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Hume-Nixon, M; Kuper, H; (2018) The association between malnutrition and childhood disability in low- and middle- income countries: Systematic review and meta-analysis of observational studies. *Tropical medicine & international health*. ISSN 1360-2276 DOI: <https://doi.org/10.1111/tmi.13139>

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Article Type: Systematic Review

The association between malnutrition and childhood disability in low- and middle- income countries: Systematic review and meta-analysis of observational studies

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Abstract

Objective: To evaluate the association between childhood disability and malnutrition in low- and middle- income countries (LMICs).

Methods: Articles were identified from 1990 to August 2017 by searching 9 electronic databases. Epidemiological studies, undertaken in LMICs that compared the prevalence of malnutrition in children with disabilities to children without disabilities were eligible for inclusion. Titles, abstracts, and full texts were screened by two reviewers, and data were extracted using a structured table for eligible papers. Meta-analyses for the association between childhood disability and undernutrition were performed.

Results: The search generated 4678 results, from which 17 articles were eligible. 53% of these studies showed a positive association between childhood disability and undernutrition. Results varied when disaggregated by type of disability, with positive associations identified for 44% of studies focussed on neurodevelopmental disability, 60% of general disability studies and 67% of studies on hearing impairment. Only four studies were identified that considered overnutrition outcomes, and these showed variable results. 18% of eligible studies were considered at low risk of bias, 53% had a medium risk, and 29% had a high risk of bias. Pooled ORs showed that children with disabilities were almost three times more likely to be underweight (OR 2.97, 95% CI 2.33, 3.79), and nearly twice as likely to experience stunting and wasting (Stunting: 1.82, 1.40, 2.36; Wasting: 1.90, 1.32-2.75), compared to controls.

Conclusions: Children with disabilities may be a vulnerable group for undernutrition in LMICs, which should be reflected in disability and nutritional programming and policy-making.

Keywords: Developing Countries; disabled children; disabled persons; malnutrition; child nutrition disorders

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/tmi.13139

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Introduction

Malnutrition is a critical issue on the global health agenda, with an estimated 45% of deaths under five being attributed to undernutrition (1). There are approximately 165 million stunted children, and 52 million wasted children worldwide, with the highest percentages living in Asia or Sub-Saharan Africa (SSA) (1). Many children living in low and middle income countries (LMIC) are now facing the dual burden of both under- and overnutrition (2), with the prevalence of childhood overweight and obesity rising in these countries while undernutrition remains common.

Like malnutrition, disability affects many people globally, and disproportionately affects those living in LMIC. One billion people, including 95 million children, are estimated to have a disability (3), and 80% of all persons with disabilities live in LMICs (3). Childhood disability may result from nutrient deficiencies (e.g. iodine deficiency), but also from congenital disorders, infections, trauma or other causes, which can result in a broad range of impairments (e.g. physical, visual, hearing, intellectual). Children with disabilities often face exclusion from school and other aspects of social life, reduced access to healthcare services, and are at higher risk of poor health and poverty (4, 5). Malnutrition and disability also share a strong foundation in human rights, as the right to have access to food, including for people with disabilities, is stated in several internationally ratified documents (6-8).

Many factors associated with disability are also linked to malnutrition, including poverty (9-12) and ill health (5). There is increasing evidence that childhood disability and malnutrition are directly related (13-15) though various pathways including feeding problems in children with disability, neglect, and exclusion of these children from school (and thus school-based feeding programmes). Groce et al (2014) describes a framework showing that malnutrition may occur when there is increased need of nutrients, increased nutrient loss, and decreased nutrient intake (13). Reasons for a decreased nutrient intake may be due to certain physical impairments such as cleft palate or cerebral palsy (CP) that affect eating or swallowing (15), resulting in prolonged feeding times, and caregivers may be unable to spend sufficient time feeding the child. Some conditions may make children with disabilities prone to nutrient loss, for example children with CP may be more likely to have vomiting episodes, and some of these children may have more frequent episodes of illness and thus have higher nutritional requirements (15). Malnutrition may also lead to disability, for example malnutrition may increase the risk of acquiring potentially disabling illnesses such as meningitis or rickets. The link between disability and malnutrition is likely to be strongest, therefore, where public health systems are weakest. Despite these similarities and potential linkages, to date there has been limited research and specific programming in this area.

Context is likely to affect the relationship between childhood disability and malnutrition. Research from high income countries has shown that children with disabilities are generally at higher risk of obesity (16-18), particularly children with intellectual disabilities. However children with disabilities living in LMICs may be more vulnerable to malnutrition (19, 20), due to failure of public health systems, as the underlying risk of malnutrition is higher in these contexts, and there are fewer services available to provide nutritional support for children with feeding difficulties (e.g. percutaneous endoscopic gastrostomy feeding). Furthermore, qualitative studies have suggested that children with disabilities in LMICs are at a high risk of hunger associated with poverty, particularly as these children may require a large burden of care limiting household productivity. Carers who are required to go to work may not have enough time for adequate care for these children, and their skills in feeding the children may be low (20-24). Gottlieb et al's (2009) ecological study (25) showed that children who were underweight were more likely to screen positive on UNICEF's '10 question screen' for disability than children who were not underweight, and that children who were stunted were more likely to screen positive than children who were not. However, other studies have not supported this finding (26).

These inconsistencies illustrate the need for a systematic review to synthesise the findings of the relationship between childhood disability and malnutrition in LMIC, which has not been previously undertaken. Considering that the majority of the burden of malnutrition and disability is in these countries, this represents an important gap in the literature.

Methods

The objective of this systematic review was to evaluate the association between childhood disability and malnutrition (both under and overnutrition) in LMIC. Primarily the exposure will be considered childhood disability, and the outcome malnutrition. However, we also identified studies that show reverse directionality: that childhood malnutrition leads to disability, to explore the complexity of this association. The review also considers whether the association between disability and malnutrition changes depending on the type of disability and contextual factors. PRISMA (27) guidelines were followed throughout the systematic review process.

Data sources

PICOST was used to formulate the research question: Do children with disability in LMIC have a higher likelihood of malnutrition than children without disability, using data from observational quantitative studies (28)? Nine electronic databases were searched in August 2017, including EMBASE, MEDLINE, Global Health, Web of Science, Academic Search Complete, FRANCIS, ERIC, Social

Policy & Practice and EconLit. Comprehensive search terms for key concepts including disability, LMIC, “child”, and “malnutrition” were informed by previous systematic reviews on similar topics (29-32), and appropriate MESH and Emtree terms relating to these topics were selected. For the full MEDLINE search strategy see Appendix 1. Filters were applied to limit results to English-language texts, and date of publication being between 1990 and August 2017, as there have been large decreases in undernutrition (33) and increases in the prevalence of obesity internationally since the 1990s, in addition to improved international commitments to the rights and health of disabled persons. References of relevant review articles were also checked to identify additional potentially eligible studies.

Inclusion criteria

Papers were included if they were undertaken in an LMIC as classified by the World Bank. Studies were required to include a measure of disability. This could include assessment of impairment, self-reported disability or functional limitations, or the presence of a long-term condition that was likely to be disabling (e.g. club foot), as measured through standardised tools or clinical assessment, or self-report. Studies also had to include at least one measure of malnutrition status as per World Health Organization (WHO) definition, including: stunting, underweight, wasting, overweight and obesity. Marasmus and kwashiorkor; forms of protein-energy malnutrition were also included (34). Studies that presented continuous values for measures of disability or nutritional status were excluded.

Studies were included where participants were children or young people with disabilities, which was defined as the mean age of participants (if available) being younger than 18 years. All included studies had an epidemiological design that included a comparison group (i.e children without disabilities).

Studies were excluded where the primary outcomes related to micronutrient deficiencies such as vitamin A and iodine, as there are already well-established interactions between micronutrient deficiency and disability (35, 36). In addition, studies conducted on institutionalised or hospitalised children were excluded, because of concerns regarding generalisability.

Study selection

Articles were screened independently by two reviewers (MHN and HK) first by title, then by abstract. Finally, the full-text of articles were screened to determine eligibility. At each stage of screening differences between the reviewers were discussed, and a consensus for eligibility and inclusion was reached on all papers.

Data extraction

Data extraction from the final selection of articles was performed by MHN using an extraction table, and all data items were checked by HK. The prevalence of malnutrition in children with and without disabilities, and effect estimates, were extracted as the primary measure of the association between childhood disability and malnutrition.

Study outcomes were classified as showing a positive, null, negative, or mixed, association between childhood disability and undernutrition. Studies were classified as showing a 'positive' association if all undernutrition outcomes measured were more common in children with disabilities, and when all undernutrition outcomes measured were less common in children with disabilities, studies were considered 'negative'. For classifications of 'positive' or 'negative' association, study results were required to show statistical significance, preferentially based on results adjusted for confounders (for studies that employed multivariate analysis). When these data were not available (if studies presented only univariate analysis), this classification was based on crude effect estimates, if necessary, calculated by the authors. An association was categorised as 'null' if none of an individual study's effect estimates for undernutrition outcomes were statistically significant, and classified as 'mixed' if it showed both negative and positive associations for different undernutrition outcomes. Studies were also classified as 'mixed' if they reported some effect estimates that were statistically significant, and some that were not. The proportion of studies showing positive, negative, null or mixed associations was disaggregated by study characteristics (type of disability, region, setting, quality rating). For studies that reported on overnutrition outcomes, the same method was used to categorize their reported associations between childhood disability and overnutrition. Studies were classified as having a positive association when they showed children with disabilities were at increased risk of overweight or obesity, and as having a negative association, when outcomes of overweight or obesity were less common in children with disabilities.

Quality Assessment

The full text of all eligible studies were assessed against quality criteria adapted from Lund et al. 2016 (37), (Table 1). Based on these criteria, overall quality ratings were assigned to each individual study. A study was judged to have a low risk of bias (++) if it fulfilled all or almost all of the relevant criteria, and those criteria that were not fulfilled were thought unlikely to alter the conclusions of the study. A study had a medium risk of bias (+) if it fulfilled some of the relevant criteria, and those criteria not fulfilled were thought unlikely to alter its conclusions. A study was considered to have a

high risk of bias (-) if it met few or no criteria, and its conclusions were thought likely or very likely to alter with the inclusion of these criteria (37).

Meta-analysis

Odds Ratios (OR) with 95% Confidence Intervals (CI) were calculated by extracting raw frequencies of malnutrition in children with disabilities and in children without disabilities. A pooled OR with 95% CIs was calculated for the prevalence of malnutrition (e.g. stunting, underweight, and wasting) in children with disabilities compared to controls with a fixed effects model for sub-groups of data that were believed to be comparable (same category of disability and same measure of malnutrition). All calculations were performed using STATA 15.0. This software package was also used to generate forest plots that showed the ORs and 95% CIs for each individual study, in addition to the overall pooled OR with CIs. Heterogeneity of the pooled studies was explored using the I^2 statistic, in addition to visual confirmation from forest plot.

Results

The search generated 4678 papers (Figure 1). After 1567 duplicates were removed, the remaining number were screened (3111). We excluded 2535 papers during title screening, and then an additional 475 during abstract screening. This led to 101 full-text articles being assessed for eligibility. We could not locate 3 full texts, and 81 texts were excluded, most commonly because they used inappropriate measures of disability and/or malnutrition, as per the inclusion and exclusion criteria (n=64). In total, 17 articles were deemed eligible and included in the final sample for review.

The descriptive characteristics of included studies are shown in Table 2. Studies in the final sample for analysis were categorised by type of disability. 'Neurodevelopmental' disability was the largest category, containing nine studies (53%) (38-45). There were five studies that considered multiple disability diagnoses, but that reported data overall for children with disabilities as a group, so were included in a 'general disability' (29%) category. There were three studies in the 'hearing' disability/impairment category (18%). Predominantly studies were from the South Asia region (n=10, 59%), and set in urban contexts (47%). There were seven case-control studies, one cohort study (with 16 years follow-up), and nine cross-sectional studies. These studies involved a wide variety of age ranges, from 0-0.25 years (46), compared to 5-19 years (47). Most studies included more boys than girls, and in Liu (2016)'s study only 8% of cases and controls were female.

Table 3 shows the prevalence of malnutrition in relation to childhood disability, including measures of effect, for included studies. This table shows there were a wide range of measures of

disability and malnutrition used. Three studies (18%) were considered to have a low risk of bias (++), nine studies (53%) had a medium risk of bias (+), and five studies (29%) had a high risk of bias (-) (see table 4). There was only one cohort study, for which only the abstract was available (48). Few papers had a response rate that was reported and acceptable (41%), and took potential confounders into account in analysis (41%). Only 59% of papers presented confidence intervals.

Table 4 presents a summary of study characteristics and their results for the association of undernutrition with disability. Overall, approximately half (53%) of studies showed a positive association between undernutrition and childhood disability. 29% of studies showed no association (categorised as a 'null' association), and 18% of studies showed a mixed association. No studies showed an inverse association between undernutrition and disability. When this association was disaggregated by disability/impairment type, 44% of studies showed a positive association between neurodevelopmental disability and undernutrition, 33% showed no association, and 22% had a mixed association. Three studies (60%) in the general disability category showed a positive association between disability and undernutrition outcomes, one study (20%) had null results (26), and one study (20%) had mixed results. 67% of studies showed a positive association between hearing impairment in children and undernutrition, and 33% showed no association. 80% of studies from South Asia showed a positive association, vs. 50% of studies from SSA. Studies from rural settings reported similar frequencies of positive association to those from urban settings (67% compared to 63%). When examined by quality, 67% of studies with a low risk of bias showed a positive association between undernutrition with disability. However, 60% of studies with a high risk of bias also showed a positive association.

Of the final sample of studies for analysis, only four reported outcomes for overweight/obesity. One of these studies (25%) showed no association between childhood disability and obesity. One study (25%), Kummer (2016), showed a positive association between neurodevelopmental disability and obesity, reporting that children with ADHD were nearly 10 times more likely (9.6, 1.1-85.7), and children with ASD were 12 times more likely to be overweight or obese (12.3, 1.6-97.4). Two of these studies showed mixed results for the association between childhood disability and obesity (50%).

Meta-analysis

Pooled estimates were calculated using raw data on prevalence of malnutrition in controls. The frequency of malnutrition in the total number of children with disabilities from each study was used for this analysis. Studies in the 'general disability' category were used in the meta-analysis because all of these studies were considered to have a low or medium risk of bias, and reported on the

prevalence of at least one of the malnutrition outcomes of stunting, underweight, or wasting.

Four studies in the 'general disability' category that reported the prevalence of underweight in children with disabilities were included in the meta-analysis for the association between disability and being underweight (Figure 2). The pooled OR showed that children with disabilities were almost three times more likely to be underweight compared to controls (Pooled OR 2.97; 95% CI 2.33, 3.79), with little or no evidence of heterogeneity (I^2 26.2%, $p=0.254$). Three studies (14, 49, 50) were included in a meta-analysis of association between disability and stunting (Figure 3), and in a meta-analysis of the association between disability and wasting (Figure 4). The pooled OR for the association between childhood disability and stunting showed that children with disabilities were almost twice as likely to experience stunting than controls (Pooled OR 1.82, 95% CI 1.40, 2.36), however statistical tests showed some evidence of heterogeneity between studies (I^2 59.8%, $p=0.08$) (Figure 3). Children with disabilities were nearly twice as likely to experience wasting than controls (Pooled OR 1.90, 95% CI 1.32-2.75), but there was evidence of heterogeneity ($p=0.05$) with a high amount of variability between studies due to heterogeneity rather than random effects (I^2 67.7%).

Discussion

This systematic review provides some evidence that undernutrition is associated with childhood disability in LMICs. This conclusion is supported by different individual studies showing a positive association between undernutrition and disability, and meta-analyses of individual studies that showed children with disabilities in LMIC were more likely to be stunted, wasted, and underweight, than children without disabilities. There were insufficient numbers of studies reporting on outcomes of overweight or obesity, to draw further conclusions about the association between childhood disability and overnutrition in LMIC. No previous systematic review was identified that examined the relationship between malnutrition and disability in LMIC, although other literature reviews (13, 15) have commented on the possible association between disability and malnutrition in these settings.

There are different proposed mechanisms for the link between childhood disability and malnutrition, and Groce et al categorised these causal pathways as 'medical', 'educational', or 'attitudinal, cultural and social' (13). Decreased nutrient intake may be caused by feeding difficulties, as some disabilities such as cleft palate or CP may affect eating or swallowing (13), an example of a 'medical' causal pathway. An example of the educational pathway is that there may be insufficient knowledge of appropriate feeding practises for these children in some LMIC (24). There may also be neglect of this group of children (51), or these children may be excluded from school and therefore school-based feeding programmes (14). Both of these represent attitudinal, cultural and social mechanisms linking childhood disability and malnutrition.

Accepted Article

Due to the designs of included studies, it was not possible to determine whether disability preceded malnutrition, or vice-versa. Determining temporality between these two conditions is especially challenging, as there is evidence suggesting that the pathways between disability and undernutrition may be bidirectional. For example, malnutrition may affect axonal, and therefore brain development, resulting in increased risk of cognitive disability in later life (15, 44). Conversely, children with disabilities in LMIC may be at increased risk of malnutrition through multiple pathways (15, 24).

A strength of this systematic review was that it used a comprehensive search strategy, particularly for subjects of 'disability' and 'LMIC'. However, the search was limited to English language studies, which may have been reflected in the low number of studies from South America being included ($n=2$, 12%). This study did not include studies examining the prevalence of micronutrient deficiencies in children with disabilities compared to children without disabilities. There are well-established examples of micronutrient deficiencies, including iodine deficiency, vitamin A deficiency and vitamin D deficiency, that lead to disabling conditions such as cretinism, visual impairment and rickets (36, 52, 53). However, given that some malnutrition states such as severe acute malnutrition are associated with micronutrient deficiency, children with disabilities may be at greater risk of developing these deficiencies. These may worsen existing conditions or cause additional morbidity, and therefore it may be beneficial to synthesise and evaluate existing research in this area.

The biggest constraint on this systematic review was the current state of literature on this topic, including few studies that were eligible. This made it difficult to quantitatively summarise study characteristics and their effects on the association between childhood disability and malnutrition (Table 4), particularly whether type of disability mediated this association, as there was also an absence of essential types of disabilities such as visual impairment in included studies. The few studies examining outcomes of overweight/obesity provided insufficient evidence regarding the relationship between disability and overnutrition, contrary to current evidence from high-income countries (17). However, given that the prevalence of childhood obesity is rising in many LMIC (54), this may become an important issue for health professionals and policymakers in these countries to consider in the future. The characteristics of the included studies also created problems for generalisability, as the majority of studies were from South Asia (59%), with little or no representation of other major regions. Finally, the underrepresentation of girls in studies was problematic, because disabled girls may face increased discrimination (67) making them more vulnerable to malnutrition compared to disabled boys.

There were also issues with the generally poor quality of included studies. Some studies did not clearly report how malnutrition was defined or assessed (39, 40), and many studies did not report whether they screened their controls for disability, and thus it was unclear whether cases and controls were clearly defined. Significantly, 41% of studies did not consider confounders in their analysis. In addition to these issues, there was variation between included studies in how they measured disability that may have affected the comparability of results, for example, three studies in the meta-analyses measured disability by clinical examination (14, 49, 55), whereas one used UNICEF's '10 question screen' (50). Large variation in the age range of study populations also limited comparability of results. This review did not formally assess the potential for publication bias, since many of the studies reported multiple results. However, we believe that the potential was small, since the proportion of studies reporting positive associations was, if anything, high among the studies with a low risk of bias (Table 4).

The findings of the review calls for the prevention and treatment of undernutrition among children with disabilities in LMICs. The implementation of these interventions could be through a "twin-track" approach which promotes the inclusion of children with disabilities in mainstream programmes as well as their targeting with specific programmes. There is a lack of robust evidence available on what works, and so best in class interventions that prevent malnutrition in children should be assessed for effectiveness for children with disabilities in LMIC (56). For instance, Hossain et al (2017) recently showed programmes that effectively reduced stunting in LMIC most commonly implemented interventions of nutrition education and counselling, growth monitoring and promotion, immunisation, water, sanitation and hygiene, and social safety nets (35). These approaches will require strengthening of the public health services in order to be effective. On the other hand, disability-targeted programmes should consider nutrition as an essential part of their services, and workers in these programmes may require additional training in identification and management of malnutrition. However, there is a lack of research into these interventions even in high-income countries. For example a recent Cochrane review examining the effects of gastrostomy feeding versus oral feeding alone for children with cerebral palsy found no trials that met the review's inclusion criteria (57). In high-income countries healthcare systems often have frequent opportunities or contacts with children to identify and manage developmental problems (4), and children with disabilities often have ongoing follow-up with secondary level healthcare providers, allowing opportunities to identify issues such as nutrition. This approach, including improved developmental and disability screening for children has been implemented by some LMIC such as Bangladesh (58).

Conclusions

This systematic review found evidence that children with disabilities may be a vulnerable group for undernutrition in LMICs, which should be reflected in disability and nutritional programming and policy-making. Preventing and treating malnutrition among children with disabilities will require stronger and more inclusive public health systems.

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Appendices/annexes

Appendix 1. Search strategy for MEDLINE database

1	(Physical* adj5 (impair* or deficienc* or disable* or disabili* or handicap*)).ti,ab.
2	((Visual* or Vision or Eye*) adj5 (loss* or impair* or deficienc* or disable* or disabili* or handicap*)).ti,ab.
3	((Hearing or Acoustic or Ear*) adj5 (loss* or impair* or deficienc* or disable* or disabili* or handicap*)).ti,ab.
4	((Intellectual* or Mental* or Psychological* or Developmental) adj5 (impair* or retard* or deficienc* or disable* or disabili* or handicap* or ill*)).ti,ab.
5	((communication or language or speech or learning) adj5 disorder*).ti,ab.
6	(Neurologic* adj5 (impair* or deficienc* or disable* or disabili* or handicap*)).ti,ab.
7	((Disable* or Disabilit* or Handicapped) adj5 (person* or people)).ti,ab.
8	(Cerebral pals* or Spina bifida or Muscular dystroph* or Osteogenesis imperfecta or juvenile rheumatoid arthritis or Musculoskeletal abnormalit* or Musculo-skeletal abnormalit* or Muscular abnormalit* or Skeletal abnormalit* or Limb abnormalit* or Brain injur* or Amputation* or Clubfoot or Poliomyeliti* or Paraplegi* or Paralys* or Paralyz* or Hemiplegi* or Deaf* or Blind* or Autis* or Dyslexi* or Down* Syndrome or Mongolism or Trisomy 21).ti,ab.
9	exp Cerebral palsy/ or exp Spina Bifida Cystica/ or exp Spina Bifida Occulta/ or exp Muscular dystrophies/ or exp musculoskeletal abnormalities/ or exp Brain Injuries/ or exp Clubfoot/ or exp Poliomyelitis/ or exp Paraplegia/ or exp Hemiplegia/ or exp Intellectual disability/ or exp Developmental Disabilities/ or exp child Developmental Disorders, Pervasive/ or exp Communication Disorders/ or exp Hearing loss/ or exp Vision, Low/ or exp Blindness/ or exp Deafness/ or exp Disabled persons/
10	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
11	(Afghanistan or Albania or Algeria or American Samoa or Angola or Antigua or Barbuda or Argentina or Armenia or Azerbaijan or Bangladesh or Belarus or Byelarus or Byelorussia or Belorussia or Belize or Benin or Bhutan or Bolivia or Bosnia or Herzegovina or Hercegovina or Bosnia-Herzegovina or Bosnia-Hercegovina or Botswana or Brazil or Brasil or Bulgaria or Burkina or Upper Volta or Burundi or Urundi or Cambodia or Republic of Kampuchea or Cameroon or Cameroons or Cape Verde or Central African Republic or Chad or Chile or China or Colombia or Comoros or Comoro Islands or Comores or Congo or DRC or Zaire or Costa Rica or Cote d'Ivoire or Ivory Coast or Cuba or Djibouti or Obock or French Somaliland or Dominica or Dominican Republic or Ecuador or Egypt or United Arab Republic or El Salvador or Eritrea or Ethiopia or Fiji or Gabon or Gabonese Republic or Gambia or Georgia or Ghana or Gold Coast or Grenada or Guatemala or Guinea or Guinea-Bisau or Guiana or Guyana or Haiti or Honduras or India or Indonesia or Iran or Iraq or Jamaica or Jordan or Kazakhstan or Kenya or Kiribati or Republic of Korea or North Korea or DPRK or Kosovo or Kyrgyzstan or Kirghizstan or Kirgizstan or Kirghizia or Kirgizia or Kyrgyz or Kirghiz or Kyrgyz Republic or Lao or Laos or Latvia or Lebanon or Lesotho or Basutoland or Liberia or Libya or Lithuania or Macedonia or Madagascar or Malagasy Republic or Malawi or Nyasaland or Malaysia or Malaya or Malay or Maldives or Mali or Marshall Islands or Mauritania or Mauritius or Mayotte or Mexico or Micronesia or Moldova or Moldovia or Mongolia or Montenegro or Morocco or Mozambique or Myanmar or Burma or Namibia or Nepal or Nicaragua or Niger or Nigeria or Pakistan or Palau or Palestine or Panama or Papua New

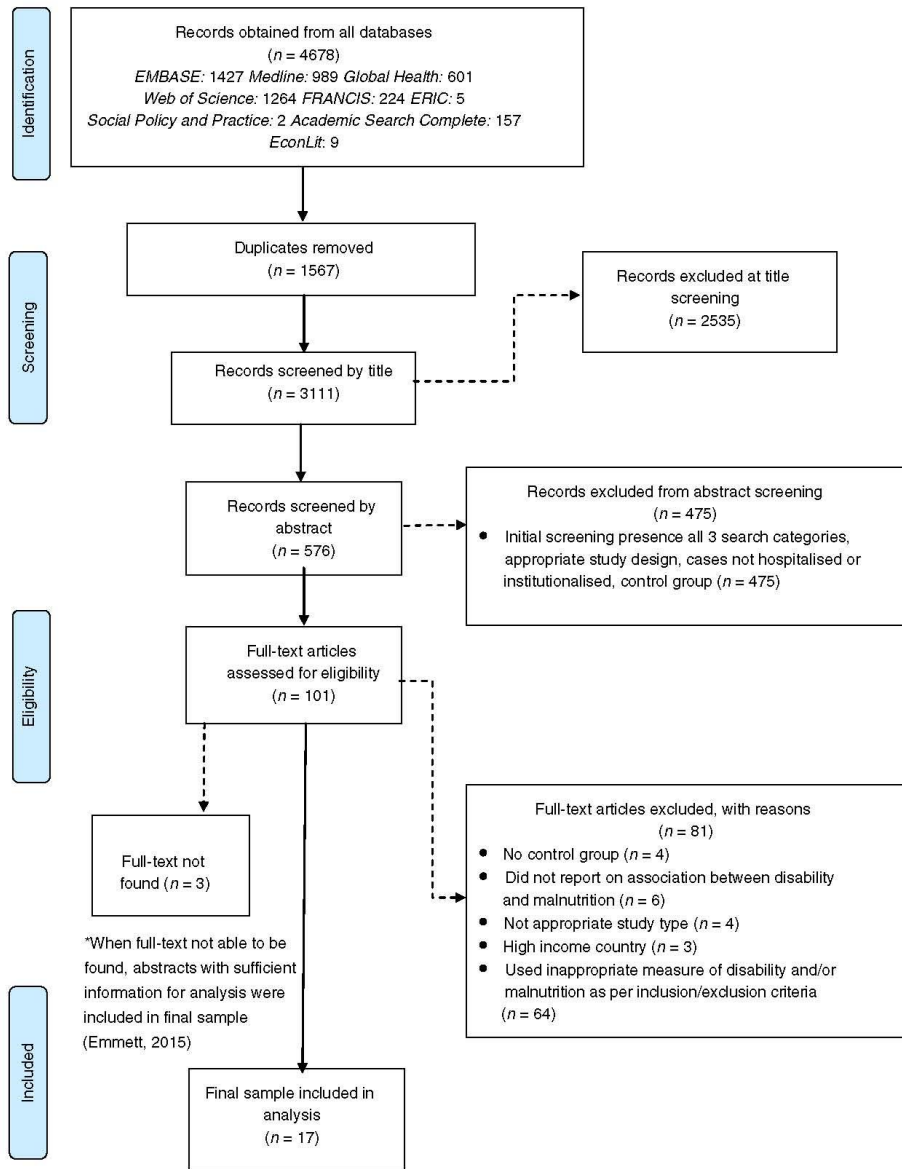
	Guinea or Paraguay or Peru or Philippines or Romania or Rumania or Roumania or Russia or Russian Federation or USSR or Soviet Union or Union of Soviet Socialist Republics or Rwanda or Ruanda-Urundi or Samoa or Samoan Islands or Sao Tome or Principe or Senegal or Serbia or Montenegro or Yugoslavia or Seychelles or Sierra Leone or Solomon Islands or Somalia or South Africa or Sri Lanka or Ceylon or Saint Kitts or St Kitts or Saint Christopher Island or Nevis or Saint Lucia or St Lucia or Saint Vincent or St Vincent or Grenadines or Sudan or Suriname or Surinam or Swaziland or Syria or Syrian Arab Republic or Tajikistan or Tadzhikistan or Tadjikistan or Tanzania or Thailand or Timor-Leste or East Timor or Togo or Togolese Republic or Tonga or Tunisia or Turkey or Turkmenistan or Turkmenia or Tuvalu or Uganda or Ukraine or Uruguay or Uzbekistan or Vanuatu or New Hebrides or Venezuela or Vietnam or Viet Nam or West Bank or Gaza or Yemen or Zambia or Zimbabwe or Rhodesia).ti,ab,cp.
12	(Africa* or Asia* or Caribbean or West Indies or Latin America* or Central America* or South America* or LIC or LICs or MIC or MICs or LMIC or LMICs or LAMIC or LAMICs or LAMI countr* or third world or Transitional countr* or Transitional econom* or Transition countr* or Transition econom*).ti,ab.
13	exp Africa South of the Sahara/ or exp Asia, Central/ or exp Asia, Southeastern/ or exp Asia, Western/ or exp Latin America/ or exp Caribbean Region/ or exp Central America/ or exp South America/ or exp Developing countries/
14	((Developing or Low-income or low income or Middle-income or Middle income or (Low and middle income) or (Low- and middle-income) or Less-Developed or Less Developed or Least Developed or Under Developed or underdeveloped or Third-World) adj5 (countr* or nation* or world or econom*)).ti,ab.
15	11 or 12 or 13 or 14
16	exp child/ or exp infant/ or exp pediatrics/ or exp Adolescent/
17	(infan* or child* or p?ediatric* or adolescen*).ti,ab.
18	16 or 17
19	(anthropometric failure or malnourish* or malnutrition or wast* or undernutrition or undernourished or marasm* or kwashiorkor or stunt* or underweight or severe acute malnutrition or SAM or body mass index or BMI or MUAC or mid-upper arm circumference or mid upper arm circumference).ti,ab.
20	exp Protein-Energy Malnutrition/ or Malnutrition/ or child malnutrition/ or infant malnutrition/
21	19 or 20
22	10 and 15 and 18 and 21
23	limit 22 to (english language and yr="1990 -Current")

Table 1 .Number and percentages of included studies meeting each quality appraisal criteria

Criteria no.	Criteria description	No. of papers meeting criteria	Percent (%)
1	Study design, sampling method is appropriate to the study question	16	94
2	Adequate sample size (>100 participants), or sample size calculations undertaken	17	100
3	Response rate reported and acceptable (>70%)	7	41
4	Disability/impairment measure is clearly defined and reliable	14	82
5	Malnutrition measure is clearly defined and reliable	13	76
6	Potential confounders taken into account in analysis	7	41
7	Confidence intervals are presented	10	59
Case-control (additional criteria)[†]			
8	Cases and controls are comparable	5	71
9	Cases and controls are clearly defined	4	57
Cohort (additional criteria)[‡]			
10	Groups being studied are comparable at baseline	1	100
11	Losses to follow up are presented and acceptable	1	100

[†] Total number of case control studies (n = 7)

[‡] Total number of cohort studies (n = 1)



This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/tmi.13139

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Table 2. Description of studies included in review

Author, year	Country	Study design	Rural/urban	Clinic, population, or school based sample	Total study population	Children with disabilities (n)	Children without disabilities (n)	Age range (years)	Mean age (years)	Percent female
General disability										
Kuper, 2015	Kenya	CC	Rural	Population	807	311	SCs 196; NCs 300	0.5-10	Cases: 2.8; SCs: 2.6; NCs: 2.7	Cases: 35%; SCs*: 41%; NCs*: 39%
Tompsett, 1999	Nigeria	CC	Rural & urban	Clinic	311	112	SCs 87; NCs 112	Under 10	Cases: 5 (SD 1.8); SCs: 4.8 (SD 2); NCs: 4.8 (SD 1.9).	Cases: 42%; SCs: 48%; NCs: 42%
Velez, 2008	Chile	CC	Urban	Clinic	963	748	215	18 or younger	Not reported	39%
Wu, 2010	Nepal	CS	Rural	Population	1902	514	1388	1-9	5.0	48.6%
Yousafzai, 2003	India	CS	Urban	Population	425	141	SCs 122; NCs 162	2-6	Cases: 4.5 (SD 1.7); SCs 4.6 (SD 2.3); NCs 4.3 (SD 1.4)	Cases: 51%, SCs 51%; NCs 49%
Hearing										
Bastos, 1993	Angola	CS	Urban	School	1030	HI 235	795	5-19	Not reported	55%
Emmett, 2015**	Nepal	Cohort	Not reported	Population	2378	140	2238	14-23	Not reported	Not reported
Olusanya, 2010	Nigeria	CS	Urban	Clinic	3386	71	3315	0-0.25	Not reported	Overall 49%; amongst CESH 38%
Neurodevelopmental disorders										
Duc, 2015	Vietnam	CS	Rural & urban	Population	1459	250	1208	3-5	Not reported	50%

Author, year	Country	Study design	Rural/urban	Clinic, population, or school based sample	Total study population	Children with disabilities (n)	Children without disabilities (n)	Age range (years)	Mean age (years)	Percent female
Durkin, 1998	Pakistan	CS	Rural & urban	Population	1363	Total 230: Serious MR 90; Mild MR 140	1133	2-9	Not reported	Not reported
Durkin, 2000	Bangladesh	CS	Rural & urban	Population	10299	Serious MR 62 [†] ; Mild MR 149	10088	2-9	Not reported	47%
Kummer, 2016	Brazil	CC	Urban	Clinic	111	ASD 69; ADHD 23	19	Not reported	ASD 8.4 +/- 4.2; ADHD 8.5 +/- 2.4; controls 8.6 +/- 2.9	ASD: 13%; ADHD 21%; Control 13%
Liu, 2016	China	CC	Urban	School	227	154	73	Less than 9	ASD 5.2 ± SD 1.8; Control 4.8 ± SD 0.8	ASD 8%; Control 8%
Mathur, 2007	India	CC	School	Population	217	117	100	7-18	Not reported	MR: 24%; Controls: 51%
Raina, 2016	India	CS	Rural & urban	Population	5300	91	5209	1-10	Not reported	Not reported
Sachdeva, 2010	India	CS	Peri-urban	Population	468	33 [‡]	435	0-3	Not reported	48%
Socrates, 2000	Philippines	CC	Rural	Population	115	31	SCs 20; NCs 64	2-10	Cases 5.8; SCs 6.5; NCs 5.9	Cases not reported; SCs 45%; NCs 47%

Study design abbreviations: CC, Case-control; CS, Cross-sectional. Abbreviations for type of disability: HI, hearing impaired; HH, hearing handicapped; MR, Mentally retarded; ASD, Autism Spectrum Disorder; ADHD, Attention Deficit/Hyperactivity Disorder; CESH, Congenital or early-onset sensorineural hearing loss. Abbreviations for prevalence of malnutrition in children without disabilities: SC, Sibling controls; NC, Neighbour controls. Mean age abbreviations: SD, Standard deviation.

*Calculated from figures in paper. **Only abstract available. †Case numbers obtained from weighting data in Phase II (CE of those screening positive for disability in Phase I, and ~10% of those screening negative. ‡Conflicting data reported in article regarding number of cases of delayed development.

Table 3. Prevalence of malnutrition in relation to disability

Author, year	Measure of disability	Method of disability assessment	Prevalence of malnutrition in children with disability	Prevalence of malnutrition in children without disabilities	Unadjusted OR	Adjusted OR	Overall quality rating	Quality appraisal criteria not fulfilled
General disability								
Kuper, 2015	Disability	CE, Washington Group-UNICEF childhood disability questionnaire	Stunting: 34% Underweight: 54% Wasting: 33% “Low BMI for age”: 37% Low MUAC for age: 25%	Stunting: SC 23%; NC 21% Underweight: SC 34%; NC 30% Wasting: SC 23%; NC 20% Low BMI for age: SC 26%; NC 24% Low MUAC for age: SC 15%; NC 10%	Stunting: SC 1.7 (1.1-2.6); NC 2.0 (1.3-3.0) Underweight: SC 2.2 (1.5-3.2); NC 2.7 (1.9-3.8) Wasting: SC 1.6 (0.9-2.8); NC 1.9 (1.1-3.3) Low BMI for age: SC 1.6 (1.1-2.5); NC 1.9 (1.3-2.8)	Stunting: SC 2.0 (1.4-3.1); NC 1.8 (1.2-2.8) Underweight: SC 2.2 (1.5-3.2); NC 2.7 (1.9-3.7) Wasting: SC 1.5 (0.8-2.7); NC 1.9 (1.1-3.2) Low BMI for age: SC 1.8 (1.2-2.7); NC 1.6 (1.0-2.4)	++	3
Tompsett, 1999	Disability	CE	Stunting: 59% Underweight: 38% Wasting: 6%	Stunting: SC 45%; NC 33%; Underweight: SC 16%; NC 12% Wasting: SC 2%; NC 1%	Stunting*: SC 1.8 (1.0-3.1); NCs 2.9 (1.7-5.0) Underweight*: SC 3.1 (1.6-6.2); NC 4.6 (2.3-9.1); Wasting*: SC 2.8 (0.6-14.0); NC 7.4 (0.9-61.2)	Not reported	+	3, 4, 6, 7
Velez, 2008	Disability	CE, MH	Underweight: 11% Overweight: 22% Obese: 12% Morbidly obese: 5%	Underweight: 2% Overweight: 33% Obese: 13% Morbidly obese: 0%	Underweight*: 5.1 (2.0-12.8) Overweight*: 0.57 (0.41-0.79) Obese/morbidly obese*:	Risk of obesity for various disability diagnoses **: CP 0.46 (0.20-1.03); <i>Developmental</i>	+	3, 8, 9

					1.42 (0.91-2.22)	<i>disabilities</i> 1.96 (1.16-3.34); <i>Neurological disorders</i> 2.58 (1.26-5.29)		
Wu, 2010	Disability	10Q	Not reported	Not reported	Stunting: <i>Moderate</i> 1.14 (0.90-1.43); <i>Severe</i> 1.51 (1.13 – 2.00) Wasting: <i>Moderate</i> 0.94 (0.74-1.19); <i>Severe</i> 0.86 (0.62 – 1.21)	Stunting: <i>Moderate</i> 1.04 (0.81-1.34); <i>Severe</i> 1.33 (0.98 – 1.82) Wasting: <i>Moderate</i> 0.96 (0.75-1.24); <i>Severe</i> 0.94 (0.66 – 1.35)	+	3
Yousafzai, 2003	Disability	10Q	Stunted: 69% Underweight: 69% Wasted: 30%	Stunted: SCs 51%; NCs 53% Underweight: SCs 42%; NCs 47% Wasted: SCs 11%; NCs 13%	Stunting*: SCs 2.1 (1.3-3.5); NCs 1.9 (1.2-3.1) Underweight*: SCs 3.1 (1.8-5.1); NCs 2.5 (1.6-4.0) Wasting*: SCs 3.6 (1.8-7.0); NCs 2.8 (1.6-5.1)	Not reported	+	3, 6, 7
Hearing								
Bastos, 1993	HI (including HH)	Audiometry, otoscopy	Not reported	Not reported	Null	Not reported	-	3, 6, 7
Emmett, 2015***	Hearing loss	Audiometry, tympanometry	Not reported	Not reported	Not reported	Stunting: 2.2-1.7 Wasting: 1.8-2.2 “(all 95% lower CL >1)”	-	3, 6, 10, 11
Olusanya, 2010	CESHL	ABR, tympanometry, visual response audiometry	Stunted: 35% Underweight: 31% Wasted: 26%	Stunted: 28% Underweight: 17% Wasted: 14%	Stunted: 1.44 (0.87-2.37) Underweight: 2.32 (1.39-3.88) Wasted: 2.30 (1.33-3.97)	“Any undernourishment”: 1.67 (1.03-2.77)	++	1
Neurodevelopmental disorders								

Duc, 2015	Early childhood development "on track"	ECDI (10 item module)	Not reported	Not reported	Not reported	Stunting: 0.71 (0.51-0.98, p-value <0.05) Wasting: 0.89 (0.43-1.81) [†]	++	5
Durkin, 1998 [‡]	MR	SB and adaptive behaviour scale, MH, CE	<i>Serious MR</i> 14%; <i>Mild MR</i> 9%	2%	<i>Serious MR & "current malnutrition":</i> 10.92 (3.62-32.97) <i>Mild MR & "current malnutrition":</i> 6.82 (3.11-14.92)	<i>Serious MR with malnourishment:</i> 10.19 (3.19-32.58) <i>Mild MR with malnourishment:</i> 4.23 (1.64-10.90)	-	5
Durkin, 2000	MR	CE, MH, SB	Not reported	Not reported	"Currently malnourished" and <i>serious CD</i> : Rural 2.48 (1.07, 5.75); <i>Mild CD</i> 1.95 (0.36-10.61)	Not reported	-	5
Kummer, 2016	ADHD, ASD	DSM-5	Underweight: ADHD 0%; ASD 7% Overweight: ADHD 18%; ASD 18% Obese: ADHD 17%; ASD 22%	Underweight: 21% Overweight: 0% Obese: 5%	Underweight*: ADHD Unable to be calculated; ASD 0.3 (0.1-1.2) Overweight/obese*: ADHD 9.6 (1.1-85.7); ASD 12.3 (1.6-97.4)	Not reported	+	6, 7, 9
Liu, 2016	ASD	DSM-5, CE, SI, CARS	Stunted: 7% Underweight: 3% Wasted: 0% Overweight: 8% Obese: 10%	Stunted: 0% Underweight: 0% Wasted: 0% Overweight: 14% Obese: 21%	Stunted*: Unable to be calculated Underweight*: Unable to be calculated Wasted*: Unable to be calculated Overweight*: 0.53 (0.22-1.30) Obese*: 0.42 (0.20-0.91)	Not reported	+	3, 6, 7
Mathur, 2007	MR	IQ tests	Underweight: 34% Overweight: 9%	Underweight: 17% Overweight: 16%	Underweight*: 2.54 (1.33-4.84)	Not reported	-	4, 5, 6, 7, 8

					Overweight*: 0.49 (0.21-1.14)			
Raina, 2016	MR	CE, MH, SB	Stunted*: 45% Wasted*: 8% Wasted & stunted*: 20%	Stunted*: 50% Wasted*: 10% Wasted & stunted*: 5%	Stunted: 1.18 (0.72-1.95) Wasted: 1.00 (0.43-2.33) Wasted & stunted: 5.57 (2.99-10.36)	Not reported	+	3, 6
Sachdeva, 2010	GDD	The IMCR Developmental Screening Test questionnaire	Stunted*: 49% Underweight*: 42% Wasted*: 9%	Stunted*: 28% Underweight*: 26% Wasted*: 8%	Stunted: 2.2 (1.1-4.6) Underweight: 1.8 (0.9-3.9) Wasted: 0.7 (0.2-3.5)	Stunting: 5.69 P=0.02	+	6
Socrates, 2000	CP	CE, MH	Stunted: 79% Wasted: 66%	Stunted: SC 45%; NC 36% Wasted: SC 10%; NC 5%	Stunting*: SC 4.2 (1.2-14.2); NC 6.1 (2.3-16.4) Wasting*: SC 16.4 (3.2-84.0); NC 37.0 (9.4-145.9)	Not reported	+	3, 4, 6, 7, 9

Measure of disability abbreviations: CESH, Congenital or early-onset sensorineural hearing loss; MR, Mental retardation; GDD, Global developmental delay. Method of disability assessment abbreviations: CE, clinical evaluation; PT, physiotherapist; MH, medical history; 10Q, Ten Questions Screen; ECDI, Early childhood development index; DSM-5, Diagnostic and Statistical Manual of Mental Disorders; SI, Structured interview; CARS, Childhood Autism Rating Scale; SB, Stanford-Binet Intelligence Test. Abbreviations for type of disability: ASD, Autism Spectrum Disorder; ADHD, Attention Deficit/Hyperactivity Disorder; CD, cognitive disability. Abbreviations for prevalence of malnutrition in children without disabilities: SC, Sibling controls; NC, Neighbour controls. *Calculated from figures in paper. **Disability diagnoses only shown that had p-values that were significant/borderline. Non-disabled children were used as the reference. ***Abstract only available. †These adjusted OR were for children with wasting/stunting having ECDI in the normal range. These results were interpreted by Duc as “children with stunting were 0.71-fold...less likely to have ECDI in the normal range”. ‡ Durkin (1998) and Durkin (2000) did not report any details on measures of malnutrition, just presented “current malnutrition” as potential risk factor for CD. In Durkin (2000), OR for risk factors and serious CD were presented separately for rural and urban, because of heterogeneity of effect, or effect modification, by rural-urban residence. No OR for association between “currently malnourished” and serious CD presented for urban residence. OR for risk factors for mild CD not presented separately.

Accepted Article

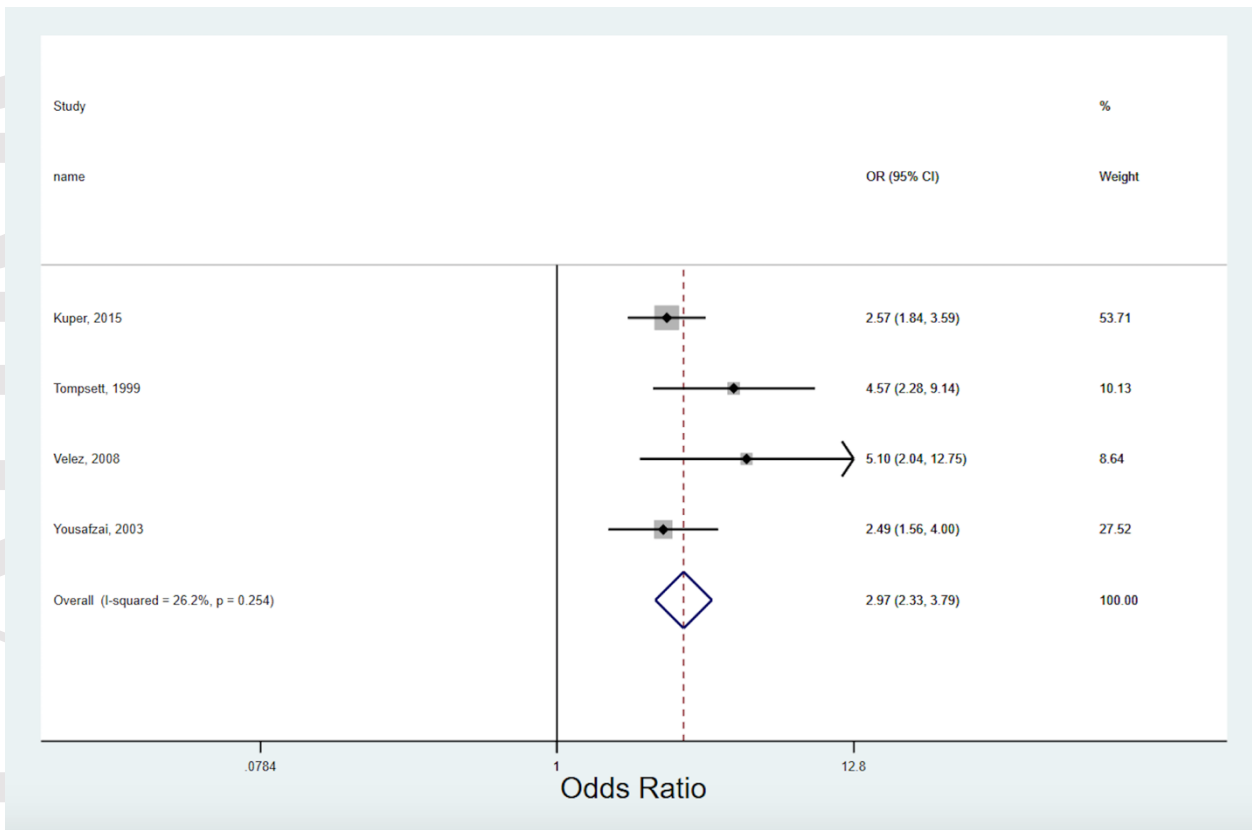
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Table 4. Summary of study characteristics and their results for the association of undernutrition with disability

		Total		Association of undernutrition			
		(n =)	(%)	Positive	Null	Negative	Mixed
Overall		17	100	53	29	0	18
Disability/impairment type	General disability*	5	29	60	20	0	20
	Hearing	3	18	67	33	0	0
	Neurodevelopmental	9	53	44	33	0	22
Region	East Asia	1	6	0	100	0	0
	South America	2	12	50	50	0	0
	South Asia	10	59	80	20	0	20
	Sub-Saharan Africa	4	24	50	25	0	25
Setting	Rural	3	18	67	33	0	0
	Urban	8	47	63	37	0	0
	Rural and urban	5	29	20	20	0	60
	Not specified	1	6	100	0	0	0
Quality	Low risk of bias (++)	3	18	67	33	0	0
	Medium risk of bias	9	53	44	33	0	22
	High risk of bias (-)	5	29	60	40	0	0

Figure 2 Odds of the association between childhood disability and underweight status



*Kuper (2015) had one adjusted OR that contained the null value (OR for wasting in SCs), but all other results were statistically significant and showed a positive association between disability and undernutrition. When crude OR was calculated for Velez (2008) for all disabled cases compared to controls, this showed a positive association with underweight.

Figure 3 Odds of the association between childhood disability and stunting

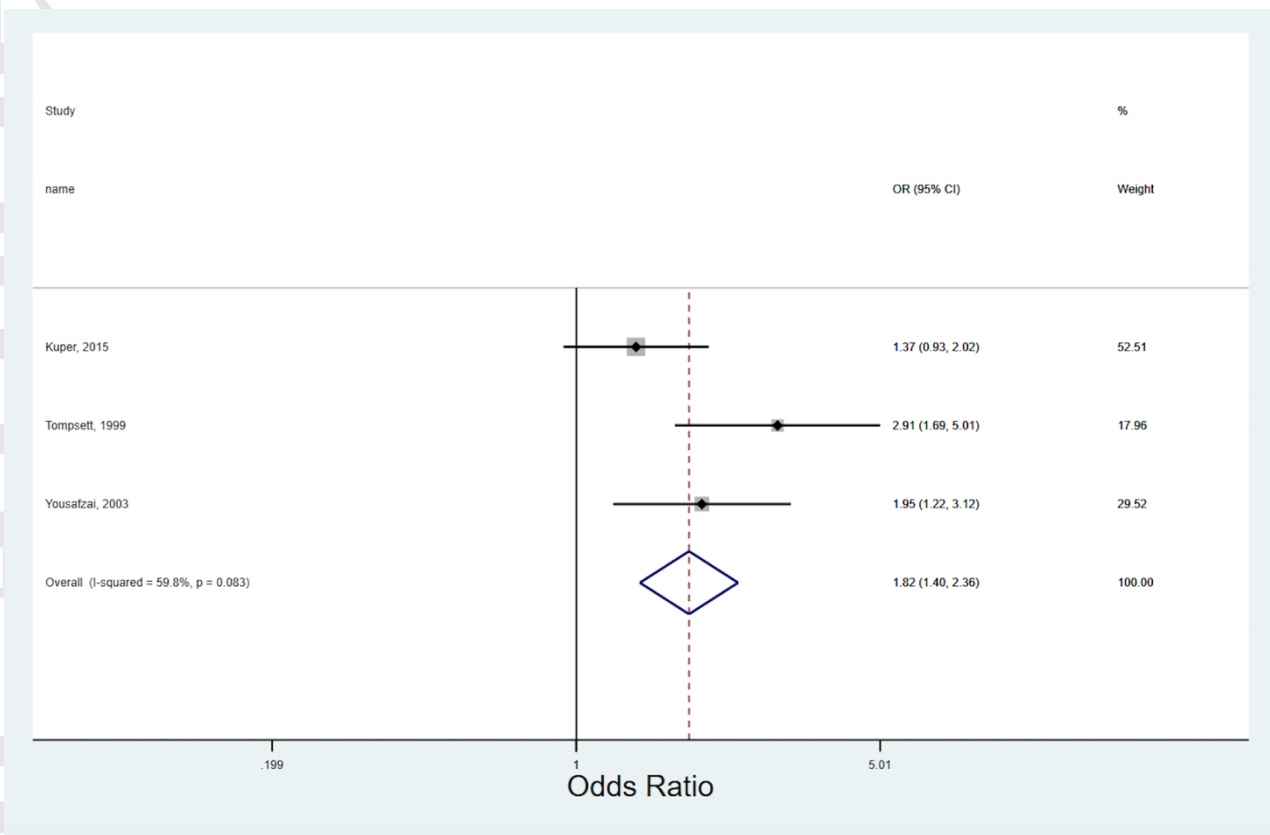


Figure 4 Odds of the association between childhood disability and wasting

