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Neurodevelopmental, cognitive, behavioural and mental health impairments following childhood malnutrition: a systematic review

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ABSTRACT

Background Severe childhood malnutrition impairs growth and development short-term, but current understanding of long-term outcomes is limited. We aimed to identify studies assessing neurodevelopmental, cognitive, behavioural and mental health outcomes following childhood malnutrition.

Methods We systematically searched MEDLINE, EMBASE, Global Health and PsycINFO for studies assessing these outcomes in those exposed to childhood malnutrition in low-income and middle-income settings. We included studies assessing undernutrition measured by low mid-upper arm circumference, weight-for-height, weight-for-age or nutritional oedema. We used guidelines for synthesis of results without meta-analysis to analyse three outcome areas: neurodevelopment, cognition/academic achievement, behaviour/mental health.

Results We identified 30 studies, including some long-term cohorts reporting outcomes through to adulthood. There is strong evidence that malnutrition in childhood negatively impacts neurodevelopment based on high-quality studies using validated neurodevelopmental assessment tools. There is also strong evidence that malnutrition impairs academic achievement with agreement across seven studies investigating this outcome. Eight of 11 studies showed an association between childhood malnutrition and impaired cognition. This moderate evidence is limited by some studies failing to measure important confounders such as socioeconomic status. Five of 7 studies found a difference in behavioural assessment scores in those exposed to childhood malnutrition compared with controls but this moderate evidence is similarly limited by unmeasured confounders. Mental health impacts were difficult to ascertain due to few studies with mixed results.

Conclusions Childhood malnutrition is associated with impaired neurodevelopment, academic achievement, cognition and behavioural problems but evidence regarding possible mental health impacts is inconclusive. Future research should explore the interplay of childhood and later-life adversities on these outcomes. While evidence on improving nutritional and clinical therapies to reduce long-term risks is also needed, preventing and eliminating child malnutrition is likely to be the best way of preventing long-term neurocognitive harms.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ High mortality risk and impaired growth are well-recognised short-term risks of childhood malnutrition.
⇒ While there is increasing appreciation of longer-term risks for survivors, notably adult cardiometabolic non-communicable disease, other longer-term risks have been poorly described.

WHAT THIS STUDY ADDS

⇒ There is strong evidence that malnutrition impairs neurodevelopment and academic achievement in childhood which has significant implications for future well-being and prospects of those affected.
⇒ Childhood malnutrition is associated with impaired cognition and behavioural problems with evidence of effects through to adolescence and adulthood but the effect of nutritional treatment and interplay with childhood adversity, coexisting illness such as HIV and environmental factors in influencing these outcomes is unclear.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE AND/OR POLICY

⇒ Study findings imply that there are likely to be long-term effects of childhood malnutrition on cognition and well-being lasting through adolescence and adulthood.
⇒ Long-term needs of malnutrition survivors need to be carefully considered in treatment programmes. Further research is needed on the effects of nutritional therapy, adversity and environmental factors to tailor future interventions, particularly with regard to mental health which has been little researched.

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INTRODUCTION

Severe childhood malnutrition is widespread and has a high disease burden concentrated in low-income and middle-income settings.[1] To date, most malnutrition policies and

treatment programmes have focused on short-term risks, notably infections and death.[2 3] There is however growing evidence of long-term risks for malnutrition survivors, including that of later-life non-communicable disease.[4] The prevalence of malnutrition has decreased in recent years due to concerted global efforts.[1] However, there is a risk of resurgence and perpetuation of childhood malnutrition due to climate change, conflict and food insecurity in many settings with fragile food supply chains.[5]

Understanding long-term outcomes following child malnutrition is especially important because improved treatment has thankfully resulted in more children with malnutrition surviving into adolescence and adulthood.[3 6] Most previous research and programmatic investment have focused on child mortality rather than thriving and long-term outcomes. Fewer studies explore long-term impacts of malnutrition on cognitive, behavioural and mental health outcomes in survivors. Improved understanding of these outcomes can inform disease burden estimates, support ongoing investment and inform follow-up care for children with malnutrition.

Causal pathways linking malnutrition with neurodevelopment, cognition, behaviour and mental health are complex. Previous studies have found children admitted to hospital with severe malnutrition often have severe developmental delays with significant implications for ongoing development, well-being and potential future capital.[7] The interaction with HIV exposure in settings where both malnutrition and HIV are highly prevalent is also important given that both are associated, and both can independently affect early childhood development. Quantifying the association between malnutrition and neurodevelopment is complicated by the fact that children with neurodisability are inherently at higher risk of becoming malnourished, potentially due to factors such as poor feeding or differing treatment within family groups with food scarcity.[8] Other factors may mediate outcomes such as socioeconomic adversity, risk of infectious disease, parental engagement and school attendance which have been found to influence early childhood development and are often associated with risk of developing severe malnutrition.[9] These mediating factors also explain in part the difficulty in predicting developmental trajectories after an episode of severe malnutrition and why studies investigating outcomes are significantly influenced by potential confounders affecting the internal validity of results.[10]

A 1995 review found school-age children who suffered from early childhood malnutrition generally had poorer IQ levels, cognitive function, school achievement and greater behavioural problems than matched controls and, to a lesser extent, siblings.[11] Despite these associations, previous evidence of direct causal relationships is limited due to a lack of long-term follow-up studies, retrospective study designs and few studies having investigated behaviour and mental health. With this lack of up-to-date evidence on an increasingly important topic we aimed to identify studies reporting neurodevelopmental, cognitive, behavioural and mental health outcomes for children exposed to malnutrition in childhood.

METHODS

We searched MEDLINE, EMBASE, Global Health and PsycINFO for studies published between 1 January 1995 and 6 January 2022 using Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[12] Detailed search strategies are included in online supplemental appendix 1.

Selection criteria

We included studies from low-income and middle-income countries reporting neurodevelopmental, cognitive, school/academic achievement, mental health or behavioural outcomes in children under five exposed to malnutrition compared with children without malnutrition (we did not exclude studies that included small numbers of children between the ages of 5 and 6 years). We defined childhood malnutrition as undernutrition using standard definitions (definitions which are commonly measured in research and often related to severe adverse outcomes)[13]: moderate or severe wasting defined by low weight for height or low mid-upper arm circumference; presence of nutritional oedema; low weight-for-age as per older definitions of severe malnutrition. Despite the overlap between those suffering from severe undernutrition and those with micronutrient deficiencies and chronic malnutrition, we focus on acute undernutrition in early childhood in this review. We, therefore, did not include studies focusing solely on stunting (low height-for-age), chronic malnutrition or micronutrient deficiencies which often have their own dedicated literature.[14 15]

We included cross-sectional, cohort, case-control and controlled trial study designs which had a comparator group not exposed to childhood malnutrition. We excluded conference papers and reviews which did not include original data. We excluded studies which failed to define how malnutrition, child neurodevelopment, cognition, school/academic achievement, mental health or behaviour were measured. We also excluded studies looking at specific sub-populations of children (eg, only children with a specific medical condition). No language restrictions were placed on studies.

Literature search

Titles and abstracts were screened by two independent reviewers (two of AK, MGo, MKE and MC). The full texts of titles and abstracts chosen by any reviewer were then independently reviewed by two reviewers (two of AK, MGo, MKE and MC) against our selection criteria. We also screened reference lists of included studies. Data extraction of included studies was done by one of AK or MGo into a standard template (including study characteristics, assessment tool, malnutrition definition, sample size, results in cases and controls, reported effect sizes, results of statistical significance tests, results of analyses adjusted for confounding variables). Data extraction was

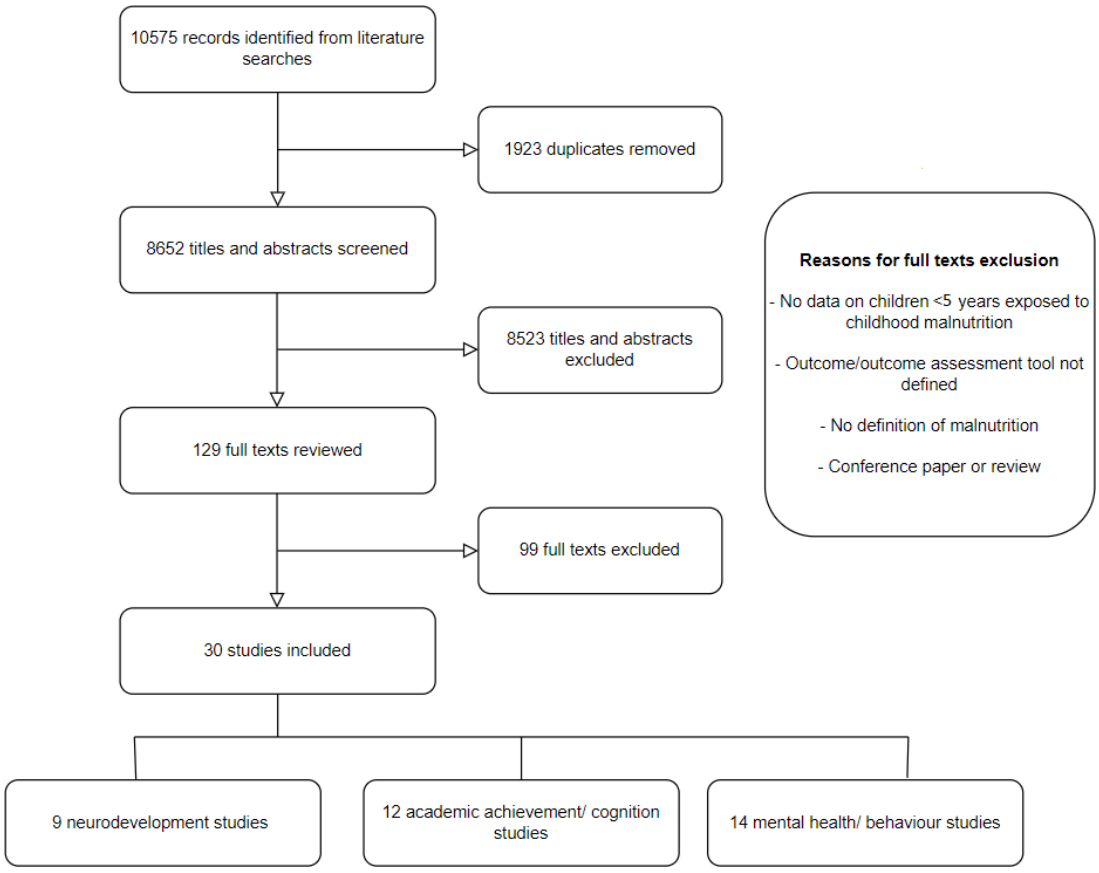

Figure 1 Flow chart of literature search.

subsequently checked by a second separate reviewer (one of AK, MKE, MC). Disagreements regarding inclusion of full texts and data extraction were resolved through mutual discussion.

Quality assessment

We assessed study quality using the National Institute for Health and Care Excellence (NICE) quality appraisal checklist.[16] Studies were scored independently by two reviewers (two of AK, MGo, MKE, MC) with scoring disagreements resolved through mutual discussion. Internal and external validity were rated as poor, acceptable and very good based on NICE quality appraisal checklist results. We considered overall study quality to be high quality when both internal and external validity scores were rated as very good, adequate quality when either score was rated as acceptable and poor quality when either internal or external validity was rated as poor.

Synthesis of study results

We grouped studies into three outcome areas: neurodevelopmental, cognition/academic achievement and mental health/behavioural outcomes (with some studies reporting outcomes from more than one category). We differentiated tools which measured general neurodevelopmental outcomes (and included a component of cognition but also include motor and speech domains) from those which specifically measured only cognition or academic language tests. We undertook a narrative synthesis of results within each of these areas as diverse outcomes and measurement tools precluded meta-analysis. We followed the Synthesis without meta-analysis (SWiM) reporting guidelines for analysing and reporting results.[17]

For neurodevelopmental studies we grouped studies and compared results by neurodevelopmental assessment tool used. For studies investigating cognition/academic achievement, we grouped those that measured IQ or executive function and those that measured either school or language performance/assessment results. For mental health/behaviour studies, we grouped studies that used behavioural assessment tools and then into groups by mental health condition or domain assessed.

For each study outcome where available, we recorded the unadjusted and adjusted results in cases and controls, reported effect sizes, and results from any statistical significance tests. When synthesising results by the groupings described above, we used vote counting by direction of effect to assess the number of studies which recorded differences between cases and controls. We summarised results in tables showing the number of studies with an effect on each outcome area. We also recorded the age group (childhood 0–10 years, adolescence 11–17 years, adulthood 18+ years) at which outcomes were measured to compare results between studies. Using SWiM guidelines we used vote counting in conjunction with study quality scores (which accounted for sample size, use

Table 1 Study characteristics

Study (year published)	Country (years conducted)	Study design (sample size)	Age exposed to malnutrition (age at follow-up if different)	Malnutrition definition (reference population)	Outcome	Outcome measurement tool
Chen *et al* (2021)[18]	China (2018)	Cross-sectional study (23 cases, 1270 controls)	3–5 years	w/h z score ≤2 (WHO)	Cognition/school achievement, Behaviour/ mental health	WPPSI-IV SDQ
Mwene-Batu *et al* (2020)[19]	DRC (1988–2019)	Retrospective cohort (524 cases, 407 controls)	Median 41 months (median 22 years)	w/h z score ≤3 (WHO)	Cognition/school achievement, Behaviour/ mental health	MMSE, Rosenberg Self-Esteem Scale, WHODAS
Asiki *et al* (2019)[20]	Uganda (1999–2011)	Retrospective cohort (12 cases with wasting, 145 cases recovered from wasting, 464 controls)	2–5 years (13–16 years)	w/h z score ≤2 (WHO)	Cognition/school achievement	Parental report of school years achieved
Dwivedi *et al* (2018)[21]	India (2014–15)	Cross-sectional study (102 cases, 101 controls)	6–30 months	WHO definition of severe acute malnutrition	Neurodevelopment	DASII (Indian modification of BSID)
Kang *et al* (2018)[22]	Bangladesh (2014), Bhutan (2011), Nepal (2015), Punjab, Pakistan (2016), Sindh, Pakistan (2015)	Cross-sectional study (31 037 participants)	36–59 months	w/h z score ≤2 (WHO)	Neurodevelopment	MICS ECDI
Lelijiveld *et al* (2018)[23]	Malawi (2006–2013)	Prospective cohort (171 cases, 155 controls)	Median 21.5 months(IQR 15–32) (9 years)	w/h<70% of the median (NCHS)	Cognition/school achievement	CANTAB, Parental report of school grade
Abessa *et al* (2017)[24]	Ethiopia (2011–13)	Cross-sectional study (310 cases, 310 controls)	Cases—mean 30.7 months (SD 15.2) controls—mean 29.6 months (SD 15.4)	w/h<70% of the median (NCHS), MUAC <110mm, or bilateral pitting oedema due to malnutrition	Neurodevelopment, behaviour/mental Health	Denver II, ASQ
Sudfeld *et al* (2015)[25]	Tanzania (2010–14)	Randomised controlled trial (47 cases, 989 controls)	18–36 months	w/h z score ≤2 (WHO)	Neurodevelopment	BSID-III
De Grandis *et al* (2014)[26]	Argentina (not stated)	Retrospective cohort (25 cases, 28 controls)	0–2 years (5–12 years)	w/h z score ≤3 (or <70% expected) (WHO)	Behaviour/mental Health	Paediatric quality of life inventory
Malhi *et al* (2013)[27]	India (not stated)	Cross-sectional study (20 cases, 44 controls)	0–6 years	w/a z-score ≤2 (WHO)	Neurodevelopment	Indian development inventory
Bogale *et al* (2013)[28]	Ethiopia (2007)	Cross-sectional study (12 cases, 88 controls)	61.0 months ±3.0	w/a z-score ≤2 (WHO)	Cognition/school achievement	Raven's CPM, KABC-II
Warsito *et al* (2012)[29]	Indonesia (not stated)	Cross-sectional study (5 cases, 48 controls)	3–5 years old	w/h z-score ≤2 (WHO)	Cognition/school achievement	Indonesian Department of National Education-Child Development Instrument
Nassar *et al* (2012)[30]	Egypt (not stated)	Cross-sectional study (33 cases, 30 controls)	3–6 years old	Wellcome classification (WHO)	Cognition/school achievement	Stanford-Binet-Intelligence-Scale (Arabic-translation) Receptive/Expressive/-Total-Language (Arabic-Language-Test)

Continued

Table 1 Continued

Study (year published)	Country (years conducted)	Study design (sample size)	Age exposed to malnutrition (age at follow-up if different)	Malnutrition definition (reference population)	Outcome	Outcome measurement tool
Baker-Henningham *et al* (2009)[31]	Bangladesh (not stated)	Cross-sectional study (212 cases, 108 controls)	6–24 months old	w/a z-score ≤2 (NCHS)	Behaviour/mental Health	Temperament Questionnaire derived from existing validated instruments (modified by Wachs, Purdue University)
El-Khayat *et al* (2007)[32]	Egypt (2006)	Cross-sectional study (42 cases, 15 controls)	6–25 months	w/h z-score ≤2 (WHO)	Neurodevelopment	BSID-II
Liu *et al* (2004)[33]	Mauritius (1972-)	Prospective Cohort (235 cases, 807 controls)	3 years (8,11, 17 years)	Malnutrition and one of angular stomatitis, kwashiorkor, sparse thin hair, haemoglobin <8.5 g/dL	Behaviour/mental Health	Child Behaviour Questionnaire at age 8, Child Behaviour Checklist at age 11, Revised Behaviour Checklist at Age 17
Liu *et al* (2003)[34]	Mauritius (1972-)	Prospective Cohort (253 cases, 837 controls	3 years (11 years)	Malnutrition and one of angular stomatitis, kwashiorkor, sparse thin hair, haemoglobin <8.5g/dL	Cognition/school achievement	Bohem Test WISC Academic Tests Holborn-Reading Scale Trail Making Test
Drewett *et al* (2001)[35]	Ethiopia (not stated)	Prospective Cohort (97 cases, 100 controls)	2 years	w/a z-score <–1.88 (NCHS)	Neurodevelopment	BSID
Vazir *et al* (1998)[36]	India (not stated)	Cross-sectional study (1456 cases, 2212 controls)	0–6 years	<75% expected w/a (NCHS)	Neurodevelopment	ICMR Psychosocial Developmental Screening Test
Perales *et al* (1996)[37]	Chile (1987 – not stated)	Retrospective Cohort (40 cases, 40 controls)	0–2 years (8–10 years)	Protein energy malnutrition (defined by Sempe (1979) *et al*)	Cognition/school achievement	Continuous Performance Task Anstey Domino Test
Kaul *et al* (1995)[38]	India (not stated)	Cross-sectional study (50 cases, 102 controls)	0–12 months	Gomez classification—moderate malnutrition (NCHS)	Neurodevelopment	BSID
Barbados Nutrition Study						
Hock *et al** (2018)[39]	Barbados (1977-not stated)	Prospective cohort (77 cases, 62 controls)	0–1 years (40–45 years)	Gomez classification	Behaviour/mental health	SCID-II-PQ, NEO PI-R FFM
Waber (1) *et al** (2014)[40]	Barbados (1977–2010)	Prospective cohort (77 cases, 59 controls)	0–1 years (38 years)	Gomez classification	Cognition/school achievement	WASI, WRAT-III
Waber (2) *et al** (2014)[41]	Barbados (1977–2010)	Prospective cohort (77 cases, 59 controls)	0–1 years (38 years)	Gomez classification	Cognition/school achievement, behaviour/mental Health	WAIS-III, D-KEFS, WRAML-II, Wisconsin card sorting, Metacognitive index, Behavioural regulation index
Galler *et al** (2013)[42]	Barbados (2006–2010)	Prospective cohort (77 cases, 57 controls)	0–1 years (37–43 years)	Gomez classification	Behaviour/mental health	NEO-PI-R personality inventory
Galler (1) *et al** (2012)[43]	Barbados (1967–2010)	Prospective cohort (80 cases, 65 controls)	0–1 years (40 years)	Gomez classification	Behaviour/mental Health	CAARS, CPT
Galler (2) *et al** (2012)[44]	Barbados (1967–1985)	Prospective cohort (56 cases, 60 controls)	0–1 years (15 years old)	Gomez classification	Behaviour/mental Health	Child-Behaviour-Questionnaire, Teacher Behaviour Questionnaire

Continued

Table 1 Continued

Study (year published)	Country (years conducted)	Study design (sample size)	Age exposed to malnutrition (age at follow-up if different)	Malnutrition definition (reference population)	Outcome	Outcome measurement tool
Waber *et al** (2011)[45]	Barbados (1967–1985)	Prospective cohort (57 cases, 60 controls)	0–1 years (11–18 years)	Gomez classification	Cognition/school achievement and behaviour/mental health	WISC, Common entrance examination (local school test), Teacher-Behaviour Questionnaire, School functioning scale Minnesota-General-Adjustment-and Morale-Scale
Galler *et al** (2011)[46]	Barbados (1967–1985)	Prospective cohort (109 cases, 107 controls)	0–1 years (9–17 years)	Gomez classification	Behaviour/mental health	Barbados-Child-Behaviour-Scale
Galler *et al** (2010)[47]	Barbados (1967–1985)	Prospective cohort (116 cases, 61 controls)	0–1 years (11–17 years old)	Gomez classification	Behaviour/mental health	Minnesota-General-Adjustment-and Morale-Scale

*Studies are drawn from the same Barbados Nutrition Study Cohort.
ASQ, Ages and Stages Questionnaire; BSID, Bayley scales of infant development; CAARS, Attention-domain: Conners-ADHD-Rating-Scales; CANTAB, Cambridge Neuropsychological Test Automated Battery; CPT, Conners-Continuous-Performance Test; DASII, Developmental Assessment Scale of Indian Infants; D-KEFS, Delis-Kaplan Executive Function System; DRC, Democratic Republic of Congo; ICMR, Indian Council Medical Research Psychosocial Developmental Screening Test; KABC-II, Kaufman Assessment Battery for Children-II; MDAT, Malawi Developmental Assessment Tool; MICS ECDI, Multiple Indicator Cluster Survey Early Child Development Index; MMSE, Mini Mental State Exam; MUAC, Mid Upper Arm Circumference; NCHS, National Centre for Health Statistics reference population; NEO PI-R FFM, NEO Personality Inventory-Revised derived Five-Factor Model; Raven's CPM, Raven's Coloured Progressive Matrices; SCID-II-PQ, Structured Clinical Interview for DSM-IV Axis II Personality Disorders Personality Questionnaire; SDQ, Strengths and Difficulties Questionnaire; WAIS-III, Wechsler Adult Intelligence Scale-III; WASI, Adult IQ: Weschler Abbreviated Scale of Intelligence – Vocabulary and Matrix Reasoning subsets; w/h, Weight-for-Height; WHO, WHO reference population; WHODAS, WHO Disability Assessment Schedule; WISC, Weschler Intelligence Scale; WPPSI-IV, Wechsler Preschool and Primary Scale of Intelligence Fourth Edition; WRAML-II, Wide Range Assessment of Memory and Learning-II; WRAT-III, Academic achievement: Wide Range Achievement Test-III-Reading Spelling and Calculation subsets.

of validated outcome tools/assessments and whether results were adjusted for confounders) to summarise the strength of conclusions.[17] Where several high-quality studies in one grouped outcome area reported results of an association with malnutrition, we graded conclusions as strong evidence. Where several adequate and high-quality studies reported an association with malnutrition, but there were uncertainties or limitations of studies identified, we graded conclusions as moderate evidence. Where there were few studies identified or studies with mixed results or poor study quality, we graded associations as inconclusive.

RESULTS

Study characteristics

Thirty studies met our selection criteria (figure 1).[18–47] Full study characteristics are included in table 1. Studies published since 1995 were conducted across several countries in Africa, Asia and South America and included long-term cohorts recruited from 1967 onwards following participants through to adolescence and adulthood. Nine studies were part of the same Barbados Nutrition Study (BNS), a prospective lifelong cohort study assessing multiple outcomes at different follow-up points for children who suffered from malnutrition in the first year of life.[39–47] Nine studies assessed neurodevelopmental outcomes, 12 studies assessed cognition or academic achievement (three from BNS) and 14 studies assessed mental health conditions or behaviour (eight from BNS). Study designs included cross-sectional, retrospective cohorts, prospective cohorts and randomised controlled trial studies. Neurodevelopmental studies were either cross-sectional or had a short follow-up time during childhood. The age at follow-up following exposure to malnutrition in other studies varied from childhood through to adulthood.

Study quality scoring is included in online supplemental table 1. Twenty-three studies had very good external validity, with the seven others apart from one with acceptable external validity. This was due to most providing good descriptions of study settings, populations and selection criteria. Fourteen studies had very good internal validity, 12 had acceptable internal validity and four studies had poor internal validity. Studies often scored poorly where important confounding variables such as socioeconomic status were not accounted for in analyses, sample size was small or study designs were poor or poorly described, leading to potential biases. Overall, 14 studies were rated as high quality, 12 were adequate quality and four were poor quality.

Malnutrition and neurodevelopment

We identified nine studies assessing neurodevelopmental outcomes of malnutrition (table 2). A summary of results from these studies is included in online supplemental table 2. Five studies used the Bayley Scales of Infant Development (BSID). Three of these were adequate-quality

Table 2 Summary of results from studies assessing the effect of malnutrition on neurodevelopment

Study (quality) country (outcome age)	Neurodevelopmental assessment tool				
	BSID	MICS ECDI	Denver	IDI	ICMR
Dwivedi *et al* 2018 (+) India (childhood)[21]	Effect (unadjusted)*				
Kang *et al* 2018 (+) multiple in Asia (childhood)[22]		No effect (adjusted)			
Abessa *et al* 2017 (++) Ethiopia (childhood)[24]			Effect (adjusted)		
Sudfeld *et al* 2015 (++) Tanzania (childhood)[25]	Effect (adjusted)				
Malhi *et al* 2013 (-) India (childhood)[27]				No effect (adjusted)	
El-Khayat *et al* 2007 (+) Egypt (childhood)[32]	Effect (unadjusted)				
Drewett *et al* 2001 (++) Ethiopia (childhood)[35]	No effect (adjusted)				
Vazir *et al* 1998 (+) India (childhood)[36]					Effect (unadjusted)
Kaul et al 1995 (+) India (childhood)[38]	Effect (unadjusted)				

Effect (marked in green) —statistically significant difference in neurodevelopment between cases and controls.
No effect (marked in red)—no difference, or statistically insignificant difference, or statistically insignificant difference after adjusting for confounding variables, in neurodevelopment between cases and controls.
Adjusted—results adjusted for confounding variables.
Unadjusted—results unadjusted for confounding variables.
++=high quality.
+=adequate quality.
-=poor quality.
*Indian modification of BSID.
BSID, Bayley Scales of Infant Development; ICMR, Indian Council Medical Research Psychosocial Developmental Screening Test; IDI, Indian Developmental Inventory; MICS ECDI, Multiple Indicator Cluster Survey Early Child Development Index.

studies which found impaired neurodevelopment in those with malnutrition unadjusted for confounding variables such as socioeconomic status and family characteristics.[21 32 38] Two high-quality studies using BSID found impaired neurodevelopment in those with malnutrition but one found that differences were no longer significant when adjusting for differences in current weight during follow-up at 2 years old.[25 35] These differences in BSID scores where present across studies for both mental and psychomotor subscales. A further high-quality study using the Denver-II tool found children with malnutrition had lower scores across fine motor, gross motor, language and personal-social domains compared with controls.[24] One adequate-quality study using a neurodevelopment tool developed in India (Indian Council Medical Research Psychosocial Developmental Screening Test) found poorer development outcomes for those with malnutrition.[36] Another adequate-quality study using UNICEF Multiple Indicator Cluster Surveys (MICS) Early Childhood Development Indicators (ECDI) did not find an effect of malnutrition on learning-cognition or socioemotional development.[22] This was carried out on a large population sample from five country surveys in Asia, but the MICS ECDI tool consists of few basic developmental items which span a large age range. This is notably different to the detailed neurodevelopmental assessments by trained assessors used in most other studies. A poor-quality study using an Indian specific development tool (Indian Development Inventory), found poorer neurodevelopment scores across social, adaptive, motor, communication and cognitive subscales in cases, but this was no longer significant when adjusted

Table 3 Summary of results from studies assessing the effect of malnutrition on cognition and academic achievement

Study (quality) (outcome age) Country	School, academic or language performance	Executive function/intelligence (assessment tool)
Chen *et al* 2021 (++) (childhood) China[18]		No effect (adjusted) (WPPSI-IV)
Mwene-Batu *et al* 2020 (+) (adulthood) DRC[19]	Effect (unadjusted)	Effect (unadjusted) (MMSE)
Asiki et al 2018 (++) (adolescence) Uganda[20]	Effect (adjusted)	
Lelijiveld *et al* 2018 (++) (childhood) Malawi[23]	Effect (adjusted)	No effect (adjusted) (CANTAB)
Bogale *et al* 2013 (++) (childhood) Ethiopia[28]		Effect (adjusted) (Raven's CPM, KABC-II)
Warsito *et al* 2012 (-) (childhood) Indonesia[29]		No effect (unadjusted) (Indonesian Department of National Education – child development instrument score)
Nassar *et al* 2012 (-) (childhood) Egypt[30]	Effect (unadjusted)	Effect (unadjusted) (Stanford-Binet-Intelligence-Scale)
Liu *et al* 2003 (++) (adolescence) Mauritius[34]	Effect (adjusted)	Effect (adjusted) (Bohem Test, Trail Making Test, WISC)
Perales *et al* 1996 (+) (childhood) Chile[37]		Effect (unadjusted) [Continuous Performance Task, Anstey Domino test]
Barbados Nutrition Study		
Waber (1) *et al* 2014* (++) (adulthood) Barbados[40]	Effect (adjusted)	Effect (adjusted) (WASI)
Waber (2) *et al* 2014* (++) (adulthood) Barbados[41]		Effect (adjusted) [WAIS-III, D-KEFS, WRAML-2, Wisconsin card sorting, Metacognitive index]
Waber *et al* 2011* (+) (adolescence) Barbados[45]	Effect (adjusted)	Effect (adjusted) (WISC)

Effect (marked in green) —statistically significant difference in academic achievement/cognition between cases and controls.
No effect (marked in red)—no difference, or statistically insignificant difference, or statistically insignificant difference after adjusting for confounding variables, in academic achievement/cognition between cases and controls.
Adjusted—results adjusted for confounding variables.
Unadjusted—results unadjusted for confounding variables.
++=high quality.
+=adequate quality.
-=poor quality.
*Studies are drawn from the same Barbados Nutrition Study.
CANTAB, Cambridge Neuropsychological Test Automated Battery; D-KEFS, Delis-Kaplan Executive Function System; KABC-II, Kaufman Assessment Battery for Children-II; MMSE, Mini-Mental State Exam; Raven's CPM, Raven's Coloured Progressive Matrices; WAIS-III, Wechsler Adult Intelligence Scale-III; WASI, Adult IQ: Wechsler Abbreviated Scale of Intelligence-Vocabulary and Matrix Reasoning subsets; WISC, Weschler Intelligence Scale for Children; WPPSI-IV, Wechsler Preschool and Primary Scale of Intelligence Fourth Edition; WRAML-II, Wide Range Assessment of Memory and Learning-II.

Table 4 Summary of results from studies assessing the effect of malnutrition on mental health and behaviour

Study (quality) (outcome age) Country	Behavioural problems (tool)	Self-esteem (tool)	Social-related disability (tool)	Quality of life (tool)	Personality (tool)	Attention (tool)	Morale (tool)
Chen *et al* 2021 (++) (childhood) China[18]	No effect (adjusted) (SDQ)						
Mwene-Batu *et al* 2020 (+) (adulthood) DRC[19]		Effect (unadjusted) (Rosenberg Self-Esteem Scale)	No effect (unadjusted) (WHODAS)				
Abessa *et al* 2017 (++) (childhood) Ethiopia[24]	Effect (adjusted) (ASQ:SE)						
De Grandis *et al* 2014 (-) (childhood) Argentina[26]				Effect (unadjusted) (Paediatric quality of life inventory)			
Baker-Henningham *et al* 2009 (++) (childhood) Bangladesh[31]	Effect (adjusted) (Wachs temperament questionnaire)						
Liu *et al* 2004 (+) (childhood, adolescence) Mauritius[33]	Effect (adjusted) (Child Behaviour Checklist)						
Barbados Nutrition Study							
Hock *et al* 2018* (+) (adulthood) Barbados[39]					Mixed (adjusted) [SCID-II-PQ, NEO PI-R FFM]		
Waber (2) *et al* 2014* (++) (adulthood) Barbados[41]	Effect (adjusted) (Behavioural regulation index)						
Galler *et al* 2013* (+) (adulthood) Barbados[42]					Effect (adjusted) (NEO-PI-R)		

Continued

Table 4 Continued

Study (quality) (outcome age) Country	Behavioural problems (tool)	Self-esteem (tool)	Social-related disability (tool)	Quality of life (tool)	Personality (tool)	Attention (tool)	Morale (tool)
Galler (1) *et al* 2012* (+) (adulthood) Barbados[43]						Mixed (adjusted) (CAARS, CPT)	
Galler (2) *et al* 2012* (+) (adolescence) Barbados[44]	No effect (adjusted) (Conduct: CBQ, Teacher behaviour questionnaire)						
Waber *et al* 2011* (+) (adolescence) Barbados[45]						No effect (adjusted) (Attention: CBQ)	No effect (adjusted) (Minnesota Adjustment and Morale Scale)
Galler *et al* 2011* (++) (adolescence) Barbados[46]	Effect (adjusted) (BCBS)						
Galler *et al* 2010* (++) (adolescence) Barbados[47]							Effect (adjusted) (Minnesota Adjustment and Morale Scale)

Effect (marked in green)—statistically significant difference in mental health/behaviour between cases and controls.
No effect (marked in red)—no difference, or statistically insignificant difference, or statistically insignificant difference after adjusting for confounding variables, in mental health/behaviour between cases and controls.
Mixed (marked in blue)-mixture of results in the same paper showing statistically significant differences of certain outcome measurements but not other
Adjusted—results adjusted for confounding variables.
Unadjusted—results unadjusted for confounding variables.
++=high quality.
+=adequate quality.
-=poor quality.
*Studies are drawn from the same Barbados Nutrition Study.
ASQ-SE, Ages and Stages Questionnaire Socio Emotional; Attention-domain, Conners-ADHD-Rating-Scales; BCBS, Barbados Child Behaviour Scale; CAARS, Attention-domain: Conners-ADHD-Rating-Scales; CBQ, Child Behaviour Questionnaire; CPT, Conners-Continuous-Performance Test; NEO PI-R, NEO Personality Inventory-Revised; NEO PI-R FFM, NEO Personality Inventory-Revised derived Five-Factor Model; SCID-II-PQ, Structured Clinical Interview for DSM-IV Axis II Personality Disorders Personality Questionnaire; SDQ, Strengths and Difficulties Questionnaire; WHODAS, WHO Disability Assessment Schedule.

for confounding variables. The results from high-quality and adequate-quality studies provides strong evidence of an association between malnutrition in childhood and impaired neurodevelopment across multiple developmental domains.

Malnutrition and cognition/academic achievement

We identified 12 studies (three from BNS) assessing cognitive outcomes of malnutrition (table 3). A summary of results from these studies is included in online supplemental table 3. Seven studies assessed academic performance, with three based on self-report of school performance or school year achieved by age at follow-up (a measure in one Malawian study where school year progression is based on performance[23]), and four based on tests of school skill such as mathematics or country specific language tests (online supplemental table 3).[19 20 23 30 34 40 45] Three studies were high quality, three were adequate quality and one was poor quality. All studies (two from BNS) found worse school/academic performance in those exposed to malnutrition in childhood compared with controls. The results from high-quality and adequate-quality studies identified provides strong evidence of an association between exposure to malnutrition and impaired academic performance/achievement in childhood and adolescence.

Eleven studies investigated cognition using several tools assessing intelligence and executive function (table 3, online supplemental table 3). Eight of these studies (three from BNS) found impaired intelligence/executive function in those exposed to malnutrition in childhood compared with controls.[19 28 30 34 37 40 41 45] Two high-quality studies found no significant association between malnutrition and cognition.[18 23] One study from China found no difference between cases and controls using Wechsler Pre-school and Primary Scale of Intelligence Fourth Edition, and the other from Malawi found the differences seen between cases and controls using CANTAB (the Cambridge Neuropsychological Test Automated Battery) were no longer significant when adjusting for confounding variables including HIV, stunting, socioeconomic status and household characteristics. Of the studies which found a significant difference in cognition between cases and controls, there were four high-quality studies (two from BNS).[28 34 40 41] These four high-quality studies all used different cognitive assessment tools, including Kauffman-ABC, Bohem Test, Trail Making Test and Wechsler Scale of Intelligence (table 3), and found poorer scores in those exposed to malnutrition compared with controls. Three adequate-quality studies (one from BNS) using different cognitive assessment tools, including Mini-Mental State Exam, Wechsler Scale of Intelligence and Anstey Domino test (table 3) also found those exposed to childhood malnutrition had impaired cognition compared with controls, however, only one of these studies adjusted for any confounding variables (BNS study which adjusted for childhood standard of living).[19 37 45] The results from high-quality and adequate-quality studies provide moderate evidence of an association between exposure to malnutrition in childhood and impaired cognition, but definitive conclusions are limited by mixed results from two high-quality studies showing no association after adjusting for important confounders such as HIV and socioeconomic status and results from several adequate-quality studies which failed to adjust for any confounding variables.

Malnutrition and mental health/behaviour

We identified 14 studies (8 from BNS) assessing mental health and behavioural outcomes of malnutrition (table 4). A summary of results from these studies is included in online supplemental table 4. Seven studies (three from BNS) assessed behaviour using different behavioural rating tools including the Strengths and Difficulties Questionnaire (SDQ), Child Behaviour Checklist, Ages and Stages (socioemotional questions) and other adapted behavioural questionnaires (table 4).[18 24 31 33 41 44 46] Five of these studies, four of which were rated as high quality, found significantly higher behavioural problems in those exposed to malnutrition in childhood.[24 31 33 41 46] One high-quality study found no difference in behavioural scores between cases and controls using SDQ and one adequate-quality study looking at conduct problems using the child behaviour questionnaire found differences in behaviour were no longer significant when adjusting for confounding variables including childhood standard of living. The results from adequate-quality and high-quality studies provide moderate evidence of an association between exposure to malnutrition in childhood and increased behavioural problems but is limited by some mixed results in high-quality studies and potential confounding in some studies reporting an association.

Seven studies (five from BNS) investigated different mental health outcomes (table 4).[19 26 39 42 43 45 47] Studies indicated possible associations with self-esteem, quality of life, personality disorders, attention deficits and low morale. There were small numbers of studies investigating specific mental health domains and there were significant study limitations in several studies such as failure to adjust for confounders and the use of multiple tools and domains within individual studies, increasing the risk of type 1 error. The results from the studies identified provide inconclusive evidence regarding possible associations between exposure to malnutrition in childhood and poorer mental health outcomes.

DISCUSSION

Our review finds strong evidence that exposure to malnutrition in childhood impairs neurodevelopment and academic achievement. There is moderate evidence that childhood malnutrition is associated with impaired cognition and is associated with more behavioural problems throughout childhood and adolescence. However, there is uncertainty around the relative contributions of

malnutrition and other associated factors (such as childhood adversity, HIV-exposure, socioeconomic status and household characteristics) to these outcomes. Research investigating mental health outcomes in children with malnutrition is inconclusive and there are few studies investigating specific mental health domains such as depression. These results have implications for policymakers surrounding the long-term care needs of those treated for childhood malnutrition and there is a need for research exploring how nutritional therapies and social interventions affect these outcomes.

Due to study heterogeneity, we were unable to perform a meta-analysis of any results. We therefore, used published guidelines to synthesise results and determine the strength of evidence for each outcome area. Despite this, there are still limitations given potential publication bias of positive associations between malnutrition and the outcomes investigated. Our review, however, builds on previously published evidence which has suggested links between malnutrition and poorer IQ levels, cognitive function, school achievement and greater behavioural problems.[11] Our findings strengthen the evidence base regarding these associations as previous findings were limited by difficulties in interpreting retrospective case control studies, but our review includes evidence from prospective studies which have sought to minimise these biases. There are however several poor-quality or adequate-quality studies we identified which failed to account for important confounders such as socioeconomic status and family characteristics. Of the 30 studies we identified, 9 were from the same prospective cohort study in Barbados, with many of these publications from the same cohort testing multiple cognitive, behavioural and mental health outcomes. This may have increased the likelihood of type 1 error. For example, different studies from the same cohort found mixed results regarding morale and personality disorder scores when different assessment tools were used (table 4).[43 45 47] However, we accounted for this when assessing the strength of conclusions. We focused on studies from low-income and middle-income countries where there is a high disease burden from severe malnutrition. Results are therefore applicable to similar settings and outcomes may differ in children with malnutrition in high-middle-income settings where other societal factors can alter development trajectories. Differentiating the relative effects of malnutrition and subsequent socioeconomic factors is therefore difficult from studies in this review but impaired cognition due to malnutrition in high-income settings has been found in other studies such as those looking at outcomes from the 'Dutch winter hunger'.[48]

Impaired neurodevelopment in childhood is likely linked to subsequently poorer academic achievement in childhood and adolescence and may also be linked to increased behavioural problems seen in some studies.[49] The studies assessing IQ/executive function outcomes spanned childhood through to adulthood and there was moderate evidence of a link between malnutrition and cognition. Two high-quality studies showed no effect[18 23] and other studies which showed an effect did not adjust for any confounding variables.[19 30 37] There are therefore remaining questions over how much an early insult to neurodevelopment from malnutrition affects future cognition and functioning, and to what extent other related environmental factors such as prenatal nutrition, family characteristics and infections contribute to these outcomes.[50 51] Several studies adjusted for sex when analysing data but there are insufficient studies with stratified data in this review to comment confidently on possible sex-specific differences in outcomes. A recent systematic review found that sex can significantly influence outcomes with higher odds of boys being wasted, underweight and stunted than girls.[52] The review also found geographical variation in outcomes and the reasons for sex-specific differences remain unclear with both plausible biological and social causes. This is therefore an important area of future research with regards to the outcomes we investigate in this study.[53] Mental health outcomes such as depression and inattention are likely to be influenced by similar confounding variables, and whether early insults from malnutrition independently contribute to poor mental health outcomes in later life is yet to be established. There is also uncertainty around the effect of nutritional therapy on long-term cognition and functioning and there has been significant interest in catch-up growth during key periods.[54] For example, previous research has indicated that weight gain in the first 2 years of life predicts schooling outcomes and there is ongoing work to determine the optimum speed and regimen of nutritional therapy to maximise long-term outcomes.[55 56] However, even if some of the effects we report are due to confounding, evidence is clear from our review that children who experience an episode of malnutrition in childhood are at high risk of poorer development, behaviour and cognition. Specific adversities prevalent in low-income and middle-income settings related to low socioeconomic status are areas of potential intervention which may improve outcomes. These can target areas such as parenting, schooling, poverty alleviation, ending child exploitation and labour, all of which are likely to influence outcomes. Policy-makers should therefore prioritise targeted support both nutritionally and societally for these vulnerable children to optimise life chances after recovery.

While there is still uncertainty around the relative contributions of associated medical and social factors, there is increasing evidence from this review that the early impacts of malnutrition are related to worse academic, cognitive and behavioural outcomes compared with well-nourished peers. Preventing and decreasing childhood malnutrition is therefore of key importance to prevent serious long-term neurocognitive issues in affected children, particularly given the ongoing high malnutrition prevalence in many low-income and middle-income settings. Further research is needed on how to optimise treatment and to best

support ongoing care for survivors to improve outcomes in the long term.

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REFERENCES

1 Development Initiatives. *Global nutrition report: the state of global nutrition*. Bristol, UK, 2021.
2 Black RE, Victora CG, Walker SP, *et al*. Maternal and child undernutrition and overweight in low-income and middle-income countries. *Lancet* 2013;382:427–51.
3 Bhutta ZA, Berkley JA, Bandsma RHJ, *et al*. Severe childhood malnutrition. *Nat Rev Dis Primers* 2017;3:17067.
4 Grey K, Gonzales GB, Abera M, *et al*. Severe malnutrition or famine exposure in childhood and cardiometabolic non-communicable disease later in life: a systematic review. *BMJ Glob Health* 2021;6:e003161.
5 United Nations Children's Fund (UNICEF) WHO, W. B. *Levels and trends in child malnutrition: key findings of the 2021 edition of the joint child malnutrition estimates*. Geneva: World Health Organization, 2021.
6 Fergusson P, Tomkins A, Kerac M. Improving survival of children with severe acute malnutrition in HIV-prevalent settings. *Int Health* 2009;1:10–16.
7 van den Heuvel M, Voskuijl W, Chidzalo K, *et al*. Developmental and behavioural problems in children with severe acute malnutrition in Malawi: a cross-sectional study. *J Glob Health* 2017;7:020416.
8 Gladstone M, Mallewa M, Alusine Jalloh A, *et al*. Assessment of neurodisability and malnutrition in children in Africa. *Semin Pediatr Neurol* 2014;21:50–7.
9 Martins VJB, Toledo Florêncio TMM, Grillo LP, *et al*. Long-Lasting effects of undernutrition. *Int J Environ Res Public Health* 2011;8:1817–46.
10 Pollitt E. Developmental sequel from early nutritional deficiencies: conclusive and probability judgements. *J Nutr* 2000;130:350S–3.
11 Grantham-McGregor S. A review of studies of the effect of severe malnutrition on mental development. *J Nutr* 1995;125:2233S–8.
12 Page MJ, Moher D, Bossuyt PM, *et al*. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. *BMJ* 2021;372:n160.
13 Kerac M, McGrath M, Connell N, *et al*. 'Severe malnutrition': thinking deeplyS, communicating simply. *BMJ Glob Health* 2020;5:e003023.
14 Swaminathan S, Edward BS, Kurpad AV. Micronutrient deficiency and cognitive and physical performance in Indian children. *Eur J Clin Nutr* 2013;67:467–74.
15 Alam MA, Richard SA, Fahim SM, *et al*. Impact of early-onset persistent stunting on cognitive development at 5 years of age: results from a multi-country cohort study. *PLoS One* 2020;15:e0227839.
16 NICE. Quality appraisal checklist - quantative studies reporting correlations and associations, 2012. Available: https://www.nice.org.uk/process/pmg4/chapter/appendix-g-quality-appraisal-checklist-quantitative-studies-reporting-correlations-and
17 Campbell M, McKenzie JE, Sowden A, *et al*. Synthesis without meta-analysis (swim) in systematic reviews: reporting guideline. *BMJ* 2020;368:l6890.
18 Chen K, Liu C, Liu X, *et al*. Nutrition, cognition, and social emotion among preschoolers in poor, rural areas of South central China: status and correlates. *Nutrients* 2021;13. doi:10.3390/nu13041322. [Epub ahead of print: 16 Apr 2021].
19 Mwene-Batu P, Bisimwa G, Baguma M, *et al*. Long-Term effects of severe acute malnutrition during childhood on adult cognitive, academic and behavioural development in African fragile countries: the Lwiro cohort study in Democratic Republic of the Congo. *PLoS One* 2020;15:e0244486.
20 Asiki G, Newton R, Marions L, *et al*. The effect of childhood stunting and wasting on adolescent cardiovascular diseases risk and educational achievement in rural Uganda: a retrospective cohort study. *Glob Health Action* 2019;12:1626184.
21 Dwivedi D, Singh S, Singh J, *et al*. Neurodevelopmental status of children aged 6-30 months with severe acute malnutrition. *Indian Pediatr* 2018;55:131–3.
22 Kang Y, Aguayo VM, Campbell RK, *et al*. Nutritional status and risk factors for stunting in preschool children in Bhutan. *Matern Child Nutr* 2018;14.
23 Lelijveld N, Jalloh AA, Kampondeni SD, *et al*. Brain MRI and cognitive function seven years after surviving an episode of severe acute malnutrition in a cohort of Malawian children. *Public Health Nutr* 2019;22:1406–14.
24 Abessa TG, Bruckers L, Kolsteren P, *et al*. Developmental performance of hospitalized severely acutely malnourished under-six children in low- income setting. *BMC Pediatr* 2017;17:197.
25 Sudfeld CR, McCoy DC, Fink G, *et al*. Malnutrition and its determinants are associated with suboptimal cognitive, communication, and motor development in Tanzanian children. *J Nutr* 2015;145:2705–14.
26 De Grandis ES, Armelini PA, Cuestas E. [Evaluation of quality of life in school children with a history of early severe malnutrition]. *An Pediatr* 2014;81:368–73.
27 Malhi P, Bharti B, Sidhu M. Developmental functioning of young Indian children with malnutrition. *Psychol Stud* 2013;58:259–64.
28 Bogale A, Stoecker BJ, Kennedy T, *et al*. Nutritional status and cognitive performance of mother-child pairs in Sidama, southern Ethiopia. *Matern Child Nutr* 2013;9:274–84.

29 Warsito O, Khomsan A, Hernawati N, *et al*. Relationship between nutritional status, psychosocial stimulation, and cognitive development in preschool children in Indonesia. *Nutr Res Pract* 2012;6:451–7.
30 Nassar MF, Shaaban SY, Nassar JF, *et al*. Language skills and intelligence quotient of protein energy malnutrition survivors. *J Trop Pediatr* 2012;58:226–30.
31 Baker-Henningham H, Hamadani JD, Huda SN, *et al*. Undernourished children have different temperaments than better-nourished children in rural Bangladesh. *J Nutr* 2009;139:1765–71.
32 El-khayat H, Shaaban S, Emam EK, *et al*. Cognitive functions in protein-energy malnutrition: in relation to long chain-polyunsaturated fatty acids. *Pak J Biol Sci* 2007;10:1773–81.
33 Liu J, Raine A, Venables PH, *et al*. Malnutrition at age 3 years and externalizing behavior problems at ages 8, 11, and 17 years. *Am J Psychiatry* 2004;161:2005–13.
34 Liu J, Raine A, Venables PH, *et al*. Malnutrition at age 3 years and lower cognitive ability at age 11 years: independence from psychosocial adversity. *Arch Pediatr Adolesc Med* 2003;157:593–600.
35 Drewett R, Wolke D, Asefa M, *et al*. Malnutrition and mental development: is there a sensitive period? a nested case-control study. *J Child Psychol Psychiatry* 2001;42:181–7.
36 Vazir S, Naidu AN, Vidyasagar P. Nutritional status, psychosocial development and the home environment of Indian rural children. *Indian Pediatr* 1998;35:959–66.
37 Perales CG, Heresi E, Pizarro F, *et al*. [Cognitive functions of school children with normal IQ and histories of severe and early malnutrition]. *Arch Latinoam Nutr* 1996;46:282–6.
38 Kaul M. Malnutrition and mental development during infancy. *J Dairying Foods & Home Sci* 1995;14:159–65.
39 Hock RS, Bryce CP, Fischer L, *et al*. Childhood malnutrition and maltreatment are linked with personality disorder symptoms in adulthood: results from a Barbados lifespan cohort. *Psychiatry Res* 2018;269:301–8.
40 Waber DP, Bryce CP, Girard JM, *et al*. Impaired IQ and academic skills in adults who experienced moderate to severe infantile malnutrition: a 40-year study. *Nutr Neurosci* 2014;17:58–64.
41 Waber DP, Bryce CP, Fitzmaurice GM, *et al*. Neuropsychological outcomes at midlife following moderate to severe malnutrition in infancy. *Neuropsychology* 2014;28:530–40.
42 Galler JR, Bryce CP, Zichlin ML, *et al*. Malnutrition in the first year of life and personality at age 40. *J Child Psychol Psychiatry* 2013;54:911–9.
43 Galler JR, Bryce CP, Zichlin ML, *et al*. Infant malnutrition is associated with persisting attention deficits in middle adulthood. *J Nutr* 2012;142:788–94.
44 Galler JR, Bryce CP, Waber DP, *et al*. Infant malnutrition predicts conduct problems in adolescents. *Nutr Neurosci* 2012;15:186–92.
45 Waber DP, Eaglesfield D, Fitzmaurice GM, *et al*. Cognitive impairment as a mediator in the developmental pathway from infant malnutrition to adolescent depressive symptoms in Barbadian youth. *J Dev Behav Pediatr* 2011;32:225–32.
46 Galler JR, Bryce CP, Waber DP, *et al*. Early malnutrition predicts parent reports of externalizing behaviors at ages 9-17. *Nutr Neurosci* 2011;14:138–44.
47 Galler JR, Bryce CP, Waber D, *et al*. Early childhood malnutrition predicts depressive symptoms at ages 11-17. *J Child Psychol Psychiatry* 2010;51:789–98.
48 de Rooij SR, Wouters H, Yonker JE, *et al*. Prenatal undernutrition and cognitive function in late adulthood. *Proc Natl Acad Sci U S A* 2010;107:16881–6.
49 Krebs NF, Lozoff B, Georgieff MK. Neurodevelopment: the impact of nutrition and inflammation during infancy in low-resource settings. *Pediatrics* 2017;139:S50–8.
50 Germine L, Dunn EC, McLaughlin KA, *et al*. Childhood adversity is associated with adult theory of mind and social affiliation, but not face processing. *PLoS One* 2015;10:e0129612.
51 McLaughlin KA, Weissman D, Bitrán D. Childhood adversity and neural development: a systematic review. *Annu Rev Dev Psychol* 2019;1:277–312.
52 Thurstans S, Opondo C, Seal A, *et al*. Boys are more likely to be undernourished than girls: a systematic review and meta-analysis of sex differences in undernutrition. *BMJ Glob Health* 2020;5:e004030.
53 Shapiro JR, Klein SL, Morgan R. Stop 'controlling' for sex and gender in global health research. *BMJ Glob Health* 2021;6:e005714.
54 Stephenson K, Callaghan-Gillespie M, Maleta K, *et al*. Low linoleic acid foods with added DHA given to Malawian children with severe acute malnutrition improve cognition: a randomized, triple-blinded, controlled clinical trial. *Am J Clin Nutr* 2022;115:1322–33.
55 Martorell R. Improved nutrition in the first 1000 days and adult human capital and health. *Am J Hum Biol* 2017;29. doi:10.1002/ajhb.22952. [Epub ahead of print: 24 01 2017].
56 Martorell R, Horta BL, Adair LS, *et al*. Weight gain in the first two years of life is an important predictor of schooling outcomes in pooled analyses from five birth cohorts from low- and middle-income countries. *J Nutr* 2010;140:348–54.

Supplementary Appendix 1 – Search strategies

EMBASE

1. severe acute malnutrition.ti,ab.
2. acute severe malnutrition.ti,ab.
3. acute malnutrition.ti,ab.
4. (acute adj2 malnutrition).ti,ab.
5. "sever* acute* maln*".ti,ab.
6. protein-energy malnutrition.ti,ab.
7. protein calorie malnutrition.ti,ab.
8. (protein malnutrition or energy malnutrition or energy-protein malnutrition).ti,ab.
9. "acute* maln*".ti,ab.
10. "kwas?io?kor*".ti,ab.
11. "marasm*".ti,ab.
12. "marasm* kwas?io?kor*".ti,ab.
13. wasting.ti,ab.
14. "acute wast*".ti,ab.
15. wasted.ti,ab.
16. (acute adj2 wasting).ti,ab.
17. (severe adj2 wasting).ti,ab.
18. acute undernutrition.ti,ab.
19. (acute adj2 undernutrition).ti,ab.
20. severe undernutrition.ti,ab.
21. (severe adj2 undernutrition).ti,ab.
22. "mid* upper arm circumference".ti,ab.
23. (mid* upper arm circumference adj "115").ti,ab.
24. (mid* upper arm circumference adj "110").ti,ab.
25. MUAC.ti,ab.
26. "acute* undernourish*".ti,ab.
27. "acut* emaciat*".ti,ab.
28. "acut* maln*".ti,ab.
29. *malnutrition/
30. exp kwashiorkor/
31. exp marasmus/
32. exp wasting syndrome/
33. exp protein calorie malnutrition/
34. *nutritional disorder/
35. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34
36. infant/
37. child/

38. exp toddler/
39. "child*".ti,ab.
40. "infan*".ti,ab.
41. "pre-school*".ti,ab.
42. "preschool*".ti,ab.
43. "toddler*".ti,ab.
44. 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43
45. 35 and 44
46. "child* developm* ".ti,ab.
47. "child* neurodevelopm*".ti,ab.
48. "neurodevelopm*".ti,ab.
49. (socio-emotion* develop* or socioemotion* develop*).ti,ab.
50. "social developm*".ti,ab.
51. "emotion* developm*".ti,ab.
52. (sensorymotor developm* or sensory-motor developm*).ti,ab.
53. "motor developm*".ti,ab.
54. "motor neurodevelopm*".ti,ab.
55. exp child development/ or exp postnatal development/
56. 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55
57. exp cognition assessment/ or exp cognition/
58. exp learning/ or exp learning disorder/
59. exp intelligence quotient/ or exp intelligence/
60. exp language development/ or exp human development/ or exp mental development/
61. *brain function/ or *central nervous system function/
62. cognition.ti,ab.
63. "cogniti* performance".ti,ab.
64. intelligence.ti,ab.
65. IQ.ti,ab.
66. "executive function*".ti,ab.
67. reasoning.ti,ab.
68. language.ti,ab.
69. attention.ti,ab.
70. memory.ti,ab.
71. memory.ti,ab.
72. learning.ti,ab.
73. early learning.ti,ab.
74. information processing.ti,ab.
75. literacy.ti,ab.
76. reading.ti,ab.
77. math.ti,ab.

78. 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77
79. education.ti,ab.
80. "school* achievement".ti,ab.
81. "school* performance".ti,ab.
82. school retention.ti,ab.
83. academic.ti,ab.
84. pre-academic.ti,ab.
85. schooling.ti,ab.
86. exp academic achievement/
87. 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86
88. exp behavior/
89. exp mental health/
90. exp psychological aspect/ or exp neuropsychology/ or exp attention/ or exp cognitive defect/ or exp mental disease/
91. exp depression/
92. *hyperactivity/ or *psychomotor disorder/
93. exp attention deficit disorder/
94. "behavi?r* problem*".ti,ab.
95. "emotion* problem*".ti,ab.
96. "temperament*".ti,ab.
97. self regulation.ti,ab.
98. attachment.ti,ab.
99. self esteem.ti,ab.
100. self efficacy.ti,ab.
101. "social competen*".ti,ab.
102. "peer relationship*".ti,ab.
103. pro-social behavi?r.ti,ab.
104. hyperactivity.ti,ab.
105. impulsivity.ti,ab.
106. attention* deficit hyperactivity disorder*.ti,ab.
107. agression.ti,ab.
108. 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97 or 98 or 99 or 100 or 101 or 102 or 103 or 104 or 105 or 106 or 107
109. 56 or 78 or 90 or 108
110. 45 and 109
111. limit 110 to (human and yr="1995 -Current")

MEDLINE

1. "acute severe malnutrition".ti,ab.

2. severe acute malnutrition.ti,ab.
3. acute malnutrition.ti,ab.
4. (acute adj2 malnutrition).ti,ab.
5. "sever* acute* maln*".ti,ab.
6. protein-energy malnutrition.ti,ab.
7. acute severe malnutrition.ti,ab.
8. (protein malnutrition or energy malnutrition or energy-protein malnutrition).ti,ab.
9. "acute* maln*".ti,ab.
10. "kwas?io?kor*".ti,ab.
11. "marasm*".ti,ab.
12. "marasm* kwas?io?kor*".ti,ab.
13. wasting.ti,ab.
14. "acute wast*".ti,ab.
15. wasted.ti,ab.
16. (acute adj2 wasting).ti,ab.
17. (severe adj2 wasting).ti,ab.
18. acute undernutrition.ti,ab.
19. (acute adj2 undernutrition).ti,ab.
20. severe undernutrition.ti,ab.
21. (severe adj2 undernutrition).ti,ab.
22. "mid* upper arm circumference".ti,ab.
23. (mid* upper arm circumference adj "115").ti,ab.
24. (mid* upper arm circumference adj "110").ti,ab.
25. MUAC.ti,ab.
26. "acute* undernourish*".ti,ab.
27. "acut* maln*".ti,ab.
28. exp child nutrition disorders/ or exp deficiency diseases/ or exp starvation/ or *wasting syndrome/
29. exp Protein-Energy Malnutrition/
30. exp Infant Nutrition Disorders/
31. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30
32. "child*".ti,ab.
33. "infan*".ti,ab.
34. "pre-school*".ti,ab.
35. "preschool*".ti,ab.
36. "toddler*".ti,ab.
37. exp Infant/
38. exp Child/
39. Child, Preschool/
40. 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39

41. 31 and 40
42. "child* developm* ".ti,ab.
43. "child* neurodevelopm*".ti,ab.
44. "neurodevelopm*".ti,ab.
45. (socio-emotion* develop* or socioemotion* develop*).ti,ab.
46. "social developm*".ti,ab.
47. "emotion* developm*".ti,ab.
48. (sensorymotor developm* or sensory-motor developm*).ti,ab.
49. "motor developm*".ti,ab.
50. "motor neurodevelopm*".ti,ab.
51. exp Child Development/
52. 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51
53. cognition.ti,ab.
54. "cogniti* performance".ti,ab.
55. intelligence.ti,ab.
56. IQ.ti,ab.
57. "executive function*".ti,ab.
58. reasoning.ti,ab.
59. language.ti,ab.
60. attention.ti,ab.
61. memory.ti,ab.
62. learning.ti,ab.
63. early learning.ti,ab.
64. information processing.ti,ab.
65. literacy.ti,ab.
66. reading.ti,ab.
67. math.ti,ab.
68. *cognition/ or exp cognitive reserve/ or exp comprehension/ or exp executive function/ or exp learning/
69. exp Mild Cognitive Impairment/
70. *Intelligence/
71. *language development/ or *child language/
72. 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71
73. education.ti,ab.
74. "school* achievement".ti,ab.
75. "school* performance".ti,ab.
76. school retention.ti,ab.
77. academic.ti,ab.
78. pre-academic.ti,ab.
79. schooling.ti,ab.

80. exp Educational Status/
81. 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80
82. "behavi?r* problem*".ti,ab.
83. "emotion* problem*".ti,ab.
84. "temperament*".ti,ab.
85. self regulation.ti,ab.
86. attachment.ti,ab.
87. self esteem.ti,ab.
88. self efficacy.ti,ab.
89. "social competen*".ti,ab.
90. "peer relationship*".ti,ab.
91. pro-social behavi?r.ti,ab.
92. hyperactivity.ti,ab.
93. impulsivity.ti,ab.
94. attention* deficit hyperactivity disorder*.ti,ab.
95. aggression.ti,ab.
96. exp Child Behavior Disorders/
97. exp Mental Health/
98. *psychology/ or exp psychology, adolescent/ or exp psychology, child/
99. exp Depression/
100. exp Attention Deficit Disorder with Hyperactivity/
101. *Anxiety Disorders/
102. 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97 or 98 or 99 or 100 or 101
103. 52 or 72 or 81 or 102
104. 41 and 103
105. limit 104 to (humans and yr="1995 -Current")

GLOBAL HEALTH

1. severe acute malnutrition.ti,ab.
2. acute severe malnutrition.ti,ab.
3. acute malnutrition.ti,ab.
4. (acute adj2 malnutrition).ti,ab.
5. "sever* acute* maln*".ti,ab.
6. protein-energy malnutrition.ti,ab.
7. protein calorie malnutrition.ti,ab.
8. (protein malnutrition or energy malnutrition or energy-protein malnutrition).ti,ab.
9. "acute* maln*".ti,ab.
10. "kwas?io?kor*".ti,ab.
11. "marasm*".ti,ab.

12. "marasm* kwas?io?kor*".ti,ab.
13. wasting.ti,ab.
14. "acute wast*".ti,ab.
15. wasted.ti,ab.
16. (acute adj2 wasting).ti,ab.
17. (severe adj2 wasting).ti,ab.
18. acute undernutrition.ti,ab.
19. (acute adj2 undernutrition).ti,ab.
20. severe undernutrition.ti,ab.
21. (severe adj2 undernutrition).ti,ab.
22. "mid* upper arm circumference".ti,ab.
23. (mid* upper arm circumference adj "115").ti,ab.
24. (mid* upper arm circumference adj "110").ti,ab.
25. MUAC.ti,ab.
26. "acute* undernourish*".ti,ab.
27. "acut* maln*".ti,ab.
28. emaciat*.ti,ab.
29. nutritional disorders/ or malnutrition/ or exp protein energy malnutrition/ or exp undernutrition/ or exp nutritional oedema/
30. wasting disease/ or exp emaciation/
31. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30
32. "child*".ti,ab.
33. "infan*".ti,ab.
34. "pre-school*".ti,ab.
35. "preschool*".ti,ab.
36. "toddler*".ti,ab.
37. exp infants/
38. exp preschool children/ or children/
39. 32 or 33 or 34 or 35 or 36 or 37 or 38
40. 31 and 39
41. "child* developm* ".ti,ab.
42. "child* neurodevelopm*".ti,ab.
43. "neurodevelopm*".ti,ab.
44. (socio-emotion* develop* or socioemotion* develop*).ti,ab.
45. "social developm*".ti,ab.
46. "emotion* developm*".ti,ab.
47. (sensorymotor developm* or sensory-motor developm*).ti,ab.
48. "motor developm*".ti,ab.
49. child development/ or exp early childhood development/ or exp infant development/ or exp psychomotor development/

50. 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49
51. cognition.ti,ab.
52. "cogniti* performance".ti,ab.
53. intelligence.ti,ab.
54. IQ.ti,ab.
55. "executive function*".ti,ab.
56. reasoning.ti,ab.
57. language.ti,ab.
58. attention.ti,ab.
59. memory.ti,ab.
60. learning.ti,ab.
61. early learning.ti,ab.
62. information processing.ti,ab.
63. literacy.ti,ab.
64. reading.ti,ab.
65. math.ti,ab.
66. exp mental ability/ or exp cognitive development/ or exp memory/
67. exp learning/
68. 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67
69. education.ti,ab.
70. "school* achievement".ti,ab.
71. "school* performance".ti,ab.
72. school retention.ti,ab.
73. academic.ti,ab.
74. schooling.ti,ab.
75. preacademic.ti,ab.
76. education/ or exp early childhood education/ or exp elementary education/ or exp extension education/ or exp higher education/ or exp primary education/ or exp professional education/ or exp secondary education/ or exp academic achievement/ or exp educational performance/
77. 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76
78. "behavi?r* problem*".ti,ab.
79. "emotion* problem*".ti,ab.
80. "temperament*".ti,ab.
81. self regulation.ti,ab.
82. attachment.ti,ab.
83. self esteem.ti,ab.
84. self efficacy.ti,ab.
85. "social competen*".ti,ab.
86. "peer relationship*".ti,ab.

87. pro-social behavi?r.ti,ab.
88. hyperactivity.ti,ab.
89. impulsivity.ti,ab.
90. attention* deficit hyperactivity disorder*.ti,ab.
91. aggression.ti,ab.
92. exp mental health/ or exp mental disorders/
93. depression/
94. psychology/ or exp adolescent development/ or exp adult development/ or exp emotional development/ or exp self esteem/ or exp self reliance/
95. exp attention deficit hyperactivity disorder/
96. 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95
97. 50 or 68 or 77 or 96
98. 40 and 97
99. limit 98 to yr="1995 -Current"

PsycINFO

1. severe acute malnutrition.ti,ab.
2. acute malnutrition.ti,ab.
3. (acute adj2 malnutrition).ti,ab.
4. "sever* acute* maln*".ti,ab.
5. protein-energy malnutrition.ti,ab.
6. protein calorie malnutrition.ti,ab.
7. (protein malnutrition or energy malnutrition or energy-protein malnutrition).ti,ab.
8. "acute* maln*".ti,ab.
9. "kwas?io?kor*".ti,ab.
10. "marasm*".ti,ab.
11. "marasm* kwas?io?kor*".ti,ab.
12. wasting.ti,ab.
13. wasted.ti,ab.
14. (acute adj2 wasting).ti,ab.
15. (severe adj2 wasting).ti,ab.
16. acute undernutrition.ti,ab.
17. (acute adj2 undernutrition).ti,ab.
18. severe undernutrition.ti,ab.
19. (severe adj2 undernutrition).ti,ab.
20. "mid* upper arm circumference".ti,ab.
21. MUAC.ti,ab.
22. "acute* undernourish*".ti,ab.
23. "emaciat*".ti,ab.

24. "acut* maln*".ti,ab.
25. nutritional deficiencies/ or protein deficiency disorders/ or exp failure to thrive/ or exp underweight/
26. exp Kwashiorkor/
27. *protein deficiency disorders/
28. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27
29. "child*".ti,ab.
30. "infan*".ti,ab.
31. "pre-school*".ti,ab.
32. "preschool*".ti,ab.
33. "toddler*".ti,ab.
34. 29 or 30 or 31 or 32 or 33
35. 28 and 34
36. "child* developm* ".ti,ab.
37. "child* neurodevelopm*".ti,ab.
38. "neurodevelopm*".ti,ab.
39. (socio-emotion* develop* or socioemotion* develop*).ti,ab.
40. "social developm*".ti,ab.
41. "emotion* developm*".ti,ab.
42. (sensorymotor developm* or sensory-motor developm*).ti,ab.
43. "motor developm*".ti,ab.
44. "motor neurodevelopm*".ti,ab.
45. psychomotor developm*.ti,ab.
46. exp infant development/ or exp early childhood development/
47. *childhood development/ or exp early childhood development/ or exp motor development/ or exp psychological development/ or exp psychomotor development/
48. exp emotional development/ or exp psychological development/
49. 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48
50. cognition.ti,ab.
51. "cogniti* performance".ti,ab.
52. intelligence.ti,ab.
53. IQ.ti,ab.
54. "executive function*".ti,ab.
55. reasoning.ti,ab.
56. language.ti,ab.
57. attention.ti,ab.
58. memory.ti,ab.
59. learning.ti,ab.
60. early learning.ti,ab.
61. information processing.ti,ab.

62. literacy.ti,ab.
63. reading.ti,ab.
64. math.ti,ab.
65. *cognitive processes/ or exp cognitive assessment/ or exp learning/ or exp memory/ or exp neurocognition/
66. *learning/ or adult learning/ or problem based learning/ or school learning/ or skill learning/ or verbal learning/
67. exp Fine Motor Skill Learning/ or exp Learning Disabilities/ or exp Learning Disorders/ or exp Gross Motor Skill Learning/
68. *language disorders/ or *specific language impairment/ or exp language delay/ or exp language development/
69. *cognitive development/ or exp brain development/ or exp speech development/
70. *cognition/ or exp cognitive impairment/
71. *intelligence/ or exp intellectual development/ or exp intelligence quotient/
72. 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71
73. education.ti,ab.
74. "school* achievement".ti,ab.
75. "school* performance".ti,ab.
76. school retention.ti,ab.
77. academic.ti,ab.
78. pre-academic.ti,ab.
79. schooling.ti,ab.
80. *education/
81. education/ or exp academic achievement/ or exp school attendance/ or exp school dropouts/ or exp school learning/
82. 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81
83. "behavi?r* problem*".ti,ab.
84. "emotion* problem*".ti,ab.
85. "temperament*".ti,ab.
86. self regulation.ti,ab.
87. attachment.ti,ab.
88. self esteem.ti,ab.
89. self efficacy.ti,ab.
90. "social competen*".ti,ab.
91. "peer relationship*".ti,ab.
92. pro-social behavi?r.ti,ab.
93. hyperactivity.ti,ab.
94. impulsivity.ti,ab.
95. attention* deficit hyperactivity disorder*.ti,ab.
96. aggression.ti,ab.

97. *mental health/
98. exp behavior problems/ or exp behavior disorders/ or exp conduct disorder/
99. exp anxiety disorders/
100. exp hyperkinesis/ or exp attention deficit disorder with hyperactivity/
101. *deprivation/ or exp psychological stress/ or exp stress/
102. *affective disorders/ or *major depression/
103. 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97 or 98 or 99 or 100 or 101 or 102
104. 49 or 72 or 82 or 103
105. 35 and 104
106. limit 105 to (human and yr="1995 –Current)

Supplementary Table 1 – Study quality scoring

Study (Year published)	External Validity	Internal Validity	Overall Study Quality
Chen *et al* (2021)	++	++	++
Mwene-Batu *et al* (2020)	++	+	+
Asiki *et al* (2019)	++	++	++
Dwivedi *et al* (2018)	+	+	+
Hock *et al* (2018)	++	+	+
Kang *et al* (2018)	++	+	+
Lelijiveld *et al* (2018)	++	++	++
Abessa *et al* (2017)	++	++	++
Sudfeld *et al* (2015)	++	++	++
De Grandis *et al* (2014)	+	-	-
Waber (1) *et al* (2014)	++	++	++
Waber (2) *et al* (2014)	++	++	++
Malhi *et al* (2013)	+	-	-
Galler *et al* (2013)	++	+	+
Bogale *et al* (2013)	++	++	++
Galler (1) *et al* (2012)	++	+	+
Galler (2) *et al* (2012)	++	+	+
Warsito *et al* (2012)	++	-	-
Nassar *et al* (2012)	-	-	-
Waber *et al* (2011)	++	+	+
Galler *et al* (2011)	++	++	++
Galler *et al* (2010)	++	++	++
Baker-Henningham *et al* (2009)	++	++	++
El-Khayat *et al* (2007)	+	+	+
Liu *et al* (2004)	++	++	++
Liu *et al* (2003)	++	++	++
Drewett *et al* (2001)	++	++	++
Vazir *et al* (1998)	++	+	+
Perales *et al* (1996)	+	+	+
Kaul *et al* (1995)	+	+	+

++ = very good

+ = adequate

- = poor

Supplementary Table 2 – Results from studies assessing neurodevelopment in children with malnutrition compared to controls

Study (quality)	Neurodevelopment tool/measurement	Summary of results
Dwivedi *et al* (2018) **(+)**	DASII (Indian modification of BSID)	Controls n=101 Cases n=102 **Mental age:** 10.4 (SE 0.5) 8.2 (SE 0.4) **Mental development quotient:** 83.5 (SE 1.0) 62.1 (SE 0.6) **Motor age:** 10.1 (SE 0.5) 7.9 (SE 0.4) **Motor development quotient:** 80.0 (SE 1.0) 59.0 (SE 0.7) **Adjusted analysis:** (unadjusted analysis) **Overall findings:** Significant developmental delay in children with severe malnutrition compared to controls unadjusted for confounding variables.
Kang *et al* 2018 **(+)**	MICS ECDI	**Learning-cognition development (odds of cases being on track compared to controls):** Country — Unadjusted Odds Ratio — Adjusted Odds Ratio Bangladesh 1.27 [95% CI 0.92, 1.75] 1.27 [95% CI 0.90, 1.79] Bhutan 1.60 [95% CI 0.32, 7.85] 1.93 [95% CI 0.39, 9.48] Nepal 1.09 [95% CI 0.66, 1.79] 1.52 [95% CI 0.90, 2.58] Punjab 0.63 [95% CI 0.50, 0.79] 0.67 [95% CI 0.53, 0.86] Sindh 0.69 [95% CI 0.53, 0.89] 0.76 [95% CI 0.59, 0.97]

		All 0.98 [95% CI 0.70, 1.37] **Socio-emotional development (odds of cases being on track compared to controls):** Country — Unadjusted Odds Ratio — Adjusted Odds Ratio Bangladesh 1.14 [95% CI 0.92, 1.42] 1.10 [95% CI 0.40, 1.88] Bhutan 1.08 [95% CI 0.58, 2.01] 1.08 [95% CI 0.58, 2.03] Nepal 2.40 [95% CI 1.25, 4.58] 2.54 [95% CI 1.33, 4.85] Punjab 0.86 [95% CI 0.73, 1.02] 0.88 [95% CI 0.74, 1.04] Sindh 0.92 [95% CI 0.74, 1.14] 0.94 [95% CI 0.76, 1.15] All 1.07 [95% CI 0.86, 1.33] **Adjusted analysis:** (results adjusted for rural/urban, wealth quintile, household size, household head, water source, toilet facility, maternal education, child age and sex, diarrhoea/cough in past 2 weeks, study design effect, early childhood education, support for learning, availability of children's books and playthings, inadequate care) **Sample size:** n = 31037, wasting prevalence = between 4.1-12.8% across study sites **Overall findings:** Mixed results between study sites with no significant difference between cases and controls including when adjusted for confounding variables
Abessa *et al* (2017) **(++)**	Denver II ASQ: social-emotional score	**Denver II score (incidence rate ratio in cases compared to controls):** Fine motor IRR 0.76 [95% CI 0.71, 0.8] Gross motor IRR 0.73 [95% CI 0.71, 0.74] Language IRR 0.98 [95% CI 0.86, 1.11] Personal-social IRR 0.7 [95% CI 0.65, 0.75] **Adjusted analysis:** (results adjusted for significant variables from age, sex, maternal religion) **Sample size:**

<table>
<tr><td></td><td></td><td>Cases n=310, Controls n=310

<u>Overall Findings:</u>
Children with malnutrition performed worse on personal-social, fine motor, and gross motor skills compared to age and sex-matched controls adjusted for confounding variables. Motor skills are the most and personal social the least affected domains assessed on the Denver II Jimma.</td></tr>
<tr><td>Sudfeld et al (2015)

(++)</td><td>BSID-III</td><td><u>BSID-II score (association between score and malnutrition):</u>
Cognitive -0.63 [95% CI -0.97, -0.29]
Communication -0.32 [95% CI -0.64, -0.01]
Motor -0.54 [95% CI -0.86, -0.23]

<u>Adjusted analysis:</u>
(results adjusted for height-for-age, stimulation category, sex, age, assessor, maternal education, wealth quintile, randomized regimen)

<u>Sample size:</u>
Cases n=47, Controls n=989

<u>Overall Findings:</u>
Children experiencing wasting had across domain deficits compared to controls adjusted for confounding variables.</td></tr>
<tr><td>Malhi et al 2013

(-)</td><td>Indian Development Inventory</td><td><table><tr><th></th><th>Controls n=20</th><th>Cases n=44</th><th>p value</th></tr><tr><td><u>Inventory domain:</u></td><td></td><td></td><td></td></tr><tr><td>Social score</td><td>104.64 (SD 17.11)</td><td>101.30 (SD 17.31)</td><td>0.036</td></tr><tr><td>Adaptive score</td><td>105.36 (SD 9.71)</td><td>105.25 (SD 8.33)</td><td>0.239</td></tr><tr><td>Motor score</td><td>112 (SD 14.5)</td><td>108.85 (SD 10.93)</td><td>0.074</td></tr><tr><td>Communication score</td><td>97.82 (SD 14.34)</td><td>94.50 (SD 8.61)</td><td>0.047</td></tr><tr><td>Cognitive score</td><td>92.82 (SD 13.92)</td><td>90.1 (SD 9.79)</td><td>0.080</td></tr><tr><td>Total score</td><td>100.86 (SD 18.15)</td><td>95 (SD 13.51)</td><td>0.007</td></tr></table></td></tr>
</table>

		Adjusted analysis: Multivariate regression revealed that 26.7% of variance was accounted by household income and stunting, indicating results were no longer significant **Overall Findings:** Children with wasting compared to controls did not have significantly lower domain scores adjusted for confounding variables.
El-Khayat *et al* 2007 **(+)**	BSID-II	Controls n=15 / Cases n=42 (before rehab) / Cases (after rehab) Mental Development Index: 97 (SD 10.92) / 76.3 (SD 8.78) / 88.19 (SD 8.93) Psychomotor Development Index: 97 (SD 12.38) / 72.76 (SD 11.27) / 87.39 (SD 8.85) **Adjusted analysis:** (unadjusted analysis) **Overall Findings:** Cases had lower scores at the start of the study compared to controls unadjusted for confounding variables. Scores were improved after 8 weeks of nutritional rehabilitation but were still significantly lower when compared to controls unadjusted for confounding variables.
Drewett *et al* 2001 **(++)**	BSID	Controls n=100 / Cases n=27 Early Malnutrition at 4 months / Cases n=70 Late Malnutrition at 12 months **BSID (score at 2 years):** Psychomotor score: 10.2 (SD3.7) / 6.6 (SD 4.2) / 8.5 (SD 4.3) Mental score: 28.9 (SD5.8) / 22.6 (SD 6.2) / 26.6 (SD 6.1) **Adjusted analysis:** Weight at 2 years associated with BSID outcome, but early and late growth faltering before 1 year not independently associated with BSID scores after adjusting for weight at 2 years and other covariates (sex, mother's education, possessions). **Overall Findings:** Significantly lower psychomotor and mental scores at 2 years in early growth falterers and late growth

		falterers compared to controls. Difference is accounted for by differences in weight at 2 years when adjusted for in analysis.
Vazir *et al* 1998 **(+)**	ICMR Psychosocial Developmental Screening Test	**ICMR Psychosocial Development Screening Test Results:** Well nourished children attained developmental milestones at a younger age in the five areas of development compared to undernourished children. **Adjusted analysis:** (unadjusted analysis) **Sample size:** Cases n=1456, Controls n=2212 **Overall Findings:** Malnourished children attained developmental milestones at a later age unadjusted for confounders.
Kaul *et al* 1995 **(+)**	BSID	Controls n=102 Cases n=50 **BSID (mental quotient):** Male (0-6 months) 98.80 (SD 11.94) 57.60 (SD 6.77) Female (0-6 months) 97.28 (SD 10.22) 59.85 (SD 11.94) Male (6-12 months) 100.86 (SD 4.39) 79.93 (SD 5.57) Female (6-12 months) 103.68 (SD 4.31) 75.15 (SD 3.39) **Adjusted analysis:** (unadjusted analysis) **Overall Findings:** Children with moderate malnutrition had a lower mental quotient than controls unadjusted for confounding variables.

95% CI – 95% confidence intervals, BSID – Bayley Scales of Infant Development, DASII – Developmental Assessment Scale of Indian Infants, ICMR – Indian Council Medical Research Psychosocial Developmental Screening Test, IDI – Indian Developmental Inventory, IRR – incidence rate ratio, MDAT – Malawi Developmental Assessment Tool, MICS ECDI – Multiple Indicator Cluster Survey Early Child Development Index, SD – Standard Deviation, SE – standard error

Supplementary Table 3 - Results from studies assessing cognitive outcomes in those exposed to childhood malnutrition compared to controls

Study (quality)	Cognition tool/measurement (outcome age)	Summary of results
Chen *et al* 2021 **(++)**	WPPSI-IV (childhood)	Controls n=1270 — Cases n=23 **WPPSI-IV:** Working Memory Index: 90.35 (SD 0.38) [95% CI 89.60, 91.09] — 95.09 (SD 2.67) [95% CI 89.86, 100.32] Verbal Comprehension Index: 86.00 (SD 0.36) [95% CI 85.30, 86.70] — 87.26 (SD 3.29) [95% CI 80.80, 93.72] **Adjusted analysis:** Wasting was not statistically associated with any developmental outcome variables after adjusting for vector of child, parent, caregiver and household-level characteristics. **Overall findings:** Wasting was not associated with impaired cognition after adjusting for confounding variables
Mwene-Batu *et al* 2020 **(+)**	MMSE Academic performance (adulthood)	Controls n=407 — Cases n=524 — p value **MMSE:** Mean score: 25.6 (SD 2.6) — 27.8 (SD 2.2) — 0.001 Normal score (%): 78.0 — 90.1 — <0.001 **Academic performance (based on self-report):** Low (%): 15.2 — 23.8 Average (%): 49.0 — 45.1 High (%): 35.8 — 31.0 — 0.014 **Adjusted analysis:** (unadjusted analysis) **Overall findings:**

		Malnutrition survivors had a significantly lower probability of attaining a high education level, reported worse academic performance and a significantly lower mean cognition score unadjusted for confounding variables.
Asiki *et al* 2019 **(++)**	Academic achievement (adolescence)	Controls n=464 Children with ongoing wasting n=12 Children recovered from wasting n=145 **School years achieved (parental report):** 9.2 years (SD 11) 6.2 (SD 2.5) 7.8 (SD 3.8) **Adjusted correlation coefficient:** -1.91 [95% CI -4.51, 0.68] - 2.05 [95% CI -3.30, -0.79] **Adjusted analysis:** (adjusted for age group, sex, education, tribe, wall of house type, reported alcohol consumption) **Overall findings:** Wasting was associated with fewer schooling years regardless of recovery from undernutrition adjusted for confounding variables.
Lelijveld *et al* 2018 **(++)**	Academic achievement CANTAB (adolescence)	Controls n=178 Cases n=315 **School grade achieved (parental report):** 3.1 (SD 1.6) 2.5 (SD 1.3) **Logistic regression comparing school grade in groups:** OR 0.5 [95% CI 0.4, 0.7] Adjusted OR 0.54 [95% CI 0.35, 0.81] **Adjusted analysis:** (adjusted for h/a z-score, age, sex, HIV, socioeconomic status) **CANTAB cognition test scores:** Malnutrition survivors had poorer scores in all CANTAB cognitive tests. **Adjusted analysis:** Adjusting for HIV and socio-economic status diminished statistically significant

		differences in CANTAB test scores. **Overall findings:** Malnutrition survivors were significantly more likely to be in a lower grade at school than controls adjusted for confounding variables. Malnutrition survivors had poorer cognition scores than controls, but differences were not statistically significant when adjusted for confounding variables.
Bogale *et al* 2013 **(++)**	Raven's CPM, KABC-II (childhood)	Controls n=88 / Cases n=12 / p value **Cognitive scores:** Visual processing: 17.0 (SD 3.9) / 12.8 (SD 2.4) / 0.003 Triangles: 4.3 (SD 2.4) / 1.7 (SD 1.0) / 0.001 Conceptual thinking: 4.7 (SD 1.8) / 3.3 (SD 1.3) / 0.017 Pattern reasoning: 8.1 (SD 1.8) / 7.9 (SD 1.7) / 0.726 Short-term memory: 21.7 (SD 5.6) / 16.2 (SD 5.1) / 0.006 Word order: 6.5 (SD 3.0) / 4.8 (SD 2.0) / 0.1 Number recall: 7.1 (SD 2.2) / 5.4 (SD 2.5) / 0.025 Hand movement: 8.1 (SD 2.1) / 5.9 (SD 1.1) / 0.004 **Adjusted analysis:** When results adjusted via stepwise regression, visual processing and short-term memory remained significantly correlated when adjusted for maternal education, family size, and household roof type. **Overall findings:** Scores on short-term memory and visual processing were significantly poorer in cases compared to controls when adjusted for confounding variables.
Warsito *et al* 2012 **(-)**	Indonesian Department of National Education – child development instrument (childhood)	Controls n=48 / Wasting n=3 / Severe Wasting n=2 **Child development score:** Percentage score: 68.7 / 73.9 / 73.8 **Adjusted analysis:** (results unadjusted)

		Overall findings: Those with wasting in this study had better development scores than those without wasting. The study is limited by small case numbers.			
Nassar *et al* 2012 **(-)**	Stanford-Binet-Intelligence-Scale Arabic-Language-Test (childhood)		Controls n=30	Cases n=33	p value
		Stanford-Binet-Intelligence-Scale (mean):			
		IQ score	92.07 (SD 11.52)	80.52 (SD 13.65)	0.001
		Mental age (months)	50.50 (SD 13.40)	42.58 (SD 8.66)	0.017
		Arabic Language Test (mean):			
		Receptive language age (months)	51.67 (SD 13.98)	40.09 (SD 17.36)	0.005
		Expressive language age (months)	51.67 (SD 14.23)	40.76 (SD 16.74)	0.003
		Total language age (months)	51.40 (SD 14.15)	40.00 (SD 17.66)	0.007
		Adjusted analysis: (results unadjusted)			
		Overall findings: Those with malnutrition had poorer scores for both tests than age- and sex-matched controls unadjusted for confounding variables.			
Liu *et al* 2003 **(++)**	Bohem Test WISC Academic Tests Holborn-Reading Scale Trail Making Test (adolescence)		Control n=837	Cases n=253	p value
		Age 3y:			
		Verbal IQ	100.92 (SD 15.04)	96.93 (SD 14.36)	0.001
		Spatial IQ	100.34 (SD 15.21)	98.95 (SD 13.52)	0.18
		Full-Scale IQ	100.92 (SD 15.04)	96.93 (SD 14.36)	0.001
		Age 11y:			
		Verbal IQ	100.90 (SD 14.41)	96.16 (SD 15.40)	0.001
		Spatial IQ	100.75 (SD 14.55)	96.23 (SD 15.41)	0.001
		Full-Scale IQ	100.88 (SD 14.43)	95.83 (SD 15.49)	0.001
		Reading	95.11 (SD 55.30)	76.81 (SD 56.58)	0.001

		School performance 10.33 (SD 7.07) 7.63 (SD 6.48) 0.001 Trails A -0.049 (SD 0.95) 0.24 (SD 1.10) 0.001 Trails B -0.023 (SD 0.98) 0.20 (SD 1.07) 0.004 **Adjusted analysis:** Differences remain after controlling for psychosocial adversity. **Overall Findings:** Malnourished children had poorer cognition and school/academic performance at both ages after controlling for psychosocial adversity.
Perales *et al* 1996 **(+)**	Continuous Performance Task Anstey Domino Test (childhood)	Controls n=40 Cases n=40 p value **Short-term Memory**: Number-of-digits score 4.5 (SD 0.87) 3.8 (SD 0.88) <0.05 **Problem-Solving:** Correct score 4.7 (SD 2.1) 3.4 (SD 1.4) <0.05 **Attention**: No differences in correct answers between groups. Lower performance in cases response time for correct answers (p<0.02). **Adjusted analysis:** (unadjusted analysis) **Overall Findings:** Cases had lower memory scores and problem solving scores unadjusted for confounding variables. Cases had worse performance than controls for response times in the attention test unadjusted for confounding variables.
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Waber (1) *et al* 2014*	Academic achievement, WASI	**WRAT-III academic achievement score (adjusted odds ratio):** Reading OR 3.44 [95% CI 1.88–6.30]

(++)	(adulthood)	Spelling OR 6.10 [95% CI 3.34–11.16] Calculation OR 6.23 [95% CI 3.15–12.32] **WASI score (adjusted odds ratio):** IQ OR 9.18 [95% CI 3.50, 24.13] **Adjusted analysis:** (Results adjusted for childhood standard of living) **Sample size:** Cases n=77, Controls n=59 **Overall findings:** Academic skills and IQ were lower in the malnourished group compared to controls after adjusting for childhood standard of living.
Waber (2) *et al* 2014* **(++)**	WAIS-III, D-KEFS, WRAML-II, Wisconsin card sorting, Metacognitive index (adulthood)	Controls n=59 Cases n=77 **Metacognitive index (General executive composite)**: Mean score 41.81 (SD 6.05) 47.36 (SD 9.33) Adjusted Mean difference 3.70 ($p<0.05$) **WRAML-2:** Scaled score 8.49 (SD 1.81) 7.45 (SD 2.28) Adjusted Mean difference -0.42 ($p>0.05$) **Wisconsin card sorting:** Total errors score 94.56 (SD 12.70) 80.67 (SD 12.53)

		Adjusted Mean difference -9.74 (p<0.001) **<u>Adjusted analysis</u>** (results adjusted for childhood standard of living and IQ) Significant differences persisted for the WAIS Digit Symbol and Letter-Number, D-KEFS Trails (Numbers) , Verbal Fluency (Letters) and Rey-Osterrieth Complex Figure after adjusting for covariates **<u>Overall findings:</u>** Malnutrition during infancy is associated with impaired IQ in adulthood. In models adjusted only for childhood standard of living, the malnutrition group performed more poorly on nearly all measures. In the IQ-adjusted models, significant differences persisted for the WAIS Digit Symbol and Letter-Number, D-KEFS Trails (Numbers) and Verbal Fluency (Letters), Rey-Osterrieth Complex Figure, and Wisconsin Card Sorting Test.
Waber *et al* 2011 **(+)**	WISC, Common entrance examination (local school test) (adolescence)	<u>Controls n=60 Malnutrition n=56 p value</u> **<u>WISC:</u>** IQ 104.92 (SD 10.54) 92.54 (SD 13.86) <0.0001 **<u>Common Entrance Exam:</u>** Score 210.42 (SD 22.13) 184.10 (29.27) <0.0001 **<u>Adjusted analysis:</u>** Early malnutrition predicted cognitive function and exam score in childhood after adjusting for childhood standard of living. **<u>Overall findings:</u>** Malnutrition predicted common entrance exam score and cognitive functioning after adjusting for childhood standard of living.

*Studies are drawn from the same Barbados Nutrition Study

95% CI – 95% Confidence Intervals, CANTAB – Cambridge Neuropsychological Test Automated Battery, D-KEFS – Delis-Kaplan Executive Function System, MMSE – Mini-Mental State Exam, OR – Odds Ratio, SD – Standard Deviation, WAIS-III – Wechsler Adult Intelligence Scale-III, WASI – Adult IQ: Weschler Abbreviated Scale of Intelligence – Vocabulary and Matrix Reasoning subsets, WISC – Weschler Intelligence Scale, WPPSI-IV – Wechsler Preschool and Primary Scale of Intelligence Fourth Edition, WRAML-II – Wide Range Assessment of Memory and Learning-II, WRAT-III – Academic achievement: Wide Range Achievement Test-III – Reading Spelling and Calculation subsets

Supplementary Table 4 - Results from studies assessing mental health outcomes in those exposed to childhood malnutrition compared to controls

Study (quality)	**Mental health tool/measurement (outcome age)**	**Summary of results**
Chen *et al* 2021 **(++)**	SDQ (childhood)	Controls n=1270 — Wasting n=23 **SDQ:** Prosocial score: 6.83 (SD 0.06) [95% CI 6.71, 6.95] — 6.70 (SD 0.42) [95% CI 5.86, 7.53] Total difficulties score: 12.35 (SD 0.13) [95% CI 12.10, 12.61] — 12.09 (SD 1.09) [95% CI 9.95, 14.22] **Adjusted analysis:** Wasting was not statistically associated with any developmental outcome variables after adjusting for vector of child, parent, caregiver and household-level characteristics. **Overall findings:** Wasting was not associated with a difference in behaviour after adjusting for confounding variables.
Mwene-Batu *et al* 2020 **(+)**	Rosenberg self-esteem scale, WHODAS (adulthood)	Controls n=407 — Cases n=524 — p value **Self-esteem:** Low (%): 12.1 — 20.5 Average (%): 78.5 — 72.6 High (%): 9.4 — 6.9 — 0.003 **Social related disability:** No disability (%): 91.0 — 94.2 Moderate disability (%): 8.8 — 5.0 Severe disability (%): 0.3 — 0.8 — 0.03 **Adjusted analysis:**

		(unadjusted results) **Overall findings:** Cases had significantly less disability in terms of social relationships than the community controls but had statistically significant lower self-esteem than the controls unadjusted for confounding variables.
Abessa *et al* (2017) **(++)**	ASQ: social-emotional score (childhood)	**ASQ: Socio-emotional score (incidence rate ratio in cases compared to controls):** Socioemotional IRR 3.1 [95% CI 2.24, 4.26] **Adjusted analysis:** (results adjusted for significant variables from age, sex, maternal religion) **Sample size:** Cases n=310, Controls n=310 **Overall findings:** Children with malnutrition performed worse on socio-emotional competences compared to age and sex-matched non-malnourished children adjusted for confounding variables.
De Grandis *et al* 2014 **(-)**	Paediatric quality of life inventory (childhood)	**Peds Q:** Global score: Controls n=28: 89.18 (SD 1.84); Malnutrition n=25: 80.82 (SD 1.94); p<0.0001 Health/physical dimension: 94.75 (SD 1.87); 87.75 (SD 3.37); p<0.0001 Psychosocial health: 86.57 (SD 1.42); 77.77 (SD 2.90); p<0.0001 Emotional dimension: 78.75 (SD 2.96); 67.80 (SD 4.40); p<0.0001 Social dimension: 95.71 (SD 1.52); 88.80 (SD 3.05); p<0.0001 School dimension: 74.58 (SD 3.80); 85.00 (SD 3.51); p<0.0001 **Adjusted analysis:** (unadjusted analysis) **Overall findings:** Those with a history of early severe malnutrition, showed significantly lower quality of life scores compared to

		controls unadjusted for confounding variables.
Baker-Henningham *et al* 2009 **(++)**	Temperament Questionnaire derived from existing validated instruments (modified by Wachs, Purdue University) (childhood)	Controls n=108 Undernourished n=212 p value **Temperament questionnaire:** Manageability 8.67 (SD 3.51) 9.56 (SD 3.26) p<0.05 Activity 10.40 (SD 3.00) 10.59 (SD 2.73) p>0.05 Emotionality 13.66 (SD 4.74) 14.80 (SD 4.24) p<0.05 Sociability 8.15 (SD 3.87) 9.29 (SD 3.98) p<0.05 Attention 12.58 (SD 3.31) 13.53 (SD 3.06) p<0.05 Soothability 8.23 (SD 2.77) 8.42 (SD 2.57) p<0.01 **Adjusted analysis:** After adjusting for significant covariates (parental schooling and occupation, sanitiation index, asset index, housing index, mother's BMI and home), the undernourished children were less sociable (regression coefficient (B) = -0.96 [95% CI -0.04, -1.88]), less attentive (B = -0.94 [95% CI -0.19, -1.69], more fearful (B = 1.43 [95% CI 2.44, 0.42]), and had more negative emotionality (B = -1.08 [95% CI -2.16, 0.006]). **Overall findings:** There were significant differences in temperament traits between undernourished and better-nourished groups after adjusting for confounding variables.
Liu *et al* (2004)	Child behaviour questionnaire at age 8, Child Behaviour Checklist at age 11, Revised Behaviour Checklist at Age 17 (childhood, adolescence)	**Externalizing behaviour problems at age 8:** Malnourished children had higher overall externalizing behaviour scores (both hyperactivity and aggression) than controls. **Adjusted analysis:** Main effect of malnutrition remained significant after controlling for psychosocial adversity but was abolished after controlling for cognitive ability. **Externalizing behaviour problems at age 11:** Malnourished children had higher externalising behaviour scores (hyperactivity only) at age 11 than non-malnourished children.

		Adjusted analysis: Main effect of malnutrition remained significant after controlling for psychosocial adversity but was abolished after controlling for cognitive ability. **Externalizing behaviour problems at age 17:** Malnourished group had significantly higher scores on conduct disorder and motor excess but not attention problems or socialized aggression. **Adjusted analysis:** Main effect of malnutrition remained significant after adjusting for psychosocial adversity and cognitive ability. **Sample size:** Malnutrition group n=235, Control group n=807 **Overall Findings:** Children with malnutrition were more aggressive or hyperactive at age 8 years, had more externalizing problems at age 11, and had greater conduct disorder and excessive motor activity at age 17 after adjusting for confounding variables.
Barbados Nutrition Study		
Hock *et al* 2018* **(+)**	SCID-II-PQ, NEO PI-R FFM (adulthood)	**SCID-II-PQ (linear regression with malnutrition as predictor of score):** Paranoid personality score 0.6 [95% CI 0.0, 1.2] (p=0.0499) **Adjusted analysis:** PD paranoid scale score had unique association with malnutrition after adjusting for maltreatment and childhood standard of living **NEO PI-R FFM (linear regression with malnutrition as predictor of score):** Avoidant personality score 1.0 [95% CI 0.2, 1.7] (p=0.009), schizoid personality score 0.7 [95% CI 0.1, 1.4] (p=0.03) and dependant personality score 0.7 [95% CI 0.1, 1.4] (p=0.04) **Adjusted analysis:**

		PD avoidant, schizoid and dependant scale scores had unique associations with malnutrition after adjusting for maltreatment and childhood standard of living **Sample size:** Malnutrition group n=77, control group n=62 **Overall findings:** Adults with history of infant malnutrition showed an increase in most SCID-II and NEO FFM PD personality scores compared to those with little or no exposure to either adversity. Few personality disorder score differences were statistically significant however and results differed depending on the assessment tool used.
Waber (2) *et al* 2014* **(++)**	Behavioural Regulation Index score (adulthood)	Controls n=59 Malnutrition n=77 **Behavioural regulation index**: Mean score 43.34 (SD 7.52) 49.51 (SD 11.21) Mean difference (adjusted) 3.40 ($p<0.05$) **Adjusted analysis** (results adjusted for childhood standard of living and IQ) **Overall findings:** Adults with a history of infant malnutrition showed a significantly higher behavioural regulation index score which is indicative of more behavioural problems, with a significant difference in score after adjusting for confounding variables.
Galler *et al* 2013* **(+)**	NEO-PI-R personality inventory (adulthood)	**NEO-PI-R score:** At the broad domain or factor level, previously malnourished participants had higher scores on Neuroticism and lower scores on Extraversion, Openness, Agreeableness and Conscientiousness than healthy controls. At the sub-domain or facet level, previously malnourished participants reported more anxiety, vulnerability, shyness and lowered sociability, less intellectual curiosity, greater suspiciousness of others, a more egocentric than altruistic

<table>
<tr><td></td><td></td><td>orientation, and a lowered sense of efficacy or competence.

<u>Adjusted analysis:</u>
(results adjusted for childhood standard of living)

<u>Sample size</u>
Malnutrition group n=77, Control group n=57

<u>Overall findings:</u>
Childhood malnutrition was associated with higher chance of personality trait scores outside of the average range after adjusting for childhood standard of living.</td></tr>
<tr><td>Galler (1) et al 2012*

(+)</td><td>CAARS, CPT

(adulthood)</td><td>
<table>
<tr><th></th><th>Controls n=63</th><th>Malnutrition n=80</th><th>p value</th></tr>
<tr><td><u>CAARS (mean score):</u></td><td></td><td></td><td></td></tr>
<tr><td>Inattentive symptoms</td><td>3.6 (SD 0.1)</td><td>3.7 (SD 0.2)</td><td><0.05</td></tr>
<tr><td>Hyperactive symptoms</td><td>3.7 (SD 0.1)</td><td>3.7 (SD 0.2)</td><td>>0.05</td></tr>
<tr><td>DSM-IV ADHD symptoms</td><td>3.6 (SD 0.1)</td><td>3.7 (SD 0.1)</td><td><0.01</td></tr>
<tr><td>ADHD index</td><td>3.8 (SD 0.2)</td><td>3.7 (SD 0.1)</td><td>>0.05</td></tr>
</table>
<table>
<tr><th></th><th>Controls n=59</th><th>Malnutrition n=77</th><th>p value</th></tr>
<tr><td><u>CPT (mean score):</u></td><td></td><td></td><td></td></tr>
<tr><td>Commission errors</td><td>3.8 (SD 0.2)</td><td>3.9 (SD 0.2)</td><td>>0.05</td></tr>
<tr><td>Omission errors</td><td>3.9 (SD 0.2)</td><td>4.1 (SD 0.3)</td><td>>0.05</td></tr>
<tr><td>Reaction time</td><td>4.0 (SD 0.2)</td><td>4.0 (SD 0.2)</td><td>>0.05</td></tr>
</table>
<u>Adjusted analysis:</u>
(results adjusted for childhood standard of living and IQ)

<u>Overall findings:</u>
CAARS scores were higher (indicating more attention problems) in the previously malnourished group. There were significant differences in inattention and DSM-IV ADHD symptom scores after adjusting for confounding variables. Differences in CPT scores were attenuated after adjusting for confounding variables.
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Galler (2) *et al* 2012* **(+)**	Conduct-problems: Child-Behaviour-Questionnaire, Teacher-Behaviour-Questionnaire (adolescence)	Controls n=60 Malnutrition n=56 p value **Child-Behaviour-Questionnaire (coefficient):** Conduct problems -0.27 (SD 0.84) 0.29 (SD 1.18) <0.01 **Teacher-behaviour-questionnaire:** All four items showed a higher level prevalence of aberrant behavior in the previously malnourished children as compared with the comparison group. **Adjusted analysis:** The difference was no-longer-significant with IQ and childhood standard of living included in the model **Overall findings:** Self-reported conduct problems were more prevalent among previously malnourished youth. The associated was no longer significant when adjusted for confounding variables.
Waber *et al* 2011* **(+)**	Teacher-Behaviour Questionnaire, School functioning scale Minnesota-General-Adjustment-and Morale-Scale (adolescence)	Controls n=60 Malnutrition n=56 p value **Teacher questionnaire:** Attention symptoms -0.36 (SD 0.81) 0.33 (SD 0.96) <0.0001 **Morale scale:** Depressive symptoms -0.33 (SD 0.93) 0.30 (SD 1.01) 0.001 **Adjusted analysis:** Association attenuated when IQ and attention problems included in model. Difference in attention symptoms not significant when adjusting childhood standard of living. **Overall findings:** Depressive symptoms and inattention were higher in those with malnutrition but there were no significant differences when adjusting for confounding variables.
Galler *et al* 2011*	Barbados-Child-Behaviour-Scale	Controls n=109 Malnutrition n=107 (correlations with mean score) **Peer aggression:**

(++)	adolescence	Time point 1 (9-15y)	-0.05 (SD 0.96)	0.39 (SD 1.16)
		Time point 2 (11-17y)	-0.34 (SD 0.79)	-0.34 (SD 0.80)
		Cooperative with adults:		
		Time point 1 (9-15y)	0.19 (SD 1.11)	-0.01 (SD 1.15)
		Time point 2 (11-17y)	0.15 (SD 0.73)	-0.28 (SD 1.00)
		Activity level:		
		Time point 1 (9-15y)	0.32 (SD 1.09)	0.18 (SD 1.03)
		Time point 2 (11-17y)	-0.35 (SD 0.72)	-0.29 (SD 0.78)
		Executive function deficits:		
		Time point 1 (9-15y)	0.0 (SD 0.94)	0.24 (SD 1.00)
		Time point 2 (11-17y)	-0.38 (SD 0.82)	-0.09 (SD 0.94)
		Sleep problems:		
		Time point 1 (9-15y)	-0.45 (SD 1.17)	-0.24 (SD 1.08)
		Time point 2 (11-17y)	0.21 (SD 0.61)	0.43 (SD 0.68)
		Adjusted analysis: Cases had increased prevalence of executive function deficits at both time points after adjusting for age, sex, childhood standard of living and maternal depressive symptoms. No significant association with aggression, cooperation, activity and sleep after adjusting for covariates at second time point. Cases had more problem aggression at the first time point than at the second.		
		Overall findings: Persisting parent-reported executive functioning deficits through adolescence at two time points after adjusting for confounding variables.		
Galler *et al* 2010*	Minnesota-General-Adjustment-and Morale-Scale		Controls n=60	Cases n=56 p value
		Morale Scale:		
(++)		Youth depression score	-0.33 (SD 0.98)	0.30 (SD 1.01) <0.001
	(adolescence)	**Adjusted analysis:** Adjusting for age, maternal depression symptoms and household standard of living the effect of malnutrition is similar to unadjusted estimates and remains significant.		

		Overall findings: Early childhood malnutrition contributed independently to depressive symptoms after adjusting for confounding variables.

*Studies are drawn from the same Barbados Nutrition Study

95% CI – 95% Confidence Intervals, CAARS - Attention-domain: Conners-ADHD-Rating-Scales, CPT – Conners-Continuous-Performance Test, NEO PI-R FFM – NEO Personality Inventory-Revised derived Five-Factor Model, SD – Standard Deviation, SDQ – Strengths and Difficulties Questionnaire, SCID-II-PQ – Structured Clinical Interview for DSM-IV Axis II Personality Disorders Personality Questionnaire, WHODAS – World Health Organization Disability Assessment Schedule