

# CHILDHOOD TRAUMA AND ADULT DEPRESSION TREATMENT

## FIRST SUBMITTED VERSION

### Supplement

#### Full Search String for the PubMed Database

Search: ((depress\*[All Fields] OR depression[MeSH Terms] OR "depressive disorder"[MeSH Terms] OR "depressive disorder"[All Fields] OR "mood disorder"[All Fields] OR "mood disorders"[All Fields] OR "affective disorder"[All Fields] OR "affective disorders"[All Fields] OR MDD[All Fields] OR "major depression"[All Fields] OR "major depressive disorder"[All Fields]) **AND** ("child abuse"[MeSH Terms] OR "child abuse"[All Fields] OR "childhood abuse"[All Fields] OR "child trauma"[All Fields] OR "childhood trauma"[All Fields] OR "child physical abuse"[All Fields] OR "childhood physical abuse"[All Fields] OR "child sexual abuse"[All Fields] OR "childhood sexual abuse"[All Fields] OR "child emotional abuse"[All Fields] OR "childhood emotional abuse"[All Fields] OR "early interpersonal trauma"[All Fields] OR "child maltreatment"[All Fields] OR "childhood maltreatment"[All Fields] OR "child neglect"[All Fields] OR "childhood neglect"[All Fields] OR "early experience"[All Fields] OR "child adversity"[All Fields] OR "childhood adversity"[All Fields] OR "early adversity"[All Fields] OR "early life adversity"[All Fields] OR "early stress"[All Fields] OR "early life stress"[All Fields]) **AND** (therapy[MeSH Terms] OR therap\*[All Fields] OR therapeutics[MeSH Terms] OR therapeutics[All Fields] OR treatment\*[All Fields] OR psychotherap\*[All Fields] OR psychotherapy[MeSH Terms] OR psychotherapy[All Fields] OR CBT[All Fields] OR pharmacotherap\*[All Fields] OR pharmacotherapy[MeSH Terms] OR pharmacotherapy[All Fields] OR antidepressant\*[All Fields] OR SSRI[All Fields] OR outcome[All Fields] OR "depressive symptoms"[All Fields] OR "depression severity"[All Fields] OR respon\*[All Fields] OR improvement[All Fields] OR remission[All Fields]) **NOT** ("brain injury"[All Fields]) **AND** ("2013/11/21"[PDAT] : "2020/03/16"[PDAT]))

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### **Childhood Trauma Questionnaire (28 item Short Form)**

Bernstein D., & Fink L. (1998). *Childhood Trauma Questionnaire. A Retrospective Self-Report Questionnaire and Manual*. San Antonio, The Psychological Corporation

*Cut-off: none/low vs. moderate/severe*

Emotional abuse: none = 5-8; low = 9-12; moderate = 13-15; severe = 16+

Physical abuse: none = 5-7; low = 8-9; moderate = 10-12; severe = 13+

Sexual abuse: none = 5; low = 6-7; moderate = 8-12; severe = 13+

Emotional neglect: none = 5-9; low = 10-14; moderate = 15-17; severe = 18+

Physical neglect: none = 5-7; low = 8-9; moderate = 10-12; severe = 13+

### **Childhood Experience of Care and Abuse (CECA) Interview**

Bifulco, A., Brown, G.W., & Harris, T. O. (1994). Childhood Experience of Care and Abuse (CECA): a retrospective interview measure. *J Child Psychol Psychiatry*, 35(8), 1419–35.

*Cut-off: none/little/some vs. moderate/marked*

Emotional abuse: none/little = 1; some = 2; moderate = 3; marked = 4

Physical abuse: none/little = 1; some = 2; moderate = 3; marked = 4

Sexual abuse: none/little = 1; some = 2; moderate = 3; marked = 4

### **Childhood Trauma Interview (CTI)**

Used in Netherlands Mental Health Survey and Incidence Study (NEMESIS): de Graaf, R., Bijl, R. V., ten Have, M., Beekman, A. T., & Vollebergh, W. A. (2004). Rapid onset of comorbidity of common mental disorders: Findings from the Netherlands Mental Health Survey and Incidence Study (NEMESIS). *Acta Psychiatr Scand*, 109(1), 55-63.

*Cut-off: no/once vs. sometimes/regularly/often/very often*

Emotional abuse: no = 0; once = 1; sometimes = 2; regularly = 3; often = 4; very often = 5

Emotional neglect: no = 0; once = 1; sometimes = 2; regularly = 3; often = 4; very often = 5

Physical abuse: no = 0; once = 1; sometimes = 2; regularly = 3; often = 4; very often = 5

Sexual abuse: no = 0; once = 1; sometimes = 2; regularly = 3; often = 4; very often = 5

### **Measure of Parental Style (MOPS)**

Parker, G., Roussos, J., Hadzi-Pavlovic, D., Mitchell, P., Wilhelm, K., & Austin, M.P. (1997). The development of a refined measure of dysfunctional parenting and assessment of its relevance in patients with affective disorders. *Psychol Med*, 27(5), 1193-203.

*Cut-off: not at all true/slightly true vs. moderately true/extremely true*

Emotional neglect (MOPS indifference scale): not at all true = 0; slightly true = 1, moderately true = 2; extremely true = 3

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Physical and emotional abuse (MOPS abuse scale): not at all true = 0; slightly true = 1, moderately true = 2; extremely true = 3

### **Traumatic Antecedents Questionnaire (TAQ)**

Luxenberg, T., Spinazzola, J., & Van der Kolk, B. A. (2001). Complex trauma and disorders of extreme stress (DESNOS) diagnosis, part one: Assessment. *Directions in Psychiatry*, 21(25), 373–392.

*Cut-off: never or not at all/rarely or a little bit vs. occasionally or moderately/often or very much*

Emotional abuse: never or not at all = 0; rarely or a little bit = 1; occasionally or moderately = 2; often or very much = 3

Neglect: never or not at all = 0; rarely or a little bit = 1; occasionally or moderately = 2; often or very much = 3

Physical abuse: never or not at all = 0; rarely or a little bit = 1; occasionally or moderately = 2; often or very much = 3

Sexual abuse: never or not at all = 0; rarely or a little bit = 1; occasionally or moderately = 2; often or very much = 3

Reference List of Studies (Examined Are Bolded)

- 1. Ammerman, R. T., Peugh, J. L., Teeters, A. R., Putnam, F. W., & Van Ginkel, J. B. (2016). Child Maltreatment History and Response to CBT Treatment in Depressed Mothers Participating in Home Visiting. *J Interpers Violence, 31(5), 774-791.*  
10.1177/0886260514556769**
2. Baldwin, D. S., Loft, H., & Dragheim, M. (2012). A randomised, double-blind, placebo controlled, duloxetine-referenced, fixed-dose study of three dosages of Lu AA21004 in acute treatment of major depressive disorder (MDD). *Eur Neuropsychopharmacol, 22(7), 482-491.* 10.1016/j.euroneuro.2011.11.008
3. Boulenger, J. P., Loft, H., & Olsen, C. K. (2014). Efficacy and safety of vortioxetine (Lu AA21004), 15 and 20 mg/day: a randomized, double-blind, placebo-controlled, duloxetine-referenced study in the acute treatment of adult patients with major depressive disorder. *Int Clin Psychopharmacol, 29(3), 138-149.* 10.1097/YIC.0000000000000018
- 4. Brakemeier, E.-L., Radtke, M., Engel, V., Zimmermann, J., Tuschen-Caffier, B., Hautzinger, M., Schramm, E., Berger, M., & Normann, C. (2015). Overcoming treatment resistance in chronic depression: A pilot study on outcome and feasibility of the Cognitive Behavioral Analysis System of Psychotherapy as an inpatient treatment program. *Psychotherapy and Psychosomatics, 84(1), 51-56.*  
10.1159/000369586**
5. Bruijniks, S. J. E., Lemmens, L., Hollon, S. D., Peeters, F., Cuijpers, P., Arntz, A., Dingemans, P., Willems, L., van Oppen, P., Twisk, J. W. R., van den Boogaard, M., Spijker, J., Bosmans, J., & Huibers, M. J. H. (2020). The effects of once- versus twice-weekly sessions on psychotherapy outcomes in depressed patients. *Br J Psychiatry, 216(4), 222-230.* 10.1192/bjp.2019.265
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- antidepressant treatment response in major depression. *The American Journal of Psychiatry*, 177(2), 143-154. 10.1176/appi.ajp.2019.18070870**
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  9. **Day, C. V., John Rush, A., Harris, A. W., Boyce, P. M., Rekshan, W., Etkin, A., DeBattista, C., Schatzberg, A. F., Arnow, B. A., & Williams, L. M. (2015). Impairment and distress patterns distinguishing the melancholic depression subtype: an iSPOT-D report. *J Affect Disord*, 174, 493-502. 10.1016/j.jad.2014.10.046**
  10. **Douglas, K. M., & Porter, R. J. (2012). The effect of childhood trauma on pharmacological treatment response in depressed inpatients. *Psychiatry Res*, 200(2-3), 1058-1061. 10.1016/j.psychres.2012.06.015**
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Table S2. Results of random-effects meta-analyses for CT types.

CT Types - Subgroup Analyses							
	<i>k<sub>comp</sub></i>	<i>n<sub>total</sub></i>	<i>g</i>	<i>95% CI</i>	<i>I<sup>2</sup></i>	<i>95% CI</i>	<i>p<sub>subgroup</sub></i>
<b>Depression Severity</b>							
<b>Baseline comparison</b>							
CT vs. No CT							0.075
• Emotional abuse	50	4767	<b>0.310</b>	0.224-0.395	2.8	0.0-27.3	
• Emotional neglect	45	3799	<b>0.196</b>	0.127-0.265	0.0	0.0-34.5	
• Physical abuse	52	3997	<b>0.344</b>	0.253-0.436	10.9	0.0-37.1	
• Physical neglect	45	3024	<b>0.268</b>	0.183-0.354	0.0	0.0-34.5	
• Sexual abuse	53	3792	<b>0.295</b>	0.212-0.378	0.0	0.0-32.2	
<b>Treatment effect</b>							
CT (within-group)							0.951
• Emotional abuse	44	2250	<b>1.277</b>	1.080-1.474	<b>85.6</b>	81.5-88.8	
• Emotional neglect	38	1929	<b>1.327</b>	1.136-1.518	<b>69.6</b>	57.7-78.2	
• Physical abuse	46	1587	<b>1.249</b>	1.046-1.451	<b>74.6</b>	66.2-80.9	
• Physical neglect	39	1066	<b>1.224</b>	1.001-1.447	<b>77.6</b>	69.7-83.4	
• Sexual abuse	47	1195	<b>1.236</b>	1.041-1.432	<b>62.6</b>	48.9-72.7	
CT vs. No CT (between-group)							0.813
• Emotional abuse	43	4381	0.089	-0.070-0.248	<b>53.0</b>	33.5-66.8	
• Emotional neglect	38	3388	0.058	-0.082-0.198	<b>42.6</b>	15.4-61.0	
• Physical abuse	45	3744	0.116	-0.027-0.260	<b>48.9</b>	27.7-63.8	
• Physical neglect	39	2775	0.001	-0.152-0.153	<b>53.8</b>	33.6-67.9	
• Sexual abuse	46	3532	0.104	-0.033-0.241	<b>33.4</b>	4.2-53.7	
<b>Treatment vs. control</b>							
CT (between-group)							0.932
• Emotional abuse	10	558	<b>0.502</b>	0.227-0.777	14.7	0.0-56.0	
• Emotional neglect	10	628	<b>0.683</b>	0.326-1.040	<b>59.3</b>	18.3-79.7	
• Physical abuse	8	304	<b>0.546</b>	0.170-0.921	7.8	0.0-70.1	
• Physical neglect	9	336	<b>0.576</b>	0.223-0.929	4.9	0.0-66.5	
• Sexual abuse	9	309	<b>0.564</b>	0.241-0.888	0.0	0.0-64.8	
<b>Dropout</b>							
CT vs. No CT (between-group)							0.384
• Emotional abuse	28	2865	1.057	0.912-1.226	0.0	0.0-41.9	
• Emotional neglect	20	1321	1.008	0.821-1.237	0.0	0.0-48.0	
• Physical abuse	26	2042	1.088	0.948-1.249	0.0	0.0-43.2	
• Physical neglect	19	1460	<b>1.190</b>	1.051-1.347	0.0	0.0-48.9	
• Sexual abuse	24	2059	<b>1.187</b>	1.066-1.321	0.0	0.0-44.6	

Note: boldface indicates significance at  $p < .05$ . CT, childhood trauma; comp, comparisons.



# CHILDHOOD TRAUMA AND ADULT DEPRESSION TREATMENT

• CT measure						0.621	0.878									
CTQ	9	<b>0.662</b>	0.339-0.985	<b>51.1</b>	0.0-77.1											
Other	2	0.379	-6.672-7.430	<b>65.5</b>	0.0-92.2											
No CT (between-group)								0.089	0.202	0.653	0.016	0.706	0.878	-0.440	<b>0.012</b>	0.144
• Country						0.093	0.558									
North America	3	-0.295	-1.439-0.849	<b>55.7</b>	0.0-87.4											
Europe	7	0.213	-0.138-0.565	0.0	0.0-70.8											
• Diagnosis						0.536	0.878									
Chronic/TRD	3	0.345	-1.351-2.042	<b>77.4</b>	26.7-93.0											
Other	8	0.075	-0.369-0.519	<b>56.3</b>	3.7-80.2											
• CT measure						0.272	0.653									
CTQ	9	0.031	-0.352-0.414	<b>50.0</b>	0.0-76.7											
Other	2	0.613	-5.772-6.997	<b>77.0</b>	0.0-94.7											
Dropout	<i>k<sub>comp</sub></i>	<i>RR</i>	<i>95% CI</i>	<i>I<sup>2</sup></i>	<i>95% CI</i>	<i>p<sub>subgroup</sub></i>	<i>B</i>	<i>p</i>	<i>p<sub>FDR</sub></i>	<i>B</i>	<i>p</i>	<i>p<sub>FDR</sub></i>	<i>B</i>	<i>p</i>	<i>p<sub>FDR</sub></i>	
CT vs. No CT (between-group)							-0.004	0.825	0.888	-0.002	0.840	0.888	0.055	0.554	0.888	
• Design						0.888	0.888									
RCT	24	1.064	0.929-1.219	0.0	0.0-44.6											
Open trial	5	1.044	0.762-1.432	0.0	0.0-79.2											
• Country						0.615	0.888									
North America	9	1.108	0.851-1.441	0.0	0.0-64.8											
Europe	15	0.978	0.793-1.207	0.0	0.0-53.6											
Other	5	1.101	0.846-1.432	0.0	0.0-79.2											
• Diagnosis						0.850	0.888									
Chronic/TRD	9	1.046	0.818-1.337	0.0	0.0-64.8											
Other	20	1.071	0.926-1.240	0.0	0.0-48.0											
• CT measure						0.575	0.888									
CTQ	16	1.107	0.930-1.318	0.0	0.0-52.3											
Other	13	1.036	0.862-1.246	0.0	0.0-56.6											
• Treatment type						0.592	0.888									
Pharmacotherapy	11	1.140	0.996-1.304	0.0	0.0-60.2											
Psychotherapy	13	1.070	0.857-1.335	0.0	0.0-56.6											

Note: boldface indicates significance at  $p < .05$ ; FDR adjustment for: 6 tests (baseline comparison), 8 tests (treatment effect; dropout), 12 tests (treatment vs. control).

CT, childhood trauma; CTQ, Childhood Trauma Questionnaire; comp, comparisons; RCT, randomized clinical trial; TRD, treatment-resistant depression

# CHILDHOOD TRAUMA AND ADULT DEPRESSION TREATMENT

## Weighted Risk-Of-Bias Summary Plots

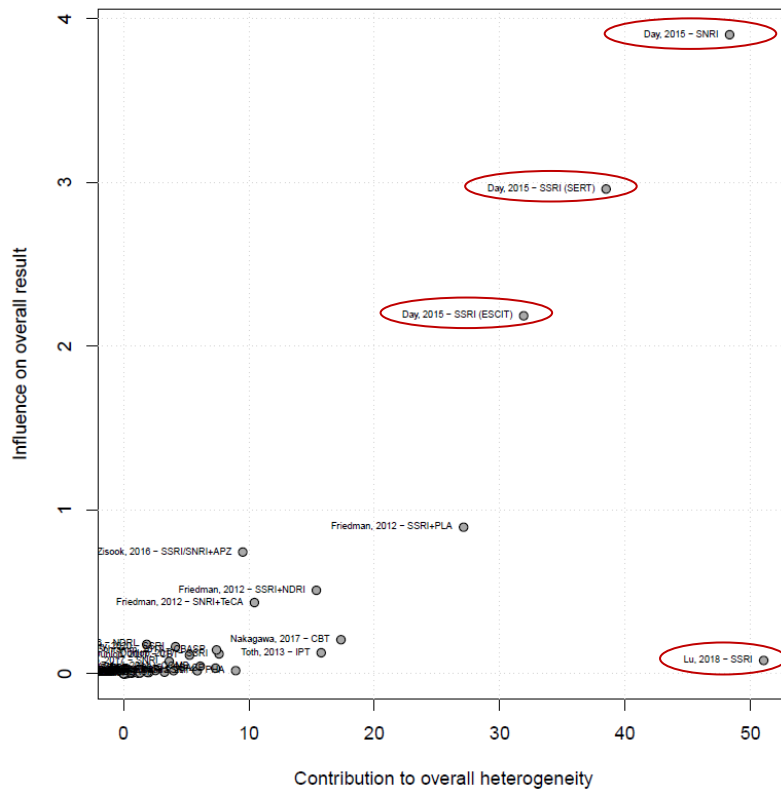




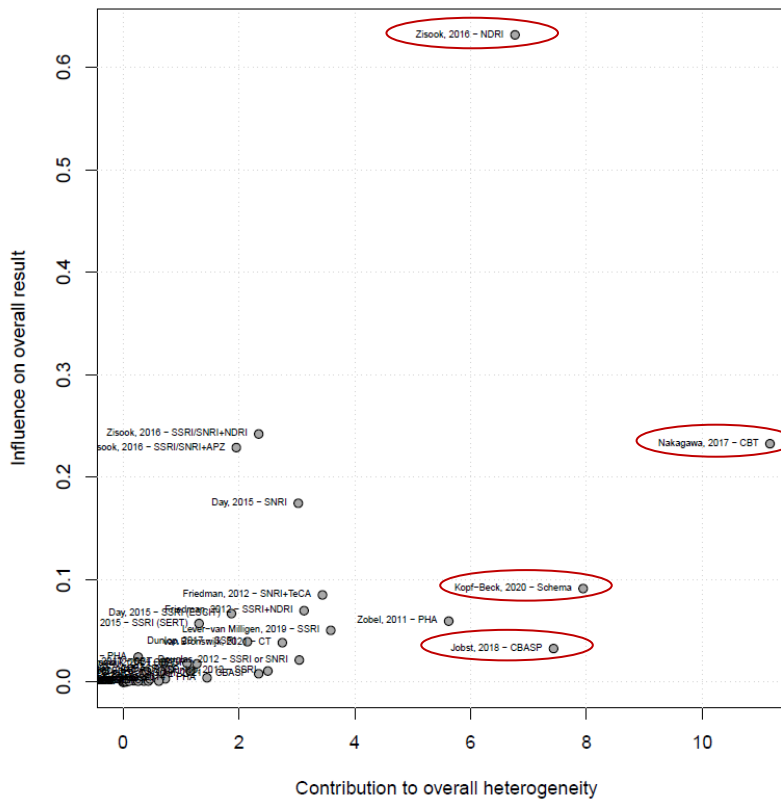


# CHILDHOOD TRAUMA AND ADULT DEPRESSION TREATMENT

## Heterogeneity of Individual Studies (NO CT Treatment Effect)

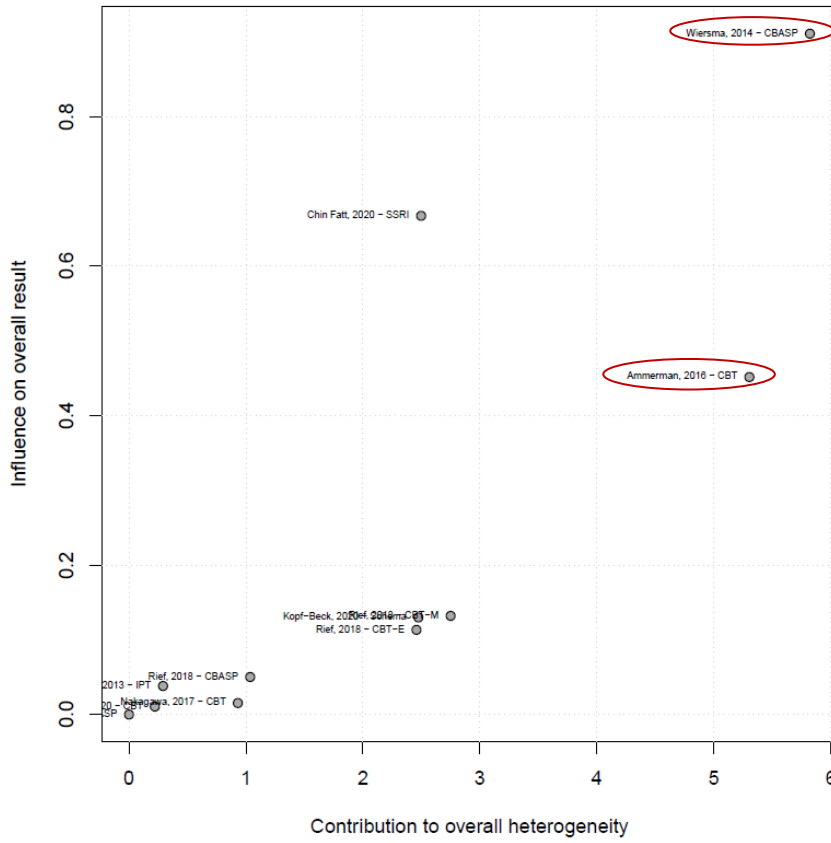


## Heterogeneity of Individual Studies (CT vs NO CT Treatment Effect)

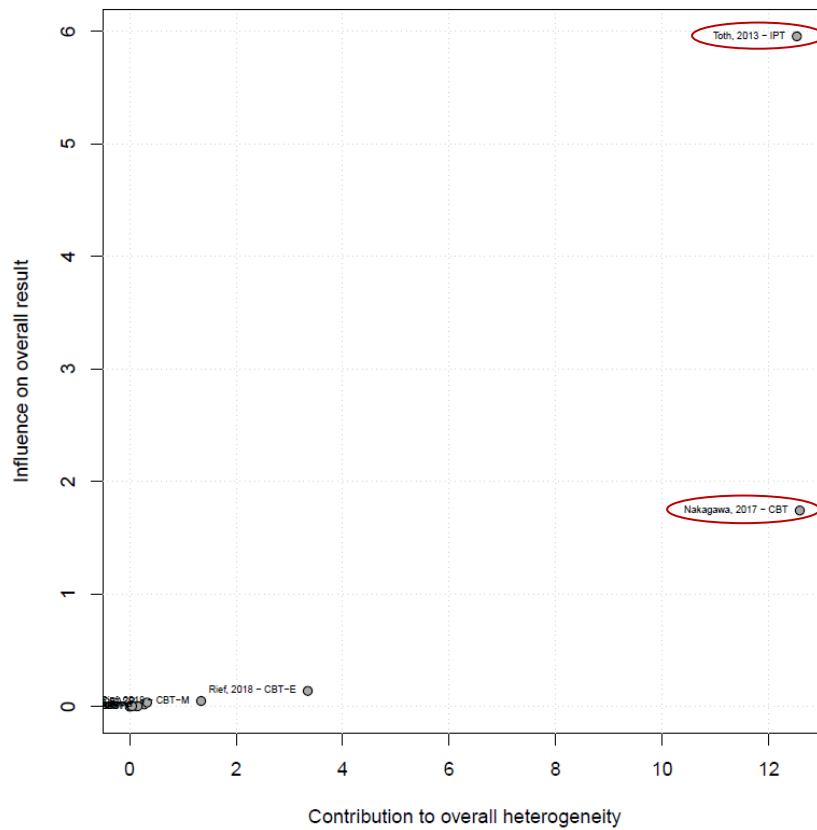


# CHILDHOOD TRAUMA AND ADULT DEPRESSION TREATMENT

## Heterogeneity of Individual Studies (CT Treatment vs Control)

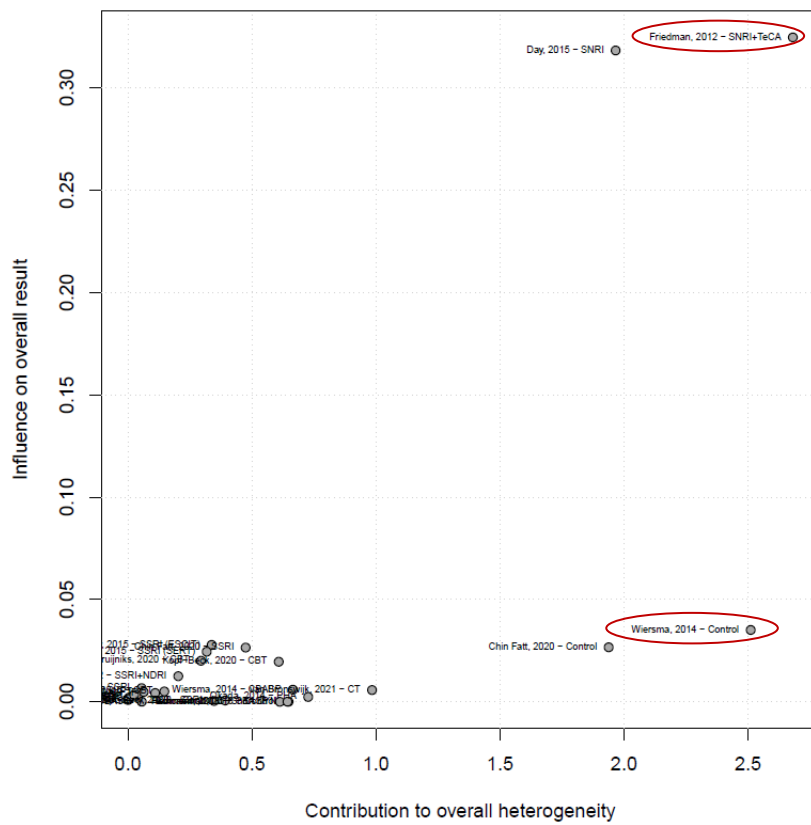


## Heterogeneity of Individual Studies (No CT Treatment vs No CT Control)



# CHILDHOOD TRAUMA AND ADULT DEPRESSION TREATMENT

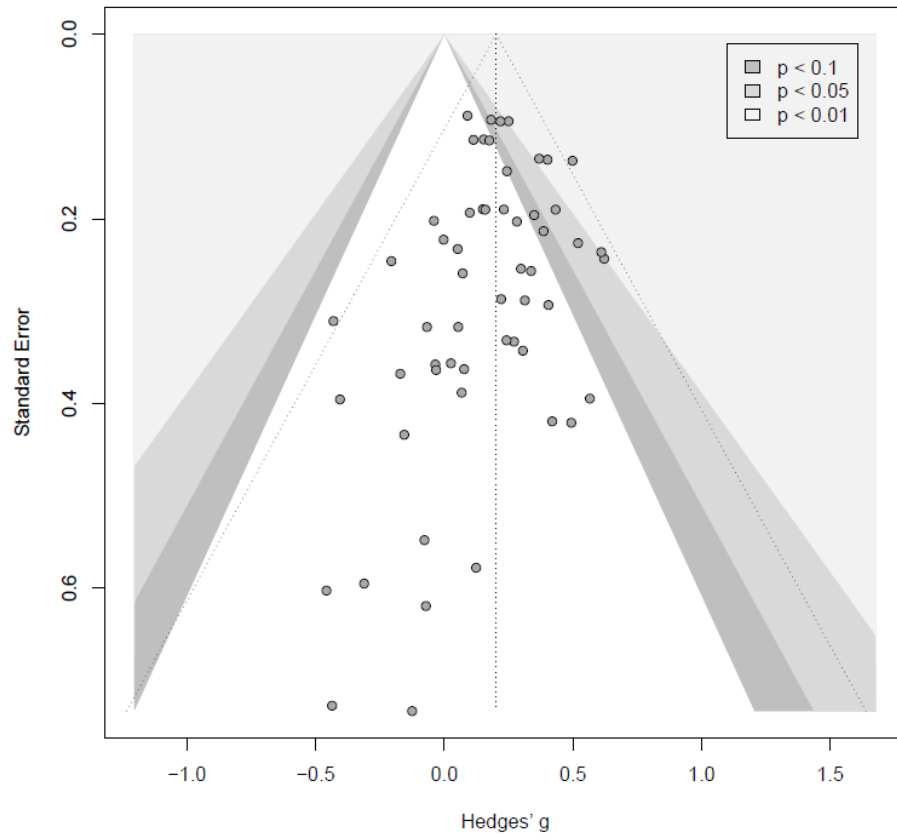
## Heterogeneity of Individual Studies (CT vs No CT - Dropout)



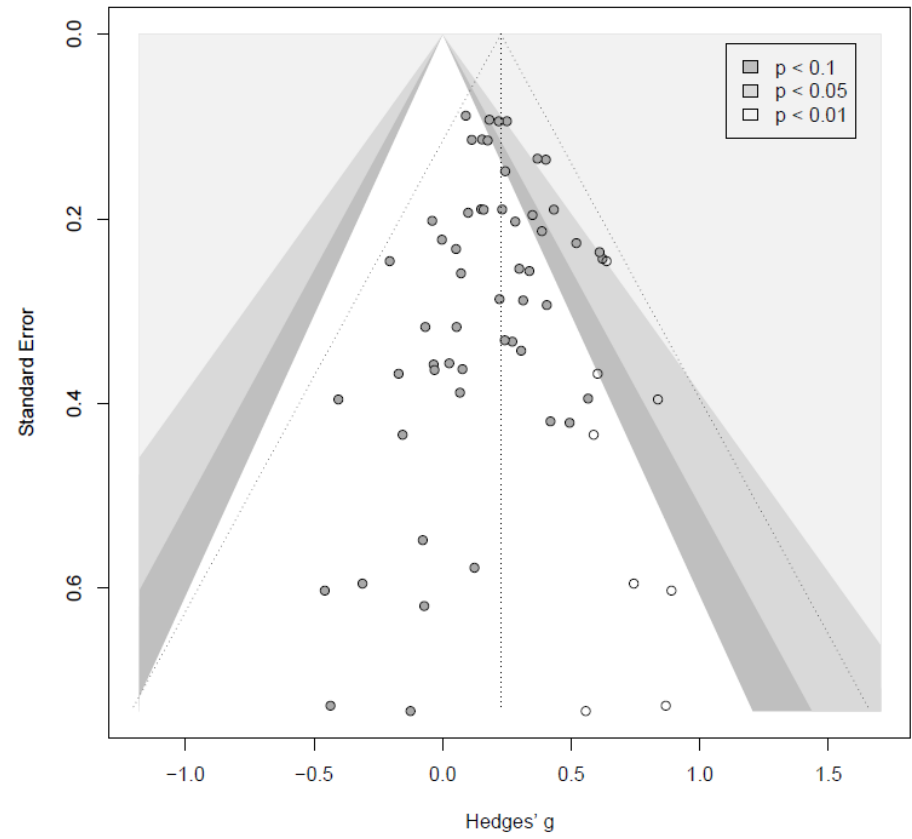
# CHILDHOOD TRAUMA AND ADULT DEPRESSION TREATMENT

## Funnel Plots

Funnel Plot CT vs No CT (Baseline)

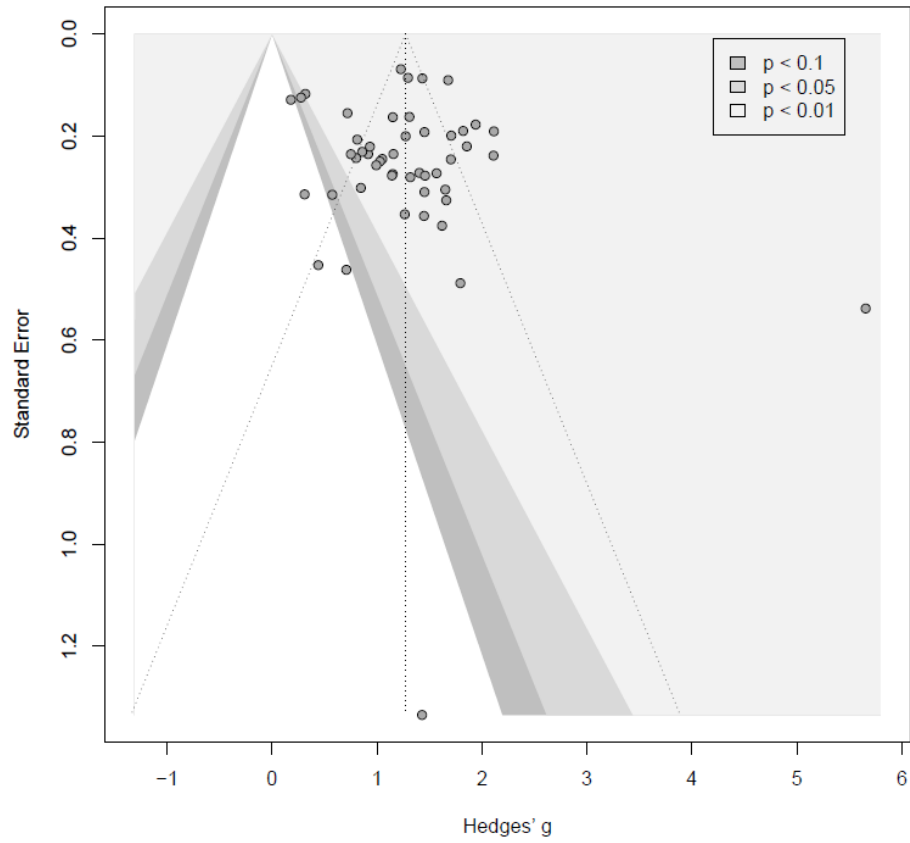


Funnel Plot CT vs No CT (Baseline; Trim & Fill Method) - Outliers Removed

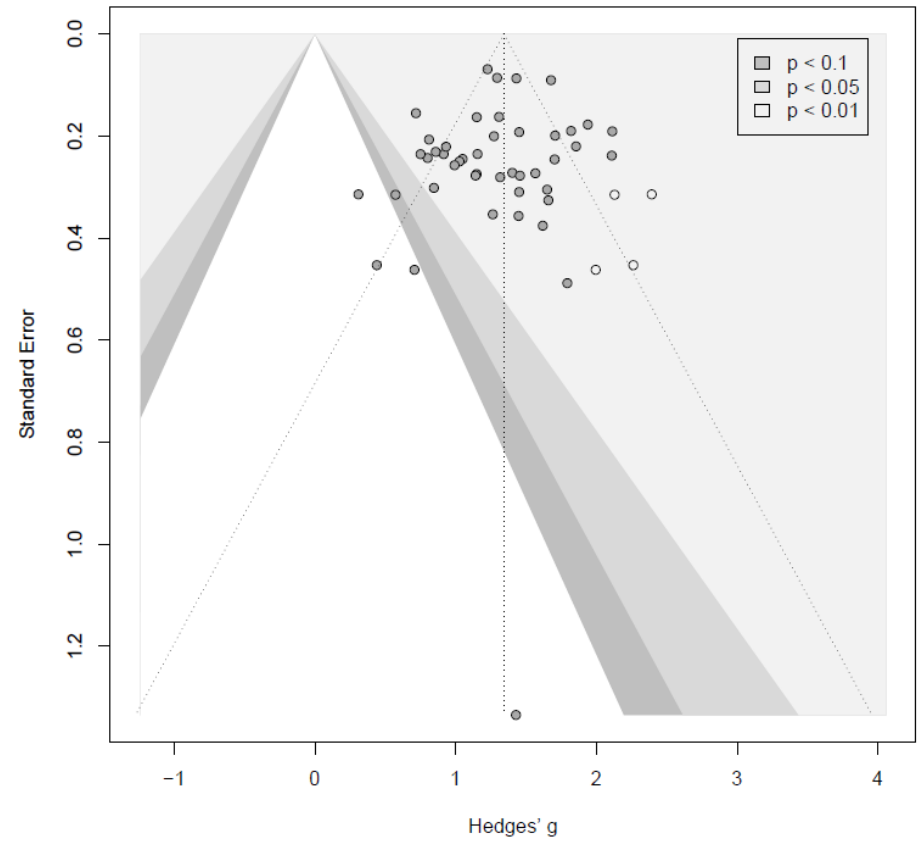


# CHILDHOOD TRAUMA AND ADULT DEPRESSION TREATMENT

### Funnel Plot CT Treatment Effect

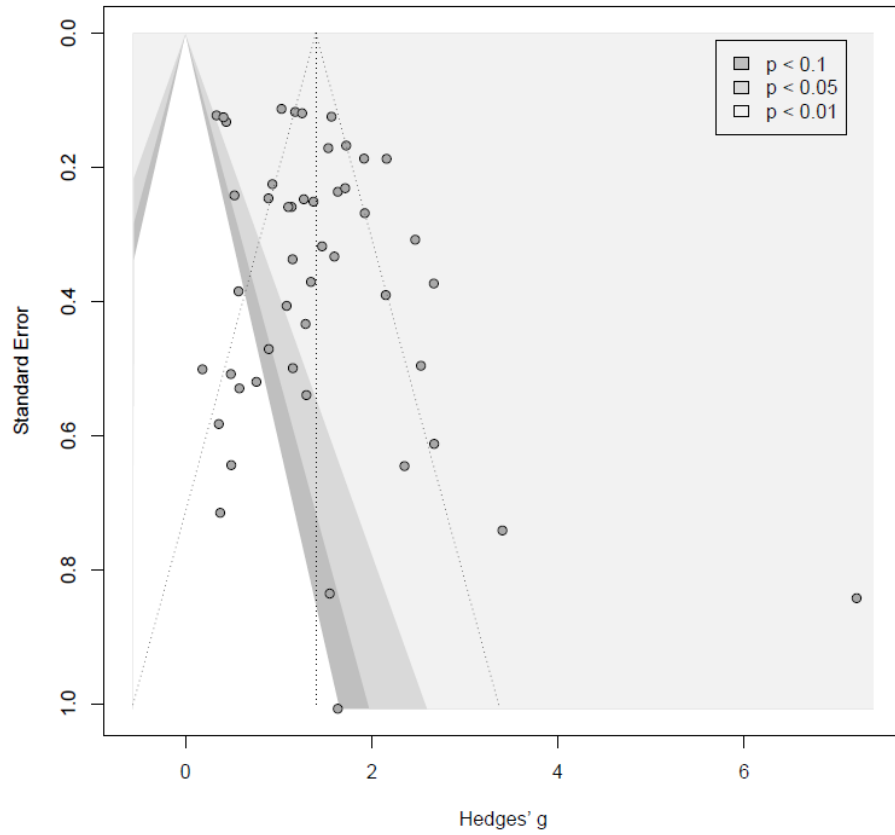


### Funnel Plot CT Treatment Effect (Trim & Fill Method) - Outliers Removed

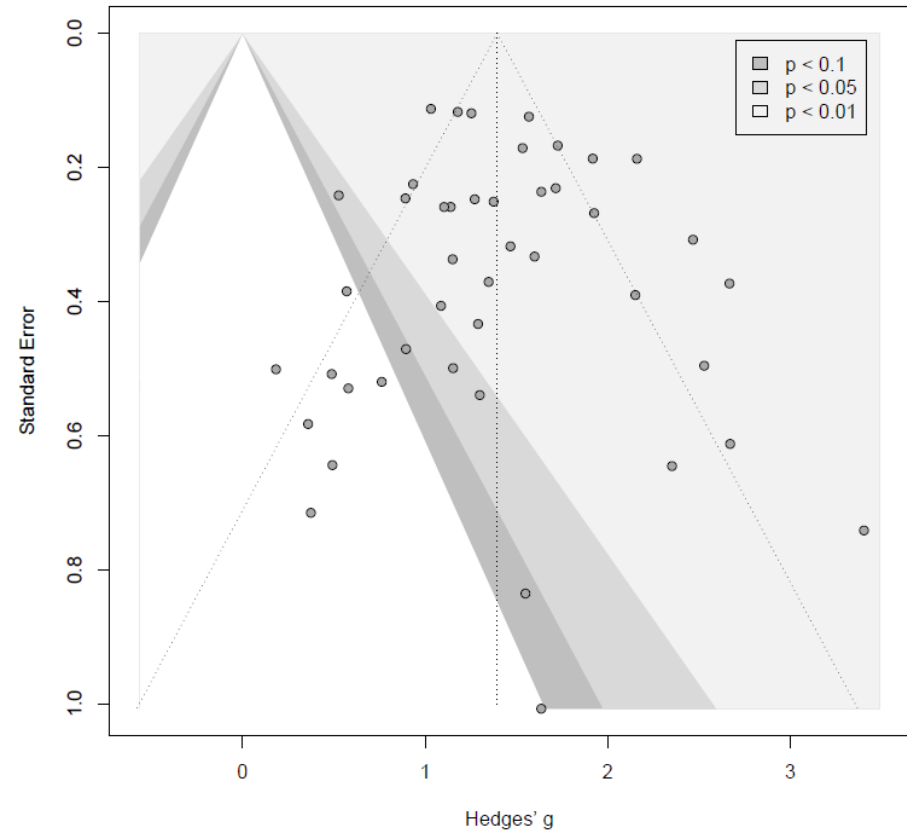


# CHILDHOOD TRAUMA AND ADULT DEPRESSION TREATMENT

### Funnel Plot No CT Treatment Effect

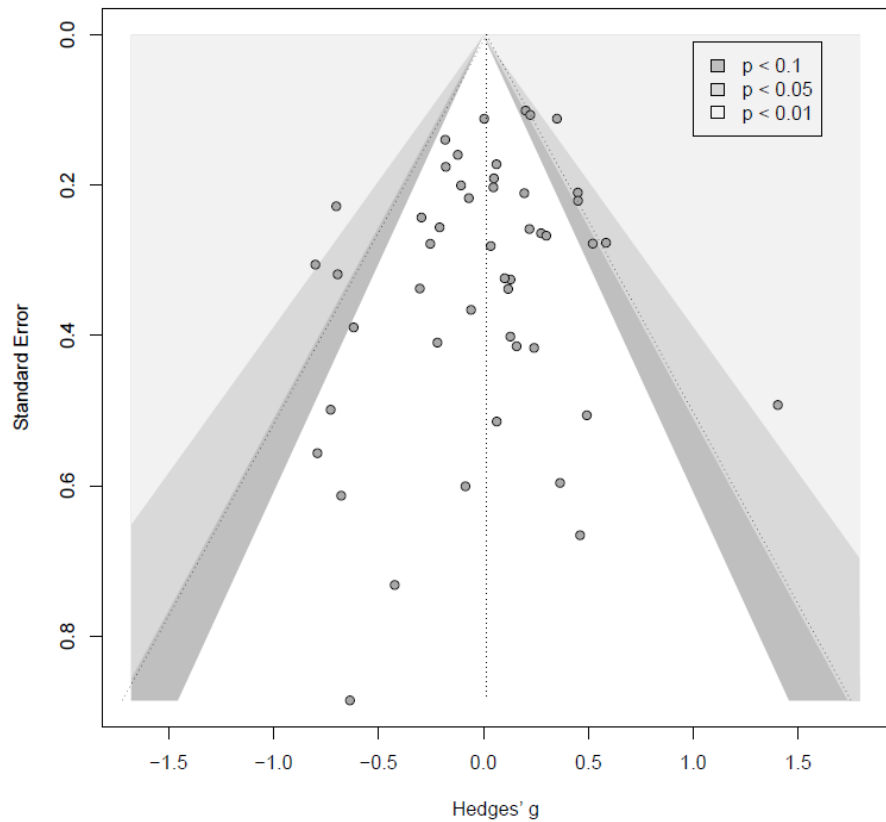


### Funnel Plot No CT Treatment Effect (Trim & Fill Method) - Outliers Removed

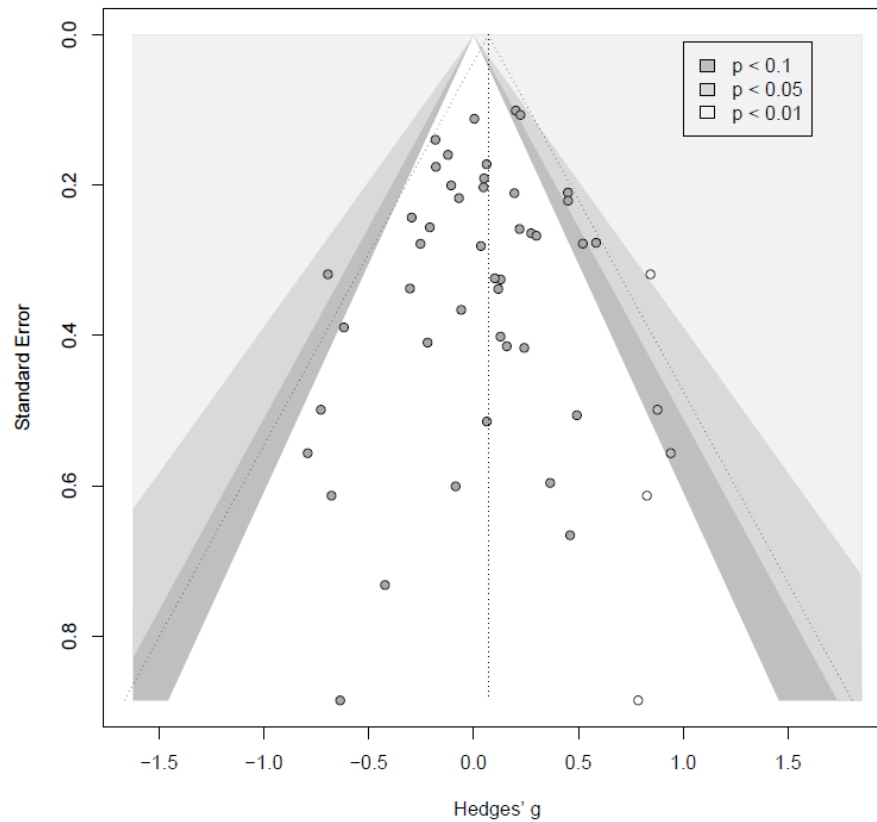


# CHILDHOOD TRAUMA AND ADULT DEPRESSION TREATMENT

### Funnel Plot CT vs No CT Treatment Effect



### Funnel Plot CT vs No CT Treatment Effect (Trim & Fill Method) – Outliers Removed

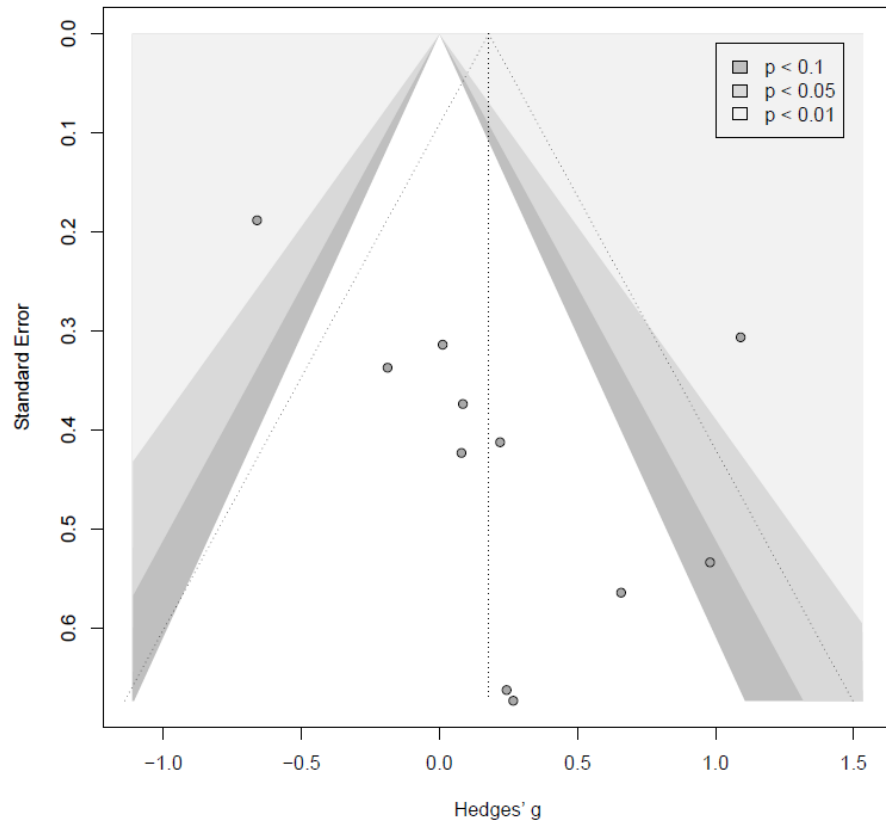




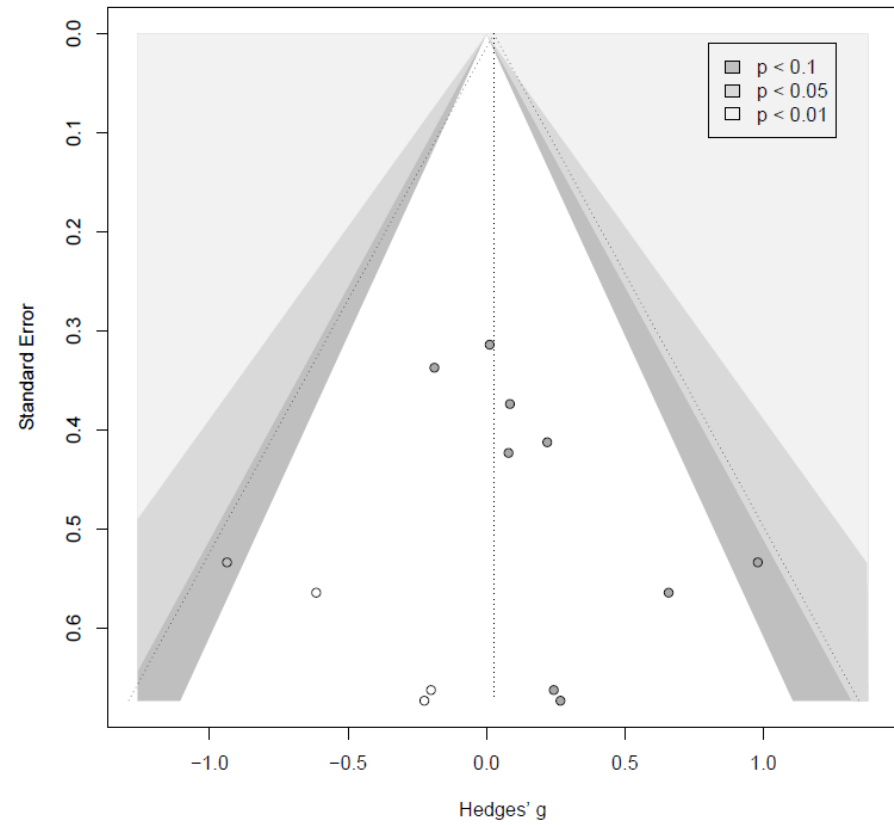


# CHILDHOOD TRAUMA AND ADULT DEPRESSION TREATMENT

### Funnel Plot No CT Treatment vs Control

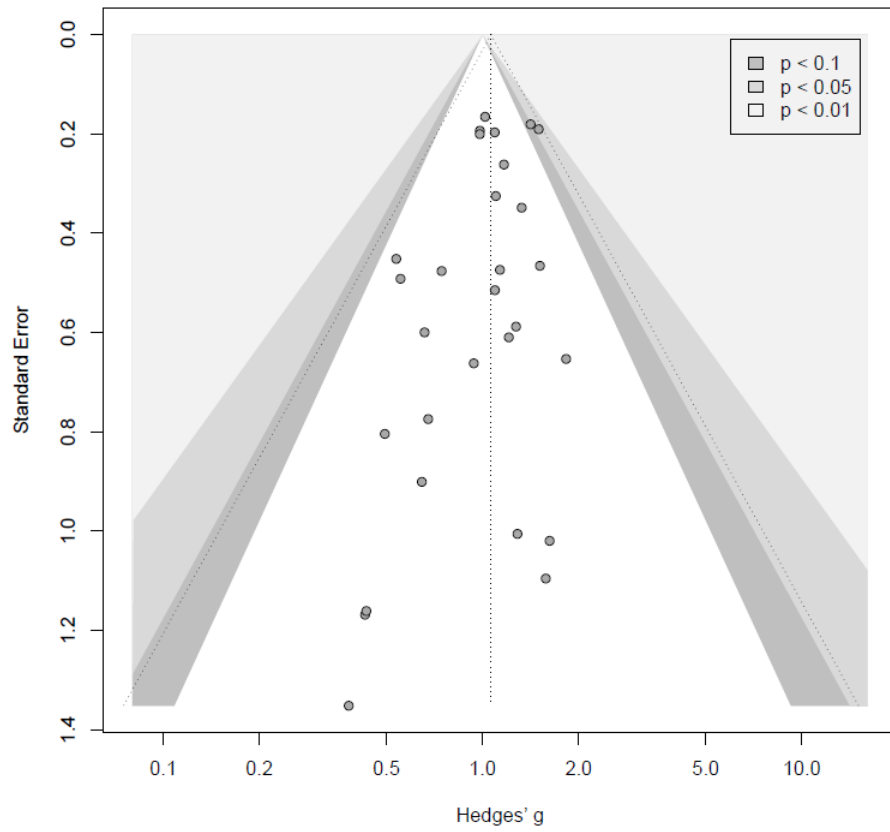


### Funnel Plot No CT Treatment vs Control (Trim & Fill Method) - Outliers Removed



# CHILDHOOD TRAUMA AND ADULT DEPRESSION TREATMENT

### Funnel Plot CT vs No CT – Dropout



### Funnel Plot CT vs No CT – Dropout (Trim & Fill Method) – Outliers Removed

