

## Supplemental Online Content

Osborn AJ, Roberts RM, Dorstyn DS, Grave BG, David DJ. Sagittal synostosis and its association with cognitive, behavioral, and psychological functioning: a meta-analysis. *JAMA Netw Open*. 2021;4(9):e2121937. doi:10.1001/jamanetworkopen.2021.21937

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### eReferences

This supplemental material has been provided by the authors to give readers additional information about their work.

## **eTable 1**

### *Electronic Search Strategy*

#### **Pubmed**

(craniosynostos\*[mh] OR craniosynostos\*[tw] OR sagittal[tw] OR scaphocephal\*[tw])

AND

(quality of life[tw] OR satisfaction with life[tw] OR life satisfaction[tw] OR anxiety[mh] OR anxiety[tw] OR anxious[tw] OR depression[mh] OR depress\*[tw] OR mood[tw] OR affect[tw] OR emotion\*[tw] OR psychol\*[tw] OR psychiat\*[TW] OR psychosocial[tw] OR psychopath\*[tw] OR body, physical appearance[mh] OR appearance[tw] OR function\*[tw] OR mental processes[mh] OR mental\*[tw] OR cognit\*[tw] OR neuropsychol\*[tw] OR learning[tw] OR neurodevelopment\*[tw] OR development\*[tw] OR behaviour[mh] OR behav\*[tw] OR neurobehav\*[tw] OR memory[tw] OR language[tw] OR verbal[tw] OR visuospatial[tw] OR attention[tw] OR information processing[tw] OR academic[tw] OR intellectual[tw] OR intelligen\*[tw] OR speech[tw])

#### **PsycINFO**

(craniosynostos\* or sagittal or scaphocephal\*).mp AND (outcome\* or quality of life or satisfaction with life or life satisfaction or anxiety or anxious or depress\* or mood or affect or emotion\* or psychol\* or psychiat\* or psychosocial or psychopath\* or appearance or function\* or mental\* or cognit\* or neuropsychol\* or learning or neurodevelopment\* or development\* or behav\* or neurobehav\* or memory or language or verbal or visuospatial or attention or information processing or academic or intellectual or intelligen\* or speech).mp

#### **SCOPUS**

(craniosynostos\* OR sagittal OR scaphocephal\*)

AND

(outcome\* OR “quality of life” OR “satisfaction with life” OR “life satisfaction” OR anxiety OR anxious OR depress\* OR mood OR affect OR emotion\* OR psychol\* OR psychiat\* OR psychosocial OR psychopath\* OR appearance OR function\* OR mental\* OR cognit\* OR neuropsychol\* OR learning OR neurodevelopment\* OR development\* OR behav\* OR neurobehav\* OR memory OR language OR verbal OR visuospatial OR attention OR “information processing” OR academic OR intellectual OR intelligen\* OR speech)

**Embase**

'craniofacial synostosis'/syn OR craniosynostos\* OR sagittal OR scaphocephal\*

AND

outcome OR 'quality of life'/syn OR 'satisfaction with life' OR 'life satisfaction' OR 'mental disease assessment'/syn OR 'mental disease'/syn OR 'mental function assessment'/syn OR 'physical appearance'/syn OR 'cognition'/syn OR 'individual behavior assessment'/syn OR 'behavior'/syn OR 'cognitive function test'/syn OR 'psychological and psychiatric procedures'/syn OR 'learning'/syn OR 'neuropsychology'/syn OR 'memory'/syn OR 'speech and language assessment'/syn OR 'academic achievement'/syn OR neurodevelopment\* OR development\* OR anxiety OR anxious OR depress\* OR psychol\* OR psychiat\* OR psychosocial OR psychopath\* OR appearance OR function\* OR mood OR affect OR emotion OR mental\* OR cognit\* OR neuropsychol\* OR learning OR behav\* OR neurobeh\* OR memory OR language OR verbal OR visuospatial OR attention OR intellect\* OR intelligen\* OR speech

**eTable 2**

*Summary Details of the Meta-analyzed Studies*

Author (year)	N	Mean age (yrs)	% male	Study origin	Surgical status of patients				Craniosynostosis risks reported		Cognitive risks reported		Outcome: domain
					CM	pre	post	mixed	Genetic status	Family history	SES	Neonatal /perinatal	
Arnaud et al., 1995 <sup>1</sup>	193	T1: 1.0 T2: -	-	France	51	142	47					general cognition, global development	
Bellew et al., 2005 <sup>2</sup> Bellew et al., 2011 <sup>3</sup> Bellew et al., 2015 <sup>4</sup> Bellew et al., 2019 <sup>5</sup>	67	Surgical : T1: 0.6 T2: 1.3 CM: T1: 2.1 T2: 2.9	83	UK	13	28	54	47				✓	general cognition, motor functioning, verbal, visuospatial, adaptive & social skills, global development
Boltshauser et al., 2003 <sup>6</sup>	30	9.3	77	Switzerland	30						✓		general cognition, verbal, visuospatial, arithmetic, attention, executive function, memory: shorter term, processing speed, quality of life, behavior: externalizing/internalizing/total
Byun et al., 2018 <sup>7</sup>	67	-	69	Sth Korea				67	✓				general cognition, motor functioning
Cabrejo et al., 2019 <sup>8</sup>	10	12.1	80	US			10						verbal, visuospatial
Care et al., 2019 <sup>9</sup>	140	3.3	-	UK			140		✓				motor functioning, verbal, adaptive & social skills, behavior: externalizing/internalizing/total
Chandler et al., 2020 <sup>10</sup>	75	10.3	64	US			75			✓	✓		executive function, memory-shorter term, behavior: externalizing/internalizing/total
Chieffo et al., 2010 <sup>11</sup>	35	13.4	77	Italy			35		✓		✓		visuospatial, processing speed
Chieffo et al., 2020 <sup>12</sup>	87	T1: 0.5 T2: 1.2	-	Italy		87	63						global development, motor functioning, verbal, visuospatial, adaptive & social skills
Chuang et al., 2018 <sup>13</sup>	9	0.4	-	US		9						✓	general cognition, verbal

Chuang et al., 2021 <sup>14</sup>	47	-	-	US			47						general cognition, verbal, visuospatial, motor functioning, executive function, behaviour: externalizing/internalizing
Da Costa et al., 2006 <sup>15</sup>	6	-	-	Australia			6				✓		general cognition
Da Costa et al., 2012 <sup>16</sup> Da Costa et al., 2013 <sup>17</sup>	26	T1: 0.7 T2: 1.8	88	Australia		26	26				✓	✓	general cognition, motor functioning
Engel et al., 2012 <sup>18</sup>	46	-	80	Germany		46							global development
Gewalli et al., 2001 <sup>19</sup>	26	T1: 0.5 T2: 1.4	81	Sweden		26	26						motor functioning, verbal, visuospatial, adaptive & social skills, global development
Hashim et al., 2014 <sup>20</sup> Patel et al., 2014 <sup>21</sup>	70	10.0	-	US			70				✓		general cognition, motor functioning, verbal, visuospatial, learning difficulties, behavior: externalizing/internalizing/total, memory: shorter term
Imahiyerobo et al., 2019 <sup>22</sup>	77	0.4	78	US		77					✓	✓	general cognition, motor functioning, verbal
Infant Learning Project Kapp-Simon et al., 2005 <sup>23</sup> Ruiz-Correa et al., 2007 <sup>24</sup> Speltz et al., 2007 <sup>25</sup> Starr et al., 2007 <sup>26</sup> Toth et al., 2008 <sup>27</sup> Naumann et al., 2012 <sup>28</sup> Starr et al., 2012 <sup>29</sup> Cradock et al., 2015 <sup>30</sup> Speltz et al., 2015 <sup>31</sup> Speltz et al., 2016 <sup>32</sup> Kapp-Simon et al., 2016 <sup>33</sup> Collett et al., 2017 <sup>34</sup> Wallace et al., 2016 <sup>35</sup>	94	T1: 0.5 T2: 1.5 T3: 3.0 T4: 7.0	83	US		62	94		✓		✓	✓	general cognition, motor functioning, verbal, visuospatial, arithmetic, attention, executive function, learning difficulties, memory: shorter term, memory: longer term, behavior: externalizing/internalizing/total
Kapp-Simon et al., 1993 <sup>36</sup> Kapp-Simon et al., 1998 <sup>37</sup>	24	T1: 0.7 T2: 1.5 T3: 4.2	86	US	4	20	20						general cognition, learning difficulties
Kljajic et al., 2019 <sup>38</sup> Kljajic et al., 2020 <sup>39</sup>	41	11.5	68	Sweden			41					✓	general cognition, verbal, visuospatial, attention, memory: shorter term, processing speed

Korpilahti et al., 2012 <sup>40</sup>	18	3.4	90	Finland			18					✓	verbal	
Lee et al., 2015 <sup>41</sup> Lee et al., 2017 <sup>42</sup>	37	-	75	Sth Korea		37	25		✓				general cognition, motor functioning,	
Magge et al., 2002 <sup>43</sup>	16	10.3	-	US			16						learning difficulties	
Mazzaferro et al., 2018 <sup>44</sup>	5	-	-	US			5						quality of life	
Moreno-Villagomez et al., 2020 <sup>45</sup>	10	4.5	80	Mexico			10						general cognition, motor functioning, verbal, visuospatial, arithmetic, memory: shorter term, processing speed	
Noetzel et al., 1985 <sup>46</sup>	3	-	-	US				3					general cognition	
Salokorpi et al., 2018 <sup>47</sup>	40	27.4	63	Finland			40						satisfaction with appearance	
Scheuerle et al., 2004 <sup>48</sup>	3	-	-	US		3	3						verbal	
Shipster et al., 2003 <sup>49</sup>	76	0.4	80	UK				76				✓	✓	general cognition, verbal, visuospatial, learning difficulties
Speltz et al., 1993 <sup>50</sup>	7	5.8	86	US			7					✓		behavior: externalizing/internalizing/total, self-concept
Speltz et al., 1997 <sup>51</sup>	19	0.3	-	US		18	19							general cognition, motor functioning
Virtanen et al., 1999 <sup>52</sup>	18	12.2	72	Finland			18							motor functioning, verbal, visuospatial, attention, memory: shorter term

Note: N = sagittal synostosis participants; descriptive statistics reflect non-syndromic metopic synostosis patient details extracted from each paper; data from non-independent papers combined & treated as a single study in analyses as appropriate. Study details above refer to the *specific* sagittal sample data extracted from each study & used in the current meta-analysis (which may differ from overall study details)

**eTable 3**

*Studies Using Overlapping Samples - Combined and Treated as Non-independent Studies in the Current Meta-analysis*

Study 'name' in meta-analysis	Papers using overlapping samples
Bellew 2005/2011/2015/2019	Bellew et al, 2005 <sup>2</sup>
	Bellew et al, 2011 <sup>3</sup>
	Bellew et al, 2015 <sup>4</sup>
	Bellew et al, 2019 <sup>5</sup>
Da Costa 2012/2013	Da Costa et al, 2012 <sup>16</sup>
	Da Costa et al, 2013 <sup>17</sup>
Hashim 2014/Patel 2014	Patel et al, 2014 <sup>21</sup>
	Hashim et al, 2014 <sup>20</sup>
Infant Learning Project (ILP)	Collett et al, 2017 <sup>34</sup>
	Cradock et al, 2015 <sup>30</sup>
	Kapp-Simon et al, 2005 <sup>23</sup>
	Kapp-Simon et al, 2016 <sup>33</sup>
	Naumann et al, 2012 <sup>28</sup>
	Ruiz-Correa et al, 2007 <sup>24</sup>
	Speltz et al, 2007 <sup>25</sup>
	Speltz et al, 2015 <sup>31</sup>
	Speltz et al, 2016 <sup>32</sup>
	Starr et al, 2007 <sup>26</sup>
	Starr et al, 2012 <sup>29</sup>
	Toth et al, 2008 <sup>27</sup>
	Wallace et al, 2016 <sup>35</sup>
Kapp-Simon 1993/1998	Kapp-Simon et al, 1993 <sup>36</sup>
	Kapp-Simon et al, 1998 <sup>37</sup>
Kljajic 2019/2020	Kljajic et al, 2019 <sup>38</sup>
	Kljajic et al, 2020 <sup>39</sup>
Lee 2015/2017	Lee et al, 2015 <sup>41</sup>
	Lee et al, 2017 <sup>42</sup>

**eTable 4**

*Data Extracted From Studies Included in the Meta-analysis (Where Reported)*

- Article title, year and authors
- Sample size
- Country of origin
- Age at assessment
- Sex
- Type of craniosynostosis
- Surgical status
- Type of surgical treatment
- Age at surgery
- Number of surgeries
- Criteria for surgery
- Length of post-surgery follow-up
- Sagittal synostosis diagnosis confirmation
- Status of genetic disorders
- Socio-economic status
- Family history of craniosynostosis
- Method of identification and recruitment
- Outcome
- Measures
- Outcome data



**eTable 5**

*Summary of the Cognitive Tests That Were Used by the Studies and Their Corresponding Cognitive Domain*

<b>Domain</b>	<b>Test</b>
General cognition	BSID, BSID-II, BSID-III: mental development index, cognitive scale McCarthy's Scale of Children's Abilities: general cognitive index K-ABC: IQ WPPSI-III, WPPSI-R-UK, WISC-III, WISC-IV, WASI, WAIS-R: FSIQ Brunet-Lezine; Nouvelle Echelle Metrique de L'Intelligence Cattell Infant Intelligence Scale; Stanford-Binet Intelligence Scale
Verbal Functions & Language Skills	British Picture Vocabulary Scale BSID, BSID-III: language , receptive, expressive CTOPP: phonological awareness composite Denver Developmental Screening Test: language Griffiths Mental Development Scale: hearing & speech/language NEPSY-II: Word generation (semantic, initial letter) PLS-3: receptive, expressive Renfrew Action Picture Test: grammar, information Renfrew Word Finding Vocabulary Scale Clinical Evaluation of Language Fundamentals: expressive, receptive Reynell Scales: receptive, expressive Token Test-II TOWRE: total words WPPSI-III, WPPSI-R-UK, WISC-III, WISC-III-UK, WISC-IV, WISC-R, WASI, WAIS-R: Verbal Comprehension Index, Verbal IQ, general language composite, information, vocabulary, similarities WRAT-4: reading composite, spelling Wechsler Fundamentals: reading-related  <i>Subjective/proxy-rated:</i> <i>ASQ-3: Communication; CCC-2: general communication composite</i>
Motor functioning	Beery-VMI: total, motor co-ordination index BSID, BSID-II, BSID-III: psychomotor development index, fine motor, gross motor Griffiths Mental Development Scale: locomotor, eye/hand co-ordination Purdue Pegboard Test: preferred, non-preferred, both, assembly WPPSI-III: motor index  <i>Subjective/proxy-rated:</i> <i>ASQ-3: gross motor skills; fine motor skills</i>
Visuospatial	Beery-VMI: visual perception Developmental Test of Visual Perception-2: motor-reduced visual perception index, visual closure Griffiths Mental Development Scale: performance Hooper Visual Organisation Test NEPSY-II: arrows Rey Complex Figure Test WPPSI-III, WPPSI-R-UK, WISC-III, WISC-III-UK, WISC-R, WISC-IV, WASI, WAIS-R: Performance IQ, Perceptual Reasoning Index, perceptual organisation, picture arrangement, picture completion, object assembly, block design Design fluency (5 point test)

Attention	CCPT-3: C, detectability, omissions, commissions, perseveration, HRT, HRT-SD, Variability, HRT-BC, HRT-iC
	Corsi Block Tapping Test
	K-ABC: sequential processing index, hand movements, number recall
	Mottier Test
	TAP: alertness tonic, alertness phasic, Go/Nogo (selective attention), divided attention, sustained attention
	TEA-Ch: sky search, score!, sky search DT, score DT
	WISC-III, WISC-IV, WISC-R, WAIS-R: digit span, digits forward, letter-number sequencing, freedom from distractibility
Processing speed	WPPSI-III, WISC-III, WISC-IV, WAIS-R: processing speed index, processing speed quotient, coding, digit symbol, symbol search
Executive Function	NEPSY-II: Inhibition
	Stroop test
Arithmetic	McCarthy Scale of Children's Abilities: quantitative index
	K-ABC: arithmetic
	WRAT-4: math computation
	Wechsler Fundamentals: numerical operations
Memory – short-term	Benton's Visual Retention: Multiple Choice Form
	McCarthy Scale of Children's Abilities: memory scale
	CMS: stories (immediate, immediate thematic); word lists (learning)
	Rey Visual Design Learning Test: immediate memory span, new learning ability, memory
	Verbal learning + memory test (VLMT): immediate memory span, susceptibility to interference
	WISC-IV: working memory index
Memory – longer-term	CMS: stories (delayed, delayed recognition, delayed thematic); word lists (delayed, delayed recognition)
	CTOPP: rapid naming composite
Global development	BSID-II, BSID-III: mental/motor developmental delays, developmental delays
	Griffiths Mental Development Scale: general quotient, global development quotient
	Developmental Brunet-Lezine Scale
Learning/literacy problems	reading-related learning disability, mathematic-related learning disability, reading learning disability, spelling learning disability, literacy impairment, learning problems (<25 <sup>th</sup> percentile on standardized tests)
	<b><i>Subjective/proxy-rated behavioral and psychological measures</i></b>
Behavior	ASEBA/CBCL externalizing index, internalizing index
	Behavior Assessment System for Children - 2: externalizing index, internalizing index
	Strengths & Difficulties Questionnaire: externalizing, internalizing
Adaptive /functional/ social	Ages & Stages Questionnaire-3: personal-social, problem solving
	Strengths & Difficulties Questionnaire: prosocial
	Griffiths Mental Development Scale: personal-social
	Behavior Assessment System for Children - 2: adaptive skills index
Satisfaction with Appearance	Visual analog scale

Self-concept	Method used by Eder
Quality of Life	TACQOL: EMOPOS, EMONEG, body, motor, auto, cognition, social WHOQOL: physical health, psychological, social, environmental
Attention	ASEBA/CBCL: parent/teacher
Executive function	BRIEF: behavioural regulation index, metacognition index, global executive composite
Memory - shorter-term	BRIEF: working memory

Note: all cognitive measures are categorised in meta-analyses as ‘objective’ except where noted above; general cognition = test scores on measures of IQ; global developmental delay = poor developmental progress in multiple domains (e.g cognition, language, motor skills); BSID = Bayley Scales of Infant Development; K-ABC = Kaufman Assessment Battery for Children; WASI: Wechsler Abbreviated Scale Intelligence; WPPSI: Wechsler Preschool and Primary Scale of Intelligence; WISC = Wechsler Intelligence Scale for Children; WAIS = Wechsler Adult Intelligence Scale; CTOPP = Comprehensive Test of Phonological Processing; WRAT-4 = Wide Range Achievement Test 4; TOWRE = Test of Word Reading Efficiency; PLS = Preschool Language Scale; NEPSY-II = A Developmental Neuropsychological Assessment; CCC-2 = Children’s Communication Checklist-2; Tea-CH = Test of Everyday Attention in Children; BRIEF = Behavioral Rating Inventory of Executive Function; CMS = Children’s Memory Scale; Beery-VMI = Beery-Buktenica Test of Visual-Motor Integration; ASQ = Ages & Stages Questionnaire ; CCPT = Connor’s Continuous Performance Test; TAP = Tests for Attentional Performance; ASEBA = Achenbach System of Empirically Based Assessment; CBCL = Child Behavior Checklist; TACQOL = TNO AZL Children’s Quality of Life; WHOQOL = World Health Organization Quality of Life.

**eTable 6**

*Adapted NIH Quality Assessment of Observational Cohort and Cross-Sectional Studies*

Study (lead author, year)	Item 1	Item 2	Item 3	Item 4a	Item 4b	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11
Arnaud 1995 <sup>1</sup>	Y	N	Y	Y	Y	N	Y	N	N	NR	NA	N
Bellew 2005, 2011, 2015, 2019 <sup>2-5</sup>	Y	Y	NR	Y	N	N	Y	Y	Y	NR	N	N
Byun 2018 <sup>7</sup>	N	N	NR	Y	Y	N	Y	N	Y	NR	NA	N
Care 2019 <sup>9</sup>	N	Y	Y	Y	Y	N	Y	Y	Y	NR	NA	N
Chandler 2020 <sup>10</sup>	Y	N	NR	NR	Y	N	Y	Y	Y	NR	NA	Y
Chieffo 2020 <sup>12</sup>	Y	N	Y	NR	N	N	Y	Y	N	NR	N	N
Chuang 2021 <sup>13</sup>	Y	Y	N	Y	Y	N	Y	Y	Y	NR	NA	Y
Da Costa 2006 <sup>15</sup>	Y	N	NR	NR	Y	N	Y	Y	Y	NR	NA	Y
Da Costa 2012/2013 <sup>16,17</sup>	Y	N	Y	NR	Y	N	Y	Y	Y	NR	NA	N
Engel 2012 <sup>18</sup>	Y	Y	NR	Y	Y	N	Y	Y	Y	NR	NA	N
Gewalli 2001 <sup>19</sup>	Y	Y	NR	Y	N	N	Y	Y	Y	NR	Y	N
Hashim 2014 / Patel 2014 <sup>20,21</sup>	Y	Y	Y	Y	Y	N	Y	Y	Y	NR	NA	Y
Imahiyerobo 2019 <sup>22</sup>	Y	Y	Y	Y	N	N	Y	N	Y	NR	NA	Y
Kapp-Simon 1993/1998 <sup>36,37</sup>	Y	N	Y	Y	Y	N	Y	Y	Y	NR	N	N
Kljajic 2019/2020 <sup>38,39</sup>	Y	Y	Y	Y	Y	N	Y	Y	Y	NR	NA	Y
Korpilahti 2012 <sup>40</sup>	Y	N	NR	NR	Y	N	Y	Y	Y	NR	NA	N
Lee 2015 / 2017 <sup>41,42</sup>	Y	N	NR	Y	N	N	Y	Y	Y	NR	N	N
Magge 2002 <sup>43</sup>	Y	Y	N	Y	Y	N	Y	Y	Y	NR	NA	N
Mazzaferro 2018 <sup>44</sup>	Y	N	N	NR	Y	N	Y	Y	Y	NR	NA	Y
Moreno-Villagomez 2020 <sup>45</sup>	Y	N	NR	NR	Y	N	Y	Y	Y	NR	NA	N
Noetzel 1985 <sup>46</sup>	N	N	NR	Y	N	N	Y	N	N	NR	NA	N
Scheuerle 2004 <sup>48</sup>	N	N	NR	N	N	N	Y	Y	N	NR	NA	N
Shipster 2003 <sup>49</sup>	Y	Y	Y	Y	Y	N	Y	Y	Y	NR	NA	N

NIH = National Institutes of Health; Y = yes; N = no; NR = not reported; NA = not applicable

1. Was the research question or objective in this paper clearly stated?
2. Was the study population clearly specified & defined (including demographics, location and time period)?
3. Was the participation rate of eligible persons at least 50%?
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)?
5. Were inclusion and exclusion criteria for being in the study prespecified, reported and applied uniformly to all participants?
6. Was a sample size justification, power description, or variance and effect estimates provided?
7. Was sagittal synostosis diagnosed prior to the outcome(s) being measured?

8. Was the diagnosis of sagittal synostosis (independent variable) clearly defined, valid, reliable, and implemented consistently across all study participants?
9. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?
10. Were the outcome assessors blinded to the exposure status of participants?
11. Was loss to follow-up after baseline 20% or less?
12. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?

**eTable 7***NIH Quality Assessment of Case-Control Studies*

Study (lead author, year)	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Item 12a	Item 12b	Item 12c
Boltshauser, 2003 <sup>6</sup>	Y	N	N	NR	NR	Y	NR	NR	Y	Y	NR	N	N	NA
Cabrejo, 2019 <sup>8</sup>	Y	N	N	NR	Y	Y	NR	NR	Y	Y	NR	N	Y	N
Chieffo, 2010 <sup>11</sup>	Y	N	N	NR	NR	Y	NR	NR	Y	Y	NR	N	Y	N
Chuang, 2018 <sup>13</sup>	N	N	N	NR	NR	Y	NR	NR	Y	N	NR	N	N	NA
Infant Learning Project <sup>23-37</sup>	Y	Y	N	Y	Y	Y	NR	NR	Y	Y	NR	Y	Y	Y
Salokorpi, 2018 <sup>47</sup>	Y	Y	N	Y	Y	Y	NR	NR	Y	N	NR	N	Y	N
Speltz, 1993 <sup>50</sup>	Y	N	N	NR	NR	Y	NR	NR	Y	Y	NR	Y	Y	NR
Speltz, 1997 <sup>51</sup>	Y	N	N	NR	Y	Y	NR	NR	Y	Y	NR	Y	Y	Y
Virtanen, 1999 <sup>52</sup>	Y	Y	N	Y	Y	Y	NR	NR	Y	Y	NR	N	Y	N

NIH = National Institutes of Health; Y = yes; N = no; NR = not reported; NA = not applicable

1. Was the research question or objective in this paper clearly stated & appropriate?
2. Was the study population clearly specified & defined (including details of demographics, time period, location)?
3. Did the authors include a sample size justification?
4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?
5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?
6. Were the cases clearly defined and differentiated from controls?
7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?
8. Was there use of concurrent controls?
9. Was the diagnosis of sagittal synostosis clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?
10. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across participants?
11. Were the assessors of outcomes blinded to the case or control status of participants?
12. Were key potential confounding variables measured and adjusted statistically in the analyses?
13. Were cases and controls matched?
14. If matching was used, did the investigators account for matching during study analysis?

**eTable 8**

*Prediction Intervals for Pooled Analyses With  $\geq 5$  Included Studies*

Post-surgical domain	No. of studies	Mean $g_w$	CI (95%) lower limit	CI (95%) upper limit	PI (95%) lower limit	PI (95%) upper limit	-1.0	-0.5	0	0.5	1.0
General cognition: norms	9	0.01	-0.26	0.27	-0.86	0.87					
Motor functioning: norms	7	0.01	-0.31	0.34	-1.09	1.12					
Verbal abilities: norms	7	0.23	-.01	0.47	-0.51	0.97					
Visuospatial: norms	6	0.31	0.18	0.44	0.12	0.49					

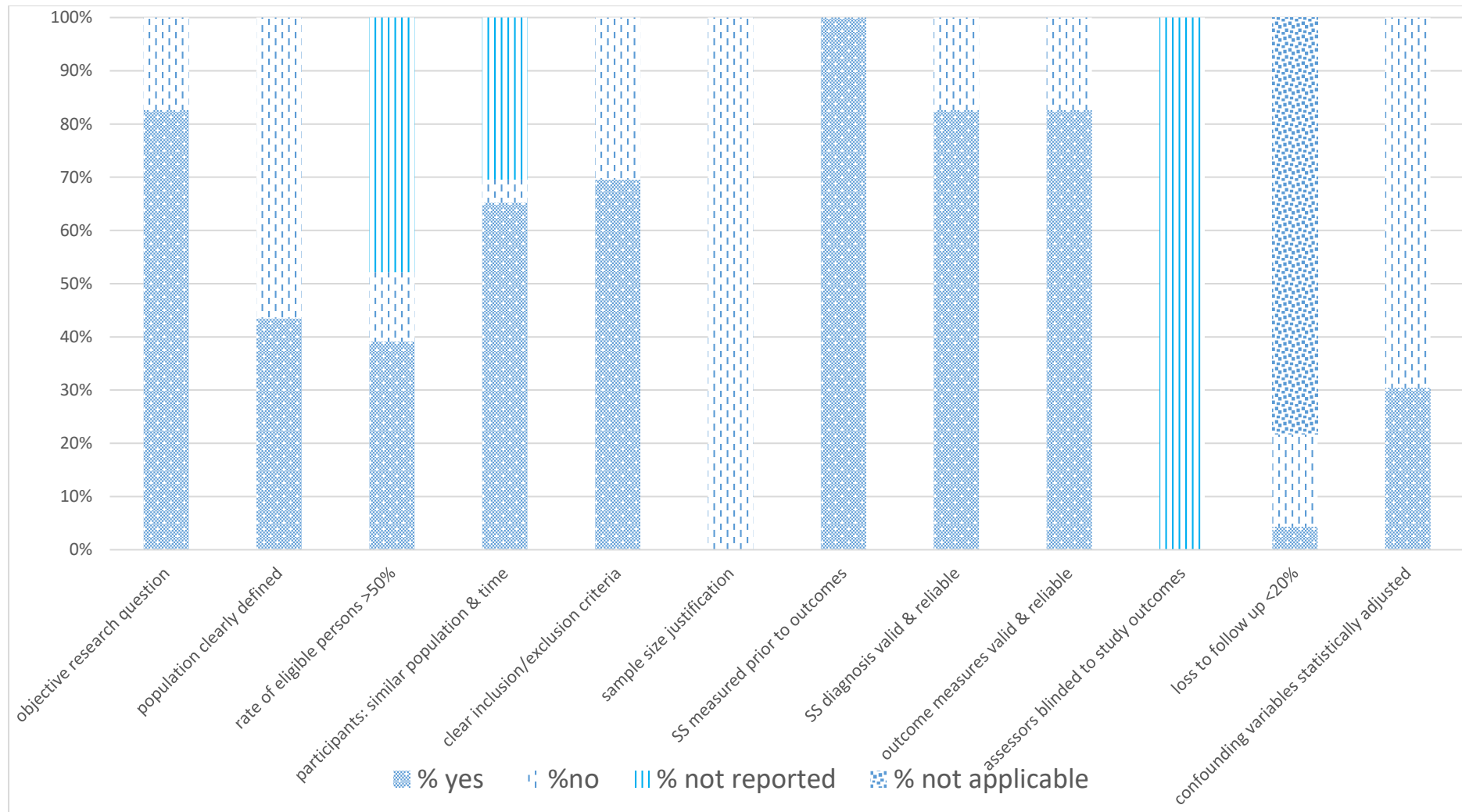
Note: CI = confidence intervals; PI = prediction intervals

**eTable 9**

*Outcomes of Mixed (Conservatively Managed + Presurgical + Postsurgical) Samples of Children With Sagittal Synostosis*

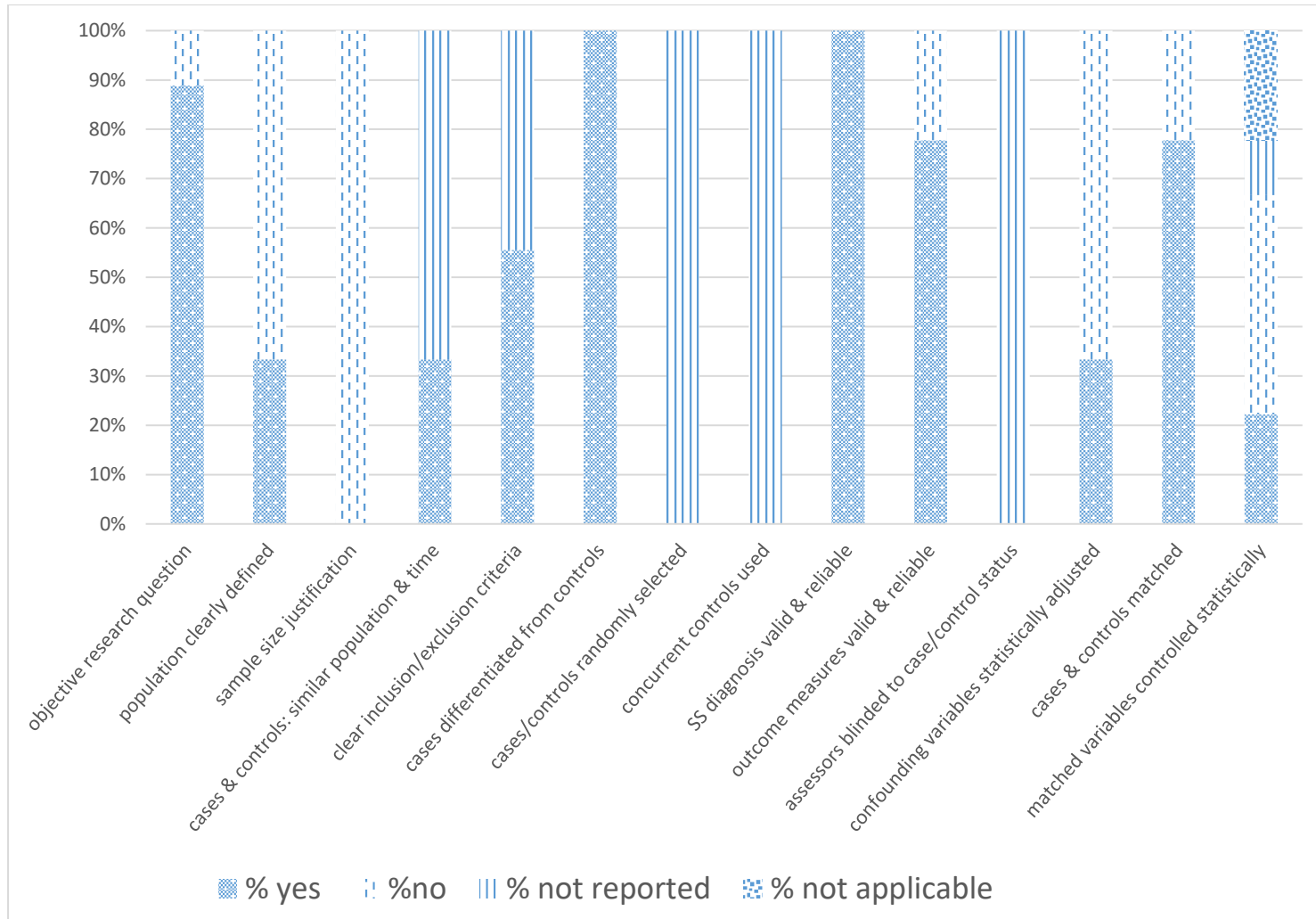
<b>COMBINED SAMPLES (combined conservatively managed, pre- and post-surgery participants)</b>																
	Standardized Mean Group Differences										Prevalence rates					
<i>Domain</i>	<i>Comparison data</i>	<i>N<sub>studies</sub></i>	<i>N<sub>SS</sub></i>	<i>Hedges' g</i>	<i>Lower 95% CI</i>	<i>Upper 95% CI</i>	<i>p</i>	<i>I<sup>2</sup></i>	<i>tau</i>	<i>N<sub>fs</sub></i>	<i>N<sub>studies</sub></i>	<i>N<sub>SS</sub></i>	<i>Prevalence (95% CI)</i>	<i>N<sub>studies</sub></i>	<i>N<sub>SS</sub></i>	<i>Odds ratio (95% CI) logarithmic scale</i>
General cognition	norms	3	185	-.33	-1.17	.51	.44	95.08	.72	2	2	73	0.20 (0.12 – 0.30)			
Motor functioning	norms	1	67	-.93	-1.18	-.69	<b>.00</b>	-	-	-						
Verbal abilities	norms	2	123	.12	-.24	.49	.51	47.63	.19	0	1	76	0.37 (0.27 – 0.48)			
Visuospatial abilities	norms	2	84	-.03	-.50	.44	.90	65.53	.28	0						





**eFigure 1**

Percentage of Observational Cross-Sectional and Cohort Studies Meeting Each of the Adapted NIH Study Quality Criteria ( $N_{\text{studies}} = 23$ ).  
 SS = sagittal synostosis







**eFigure 2**

Percentage of Case-Control Studies Meeting Each of the Adapted NIH Study Quality Criteria ( $N_{\text{studies}} = 9$ ). SS = sagittal synostosis.

CONSERVATIVELY MANAGED SAGITTAL SYNOSTOSIS

Study details		Standardized Mean Group Differences					Prevalence Rates													
Authors	N	Comparisons with healthy peers		Comparisons with norms		Hedges' g and 95% CI					Prevalence and 95% CI (single group studies)					Odds ratio and 95% CI (2 group studies; logarithmic scale)				
Objective measures		g	p	g	p	-2.0	-1.0	0.0	1.0	2.0	0	25	50	75	100	0.01	0.1	1	10	100
						SS outcomes worse					→ increasing prevalence					SS outcomes better		SS outcomes worse		
<b>General cognition</b>																				
Arnaud, <sup>1</sup> 1995	51										4%									
Boltshauser et al, <sup>6</sup> 2003	30	-0.08	.79								7%									
Bellew et al, (2005-2019)*	13			.13	.64															
Kapp-Simon 1993/1998*	4			.40	.42															
<b>OVERALL</b>	<b>98</b>			<b>.19</b>	<b>.43</b>						<b>5%</b>									
<b>Motor functioning</b>																				
Bellew et al, (2005-2019)*	13			-.15	.59															
<b>Verbal abilities/ language</b>																				
Bellew et al, (2005-2019)*	14			.09	.74															
Boltshauser et al, <sup>6</sup> 2003	14										7%					0.33				
<b>Visuospatial abilities</b>																				
Bellew et al, (2005-2019)*	14			.02	.93															
Boltshauser et al, <sup>6</sup> 2003											7%					0.69				
<b>Adaptive &amp; social skills</b>																				
Bellew et al, (2005-2019)*	13			-.14	.62															
<b>Arithmetic</b>																				
Boltshauser et al, <sup>6</sup> 2003	18															0.71				
<b>Attention</b>																				
Boltshauser et al, <sup>6</sup> 2003	19										13%					1.04				
<b>Executive function</b>																				
Boltshauser et al, <sup>6</sup> 2003	12										8%									
<b>Global development</b>																				
Bellew et al, (2005-2019)*	23			.58	.01															
<b>Memory: shorter term</b>																				
Boltshauser et al, <sup>6</sup> 2003	18										9%					0.70				
<b>Processing speed</b>																				
Boltshauser et al, <sup>6</sup> 2003	14										7%					0.31				

<i>Subjective measures</i>							
<b>Behavior- externalizing</b>							
Boltshauser et al, <sup>6</sup> 2003	24	-0.25	.22				
<b>Behavior: internalizing</b>							
Boltshauser et al, <sup>6</sup> 2003	24	-0.30	.14				
<b>Behavior: overall</b>							
Boltshauser et al, <sup>6</sup> 2003	24	-0.29	.16				
<b>Quality of life</b>							
Boltshauser et al, <sup>6</sup> 2003	24	.00	1.0				

Note: *N* refers to sagittal synostosis participants; \* = details for studies comprising the same participants across multiple papers are provided in eTable 2 in the Supplement; green forest plots = comparisons between SS and healthy norms; black forest plots = comparisons between SS and normative data.

### eFigure 3

*Outcomes of Children With Conservatively Managed Sagittal Synostosis.*

PRE-SURGICAL SAGITTAL SYNOSTOSIS

Study details		Standardized Mean Group Differences						Prevalence Rates						
Authors	N	Comparisons with healthy peers		Comparisons with norms		Hedges' g and 95% CI		Prevalence and 95% CI						
Objective measures		g	p	g	p	-2.0	-1.0	0.0	1.0	2.0	0	25	50	75
						SS outcomes worse		SS outcomes better				→ increasing prevalence		
<b>General cognition</b>														
Chuang et al, <sup>13</sup> 2018	9	.31	.45											
Da Costa et al, 2012/2013*	26			-.24	.22									
ILP (2005 – 2017)*	62	-.46	.00											
Imahiyerobo et al, <sup>22</sup> 2019	77			.52	.00									
Kapp-Simon 1993/1998*	20			.17	.46									
Lee et al, 2015/2017*	37			-1.03	.00						37%			
Speltz et al, <sup>51</sup> 1997	18	.29	.37											
<b>OVERALL</b>	<b>249</b>	<b>-.28</b>	<b>.15</b>	<b>-.15</b>	<b>.70</b>									
<b>Motor functioning</b>														
Bellew et al, (2005-2019)*	28	-.44	.10											
Chieffo et al, <sup>12</sup> 2020	87										11%			
Da Costa et al, 2012/2013*	26			-.82	.00									
Gewalli et al, <sup>19</sup> 2001	26			.44	.03									
ILP (2005 – 2017)*	62	-.41	.01											
Imahiyerobo et al, <sup>22</sup> 2019	77			.21	.07									
Lee et al, 2015/2017*	37			-1.04	.00						26%			
Speltz et al, <sup>51</sup> 1997	18	-.47	.15											
<b>OVERALL</b>	<b>361</b>	<b>-.42</b>	<b>.00</b>	<b>-.30</b>	<b>.41</b>						<b>17%</b>			
<b>Verbal abilities / language</b>														
Bellew et al, (2005-2019)*	28	-.01	.96											
Chieffo et al, <sup>12</sup> 2020	87										8%			
Chuang et al, <sup>13</sup> 2018	9	.32	.45											
Gewalli et al, <sup>19</sup> 2001	26			.24	.23									
ILP (2005 – 2017)*	62	-.03	.85											
Imahiyerobo et al, <sup>22</sup> 2019	77			.15	.22									
Scheuerle 2004	3										33%			
<b>OVERALL</b>	<b>292</b>	<b>.01</b>	<b>.96</b>	<b>.17</b>	<b>.09</b>						<b>13%</b>			
<b>Visuospatial abilities</b>														
Bellew et al, (2005-2019)*	28	-.09	.73											
Chieffo et al, <sup>12</sup> 2020	87										7%			
Gewalli et al, <sup>19</sup> 2001	26			.44	.03									
<b>OVERALL</b>	<b>141</b>													
<b>Adaptive &amp; social skills</b>														
Bellew et al, (2005-2019)*	28	-.21	.44											
Chieffo et al, <sup>12</sup> 2020	87										6%			
Gewalli et al, <sup>19</sup> 2001	26			.21	.30									
<b>OVERALL</b>	<b>141</b>													
<b>Global development</b>														
Arnaud, <sup>1</sup> 1995	142										8%			
Bellew et al, (2005-2019)*	28	-.31	.25											
Chieffo et al, <sup>12</sup> 2020	87										25%			
Engel et al, <sup>18</sup> 2012	46										17%			
Gewalli et al, <sup>19</sup> 2001	26			.30	.13						8%			
Imahiyerobo et al, <sup>22</sup> 2019	77										18%			

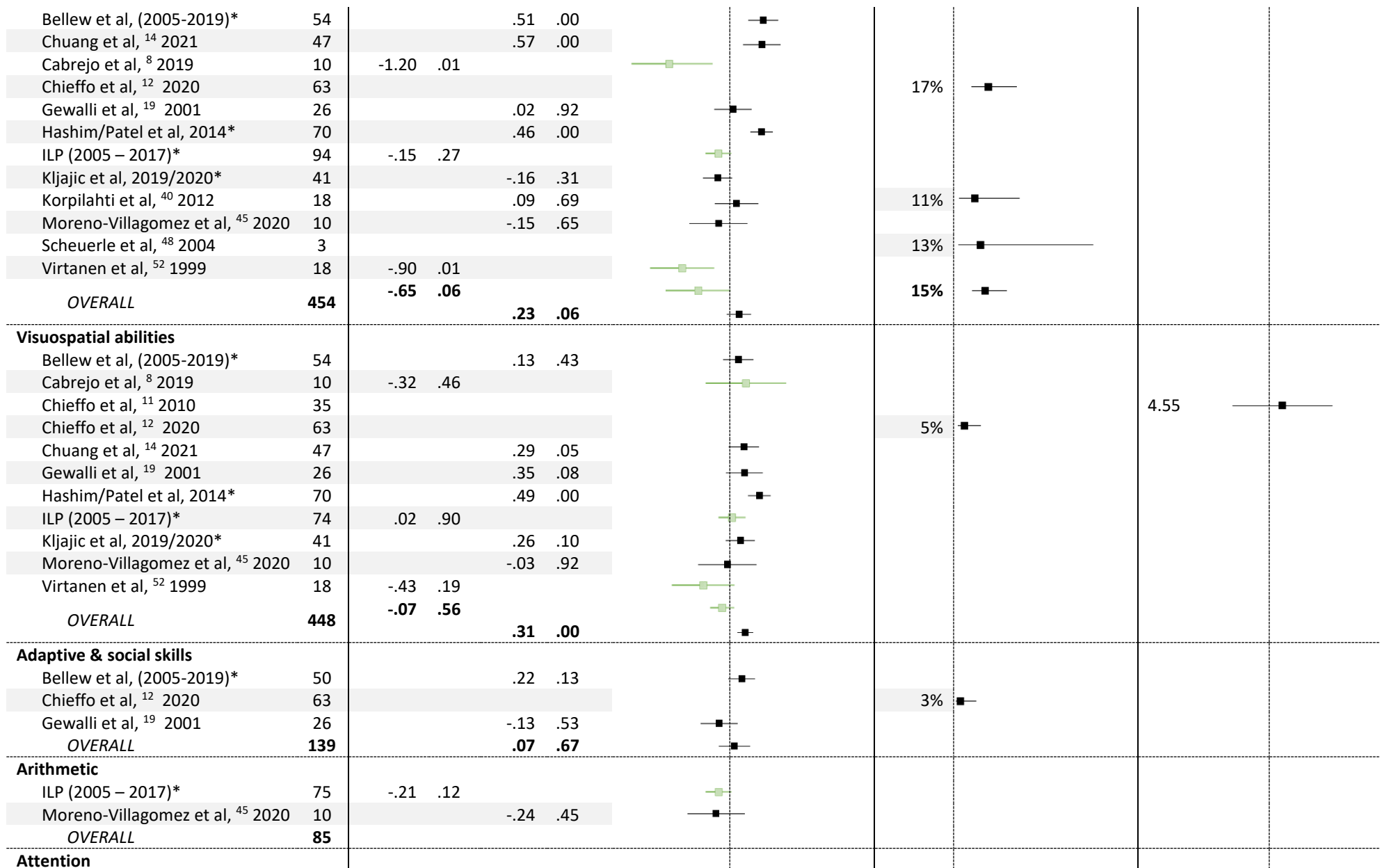
Note: *N* refers to sagittal synostosis participants; ILP = Infant Learning Project combined papers; \* = details for studies comprising the same participants across multiple papers are provided in eTable 2 in the Supplement; green forest plots = comparisons between SS and healthy norms; black forest plots = comparisons between SS and normative data.

**eFigure 4**

*Presurgical Functioning of Children With Sagittal Synostosis: Had Not Yet Undergone Surgery Prior to Being Assessed.*

POST-SURGICAL SAGITTAL SYNOSTOSIS

Study details		Standardized Mean Group Differences					Prevalence Rates												
Authors	N	Comparisons with healthy peers		Comparisons with norms		Hedges' g and 95% CI					Prevalence and 95% CI (single group studies)		Odds ratio and 95% CI (2 group studies; logarithmic scale)						
Objective measures		g	p	g	p	-2.0	-1.0	0.0	1.0	2.0	0	25	50	75	0.01	0.1	1	10	100
<b>General cognition</b>																			
Arnaud, <sup>1</sup> 1995	47										11%								
Bellew et al, (2005-2019)*	54			.10	.59						28%								
Chuang et al, <sup>14</sup> 2021	47			.43	.00														
Da Costa et al, <sup>15</sup> 2006	6			-.03	.94														
Da Costa et al, 2012/2013*	26			-.42	.10														
Hashim/Patel et al, 2014*	70			.52	.00														
ILP (2005 – 2017)*	94	-.28	.04																
Kapp-Simon et al, 1993/1998*	20			-.13	.63														
Kljajic et al, 2019/2020*	41			-.25	.11														
Lee et al, 2015/2017*	25			-.38	.06						22%								
Moreno-Villagomez et al, <sup>45</sup> 2020	10			.01	.98														
Speltz et al, <sup>51</sup> 1997	19	.21	.51								20%								
<b>OVERALL</b>	<b>459</b>	<b>-.12</b>	<b>.60</b>	<b>.01</b>	<b>.96</b>														
<b>Motor functioning</b>																			
Bellew et al, (2005-2019)*	50			.58	.00														
Chieffo et al, <sup>12</sup> 2020	63										6%								
Chuang et al, <sup>14</sup> 2021	47			.27	.07														
Da Costa et al, 2012/2013*	16			-.89	.00														
Gewalli et al, <sup>19</sup> 2001	26			.16	.42														
Hashim/Patel et al, 2014*	70			.27	.03														
ILP (2005 – 2017)*	94	-.22	.12																
Lee 2015/2017	25			-.41	.04						22%								
Moreno-Villagomez et al, <sup>45</sup> 2020	10			-.14	.66														
Speltz et al, <sup>51</sup> 1997	19	.00	1.0																
Virtanen et al, <sup>52</sup> 1999	18	-.15	.65																
<b>OVERALL</b>	<b>438</b>	<b>-.18</b>	<b>.13</b>	<b>.01</b>	<b>.93</b>														
<b>Verbal abilities / language</b>																			





ILP (2005 – 2017)*	76	-0.11	.43					
Kljajic et al, 2019/2020*	38			-0.51	.00			
Virtanen et al, <sup>52</sup> 1999	18	-0.82	.02					
<b>OVERALL</b>	<b>132</b>	<b>-0.40</b>	<b>.26</b>					
<b>Executive function</b>								
ILP (2005 – 2017)*	75	-0.18	.19					
<b>Global development</b>								
Bellew et al, (2005-2019)*	50			.53	.00			
Gewalli et al, <sup>19</sup> 2001	26			.09	.64	15%		
<b>OVERALL</b>	<b>76</b>			<b>.34</b>	<b>.13</b>			
<b>Learning difficulties</b>								
Chuang et al, <sup>14</sup> 2021	47					12%		
ILP (2005 – 2017)*	70						0.64	
Hashim/Patel et al, 2014*	70					23%		
Kapp-Simon et al, 1993/1998*	10					13%		
Magge et al, <sup>43</sup> 2002	16					50%		
<b>OVERALL</b>	<b>213</b>					<b>22%</b>		
<b>Memory: shorter term</b>								
ILP (2005 – 2017)*	74	-0.24	.09					
Kljajic et al, 2019/2020*	41			-0.49	.00			
Moreno-Villagomez et al, <sup>45</sup> 2020	10			-0.28	.38			
Virtanen et al, <sup>52</sup> 1999	18	.00	1.0					
<b>OVERALL</b>	<b>143</b>	<b>-0.20</b>	<b>.12</b>					
				<b>-0.45</b>	<b>.00</b>			
<b>Memory: longer term</b>								
ILP (2005 – 2017)*	74	-0.18	.20					
<b>Processing speed</b>								
Kljajic et al, 2019/2020*	41			-0.65	.00			
Moreno-Villagomez et al, <sup>45</sup> 2020	7			.27	.48			
<b>OVERALL</b>	<b>48</b>			<b>-0.26</b>	<b>.57</b>			
<i>Subjective measures</i>								
<b>Motor functioning</b>								
Care et al, <sup>53</sup> 2019	138					10%		
<b>Verbal abilities / language</b>								
ILP (2005 – 2017)*	70	-0.01	.93					
Care et al, <sup>53</sup> 2019	138					9%		
<b>OVERALL</b>	<b>208</b>							



Chuang et al, <sup>14</sup> 2021	47								
Hashim/Patel et al, 2014*	70								
<b>OVERALL</b>	<b>192</b>								
<b>Quality of life</b>									
Mazzaferro et al, <sup>44</sup> 2018	5								
<b>Satisfaction with appearance</b>									
Salokorpi et al, <sup>54</sup> 2018	40								
<b>Self-concept</b>									
Speltz et al, <sup>50</sup> 1993	7								

Note: *N* refers to sagittal synostosis participants; ILP = Infant Learning Project combined papers; \* = details for studies comprising the same participants across multiple papers are provided in eTable 2 in the Supplement; green forest plots = comparisons between SS and healthy norms; black forest plots = comparisons between SS and normative data.

#### eFigure 5

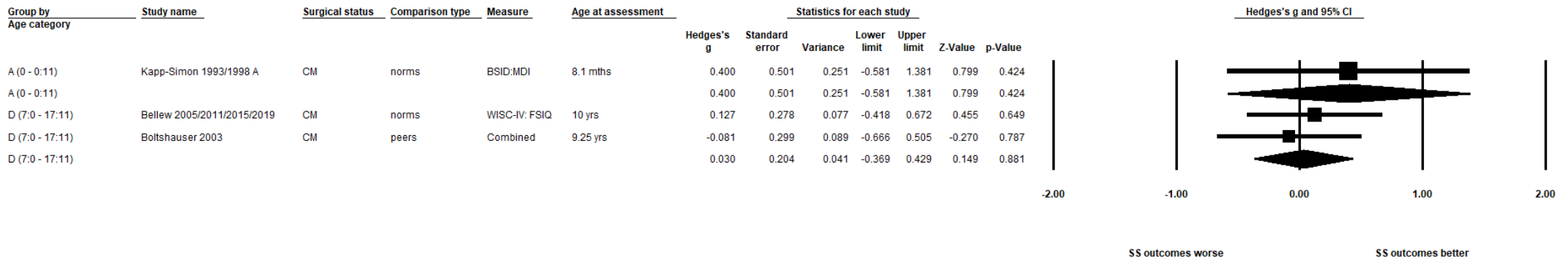
*Outcomes of Children With Operated Sagittal Synostosis: Had Undergone Surgery Prior to Being Assessed.*

**eFigure 6**

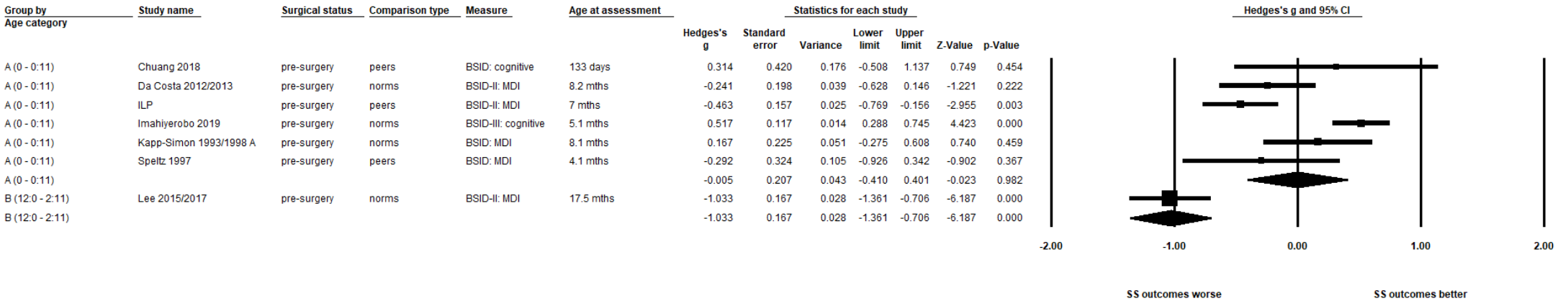
*Pooled Analyses for Each Cognitive, Behavioral and Psychological Domain, Partitioned According to Surgical Status (Conservatively Managed, Presurgical, Postsurgical) and Age at Assessment: A (0 – 0.11); B (1:0 – 2:11); C (3:0 – 6:11); D (7:0 – 17:11); E (>18:0)*

**OBJECTIVE MEASURES**

**3a. General cognition: conservatively managed samples**

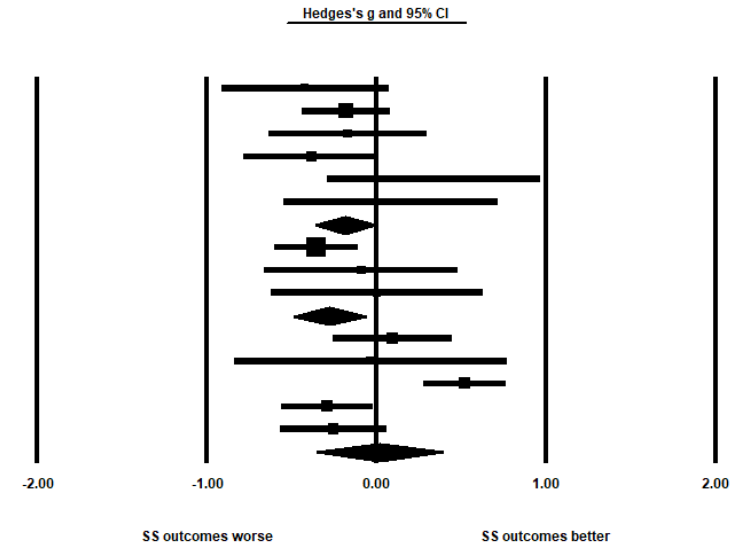


**3b. General cognition: pre-surgical samples**



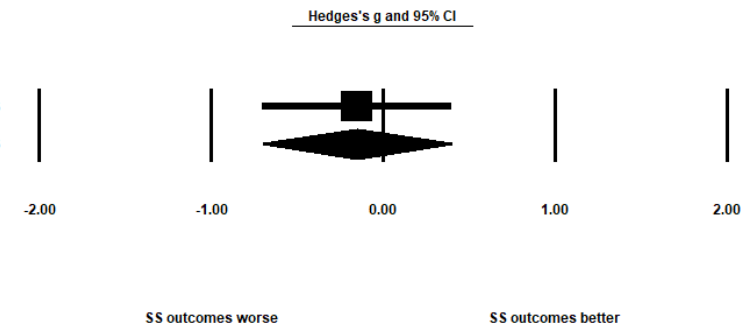
### 3c. General cognition: post-surgical samples

Group by Age category	Study name	Surgical status	Comparison type	Measure	Age at assessment	Statistics for each study						
						Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
B (12:0 - 2:11)	Da Costa 2012/2013	post-surgery	norms	BSID-II: MDI	21.2 mths	-0.419	0.251	0.063	-0.911	0.073	-1.668	0.095
B (12:0 - 2:11)	ILP B	post-surgery	peers	BSID-II: MDI	18 mths	-0.180	0.132	0.017	-0.438	0.078	-1.366	0.172
B (12:0 - 2:11)	Kapp-Simon 1993/1998 B	post-surgery	norms	BSID: MDI	21 mths	-0.167	0.237	0.056	-0.632	0.298	-0.704	0.481
B (12:0 - 2:11)	Lee 2015/2017	post-surgery	norms	BSID-II: MDI	31.5 mth	-0.383	0.201	0.041	-0.778	0.012	-1.900	0.057
B (12:0 - 2:11)	Speltz 1997 A	post-surgery	peers	BSID: MDI	12.4 mths	0.337	0.320	0.102	-0.290	0.965	1.054	0.292
B (12:0 - 2:11)	Speltz 1997 B	post-surgery	peers	BSID: MDI	24.4 mths	0.085	0.322	0.104	-0.546	0.716	0.263	0.793
B (12:0 - 2:11)						-0.186	0.089	0.008	-0.360	-0.012	-2.092	0.036
C (3:0 - 6:11)	ILP C	post-surgery	peers	BSID-II: MDI	3 yrs	-0.356	0.125	0.016	-0.601	-0.111	-2.851	0.004
C (3:0 - 6:11)	Kapp-Simon 1993/1998 C	post-surgery	norms	BSID: MDI	50 mths	-0.089	0.290	0.084	-0.657	0.480	-0.305	0.760
C (3:0 - 6:11)	Moreno-Villagomez 2020	post-surgery	norms	WPPSI-III: FSIQ	54.2 mths	0.007	0.317	0.100	-0.615	0.628	0.021	0.983
C (3:0 - 6:11)						-0.277	0.108	0.012	-0.489	-0.066	-2.568	0.010
D (7:0 - 17:11)	Bellew 2005/2011/2015/2019	post-surgery	norms	WISC-IV: FSIQ	Combined	0.095	0.177	0.031	-0.253	0.442	0.534	0.593
D (7:0 - 17:11)	Da Costa 2006	post-surgery	norms	WISC-III: FSIQ	10.9 yrs	-0.033	0.409	0.167	-0.834	0.768	-0.082	0.935
D (7:0 - 17:11)	Hashim 2014/Patel 2014	post-surgery	norms	WASI: FSIQ	10.04 yrs	0.521	0.122	0.015	0.283	0.759	4.285	0.000
D (7:0 - 17:11)	ILP D	post-surgery	peers	WISC-IV: FSIQ	7 yrs	-0.290	0.137	0.019	-0.558	-0.022	-2.122	0.034
D (7:0 - 17:11)	Kljajic 2019/2020	post-surgery	norms	WISC-IV: FSIQ	11.5 yrs	-0.254	0.158	0.025	-0.563	0.055	-1.610	0.107
D (7:0 - 17:11)						0.016	0.190	0.036	-0.357	0.388	0.083	0.934



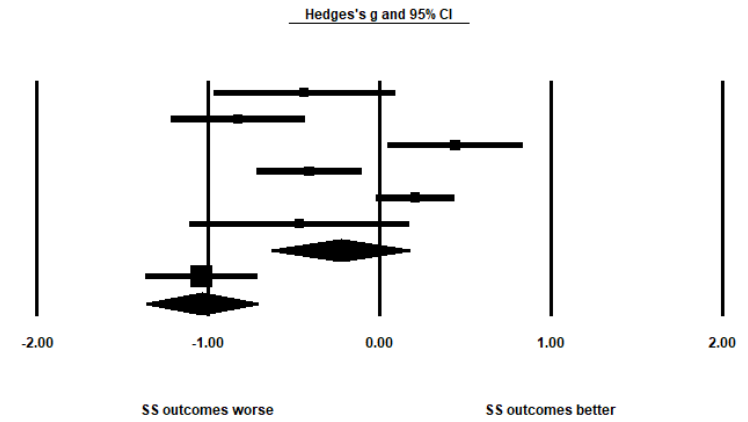
### 3d. Motor functioning: conservatively managed samples

Group by Age category	Study name	Surgical status	Comparison type	Measure	Age at assessment	Statistics for each study						
						Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
B (1:0 - 2:11)	Bellew 2005/2011/2015/2019 B	CM	norms	Combined	Combined	-0.152	0.278	0.077	-0.697	0.394	-0.545	0.586
B (1:0 - 2:11)						-0.152	0.278	0.077	-0.697	0.394	-0.545	0.586



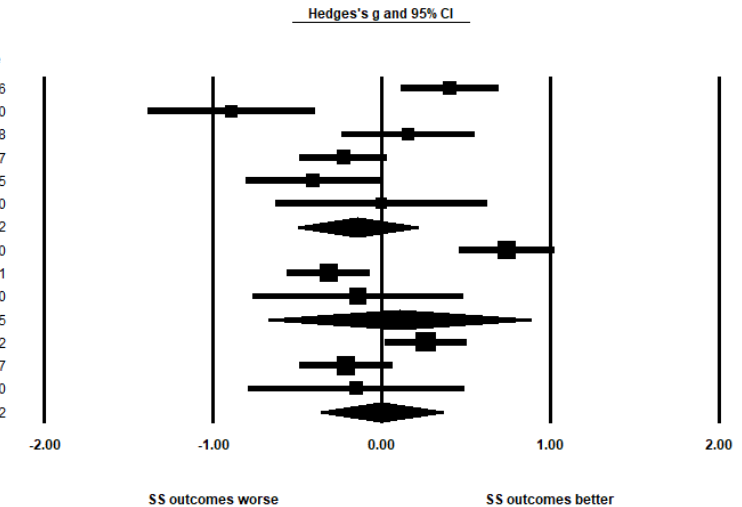
### 3e. Motor functioning: pre-surgical samples

Group by Age category	Study name	Surgical status	Comparison type	Measure	Age at assessment	Statistics for each study						
						Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
A (0 - 0:11)	Bellew 2005/2011/2015/2019 A	pre-surgery	peers	Combined	6.9 mths	-0.436	0.268	0.072	-0.961	0.090	-1.626	0.104
A (0 - 0:11)	Da Costa 2012/2013	pre-surgery	norms	BSID-II PDI	8.2 mths	-0.822	0.198	0.039	-1.210	-0.434	-4.153	0.000
A (0 - 0:11)	Gewalli 2001	pre-surgery	norms	Combined	6.9 mths	0.442	0.201	0.040	0.049	0.836	2.202	0.028
A (0 - 0:11)	ILP A	pre-surgery	peers	BSID-II PDI	7 mths	-0.409	0.156	0.024	-0.715	-0.103	-2.621	0.009
A (0 - 0:11)	Imahiyerobo 2019	pre-surgery	norms	Combined	5.1 mths	0.211	0.117	0.014	-0.018	0.439	1.808	0.071
A (0 - 0:11)	Speltz 1997	pre-surgery	peers	BSID I PDI	4.1 mths	-0.467	0.326	0.107	-1.107	0.173	-1.431	0.153
A (0 - 0:11)						-0.228	0.205	0.042	-0.630	0.174	-1.113	0.266
B (1:0 - 2:11)	Lee 2015/2017	pre-surgery	norms	BSID-II PDI	17.5 mths	-1.037	0.167	0.028	-1.365	-0.710	-6.209	0.000
B (1:0 - 2:11)						-1.037	0.167	0.028	-1.365	-0.710	-6.209	0.000

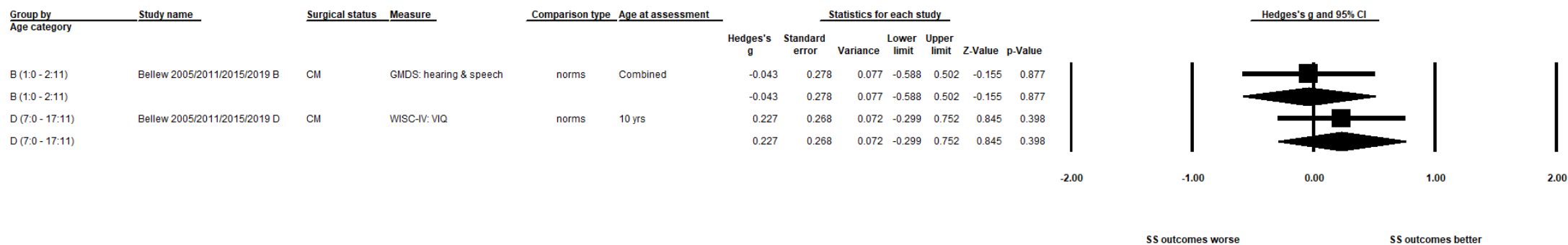


### 3f. Motor functioning: post-surgical samples

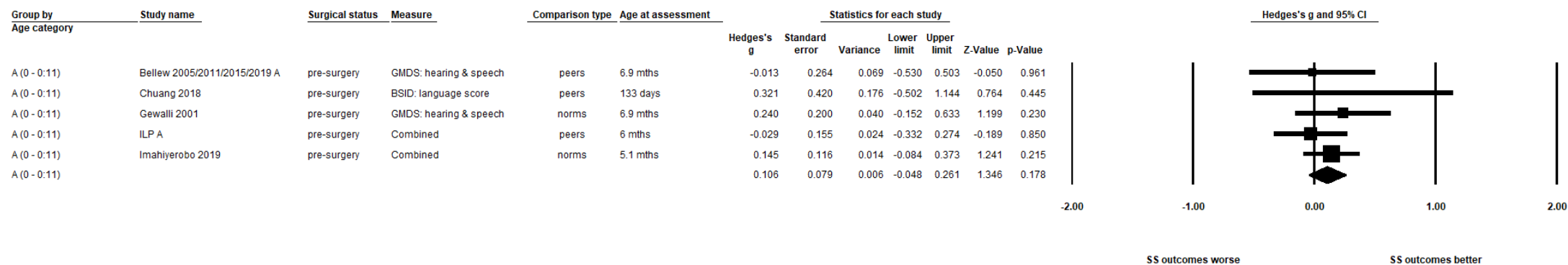
Group by Age category	Study name	Surgical status	Comparison type	Measure	Age at assessment	Statistics for each study						
						Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
B (1:0 - 2:11)	Bellew 2005/2011/2015/2019 B	post-surgery	norms	Combined	15.2 mths	0.406	0.148	0.022	0.117	0.696	2.750	0.006
B (1:0 - 2:11)	Da Costa 2012/2013	post-surgery	norms	BSID-II PDI	21.2 mths	-0.887	0.252	0.063	-1.380	-0.394	-3.528	0.000
B (1:0 - 2:11)	Gewalli 2001	post-surgery	norms	Combined	16.3 mths	0.162	0.200	0.040	-0.230	0.555	0.810	0.418
B (1:0 - 2:11)	ILP B	post-surgery	peers	BSID-II PDI	18 mths	-0.225	0.132	0.017	-0.483	0.033	-1.710	0.087
B (1:0 - 2:11)	Lee 2015/2017	post-surgery	norms	BSID-II PDI	31.5 mths	-0.405	0.201	0.041	-0.800	-0.010	-2.009	0.045
B (1:0 - 2:11)	Speltz 1997	post-surgery	peers	BSID I PDI	Combined	0.000	0.320	0.102	-0.627	0.627	0.000	1.000
B (1:0 - 2:11)						-0.143	0.182	0.033	-0.499	0.213	-0.786	0.432
C (3:0 - 6:11)	Bellew 2005/2011/2015/2019 C	post-surgery	norms	Combined	5 yrs	0.744	0.143	0.021	0.463	1.026	5.188	0.000
C (3:0 - 6:11)	ILP C	post-surgery	peers	BSID-II PDI	3 yrs	-0.313	0.124	0.015	-0.556	-0.071	-2.534	0.011
C (3:0 - 6:11)	Moreno-Villagomez 2020	post-surgery	norms	WPPSI-III: motor	54.2 mths	-0.139	0.317	0.101	-0.761	0.482	-0.440	0.660
C (3:0 - 6:11)						0.108	0.397	0.157	-0.669	0.885	0.272	0.785
D (7:0 - 17:11)	Hashim 2014 / Patel 2014	post-surgery	norms	Beery VMI	10.04 yrs	0.265	0.124	0.015	0.022	0.507	2.141	0.032
D (7:0 - 17:11)	ILP D	post-surgery	peers	Combined	7 yrs	-0.209	0.140	0.020	-0.484	0.066	-1.488	0.137
D (7:0 - 17:11)	Virtanen 1999	post-surgery	peers	Combined	146.8 mths	-0.148	0.327	0.107	-0.789	0.492	-0.454	0.650
D (7:0 - 17:11)						-0.002	0.185	0.034	-0.365	0.361	-0.010	0.992



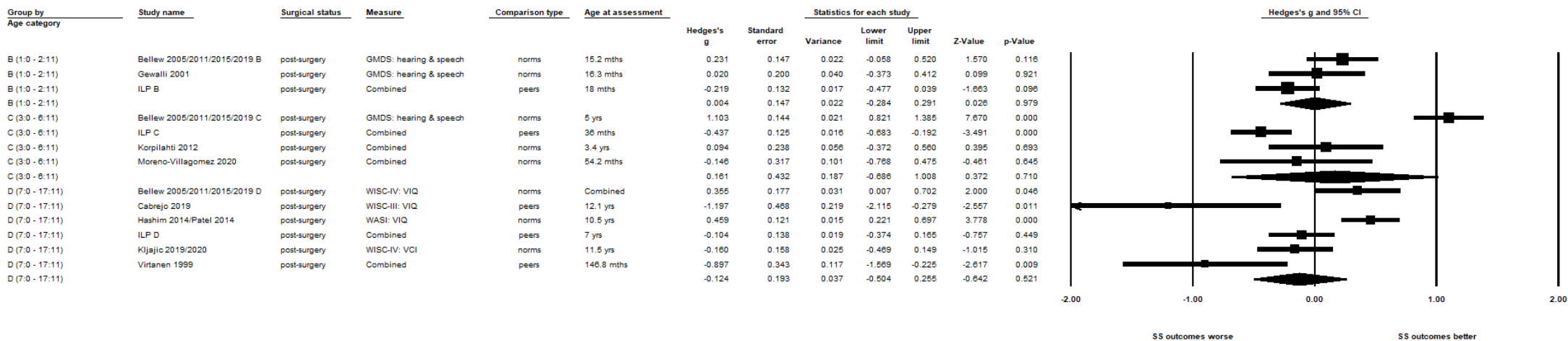
### 3g. Verbal ability / language: conservatively managed samples



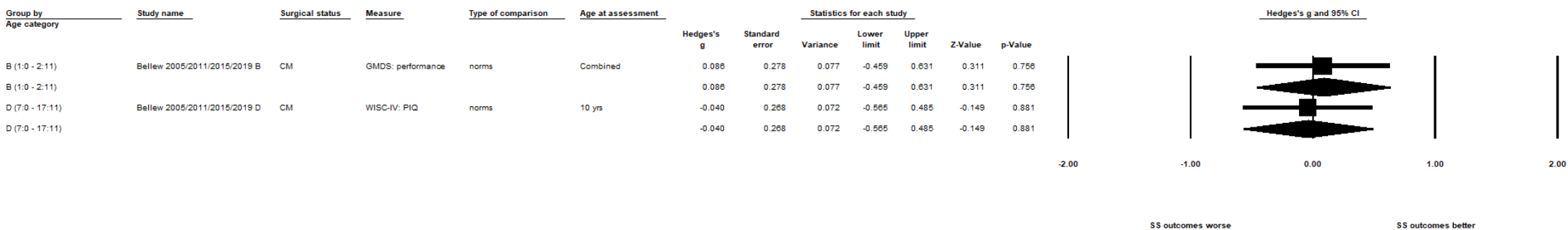
### 3h. Verbal ability / language: pre-surgical samples



### 3i. Verbal ability / language: post-surgical samples



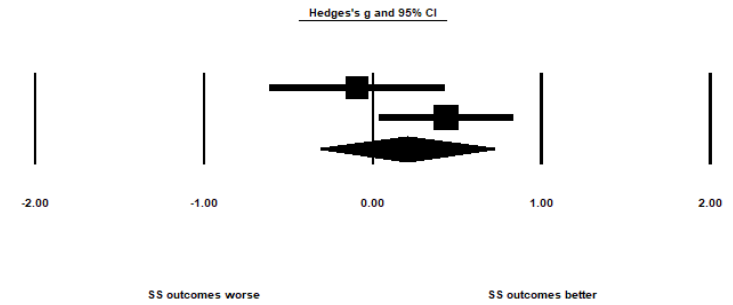
### 3j. Visuospatial ability / language: conservatively managed samples





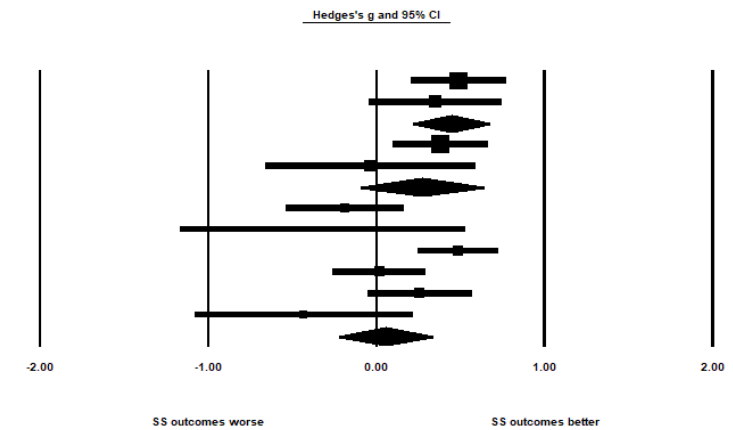
### 3k. Visuospatial ability / language: pre-surgical samples

Group by Age category	Study name	Surgical status	Measure	Type of comparison	Age at assessment	Statistics for each study						
						Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
A (0 - 0:11)	Bellew 2005/2011/2015/2019 A	pre-surgery	GMDS: performance	peers	6.9 mths	-0.090	0.284	0.070	-0.607	0.427	-0.341	0.733
A (0 - 0:11)	Gewalli 2001	pre-surgery	GMDS: performance	norms	6.9 mths	0.438	0.201	0.040	0.044	0.831	2.181	0.029
A (0 - 0:11)						0.202	0.282	0.069	-0.313	0.716	0.788	0.442

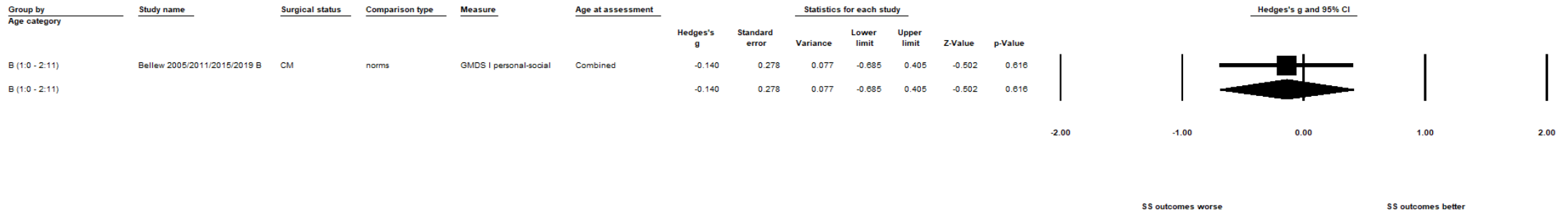


### 3l. Visuospatial ability / language: post-surgical samples

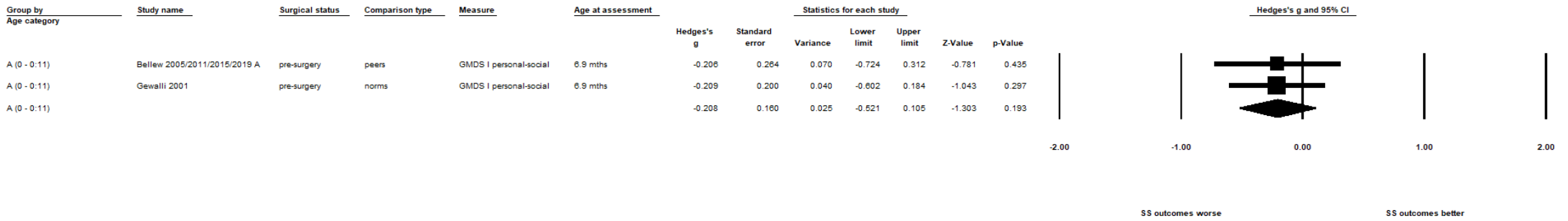
Group by Age category	Study name	Surgical status	Measure	Type of comparison	Age at assessment	Statistics for each study						
						Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
B (1:0 - 2:11)	Bellew 2005/2011/2015/2019 B	post-surgery	WISC-IV: performance	norms	15 mths	0.492	0.143	0.020	0.211	0.772	3.434	0.001
B (1:0 - 2:11)	Gewalli 2001	post-surgery	GMDS: performance	norms	16.3 mths	0.354	0.201	0.040	-0.039	0.747	1.763	0.078
B (1:0 - 2:11)						0.445	0.117	0.014	0.217	0.673	3.819	0.000
C (3:0 - 6:11)	Bellew 2005/2011/2015/2019 C	post-surgery	WISC-IV: performance	norms	60 mths	0.385	0.143	0.020	0.105	0.666	2.692	0.007
C (3:0 - 6:11)	Moreno-Villagomez 2020	post-surgery	WPPSI-III: PIQ	norms	54.2 mths	-0.033	0.317	0.101	-0.655	0.588	-0.105	0.916
C (3:0 - 6:11)						0.271	0.188	0.035	-0.093	0.636	1.458	0.145
D (7:0 - 17:11)	Bellew 2005/2011/2015/2019 D	post-surgery	WISC-IV: PIQ	norms	Combined	-0.186	0.177	0.031	-0.533	0.162	-1.047	0.295
D (7:0 - 17:11)	Cabrejo 2019	post-surgery	WISC-III: PIQ	peers	12.1 yrs	-0.319	0.431	0.186	-1.165	0.526	-0.740	0.459
D (7:0 - 17:11)	Hashim 2014/Patel 2014	post-surgery	WASI: PIQ	norms	10.04 yrs	0.486	0.121	0.015	0.248	0.724	3.999	0.000
D (7:0 - 17:11)	ILP D	post-surgery	Combined	peers	7 yrs	0.018	0.140	0.020	-0.256	0.293	0.131	0.896
D (7:0 - 17:11)	Kijajic 2019/2020	post-surgery	WISC-IV: PRI	norms	11.5 yrs	0.261	0.158	0.025	-0.048	0.570	1.656	0.098
D (7:0 - 17:11)	Virtanen 1999	post-surgery	WISC-R: block design	peers	146.8 mths	-0.430	0.330	0.109	-1.077	0.216	-1.304	0.192
D (7:0 - 17:11)						0.058	0.141	0.020	-0.219	0.334	0.407	0.684



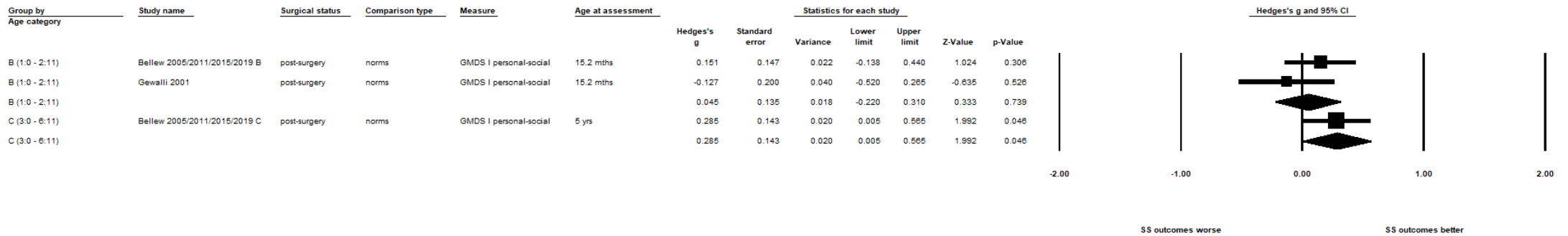
### 3m. Adaptive & social skills: conservatively managed samples



### 3n. Adaptive & social skills: pre-surgical samples

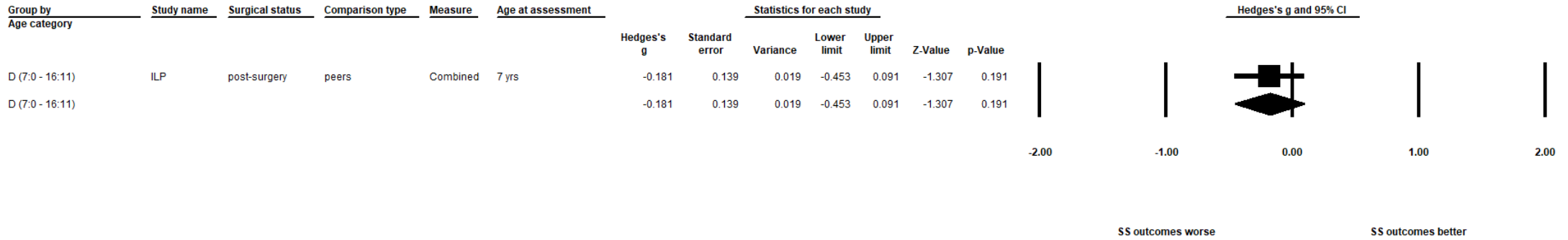


### 3o. Adaptive & social skills: post-surgical samples

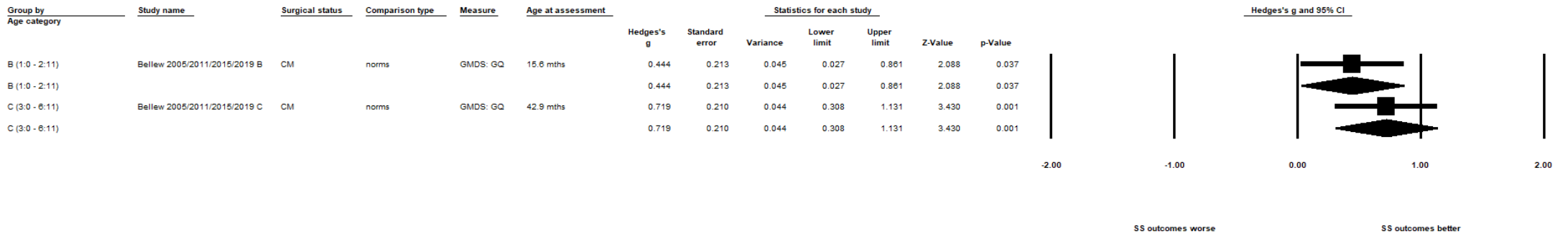




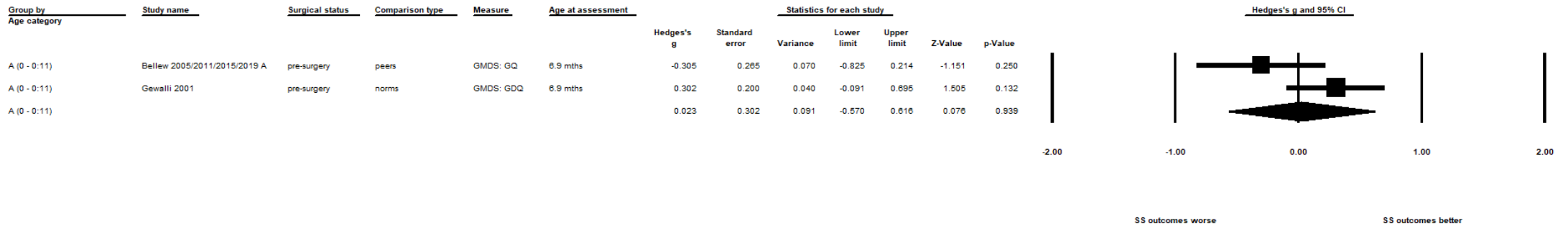
### 3r. Executive Function: post-surgical samples



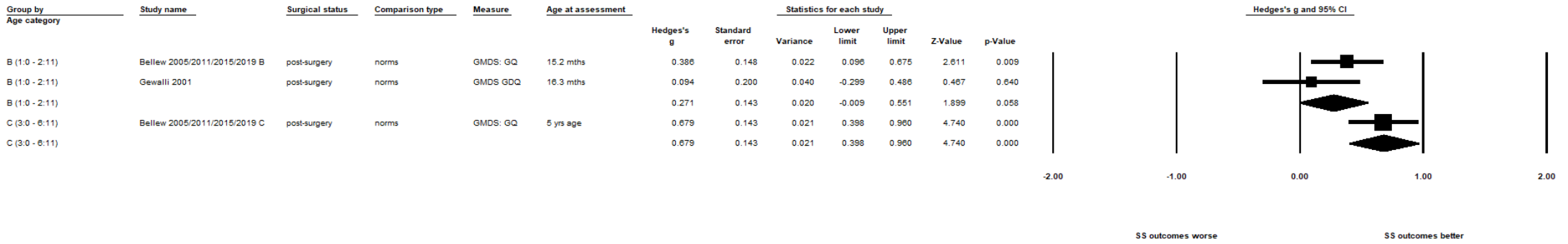
### 3s. Global development: conservatively managed samples



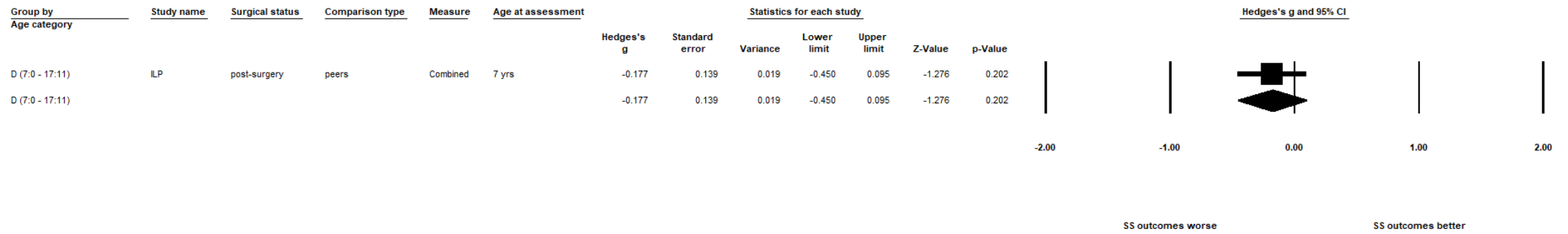
### 3t. Global development: pre-surgical samples



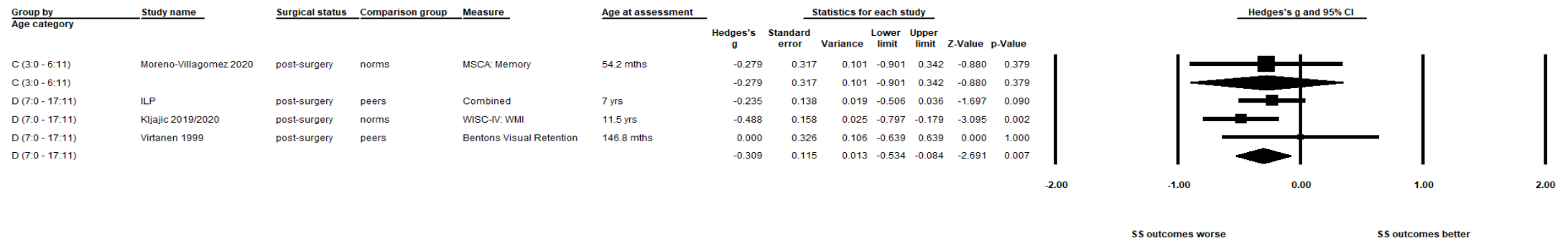
### 3u. Global development: post-surgical samples



### 3v. Memory – longer-term: post-surgical samples



### 3w. Memory – shorter-term: post-surgical samples



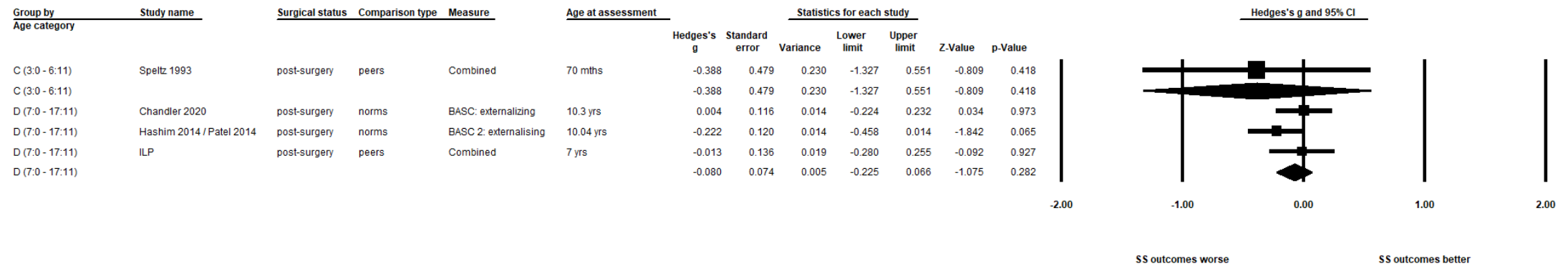


SUBJECTIVE MEASURES

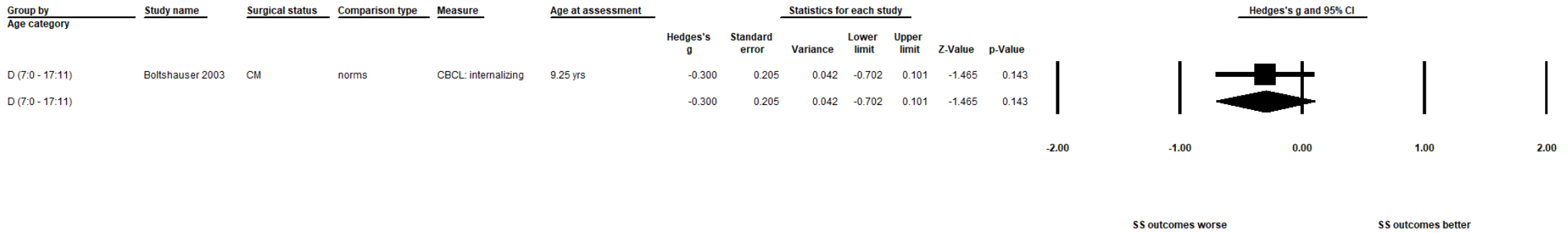
3y. Behavior - externalizing: conservatively managed samples



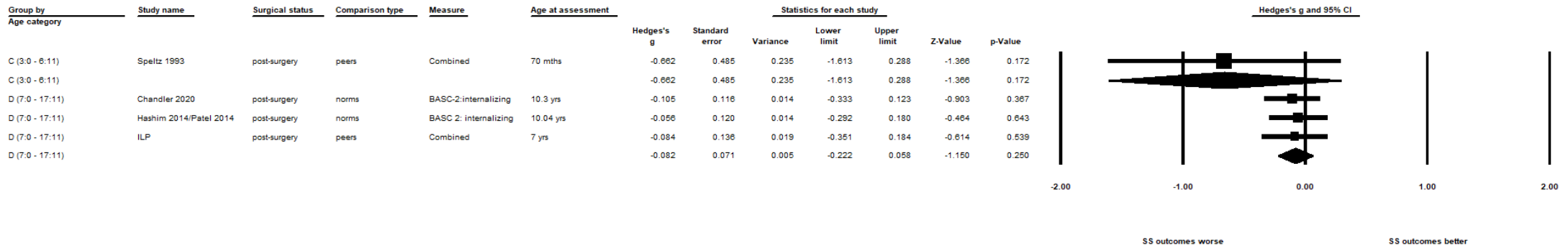
3z. Behavior - externalizing: post-surgical samples



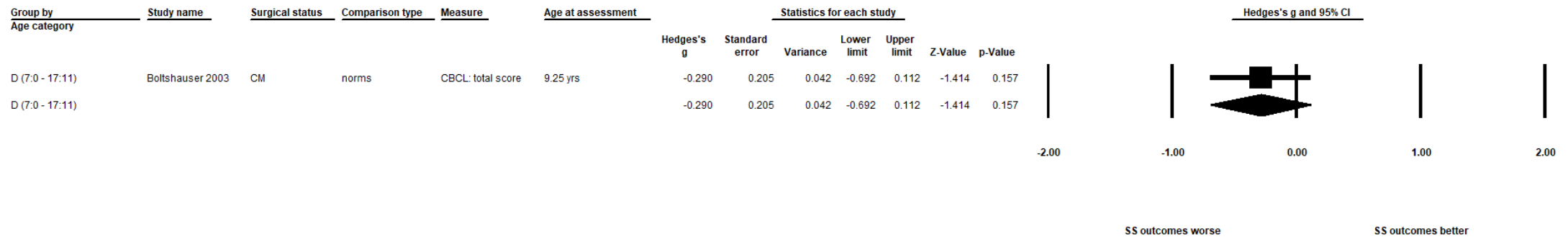
### 3aa. Behavior - internalizing: conservatively managed samples



### 3ab. Behavior - internalizing: post-surgical samples



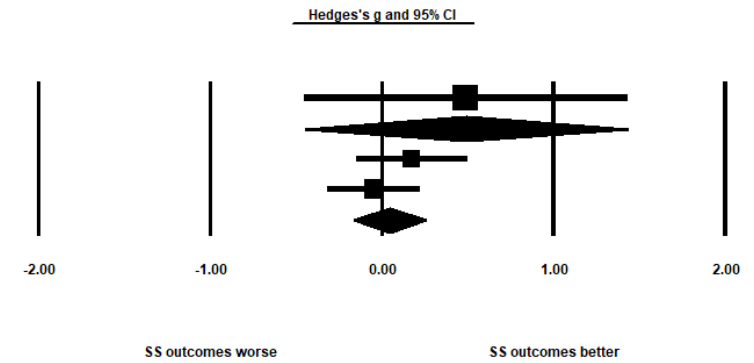
### 3ac. Behavior - total: conservatively managed samples





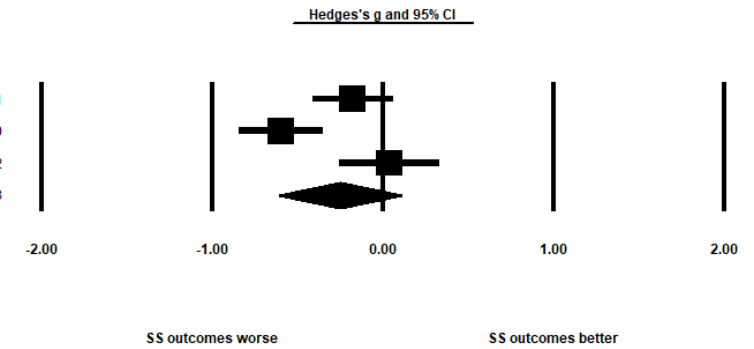
### 3ad. Behavior - total: post-surgical samples

Group by Age category	Study name	Surgical status	Comparison type	Measure	Age at assessment	Statistics for each study						
						Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
C (3:0 - 6:11)	Speltz 1993	post-surgery	peers	Combined	70 mths	0.488	0.481	0.231	-0.455	1.431	1.015	0.310
C (3:0 - 6:11)						0.488	0.481	0.231	-0.455	1.431	1.015	0.310
D (7:0 - 17:11)	Chandler 2020	post-surgery	norms	Combined	10.3 yrs	0.171	0.164	0.027	-0.150	0.493	1.043	0.297
D (7:0 - 17:11)	ILP	post-surgery	peers	Combined	7 yrs	-0.048	0.136	0.019	-0.316	0.219	-0.354	0.723
D (7:0 - 17:11)						0.043	0.108	0.012	-0.169	0.254	0.393	0.694

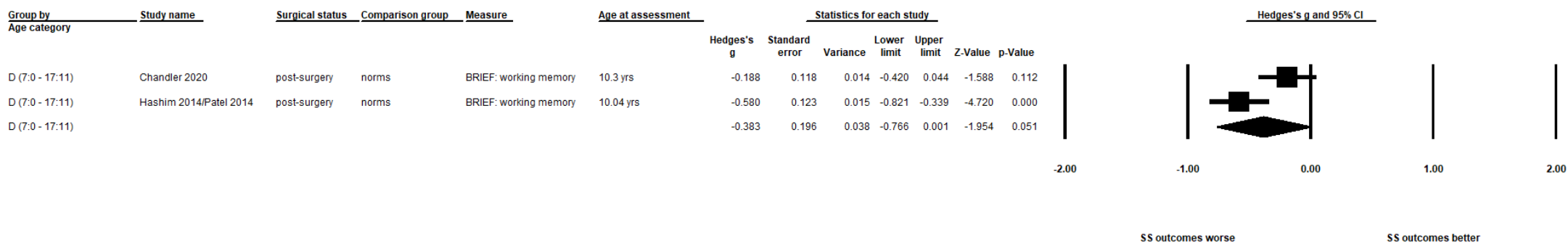


### 3ae. Executive function: post-surgical samples

Group by Age category	Study name	Surgical status	Comparison type	Measure	Age at assessment	Statistics for each study						
						Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
D (7:0 - 16:11)	Chandler 2020	post-surgery	norms	BRIEF- parent GEC	10.3 yrs	-0.175	0.118	0.014	-0.407	0.058	-1.474	0.141
D (7:0 - 16:11)	Hashim 2014/Patel 2014	post-surgery	norms	BRIEF: GEC	10.04 yrs	-0.598	0.123	0.015	-0.839	-0.357	-4.869	0.000
D (7:0 - 16:11)	ILP	post-surgery	peers	Combined	7 yrs	0.039	0.149	0.022	-0.253	0.331	0.264	0.792
D (7:0 - 16:11)						-0.251	0.184	0.034	-0.611	0.110	-1.364	0.173



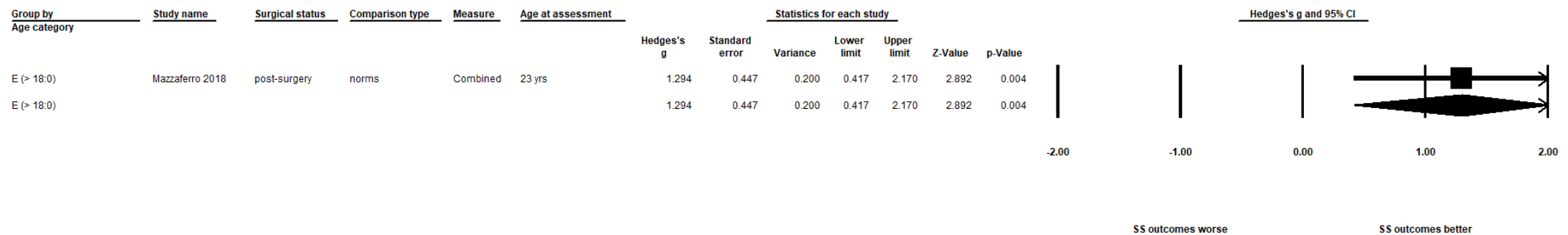
### 3af. Memory – shorter-term: post-surgical samples



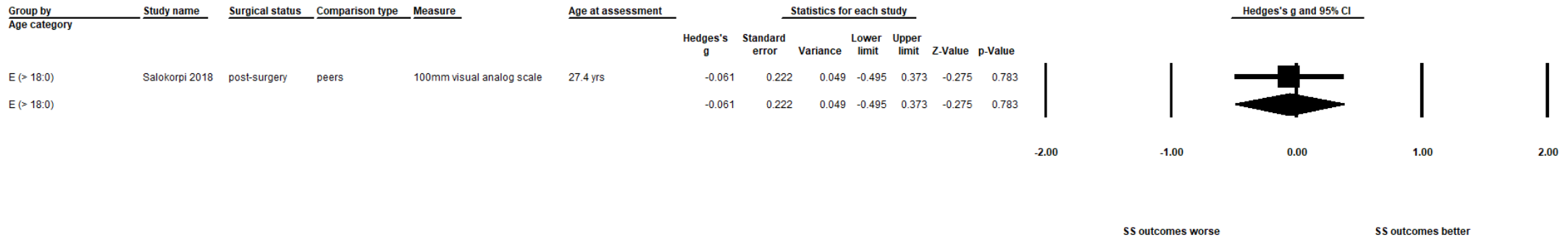
### 3ag. Quality of life: conservatively managed samples



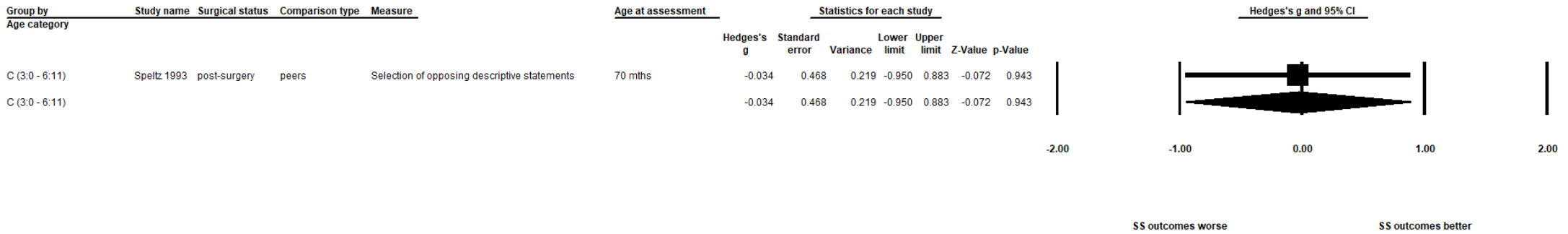
### 3ah. Quality of life: post-surgical samples



### 3ai. Satisfaction with appearance: post-surgical samples



### 3aj. Self-concept: post-surgical samples



### eFigure 3

Pooled analyses for each cognitive, behavioral and psychological domain, partitioned according to surgical status (conservatively managed, presurgical, postsurgical) and age at assessment: A (0 – 0:11); B (1:0 – 2:11); C (3:0 – 6:11); D (7:0 – 17:11); E (>18:0)

Note: ILP = Infant Learning Project

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