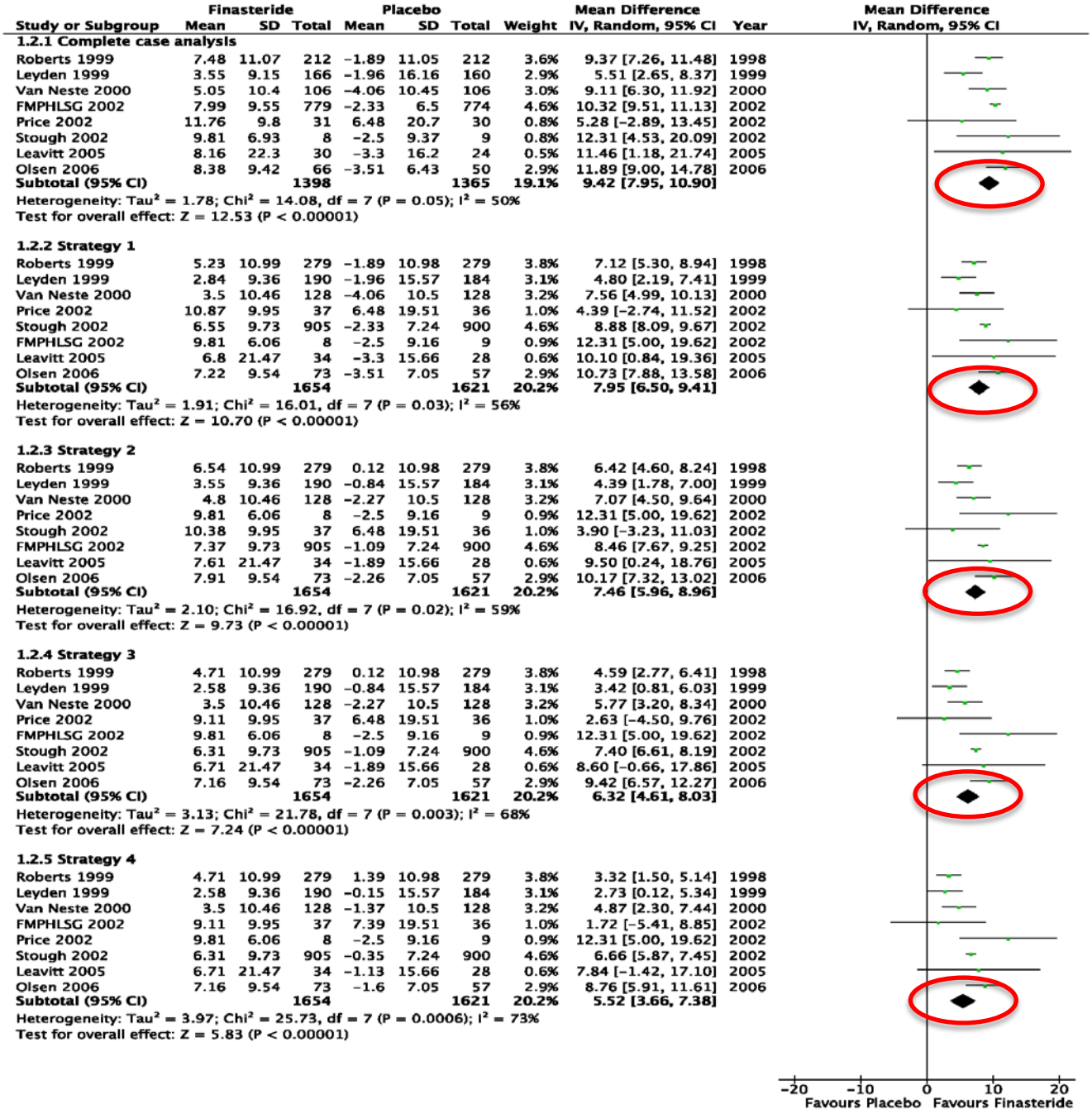
Study or Subgroup	CBT Mean	CBT SD	CBT Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
1.1.1 Complete case analysis								
DeGraaf 2009	17.87	10.72	75	19.69	9.62	81	2.7%	−1.82 [−5.03, 1.39]
Dozois 2009	9.65	10.29	17	13.8	10.35	20	1.3%	−4.15 [−10.82, 2.52]
Faramarzi 2007	7.7	4.8	29	19.7	8.4	30	2.6%	−12.00 [−15.48, −8.52]
Hollon 1992	6.8	9.5	16	10.5	9.5	32	1.6%	−3.70 [−9.40, 2.00]
Miranda 2003	13.3	7.34	90	14.47	7.3	89	3.3%	−1.17 [−3.31, 0.97]
Misri 2004	7	8.27	19	5.25	4.98	16	2.1%	1.75 [−2.70, 6.20]
Naeem 2011	16.8	8.1	17	28.5	8.7	17	1.6%	−11.70 [−17.35, −6.05]
Rahman 2008	5.25	7	418	10.15	8.63	400	3.7%	−4.90 [−5.98, −3.82]
Subtotal (95% CI)			**681**			**685**	**19.0%**	**−4.56 [−7.35, −1.76]**
Heterogeneity: Tau² = 11.93; Chi² = 44.20, df = 7 (P < 0.00001); I² = 84%								
Test for overall effect: Z = 3.20 (P = 0.001)								
1.1.2 Strategy 1								
DeGraaf 2009 (1)	18.05	10.56	83	19.69	9.52	92	2.8%	−1.64 [−4.63, 1.35]
Dozois 2009 (1)	9.88	10.29	18	13.8	10.44	20	1.4%	−3.92 [−10.52, 2.68]
Faramarzi 2007 (1)	11.41	6.22	42	19.7	8.48	43	2.7%	−8.29 [−11.45, −5.13]
Hollon 1992 (1)	8.13	9.22	25	10.5	9.15	57	2.2%	−2.37 [−6.69, 1.95]
Miranda 2003 (1)	13.3	7.32	90	14.47	7.28	89	3.3%	−1.17 [−3.31, 0.97]
Misri 2004 (1)	6.83	8.29	21	5.25	7.07	32	2.2%	1.58 [−2.73, 5.89]
Naeem 2011 (1)	18.56	8.16	20	28.5	8.68	34	2.0%	−9.94 [−14.56, −5.32]
Rahman 2008 (1)	5.78	7.2	469	10.15	8.63	401	3.7%	−4.37 [−5.44, −3.30]
Subtotal (95% CI)			**768**			**768**	**20.3%**	**−3.69 [−5.86, −1.51]**
Heterogeneity: Tau² = 6.51; Chi² = 29.88, df = 7 (P < 0.0001); I² = 77%								
Test for overall effect: Z = 3.33 (P = 0.0009)								

1.1.4 Strategy 3								
DeGraaf 2009 (3)	18.89	10.56	83	17.96	9.52	92	2.8%	0.93 [−2.06, 3.92]
Dozois 2009 (3)	10.7	10.29	18	13.8	10.44	20	1.4%	−3.10 [−9.70, 3.50]
Faramarzi 2007 (3)	14.14	6.22	42	15.33	8.48	43	2.7%	−1.19 [−4.35, 1.97]
Hollon 1992 (3)	14.61	9.22	25	8.2	9.15	57	2.2%	6.41 [2.09, 10.73]
Miranda 2003 (3)	13.3	7.32	90	14.47	7.28	89	3.3%	−1.17 [−3.31, 0.97]
Misri 2004 (3)	9.05	8.29	21	5.25	7.07	32	2.2%	3.80 [−0.51, 8.11]
Naeem 2011 (3)	18.56	8.16	20	16.88	8.68	34	2.0%	1.68 [−2.94, 6.30]
Rahman 2008 (3)	7.78	7.2	469	10.14	8.63	401	3.7%	−2.36 [−3.43, −1.29]
Subtotal (95% CI)			**768**			**768**	**20.3%**	**0.36 [−1.65, 2.37]**
Heterogeneity: Tau² = 5.23; Chi² = 25.37, df = 7 (P = 0.0007); I² = 72%								
Test for overall effect: Z = 0.35 (P = 0.72)								
1.1.5 Strategy 4								
DeGraaf 2009 (4)	18.89	10.56	83	17.96	9.52	92	2.8%	0.93 [−2.06, 3.92]
Dozois 2009 (4)	10.7	10.29	18	13.8	10.44	20	1.4%	−3.10 [−9.70, 3.50]
Faramarzi 2007 (4)	14.14	6.22	42	15.33	8.48	43	2.7%	−1.19 [−4.35, 1.97]
Hollon 1992 (4)	14.61	9.22	25	8.2	9.15	57	2.2%	6.41 [2.09, 10.73]
Miranda 2003 (4)	13.3	7.32	90	14.47	7.28	89	3.3%	−1.17 [−3.31, 0.97]
Misri 2004 (4)	9.05	8.29	21	5.25	7.07	32	2.2%	3.80 [−0.51, 8.11]
Naeem 2011 (4)	18.56	8.16	20	16.88	8.68	34	2.0%	1.68 [−2.94, 6.30]
Rahman 2008 (4)	7.78	7.2	469	10.14	8.63	401	3.7%	−2.36 [−3.43, −1.29]
Subtotal (95% CI)			**768**			**768**	**20.3%**	**0.36 [−1.65, 2.37]**
Heterogeneity: Tau² = 5.23; Chi² = 25.37, df = 7 (P = 0.0007); I² = 72%								
Test for overall effect: Z = 0.35 (P = 0.72)								

Application of approach: 2

- Finasteride therapy versus placebo on improvement in scalp hair for men with androgenetic alopecia
- 8 RCTs
- Median missing participant data rate = 14% (range 0% to 24%)

Mella et al. Arch Dermatol. 2010 Oct;146(10):1141-50.


Finasteride
Placebo
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI Year
IV, Random, 95% CI
1.2.1 Complete case analysis
Roberts 1999 7.48 11.07 212 -1.89 11.05 212 3.6% 9.37 [7.26, 11.48] 1998
Leyden 1999 3.55 9.15 166 -1.96 16.16 160 2.9% 5.51 [2.65, 8.37] 1999
Van Neste 2000 5.05 10.4 106 -4.06 10.45 106 3.0% 9.11 [6.30, 11.92] 2000
FMPHLSG 2002 7.99 9.55 779 -2.33 6.5 774 4.6% 10.32 [9.51, 11.13] 2002
Price 2002 11.76 9.8 31 6.48 20.7 30 0.8% 5.28 [-2.89, 13.45] 2002
Stough 2002 9.81 6.93 8 -2.5 9.37 9 0.8% 12.31 [4.53, 20.09] 2002
Leavitt 2005 8.16 22.3 30 -3.3 16.2 24 0.5% 11.46 [1.18, 21.74] 2005
Olsen 2006 8.38 9.42 66 -3.51 6.43 50 2.9% 11.89 [9.00, 14.78] 2006
Subtotal (95% CI) 1398 1365 19.1% 9.42 [7.95, 10.90]
Heterogeneity: Tau² = 1.78; Chi² = 14.08, df = 7 (P = 0.05); I² = 50%
Test for overall effect: Z = 12.53 (P < 0.00001)
1.2.2 Strategy 1
Roberts 1999 5.23 10.99 279 -1.89 10.98 279 3.8% 7.12 [5.30, 8.94] 1998
Leyden 1999 2.84 9.36 190 -1.96 15.57 184 3.1% 4.80 [2.19, 7.41] 1999
Van Neste 2000 3.5 10.46 128 -4.06 10.5 128 3.2% 7.56 [4.99, 10.13] 2000
Price 2002 10.87 9.95 37 6.48 19.51 36 1.0% 4.39 [-2.74, 11.52] 2002
Stough 2002 6.55 9.73 905 -2.33 7.24 900 4.6% 8.88 [8.09, 9.67] 2002
FMPHLSG 2002 9.81 6.06 8 -2.5 9.16 9 0.9% 12.31 [5.00, 19.62] 2002
Leavitt 2005 6.8 21.47 34 -3.3 15.66 28 0.6% 10.10 [0.84, 19.36] 2005
Olsen 2006 7.22 9.54 73 -3.51 7.05 57 2.9% 10.73 [7.88, 13.58] 2006
Subtotal (95% CI) 1654 1621 20.2% 7.95 [6.50, 9.41]
Heterogeneity: Tau² = 1.91; Chi² = 16.01, df = 7 (P = 0.03); I² = 56%
Test for overall effect: Z = 10.70 (P < 0.00001)
1.2.3 Strategy 2
Roberts 1999 6.54 10.99 279 0.12 10.98 279 3.8% 6.42 [4.60, 8.24] 1998
Leyden 1999 3.55 9.36 190 -0.84 15.57 184 3.1% 4.39 [1.78, 7.00] 1999
Van Neste 2000 4.8 10.46 128 -2.27 10.5 128 3.2% 7.07 [4.50, 9.64] 2000
Price 2002 9.81 6.06 8 -2.5 9.16 9 0.9% 12.31 [5.00, 19.62] 2002
Stough 2002 10.38 9.95 37 6.48 19.51 36 1.0% 3.90 [-3.23, 11.03] 2002
FMPHLSG 2002 7.37 9.73 905 -1.09 7.24 900 4.6% 8.46 [7.67, 9.25] 2002
Leavitt 2005 7.61 21.47 34 -1.89 15.66 28 0.6% 9.50 [0.24, 18.76] 2005
Olsen 2006 7.91 9.54 73 -2.26 7.05 57 2.9% 10.17 [7.32, 13.02] 2006
Subtotal (95% CI) 1654 1621 20.2% 7.46 [5.96, 8.96]
Heterogeneity: Tau² = 2.10; Chi² = 16.92, df = 7 (P = 0.02); I² = 59%
Test for overall effect: Z = 9.73 (P < 0.00001)
1.2.4 Strategy 3
Roberts 1999 4.71 10.99 279 0.12 10.98 279 3.8% 4.59 [2.77, 6.41] 1998
Leyden 1999 2.58 9.36 190 -0.84 15.57 184 3.1% 3.42 [0.81, 6.03] 1999
Van Neste 2000 3.5 10.46 128 -2.27 10.5 128 3.2% 5.77 [3.20, 8.34] 2000
Price 2002 9.11 9.95 37 6.48 19.51 36 1.0% 2.63 [-4.50, 9.76] 2002
FMPHLSG 2002 9.81 6.06 8 -2.5 9.16 9 0.9% 12.31 [5.00, 19.62] 2002
Stough 2002 6.31 9.73 905 -1.09 7.24 900 4.6% 7.40 [6.61, 8.19] 2002
Leavitt 2005 6.71 21.47 34 -1.89 15.66 28 0.6% 8.60 [-0.66, 17.86] 2005
Olsen 2006 7.16 9.54 73 -2.26 7.05 57 2.9% 9.42 [6.57, 12.27] 2006
Subtotal (95% CI) 1654 1621 20.2% 6.32 [4.61, 8.03]
Heterogeneity: Tau² = 3.13; Chi² = 21.78, df = 7 (P = 0.003); I² = 68%
Test for overall effect: Z = 7.24 (P < 0.00001)
1.2.5 Strategy 4
Roberts 1999 4.71 10.99 279 1.39 10.98 279 3.8% 3.32 [1.50, 5.14] 1998
Leyden 1999 2.58 9.36 190 -0.15 15.57 184 3.1% 2.73 [0.12, 5.34] 1999
Van Neste 2000 3.5 10.46 128 -1.37 10.5 128 3.2% 4.87 [2.30, 7.44] 2000
FMPHLSG 2002 9.11 9.95 37 7.39 19.51 36 1.0% 1.72 [-5.41, 8.85] 2002
Price 2002 9.81 6.06 8 -2.5 9.16 9 0.9% 12.31 [5.00, 19.62] 2002
Stough 2002 6.31 9.73 905 -0.35 7.24 900 4.6% 6.66 [5.87, 7.45] 2002
Leavitt 2005 6.71 21.47 34 -1.13 15.66 28 0.6% 7.84 [-1.42, 17.10] 2005
Olsen 2006 7.16 9.54 73 -1.6 7.05 57 2.9% 8.76 [5.91, 11.61] 2006
Subtotal (95% CI) 1654 1621 20.2% 5.52 [3.66, 7.38]
Heterogeneity: Tau² = 3.97; Chi² = 25.73, df = 7 (P = 0.0006); I² = 73%
Test for overall effect: Z = 5.83 (P < 0.00001)
-20 -10 0 10 20
Favours Placebo Favours Finasteride

Discussion

CBT review:

- Effect diminished, lost significance as strategies became more stringent
- Rate down for risk of bias

Finasteride review:

- Even most stringent: effect important, statistical sig remains
- Do not need to rate down for risk of bias

Conclusions

- Approach involving progressively more stringent assumptions about results in participants with missing data
- Provides guidance on rigorously determining the extent to which missing data increases risk of bias in systematic reviews
- To the extent that results change with the sensitivity analyses, risk of bias as a result of missing data increases

ELSEVIER

Journal of Clinical Epidemiology ■ (2013) ■

Journal of Clinical Epidemiology

ORIGINAL ARTICLE

Addressing continuous data for participants excluded from trial analysis: a guide for systematic reviewers

Shanil Ebrahim[a,b], Elie A. Akl[a,c,d], Reem A. Mustafa[a,e], Xin Sun[a,f], Stephen D. Walter[a], Diane Heels-Ansdell[a], Pablo Alonso-Coello[g], Bradley C. Johnston[a,h,i,j], Gordon H. Guyatt[a,k,*]