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SYSTEMATIC REVIEW

Childhood outcomes after low-grade intraventricular haemorrhage: A systematic review and meta-analysis

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Abstract

Aim: To undertake a systematic review and meta-analysis exploring school-age neurodevelopmental outcomes of children after low-grade intraventricular haemorrhage (IVH).

Method: The published and grey literature was extensively searched to identify observational comparative studies exploring neurodevelopmental outcomes after IVH grades 1 and 2. Our primary outcome was neurodevelopmental impairment after 5 years of age, which included cognitive, motor, speech and language, behavioural, hearing, or visual impairments.

Results: This review included 12 studies and over 2036 infants born preterm with low grade IVH. Studies used 30 different neurodevelopmental tools to determine outcomes. There was conflicting evidence of the composite risk of neurodevelopmental impairment after low-grade IVH. There was evidence of an association between low-grade IVH and lower IQ at school age (−4.23, 95% confidence interval [CI] −7.53, −0.92, $I^2 = 0\%$) but impact on school performance was unclear. Studies reported an increased crude risk of cerebral palsy after low-grade IVH (odds ratio [OR] 2.92, 95% CI 1.95, 4.37, $I^2 = 41\%$). No increased risk of speech and language impairment or behavioural impairment was found. Few studies addressed hearing and visual impairment.

Interpretation: This systematic review presents evidence that low-grade IVH is associated with specific neurodevelopmental impairments at school age, lending support to the theory that low-grade IVH is not a benign condition.

Globally, over 10% of infants are born preterm, making preterm birth the foremost cause of death and disability.[1,2] Intraventricular haemorrhage (IVH) is a common neuropathological consequence of preterm birth.[3,4] Unfortunately, despite many advances in neonatal care—which have dramatically reduced mortality for the population born preterm—the incidence of IVH has remained static.[4,5] Amongst infants born very preterm (less than 32 weeks' gestation) the incidence of IVH is reported to be in the region of 20%.[3,4,6] The neurological sequelae of severe IVH (grade 3 or 4) are widely recognized.[6,7] However until recently, lower grade IVH (1 or 2) was felt to be relatively benign, with little impact on childhood development.[4–6,8] There is now, however, increasing evidence that even low-grade IVH results in an increased risk of neurodevelopmental impairment at 2 to 3 years of age, above and beyond the risks posed by prematurity alone.[6,7]

Parents have highlighted that the longer-term functional impact of brain injuries such as IVH is a priority area for further research.[9,10] Although there is growing evidence of an impact of low-grade IVH on development in infancy,[7] this does not necessarily translate into an ongoing impact throughout childhood. Early developmental assessment is widely acknowledged to be poorly predictive of future

Abbreviation: IVH intraventricular haemorrhage

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childhood functioning.[11,12] Additionally, neurodevelopmental impairment is often not fixed: it can deteriorate or improve over time, influenced by the neuroplasticity of the early brain and external environmental factors. As such, there are unanswered questions around the developmental trajectories of children with a history of low-grade IVH. This information is essential to inform developmental follow-up and provision of early intervention services, in addition to preparing affected families for the future. We therefore undertook a systematic review with the aim of exploring school-aged childhood outcomes after low-grade IVH.

What this paper adds

- The functional impact of low-grade intraventricular haemorrhage (IVH) at school age is unknown.
- Low-grade IVH is associated with a lower IQ at school age.
- The risk of cerebral palsy is increased after low-grade IVH.
- Low-grade IVH is not associated with speech and language impairment.

METHOD

The systematic review was conducted as per our a priori registered protocol (CRD 42021278572) and in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. Observational comparative studies, published between 2000 and 2021, exploring neurodevelopmental outcomes of school-aged children after IVH grades 1 and 2, compared to those of children born preterm without IVH, were included (Table 1). Only cohort study designs were included because of the nature of the review question and with a view to seeking the highest level of evidence available. Therefore, intervention studies, cross-sectional studies, case–control studies, and case series were excluded. A composite outcome of neurodevelopmental impairment, however defined by study authors, was the primary study outcome. Secondary outcomes included cognitive impairment (including poor academic attainment and special educational needs), motor impairment (including cerebral palsy), speech and language deficits, behavioural outcomes, visual impairment, and hearing impairment.

An extensive search strategy was developed in Medline Ovid which consisted of 99 key terms and MeSH headings (Appendix S1). This was adapted and employed across 10 databases (Appendix S2). In addition to searching the published and grey literature, searches were augmented by hand searching the reference lists of included studies. All identified abstracts were screened for relevance independently, by two reviewers. The full texts of potentially relevant abstracts were retrieved and again reviewed for inclusion by two trained reviewers independently. This included an assessment of studies' risk of bias as a result of population selection, the comparability of the exposed and comparator groups (with IVH grade 1 or 2 and without IVH), and outcome assessment, using the Newcastle-Ottawa Scale for cohort studies.[13] Disagreements were resolved through third reviewer arbitration.

Key data from included studies were extracted to a purpose-built Microsoft Excel spreadsheet by two reviewers independently. Results from studies were narratively synthesized and described for each developmental domain. Where possible, data from suitably clinically and contextually comparable studies were pooled in random effects meta-analyses using RevMan 5.4.[14] Dichotomous study data were combined using the Mantel–Haenszel method and continuous data were combined using the inverse variance method. Heterogeneity was assessed using the I^2 statistic.[14] Caution was advised in interpreting meta-analyses where there was substantial (>85%) heterogeneity across studies, and, where possible, heterogeneity was explored through subgroup analyses.

RESULTS

Overview

Searches yielded 14 210 records, 10 178 of these were screened, and 12 studies were included (Figure S1). Studies were undertaken in Australia ($n=3$), the UK ($n=2$), the USA ($n=2$), France ($n=1$), the Netherlands ($n=1$), Germany ($n=1$), Austria ($n=1$), and Canada ($n=1$) (Table S1). They were either prospective ($n=9$) or retrospective cohort studies ($n=3$) from single-centres ($n=6$), multiple-centres ($n=2$), or population-registries ($n=4$), and regarded as either low ($n=7$) or moderate ($n=5$) risk of bias (Table S2).

The 12 studies included over 2036 infants with IVH grade 1 to 2 and 53 067 comparator infants born preterm without IVH (five studies contained a partially overlapping population). Infants were mostly born at less than 33 weeks' gestation or had a birthweight of less than 1500 g. IVH grade 1 to 2 was mainly confirmed on ultrasound imaging ($n=11$) and occasionally on magnetic resonance imaging (MRI) ($n=2$). The Papile classification was used by most studies to classify the severity of IVH ($n=8$) based on the most severe IVH observed on imaging (whether unilateral or bilateral). Images were reviewed and classified by neonatologists ($n=3$), radiologists ($n=2$), and sonographers ($n=1$), although most studies did not specify who reviewed the imaging and whether imaging review was blinded. Studies used 30 different neurodevelopmental assessment tools to determine outcomes at varying time points.

Neurodevelopmental impairment

Four studies explored neurodevelopmental impairment at school age of infants born preterm with IVH grade 1 to 2.[15–18] These studies reported conflicting results and were not comparable (Table S1 and Table 2).

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TABLE 1 Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
Prospective or retrospective cohort studies	Cross-sectional studies, case–control studies, non-comparative studies, and lab studies
Studies in any language	Studies where comparable outcome data for infants born preterm with and without low-grade IVH cannot be extracted
Studies published after 2000	Studies where outcome data for infants with low-grade IVH cannot be isolated from those with other brain injuries or those with higher grades of IVH
Infants born preterm at less than 37 weeks' gestation or with a birthweight of less than 2500 g	Studies not reporting quantitative neurodevelopmental outcomes
Studies including infants with low-grade IVH (i.e. IVH grades 1 and 2 defined as unilateral or bilateral germinal matrix haemorrhage that may extend into the lateral ventricle but does not occupy more than 50% of the lateral ventricle) identified through neuroimaging during the neonatal period[37]	
Studies focused on school-aged neurodevelopmental outcomes (of children between 5–18 years of age) including at least one of the following:	
Primary outcome(s) Neurodevelopmental impairment, as defined by authors (including direct testing, clinical record review, and parental interview/survey)	
Secondary outcome(s) Any cognitive impairment, as defined by authors (direct testing) Mild cognitive impairment (IQ or developmental quotient 1–2 SD below the mean) Moderate–severe cognitive impairment (IQ or developmental quotient more than 2 SD below the mean) Executive dysfunction, as defined by authors (direct testing) Low numeracy, as defined by authors (by direct testing or educational achievement tests) Low literacy, as defined by authors (by direct testing or educational achievement tests) Special educational needs as defined by authors (school or parental report) Motor impairment, as defined by authors (including direct testing, clinical record review, and reporting) Visual-motor impairment, as defined by authors (on direct testing) Emotional-behavioural difficulty, as defined by authors (including direct testing, clinical record review, and parental reporting) Speech and language impairment, as defined by authors (on direct testing) Visual impairment, as defined by authors (including direct testing, clinical record review, and parental reporting) Hearing impairment, as defined by authors (including direct testing, clinical record review, and parental reporting)	

Cognitive

Six included studies reported cognitive outcomes after IVH grade 1 to 2 at school age.[16,17,19–22] These studies used 17 different cognitive assessment tools and reported conflicting results for children born across a wide time-period (1983–2005). Two comparable studies highlighted a significant pooled mean difference in IQ scores of 4 points at 8 years of age between those with and without IVH grade 1 to 2 and heterogeneity was low (−4.23, 95% confidence interval [CI] −7.53, −0.92, $I^2 = 0\%$) (Figure 1).[21,22] These studies were of low and moderate risk of bias. This was largely because of the risk of bias stemming from how the exposed and comparator cohorts were selected by Wy et al.[22] and in the ascertainment of low-grade IVH (Table S3). Although this difference was attenuated and not statistically significant on including only those with left-sided IVH grade 1 to 2 (−2.96, 95% CI −6.61, 0.7, $I^2 = 0\%$) and equivocal on including only those with right-sided IVH grade 1 to 2 (−0.12, 95% CI −5.89, 5.66, $I^2 = 50\%$) from Vollmer et al.[21] in sensitivity analyses (Figure S2 and S3). Wy et al.[22] did not report outcomes by laterality.

Van de Bor and den Ouden[17] also highlighted a cognitive impact of IVH grade 1 to 2 with 22.5% having special educational needs at 5 years of age compared to 8.7% of comparators. These needs persisted at 9 and 14 years of age after adjusting for key confounders (adjusted OR [aOR] 2.1, 95% CI 1.01, 4.35).[17] On the other hand Wy et al.[22] (after adjusting for covariates) and Hollebrandse et al.[19] which included children born more recently than Van de Bor and den Ouden[17] reported no increased risk of cognitive impairment. Hollebrandse et al.[19] also did not find any increased risk of impaired academic performance in reading, spelling, or arithmetic (OR 0.7, 95% CI 0.39, 1.27).

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TABLE 2 Overview of key findings for school age outcomes of infants with perinatal brain injury compared to those without brain injury.

	NDI	Cognitive	Motor	Speech and language	Behavioural	Hearing[b]	Vision[b]
IVH grades 1 and 2[a]	Four studies[15–18] Not comparable Small studies with conflicting results	Six studies[16,17,19–22] Two comparable studies in meta-analysis Conflicting results **Meta-analysis** (two studies): mean IQ difference −4.23, 95% CI −7.53, −0.92, $I^2 = 0\%$ **Van de Bor and den Ouden:**[17] increased prevalence of special educational needs **Hollebrandse et al.:**[19] no increased risk of cognitive impairment or impaired academic performance OR 0.7, 95% CI 0.39, 1.27	Six studies[16,19–21,23,24] **Sherlock et al.:**[16] similar prevalence of abnormal movement scores ($n = 17$, 23.6% vs $n = 39$, 22.5%) **Hollebrandse et al.:**[19] increased prevalence of low movement ABC score (below the 5th centile) or cerebral palsy ($n = 42$, 31.6% vs $n = 81$, 24%) after IVH grades 1 and 2 but only statistically significant for IVH grade 2 OR 1.93, 95% CI 1.05, 3.56 **Vollmer et al.:**[21] worse motor outcomes for left-sided IVH grades 1 and 2 vs right-sided IVH grades 1 and 2 but similar to bilateral IVH grades 1 and 2 **Cerebral palsy** Six studies[16,19–21,23,24] Three included in meta-analysis OR 2.92, 95% CI 1.95, 4.37, $I^2 = 41\%$	Four studies[16,17,19,22] **Hollebrandse et al.:**[19] no increased risk of impaired reading OR 0.85, 95% CI 0.44, 1.66 No increased risk impaired spelling OR 0.46, 95% CI 0.16, 1.29 **Sherlock et al.:**[16] no significant difference in verbal comprehension scores **Van de Bor and den Ouden:**[17] no significant difference in speech and language impairment **Wy et al.:**[22] no significant mean difference in vocabulary score 3.82, 95% CI −1.12, 8.75; $p = 0.13$	Two studies[22,25] No significant difference in behaviour scores on Child Behaviour Checklist	Three studies[17,20,26] Not comparable Outcome too rare for inferential analysis in most studies **Kaur et al.:**[26] risk of hospitalization for otological reasons after IVH grade 2 HR 1.28, 95% CI 0.98, 1.69 and IVH grade 1 HR 1.21, 95% CI 1.05, 1.40	Four studies[17,20,21,26] Not comparable Outcome too rare in most studies for inferential analysis **Klebermass-Schrehof et al.:**[20] increased risk of visual impairment (including needing glasses or blindness) OR 4.5, 95% CI 2.09, 7.83 **Kaur et al.:**[26] increased adjusted risk of hospitalization for ophthalmic reasons after IVH grade 2 aHR 3.00, 95% CI 1.78, 5.07 and IVH grade 1 aHR 1.76, 95% CI 1.20, 2.57 **Vollmer et al.:**[21] lower visuomotor integration scores after bilateral lesions (mean 55.1, SD 32.1) and left-sided lesions (mean 46.8, SD 31.0) compared to right-sided lesions (mean 64.2, SD 30.2)

[a]Does not include studies where infants with IVH grades 1 and 2 cannot be separated from those with other brain injuries such as IVH grades 3 and 4 or white matter injury.

[b]Does not include studies using hearing or visual outcomes only as part of their composite outcome.

Abbreviations: aHR, adjusted hazard ratio; CI, confidence interval; HR, hazard ratio; IVH, intraventricular haemorrhage; NDI, neurodevelopmental impairment; OR, odds ratio.

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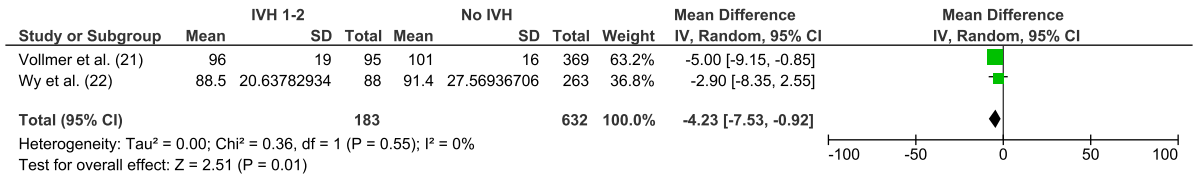

FIGURE 1 Forest plot reporting the mean difference in IQ score at 8 years of age after intraventricular haemorrhage (IVH) grades 1 and 2. Abbreviation: CI, confidence interval.

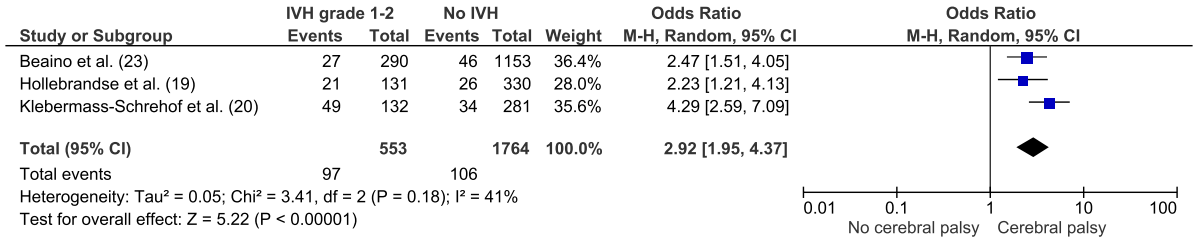

FIGURE 2 Forest plot reporting the crude risk of cerebral palsy after intraventricular haemorrhage (IVH) grades 1 and 2. Abbreviation: CI, confidence interval.

Motor and cerebral palsy

Six studies presented motor outcomes after low-grade IVH.[16,19–21,23,24] They all focused on cerebral palsy and three were sufficiently comparable for pooling in a meta-analysis.[16,19–21,23] An increased combined crude risk of cerebral palsy at school age after IVH grade 1 to 2 was reported (OR 2.92, 95% CI 1.95, 4.37, $I^2 = 41\%$) with moderate heterogeneity (Figure 2). There was clinical heterogeneity in terms of outcome assessment (timing and method) which may account for the moderate statistical heterogeneity. Two of these studies had a low risk of bias and one had a moderate risk of bias because of the poor comparability of the exposed and comparator cohort and high loss to follow-up in the absence of a clear explanation (Table S4). Sherlock et al.[16] highlighted similar rates of abnormal movement scores amongst those with previous IVH grade 1 to 2 ($n = 17$, 23.6%) compared to those without IVH at 8 years of age ($n = 39$, 22.5%).[16] However, Hollebrandse et al.[19] reported a stepwise increase in the prevalence of motor dysfunction, defined as a low movement ABC score (below the 5th centile) or cerebral palsy, from those with no IVH ($n = 81$, 24%), to those with IVH grade 1 ($n = 22$, 28%) and those with IVH grade 2 ($n = 20$, 38%). This was statistically significant for those with IVH grade 2 (OR 1.93, 95% CI 1.05, 3.56) but not those with IVH grade 1 (OR 1.17, 95% CI 0.67, 2.03) (Table S1).[19] Vollmer et al.[21] also explored motor outcomes at school age but by laterality of IVH. They highlighted that children with previous left-sided IVH grade 1 to 2 performed worse than those with right-sided IVH grade 1 to 2 (mean test of motor impairment score 4.5 [SD 3.8] compared to 2.7 [SD 1.8]), but on a similar level to those with bilateral IVH grade 1 to 2 (mean test of motor impairment score 4.1 [SD 3.7]) (Table S1). Children with right-sided IVH performed similarly to those without IVH (mean test of motor impairment score 2.7 [SD 1.8] vs 2.78 [SD 2.1] respectively).[21]

Speech and language

Four studies explored speech and language outcomes at school age after low-grade IVH.[16,17,19,22] They consistently reported no significant difference in speech and language between infants born preterm with low-grade IVH and infants born preterm without IVH at school age (Table 2). Sherlock et al.[16] reported no significant difference in mean verbal comprehension scores after IVH grade 1 (96.3 [15.7]) or IVH grade 2 (99.6 [12.8]) compared to no IVH (96.6 [16.2]) (Table S1). Additionally Van de Bor and den Ouden[17] did not find any significant differences in the incidence of speech disability at 5 years of age after IVH grades 1 and 2 ($n = 12$, 26.6%) compared to those without IVH ($n = 34$, 15.7%) (Table S1). Wy et al.[22] also found no significant difference in vocabulary scores between those with IVH grade 1 to 2 and those without IVH at 3, 8, or 18 years of age (mean difference in Peabody Picture Vocabulary Test score 2.59, 95% CI −1.51, 6.69; 3.82, 95% CI −1.12, 8.75; 2.02, 95% CI −2.93, 6.98 respectively) (Table S1). Hollebrandse et al.[19] explored functional outcomes and reported no increased risk of impaired reading (OR 0.85, 95% CI 0.44, 1.66) or spelling after IVH grade 1 to 2 (OR 0.46, 95% CI 0.16, 1.29).

Behaviour

Two studies explored behavioural outcomes at school age.[22,25] They did not report any significant differences on the Child Behaviour Checklist between those with and

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without IVH grade 1 to 2.[22,25] Wy et al.[22] reported no significant mean difference in Child Behaviour Checklist internalizing (0.91, 95% CI −0.76, 2.58), externalizing (−0.14, 95% CI −2.19, 1.90), or total raw scores (0.56, 95% CI −4.60, 5.72) between infants born preterm with low-grade IVH and infants born preterm without IVH at 8 years of age.[22]

Hearing and vision

Three studies explored hearing outcomes after low-grade IVH and four explored visual outcomes.[17,20,21,26] These studies were not comparable and the outcome of hearing or visual impairment was often too rare to enable inferential analysis. However, Kaur et al.[26] reported an increased adjusted risk of hospitalization for ophthalmic reasons after IVH grade 2 (adjusted hazard ratio [aHR] 3.00, 95% CI 1.78, 5.07) and IVH grade 1 (aHR 1.76, 95% CI 1.20, 2.57) after adjusting for key covariates including retinopathy of prematurity. Additionally Klebermass-Schrehof et al.[20] reported that those with IVH grade 1 to 2 had an increased crude risk of visual impairment (including needing glasses or blindness) at 5 years 6 months of age (OR 4.5, 95% CI 2.09, 7.83) although retinopathy of prematurity was more common in the IVH group and this was not adjusted for in the analysis.[20] No significant difference in visuomotor integration scores after IVH grade 1 to 2 was reported.[20,21]

DISCUSSION

This review adds to the growing evidence that low-grade IVH is not a benign pathology by reporting on its association with specific persisting neurodevelopmental impairments at school age. Evidence of an increased composite risk of neurodevelopmental impairment after low-grade IVH was conflicting. There was however evidence of an impact of low-grade IVH on IQ at school age—although the impact of this on school performance and the functional importance of a 4-point reduction in IQ was less clear. There was also a demonstrably increased risk of cerebral palsy after low-grade IVH and some suggestion of an impact on motor performance outside of cerebral palsy. Promisingly, studies consistently reported no increased risk of speech and language impairment after low-grade IVH and no increased risk of behavioural impairment was found. There was a suggestion of increased risk of visual impairment after IVH grade 1 to 2, although few studies addressed this.

Strengths and limitations

This systematic review included a sensitive search strategy, covering an extensive time-period, and a rigorous review and appraisal process was followed. Data synthesis and review findings were limited by the heterogeneity of included studies. The 12 included studies employed 30 different neurodevelopmental assessment tools at varying time points. Data extraction was limited by the presentation of results within studies. For example, disaggregated outcome data for those with IVH grade 1, IVH grade 2, and no IVH were typically not presented. Additionally, outcomes were often not presented by laterality of injury. Most studies used ultrasound imaging to diagnose low-grade IVH despite concerns about interrater variability in the classification of IVH severity on ultrasound. Additionally using ultrasound imaging over MRI poses a risk of not detecting additional confounding lesions such as white matter injuries which may affect outcomes.[4,8] Although we required the study to have a non-brain injured preterm comparator group for inclusion, many studies did not account for other key confounders including comorbidities such as retinopathy of prematurity and necrotizing enterocolitis.

Context of literature

A previous review reported an increased adjusted risk of moderate to severe neurodevelopmental impairment after IVH grade 1 to 2 at 2 to 3 years of age (aOR 1.35, 95% CI 1.05, 1.75).[7] Unfortunately it was not possible to determine whether this risk persists to school age. Previous reviews of this topic have also been limited by heterogeneity across studies.[6] However, we were able to report that the cognitive impact associated with low-grade IVH at age 2 to 3 years of age (an increased risk of Bayley Scale of Infant Development scores <70) may persist at school age in the form of reduced IQ scores at 8 years of age.[21,22] However, it was unclear whether this translated into a functional impact on school performance.[17,19,22] Unsurprisingly, the previously reported increased risk of cerebral palsy at 2 to 3 years after low-grade IVH was also seen at school age.[7] The overall crude risk of cerebral palsy after IVH grade 1 to 2 (combining this review's data with a previously review's meta-analysis at 2–3 years of age) is OR 1.79, 95% CI 1.44, 2.24, $I^2 = 48\%$ (Figure S4).[3,16,19–21,27–34]

There are many postulated mechanisms through which grade 1 to 2 IVH may affect neurodevelopment including through direct (primary) damage to the germinal matrix or through secondary damage by impacting adjacent brain development (e.g. cerebral white matter injury).[8,35] After 24 weeks' gestation the germinal matrix plays a key role in the development and migration of glial precursor cells and GABAergic interneurons to the cerebral cortex and thalamus.[4,8,36] Disruption to these processes by IVH and its deleterious effects could impact neurodevelopment especially motor and cognitive development.[4,35,36]

Implications

This review provides further evidence that low-grade IVH is unlikely to be a benign pathology (as previously thought) by highlighting that it has a measurable impact on children's cognitive and motor development at school

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age. These findings, including the outstanding gaps in our knowledge, should inform counselling of parents of infants born preterm with low-grade IVH on the neonatal unit. The findings also provide further evidence to support the importance of ongoing quality improvement initiatives to prevent IVH amongst infants born preterm on the neonatal unit in addition to reiterating the importance of neurodevelopmental follow-up and support for this population. Further studies which are adequately powered to explore school-aged outcomes after low-grade IVH, which adjust for key confounders (including white matter injury), and report outcomes by laterality and specific grade of IVH, are needed to more fully understand the implications of low-grade IVH for affected children. Additionally, use of a core outcome set and more transparent reporting would reduce heterogeneity across studies enabling powerful meta-analyses which could efficiently address these outstanding questions.

Conclusions

This review provides evidence that low-grade IVH is associated with specific neurodevelopmental impairments at school age.

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DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study

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SUPPORTING INFORMATION

The following additional material may be found online:

Appendix S1: Medline search strategy.

Appendix S2: Databases searched.

Figure S1: PRISMA flow chart of included and excluded studies.

Figure S2: Sensitivity analysis of the mean difference in IQ on including only those with left-sided IVH grades 1 and 2.

Figure S3: Sensitivity analysis of the mean difference in IQ on including only those with right-sided IVH grades 1 and 2.

Figure S4: Forest plot of the overall crude risk of cerebral palsy after IVH grades 1 and 2.

Table S1: Included studies of school-aged outcomes after low-grade IVH.

Table S2: Risk of bias table.

Table S3: Risk of bias table of studies included in meta-analysis of cognitive outcomes after IVH grades 1 and 2.

Table S4: Risk of bias table of studies included in meta-analysis of cerebral palsy after IVH grades 1 and 2.

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