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Journal Summary

Lifelong learning in paediatrics

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1. Excessive noise in neonatal intensive care units: A persistent challenge with modifiable solutions

Source: Andy L, Fan H, Valerie S, Jing W. Systematic review of environmental noise in neonatal intensive care units. *Acta Paediatr*. 2025 Jan; 114(1): 35–50. doi: 10.1111/apa.17445. Epub 2024 Oct 3. PMID: 39363441.

This systematic review provides an updated analysis of noise measurement methods in neonatal intensive care units (NICUs) since 2005, highlighting the persistent issue of excessive noise exposure in these environments. The study systematically summarised noise characteristics, sources and measurement methodologies, employing a rigorous search strategy across major databases and independent reviewers to minimise bias. However, findings were limited by small sample sizes and significant heterogeneity in measurement techniques, preventing direct comparisons across studies and precluding meta-analysis.

A key finding was that all reported equivalent continuous noise levels (Leq) and L10 exceeded the recommended limits of 45 decibels (dBA) and 50 dBA, respectively, suggesting that NICU noise levels were consistently above acceptable thresholds. In ten studies, even minimum noise levels surpassed the recommended 45 dBA, indicating that ambient noise never fell within safe limits. However, maximum noise levels remained within the 65 dBA threshold in some NICUs. Notably, NICUs exhibited high-frequency noise exposure averaging 71.5 dBA between 1000 and 8000 Hz, significantly higher than the foetal *in utero* exposure, which is typically below 500 Hz. In addition, transient high-frequency noises were observed, though their physiological significance remains unclear.

The primary contributors to noise varied between NICUs, though five studies consistently identified people congregation as a key factor in elevated noise levels. Staff perception surveys regarding noise sources showed substantial variability, emphasising the subjective nature of this assessment. Only one study attempted to quantify sound pressure levels at different frequencies from potential noise sources, limiting generalizability. Moreover, many studies failed to adhere to IEC 61672 standards for noise measurement, raising concerns about measurement accuracy. Even among studies that used standard-compliant devices, variations in interval measurements and microphone placements introduced inconsistencies.

The quality assessment identified only four studies that met the criteria for accurate sound measurement and comprehensive noise parameter reporting. These studies showed smaller variability in noise measurements across NICUs, reinforcing the need for stringent methodology. Despite these methodological challenges, the conclusions remained unchanged: NICU noise exposure exceeds recommended levels, with people congregation emerging as a modifiable

factor that should be considered in NICU noise reduction strategies.

This review underscores the persistent methodological inconsistencies in NICU noise studies over the past two decades, limiting the ability to compare findings or establish causal relationships between noise exposure and neonatal outcomes. To improve research in this area, future studies should adopt standardised methodologies, including accumulative noise measurements (Leq, L10, L90) using class 1 sound level meters with A-weighted slow parameters and short interval measurements. Microphones should be placed as close as possible to the infant's ear, ideally within the incubator. In addition, large-scale, state-wide studies encompassing multiple NICUs and special care nurseries would provide more generalizable data and minimise heterogeneity.

In conclusion, NICUs continue to exceed recommended noise exposure levels, with transient high-frequency noises and people congregations identified as consistent contributors. Given the critical impact of excessive noise on neonatal physiological and neurodevelopmental outcomes, policies should incorporate noise reduction strategies, particularly targeting modifiable sources such as staff congregation and conversational noise. Future research should prioritise methodological consistency and larger sample sizes to facilitate robust comparisons and causal analyses, ultimately guiding evidence-based interventions for improving neonatal care environments.

2. Systemic targeted therapies for paediatric atopic dermatitis: Balancing efficacy and safety

Source: Kawamoto N, Murai H, Nogami K, Yamamoto T, Kikkawa T, Yasutomi-Sakai M, *et al*. Efficacy and safety of systemic targeted therapies for atopic dermatitis in children: A systematic review and meta-analysis. *Allergol Int*. 2025 Feb 4:S1323-8930(25)00001-2. doi: 10.1016/j.alit.2024.11.007. Epub ahead of print. PMID: 39909768.

This systematic review and meta-analysis evaluated the efficacy and safety of systemic targeted therapies in children with moderate-to-severe refractory atopic dermatitis (AD). A total of 11 studies examining three targeted agents were included in the study. The meta-analysis demonstrated that systemic targeted therapies significantly improved clinical outcomes across multiple efficacy measures, including the eczema area and severity index, investigator's global assessment, SCORing atopic dermatitis, patient-oriented eczema measure, numeric rating scale for pruritus, children's dermatology life quality index and dermatitis family impact. These findings reinforce the potential of systemic therapies to enhance symptom control in paediatric AD.

Regarding safety, systemic targeted therapies were associated with an increased risk of treatment-emergent adverse events (TEAEs), particularly for small molecules, while biologics did not show a similar trend. However, there were no significant differences in serious adverse events, mortality, or treatment withdrawals due to adverse events. These results suggest that while systemic therapy carries some risks, it remains a viable option for carefully selected paediatric patients when appropriately monitored.

The included studies had largely comparable baseline characteristics, with a few exceptions, such as Paller 2020, which reported slightly higher disease severity at enrolment. Most randomised controlled trials examined systemic agents in combination with topical therapies, further supporting their real-world applicability. The results align with previous meta-analyses, which have consistently reported that systemic therapies, including dupilumab, abrocitinib and upadacitinib, provide significant symptom relief in children with AD, particularly in reducing pruritus. However, prior studies primarily included both paediatric and adult populations, limiting the specificity of conclusions drawn for children. This study uniquely addresses that gap by focusing exclusively on paediatric patients.

Despite its strengths, the meta-analysis has notable limitations. Two potentially relevant studies were excluded due to the inability to extract paediatric-specific data. In addition, variability in study endpoints, with treatment durations ranging from 12 weeks (abrocitinib) to 16 weeks (dupilumab and upadacitinib), complicates direct comparisons. Long-term safety data were also lacking, as only open-label studies were available beyond the initial treatment period. Furthermore, newer systemic targeted therapies introduced after the study's search period were not included, indicating a need for ongoing research.

In conclusion, systemic targeted therapies represent an effective treatment option for paediatric AD, offering substantial symptom relief with an overall acceptable safety profile. While biologics appear well-tolerated, small molecules are associated with a higher risk of TEAEs. Given the limited number of paediatric-focused studies and the lack of long-term data, further large-scale trials are essential to establish the durability of treatment benefits and long-term safety. Systemic therapies should be considered as part of a comprehensive treatment strategy for children with refractory AD, ensuring individualised patient selection and close monitoring for adverse effects.

3. Combination therapy with mometasone and montelukast for paediatric adenoid hypertrophy: A step toward non-surgical management?

Source: Joseph M, Krishna MM, Franco AJ, Jekov L, Sudo RYU, Cabral TDD. Efficacy of combination therapy

with mometasone and montelukast versus mometasone alone in the treatment of adenoid hypertrophy in children: A systematic review and meta-analysis. *Am J Otolaryngol*. 2025 Jan-Feb;46(1):104566. doi: 10.1016/j.amjoto.2024.104566. Epub 2024 Dec 19. PMID: 39709899.

This systematic review and meta-analysis evaluated the efficacy of combination therapy with intranasal mometasone furoate and oral montelukast compared to mometasone alone in children with adenoid hypertrophy. Based on three randomised controlled trials (RCTs) involving 207 children aged 12 years or younger, the pooled analysis demonstrated significant reductions in rhinorrhoea, snoring and mouth breathing in the combination therapy group. In addition, there was a reduction in the adenoid/nasopharynx ratio, though statistical significance was observed only after a sensitivity analysis excluding a study with higher baseline adenoid/nasopharynx ratios. These findings highlight the potential of combination therapy as an effective non-surgical approach for managing moderate-to-severe adenoid hypertrophy.

Adenoid hypertrophy can cause nasal obstruction, recurrent otitis media and chronic rhinosinusitis, often necessitating surgical intervention. While adenoidectomy remains a standard treatment, concerns over intraoperative and post-operative complications have prompted interest in conservative management strategies. Both mometasone and montelukast have been investigated as potential therapies due to their anti-inflammatory properties and ability to reduce adenoid tissue size. Mometasone, a corticosteroid with minimal systemic absorption, directly decreases lymphoid tissue size and inflammation, while montelukast, a leukotriene receptor antagonist, has been shown to modulate immune responses within adenotonsillar tissue, reducing inflammatory cell infiltration and mucus hypersecretion.

Previous studies have reported that intranasal mometasone alone can improve snoring, but its effects on other symptoms such as rhinorrhoea and mouth breathing, have been inconsistent. The current meta-analysis demonstrated that the addition of montelukast significantly enhanced symptom relief and contributed to reducing adenoid size. These findings are consistent with prior research suggesting that leukotriene receptor antagonists may enhance the therapeutic effects of corticosteroids, particularly in upper airway inflammatory conditions. However, some heterogeneity in study methodologies and baseline characteristics suggests that further investigation is needed to confirm these effects across diverse populations.

An important strength of this meta-analysis is its focus on children with Grade 3 or 4 adenoid hypertrophy, providing valuable evidence for non-surgical management in cases where surgery might otherwise be indicated. In addition, the improvements observed during both the treatment period and the 3-month follow-up suggest that combination therapy may have lasting benefits beyond the active treatment phase. However, the study has notable limitations, including a small number of RCTs and variability in sample sizes, patient selection criteria and study methodologies. One of the included studies had a high risk of bias, and only two studies reported outcomes related to rhinorrhoea, snoring and mouth breathing, limiting the robustness of the findings. While a random-effects model was used to address heterogeneity, caution is needed when interpreting the results.

In conclusion, combination therapy with intranasal mometasone and oral montelukast offers a promising alternative for managing adenoid hypertrophy in children, demonstrating superior symptom control and potential for adenoid size reduction compared to mometasone alone. These findings suggest that targeted pharmacologic interventions could help delay or even prevent the need for surgical intervention in select cases. However, further high-quality RCTs with larger sample sizes and longer follow-up durations are needed to validate these findings and determine the long-term impact of combination therapy on disease progression and quality of life.

4. Chest computed tomography for paediatric foreign body aspiration: High accuracy but at what cost?

Source: Goodarzy B, Rahmani E, Farrokhi M, Tavakoli R, Moghadam Fard A, Ranjbaran Ghaleh M, *et al*. Diagnostic value of chest computed tomography scan for identification of foreign body aspiration in children: A systematic review and meta-analysis. *Arch Acad Emerg Med*. 2024 Sep 5;13(1):e3. doi: 10.22037/aaem.v12i1.2431. PMID: 39318866; PMCID: PMC11417639.

This systematic review and meta-analysis evaluated the diagnostic performance of chest computed tomography (CT) for detecting foreign body aspiration (FBA) in children. The pooled analysis of included studies demonstrated excellent diagnostic accuracy, with a sensitivity of 99%, specificity of 97%, positive likelihood ratio (PLR) of 10.11, negative likelihood ratio (NLR) of 0.05 and a diagnostic odds ratio (DOR) of 252.22. The overall accuracy of chest CT for FBA was 98%, reinforcing its utility as a diagnostic tool in paediatric cases.

These findings align with prior systematic reviews, such as that by Tuckett *et al*., which reported sensitivity and specificity ranging from 90–100% to 75–100%, respectively. However, their study did not conduct a meta-analysis, limiting the ability to derive pooled estimates. More recently, a meta-analysis by Azzi *et al*. included 16 studies and reported slightly lower sensitivity (98.8%) and specificity (96.6%) than our results, likely due to differences in the

number of included studies, imaging quality, and study selection criteria.

Despite its diagnostic accuracy, the routine use of CT scans in paediatric FBA cases raises concerns regarding radiation exposure. Evidence suggests that CT radiation exposure increases the risk of malignancies, with an Australian cohort study reporting a 24% higher cancer incidence in individuals exposed to CT scans. The cumulative radiation dose is particularly concerning in children, given their increased susceptibility to radiation-induced malignancies. Moreover, the requirement for sedation in younger children introduces additional risks, including respiratory depression, hypoxia and aspiration, further complicating its use as a first-line diagnostic modality. The cost-effectiveness of routine CT scans for suspected FBA cases remains another critical consideration.

Significant heterogeneity was observed across the included studies in sensitivity, specificity, PLR, NLR and DOR. Several factors likely contributed to this variability, including differences in radiation dosages, CT scanner types, use of sedation, operator expertise and inclusion criteria for paediatric patients. The lack of standardised protocols for performing and interpreting CT scans in paediatric FBA cases further underscores the need for more uniform guidelines to improve reliability and reproducibility across studies.

This meta-analysis had limitations, primarily the heterogeneity in inclusion criteria, study methodologies and sample populations, which may affect the generalizability of findings. In addition, some subgroups had an insufficient number of studies to allow meta-regression analyses, limiting deeper exploration of potential confounding factors.

In conclusion, chest CT demonstrates high diagnostic accuracy for paediatric FBA and may be a valuable tool in settings where bronchoscopy is unavailable. However, its routine use must be carefully weighed against the risks of radiation exposure, sedation-related complications and cost-effectiveness. Future research should focus on optimising imaging protocols, minimising radiation doses and establishing clear clinical guidelines to ensure the judicious use of CT scans in paediatric FBA diagnosis.

5. Safety of inhaled salbutamol in infants with acute wheezing: Reassessing the risks

Source: Pierantoni L, Muratore E, Cerasi S, Zama D, Del Bono C, Gori D, *et al*. Salbutamol safety in children under 2 years of age with acute wheezing: a meta-analysis of randomised controlled trials. *Arch Dis Child*. 2025 Jan 24;110(2):111-119. doi: 10.1136/archdischild-2023-326556. PMID: 39266286.

This systematic review and meta-analysis evaluated the safety of short-term inhaled salbutamol use in children under 2 years of age presenting with acute wheezing. A comprehensive search of electronic databases identified 3532 references, from which 24 studies met the inclusion criteria. The meta-analysis, conducted following Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, primarily assessed the incidence of adverse drug reactions associated with salbutamol compared to placebo.

The findings indicated no statistically significant difference in adverse reaction incidence between the salbutamol and control groups across seven studies involving 597 patients (odd ratios [OR] = 2.12, 95% confidence intervals [CI] = 0.69–6.51; P = 0.19). However, when administered through nebulisation, salbutamol was associated with an increased risk of adverse effects (OR = 6.76, 95% CI = 2.01–22.71; P = 0.002). Notably, none of the included studies reported severe cardiac side effects requiring treatment discontinuation. The only significant non-cardiac adverse effect necessitating withdrawal was severe tremulousness in a single study.

These results suggest that inhaled salbutamol can be safely used in infants with acute wheezing, with a metered-dose inhaler (MDI) potentially offering a safer administration route than nebulisation. While nebulised salbutamol was associated with a higher incidence of side effects, none were life-threatening. The absence of severe cardiovascular complications reinforces the safety of short-term salbutamol use in this population.

Despite these promising findings, some limitations must be acknowledged. The included studies varied in sample sizes and methodologies, which may introduce heterogeneity. Furthermore, long-term safety data were lacking, and most studies did not assess the cumulative impact of repeated salbutamol exposure. Future research should focus on identifying patient subgroups most at risk for adverse effects and further exploring the safety profile of different administration methods.

In conclusion, inhaled salbutamol remains a viable and safe option for managing acute wheezing in infants under 2 years of age. However, clinicians should consider administering the drug through MDI rather than nebulisation to minimise adverse effects. Further high-quality research is warranted to refine dosing strategies and confirm these findings in larger, more diverse populations.

6. Neonatal palliative care: A fragmented landscape in urgent need of standardisation

Source: Gallagher K, Chant K, Parisi V, Patel M, Dunbar H, Paize F, *et al*. Outcomes used to measure the clinical application of neonatal palliative and/or end-of-life care in neonatal settings: A systematic review. *Arch Dis Child Fetal Neonatal Ed*. 2025 Jan 31: Fetalneonatal-2024-328252.

doi: 10.1136/archdischild-2024-328252. Epub ahead of print. PMID: 39890444.

This narrative review sought to identify reported outcomes following neonatal palliative care, yet despite a substantial body of literature, only 20 retrospective chart review studies met the inclusion criteria. The reliance on proxy outcomes and inconsistent documentation across studies underscores the critical gaps in assessing the efficacy of neonatal palliative interventions. A significant concern identified was the lack of standardised reporting, with several studies noting minimal documentation of the care provided during an infant's final hours, making it difficult to determine the level of support available to families. These findings highlight an urgent need for prospective, standardised data collection to evaluate palliative care strategies and establish best practices.

One of the key challenges in neonatal palliative care research is the absence of clear and consistent terminology. Terms such as 'withdrawal of treatment', 'comfort care', 'redirection of care' and 'parallel planning' are used variably across studies, leading to ambiguity in clinical documentation and research. Effective interprofessional communication depends on precise and inclusive language to ensure consistency in patient care. Furthermore, symptom identification and management remain inadequately characterised in neonatal palliative care, despite their established importance in paediatric oncology. While pain, dyspnoea, nausea and restlessness are well-documented in end-of-life care for older children, neonatal symptoms and their management remain poorly described. Variations in opioid prescribing practices and the absence of standardised pain or comfort scales further complicate efforts to assess and improve care quality.

Parental presence at the time of an infant's passing is an essential component of neonatal palliative care, yet documentation on this practice is inconsistent. Cultural factors, timing of deterioration and parental preferences may influence whether parents are present, and in cases where they are not, staff members may step in to hold the infant. However, the absence of clear documentation on parental involvement raises concerns about whether families' preferences and emotional needs are being adequately addressed. Similarly, support services for both parents and healthcare providers are frequently underreported in care records. While parental support from families, communities and spiritual advisors may play a crucial role, it is rarely documented. Neonatal staff, who operate in a high-stress, emotionally demanding environment, are also at an increased risk of burnout, yet little is recorded regarding the psychological support available to them.

A notable discrepancy was found in the recording of medical interventions compared to social and emotional support. While clinical procedures are documented with relative consistency, the social, cultural and spiritual needs of families remain poorly understood, particularly among different ethnic and socio-economic groups. Given that neonatal mortality disproportionately affects certain populations, there is a pressing need for research that considers the broader social determinants of neonatal death and how support structures can be optimised for diverse communities.

The review highlights that neonatal deaths account for the majority of child mortality within the first 5 years of life, making it imperative that neonatal palliative care services are robust, evidence-based and effective. However, the lack of standardised outcome measures remains a major barrier to evaluating and improving care. Establishing a core outcome set for neonatal palliative and end-of-life care would enable better data collection, facilitate comparisons across studies and ultimately improve care delivery. Future research must move beyond retrospective chart reviews and incorporate prospective studies with well-defined outcomes, ensuring that symptom management, family support and ethical considerations are rigorously evaluated. This review underscores the urgent need to develop a more comprehensive, standardised and patient-centred approach to neonatal palliative care, bridging the current gaps in research and practice.

7. Intergenerational risk of preterm birth: Strengthening screening and targeted interventions

Source: Seid A, Cumpston MS, Ahmed KY, Bizuayehu HM, Thapa S, Tegegne TK, *et al*. The intergenerational association of preterm birth: A systematic review and meta-analysis. *BJOG*. 2025 Jan;132(1):18-26. doi: 10.1111/1471-0528.17924. Epub 2024 Aug 7. PMID: 39113242; PMCID: PMC11612607.

This systematic review and meta-analysis provide compelling evidence that women with a family history of preterm birth – particularly those with a maternal lineage of preterm birth – face a significantly increased risk of delivering preterm. The findings highlight a strong intergenerational association along the maternal line, with women who were themselves born preterm, had siblings born preterm or had mothers or aunts with a history of preterm birth, all showing increased odds of delivering preterm. In contrast, the paternal contribution to preterm birth risk appears less consistent, with only a small increase in risk observed among women whose partners were born preterm, while no significant association was found for paternal sibling history.

A major strength of this review lies in its inclusion of large population-based studies with robust sample sizes, enhancing the reliability of the findings. The comprehensive search strategy, spanning multiple databases without geographical or temporal restrictions, further strengthens the validity of the results. However, limitations must be acknowledged. A key challenge was the inability to

distinguish between spontaneous and iatrogenic preterm births due to inconsistent reporting in primary studies. While both types share common risk factors, iatrogenic preterm births are often medically indicated due to maternal or foetal complications, which may obscure the true genetic and epigenetic influences on preterm birth. In addition, given that most included studies originated from high-income countries, the findings may not be directly generalizable to low-income settings, where different environmental and healthcare factors may play a role. The small number of included studies and the heterogeneity in some analyses also necessitate cautious interpretation.

The findings align with emerging research suggesting a genetic and epigenetic basis for preterm birth risk transmission. Prior studies estimate that maternal genetic factors contribute between 15% and 40% to preterm birth risk, whereas paternal genetic influence appears to be minimal, at around 6%. This difference may be partly attributed to intrauterine environmental factors, maternal health behaviours and biological mechanisms unique to pregnancy. The review also found that women born at earlier gestational ages were at a particularly high risk of delivering preterm, reinforcing the idea of a direct relationship between a mother's gestational age at birth and that of her offspring.

Notably, the study underscores the importance of incorporating family history screening into antenatal care. A history of preterm birth in a woman's immediate maternal lineage should serve as a strong risk indicator, warranting closer monitoring and specialised prenatal care. In resource-limited settings where prioritisation is necessary, screening efforts should focus on identifying women born preterm themselves, as they appear to have the highest risk. In addition, while existing research has identified prior preterm birth as a major risk factor for recurrence, this review's subgroup analysis of 1st-time mothers born preterm showed a similarly increased risk, suggesting that screening should extend to all pregnant women, not just those with prior births.

Future research should aim to differentiate between spontaneous and iatrogenic preterm births to refine our understanding of hereditary and non-hereditary influences. Expanding studies to diverse populations, particularly in low-income countries, is essential to determine how environmental and healthcare factors interact with genetic predisposition. Furthermore, targeted interventions should be developed for high-risk groups, focusing on early detection, enhanced prenatal care and potential therapeutic strategies to mitigate the risk of preterm delivery.

In conclusion, this study reinforces the critical role of family history – especially maternal history – in assessing preterm birth risk. Integrating family history screening into routine prenatal care and prioritising close monitoring for high-risk pregnancies could significantly improve perinatal outcomes. As research advances, distinguishing between different types of preterm births and understanding their underlying mechanisms will be essential for developing targeted interventions that improve maternal and neonatal health outcomes globally.

8. Transcranial Doppler screening in sickle cell disease: Reducing stroke risk but raising questions

Source: Guy D, Bagnall R, Morgan RL, Babatunde I, Nevière A, Friedrich G, *et al*. Impact of transcranial Doppler screening on stroke prevention in children and adolescents with sickle cell disease: A systematic review and meta-analysis. *Blood Rev*. 2025 Jan;69:101253. doi: 10.1016/j.blre.2024.101253. Epub 2024 Dec 12. Erratum in: Blood Rev. 2025 Jan 17:101258. doi: 10.1016/j.blre.2025.101258. PMID: 39710547.

This systematic review and meta-analysis provide crucial evidence supporting the role of transcranial Doppler (TCD) screening in the management of stroke risk in children with sickle cell disease (SCD). The findings reaffirm the impact of the Stroke Prevention Trial in Sickle Cell Anaemia (STOP) trial, which established annual TCD screening as a critical tool for early stroke risk detection and intervention in children with sickle cell anaemia (SCA). The review highlights that TCD screening, when compared to no screening, is associated with a reduction in stroke incidence. Despite this, important gaps remain, particularly in understanding its impact on stroke-related morbidity, mortality and quality of life.

The evidence synthesised from non-randomised studies aligns with STOP trial findings, consistently demonstrating that TCD effectively identifies children at high risk of stroke, enabling timely preventive interventions such as chronic transfusion therapy or hydroxyurea. Elevated blood flow velocities in the internal carotid artery or middle cerebral artery are strongly associated with increased stroke risk, emphasising the role of TCD in monitoring cerebrovascular changes in SCD patients. However, this review did not identify studies that directly assessed the effects of TCD screening on stroke-related morbidity or long-term quality of life outcomes. Given the profound impact of stroke on neurological function and overall well-being, further research into these aspects is warranted.

Despite its strengths, this review faces several limitations. Significant heterogeneity was observed across studies in terms of TCD implementation, including screening frequency and diagnostic criteria. While the STOP trial protocol recommends annual screening, only three included studies explicitly reported adherence to this schedule, making cross-study comparisons challenging. Another

major limitation is the geographic bias, as most studies were conducted in high-income countries, limiting the applicability of findings to low- and middle-income countries (LMICs), where healthcare resources for TCD screening and chronic transfusion programs may be limited. In addition, most studies focused exclusively on children with SCA, leaving uncertainty about the utility of TCD screening in children with other SCD genotypes, such as homozygous haemoglobin C, who also face a stroke risk. The exclusion of children with a prior history of stroke in most studies may further underestimate the overall prevalence of stroke and the full impact of TCD screening in high-risk populations.

The review underscores the importance of expanding research efforts to fill these knowledge gaps. High-quality observational studies and randomised controlled trials are needed to strengthen the evidence base on TCD screening's effectiveness, particularly in LMICs. Furthermore, studies evaluating alternative stroke prevention strategies, such as hydroxyurea use instead of chronic transfusion for children with abnormal TCD velocities, could provide valuable insights into cost-effective management approaches. Given the significant healthcare burden of SCD-related strokes, integrating TCD screening into routine care should remain a priority, with additional research exploring its broader impacts on health outcomes and quality of life.

In conclusion, this review reinforces the critical role of TCD screening in identifying children with SCD at high risk of stroke and enabling timely intervention. However, the high risk of bias in existing studies and the lack of data on long-term outcomes highlight the urgent need for further research. Expanding TCD screening programs, particularly in resource-limited settings, and exploring alternative management strategies, such as hydroxyurea, could optimise stroke prevention efforts in children with SCD worldwide.

9. Foetal sex and adverse neonatal outcomes in gestational diabetes: A neglected risk factor?

Source: Maghalian M, Alizadeh-Dibazari Z, Mirghafourvand M. Impact of foetal sex on neonatal outcomes in women with gestational diabetes mellitus: A systematic review and meta-analysis. *BMC Pregnancy Childbirth*. 2025 Feb 3;25(1):110. doi: 10.1186/s12884-025-07250-7. PMID: 39901155; PMCID: PMC11792264.

The influence of foetal sex on neonatal outcomes in gestational diabetes mellitus (GDM) is an underappreciated yet significant factor. This systematic review and meta-analysis revealed that male foetuses are at a higher risk of adverse outcomes, including macrosomia, large-for-gestational-age (LGA) and small-for-gestational-age births, caesarean delivery and lower 5-min Apgar scores. Interestingly, no significant differences were found in preterm birth, jaundice or 1-min Apgar scores, though the trend suggested a slight disadvantage for male infants. These findings suggest that foetal sex may act as a biological determinant in GDM pregnancies, influencing both maternal and neonatal risks.

The mechanisms underlying these differences remain speculative, but emerging evidence points to metabolic and placental factors. Pregnancies with male foetuses appear to impose a greater metabolic burden on the mother, leading to increased insulin resistance, impaired β-cell function and elevated glucose levels. This could explain the higher incidence of GDM among women carrying male foetuses, as well as the increased risk of developing type 2 diabetes postpartum. The placenta itself may also play a role, with sex-specific gene expression influencing foetal growth patterns. Glucose Transporter 1, a key glucose transporter, is upregulated in male placentas, which could contribute to excessive foetal growth and, consequently, higher rates of macrosomia and LGA births.

While the biological basis of these disparities is compelling, regional and methodological inconsistencies complicate interpretation. The analysis revealed striking geographic variations, with studies from China reporting markedly higher risks of LGA and macrosomia compared to those from Europe. Whether these differences stem from genetic predispositions, environmental factors, or disparities in healthcare practices remains unclear. In addition, the limited representation of studies from the Middle East, despite its high GDM prevalence, raises concerns about the broader applicability of these findings. The lack of standardised definitions for key neonatal complications, such as respiratory distress syndrome and neonatal hypoglycaemia, further limits comparability across studies.

From a clinical standpoint, these findings highlight the need to consider foetal sex when assessing risks in GDM pregnancies. Male foetuses appear to be more vulnerable to growth abnormalities and delivery complications, suggesting that tighter glucose control and closer foetal surveillance may be warranted in these cases. Beyond the immediate perinatal period, the potential link between male foetal sex and an increased maternal risk of postpartum type 2 diabetes calls for tailored follow-up strategies, emphasising early screening and intervention.

The need for further research is evident. More studies are required in underrepresented regions, particularly in the Middle East and South Asia, to ensure that findings are globally relevant. Standardising diagnostic criteria and neonatal outcome definitions would improve comparability and strengthen the evidence base. In addition, long-term studies examining the metabolic health of children born to mothers with GDM, particularly in relation to foetal sex, could provide valuable insights into the developmental origins of metabolic disease.

Foetal sex, often overlooked in clinical decision-making, emerges as a significant factor in shaping neonatal outcomes in GDM pregnancies. While the current evidence suggests that male foetuses are at greater risk of adverse outcomes, further investigation is needed to refine risk assessment strategies and optimise maternal and neonatal care. By recognising the role of foetal sex in pregnancy complications, clinicians can adopt a more personalised approach, improving outcomes for both mothers and infants.

10. Allergens responsible for contact allergy in children from 2010 to 2024

Source: Isufi D, Jensen MB, Kursawe Larsen C, Alinaghi F, Schwensen JFB, Johansen JD. Allergens responsible for contact allergy in children from 2010 to 2024: A systematic review and meta-analysis. *Contact Dermatitis*. 2025 Jan 19. doi: 10.1111/cod.14753. Epub ahead of print. PMID: 39827476.

Nickel remains the most prevalent allergen in children, followed closely by cobalt. Despite regulatory efforts, its presence in everyday consumer products like jewellery and clothing fasteners continues to drive sensitisation. The European Union (EU) Nickel Directive has led to a decline in cases in Europe, yet our findings suggest persistent sensitisation rates, indicating a need for re-evaluating regulatory measures. Cobalt also showed significant prevalence, though its variability across studies highlights the influence of regional exposure patterns and the absence of universal regulatory limits.

Fragrances continue to be major contributors to contact allergy, particularly Fragrance Mix (FM) I and FM II, with prevalence rates notably higher in the U.S. compared to Europe. This disparity likely reflects regulatory differences, as the EU has implemented stricter fragrance restrictions, while the United States of America has yet to follow suit. Similarly, preservatives such as methylisothiazolinone (MI) and methylchloroisothiazolinone/MI exhibited higher prevalence rates in the U.S., a trend that aligns with laxer regulations compared to Europe, where their use has been restricted. These patterns underscore the powerful role of policy in shaping allergen exposure and the pressing need for harmonised global regulations.

Geographical disparities were evident across multiple allergens, reinforcing the necessity for region-specific studies. The absence of robust epidemiological data from Asia and the Middle East is particularly concerning, as these regions cannot rely on Western prevalence estimates to guide clinical practice. The lack of regulatory oversight in these areas further complicates the landscape, making it difficult to assess and address potential allergen exposure risks.

Children with atopic dermatitis (AD) displayed higher sensitisation rates to specific allergens, including nickel and fragrances, suggesting that a compromised skin barrier may facilitate allergen penetration. The increased prevalence of contact allergy to cocamidopropyl betaine and propylene glycol in children with AD raises questions about the potential misclassification of irritant versus allergic reactions. The overlapping clinical presentations of AD and allergic contact dermatitis make precise diagnosis challenging, emphasising the need for refined patch testing protocols tailored to paediatric patients with AD.

This study benefits from a comprehensive literature search and a large pooled sample size, allowing for robust prevalence estimates. However, the high variability between studies, regional disparities in data availability and the lack of standardised patch test series for children complicate direct comparisons. These limitations highlight the urgent need for paediatric-specific baseline patch test recommendations and more consistent methodologies in allergy research.

Clinicians should consider contact allergy more frequently in paediatric patients, especially those with AD, and incorporate patch testing as a standard diagnostic tool. Policymakers must recognise the impact of regulatory interventions on allergen exposure and ensure that measures are continually updated to reflect emerging sensitisation trends. The fluctuating prevalence of allergens underscores the need for ongoing surveillance and adaptive regulations to minimise contact allergy risks in children.

The findings of this study reinforce the necessity for standardised patch testing, improved global regulations, and further region-specific research. While Europe has seen some success in reducing sensitisation through regulatory measures, the lack of similar interventions in other regions suggests a broader need for global harmonisation. This review highlights the persistent burden of paediatric contact allergy and underscores the importance of continuous monitoring and policy adjustments to protect children from preventable sensitisation. Future research should focus on underrepresented regions, standardising testing protocols and assessing the long-term effectiveness of regulatory actions in reducing contact allergy rates in children.

11. Delivery mode and neonatal thyrotropin levels

Source: Dashtkoohi M, Parsaei M, Najafi MS, Amirkhalili E, Chashmyazdan M, Nazeri P. Delivery mode and neonatal thyrotropin levels: Insights from a systematic review and meta-analysis. *Endocr Pract*. 2025 Feb 13:S1530-891X(25)00045-X. doi: 10.1016/j.eprac.2025.02.006. Epub ahead of print. PMID: 39954784.

The study provides an in-depth analysis of the relationship between delivery mode and neonatal thyrotropin (thyroid-stimulating hormone [TSH]) levels, a crucial factor in early thyroid function assessment. By synthesising data from

multiple studies, it reveals that neonates born through vaginal delivery exhibit significantly higher TSH levels compared to those delivered through caesarean section. This difference is particularly pronounced in umbilical cord blood samples, whereas no significant variation is observed in heel blood samples.

These findings emphasise the importance of considering delivery mode when interpreting TSH levels, particularly in the context of newborn screening programs. Given the widespread reliance on TSH measurements for congenital hypothyroidism screening, the study underscores the need for clinicians to account for the physiological stress of labour, which may transiently elevate TSH levels in vaginally delivered infants.

The study's rigorous methodology, including a systematic review of major databases and adherence to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, strengthens its conclusions. However, heterogeneity among included studies and potential confounding factors, such as gestational age and maternal thyroid function, warrant further investigation. Future research should explore whether adjusting neonatal TSH reference ranges based on delivery mode could improve screening accuracy and reduce unnecessary follow-ups.

By reinforcing the reliability of heel blood TSH measurements and shedding light on the variability in cord blood readings, this study contributes valuable insights to neonatal endocrinology. It calls for a nuanced approach to interpreting neonatal TSH levels, ensuring that newborn screening remains an effective tool for early thyroid dysfunction detection.

12. Defining neonatal status epilepticus

Source: Nunes ML, Yozawitz EG, Wusthoff CJ, Shellhaas RA, Olivas-Peña E, Wilmshurst JM, *et al*. Defining neonatal status epilepticus: A scoping review from the ILAE neonatal task force. *Epilepsia Open*. 2025 Feb;10(1):40-54. doi: 10.1002/epi4.13090. Epub 2024 Nov 14. PMID: 39540265; PMCID: PMC11803272.

This scoping review highlights the significant variation in how neonatal status epilepticus (SE) is defined across the literature. Current definitions lack uniformity, particularly concerning seizure duration and burden, making it difficult to establish evidence-based criteria for identifying and managing SE in neonates. Most studies define SE using Electroencephalography-based assessments, commonly relying on a 30-min threshold for continuous or accumulated seizure activity within a 1-h period. However, there is insufficient evidence to support the 30-min cutoff as a reliable marker for pharmacoresistance or adverse neurological outcomes.

The review also underscores the limitations of using clinical criteria, such as return to a normal neurological state, in critically ill neonates who may be sedated or encephalopathic due to underlying brain injury. While a higher seizure burden has been linked to unfavourable outcomes, there is no consensus on what constitutes a 'high' burden. Moreover, experimental studies suggest that the neonatal brain may be more resistant to seizure-induced structural damage, though prior insults and underlying aetiology likely influence the impact of seizures on neurodevelopment.

A critical finding is an urgent need for a standardised, evidence-based classification system for neonatal SE. Aligning neonatal SE definitions with the international league against epilepsy (ILAE) criteria used in older children and adults could facilitate cross-study comparisons and improve clinical translation. The ILAE Neonatal Task Force aims to address this gap by developing consensus-based recommendations through a structured Delphi process, integrating expertise from multiple disciplines.

This study reinforces the necessity of refining neonatal seizure burden assessment and classification, ensuring more precise diagnosis, treatment and prognosis evaluation in both research and clinical settings.

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