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Language abilities in preschool children with critical CHD: a systematic review

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Review

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Abstract

Context: Children with critical CHD are at risk for neurodevelopmental impairments, including delays in expressive and receptive language development. However, no study has synthesised the literature regarding language abilities in children with this condition. *Objective:* We summarised the literature regarding expressive and receptive language in preschool children with critical CHD. *Data sources:* MEDLINE, Embase, Scopus, Child Development and Adolescent Studies, ERIC, PsycINFO, and CINAHL. *Study selection:* We included studies published between January, 1990 and 1 July, 2021, focused on children aged ≤5 years with critical CHD requiring a complex cardiac procedure at age <1 year. Language ability was documented using standardised, validated tools assessing both expressive and receptive language outcomes. *Data extraction:* Data (study, patient and language characteristics, and results) were extracted by two reviewers. *Results:* Seventeen studies were included. Among children 2–5 years old with critical CHD, there were statistically significant deficits in overall (standardised mean difference: −0.46; 95 % confidence interval: −0.56, −0.35), expressive (standardised mean difference: −0.45;95 % confidence interval: −0.54, −0.37), and receptive (standardised mean difference: −0.32; 95 % confidence interval: −0.40, −0.23) language compared to normative data. Results reported as medians were similar to meta-analysis findings. Subgroup analysis showed that children with univentricular physiology had lower language scores than children with biventricular physiology. *Conclusions:* Preschool children with critical CHD had statistically significantly lower language outcomes compared to expected population norms. Healthcare professionals should test early and often for language deficits, referring to individually tailored supports.

CHD is the most common congenital defect, presenting in approximately 8 per 1000 live births.[1] Of all children with this condition, approximately 25% have a critical form (i.e., critical CHD); for these children, survival is dependent on early complex surgical interventions.[2] While advances in the surgical and medical care of children with critical CHD have led to increased survival rates, children with critical CHD, and particularly those with univentricular CHD, are at high risk for neurodevelopmental impairments. The common developmental profile of children with critical CHD includes mild to moderate difficulties in motor, cognitive, attention, and language skills, which have all been linked to different prenatal, perioperative, and post-surgical factors.[3–6]

Until now, most studies examining the neurodevelopmental outcomes of children with critical CHD have concentrated on the motor and/or cognitive development, resulting in the synthesis of the literature on cognition and motor domains.[7–10] Despite the critical role language skills play in social connection and academic performance[11], there has been notably less attention on the receptive (comprehension of language)[12] and expressive (communication of language)[12] language outcomes of children with critical CHD; to date, no study has synthesised the literature regarding language abilities in children with this condition.

As a result, this systematic review and meta-analysis aimed to determine the language abilities of preschool children with critical CHD, including a comparison of language outcomes between those with univentricular versus biventricular CHD.

Materials and methods

Search strategy

An initial search (11 January, 1990-1 July, 2020) was completed on 1 July, 2020 to identify relevant literature on expressive and receptive language outcomes in MEDLINE, Embase, Scopus, Child Development and Adolescent Studies, ERIC, PsycINFO, and CINAHL databases. In July

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of 2021, the same search strategy was repeated to identify any subsequently published studies. The search strategies were performed using the constructs of preschool children, critical CHD, and language outcomes to formulate the search, with adaptations to the search strategy according to each database. The search strategy is available from the authors upon request.

Inclusion criteria

This review included studies published in English from 1990–2021 that examined the receptive and expressive language outcomes of children aged 5 years or younger with critical CHD who required a complex cardiac procedure within the first year of life. Complex cardiac procedure was defined as having undergone surgery with cardiopulmonary bypass or catheter-based intervention. Studies had to involve direct assessment of a child's expressive and receptive language ability through standardised testing using a validated tool to be included in the review. Study designs included in the review were cross-sectional, case–control, cohort, as well as randomised controlled trial.

We excluded studies of children: (1) who did not require surgery or (2) who had their initial heart surgery after one year of age or (3) non-bypass surgeries. Studies that assessed language abilities using screening tools or parent-completed questionnaires were also excluded.

The protocol was registered and submitted to Prospero,[13] an international prospective register for systematic reviews (CRD42020192505).

Study selection

The study selection was completed through a two-step process. Two reviewers (Reviewer 1, Reviewer 2) independently screened titles and, where available, abstracts. The reviewers categorised each study as "include," "unsure," or "exclude." The full text of potentially relevant studies, the "include" or "unsure" categories, was obtained. The formal a priori inclusion criteria were independently applied to each potentially relevant study by Reviewer 1 and Reviewer 2 Discrepancies were resolved by a third reviewer (Reviewer 3).

The authors of articles were contacted if the expressive and receptive outcomes were assessed but the results were not reported. If the author was able to provide the required data, the study was included.

Data extraction

A standardised form to facilitate data extraction was developed based on the Cochrane Handbook for Systematic Reviews of Interventions, Systematic Reviews: CRD's guidance for undertaking reviews in health care, and clinical acumen by healthcare professionals and researchers.[14,15] General and demographic information extracted included article title, author names, date of publication, country of study, study design, single or multicentre study, sample size, population age, population sex, and cardiac diagnoses. Extraction of perioperative variables included procedures performed, number of cardiac surgeries under cardiopulmonary bypass, length of hospital stay, and comorbidities. Language data included age at language assessment, language tool used, and language outcome results for children with critical CHD and control data, if available. Data extraction was first performed independently by two reviewers (Reviewer 1, Reviewer 4) and then reviewed together to resolve any discrepancies.

Quality assessment

Quality assessment was completed using the Revised Cochrane Risk-of-Bias tool for randomised trials[16] and Risk Of Bias In Non-randomised Studies of Interventions[17] assessment tool and template, as per the study design. The Revised Cochrane Risk-of-Bias tool for randomised trials tool assesses randomised studies through 5 domains for potential bias: randomisation process, deviations from intended interventions, missing outcome data, measurements of the outcome, and the selection of reported results. The Revised Cochrane Risk-of-Bias tool for randomised trials tool then classifies the randomised studies as low, some concerns, or high risk of bias.[16] The Risk Of Bias In Non-randomised Studies of Interventions tool assesses non-randomised studies through 7 different domains of potential bias: confounding, selection of study participants, classification of interventions, deviations from intended interventions, missing data, measurement of outcome, and the selection of reported results. The Risk Of Bias In Non-randomised Studies of Interventions tool then classifies each non-randomised study as low, moderate, serious, or critical risk of bias.[18]

Two reviewers (Reviewer 1 and Reviewer 2) independently assessed each article. The reviewers first pilot-tested 3 articles to ensure they operationalised each domain similarly based on the detailed guide and tool provided. Any disagreements were resolved by discussion or a third reviewer (Reviewer 3).

Statistical analyses

Review Manager[19] software (version 5.4) was used to pool the study results into a standardised mean difference for overall, expressive, and receptive language outcomes when individual study results provided the mean and standard deviation, and it was statistically and clinically appropriate. Both fixed and random effects meta-analyses were performed. A standardised mean difference pooled result was calculated and displayed as a random effects model with a 95% confidence interval since different language outcome tools were used by different studies. Four studies[24,31,35,37] reported results using the median, interquartile range, or range as described in Table 1. If studies reported critical CHD subgroups without a score for the entire critical CHD cohort, such as children with normal hearing as compared to those with hearing loss,[20] a combined summary statistic was calculated through the formulae provided by the Cochrane Handbook for Systematic Reviews of Interventions.[14,21] For studies that compared univentricular to biventricular critical CHD, a subgroup analysis compared language scores. Statistical heterogeneity between studies was measured using the I2 statistic as suggested by the Cochrane Collaboration, in which values of 0–40% may be considered unimportant, 30–60% as moderate, 50–90% as representing substantial heterogeneity, and 75–100% as considerable heterogeneity (overlapping proportions are intentional).[14,21] If the fixed and random effects results were similar, the random effects models were reported.[14] Publication bias was assessed through visual interpretation of funnel plot symmetry and formally with the Egger test[22] using STATA software[23] where $p < 0.05$ indicated likely publication bias.

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Table 1. Description of included studies and language results summary

First Author, Year	Country, Study design	Population (diagnosis)	Number of Children (N) Mean Age (SD)	Outcome tool	Overall Language Mean (SD)	Expressive Mean (SD)	Receptive Mean (SD)
Age 2–5 years							
Bellinger 1999[38]	United States, Randomized single centre trial	Biventricular	IVS TGA CA: N = 61 IVS TGA LFB: N = 61 VSD TGA CA: N=18 VSD TGA LFB: N = 18 IVS TGA CA: 49.5mo (2.3) LFB: 49.8 (2.5) VSD CA: 49.4mo (3.4) LFB: 49.2 (1.1)	ROWPVT EOWPVT	Not reported	IVS: CA: 94.1 (16.1) LFB: 90.8 (14.4) VSD: CA: 91.4 (18.2) LFB: 93.8 (16.3)	IVS: CA: 99.2 (15.1) LFB: 97.2 (14.8) VSD: CA: 91.3 (19.0) LFB: 95.4 (16.1)
Brosig 2007[24]	United States, Cross-sectional	Univentricular and biventricular	N = 26 4.7y (10mo)	ROWPVT (2nd edition) EOWPVT (3rd edition)	Not reported	97.5 (65-122) (median, range)	106 (81-140) (median, range)
Acton 2011[27]	Canada, Prospective longitudinal study	Univentricular and biventricular	N = 110 21.3mo (3.9)	Bayley-III	90.8 (18.1)	8.0 (3.2)	8.9 (3.2)
Brosig 2013[32]	United States, Prospective longitudinal study	Univentricular	N = 34 5.0y (0.6)	CELF-P2 Word Structure and sentence structure subtests	Not reported	8.7 (2.2)	9.3 (2.8)
Sood 2013[30]	United States, Cross-sectional	Univentricular and biventricular	N = 31 24mo (3)	Bayley-III	Not reported	9.8 (4.0)	9.3 (3.8)
Pizarro 2014[31]	United States, Cross-sectional	Univentricular and biventricular	N = 40 24mo (3)	Bayley-III	IP-DHCA: 103 (81-109) U-DHCA: 94 (79-106) median (IQR)	IP- DHCA: 10 (7-12) U-DHCA: 9 (7-10) median (IQR)	IP - DHCA: 10 (7-11.75) U-DHCA: 9 (6-13) median (IQR)
Gunn 2016[29]	Australia, Cohort	Univentricular and biventricular	N = 130 24.0mo (1.8)	Bayley-III	93.6 (16.1)	8.86 (3.0)*	8.88 (2.9)*
Hicks 2016[26]	Canada, Cohort	Biventricular	N = 91 2y (18-24mo) (range)	Bayley-III	92.6 (17.0)	8.4 (3.2)	9.1 (3.0)
Noeder 2017[25]	United States, Cohort	Univentricular and biventricular	24.3mo (2.2): N = 69 overall language N = 79 expressive N = 77 receptive 36.5mo (1.5): N = 32 overall language N = 29 expressive N = 26 receptive	Bayley-III	24mo: 89.3 (18.9) 36mo: 94.7 (17.4)	24mo: 8.2 (3.7) 36mo: 9.4 (3.1)	24mo: 8.5 (3.4) 36mo: 9.4 (2.8)
Grasty 2018[20]	United States, Prospective observational study	Univentricular and biventricular	N = 381 4.8y (0.2)	PLS-4	Normal hearing: 100.8 (15.4) Hearing loss: 92.4 (20.4)	Normal hearing: 100.1 (14.0) Hearing loss: 91.9 (19.2)	Normal hearing: 101.2 (15.0) Hearing loss: 93.8 (19.4)
Fourdain 2019[33]	Canada, Longitudinal study	Univentricular and Biventricular	N = 49 24.6 (0.6)	Bayley-III	94.65 (13.60)	8.78 (2.49)	9.35 (2.57)
Yoshida 2020[36]	Japan, Cohort	Univentricular and biventricular	n = 67 congenital heart disease n = 67 VLBW n = 81 control 3y (variance not reported)	Bayley-III	Congenital heart disease: 91.1 (12.2) SV: 86.5 (13.7) 2V: 92.9 (11.1) VLBW: 91.5 (11.2) Control: 99.2 (8.4)	Congenital heart disease: 8.2 (2.0) SV: 7.7 (2.5) 2V: 8.5 (1.6) VLBW: 8.1 (2.0) Control: 9.4 (1.3)	Congenital heart disease: 8.7 (2.3) SV: 7.7 (2.4) 2V: 9.1 (2.1) VLBW: 9.2 (1.9) Control: 10.3 (2.1)

(*Continued*)

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Table 1. (*Continued*)

First Author, Year	Country, Study design	Population (diagnosis)	Number of Children (N) Mean Age (SD)	Outcome tool	Overall Language Mean (SD)	Expressive Mean (SD)	Receptive Mean (SD)
Favilla 2021[37]	United States, Cohort	Biventricular	N = 28 25mo (24, 26) median (IQR)	Bayley-III	89 [75.5-98.5] median (IQR)	Normal development via earlier screener: 100.5 (88.6-108.5) Emerging/at risk development via earlier screener: 90.1 (67.7-102.5) median (IQR)	Normal development via earlier screener: 102.5 (88.6-111.5) Emerging/at risk development via earlier screener: 88.6 (67.7-100.5) median (IQR)
Age 12 months							
Noeder 2017[25]	United States, Cohort	Univentricular and biventricular	N = 90 overall language N = 90 expressive N = 87 receptive 12.9mo (1.5)	Bayley-III	88.9 (17.0)	8.5 (3.3)	7.7 (3.2)
Verrall 2018[35]	Australia, Cohort	Univentricular and biventricular	N = 120 12mo (variance not reported)	Bayley-III	Not reported	Norwood: 7 (4.5-8.5) Non - Norwood: 9 (7-10) median (IQR)	Norwood: 7 (5-10.5) Non-Norwood: 7 (6-9) median (IQR)
Fourdain 2019[33]	Canada, Longitudinal study	Univentricular and biventricular	N = 49 12.27mo (0.42)	Bayley-III	90.36 (15.52)	8.73 (2.43)	8.36 (1.81)
Graham 2019[39]	United States, Randomized control trial	Univentricular and biventricular	N = 97 12.5mo (0.6)	Bayley-III	101 (13)	9.3 (2.5)	11.1 (2.5)*
Meuwly 2019[28]	Switzerland, Cohort	Univentricular and biventricular	N = 77 congenital heart disease N = 44 controls 12.0mo (12.0-3.0) median (IQR)	Bayley-III	93.06 (13.8)* Controls: 97.5+/-9.9	8.73 (2.4)*	8.72 (3.0)*
Favilla 2021[37]	United States, Cohort	Biventricular	N = 29 13 mo (12, 17.5) median (IQR)	Bayley III	97 [79-106] median (IQR)	Normal development via earlier screener: 111.5 (100.5-118.4) Emerging/ at risk development via earlier screener: 88.6 (70.7-114,5) median (IQR)	Normal development via earlier screener: 111.5 (105.5-126.4) Emerging/ at risk development via earlier screener: 88.6 (70.7-111.5) median (IQR)
Age 6 months							
Brosig Soto 2011[34]	United States, Cohort	Univentricular and biventricular	N = 95 7.2mo (1.2)	Bayley-III	96.3 (12.7)	9.7 (2.3)	9.1 (2.3)
Noeder 2017[25]	United States, Cohort	Univentricular and biventricular	N = 59 overall language N = 61 expressive N = 63 receptive 6.4mo (1.0)	Bayley-III	84.1 (15.0)	6.9 (2.9)	7.9 (3.1)

Bayley-III = Bayley Scales of Infant and Toddler Development, Third Edition; CA = cardiac arrest; CELF-P2 = Clinical Evaluation of Language Fundamentals Preschool-2; CHD = congenital heart disease; EOWPVT = Expressive One-Word Picture Vocabulary Test; EOWPVT (3rd ed.) = Expressive One-Word Picture Vocabulary Test, Third Edition; IP-DHCA = Total body intermittent perfusion-Deep hypothermic circulatory arrest group; IQR = interquartile range; IVS = interventricular septum; LFB = low flow bypass; Mo = months; ROWPVT = Receptive One-Word Picture Vocabulary Test; ROWPVT (2nd ed.) = Receptive One-Word Picture Vocabulary Test, Second Edition; SV = single ventricle; TGA = transposition of the great arteries; U-DHCA = uninterrupted-deep hypothermic circulatory arrest group; VLBW = very low birth weight; VSD = ventricular septal defect; 2V = two ventricle.
*Unpublished data provided by author.

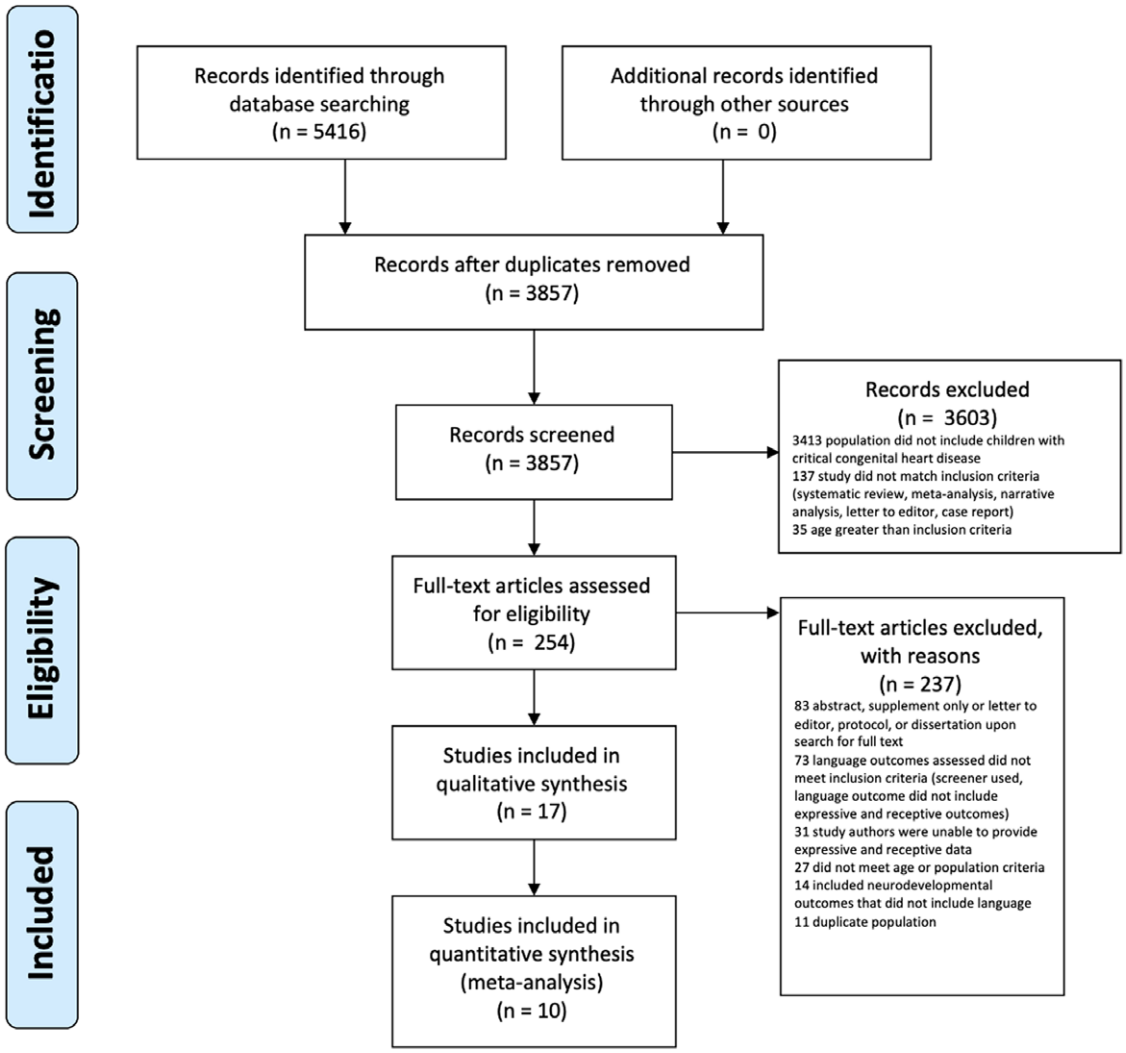


Figure 1. PRISMA flow diagram.

Results

Literature search results

A total of 5001 articles were identified through the initial database literature search, and an additional 268 articles were identified in the follow-up year of 2021. Ultimately, 17 articles (15 observational, 2 randomised) met the inclusion criteria (Fig 1), with thirteen articles published in the last ten years.[20,25,26,28,35–37,39]

Characteristics of the seventeen included studies are provided in Table 1. To summarise, 13 (77%)[20,24–27,29–33,36–38] included language outcomes for preschool children aged 2 to 5 years; six[25,28,33,35,37,39] assessed language outcomes at approximately 12 months of age, and two[25,34] reported language outcomes at approximately 6 months of age. Thirteen studies (76%)[20,24–27,30–34,37–39] were conducted in North America, two (12%)[29,35] in Australia, one (6%)[28] was in Switzerland, and one (8%)[36] in Japan. Study designs included cohort (8; 47%),[25,26,28,29,34–37] prospective case series (4; 24%),[20,27,32,33] cross-sectional (3; 18%),[24,30,31] and randomised controlled trial (2; 12%)[38,39]. Most studies included both cardiac pathologies (13; 76%),[20,24,25,27–31,33–36,39], one study examined only univentricular cardiac physiology (6%),[32] and three examined only biventricular physiology (18%).[26,37,38]

Of the 13 studies focused on preschool children, 13 (76%)[25–31,33–37,39] used the Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III), a standardised assessment tool that measures cognitive, motor, and language (expressive and receptive) development of children up to the age of 42 months (general population mean of 100 and a standard deviation of 15; expressive and receptive subscales: mean of 10 and a standard deviation of 3).[40,41] The other 4 studies completed language assessment using either the Receptive and Expressive One-Word Picture Vocabulary tests (mean of 100, standard deviation of 15),[42–45] the Preschool Language Scale, Fourth Edition (mean of 100, standard deviation of 15),[46] or the Clinical Evaluation of Language Fundamentals Preschool-2 Word Sentence and Sentence Structure Subtests (mean of 10, standard deviation of 3).[47]

Methodological quality of included studies

Of the 15 observational studies using the Risk Of Bias In Non-randomised Studies of Interventions tool, 7 (47%)[20,24–29] studies were at serious risk of bias, and eight (53%)[30–37] had a critical risk of bias. Sources of bias included confounding, the selection of study participants, and the measurement of outcome due to lack

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Table 2. Methodological quality of included studies

Quality Assessment Using ROBINS-I (Observational Studies)								
Article	Bias due to confounding	Bias of selection of participants into study	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcome	Bias in selection of reported results	Overall
Brosig 2007	Serious	Serious	Low	Low	Moderate	Moderate	Moderate	Serious
Acton 2011	Moderate	Serious	Moderate	Low	Moderate	Moderate	Moderate	Serious
Brosig Soto 2011	Serious	Critical	Serious	Moderate	Serious	Serious	Serious	Critical
Brosig 2013	Critical	Critical	Low	Low	Serious	Serious	Moderate	Critical
Sood 2013	Serious	Critical	Low	Moderate	Moderate	Serious	Serious	Critical
Pizarro 2014	Serious	Critical	Low	Serious	Moderate	Serious	Serious	Critical
Gunn 2016	Serious	Moderate	Moderate	Low	Moderate	Serious	Serious	Serious
Hicks 2016	Serious	Moderate	Low	Low	Moderate	Serious	Moderate	Serious
Noeder 2017	Serious	Serious	Moderate	Moderate	Serious	Serious	Serious	Serious
Grasty 2018	Moderate	Serious	Moderate	Low	Moderate	Serious	Moderate	Serious
Verrall 2018	Serious	Moderate	Low	Low	Critical	Serious	Serious	Critical
Fourdain 2019	Serious	Critical	Moderate	Moderate	Moderate	Serious	Moderate	Critical
Meuwly 2019	Serious	Serious	Low	Low	Moderate	Serious	Moderate	Serious
Yoshida 2020	Serious	Critical	Moderate	Serious	Serious	Serious	Serious	Critical
Favilla 2021	Critical	Serious	Moderate	Serious	Serious	Serious	Serious	Critical

Quality Assessment RoB2 (Randomized Studies)						
Article	Bias arising from the randomization process	Bias due to deviations from intended interventions	Bias due to missing outcome data	Bias in measurement of the outcome	Bias in selection of the reported result	Overall
Bellinger 1999	Some concerns	Low	Low	Low	Some concerns	Some concerns
Graham 2019	High	Some concerns	High	Low	Low	High

of blinding. Of the 2 randomised studies that were assessed using the Revised Cochrane Risk-of-Bias tool for randomised trials tool, one study[38] had some concerns and the other[39] was rated as high risk of bias. Sources of bias included the randomisation process and the selection of the reported results. Specific details are provided in Table 2.

Language outcomes at 2–5 year of age

Thirteen studies examined language outcomes for children aged 2–5 years of age.[20,24–27,29–33,36–38]

Expressive language outcomes

Ten studies (77%)[20,25–27,29,30,32,33,36,38] reported data on expressive language outcomes that could be used for the meta-analysis. The standardised mean difference for expressive language score was statistically significantly lower for children with critical CHD compared to those without this condition (standardised mean difference: –0.45; 95 % confidence interval: –0.54, –0.37; Fig 2a).

Four studies (31%)[32,33,36,38] reported an expressive language score statistically significantly lower than the normative population data (but still within one standard deviation of the population mean).

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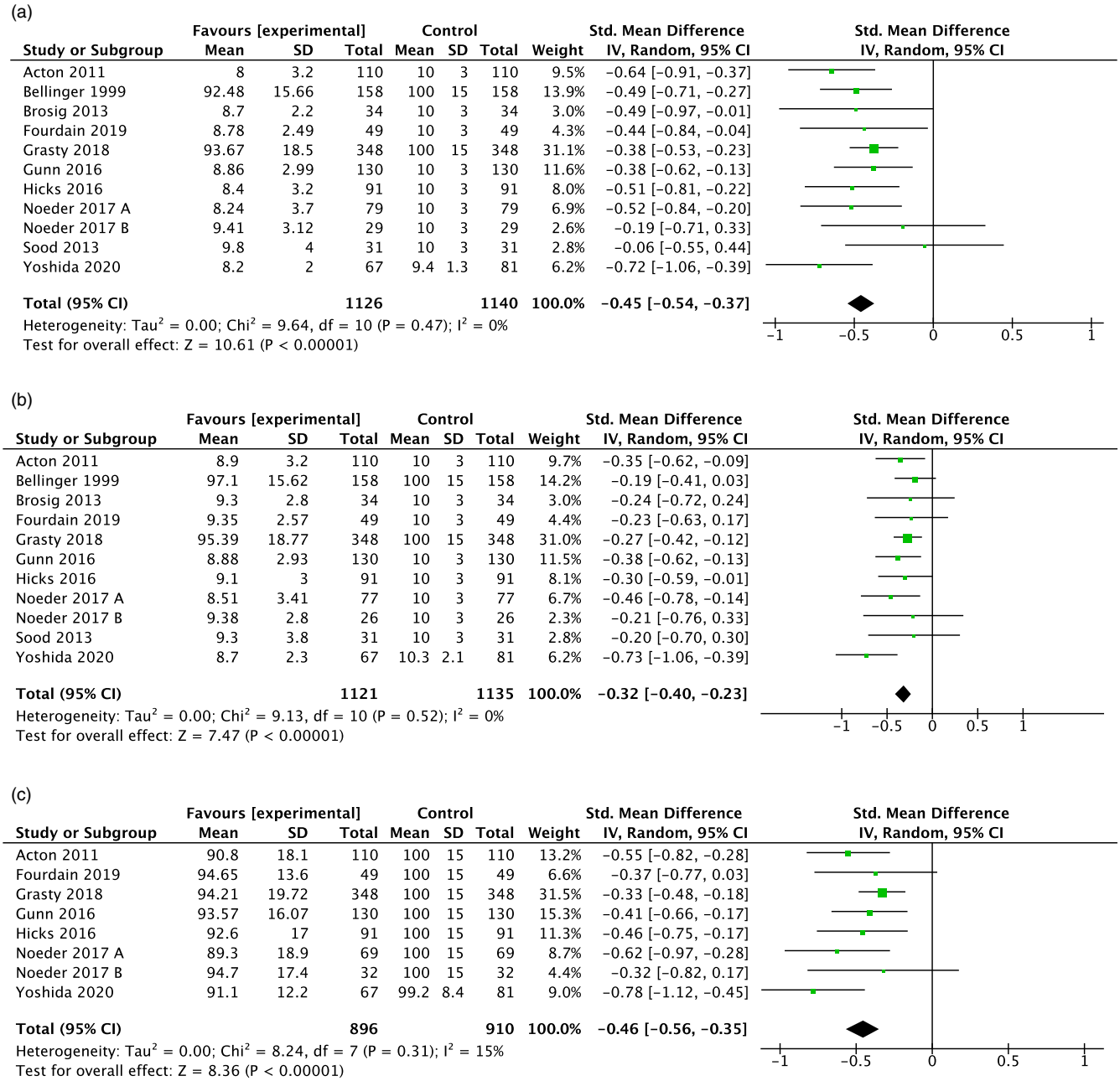


Figure 2. Forest plot and standard mean difference for expressive (2a), receptive (2b) and overall (2c) language scores of children 2–5y with critical congenital heart disease The standard mean difference for each study is represented by a square with confidence interval bars. The size of the box indicates the relative weight of the study, The total meta-analysis result is represented by the diamond. Negative values indicate lower scores for the critical congenital heart disease.

Receptive language outcomes

In the meta-analysis, 10 studies (77%)[20,25–27,29,30,32,33,36,38] reported receptive language outcomes that could be pooled. The standardised mean difference for receptive language was statistically significantly lower for children with critical CHD compared to those without this condition (standardised mean difference: −0.32; 95 % confidence interval: −0.40, −0.23; Fig 2b).

Three studies (23%)[33,36,38] provided a receptive language outcome score statistically significantly lower than the normative population data and within one standard deviation of the population mean.

Overall language outcomes

The 7 studies (78%)[20,25–27,29,33,36] with data available for overall language resulted in a pooled estimate that showed that the overall language standardised mean difference was statistically significantly lower for children with than without critical CHD (standardised mean difference: −0.46; 95 % confidence interval: −0.56, −0.35; Fig 2c).

Nine studies[20,25–27,29,31,33,36,37] reported an overall language score: 2 (22%)[29,36] were statistically significantly lower than the normative mean (but still within one standard deviation of the general population mean).

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Subgroup analysis based on cardiac physiology

Only 4 studies (24%)[24,27,29,36] described language outcomes for children with univentricular as compared to biventricular cardiac physiologies. The I^2 statistic assessing statistical heterogeneity within the 2 studies was substantial ($I^2 = 64\%$) for expressive language scores, precluding a formal meta-analysis.[14] Two studies reported significantly lower overall language scores for children with univentricular critical CHD as compared to biventricular physiology.[29,30,36] One study[24] found expressive language values to be significantly lower for children with univentricular versus biventricular physiology. Two studies[24,36] reported significantly lower receptive language values for univentricular physiology as compared to biventricular physiology.

Language outcomes at 12 months

The I^2 statistic assessing statistical heterogeneity for all language outcomes was significant, therefore, precluding a meta-analysis. However, all 6 studies[25,28,33,35,37,39] reported overall, expressive, and receptive language scores on the Bayley-III language tool within one standard deviation of the normative mean. One study[33] reported statistically significantly lower expressive and receptive language scores for children with critical CHD when compared to the general population mean. Overall language was not determined to be statistically significantly different in any study.[25,28,33,37,39]

Language outcomes at 6 months

The I^2 statistic assessing statistical heterogeneity for all language outcomes was significant; therefore, a meta-analysis was not performed. Both studies[25,34] reported expressive and receptive language scores below the mean. Brosig Soto et al (2011)[34] reported a language outcome significantly lower than the normative population mean at 96.8 (SD: 12.7, $p = .005$), while Noeder et al (2017)[25] reported a language score greater than one standard deviation below the population mean at 84.1 (SD: 15.0).

Publication bias

Publication bias could only be assessed for language outcomes for children 2 to 5 years of age. Funnel plots showed little evidence of publication bias for overall ($p = 0.14$), expressive ($p = 0.89$), and receptive ($p = 0.62$) language outcomes.

Discussion

Findings of this systematic review and meta-analysis indicate that preschool children with critical CHD have statistically significantly lower expressive, receptive, and overall language abilities when compared to their peers and that they struggle more with expressive than with receptive language skills. Additionally, although statistical heterogeneity precluded determining a pooled overall effect to quantify the difference, children with univentricular physiology appear to have higher rates of language delay than children with biventricular physiology. The importance of studying language outcomes relies on the significant role language plays in a child's development; language is essential for communication and is a key component of academic functioning. Even modest deficits in language abilities are known to significantly impact a child's day-to-day function, communication, and to negatively influence social interaction.[48]

The results of this study are consistent with previous reports and recommendations. The Cardiac Neurodevelopmental Outcome Collaborative indicates expressive language delays are a common concern for children with critical CHD and should be monitored.[49] The guidelines developed by American Heart Association also highlight the need to assess language development and to refer to speech-language pathology when language deficits are identified.[49,50] Findings that children with univentricular critical CHD struggle more in certain areas of neurodevelopment than children with biventricular critical CHD have been previously reported and determined to be statistically significant .[51–54]

This review found similar findings to those of studies looking at the longer-term language outcomes of school-aged children with critical CHD. In an article by Bellinger et al (2003),[55] school-aged children within the critical CHD cohort were found to have significantly lower scores than the expected mean. Similarly, in an article by Mahle et al (2000),[56] children with hypoplastic left heart syndrome at school age had expressive and receptive skills that were statistically significant and below the norm. In a study by Hövels-Gürich (2006),[57] expressive and receptive language values in children at school age were found to be within one standard deviation of the normative mean within the cohort studied and were statistically significant findings as compared to the normative population mean. In a second study by Hövels-Gürich (2008),[58] school-aged children were more impaired in expressive language testing than overall or receptive language testing. Such studies then highlight the importance of long-term follow-up as children with critical CHD appear to continue to be at high risk for language delays (and particularly expressive language delays). A lack of significant language difference found at 12 months compared to those differences found at 2–5 years suggests a need for continuous follow-up that is supported by the literature.[50]

The results of this language-focused systematic review are also consistent with reviews of studies in motor and cognitive neurodevelopmental delay in children with critical CHD.[7–9] Reviews of both motor and cognitive abilities of preschool children with critical CHD have shown that children with this condition score significantly lower than their non-critical CHD peers.[7–9] Proposed explanations of such delays in multiple developmental domains include chronic brain hypoxia, increased incidences of pre- and post-natal brain injury, brain immaturity, and other clinical and environmental factors.[59–63]

Importantly, some of the literature suggests the Bayley-III overestimates language ability for both healthy developing and children with critical CHD;[27,64–66] which could mean that children with critical CHD have even worse language skills than this systematic review and meta-analysis reports. Anderson et al (2017)[65] found an increase in language scores on the most recent edition of the Bayley-III compared to the Bayley-II. Moreover, Goldstone et al (2020)[66] found this increase to be significant in children with critical CHD. Notably, our review included publications that used other language assessment tools and determined that those findings were consistent with the results of studies that utilised the Bayley-III. This consistency suggests that the language abilities of preschool children with critical CHD are typically below average.

Limitations

There are several limitations to our systematic review and meta-analysis. First, the methodological quality of the included studies was rated quite poorly. This rating is unsurprising given that the

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detailed guide of the Risk Of Bias In Non-randomised Studies of Interventions tool indicates that "... it will be rare that an NRSI [non-randomised studies of the effects of interventions] is judged as at low risk of bias due to confounding, we anticipate that most NRSI will be judged as at least at moderate overall risk of bias."[18] Often, the overall risk of bias was rated as serious or critical and was typically due to the first domain regarding confounders, missing statements of possible confounders, selection of participants, and lack of blinding. However, the results of the two randomised controlled trials that focused on 2 to 5 year-old-children, which should have a balance of known and unknown confounders between the 2 groups, were similar to the non-randomised controlled trial results. The expressive and receptive scores led to the consistent conclusion that children with critical CHD at 2–5 years of age are below the normative means. While many studies were classified at critical risk, basing the use of articles solely on the quality assessment of studies that are not amenable to randomised control trials may prevent the inclusion of critical results in many different areas of research.[67]

Comparing outcomes to normative population data without further adjustments may introduce bias into the results as any difference found between children with critical CHD and the normative population may seem to be causal, when in reality differences such as socioeconomic status, support interventions, or other differences may have large effects in children with critical CHD that may not be accounted for.

Finally, only two studies[27,36] reported language outcome data comparing univentricular and biventricular cardiac physiologies. Although heterogeneity precluded pooling the individual results, reports of lower language scores and other neurodevelopmental domains support the findings of our review.[51,52,54] Likewise, although the presence of a genetic anomaly among children with critical CHD is known to impact developmental outcomes, this review was unable to examine language outcomes based on the presence or absence of genetic anomalies as the included studies did not consistently stratify their results by this variable. Future research to determine the exact clinical and statistical significance of differences in language outcomes between these two cardiac physiologies and the stratification of language abilities in children with additional genetic anomalies is recommended.

Conclusion

This systematic review and meta-analysis is the first to review and assess the results from the literature on overall, expressive, and receptive language abilities in preschool children with critical CHD. The findings indicate that preschool children with critical CHD have significantly lower language abilities when compared to the general population and may be more affected in the expressive language domain than in their receptive language skills. Future research should focus on determining language outcomes among older children with critical CHD as well as on testing interventions to improve language skills in this population.

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