Supplemental Online Content

Ko MSM, Poh PF, Heng KYC, et al. Assessment of long-term psychological outcomes after pediatric intensive care unit admission: a systematic review and meta-analysis. *JAMA Pediatr*. Published online January 18, 2022. doi:10.1001/jamapediatrics.2021.5767

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

eTable 1. PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page 3 - 4
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 5 - 6
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 6
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 7 - 8
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 7
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	eTable 2
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 7 - 8
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 8
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 8
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	eTable 2
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 8, eTable 3
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Page 8
Synthesis	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention	Page 7 - 8

Section and Topic	Item #	Checklist item	Location where item is reported
methods		characteristics and comparing against the planned groups for each synthesis (item #5)).	
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 8
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page 8
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 8
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Not applicable
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Not applicable
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Not applicable
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Not applicable
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page 9, Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Figure 1
Study characteristics	17	Cite each included study and present its characteristics.	Table 1, eTable 4
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Page 10, eTable 3
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Figure 2 – 3, eFigure 2
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	eTable 4
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Page 10 – 13, Figure 2 – 3, eFigure 2
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Table 1, eTable 4
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Not applicable
Reporting	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Not applicable

Section and Topic	Item #	Checklist item	Location where item is reported
biases			
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Figure 2 – 3, eFigure 2
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 14
	23b	Discuss any limitations of the evidence included in the review.	Page 16
	23c	Discuss any limitations of the review processes used.	Page 16
	23d	Discuss implications of the results for practice, policy, and future research.	Page 16 – 17
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Page 7
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Page 7
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Not applicable
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 18
Competing interests	26	Declare any competing interests of review authors.	Page 18
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Page 7

eTable 2. Detailed Search Strategy

MEDLINE (PubMed)

1	**(("picu" [tw] OR "Intensive care units, pediatric" [Mesh:NoExp]) AND ((((("Emotional Adjustment"[Mesh:NoExp] OR "Posttraumatic Growth, Psychological"[Mesh] OR "Stress Disorders, Post-Traumatic"[Mesh] OR "ptsd" [tw] OR "post traumatic stress disorders" [tw] OR "post-traumatic stress disorders" [tw] OR "Anxiety Disorders"[Mesh] OR "anxiety" [tw] OR "anxieties" [tw] OR "obsessive-compulsive disorder" [tw] OR "obsessive compulsive disorder" [tw] OR "OCD" [tw] OR "panic" [tw]) OR ("Bipolar and Related Disorders"[Mesh] OR "Disruptive, Impulse Control, and Conduct Disorders" [Mesh] OR "conduct disorders" [tw] OR "Dissociative Disorders" [Mesh] OR "Elimination Disorders" [Mesh] OR "encopresis" [tw] OR "enuresis" [tw] OR "Depressive Disorder" [Mesh:NoExp] OR "Depressive Disorder, Major" [Mesh] OR "Depressive Disorder, Treatment-Resistant" [Mesh] OR "Dysthymic Disorder" [Mesh] OR "Depression" [Mesh] OR "depression" [tw])) OR ("Auditory Perceptual Disorders" [Mesh] OR "Cognitive Dysfunction" [Mesh] OR "Cognition Disorders" [Mesh:NoExp] OR "cognition" [tw] OR "Neurodevelopmental Disorders" [Mesh] OR "neurodevelopmental" [tw] OR "neurodevelopment" [tw] OR "Neurotic Disorders" [Mesh] OR "Personality Disorders" [Mesh] OR "Substance-Related Disorders" [Mesh])) OR ("psychological outcome" [tw] OR "psychological outcomes" [tw] OR "psychiatric outcome" [tw] OR "psychiatric outcomes" [tw]))) OR ((("Intensive Care Units"[Mesh] OR critical care[Mesh:NoExp] OR "intensive care" [tw] OR "icu" [tw] OR "critical care" [tw]) AND ((((("Emotional Adjustment"[Mesh:NoExp] OR "Posttraumatic Growth, Psychological"[Mesh] OR "Stress Disorders, Post-Traumatic"[Mesh] OR "ptsd" [tw] OR "post traumatic stress disorders" [tw] OR "post-traumatic stress disorders" [tw] OR "Anxiety Disorders"[Mesh] OR "anxiety" [tw] OR "anxieties" [tw] OR "obsessive-compulsive disorder" [tw] OR "obsessive compulsive disorder" [tw] OR "OCD" [tw] OR "panic" [tw]) OR ("Bipolar and Related Disorders"[Mesh] OR "Disruptive, Impulse Control, and Conduct Disorders" [Mesh] OR "conduct disorders" [tw] OR "Dissociative Disorders" [Mesh] OR "Elimination Disorders" [Mesh] OR "encopresis" [tw] OR "enuresis" [tw] OR "Depressive Disorder" [Mesh:NoExp] OR "Depressive Disorder, Major" [Mesh] OR "Depressive Disorder, Treatment-Resistant" [Mesh] OR "Dysthymic Disorder" [Mesh] OR "Depression" [Mesh] OR "depression" [tw])) OR ("Auditory Perceptual Disorders" [Mesh] OR "Cognitive Dysfunction" [Mesh] OR "Cognition Disorders" [Mesh:NoExp] OR "cognition" [tw] OR "Neurodevelopmental Disorders" [Mesh] OR "neurodevelopmental" [tw] OR "neurodevelopment" [tw] OR "Neurotic Disorders" [Mesh] OR "Personality Disorders" [Mesh] OR "Substance-Related Disorders" [Mesh])) OR ("psychological outcome" [tw] OR "psychological outcomes" [tw] OR "psychiatric outcome" [tw] OR "psychiatric outcomes" [tw])) AND (adolescent[Filter] OR infant[Filter] OR preschoolchild[Filter] OR child[Filter])) OR ((("Intensive Care Units"[Mesh] OR critical care[Mesh:NoExp] OR "intensive care" [tw] OR "icu" [tw] OR "critical care" [tw]) AND ((((("Emotional Adjustment"[Mesh:NoExp] OR "Posttraumatic Growth, Psychological"[Mesh] OR "Stress Disorders, Post-Traumatic"[Mesh] OR "ptsd" [tw] OR "post traumatic stress disorders" [tw] OR "post-traumatic stress disorders" [tw] OR "Anxiety Disorders"[Mesh] OR "anxiety" [tw] OR "anxieties" [tw] OR "obsessive-compulsive disorder" [tw] OR "obsessive compulsive disorder" [tw] OR "OCD" [tw] OR "panic" [tw]) OR ("Bipolar and Related Disorders"[Mesh] OR "Disruptive, Impulse Control, and Conduct Disorders" [Mesh] OR "conduct disorders" [tw] OR "Dissociative Disorders" [Mesh] OR "Elimination Disorders" [Mesh] OR "encopresis" [tw] OR "enuresis" [tw] OR "Depressive Disorder" [Mesh:NoExp] OR "Depressive Disorder, Major" [Mesh] OR "Depressive Disorder, Treatment-Resistant" [Mesh] OR "Dysthymic Disorder" [Mesh] OR "Depression" [Mesh] OR "depression" [tw])) OR ("Auditory Perceptual Disorders" [Mesh] OR "Cognitive Dysfunction" [Mesh] OR "Cognition Disorders" [Mesh:NoExp] OR "cognition" [tw] OR "Neurodevelopmental Disorders" [Mesh] OR "neurodevelopmental" [tw] OR "neurodevelopment" [tw] OR "Neurotic Disorders" [Mesh] OR "Personality Disorders" [Mesh] OR "Substance-Related Disorders" [Mesh])) OR ("psychological outcome" [tw] OR "psychological outcomes" [tw] OR "psychiatric outcome" [tw] OR "psychiatric outcomes" [tw]))) AND (pediatric [tw] OR pediatrics [tw] OR pediatric [tw] OR paediatrics [tw] OR infant [tw] OR infants [tw] OR infancy [tw] OR infancies [tw] OR child [tw] OR children [tw] OR adolescence [tw] OR adolescent [tw] OR adolescents [tw] OR adolescense [tw] OR adolecent [tw] OR adolecents [tw] OR adolecence [tw] OR adolecense [tw] OR teen [tw] OR teens [tw] OR teenager [tw] OR teenagers [tw] OR toddler [tw] OR toddlers [tw] OR juvenille [tw] OR juvenilles [tw] OR juvenile [tw] OR juveniles [tw]))) Filters: English**
2	(Editorial[ptyp] OR Letter[ptyp] OR Case Reports[ptyp] OR Comment[ptyp])
3	#1 NOT #2

CINAHL (EBSCO)

S1	(((MH "Intensive Care Units+") OR (MH "Critical Care") OR (MH "Rapid Response (Emergency Care)")) OR (TI ("intensive care" OR icu OR "critical care"))) AND (((MH "Emotional Regulation") OR (MH "Posttraumatic Growth, Psychological") OR (MH "Adaptation, Psychological") OR TI("emotional adjust*") OR (MH "Stress Disorders, Post-Traumatic+") OR (MH "Anxiety Disorders+") OR TI (ptsd OR "post traumatic stress*" OR "post-traumatic stress*" OR "anxiet*" OR "obsessive-compulsive*" OR "obsessive compulsive*" OR OCD OR panic) OR (MH "Bipolar Disorder+") OR (MH "Disruptive Behavior") OR (MH "Impulse Control Disorders+") OR (MH "Trichotillomania") OR (MH "Child Behavior Disorders+") OR TI ("conduct disorder*") OR (MH "Dissociative Disorders+") OR (MH "Enuresis+") OR (MH "Fecal Incontinence") OR TI (encopre* OR enure* OR "fecal

	incontinen*") OR (MH "Depression") OR (MH "Dysthymic Disorder") OR TI depression OR (MH "Cognition Disorders+") OR (MH "Neurobehavioral Manifestations") OR (MH "Huntington's Disease") OR TI (cognition) OR (MH "Mental Disorders Diagnosed in Childhood+") OR (MH "Tic+") OR TI (neurodevelopmen*) OR (MH "Neurotic Disorders+") OR (MH "Personality Disorders+") OR (MH "Substance Use Disorders+") OR (MH "Cannabis+") OR (MH "Organic Mental Disorders, Substance-Induced") OR TI "psych* outcome*"))
S2	((((MH "Intensive Care Units+") OR (MH "Critical Care") OR (MH "Rapid Response (Emergency Care)")) OR (TI ("intensive care" OR icu OR "critical care"))) AND (((MH "Emotional Regulation") OR (MH "Posttraumatic Growth, Psychological") OR (MH "Adaptation, Psychological") OR TI("emotional adjust*") OR (MH "Stress Disorders, Post-Traumatic+") OR (MH "Anxiety Disorders+") OR TI (ptsd OR "post traumatic stress*" OR "post-traumatic stress*" OR "anxiet*" OR "obsessive-compulsive*" OR "obsessive compulsive*" OR OCD OR panic) OR (MH "Bipolar Disorder+") OR (MH "Disruptive Behavior") OR (MH "Impulse Control Disorders+") OR (MH "Trichotillomania") OR (MH "Child Behavior Disorders+") OR TI ("conduct disorder*") OR (MH "Dissociative Disorders+") OR (MH "Enuresis+") OR (MH "Fecal Incontinence") OR TI (encopre* OR enure* OR "fecal incontinen*") OR (MH "Depression") OR (MH "Dysthymic Disorder") OR TI depression OR (MH "Cognition Disorders+") OR (MH "Neurobehavioral Manifestations") OR (MH "Huntington's Disease") OR TI (cognition) OR (MH "Mental Disorders Diagnosed in Childhood+") OR (MH "Tic+") OR TI (neurodevelopmen*) OR (MH "Neurotic Disorders+") OR (MH "Personality Disorders+") OR (MH "Substance Use Disorders+") OR (MH "Cannabis+") OR (MH "Organic Mental Disorders, Substance-Induced") OR TI "psych* outcome*"))) AND (TI (pediatric* OR paediatric* OR infant* OR infanc* OR child* OR adolesc* OR adolec* OR teen* OR toddler* OR juvenille* OR juvenile*) OR (MH "Intensive Care Units, Pediatric") OR TI (picu))
S3	(((MH "Intensive Care Units+") OR (MH "Critical Care") OR (MH "Rapid Response (Emergency Care)")) OR (TI ("intensive care" OR icu OR "critical care"))) AND (((MH "Emotional Regulation") OR (MH "Posttraumatic Growth, Psychological") OR (MH "Adaptation, Psychological") OR TI("emotional adjust*") OR (MH "Stress Disorders, Post-Traumatic+") OR (MH "Anxiety Disorders+") OR TI (ptsd OR "post traumatic stress*" OR "post-traumatic stress*" OR "anxiet*" OR "obsessive-compulsive*" OR "obsessive compulsive*" OR OCD OR panic) OR (MH "Bipolar Disorder+") OR (MH "Disruptive Behavior") OR (MH "Impulse Control Disorders+") OR (MH "Trichotillomania") OR (MH "Child Behavior Disorders+") OR TI ("conduct disorder*") OR (MH "Dissociative Disorders+") OR (MH "Enuresis+") OR (MH "Fecal Incontinence") OR TI (encopre* OR enure* OR "fecal incontinen*") OR (MH "Depression") OR (MH "Dysthymic Disorder") OR TI depression OR (MH "Cognition Disorders+") OR (MH "Neurobehavioral Manifestations") OR (MH "Huntington's Disease") OR TI (cognition) OR (MH "Mental Disorders Diagnosed in Childhood+") OR (MH "Tic+") OR TI (neurodevelopmen*) OR (MH "Neurotic Disorders+") OR (MH "Personality Disorders+") OR (MH "Substance Use Disorders+") OR (MH "Cannabis+") OR (MH "Organic Mental Disorders, Substance-Induced") OR TI "psych* outcome*")) **Limiters - Age Groups: Infant: 1-23 months, Child, Preschool: 2-5 years, Child: 6-12 years, Adolescent: 13-18 years**
S4	S2 OR S3
S5	S4 NOT PT (editorial or letter or commentary or "case study") **Limiters - English Language**

Embase (Elsevier)

#1	(('intensive care'/de OR 'artificial ventilation'/exp OR 'early goal-directed therapy'/exp OR 'intensive care nursing'/de OR 'patient monitoring'/exp OR 'resuscitation'/de OR 'intensive care unit'/de OR 'burn unit'/de OR 'coronary care unit'/exp OR 'medical intensive care unit'/de OR 'neurological intensive care unit'/de OR 'psychiatric intensive care unit'/de OR 'stroke unit'/de OR 'surgical intensive care unit'/de OR 'critical care outcome'/de OR 'critical care':ti OR 'intensive care':ti OR 'icu':ti) AND ('coping behavior'/exp OR 'emotion regulation'/de OR 'emotional disorder'/de OR 'psychological adjustment'/de OR 'psychological adjustment':ti OR 'emotional adjustment':ti OR 'anxiety disorder'/exp OR 'ptsd':ti OR 'post traumatic stress*':ti OR 'post-traumatic stress*':ti OR 'anxiet*':ti OR 'obsessive-compulsive*':ti OR 'obsessive compulsive*':ti OR 'ocd':ti OR 'panic':ti OR 'bipolar disorder'/exp OR 'disruptive behavior'/exp OR 'impulse control disorder'/exp OR 'behavior disorder'/exp OR 'conduct disorder*':ti OR 'dissociative disorder'/exp OR 'enuresis'/exp OR 'feces incontinence'/de OR 'encopresis':ti OR 'enuresis':ti OR 'fecal incontine*':ti OR 'depression'/de OR 'major depression'/de OR 'treatment resistant depression'/de OR 'adolescent depression'/de OR 'depressive psychosis'/de OR 'mixed anxiety and depression'/de OR 'dysthymia'/de OR 'depression':ti OR 'cognitive defect'/de OR 'perception deafness'/de OR 'huntington disease like syndrome'/de OR 'cognition':ti OR 'mental disease'/de OR 'personality disorder'/exp OR 'neurosis'/exp OR 'neurodevelopment*':ti OR 'thought disorder'/exp OR 'addiction'/exp OR 'drug induced psychosis'/exp OR 'psych* outcome*':ti) AND ([adolescent]/lim OR [child]/lim OR [infant]/lim OR [preschool]/lim OR [school]/lim) OR (('intensive care'/de OR 'artificial ventilation'/exp OR 'early goal-directed therapy'/exp OR 'intensive care nursing'/de OR 'patient monitoring'/exp OR 'resuscitation'/de OR 'intensive care unit'/de OR 'burn unit'/de OR 'coronary care unit'/exp OR 'medical intensive care unit'/de OR 'neurological intensive care unit'/de OR 'psychiatric intensive care unit'/de OR 'stroke unit'/de OR 'surgical intensive care unit'/de OR 'critical care outcome'/de OR 'critical care':ti OR 'intensive care':ti OR 'icu':ti) AND ('coping behavior'/exp OR 'emotion regulation'/de OR 'emotional disorder'/de OR 'psychological adjustment'/de OR 'psychological adjustment':ti OR 'emotional adjustment':ti OR 'anxiety disorder'/exp OR 'ptsd':ti OR 'post traumatic stress*':ti OR 'post-traumatic stress*':ti OR 'anxiet*':ti OR 'obsessive-compulsive*':ti OR 'obsessive compulsive*':ti OR 'ocd':ti OR 'panic':ti OR 'bipolar disorder'/exp OR 'disruptive behavior'/exp OR 'impulse control disorder'/exp OR 'behavior disorder'/exp OR 'conduct disorder*':ti OR 'dissociative disorder'/exp OR 'enuresis'/exp OR 'feces incontinence'/de OR 'encopresis':ti

	OR 'enuresis':ti OR 'fecal incontine*':ti OR 'depression'/de OR 'major depression'/de OR 'treatment resistant depression'/de OR 'adolescent depression'/de OR 'depressive psychosis'/de OR 'mixed anxiety and depression'/de OR 'dysthymia'/de OR 'depression':ti OR 'cognitive defect'/de OR 'perception deafness'/de OR 'huntington disease like syndrome'/de OR 'cognition':ti OR 'mental disease'/de OR 'personality disorder'/exp OR 'neurosis'/exp OR 'neurodevelopment*':ti OR 'thought disorder'/exp OR 'addiction'/exp OR 'drug induced psychosis'/exp OR 'psych* outcome*':ti) AND ('pediatric*':ti OR 'pediatric*':ti OR 'infant*':ti OR 'infanc*':ti OR 'child*':ti OR 'adolesc*':ti OR 'adolec*':ti OR 'teen*':ti OR 'toddler*':ti OR 'juvenille*':ti OR 'juvenile*':ti)) OR (('coping behavior'/exp OR 'emotion regulation'/de OR 'emotional disorder'/de OR 'psychological adjustment'/de OR 'psychological adjustment':ti OR 'emotional adjustment':ti OR 'anxiety disorder'/exp OR 'ptsd':ti OR 'post traumatic stress*':ti OR 'post-traumatic stress*':ti OR 'anxiet*':ti OR 'obsessive-compulsive*':ti OR 'obsessive compulsive*':ti OR 'ocd':ti OR 'panic':ti OR 'bipolar disorder'/exp OR 'disruptive behavior'/exp OR 'impulse control disorder'/exp OR 'behavior disorder'/exp OR 'conduct disorder*':ti OR 'dissociative disorder'/exp OR 'enuresis'/exp OR 'feces incontinence'/de OR 'encopresis':ti OR 'enuresis':ti OR 'fecal incontine*':ti OR 'depression'/de OR 'major depression'/de OR 'treatment resistant depression'/de OR 'adolescent depression'/de OR 'depressive psychosis'/de OR 'mixed anxiety and depression'/de OR 'dysthymia'/de OR 'depression':ti OR 'cognitive defect'/de OR 'perception deafness'/de OR 'huntington disease like syndrome'/de OR 'cognition':ti OR 'mental disease'/de OR 'personality disorder'/exp OR 'neurosis'/exp OR 'neurodevelopment*':ti OR 'thought disorder'/exp OR 'addiction'/exp OR 'drug induced psychosis'/exp OR 'psych* outcome*':ti) AND ('pediatric intensive care nursing'/de OR 'pediatric intensive care unit'/exp OR 'pediatric advanced life support'/exp OR 'picu':ti))) AND [english]/lim NOT ('case report'/exp OR 'case study'/exp OR 'editorial'/exp OR 'letter'/exp OR 'note'/exp)

PsycInfo (EBSCO)

S1	(DE "Intensive Care" OR ("intensive care" OR "icu" OR "critical care")) AND (((DE "Adaptive Behavior" OR DE "Emotional Adjustment" OR DE "Emotional Control" OR DE "Emotional Disturbances" OR DE "Emotional Processing") OR TI "emotional adjustment*") OR ((DE "Posttraumatic Growth" OR DE "Posttraumatic Stress" OR DE "Anxiety Disorders" OR DE "Generalized Anxiety Disorder" OR DE "Obsessive Compulsive Disorder" OR DE "Hoarding Disorder" OR DE "Koro" OR DE "Panic Attack" OR DE "Panic Disorder" OR DE "Phobias" OR DE "Acrophobia" OR DE "Agoraphobia" OR DE "Claustrophobia" OR DE "Ophidiophobia" OR DE "School Phobia" OR DE "Social Phobia" OR DE "Trichotillomania")) OR (TI ("ptsd" OR "post traumatic stress*" OR "post-traumatic stress*" OR "anxiet*" OR "obsessive-compulsive*" OR "obsessive compulsive*" OR "OCD" OR "panic")) OR ((DE "Bipolar Disorder" OR DE "Bipolar I Disorder" OR DE "Bipolar II Disorder" OR DE "Cyclothymic Disorder" OR DE "Mania" OR DE "Hypomania" OR DE "Disruptive Behavior Disorders" OR DE "Conduct Disorder" OR DE "Oppositional Defiant Disorder" OR DE "Behavior Problems" OR DE "Tantrums" OR DE "Impulse Control Disorders" OR DE "Explosive Disorder") OR TI "conduct disorder*" OR (DE "Dissociative Disorders" OR DE "Depersonalization" OR DE "Depersonalization/Derealization Disorder" OR DE "Dissociative Amnesia" OR DE "Dissociative Identity Disorder" OR DE "Fugue Reaction" OR DE "Urinary Incontinence" OR DE "Fecal Incontinence") OR TI ("encopresis" OR "enuresis" OR "fecal incontine*")) OR ((DE "Major Depression" OR DE "Dysthymic Disorder" OR DE "Treatment Resistant Depression" OR DE "Internalizing Symptoms" OR DE "Depression (Emotion)" OR DE "Sadness") OR TI depression OR (DE "Cognitive Impairment" OR DE "Huntingtons Disease" OR DE "Neurocognitive Disorders" OR DE "Mild Cognitive Impairment" OR DE "Neurodevelopmental Disorders" OR DE "Attention Deficit Disorder" OR DE "Autism Spectrum Disorders" OR DE "Developmental Disabilities" OR DE "Disruptive Behavior Disorders" OR DE "Emotional and Behavioral Disorders" OR DE "Intellectual Development Disorder" OR DE "Learning Disorders") OR TI (cognition OR "auditory perceptual" OR neurobehavioral) OR TI neurodevelopment* OR (DE "Personality Disorders" OR DE "Antisocial Personality Disorder" OR DE "Avoidant Personality Disorder" OR DE "Borderline Personality Disorder" OR DE "Dependent Personality Disorder" OR DE "Histrionic Personality Disorder" OR DE "Narcissistic Personality Disorder" OR DE "Obsessive Compulsive Personality Disorder" OR DE "Paranoid Personality Disorder" OR DE "Passive Aggressive Personality Disorder" OR DE "Sadomasochistic Personality" OR DE "Schizoid Personality Disorder" OR DE "Schizotypal Personality Disorder" OR DE "Substance Related and Addictive Disorders" OR DE "Nonsubstance Related Addictions" OR DE "Substance Use Disorder" OR DE "Cannabis Use Disorder" OR DE "Opioid Use Disorder" OR DE "Heroin Addiction" OR DE "Morphine Dependence") OR TI "psych* outcome*"))
S2	S1 AND (pediatric* OR paediatric* OR infant* OR infanc* OR child* OR adolesc* OR adolec* OR teen* OR toddler* OR juvenille* OR juvenile*)
S3	S1 - **Limiters - Age Groups: Childhood (birth-12 yrs), Adolescence (13-17 yrs)**
S4	picu AND (((DE "Adaptive Behavior" OR DE "Emotional Adjustment" OR DE "Emotional Control" OR DE "Emotional Disturbances" OR DE "Emotional Processing") OR TI "emotional adjustment*") OR ((DE "Posttraumatic Growth" OR DE "Posttraumatic Stress" OR DE "Anxiety Disorders" OR DE "Generalized Anxiety Disorder" OR DE "Obsessive Compulsive Disorder" OR DE "Hoarding Disorder" OR DE "Koro" OR DE "Panic Attack" OR DE "Panic Disorder" OR DE "Phobias" OR DE "Acrophobia" OR DE "Agoraphobia" OR DE "Claustrophobia" OR DE "Ophidiophobia" OR DE "School Phobia" OR DE "Social Phobia" OR DE "Trichotillomania")) OR (TI ("ptsd" OR "post traumatic stress*" OR "post-traumatic stress*" OR "anxiet*" OR "obsessive-compulsive*" OR "obsessive compulsive*" OR "OCD" OR "panic")) OR ((DE "Bipolar Disorder" OR DE "Bipolar I Disorder" OR DE "Bipolar II Disorder" OR DE "Cyclothymic Disorder" OR DE "Mania" OR DE "Hypomania" OR DE "Disruptive Behavior Disorders" OR DE "Conduct Disorder" OR DE "Oppositional Defiant Disorder" OR DE "Behavior Problems" OR DE

	"Tantrums" OR DE "Impulse Control Disorders" OR DE "Explosive Disorder") OR TI "conduct disorder*" OR (DE "Dissociative Disorders" OR DE "Depersonalization" OR DE "Depersonalization/Derealization Disorder" OR DE "Dissociative Amnesia" OR DE "Dissociative Identity Disorder" OR DE "Fugue Reaction" OR DE "Urinary Incontinence" OR DE "Fecal Incontinence") OR TI ("encopresis" OR "enuresis" OR "fecal incontine*")) OR ((DE "Major Depression" OR DE "Dysthymic Disorder" OR DE "Treatment Resistant Depression" OR DE "Internalizing Symptoms" OR DE "Depression (Emotion)" OR DE "Sadness") OR TI depression OR (DE "Cognitive Impairment" OR DE "Huntingtons Disease" OR DE "Neurocognitive Disorders" OR DE "Mild Cognitive Impairment" OR DE "Neurodevelopmental Disorders" OR DE "Attention Deficit Disorder" OR DE "Autism Spectrum Disorders" OR DE "Developmental Disabilities" OR DE "Disruptive Behavior Disorders" OR DE "Emotional and Behavioral Disorders" OR DE "Intellectual Development Disorder" OR DE "Learning Disorders") OR TI (cognition OR "auditory perceptual" OR neurobehavioral) OR TI neurodevelopment* OR (DE "Personality Disorders" OR DE "Antisocial Personality Disorder" OR DE "Avoidant Personality Disorder" OR DE "Borderline Personality Disorder" OR DE "Dependent Personality Disorder" OR DE "Histrionic Personality Disorder" OR DE "Narcissistic Personality Disorder" OR DE "Obsessive Compulsive Personality Disorder" OR DE "Paranoid Personality Disorder" OR DE "Passive Aggressive Personality Disorder" OR DE "Sadomasochistic Personality" OR DE "Schizoid Personality Disorder" OR DE "Schizotypal Personality Disorder" OR DE "Substance Related and Addictive Disorders" OR DE "Nonsubstance Related Addictions" OR DE "Substance Use Disorder" OR DE "Cannabis Use Disorder" OR DE "Opioid Use Disorder" OR DE "Heroin Addiction" OR DE "Morphine Dependence") OR TI "psych* outcome*")))
S5	S2 OR S3 OR S4 **Limiters - English**
S6	PZ (editorial OR letter OR "column/opinion" OR "comment/reply")
S7	S5 NOT S6

Search strategy was performed for Medline (Pubmed), CINAHL (EBSCO), Embase (Elsevier), and PsycInfo (EBSCO) on 18 June 2021 with no restriction in start date.

eTable 3. Risk of Bias Assessment

A. Cochrane risk of bias (ROB) tool for RCTs

	Random sequence Generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Verstraete et al, 2019 [26]	+	+	-	+	-	+	+
Jacobs et al, 2020 [50]	+	+	-	+	-	+	+
Guiza et al, 2020 [49]	+	+	-	+	-	+	+
Melnyk et al, 2004 [28]	+	-	-	-	+	+	+
Small et al, 2006 [53]	+	-	-	-	+	+	+
Small et al, 2009 [54]	+	-	-	-	+	+	+
Watson et al, 2018 [24]	+	-	+	+	-	+	+
Mesotten et al, 2012 [27]	+	+	-	+	+	+	+
Rennick et al, 2018 [25]	+	-	-	-	+	+	-

B. Newcastle-Ottawa Scale (NOS) for cohort studies

	Selection (max 4 ★)	Comparability (max 2 ★)	Outcome (max 3 ★)
Colville et al, 2008	★★★		★
Colville et al, 2013 [32]	★★★		★★
Meert et al, 2019 [51]	★★		★★★
Slomine et al, 2018 [29]	★★		★★★
Dow et al, 2013 [59]	★★★		★★
Dow et al, 2012 [58]	★★★		★★
Buysse et al, 2008 [41]	★★★		★★★
Buysse et al, 2010 [52]	★★★		★★★
Vermunt et al, 2009 [56]	★★★		★★★
Vermunt et al, 2008 [55]	★★★		★★★
Rennick et al, 2004 [10]	★★		★★★
Rennick et al, 2002 [5]	★★		★★★
Verstraete et al, 2015 [7]	★★★★	★★	★★
Gemke et al, 1995 [13]	★★★		★★★
Berger et al, 2018 [14]	★★		★★
Rees et al, 2004 [12]	★★★★	★	★★
Shevell et al, 2020 [40]	★★		★★★
Abend et al, 2015 [36]	★★★		★★
Bronner et al, 2008 [33]	★★★		★★
Jones et al, 2006 [44]	★★★		★★
Nelson et al, 2019 [35]	★★		★
Le Brocque et al, 2020 [34]	★★★		★★
Bronner et al, 2009 [39]	★★★		★★
Lequier et al, 2008 [37]	★★★		★★

Kyosti et al, 2019 [43]	★★★		★★★
Ballweg et al, 2007 [15]	★★		★★
Limperopoulos et al, 2002 [38]	★★★		★★★
Forbess et al, 2002 [42]	★★★		★★
Boeschoten et al, 2020 [30]	★★★★		★
Shein et al, 2020 [45]	★★★		★★
Biagas et al, 2020 [31]	★★★		★★

C. Adapted NOS for case control and cross-sectional studies

	Selection (max 4 ★)	Comparability (max 2 ★)	Outcome (max 2 ★)
Vermunt et al, 2011 [57]	★★	★	★
Elison et al, 2008 [46]	★★★	★	★
Meyburg et al, 2018 [47]	★		
Fiser et al, 2000 [48]	★★★★		★

RCTs were given a quality rating of either low (+) or high (-) risk of bias for each of the seven different domains – random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias using the ROB checklist. Observational studies were scored according to three domains – selection, comparability, and outcome using the NOS checklist. Studies were rated as good quality if they obtained 3 or 4 stars in the selection domain, 1 or 2 stars in the comparability domain and 2 or 3 stars in the outcome domain; fair quality if they obtained 2 stars in the selection domain, 1 or 2 stars in the comparability domain and 2 or 3 stars in the outcome domain; poor quality if they obtained 0 or 1 stars in the selection domain, 0 stars in the comparability domain, or 0 or 1 stars in the outcome domain

eTable 4. Summary of Included Studies

Study	Design, Country	Participants (sample size, age at admission, gender, race)	Aim of study	Study inclusion and exclusion criteria	Instrument, follow-up	Point prevalence	Results
Post-Traumatic Stress Disorder (PTSD)							
Colville et al, 2013[32]	Prospective cohort study, United Kingdom	38 PICU; 11 (7-17) years; 57% male; 56% white	The main aim of this study was to elicit children's own views about their quality of life in the year following their discharge from intensive care, using a well-validated assessment tool, the Pediatric Quality of Life Inventory (PedsQL)	**Inclusion criteria:** Families of surviving children, aged over 7 years and consecutively admitted over an 18-month period, were approached by letter, 6 wk after discharge from PICU, to take part in the research project. **Exclusion criteria:** Children were excluded if they had significant learning difficulties, or if they were not registered with a general practitioner.	CRIES-8, 1 year	7 out of 38 children scored above the clinical cut-off on the CRIES-8.	
Rees et al, 2004[12]	Retrospective cohort study, United Kingdom	19 PICU, 27 general pediatric ward; 8.8 (7.1-10.8) years for PICU, 9.3 (7.3-12.2) years for no-PICU; 66% male for PICU, 55% male for general pediatric ward; 60% white for PICU, 42% white for general pediatric ward	To determine whether PICU admission is associated with greater psychiatric morbidity in children and parents as compared with general pediatric ward admissions.	**Inclusion criteria:** Children aged 5–18 years discharged from PICU (exposed cohort) and general pediatric wards (unexposed cohort) 6–12 months previously. **Exclusion criteria:** Children with meningococcal disease were excluded. Children with terminal illness, underlying neurological disorder or admission resulting from an intentional overdose were also excluded. Individuals with recognised pre-contact learning difficulties, insufficient English to complete the study instruments and families not contactable by telephone were also excluded.	CAPS-C, 6 to 12 months CIES, 6 to 12 months	CAPS-C PICU (n = 19) = 5.3%; Non-PICU (n = 27) = 0% IES PICU (n = 21) = 17.4%; Non-PICU (n = 17) = 9.5%	**IES scores (median (IQR):** PICU = 10 (6 – 24); Non-PICU = 6 (1.0 – 15.0)
[a]Rennick et al, 2002[5]	Prospective cohort study, Canada[a]	60 PICU, 60 ward controls; PICU = 11.33 (3.22) years Ward (control)	The purposes of this study were to compare the psychological responses of children hospitalized in a PICU with those of children hospitalized on a general	**Inclusion criteria:** Eligible children were (1) between 6 and 17 years of age; (2) had been in the PICU at least 24 hours and were ready for discharge; (3) understood and spoke English or French;	CIES, 6 months CMFS, 6 months		**CIES score** PICU = 0.29 (0.19) Ward controls = 0.29 (0.19) **CMFS score**

		= 11.33 (3.30) years; PICU = 50% male, Ward controls = 40% male	ward and to identify clinically relevant factors that might be associated with psychological outcome.	and (4) had at least one parent who read, wrote, and spoke English or French. **Exclusion criteria:** Not indicated			PICU = 0.23 (0.18) Ward controls = 0.27 (0.19)
[a]Rennick et al, 2004[10]	Retrospective cohort study, Canada[a]	60 PICU; Low risk of psychological sequelae (n = 40) = 11.5 (10.5–12.5), High risk of psychological sequelae (n = 20) = 11.1 (9.5–12.6); Low risk = 47.5% male, High risk = 55.0% male	To identify those patients in a pediatric intensive care unit who may be at highest risk for developing persistent psychological sequelae after hospital discharge.	**Inclusion criteria:** Children were between 6 and 17 yrs of age, had been in the PICU for at least 24 hrs, and were judged by the attending physician as ready for discharge. Children understood and spoke either English or French, and at least one of the children's parents read, wrote, and spoke English or French. **Exclusion criteria:** Not indicated	CIES, 6 months CMFS, 6 months	10% (6/60) of children scored at risk of PTSD according to CIES.	**CIES score (mean (95% CI))** Low risk of psychological sequelae (n = 40) = 0.25 (95% CI = 0.19 – 0.30) High risk of psychological sequelae (n = 20) = 0.37 (95% CI = 0.27 – 0.47) **CMFS score (mean (95% CI))** Low risk of psychological sequelae (n = 40) = 0.21 (95% CI = 0.16 – 0.26) High risk of psychological sequelae (n = 20) = 0.29 (95% CI = 0.19 – 0.38)
[b]Dow et al, 2013[59]	Prospective cohort study, Australia[b]	59 PICU; 10.76 (2.59) years; 56% male	This study explored the diagnosis of posttraumatic stress disorder (PTSD) in children and adolescents following pediatric intensive care unit (PICU) admission.	**Inclusion criteria:** As part of a prospective longitudinal research project investigating the psychological impact of PICU admission on families, surviving children aged 6–16 years admitted to the Royal Children's Hospital PICU, Brisbane, Australia for at least 8 hours (equivalent to an overnight stay) between June 2008 and January 2011 were recruited consecutively **Exclusion criteria:** Exclusion criteria were (1) prior PICU admission, (2) length of stay > 28 days, (3) posttraumatic amnesia >28 days; (4) non-accidental injury, and (5) developmental delay or intellectual impairment.	CPTSDI, 6 months	25% of children scored at risk of PTSD according to CPTSDI (based on DSM-IV criteria).	
[b]Dow et al, 2012[58]	Prospective cohort study, Australia[b]	55 PICU; 11 (6 – 16) years; 58% male	This study investigated the utility of 2 versions, the CRIES-8 and CRIES-13, in identifying those children meeting criteria for PTSD following admission to a pediatric intensive care unit (PICU).	**Inclusion criteria:** Children, families of surviving children aged 6–16 years admitted to the Royal Children's Hospital PICU, Brisbane, Australia for at least 8 hours between June 2008 and January 2011 were recruited consecutively. **Exclusion criteria:**	CPTSDI, 6 months	25% (14/55)	

				Exclusion criteria were (a) prior PICU admission, (b) stay > 28 days, (c) posttraumatic amnesia > 28 days; (d) nonaccidental injury, (e) developmental delay or intellectual impairment, and (f) death of the child.			
Bronner et al, 2008[33]	Prospective cohort study, Netherlands	29 (3 months follow-up) and 28 (9 months follow-up) PICU patients, 355 children who survived a major fire disaster; PICU = 13.4 (SD = 2.6, range 8.0–17.1) years, Major fire disaster = 15.2 (SD = 1.7, range 11–19) years; PICU = 28.6% male, Major fire disaster = 49.3% male	The goals were to determine the presence of posttraumatic stress disorder (PTSD) in children after pediatric intensive care treatment, to identify risk factors for PTSD, and to compare this data with data from a major fire disaster in the Netherlands.	**Inclusion criteria:** In this study, we included previously healthy children, unexpectedly referred to the PICU with an acute life-threatening medical event. In an attempt to include seriously ill patients only, we defined our inclusion criteria as admissions for respiratory insufficiency necessitating ventilatory support for at least 24 hours and/or patients admitted to the PICU for at least 7 days, including all trauma types. **Exclusion criteria:** We excluded children with known underlying illnesses or patients after elective surgery. Exclusion criteria were admission due to abuse or self-intoxication and the inability to complete Dutch questionnaires	CRTI, 3 and 9 months	**3 months** 34.5% (10/29) had subclinical PTSD, with 4 (13.8%) likely to meet criteria for PTSD. **9 months** 35.7% (10/28) had at least subclinical levels of PTSD, with 5 (17.9%) likely to meet criteria for PTSD.	**CRTI score (n = 28) at 9 months follow-up** PICU = 36.5 (8.1) Major fire disaster = 38.6 (8.8) Logistic regression models for both subclinical PTSD and PTSD corrected for gender, age, and gender × age produced no significant odds ratios for group (PICU children versus Volendam fire disaster children) on either subclinical PTSD (OR = 0.58, 95% CI 0.24 –1.42, p = 0.231) or PTSD (OR = 0.99, 95% CI 0.33 – 2.97, p = 0.982).
Boeschoten et al, 2020[30]	Prospective cohort study, Netherlands	50 PICU, 62 General ward; PICU = 8 (6-12) years, General ward = 5 (3-6) years; 62% PICU, 57% General ward male	Prospective study to evaluate quality of life (QoL) and psychosocial outcomes in children with severe acute asthma (SAA) after pediatric intensive care (PICU) admission compared to children with SAA who were admitted to a general ward (GW).	**Inclusion criteria:** All children (2-18 years old) with SAA admitted to all seven Dutch academic PICUs (N = 110) and the pediatric wards of four participating general hospitals (N = 111). **Exclusion criteria:** Not indicated	CRTI, 5 (1-12) months		**CRTI mean (SD) for PICU (n=17); General ward (n=5)** Total score = 60.1 (35.5); 48 (14.2) Intrusion = 11.9 (7.6); 7.8 (1.8) Avoidance = 18.7 (12.6); 17.2 (6.6) Arousal = 11.8 (6.7); 8.2 (3.2) Other child-specific responses = 17.8 (10.0); 14.8 (4.8) PTSD—total score = 30.9 (18.5); 8.2 (3.7) PTSD—intrusion = 9.1 (5.7); 5.8 (1.8) PTSD—avoidance = 12.1 (8.0); 12.4 (5.3) PTSD—arousal = 9.7 (5.6); 7.0 (3.1)
Watson et al, 2018[24]	Randomized controlled trial, USA	1073 PICU (sedation protocol = 576; usual care = 497);	To compare post-discharge outcomes in children with acute respiratory failure cluster-randomized to a sedation protocol or usual care.	**Inclusion criteria:** Patients were 2 weeks to 17 years old at enrollment and were expected to require invasive mechanical ventilation for at least 24 hours	CPSS, 6 months	30% (31/102)	CPSS score = 8.5 (9.1)

		Sedation protocol = 1.4 (0.3–6.8) years, Usual care = 3.4 (0.8–8.9) years; Sedation protocol = 53% male, Usual care = 58% male; 53% non-Hispanic white		for acute respiratory failure from lower airway or parenchymal disease. **Exclusion criteria:** Patients and families were considered ineligible for follow-up if they did not live in the United States, if they could not understand English or Spanish, or if consenting parents/guardians no longer had custody of the patient.			
[b]Brocque et al, 2020[34]	Prospective cohort study, Australia	272 PICU; 7.67 (4.44) years; 57% male	This study investigated trauma symptom trajectories of children 2–16 years old following admission to pediatric intensive care and identified factors that predicted a child's trauma symptom trajectory.	**Inclusion criteria:** Children 2–16 years old admitted to the PICU at the Royal Children's Hospital and Mater Children's Hospital, Brisbane, Qld, Australia for more than 8 hours between June 2007 and January 2011 were recruited consecutively within 72 hours of admission. **Exclusion criteria:** Exclusion criteria included the following: PICU length of stay less than 8 hours or more than 28 days, parental English insufficient for completion of questionnaires, or nonaccidental injury.	TSCYC, 12 months	12.9% (35/272) at 6 and 12 months	
Nelson et al, 2019[35]	Prospective cohort study, USA	69 PICU; 13.06 (2.71) years; 57% male; 19% white	To report the rate of acute stress (AS) and posttraumatic stress (PTS) among children and parents following pediatric intensive care unit (PICU) admission and the relation between family function and PTS.	**Inclusion criteria:** Eligible children were between eight and 17-years-old with an expected PICU stay > 24 hours. Both English- and Spanish-speaking families were recruited. **Exclusion criteria:** Children with severe neurologic injury, psychiatric disorder, or developmental delay were excluded from the study.	UCLA PTSD-RI, 3 months	53% endorsed PTS symptoms 13% met diagnostic criteria for PTSD	
Anxiety							
Rennick et al, 2018[25]	Nonblinded, pilot randomized	10 PICU; 8.5 (4.1) years; 80% male	To examine the feasibility and acceptability of a PICU	**Inclusion criteria:** Eligible participants were age 2–17 years old, spoke English or French, and had a	RCMAS, 3 months		RCMAS score (n = 10) = 41 (14.45)

	controlled trial, Canada		soothing intervention using touch, reading, and music.	parent who spoke and read English or French and agreed to be present during the intervention. **Exclusion criteria:** Children with a diagnosed sleep, seizure, or hearing disorder, cognitive delay, previous PICU admission, or not expected to survive were excluded.			
Bronner et al, 2009[39]	Retrospective cohort study, Netherlands	50 PICU; 4.2 (0.0–17.0) years; 54% male	To evaluate self-reported health-related quality of life, anxiety, depression, and cognitive function in pediatric septic shock survivors.	**Inclusion criteria:** Previously, healthy children who survived septic shock in our PICU between 1995 and 2004 were included in this study. Inclusion criteria were survival of the clinical diagnosis of septic shock according to the Conference Consensus Criteria, the administration of inotropic and/or vasoconstrictive agents for ≥ 24 hrs, and age ≥ 8 yrs at the time of the follow-up study. **Exclusion criteria:** Children with language barriers were excluded due to the inability to complete Dutch questionnaires. In addition, children < 8 yrs were excluded because they were unable to complete the questionnaires by themselves.	STAIC, 6.5 years		Females with septic shock (n = 23) = 28.3 ± 6.7 Female controls = 33.0 ± 6.5 Effect size = 0.7 p < 0.05 Males with septic shock (n = 27) = 28.2 ± 6.1 Male controls = 30.0 ± 6.0 Effect size = 0.3 p > 0.05
Cognitive impairment							
Verstraete et al, 2016[7]	Retrospective cohort study, Belgium	449 PICU (developmental cohort = 228, validation cohort = 221), 100 healthy controls; 3.4 (2.9-4.0) for development cohort, 3.3 (2.7-3.8) for validation cohort, 4.2 (3.5-4.9) for healthy controls;	The primary study aim was to assess, in a multivariable regression analysis adjusting for other risk factors, the presence of an independent association between ‘‘exposure’’ to the total circulating DEHP metabolites during PICU stay and the attention deficit 4 years later. Secondary study aims were similar analyses for the other neurocognitive outcomes, and for the individual DEHP	**Inclusion criteria:** Critically ill infants and children (0–16 years upon PICU admission). Anticipated to require intensive care for at least 24-hours. Plasma taken during PICU admission. Undergone neurocognitive testing at 4-year follow-up. **Exclusion criteria:** Estimated stay in PICU < 24-hours. Therapy restriction upon admission. Other study enrolment. No informed consent. Lost to follow-up.	WIQS, 4 years		PICU Developmental cohort = 88 (86 – 90); validation cohort = 85 (83 – 88) Healthy controls = 102 (100 – 104)

		54.0% male for developmental cohort, 60.2% male for validation cohort, 58.0% male for healthy children; 96.1% white for developmental cohort, 90.5% white for validation cohort, 93.0% white for healthy children	metabolites and the sum of MEHP metabolites.				
[c]Verstraete et al, 2019[26]	Randomized controlled trial, Belgium, Netherlands, Canada[c]	391 PICU, 405 healthy controls; age at 2-year follow-up: PICU = 5.7 (4.5) years, healthy controls = 6.0 (4.7) years; 58% male for PICU, 54% male for healthy controls; 92% white for PICU and healthy controls	We aimed to investigate whether withholding supplemental parenteral nutrition during the first week in PICU, rather than giving parenteral nutrition to reach nutritional targets as soon as possible, while adequately providing micronutrients, has an impact on survival, health status, and anthropometrics, clinically assessed neurological function, and parent-reported or caregiver-reported and clinically tested neurocognitive outcomes at the 2-year follow-up, compared with matched healthy children.	**Inclusion criteria:** Admitted to participating PICUs. Written informed consent from parents or legal guardians or from the adolescent according to local regulations. Siblings and relatives of the patients were preferably recruited into the control group besides unrelated children recruited from the same geographical area. **Exclusion criteria:** Exclusion criteria for the control group were previous admission to a neonatal ICU or a PICU, or hospital admission for at least 7 days with need for an intravenous line, history of suspicious or established inborn chronic metabolic diseases requiring a specific diet, such as diabetes, and history of short bowel syndrome on home parenteral nutrition or other conditions that require home parenteral nutrition.	WPPSI, 2 years BRIEF, 2 years		**WPPSI** Healthy controls = 100.7 (13.0) PICU = 90.3 (16.6) **BRIEF** Healthy controls = 45.9 (11.6) PICU = 51.1 (14.5)
[c]Jacobs et al, 2020[50]	Randomized controlled trial, Belgium, Netherlands, Canada[c]	684 PICU, 369 healthy controls; PICU = 7·3 (4·3) years, healthy controls = 7·5 (4·3) years; PICU = 55% male, Healthy controls = 57% male;	We aimed to determine the effect of late-parenteral nutrition versus early-parenteral nutrition on physical, neurocognitive, and emotional and behavioral development 4 years after randomization.	**Inclusion criteria:** Healthy children were only included if they had not been previously admitted to a neonatal or pediatric intensive care unit, or admitted to hospital with need for an intravenous line for 7 days or more. **Exclusion criteria:** History of inborn chronic metabolic diseases requiring a specific diet, such as diabetes, and conditions that require home parenteral	WPPSI, 4 years BRIEF, 4 years		**WPPSI** Healthy controls = 105·7 (13.4) PICU = 93·1 (18.2) **BRIEF** Healthy controls = 44·8 (9.8) PICU = 49·9 (13.2)

		PICU = 92% white, healthy controls = 93% white		nutrition, such as short bowel syndrome, were additional exclusion criteria.			
[c]Güiza et al, 2020[49]	Randomized controlled trial, Belgium, Netherlands, Canada[c]	473 PICU, 119 healthy controls; PICU = 4.0 (4.6) years, healthy controls = 4.2 (4.7) years; PICU = 58% male, healthy controls = 57% male	We aimed to test the hypothesis that DNA methylation changes occur during critical illness and that early parenteral nutrition (or a specific macronutrient component hereof) contributes to these changes, which could explain its negative effects on neurocognitive development.	**Inclusion criteria:** The PEPaNIC study included children, from full-term newborns to children aged 17 years, for whom a stay of 24 hours or more in the PICU was expected, who had a score on the Screening Tool for Risk on Nutritional Status and Growth (STRONGkids) of 2 or more (0: low risk of malnutrition; 1–3: medium risk; and 4–5: high risk), and who did not meet any of the criteria for exclusion. **Exclusion criteria:** Exclusion criteria for the control group were previous admission to a neonatal ICU or a PICU, or hospital admission for at least 7 days with need for an intravenous line, history of suspicious or established inborn chronic metabolic diseases requiring a specific diet, such as diabetes, and history of short bowel syndrome on home parenteral nutrition or other conditions that require home parenteral nutrition.	WPPSI, 2 years BRIEF, 2 years		Not indicated
Forbess et al, 2002[42]	Retrospective cohort study, USA	243 PICU; 277.3 (471.2) days; 92% white	Increased survival in children with critical congenital heart disease (CHD) has raised interest in the neurodevelopmental sequelae of these lesions. This investigation is part of an institutional effort to examine the neurodevelopment of 5-year-old children following repair or palliation of CHD.	**Inclusion criteria:** In this study, patients were eligible for inclusion if they underwent repair or palliation of congenital heart disease, were 5 years of age, and lived in New England or eastern New York. **Exclusion criteria:** Exclusion criteria included residence outside of the New England/ eastern New York region, a non–English speaking patient and family, surgery at other institutions, additional congenital syndromes known to severely affect cognition (e.g., Down syndrome or Williams syndrome), acquired cardiomyopathy, or isolated electrophysiologic interventions.	WPPSI-R, 5 years WRAML, 5 years		**Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R)** Full-scale (FSIQ) = 96.8 (15.9); range = 49-135 Verbal IQ (VIQ) = 97.8 (14.6); range = 55-135 Performance IQ (PIQ) = 96.3 (17.1); range = 49-145 **Wide Range Assessment of Memory and Learning screener (WRAML-screener)** Composite score = 97.5 (14.8); range = 19-144 Picture memory = 10.8 (3.2); range = 4-19 Design memory = 8.9 (2.1); range = 4-16 Verbal learning = 10.6 (3.1); range = 3-19 Story memory = 7.9 (2.9); range = 4-19

Gemke et al, 1995[13]	Prospective cohort study, Netherlands	226 PICU; Mean age = 55 months Median age = 24.6 months	The purpose of the present study was to assess long term survival and health related quality of life of children admitted to an ICU.	**Inclusion criteria:** Patients aged 1 month to 16 years. **Exclusion criteria:** Trauma patients excluded. Excluded from health status analysis were infants under 1 year of age, in whom MAHSC has not been validated, and survivors who stayed less than 24 hours (mainly patients for post-operative monitoring).	MAHSC, 1 year	12.4% (28/226) failed age appropriate developmental and cognitive performance	
Shevell et al, 2020[40]	Retrospective cohort study, Canada	72 PICU; 15.8 (1.7) years; 45.8% male	The relationship between patient-related factors specific to the postoperative course in the PICU following cardiac surgery with long-term neurodevelopmental outcomes in adolescents was examined.	**Inclusion criteria:** Adolescents (12–19-year-old) born between 1991 and 1999 with CHD who underwent open-heart surgery at the Montreal Children's Hospital (MCH) in Montreal, Quebec, Canada, during the first 2 years of life were recruited. Participants were included if they were English or French speaking. **Exclusion criteria:** Participants were excluded if their medical charts were unavailable at the time of review or if the participant had a known genetic abnormality or syndrome.	Leiter Brief Intelligence Quotient, 15 years	29.9% had Brief IQ less than 80.	
[d]Meert et al, 2019[51]	Prospective cohort study, USA, Canada, UK[d]	44 PICU; 80.7% < 6 years old; 64.9% male; 45.6% white	To describe one-year cognitive and neurologic outcomes among extracorporeal cardiopulmonary resuscitation (ECPR) survivors enrolled in the Therapeutic Hypothermia after Pediatric Cardiac Arrest In-Hospital (THAPCA-IH) trial; and compare outcomes between survivors who received ECPR, later extracorporeal membrane oxygenation (ECMO), or no ECMO.	**Inclusion criteria:** Only children with broadly normal pre-arrest function Children eligible for the THAPCA-IH trial were > 48 hours and < 18 years of age, had an in- hospital cardiac arrest with chest compressions for ≥ 2 minutes, and required mechanical ventilation after return of circulation. Additional inclusion criteria for this secondary analysis included having broadly normal pre-arrest neurobehavioral function defined as pre-arrest VABS-II ≥ 70, survival to 12 months, and completion of at least one 12-month follow-up measure. **Exclusion criteria:** Major exclusion criteria were a Glasgow Coma Scale motor subscale score of 5 or 6 (i.e., purposeful lateralizing response to painful stimulus), inability to be randomized within 6 hours of return of circulation, and a	MSEL (<6 years) or WASI (>6 years), 1 year	45.4% (20/44) had scores < 70	For survivors < 6 years old, 1 (2.9%) had a Mullen composite score in the above average range, 8 (23.5%) average, 6 (17.6%) below average, 9 (26.5%) impaired and 10 (29.4%) severely impaired. For survivors ≥ 6 years old, 8 (80.0%) had WASI Full- Scale IQ in the average range, 1 (10.0%) below average, and 1 (10.0%) impaired.

				decision by the clinical team to withhold aggressive treatment.			
[d]Slomine et al, 2018[29]	Randomized controlled trial, USA, Canada, UK[d]	160 PICU; 2.5 (1.3 - 6.1) years; 60% male; 60.0% white	To describe the neuropsychological outcomes of CA survivors enrolled in the Therapeutic Hypothermia After Pediatric Cardiac Arrest In-Hospital (THAPCA-IH) and Out-of-Hospital (THAPCA-OH) trials and compare the results with the primary outcome measure for these trials.	**Inclusion criteria:** Children older than 48 hours and younger than 18 years who were resuscitated after out-of-hospital CA or in-hospital CA with chest compressions for 2 minutes or longer and were unresponsive and required mechanical ventilation after return of circulation met inclusion criteria. Eligibility for inclusion in the primary outcome analyses included absence of significant development delays before CA (VABS-II score ≥ 70). **Exclusion criteria:** Major exclusion criteria included trauma, inability to randomize within 6 hours of return of circulation, a Glasgow Coma Scale motor score of 5 or 6 (i.e., purposeful lateralizing response to painful stimulus), a clinical decision to withhold aggressive treatment, or non–English-speaking or Spanish-speaking parent or guardian.	MSEL (<6 years) or WASI (>6 years), 1 year	25.2% had global cognitive impairment (28/111)	**Younger than 6 years old** 50% impaired (at least 2 SD below the mean for age) Mullen score = 67 (49 – 83) **Older than 6 years old** WASI score = 90 (79 – 103)
Abend et al, 2015[36]	Prospective cohort study, USA	20 PICU; 10.6 (6.7-15.4) years; 75% male	To determine if electrographic status epilepticus (ESE) was associated with worse outcomes using more detailed neurobehavioral measures.	**Inclusion criteria:** This study only included subjects who were reported to be neurodevelopmentally normal prior to PICU admission by parents and any available prior medical records. **Exclusion criteria:** Neonates (age <1 month) were excluded.	BRIEF, 2.6 (1.2–3.8) years		No seizure (n = 11) = 54 (42 – 63) Electrographic seizure (n = 4) = 57 (46 – 65) Electrographic status epilepticus (n = 5) = 73 (59 – 79)
[e]Buysse et al, 2008[41]	Retrospective cohort study, Netherlands[e]	120 PICU; 3.1 (0.1-17.9) years; 52.5% male	To assess long-term health status in patients who survived meningococcal septic shock in childhood.	**Inclusion criteria:** All consecutive surviving patients aged 1 month to 18 years with a clinical picture of MSS and their parents were eligible for this study. **Exclusion criteria:** Those with an insufficient command of the Dutch language were excluded.	WISC III (6 to 15-year-olds) or GIT2 (16 to 31-year-olds), 9.8 years	3% of patients had severe mental retardation (total IQ < 70) with epilepsy.	
[e]Buysse et al, 2010[52]	Retrospective cohort study, Netherlands[e]	120 PICU;	The purpose of this study was to evaluate associations between long-term physical	**Inclusion criteria:** Eligible for inclusion were all consecutive surviving patients aged 1 month to 18 years	WISC III (6 to 15-year-olds) or GIT2 (16 to 31-	6.67% (8/120) of patients had total IQ < 85	

		3.1 (0.1-17.9) years; 52.5% male	and psychological outcome variables in patients who survived meningococcal septic shock (MSS) in childhood.	with a clinical picture of MSS, as well as their parents. **Exclusion criteria:** Those with insufficient command of the Dutch language were excluded.	year-olds), 9.8 years		
[e]Vermunt et al, 2009[56]	Retrospective cohort study, Netherlands[e]	66 PICU; 3 (2.7) years; 52% male	To assess long-term cognitive functioning and its predictors, in children and adolescents who survived meningococcal septic shock (MSS) 4 to 16 years ago.	**Inclusion criteria:** For the present study 106 patients, aged 6–17 years at follow-up (age range used in this study), were eligible. **Exclusion criteria:** Patients who were not Dutch speaking were excluded.	WISC, 8 (3.4) years		Mean z scores on verbal memory (15-Word Test 1–5 and long-term 15-Word Test) were significantly higher than the mean z scores of FSIQ, VIQ and PIQ (all $p < .05$). All these differences remained significant after Bonferroni's correction for multiple independent testing.
[e]Vermunt et al, 2011[57]	Cross-sectional study, Netherlands[e]	58 PICU; At follow-up median (range) = 21 (16-31) years; 48.3% male	To investigate long-term psychosocial outcomes in young adults who survived septic shock caused by Neisseria meningitidis (meningococcal septic shock) during childhood. To explore biographical characteristics (such as living conditions, educational, occupational, and marital status) and illness-related physical or social consequences a structured interview was used. To assess intellectual functioning the Groninger Intelligence Test 2 was used and to assess behavioral/ emotional problems, the Adult Self-Report was used.	**Inclusion criteria:** For the present study, patients aged 16–31 years were included. **Exclusion criteria:** Patients with insufficient command of the Dutch language were excluded.	GIT2, 13 years Structured interview, 13 years ASR, 13 years		**Groninger intelligence test 2, intelligence quotient** Meningococcal septic shock = 96.2 (13.9) Reference group = 100 (15) $p = 0.07$ **Verbal comprehension** Meningococcal septic shock = 4.74 (1.9) Reference group = 5.3 (2) $p < 0.05$ **Visualization** Meningococcal septic shock = 5.57 (2.1) Reference group = 5.2 (2) $p = 0.25$ **Closure** Meningococcal septic shock = 5.89 (1.9) Reference group = 5.1 (2) $p < 0.01$ **Number** Meningococcal septic shock = 4.37 (2.2) Reference group = 5.1 (2) $p < 0.05$ **Reasoning/ induction/ deduction** Meningococcal septic shock = 4.76 (2.1) Reference group = 5.3 (2) $p = 0.09$ **Word fluency**

							Meningococcal septic shock = 4 (1.6) Reference group = 5.1 (2) p < 0.01
Mesotten et al, 2012[27]	Randomized controlled trial, Belgium	456 PICU (usual care = 234, tight glycemic control = 222), 216 healthy controls; At follow-up: PICU = 5.2 (4.2-8.3) years, Healthy controls = 6.7 (4.7-11.5) years; PICU = 57.24% male, healthy controls = 43.52% male; PICU = 93.42% white, Healthy controls = 97.69% white	As both hyperglycemia and hypoglycemia may adversely affect the developing brain, long-term follow-up was required to exclude harm and validate short- term benefits of tight glycemic control (TGC).	**Inclusion criteria:** Not indicated **Exclusion criteria:** Not indicated	WIQS, 3 years		Full-scale IQ scores were 9 points lower in post-ICU patients than in healthy control children (95% CI, 6-12; P < .001). PICU usual care = 88.5 (74.3–99.0) PICU TGC = 88.0 (74.0–100.0) Healthy controls = 103 (91–111)
Meyburg et al, 2018[47]	Single-center point prevalence study, Germany	47 PICU; 5.1 (4.6) years; 51.10% male	To investigate the long-term impact of postoperative delirium in children.	**Inclusion criteria:** Ninety patients who participated in a prospective study on PD and received intensive care between April 2014 and October 2014 following major surgery (in which the operation had been electively planned, and postoperative treatment in the PICU was highly likely prior to surgery) were included into this follow-up study 12–24 months after the initial PICU hospitalization. **Exclusion criteria:** Not indicated	Bayley-III, 17.7 ± 2.9 months WIQS, 17.7 ± 2.9 months WPPSI, 17.7 ± 2.9 months		Although children's cognitive performance was in the normal range at the follow-up evaluation, the mean cognitive score in PICU survivors was significantly lower than in the normal population (t [df 45] = –3.679; p = 0.001; mean difference, –11.17; 95% CI, –17.29 to –5.06). Respectively, the proportion of patients with cognitive delay or cognitive impairment was substantially higher than in the normal population.
Shein et al, 2020[45]	Retrospective cohort study, USA	18 PICU; Median (IQR) age at follow-up = 2.3 (1.9–2.8) years; 78% male	To assess the long-term outcomes of initially normally developing children who had survived critical bronchiolitis.	**Inclusion criteria:** Inclusion criteria were (1) PICU admission at age < 2 years with a diagnosis of bronchiolitis and (2) age 18 to 36 months at the time of invitation to this study	Bayley-III, 1.8 (1.7–2.2) years	Cognitive domain Moderate disability = 16.7%	

				Exclusion criteria: Children who were already > 36 months at the onset of this study were excluded. Additional exclusion criteria were (1) abnormal developmental status at the time of PICU admission and (2) any subsequent PICU admission after the index bronchiolitis admission.		Severe disability = 5.6% Language domain Moderate disability = 35.3% Severe disability = 5.9% Motor domain Moderate disability = 35.3% Severe disability = 0%	
Lequier et al, 2008[37]	Prospective cohort study, Canada	16 PICU; 53 (12) months; 51% male	Comprehensive outcome assessment of children receiving cardiac extracorporeal life support.	**Inclusion criteria:** All consecutive patients given venoarterial cardiac-related ECLS at an age of less than 5 years over the 5-year period were registered. **Exclusion criteria:** There were no exclusion criteria.	Bayley-II or WPPSI, 53 (12) months		Intelligence score = 73 (16) (ranged from less than 55 to 116) Normal intelligence score = 100 (15) Overall, 8 (50%) survivors had mental delay (mental score < 70.
Bronner et al, 2009[39]	Retrospective cohort study, Netherlands	50 PICU; Median age = 4.2 years, range = 0.0–17.0 years; 54% male	To evaluate self-reported health-related quality of life, anxiety, depression, and cognitive function in pediatric septic shock survivors.	**Inclusion criteria:** Previously, healthy children who survived septic shock in our PICU between 1995 and 2004 were included in this study. Inclusion criteria were survival of the clinical diagnosis of septic shock according to the Conference Consensus Criteria, the administration of inotropic and/or vasoconstrictive agents for ≥ 24 hrs, and age ≥ 8 yrs at the time of the follow-up study. **Exclusion criteria:** Children with language barriers were excluded due to the inability to complete Dutch questionnaires. In addition, children < 8 years were excluded because they were unable to complete the questionnaires by themselves.	TACQOL, 6.5 yrs (range, 1.5–10.1 yrs)		PICU patients with septic shock (n = 31) = 25.2 (4.9) Healthy controls = 28.4 (3.9) Effect size = 0.8 $p < 0.05$ 44% of the children had cognitive scores < 25% of the norm population.

Emotional and Behavioral Problems (Adjustment Difficulties)							
Verstraete et al, 2016[7]	Retrospective cohort study, Belgium	449 PICU (developmental cohort = 228, validation cohort = 221), 100 healthy controls; 3.4 (2.9-4.0) years for development cohort, 3.3 (2.7-3.8) for validation cohort, 4.2 (3.5-4.9) for healthy controls; 54.0% male for developmental cohort, 60.2% male for validation cohort, 58.0% male for healthy children; 96.1% white for developmental cohort, 90.5% white for validation cohort, 93.0% white for healthy children	The primary study aim was to assess, in a multivariable regression analysis adjusting for other risk factors, the presence of an independent association between ''exposure'' to the total circulating DEHP metabolites during PICU stay and the attention deficit 4 years later. Secondary study aims were similar analyses for the other neurocognitive outcomes, and for the individual DEHP metabolites and the sum of MEHP metabolites.	**Inclusion criteria:** Critically ill infants and children (0–16 years upon PICU admission). Anticipated to require intensive care for at least 24-hours. Plasma taken during PICU admission. Undergone neurocognitive testing at 4-year follow-up. **Exclusion criteria:** Estimated stay in PICU < 24-hours. Therapy restriction upon admission. Other study enrolment. No informed consent. Lost to follow-up.	CBCL, 4 years		**Total problems** PICU: developmental cohort = 52 (95% CI = 51–54); validation cohort = 52 (95% CI = 51–54) Healthy controls = 48 (95% CI = 46–49) **Internalizing problems** PICU: developmental cohort = 54 (95% CI = 52–55); validation cohort = 52 (95% CI = 51–54) Healthy controls = 49 (95% CI = 47–50) **Externalizing problems** PICU: developmental cohort = 50 (95% CI = 49–52); validation cohort = 50 (95% CI = 49–52) Healthy controls = 48 (95% CI = 46–49)
[c]Verstraete et al, 2019[26]	Randomized controlled trial, Belgium, Netherlands, Canada[c]	391 PICU, 405 healthy controls; Age at 2-year follow-up: PICU = 5.7 (4.5), healthy controls = 6.0 (4.7); 58% male for PICU, 54% male for healthy controls;	We aimed to investigate whether withholding supplemental parenteral nutrition during the first week in PICU, rather than giving parenteral nutrition to reach nutritional targets as soon as possible, while adequately providing micronutrients, has an impact on survival, health status, and anthropometrics, clinically assessed neurological	**Inclusion criteria:** Admitted to participating PICUs. Written informed consent from parents or legal guardians or from the adolescent according to local regulations. Siblings and relatives of the patients were preferably recruited into the control group besides unrelated children recruited from the same geographical area. **Exclusion criteria:** Exclusion criteria for the control group were previous admission to a neonatal ICU or a PICU, or hospital admission for at least 7	CBCL, 2 years		**Total problems** PICU (n = 391) = 51.6 (13.0) Healthy controls (n = 405) = 46.1 (10.4) **Internalizing problems** PICU (n = 391) = 51.4 (13.3) Healthy controls (n = 405) = 46.7 (10.7) **Externalizing problems** PICU (n = 391) = 50.5 (12.7) Healthy controls (n = 405) = 46.8 (10.1)

		92% white for PICU and healthy controls	function, and parent-reported or caregiver-reported and clinically tested neurocognitive outcomes at the 2-year follow-up, compared with matched healthy children.	days with need for an intravenous line, history of suspicious or established inborn chronic metabolic diseases requiring a specific diet, such as diabetes, and history of short bowel syndrome on home parenteral nutrition or other conditions that require home parenteral nutrition.			
[c]Jacobs et al, 2020[50]	Randomized controlled trial, Belgium, Netherlands, Canada[c]	684 PICU, 369 healthy controls; PICU = 7·3 (4·3) years, healthy controls = 7·5 (4·3) years; PICU = 55% male, Healthy controls = 57% male; PICU = 92% white, healthy controls = 93% white	We aimed to determine the effect of late-parenteral nutrition versus early-parenteral nutrition on physical, neurocognitive, and emotional and behavioral development 4 years after randomization.	**Inclusion criteria:** Healthy children were only included if they had not been previously admitted to a neonatal or pediatric intensive care unit, or admitted to hospital with need for an intravenous line for 7 days or more. **Exclusion criteria:** History of inborn chronic metabolic diseases requiring a specific diet, such as diabetes, and conditions that require home parenteral nutrition, such as short bowel syndrome, were additional exclusion criteria.	CBCL, 4 years		**Total problems** PICU (n = 684) = 50·1 (11·9) Healthy controls (n = 369) = 45·4 (9·9) **Internalizing problems** PICU (n = 684) = 51·0 (12·3) Healthy controls (n = 369) = 46·7 (10·5) **Externalizing problems** PICU (n = 684) = 48·8 (11·2) Healthy controls (n = 369) = 45·6 (9·7)
[c]Güiza et al, 2020[49]	Randomized controlled trial, Belgium, Netherlands, Canada[c]	473 PICU, 119 healthy controls; PICU = 4.0 (4.6) years, healthy controls = 4.2 (4.7) years; PICU = 58% male, healthy controls = 57% male	We aimed to test the hypothesis that DNA methylation changes occur during critical illness and that early parenteral nutrition (or a specific macronutrient component hereof) contributes to these changes, which could explain its negative effects on neurocognitive development.	**Inclusion criteria:** The PEPaNIC study included children, from full-term newborns to children aged 17 years, for whom a stay of 24 h or more in the PICU was expected, who had a score on the Screening Tool for Risk on Nutritional Status and Growth (STRONGkids) of 2 or more (0: low risk of malnutrition; 1–3: medium risk; and 4–5: high risk), and who did not meet any of the criteria for exclusion. **Exclusion criteria:** Exclusion criteria for the control group were previous admission to a neonatal ICU or a PICU, or hospital admission for at least 7 days with need for an intravenous line, history of suspicious or established inborn chronic metabolic diseases requiring a specific diet, such as diabetes, and history of short bowel syndrome on home parenteral nutrition or other conditions that require home parenteral nutrition.	CBCL, 2 years		Not indicated

Abend et al, 2015[36]	Prospective cohort study, USA	20 PICU; 10.6 (6.7-15.4) years; 75% male	To determine if electrographic status epilepticus (ESE) was associated with worse outcomes using more detailed neurobehavioral measures.	**Inclusion criteria:** This study only included subjects who were reported to be neurodevelopmentally normal prior to PICU admission by parents and any available prior medical records. **Exclusion criteria:** Neonates (age < 1 month) were excluded.	ABAS-II, 2.6 (IQR 1.2–3.8) years CBCL, 2.6 (IQR 1.2–3.8) years		**ABAS-II score (n = 32)** No seizures = 105 (100–118) Electrographic seizures = 92 (47–106) Electrographic status epilepticus = 73 (48–102) **CBCL score (n = 36)** No seizures = 43 (37–54) Electrographic seizures = 37 (34–52) Electrographic status epilepticus = 61 (34–65)
[e]Buysse et al, 2010[52]	Retrospective cohort study, Netherlands[e]	120 PICU; 3.1 (0.1-17.9) years; 52.5% male	The purpose of this study was to evaluate associations between long-term physical and psychological outcome variables in patients who survived meningococcal septic shock (MSS) in childhood.	**Inclusion criteria:** Eligible for inclusion were all consecutive surviving patients aged 1 month to 18 years with a clinical picture of MSS, as well as their parents. **Exclusion criteria:** Those with insufficient command of the Dutch language were excluded.	CBCL, median follow-up = 9.8 years	5.83% (7/120) had problem behavior.	
Mesotten et al, 2012[27]	Randomized controlled trial, Belgium	456 PICU (usual care = 234, tight glycemic control = 222), 216 healthy controls; At follow-up: PICU = 5.2 (4.2-8.3) years, Healthy controls = 6.7 (4.7-11.5) years; PICU = 57.24% male, healthy controls = 43.52% male; PICU = 93.42% white, Healthy controls = 97.69% white	As both hyperglycemia and hypoglycemia may adversely affect the developing brain, long-term follow-up was required to exclude harm and validate short- term benefits of tight glycemic control (TGC).	**Inclusion criteria:** Not indicated **Exclusion criteria:** Not indicated	CBCL, 3 years		**CBCL internalizing** Healthy controls = 48 (41 – 57) Usual care = 52 (45 – 61) TGC = 55 (45 – 61) **CBCL externalizing** Healthy controls = 46 (40 – 55) Usual care = 50 (42 – 57) TGC = 51 (44 – 56) **CBCL total problems** Healthy controls = 47 (40 – 55) Usual care = 52 (45 – 59) TGC = 53 (45 – 59)
[e]Vermunt et al, 2008[55]	Retrospective cohort study, Netherlands[e]	89 PICU; 6 – 17 years old	To assess the occurrence of a wide range of behavioral, emotional, and post-	**Inclusion criteria:** 6 to 17 year old patients who survived MSS and were admitted to the PICU of the	CBCL, at least 4 years	The proportion of older MSS boys (12-17	**<u>Mothers' scoring of child</u>** CBCL internalizing (mean) MSS (n = 86) = 7.3

			traumatic stress problems in children and adolescents, long term after septic shock caused by Neisseria meningitidis (MSS).	Medical Centre between 1988 and 2001. Eligible were consecutive surviving patients with a clinical picture of meningococcal septic shock (MSS), who required intensive care treatment at the PICU of Erasmus MC-Sophia Children's Hospital at least 4 years ago (between 1 August 1988 and 1 June 2001). **Exclusion criteria:** Parents and patients who were not Dutch speakers were excluded.		years) scoring in the deviant range was significantly greater (40%) than that of same-aged boys in the reference group (10%).	Reference (n = 1538) = 6.9 CBCL externalizing (mean) MSS (n = 86) = 6.7 Reference (n = 1538) = 6.7 CBCL total problems MSS (n = 86) = 26.9 Reference (n = 1538) = 25.4 Fathers' scoring of child CBCL internalizing (mean) MSS (n = 78) = 6.3 Reference (n = 1538) = 6.9 CBCL externalizing (mean) MSS (n = 78) = 6.3 Reference (n = 1538) = 6.7 CBCL total problems MSS (n = 78) = 24.5 Reference (n = 1538) = 25.4
Boeschoten et al, 2020[30]	Prospective cohort study, Netherlands	50 PICU, 62 General ward; PICU = 8 (6-12) years, General ward = 5 (3-6) years; PICU = 62% male, General ward = 57% male	To prospectively evaluate quality of life (QoL) and psychosocial outcomes in children with severe acute asthma (SAA) after pediatric intensive care (PICU) admission compared to children with SAA who were admitted to a general ward (GW).	**Inclusion criteria:** All children (2-18 years old) with SAA admitted to all seven Dutch academic PICUs (N = 110) and the pediatric wards of four participating general hospitals (N = 111). **Exclusion criteria:** Not indicated	CBCL, 5 (1-12) months		**CBCL total problems (mean (SD))** PICU (n = 10) = 39.4 (14.3) GW (n = 1) = 60 **Internalizing problems (mean (SD))** PICU (n = 10) = 7.3 (5.9) GW (n = 1) = 7 **Externalizing problems (mean (SD))** PICU (n = 10) = 8.1 (4.1) GW (n = 1) = 12
Biagas et al, 2020[31]	Prospective cohort study, USA	214 PICU; 10.1 (5.1-14.1) years; 50% male	To investigate adaptive skills, behavior, and quality health-related quality of life (HRQoL) in children.	**Inclusion criteria:** Patients aged 2 to 16 years old enrolled between April 2012 and September 2016 were studied one-year post-ICU discharge. **Exclusion criteria:** Patients were excluded from follow up if they did not survive, were under the care of persons with insufficient knowledge about regular behavior to complete assessment, or for whom consent was withdrawn.	VABS-II, 1 year CBCL, 1 year		**VABS-II** Lower glycemic target (n=97) = 79.9 (25.5) Higher glycemic target (n=111) = 79.4 (26.9) **CBCL total problems** Lower glycemic target (n=101) = 51.5 (12.0) Higher glycemic target (n=110) = 51.9 (12.5) **CBCL internalizing problems** Lower glycemic target (n=101) = 52.2 (11.4) Higher glycemic target (n=110) = 51.6 (11.8)

							CBCL externalizing problems Lower glycemic target (n=101) = 49.6 (11.6) Higher glycemic target (n=110) = 48.9 (10.9)
Fiser et al, 2000[48]	Cross-sectional analysis with prospective follow-up, USA	143 PICU; 5.96 (5.99) years; 62% male; 68% white	The purpose of this study is to significantly extend the research on two such promising measures: the Pediatric Overall Performance Category (POPC) and the Pediatric Cerebral Performance Category (PCPC).	**Inclusion criteria:** Subjects were recruited if the child's age was < 21 yrs and if the child was discharged from the PICU, and subsequently from the hospital, after an emergent PICU admission during the 34-month enrollment period. **Exclusion criteria:** Previous participants and siblings of participating subjects were ineligible to participate. Children with PCPC scores of 5 or 6 at the time of hospital discharge were excluded. Children discharged to homes in which their mothers were not residing were excluded, except for a few rare cases in which children in PCPC category 4 were living in institutional settings or foster care.	VABS-II, 6 months		Vineland Adaptive Behavior Scales scores varied significantly across Pediatric Overall Performance Category (POPC) categories ($p < .0001$). The "normal" category-1 children improved an average of 6 points from 1 month to 6 months after discharge ($p < .001$), whereas the category-2 children experienced a decrease in function with a mean decline of 4.1 points ($p < .02$). There were no statistically significant differences over time for categories 3 and 4.
[d]Meert et al, 2019[51]	Prospective cohort study, USA, Canada, UK[d]	44 PICU; 80.7% < 6 years old; 64.9% male; 45.6% white	To describe one-year cognitive and neurologic outcomes among extracorporeal cardiopulmonary resuscitation (ECPR) survivors enrolled in the Therapeutic Hypothermia after Pediatric Cardiac Arrest In-Hospital (THAPCA-IH) trial; and compare outcomes between survivors who received ECPR, later extracorporeal membrane oxygenation (ECMO), or no ECMO.	**Inclusion criteria:** Only children with broadly normal pre-arrest function Children eligible for the THAPCA-IH trial were > 48 hours and < 18 years of age, had an in-hospital cardiac arrest with chest compressions for ≥ 2 minutes, and required mechanical ventilation after return of circulation. Additional inclusion criteria for this secondary analysis included having broadly normal pre-arrest neurobehavioral function defined as pre-arrest VABS-II ≥ 70, survival to 12 months, and completion of at least one 12-month follow-up measure. **Exclusion criteria:** Major exclusion criteria were a Glasgow Coma Scale motor subscale score of 5 or 6 (i.e., purposeful lateralizing response to painful stimulus), inability to be randomized within 6 hours of return of circulation, and a decision by the clinical team to withhold aggressive treatment.	VABS-II , 1 year	16 (29.1%) ECPR survivors had VABS-II scores < 70	

[d]Slomine et al, 2018[29]	Randomized controlled trial, USA, Canada, UK[d]	160 PICU; 2.5 (1.3 - 6.1) years; 60% male; 60.0% white	To describe the neuropsychological outcomes of CA survivors enrolled in the Therapeutic Hypothermia After Pediatric Cardiac Arrest In-Hospital (THAPCA-IH) and Out-of-Hospital (THAPCA-OH) trials and compare the results with the primary outcome measure for these trials.	**Inclusion criteria:** Children older than 48 hours and younger than 18 years who were resuscitated after out-of-hospital CA or in-hospital CA with chest compressions for 2 minutes or longer and were unresponsive and required mechanical ventilation after return of circulation met inclusion criteria. Eligibility for inclusion in the primary outcome analyses included absence of significant development delays before CA (VABS-II score ≥ 70). **Exclusion criteria:** Major exclusion criteria included trauma, inability to randomize within 6 hours of return of circulation, a Glasgow Coma Scale motor score of 5 or 6 (i.e., purposeful lateralizing response to painful stimulus), a clinical decision to withhold aggressive treatment, or non–English-speaking or Spanish-speaking parent or guardian.	VABS-II, 1 year	28.8% (46/160) scored VABS-II < 70	
[f]Melnyk et al, 2004[28]	Randomized controlled trial, USA[f]	163 PICU; 50.3 (18.9) months; 60.7% male, 71.2% white	Primary outcomes included maternal anxiety, negative mood state, depression, maternal beliefs, parental stress, and parent participation in their children's care, as well as child adjustment, which was assessed with the Behavioral Assessment System for Children (parent form).	**Inclusion criteria:** All mothers who could read and speak English with children admitted to either of the 2 PICU study sites were eligible to participate if their children 1) had an unplanned medical or surgical admission to the PICU, 2) were between 2 and 7 years of age, 3) were expected to survive, 4) had no prior ICU admissions, 5) had no cancer, and 6) had no suspected or diagnosed physical or sexual abuse. **Exclusion criteria:** Mothers were excluded from data analysis if 1) their children were readmitted to the PICU after transfer from the PICU to the general pediatric unit, 2) their children were hospitalized in the PICU for > 21 days, or 3) they made a personal decision to withdraw from the study.	BASC, 3, 6, and 12 months	25.9% of control group children have clinically significant behavioral symptoms 1 year after PICU admission.	**BASC Behavior Symptoms Composite (mean (SD))** 3mth (n = 40) = 307.7 (69.1) 6mth (n = 34) = 299.6 (59.9) 12mth (n = 25) = 320.5 (72.9) **BASC Externalizing Behaviors Composite (mean (SD))** 3mth (n = 41) = 107.9 (28.2) 6mth (n = 34) = 103.6 (27.5) 12mth (n = 25) = 111/6 (28.3)
[f]Small et al, 2006[53]	Randomized controlled trial, USA[f]	76 PICU; 50.3 (18.9) months;	The purpose of this predictive secondary analysis was to determine demographic and clinical	**Inclusion criteria:** All mothers who could read and speak English with children admitted to either of the 2 PICU study sites were eligible to	PBQ, 3 and 6 months BASC		**Post-Hospital Behavior Questionnaire (PBQ)** 3mth = 84.8 (11.6) 6mth = 83.5 (7.4)

		60.7% male, 71.2% white	variables that could be assessed early during hospitalization to predict internalizing and externalizing behaviors and negative behavioral change of 2- to 7-year-old children at 3 and 6 months following an unanticipated critical care hospitalization	participate if their children 1) had an unplanned medical or surgical admission to the PICU, 2) were between 2 and 7 years of age, 3) were expected to survive, 4) had no prior ICU admissions, 5) had no cancer, and 6) had no suspected or diagnosed physical or sexual abuse. **Exclusion criteria:** Mothers were excluded from data analysis if 1) their children were readmitted to the PICU after transfer from the PICU to the general pediatric unit, 2) their children were hospitalized in the PICU for > 21 days, or 3) they made a personal decision to withdraw from the study.	internalizing behaviors, 3 and 6 months BASC externalizing behaviors, 3 and 6 months		**BASC internalizing behaviors** 3mth = 150.8 (36.9) 6mth = 149.0 (31.4) **BASC externalizing behaviors** 3mth = 103.2 (24.4) 6mth = 101.3 (21.7)
[f]Small et al, 2009[54]	Randomized controlled trial, USA[f]	163 PICU; 50.3 (18.9) months; 60.7% male, 71.2% white	A prior evaluation of the predictors of child coping outcomes following an unanticipated critical hospitalization revealed gender differences, which were explored in this study to examine patterns of behavioral change over time.	**Inclusion criteria:** All mothers who could read and speak English with children admitted to either of the 2 PICU study sites were eligible to participate if their children 1) had an unplanned medical or surgical admission to the PICU, 2) were between 2 and 7 years of age, 3) were expected to survive, 4) had no prior ICU admissions, 5) had no cancer, and 6) had no suspected or diagnosed physical or sexual abuse. **Exclusion criteria:** Data from mother–child dyads were excluded from these analyses if the child had a prior hospitalization experience, a diagnosis of childhood cancer was made at any point prior to or during the study period, the intensive care period extended beyond 21 days, the child experienced a hospital readmission during the 6-month post-hospitalization period, any suspected child abuse or neglect was uncovered, or the mother had made the decision to withdraw from primary study participation.	BASC, 3 and 6 months PBQ, 3 and 6 months		**BASC externalizing** 3 months (n = 88) = 101.92 (24.07) 6 months (n = 66) = 100.17 (21.44) **BASC internalizing** 3 months (n = 85) = 150.24 (37.27) 6 months (n = 63) = 149.26 (32.21) **PBQ (n = 55)** 3 months = 83.75 (11.21) 6 months = 83.10 (7.37)
Lequier et al, 2008[37]	Prospective cohort study, Canada	16 PICU; 53 (12) months; 51% male	Comprehensive outcome assessment of children receiving cardiac extracorporeal life support.	**Inclusion criteria:** All consecutive patients given venoarterial cardiac-related ECLS at an age of less than 5 years over the 5-year period were registered.	MAHSC, 53 (12) months ABAS-II, 53 (12) months	88% (14/16) had behavioral concerns: 62.5% (10/16) were noted to	ABAS = 79 (19)

				Exclusion criteria: There were no exclusion criteria.		have behavioral abnormalities by physicians and 69% (11/16) noted to have behavioral concerns by parents on the MAHSC	
Gemke et al, 1995[13]	Prospective cohort study, Netherlands	226 PICU; Mean age = 55 months Median age = 24.6 months	The purpose of the present study was to assess long term survival and health related quality of life of children admitted to an ICU.	**Inclusion criteria:** Patients aged 1 month to 16 years. **Exclusion criteria:** Trauma patients excluded. Excluded from health status analysis were infants under 1 year of age, in whom MAHSC has not been validated, and survivors who stayed less than 24 hours (mainly patients for post-operative monitoring).	MAHSC, 1 year	Emotional deterioration was found in 50/226 (22.1%).	
Shevell et al, 2020[40]	Retrospective cohort study, Canada	72 PICU; 15.8 (1.7) years; 45.8% male	The relationship between patient-related factors specific to the postoperative course in the PICU following cardiac surgery with long-term neurodevelopmental outcomes in adolescence was examined.	**Inclusion criteria:** Adolescents (12–19 year old) born between 1991 and 1999 with CHD who underwent open-heart surgery at the Montreal Children's Hospital (MCH) in Montreal, Quebec, Canada, during the first 2 years of life were recruited. Participants were included if they were English or French speaking. **Exclusion criteria:** Participants were excluded if their medical charts were unavailable at the time of review or if the participant had a known genetic abnormality or syndrome.	SDQ, 15 years	23.7% had behavioral challenges (with greater difficulties in subscores for emotional symptoms (32.9%) and peer problems (38.1%)).	
Kyösti et al, 2019[43]	Retrospective cohort study, Finland	1105 PICU; 4.66 (5.52) years; 54.6% male	We investigated the long-term psychologic symptoms of patients who survived pediatric intensive care admission.	**Inclusion criteria:** This study included all children who were less than 17 years old at admission to PICUs or to general ICUs in Finland between January 1, 2009, and December 31, 2010, and who were alive on July 1, 2015. **Exclusion criteria:** Not indicated	SDQ, 6.33 (0.68) years	7.2% (80/1105) had borderline scores 7.6% (84/1105) had abnormal scores.	**Age** 5 to 10 years old = 8.1 (5.6) More than 11 years old = 8.7 (5.4) **SDQ subscale scores** Total difficulties = 8.2 (5.5) Emotional problems = 1.7 (1.9) Conduct problems = 1.7 (1.6) Hyperactivity = 3.0 (2.4) Peer problems = 1.8 (1.8)

							Prosocial = 7.7 (2.0) Impact score = 0.7 (1.7)
[a]Rennick et al, 2002[5]	Prospective cohort study, Canada[a]	60 PICU, 60 ward controls; PICU = 11.33 (3.22) years Ward (control) = 11.33 (3.30) years; PICU = 50% male, Ward controls = 40% male	The purposes of this study were to compare the psychological responses of children hospitalized in a PICU with those of children hospitalized on a general ward and to identify clinically relevant factors that might be associated with psychological outcome.	**Inclusion criteria:** Eligible children were (1) between 6 and 17 years of age; (2) had been in the PICU at least 24 hours and were ready for discharge; (3) understood and spoke English or French; and (4) had at least one parent who read, wrote, and spoke English or French. **Exclusion criteria:** Not indicated	CHLOC, 6 months PBQ, 6 months		**CHLOC score** PICU = 0.72 (0.17) Controls = 0.74 (0.17) **PBQ score** PICU = 77.0 (8.04) Controls = 76.97 (9.36)
[a]Rennick et al, 2004[10]	Retrospective cohort study, Canada[a]	60 PICU; Low risk of psychological sequelae (n = 40) = 11.5 (10.5–12.5), High risk of psychological sequelae (n = 20) = 11.1 (9.5–12.6); Low risk = 47.5% male, High risk = 55.0% male	To identify those patients in a pediatric intensive care unit who may be at highest risk for developing persistent psychological sequelae after hospital discharge.	**Inclusion criteria:** Children were between 6 and 17 years of age, had been in the PICU for at least 24 hours, and were judged by the attending physician as ready for discharge. Children understood and spoke either English or French, and at least one of the children's parents read, wrote, and spoke English or French. **Exclusion criteria:** Not indicated	CHLOC, 6 months		Low risk of psychological sequelae (n = 40) = 0.74 (95% CI = 0.69 – 0.79) High risk of psychological sequelae (n = 20) = 0.70 (95% CI = 0.61 – 0.79)
Attention deficits							
Verstraete et al, 2016[7]	Retrospective cohort study, Belgium	449 PICU (developmental cohort = 228, validation cohort = 221), 100 healthy controls; 3.4 (2.9-4.0) for development cohort, 3.3 (2.7-3.8) for validation cohort, 4.2 (3.5-	The primary study aim was to assess, in a multivariable regression analysis adjusting for other risk factors, the presence of an independent association between ''exposure'' to the total circulating DEHP metabolites during PICU stay and the attention deficit 4 years later. Secondary study aims were	**Inclusion criteria:** Critically ill infants and children (0–16 years upon PICU admission). Anticipated to require intensive care for at least 24-hours. Plasma taken during PICU admission. Undergone neurocognitive testing at 4-year follow-up. **Exclusion criteria:** Estimated stay in PICU < 24-hours. Therapy restriction upon admission. Other study enrolment. No informed consent. Lost to follow-up.	ANTB, 4 years		**Reaction time dominant hand (msec)** Healthy children = 558 (95% CI = 521–595) Development cohort = 697 (95% CI = 649–745) Validation cohort = 730 (95% CI = 682–778) **Reaction time nondominant hand (msec)** Healthy children = 562 (95% CI = 542–600) Development cohort = 670 (95% CI = 626–713) Validation cohort = 709 (95% CI = 663–754)

		4.9) for healthy controls; 54.0% male for developmental cohort, 60.2% male for validation cohort, 58.0% male for healthy children; 96.1% white for developmental cohort, 90.5% white for validation cohort, 93.0% white for healthy children	similar analyses for the other neurocognitive outcomes, and for the individual DEHP metabolites and the sum of MEHP metabolites.				**Reaction time overall (msec)** Healthy children = 560 (95% CI = 524–596) Development cohort = 680 (95% CI = 635–724) Validation cohort = 718 (95% CI = 672–764)
[c]Jacobs et al, 2020[50]	Randomized controlled trial, Belgium, Netherlands, Canada[c]	684 PICU, 369 healthy controls; PICU = 7·3 (4·3) years, healthy controls = 7·5 (4·3) years; PICU = 55% male, Healthy controls = 57% male; PICU = 92% white, healthy controls = 93% white	We aimed to determine the effect of late-parenteral nutrition versus early-parenteral nutrition on physical, neurocognitive, and emotional and behavioral development 4 years after randomization.	**Inclusion criteria:** Healthy children were only included if they had not been previously admitted to a neonatal or pediatric intensive care unit or admitted to hospital with need for an intravenous line for 7 days or more. **Exclusion criteria:** History of inborn chronic metabolic diseases requiring a specific diet, such as diabetes, and conditions that require home parenteral nutrition, such as short bowel syndrome, were additional exclusion criteria.	ANTB, 4 years		**Reaction time right hand (Z score)** PICU patients = 1.7 (12.6) Healthy controls = 0.8 (4.3) **Reaction time left hand (Z score)** PICU patients = 1.0 (5.8) Healthy controls = 0.3 (2.5)
Mesotten et al, 2012[27]	Randomized controlled trial, Belgium	456 PICU (usual care = 234, tight glycemic control = 222), 216 healthy controls; At follow-up: PICU = 5.2 (4.2-8.3) years, Healthy controls = 6.7	As both hyperglycemia and hypoglycemia may adversely affect the developing brain, long-term follow-up was required to exclude harm and validate short-term benefits of TGC.	**Inclusion criteria:** Not indicated **Exclusion criteria:** Not indicated	ANTB, 3 years		**Reaction time dominant hand (msec)** Healthy children = 488 (320–704) Usual care PICU cohort = 679 (449–938) Tight glycemic control PICU cohort = 641 (383–933) **Reaction time nondominant hand (msec)** Healthy children = 501 (326–729) Usual care PICU cohort = 647 (458–933) Tight glycemic control PICU cohort = 612 (362–925)

		(4.7-11.5) years; PICU = 57.24% male, healthy controls = 43.52% male; PICU = 93.42% white, Healthy controls = 97.69% white					
Developmental delay							
Berger et al, 2018[14]	Prospective cohort study, USA	111 PICU; 86% less than 3 months old at admission; 41% male; 73% white	The aim of this study was to assess cognitive development of infants with critical pertussis 1 year after pediatric intensive care unit (PICU) discharge.	**Inclusion criteria:** Eligible patients had laboratory confirmation of pertussis infection, were < 1 year of age, and were admitted to the PICU for at least 24 hours. **Exclusion criteria:** Died prior to one year follow-up or lost to follow-up	MSEL, 1 year	21% (23/111) patients had expressive language delay and 14% (16/111) had delays in the receptive language domain.	
Ballweg et al, 2007[15]	Retrospective cohort study, USA	188 PICU; 38.5 (2.1) weeks; 41% male; 70% white	To determine whether early post- operative hyperglycemia after cardiac surgery in infants is associated with a worse neurodevelopmental outcome at 1 year of age.	**Inclusion criteria:** Patients younger than 6 months of age who were undergoing repair of congenital cardiac defects using cardio- pulmonary bypass, with or without DHCA, were eligible for the original study. **Exclusion criteria:** Exclusion criteria at the time of surgical intervention included (1) multiple congenital anomalies, (2) recognizable genetic or phenotypic syndrome other than chromosome 22q11 microdeletions at birth, or (3) language other than English spoken in the home. Patients undergoing more than one operation with cardiopulmonary bypass or more than one episode of DHCA were excluded from the secondary analysis.	MDI, 6 months PDI, 6 months		**Mental Developmental Index (MDI)** PICU = 90.6 (14.9) Normal healthy population scores = 100 (15) **Psychomotor Developmental Index** (PDI) = 81.6 (17.2) Normal healthy population scores = 100 (15)
Limperopoulos et al, 2002[38]	Prospective cohort study, Canada	61 PICU; 20.1 (7.8) months	To determine the prevalence of persistent developmental impairments in children with congenital heart defects and	**Inclusion criteria:** Subjects included term infants with a diagnosis of a CHD undergoing their first corrective or palliative OHS before 2 years	GMDS, 20.7 (8.3) months	Behavioral difficulties in 33% (20/61), which included	GMDS Personal-Social = 96.2 (20.2) (range = 61 – 139) GMDS practical reasoning = 101.2 (20.7)

			to identify factors that enhance risk for an adverse outcome.	of age, with no clinical evidence of a disorder or impairment of the central nervous system due to causes other than complications of the heart defect at the time of admission for heart surgery. **Exclusion criteria:** Children with hypoplastic left heart syndrome were specifically excluded. Subjects identified as having genetic syndromes or brain malformations in the context of clinical care were specifically excluded.		an increased level of activity/ decreased attention (n = 14), decreased activity level (n = 4), and oppositional behaviors (n = 2).	(range = 37 – 141) GMDS developmental quotient = 100.6 (15.9) (range = 60 – 128)
Depression							
Bronner et al, 2009[39]	Retrospective cohort study, Netherlands	48 PICU; 4.2 (0.0 – 17.0) years; 54% male	To evaluate self-reported health-related quality of life, anxiety, depression, and cognitive function in pediatric septic shock survivors.	**Inclusion criteria:** Previously, healthy children who survived septic shock in our PICU between 1995 and 2004 were included in this study. Inclusion criteria were survival of the clinical diagnosis of septic shock according to the Conference Consensus Criteria, the administration of inotropic and/or vasoconstrictive agents for ≥ 24 hours, and age ≥ 8 years at the time of the follow-up study. **Exclusion criteria:** Children with language barriers were excluded due to the inability to complete Dutch questionnaires. In addition, children < 8 years were excluded because they were unable to complete the questionnaires by themselves.	CDI, 6.5 years		Females with septic shock (n = 22) = 5.1 (4.1) Female controls = 9.3 (6.5) Males with septic shock (n = 26) = 5.5 (4.1) Male controls = 8.2 (5.7)
Memory impairment							
Verstraete et al, 2016[7]	Retrospective cohort study, Belgium	449 PICU (developmental cohort = 228, validation cohort = 221), 100 healthy controls;	The primary study aim was to assess, in a multivariable regression analysis adjusting for other risk factors, the presence of an independent association between ‘‘exposure’’ to the total circulating DEHP	**Inclusion criteria:** Critically ill infants and children (0–16 years upon PICU admission). Anticipated to require intensive care for at least 24-hours. Plasma taken during PICU admission. Undergone neurocognitive testing at 4-year follow-up.	CMS, 4 years		**Memory span (repeating numbers forward)** Healthy control = 9 (9–10) Developmental cohort = 8 (7–9) Validation cohort = 8 (7–8) **Working memory (repeating numbers backward)**

		3.4 (2.9-4.0) years for development cohort, 3.3 (2.7-3.8) for validation cohort, 4.2 (3.5-4.9) for healthy controls; 54.0% male for developmental cohort, 60.2% male for validation cohort, 58.0% male for healthy children; 96.1% white for developmental cohort, 90.5% white for validation cohort, 93.0% white for healthy children	metabolites during PICU stay and the attention deficit 4 years later. Secondary study aims were similar analyses for the other neurocognitive outcomes, and for the individual DEHP metabolites and the sum of MEHP metabolites.	**Exclusion criteria:** Estimated stay in PICU < 24-hours. Therapy restriction upon admission. Other study enrolment. No informed consent. Lost to follow-up.			Healthy control = 11 (95% CI = 10–11) Developmental cohort = 9 (95% CI = 8–9) Validation cohort = 9 (95% CI = 8–9) **Learning index** Healthy control = 100 (range = 97–102) Developmental cohort = 92 (range = 89–94) Validation cohort = 89 (range = 86–92) **Verbal immediate index** Healthy control = 0.50 (95% CI = 0.46–0.53) Developmental cohort = 0.36 (95% CI = 0.32–0.40) Validation cohort = 0.33 (95% CI = 0.29–0.37) **Verbal delayed index** Healthy control = 0.42 (95% CI = 0.38–0.45) Developmental cohort = 0.31 (95% CI = 0.27–0.34) Validation cohort = 0.27 (95% CI = 0.23–0.30) **Verbal delayed recognition index** Healthy control = 0.96 (95% CI = 0.95–0.98) Developmental cohort = 0.93 (95% CI = 0.90–0.95) Validation cohort = 0.90 (95% CI = 0.87–0.93)
[c]Jacobs et al, 2020[50]	Randomized controlled trial, Belgium, Netherlands, Canada[c]	684 PICU, 369 healthy controls; PICU = 7.3 (4.3) years, healthy controls = 7.5 (4.3) years; PICU = 55% male, Healthy controls = 57% male; PICU = 92% white, healthy controls = 93% white	We aimed to determine the effect of late-parenteral nutrition versus early-parenteral nutrition on physical, neurocognitive, and emotional and behavioral development 4 years after randomization.	**Inclusion criteria:** Healthy children were only included if they had not been previously admitted to a neonatal or pediatric intensive care unit or admitted to hospital with need for an intravenous line for 7 days or more. **Exclusion criteria:** History of inborn chronic metabolic diseases requiring a specific diet, such as diabetes, and conditions that require home parenteral nutrition, such as short bowel syndrome, were additional exclusion criteria.	CMS, 4 years		**Memory span (repeating numbers forward)** Healthy control = 9.9 (3.1) PICU patients (n = 418) = 8.7 (4.3) **Working memory (repeating numbers backward**) Healthy control = 10.3 (3.1) PICU patients (n = 394) = 9.5 (5.3) **Learning index** Healthy control = 101.0 (22.6) PICU patients (n = 341) = 88.1 (33.2) **Verbal immediate index** Healthy control = 0.4 (0.5) PICU patients = 0.4 (1.3)

							Verbal delayed index Healthy control = 0.4 (0.7) PICU patients = 0.4 (1.6) **Verbal delayed recognition index** Healthy control = 0.9 (0.5) PICU patients = 0.9 (1.3)
Elison et al, 2008[46]	Case control study, United Kingdom	16 PICU, 16 healthy controls; PICU = 9.44 ± 2.85 years, Controls = 9.5 ± 2.97 years; 68.8% male, 56.2% white	This pilot study explored the effects on memory function of severe acute pediatric illness and associations between memory functioning and psychiatric sequelae	**Inclusion criteria:** Not indicated **Exclusion criteria:** We excluded admissions due to neurological or psychiatric disorders such as deliberate self-harm, children with a prior history of neurological or learning disability and those not fluent in English.	CANTAB, 4.8 (1.4) months CMS, 4.8 (1.4) months		**CANTAB Spatial Working Memory (between errors) subtest** Healthy controls = 0.07 (0.80) PICU = −0.70 (0.80) P = 0.01 **CANTAB Spatial Working Memory (strategy) subtest** Healthy controls = 0.08 (1.22) PICU = −0.63 (0.67) P = 0.05 **CANTAB Rapid Visual Information Processing subtest** Controls (n = 12) = −1.10 (1.36) PICU (n = 15) = −2.78 (1.65) P = 0.009 **Children's Memory Scale word-pairs total score** Controls (n = 15) = 10.00 (3.55) PICU (n = 15) = 7.80 (2.04) P = 0.05 **Children's Memory Scale word-pairs Learning subtest** Controls (n = 15) = 10.40 (3.29) PICU (n = 15) = 8.20 (1.93) P = 0.03 **Children's Memory Scale word-pairs Delayed Recognition subtest** Controls (n = 15) = 11.60 (1.06) PICU (n = 15) = 9.67 (2.44) P = 0.009
Mesotten et al, 2012[27]	Randomized controlled trial, Belgium	198 PICU (usual care = 100, tight glycemic	As both hyperglycemia and hypoglycemia may adversely affect the developing brain, long-term follow-up was	**Inclusion criteria:** Not indicated **Exclusion criteria:**	CMS, 3 years		**Memory span (repeating numbers forward)** Healthy control = 9 (7–11) Usual care = 8 (6–9)

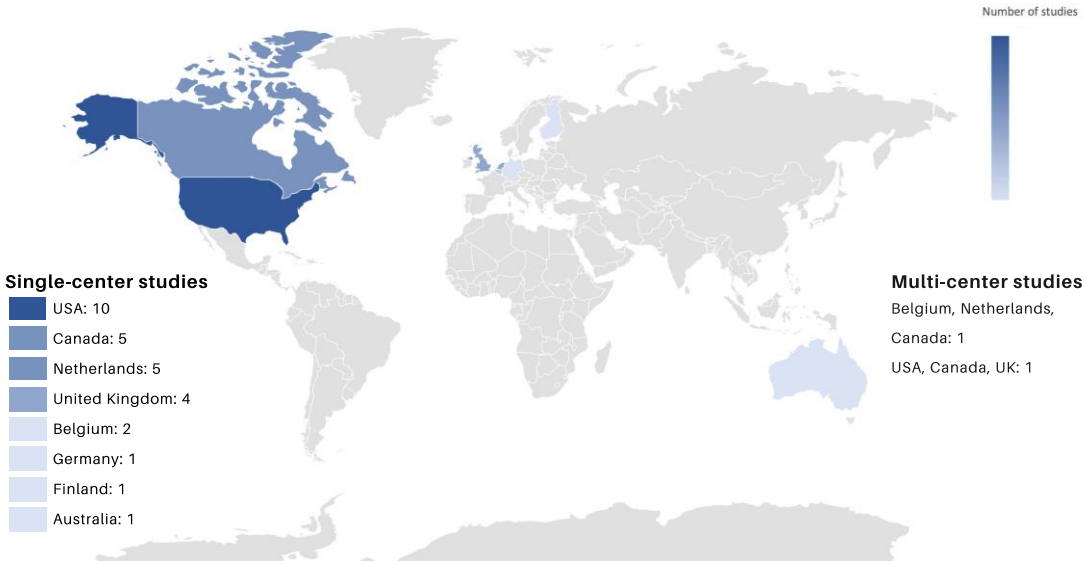
		control = 98), 124 healthy controls; At follow-up: PICU = 5.2 (4.2-8.3) years, Healthy controls = 6.7 (4.7-11.5) years; PICU = 57.24% male, healthy controls = 43.52% male; PICU = 93.42% white, Healthy controls = 97.69% white	required to exclude harm and validate short- term benefits of TGC.	Not indicated			Tight glycemic control = 7 (5.7–9) **Working memory (repeating numbers backward)** Healthy control = 10 (8–13) Usual care = 8.5 (6–11) Tight glycemic control = 9 (6–10) **Learning index** Healthy control = 101 (90–109) Usual care = 93 (78–103) Tight glycemic control = 90 (82–99) **Verbal immediate index** Healthy control = 0.50 (0.36–0.64) Usual care = 0.30 (0.20–0.50) Tight glycemic control = 0.40 (0.20–0.50) **Verbal delayed index** Healthy control = 0.40 (0.30–0.50) Usual care = 0.28 (0.10–0.40) Tight glycemic control = 0.30 (0.20–0.40) **Verbal delayed recognition index** Healthy control = 1.00 (0.95–1.00) Usual care = 0.96 (0.87–1.00) Tight glycemic control = 0.97 (0.92–1.00)
Overall health							
Jones et al, 2006[44]	Retrospective cohort study, United Kingdom	1455 PICU; 4.7 (1.7–10.1) years; 54.3% male	The goal was to measure, by using the Health Utilities Index, the health status of children 6 months after admission to PICUs in the United Kingdom.	**Inclusion criteria:** All PICUs in the United Kingdom were invited to participate. Children who were ≥ 6 months of age at admission and were discharged alive from participating units during a 1-year period were eligible for this study. Children with completed consent forms who had survived to 6 months after admission received the Health Utilities Index questionnaire. **Exclusion criteria:** Not indicated	HUI2, 6 months	72.7% (1058/1455) had at least 1domain of affected HUI2 attribute 4.4% had some level of impairment in all the outcome measures	For the sensation, cognition, emotion, pain, mobility, and self-care attributes, 767 (57.1%), 951 (69.6%), 940 (66.8%), 919 (64.9%), 962 (68.7%), and 939 (67.0%) children, respectively, were at level 1 and thus had no attribute- specific impairment at 6 months after admission. HUI score = 0.73 (0.01)

Data presented as mean (SD), median (IQR) or frequency (%) unless otherwise stated. Abbreviations: ABAS-II = Adaptive Behavior Assessment System-II; ANTB = Amsterdam Neuropsychological Task Battery; ASR = Adult Self-Report; BASC = Behavioral Assessment System for Children; Bayley-II = Bayley Scales of Infant and Toddler Development, Second Edition; Bayley-III = Bayley Scales of Infant

and Toddler Development, Third Edition; BRIEF = Behavior Rating Inventory of Executive Function; CANTAB = Cambridge Neuropsychological Test Automated Battery; CAPS-C = Post Traumatic Stress Disorder (PTSD) Scale for Children; CBCL = Child Behavior Checklist; CDI = Children's Depression Inventory; CHLOC = Children's Health Locus of Control Scale; CIES = Children's Impact of Events Scale; CMFS = Child Medical Fear Scale; CMS = Children's Memory Scale; CPSS = Child PTSD Symptom Scale; CPTSDI = Children's PTSD Inventory; CRIES = Children's Revised Impact of Event Scale; CRTI = Children's Responses to Trauma Inventory; GIT2 = Groninger Intelligence Test 2; GMDS = Griffiths Mental Development Scale; HUI2 = Health Utilities Index 2; MAHSC = Multiattribute health status classification system; MDI = Mental Developmental Index; MSEL = Mullen Scales of Early Learning; PBQ = Post-Hospital Behavior Questionnaire; PDI = Psychomotor Developmental Index; PTSD = Post-Traumatic Stress Disorder; RCMAS = Revised Children's Manifest Anxiety Scale; SDQ = Strength and Difficulties Questionnaire; STAIC = State Trait Anxiety Inventory for Children; TACQOL = TNO-AZL Children's Quality of Life Questionnaire Child Form; TGC = Tight glycemic control; TSCYC = Trauma Symptom Checklist for Young Children; UCLA PTSD-RI = UCLA Posttraumatic Stress Disorder Reaction Index; VABS-II = Vineland Adaptive Behavior Scales, Second Edition; WASI = Wechsler Abbreviated Scale of Intelligence; WIQS = Wechsler Intelligence Quotient Scale; WISC = Wechsler Intelligence Scale for Children; WPPSI = Wechsler Preschool and Primary Scale of Intelligence; WPPSI-R = Wechsler Preschool and Primary Scale of Intelligence-Revised; WRAML = Wide Range Assessment of Memory and Learning screener.

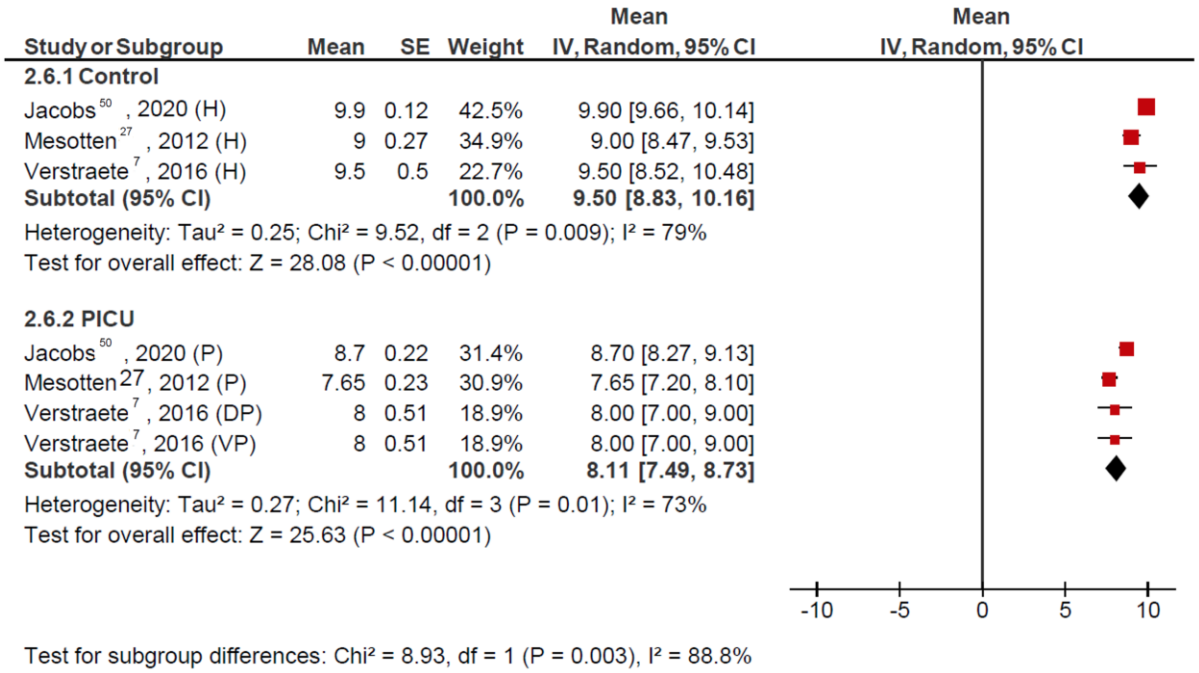
Six studies (2 RCTs and 4 observational studies) had multiple publications (18 articles). The following studies used the same study sample: RCTs by [c] Verstraete et al (2019)[26,49,50] and [f] Melnyk et al (2004)[28,53,54] had 3 published articles each. Prospective cohort studies by [a] Rennick et al (2002)[5,10], [b] Brocque et al (2009)[34,58,59], and [d] Slomine et al (2018)[29,51] had 2, 3 and 2 published articles respectively. A retrospective cohort study by [e] Buysse et al (2008)[41,52,55–57] had 5 published articles.

eFigure 1. Global Distribution of Single-Center and Multicenter Studies Included in Review

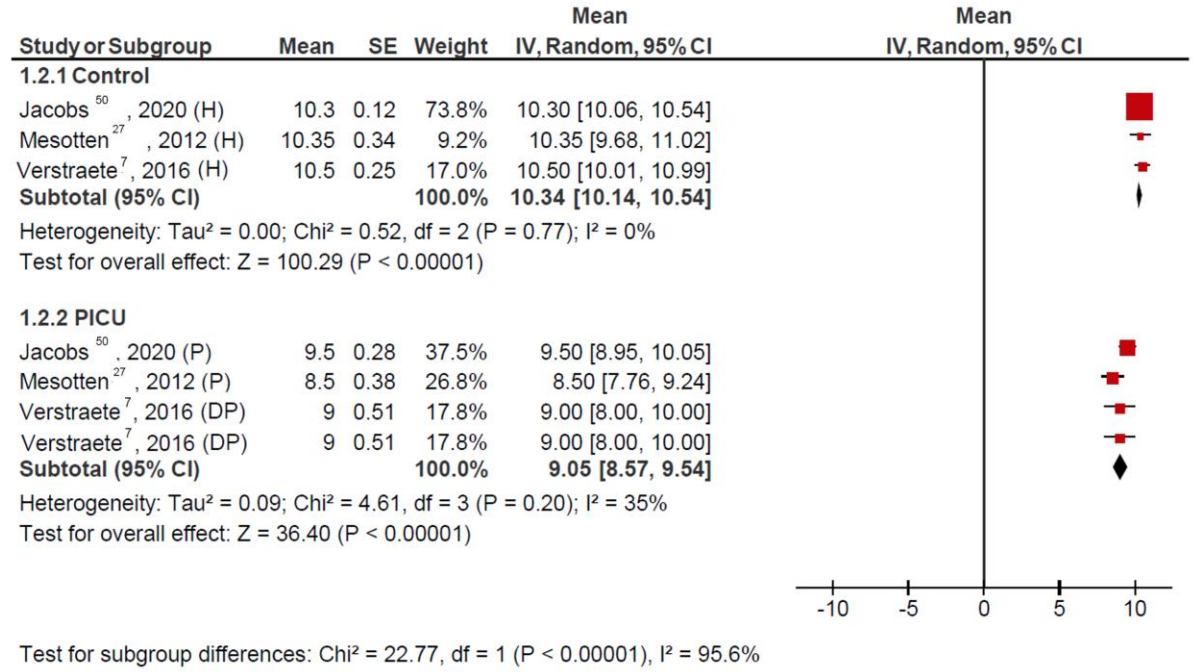


eFigure 2. Random-Effects Model for Memory Impairment Measured at 4-Year Follow-up Using Children's Memory Scale

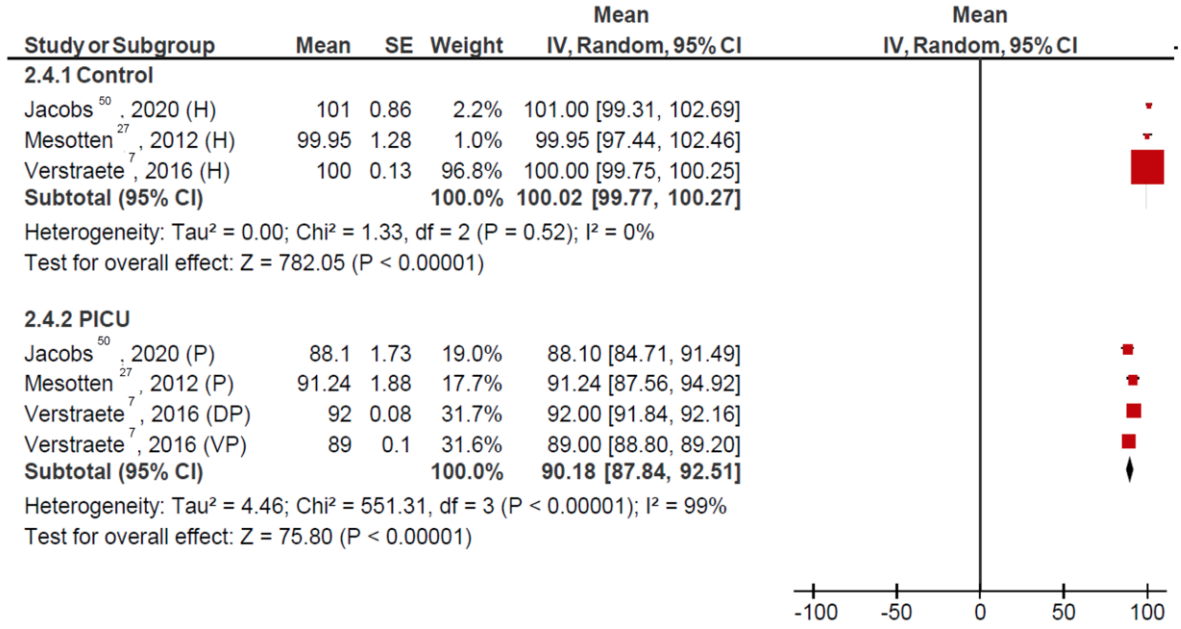
A. Memory span



B. Working memory

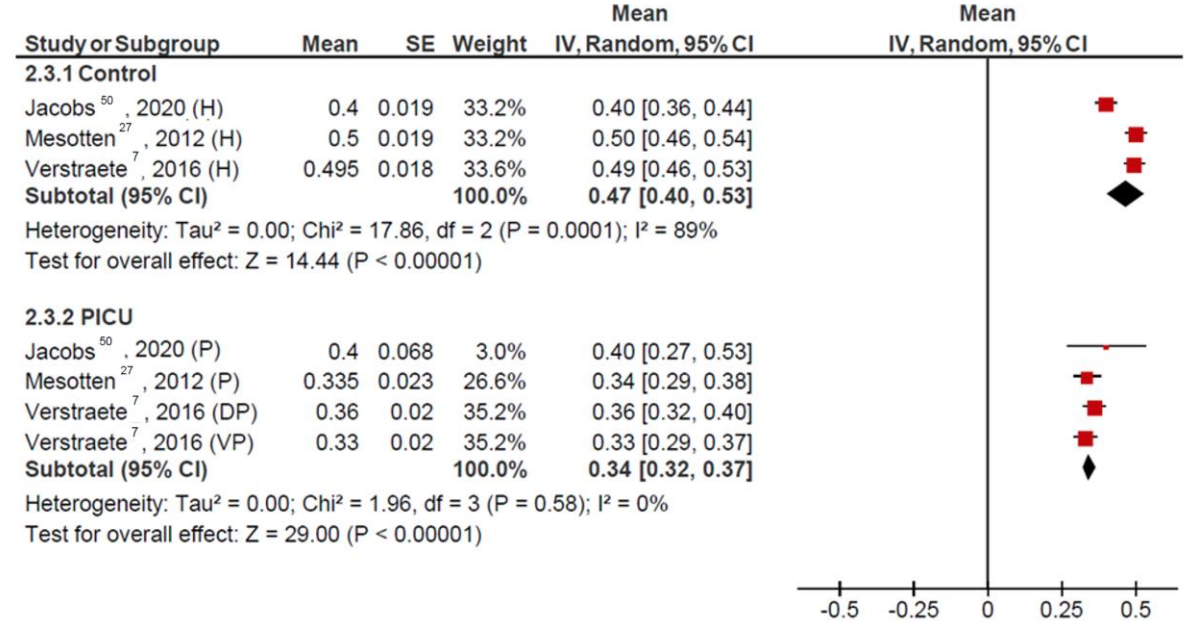


C. Learning index



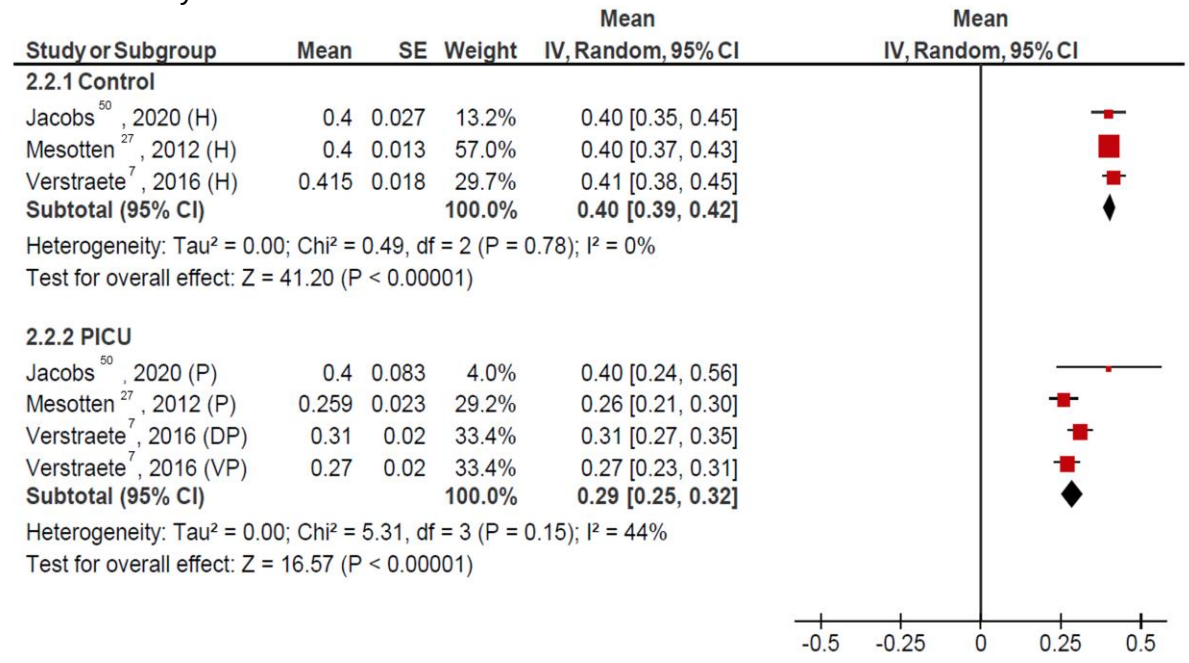
Test for subgroup differences: Chi² = 67.72, df = 1 (P < 0.00001), I² = 98.5%

D. Verbal immediate index



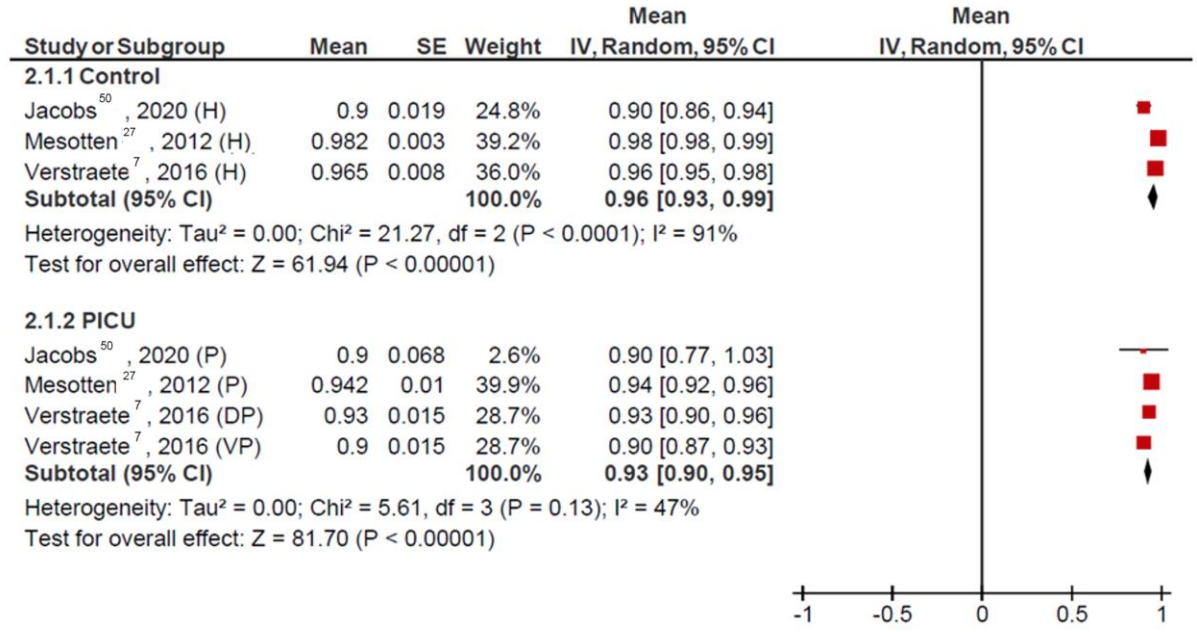
Test for subgroup differences: Chi² = 12.45, df = 1 (P = 0.0004), I² = 92.0%

E. Verbal delayed index



Test for subgroup differences: Chi² = 36.09, df = 1 (P < 0.00001), I² = 97.2%

F. Verbal delayed recognition index



Test for subgroup differences: Chi² = 2.48, df = 1 (P = 0.12), I² = 59.7%

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