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## In this issue:

- Oral vs intravenous antibiotics in children and adolescents with bone and joint infections
- Impact of wearable activity trackers on physical activity in children and adolescents
- Potential impact of replacing PCV13 with PCV15 or PCV20 in infant schedules
- Ivermectin therapy for young children with scabies
- Durability of immune responses to mRNA-based COVID-19 vaccine in adolescents
- A text message programme for vaping cessation in adolescents
- Impact of pandemic stringency measures on hospitalisations for eating disorders
- Global prevalence of overweight and obesity in young people
- Characteristics of young children presenting with poisoning
- Scurvy presentations in an Australian tertiary children's hospital

#### Abbreviations used in this issue:

COVID-19 = coronavirus disease 2019; PCV = pneumococcal conjugate vaccine; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

# Welcome to the latest issue of Paediatrics Research Review.

This issue covers a variety of topics, including a comparison of oral versus intravenous antibiotics for young people with uncomplicated bone or joint infections, the use of oral ivermectin for young children with scabies, the effectiveness of a text message programme for nicotine vaping cessation in adolescents, the worldwide prevalence of overweight and obesity in young people, and paediatric scurvy presentations at The Royal Children's Hospital in Melbourne.

We hope you find these and the other selected articles interesting and welcome any feedback you may have.

Kind Regards,

**Professor Nicholas Freezer** 

nick.freezer@researchreview.com.au

# Oral versus intravenous empirical antibiotics in children and adolescents with uncomplicated bone and joint infections

Authors: Nielsen AB et al.

Summary: This randomised non-inferiority trial in Denmark investigated the efficacy and safety of initial oral antibiotics compared with initial intravenous antibiotics followed by oral antibiotics in children and adolescents with uncomplicated bone and joint infections. 248 children and adolescents aged 3 months to 17 years with bone and joint infections who presented to one of 18 paediatric hospital departments in Denmark were randomised to initially receive either high-dose oral antibiotics (amoxicillin 100 mg/kg/day + clavulanic acid 12.5 mg/kg/day in three doses for patients aged <5 years or dicloxacillin 200 mg/kg/day in four doses for those aged ≥5 years) or intravenous ceftriaxone (100 mg/kg/day in one dose). After at least 3 days, patients in both groups were then given standard-dose oral antibiotics. At 6 months, none of the patients in either group had atypical mobility or function of the affected bone or joint (primary outcome).

**Comment:** Initial antimicrobial therapy for acute osteomyelitis and septic arthritis usually is initially administered parenterally. The empiric regimen is determined by the most likely pathogens and antimicrobial susceptibilities based on epidemiologic factors, including the child's age, clinical features, whether the infection is life threatening, and organisms prevalent in the community. This paper suggests that oral antibiotic treatment alone may be adequate in milder infections. The choice of agent(s) for oral therapy depends upon whether an organism was isolated from the synovial fluid, blood, or other culture. Additional considerations include the bioavailability and palatability of the oral medication. Consultation with an expert in infectious diseases may be helpful in choosing the optimal oral agent, particularly if the child has an unusual pathogen or allergy to antibiotics.

Reference: Lancet Child Adolesc Health 2024;8(9):625–35 Abstract



**Independent commentary by Professor Nick Freezer,** who is a Paediatric Respiratory Physician and the Medical Director of the Monash Children's Hospital, Melbourne at Monash Health. He is also a Professor of Paediatrics at Monash University, and until recently the Leader of the Children's Health research theme of Monash Partners Academic Health Science Centre and Monash Health Translation Precinct. A practicing respiratory and sleep physician for over 20 years and with over 100 papers and abstracts published in peer review journals, Prof Freezer was among the first researchers to alert the world to the dangers of overdosing asthmatic children with inhaled corticosteroids and the benefits of using steroids to treat croup. Previous roles include the Director of Respiratory Medicine at Royal Children's Hospital, Melbourne (2000-2005) and Monash Medical Centre (1995-2006).

 $\textbf{RESEA} \textbf{RCH} \; \texttt{REVIEW} \tilde{} \text{Australia's Leader in Specialist Publications}$ 



Authors: Au WW et al.

**Summary:** This systematic review and meta-analysis evaluated the effects of wearable trackers on physical activity in children and adolescents. A search of PubMed, Embase, SPORTDiscus, and Web of Science identified 21 randomised controlled trials (involving 3676 participants) that were suitable for inclusion. The two primary outcomes were objectively-measured daily steps (assessed in 10 studies) and moderate-to-vigorous physical activity (11 studies). Meta-analysis of the data showed that the wearable devices significantly increased objectively-measured daily steps compared with controls, but had no significant impact on moderate-to-vigorous physical activity.

**Comment:** Regular exercise in childhood and adolescence is to be encouraged. Increased levels of physical activity and fitness during childhood and adolescence are associated with reduced risk of disease in adulthood (e.g. cardiovascular disease, diabetes, and musculoskeletal conditions). However, these benefits usually are not the motivating factors for children and adolescents who participate in programmes to improve their physical fitness, performance, body composition, and body image, or to alleviate boredom and to socialise. Other benefits include reduced blood pressure and cholesterol, with improved psychosocial wellbeing and cognitive performance.

Reference: Lancet Digit Health 2024;6(9):e625–39 Abstract

# Potential impact of replacing the 13-valent pneumococcal conjugate vaccine with 15-valent or 20-valent pneumococcal conjugate vaccine in the 1 + 1 infant schedule in England

Authors: Choi YH et al.

**Summary:** This study used pneumococcal transmission models to investigate the potential impact of replacing the 13-valent PCV in the infant schedule in England with 15- or 20-valent PCVs. The effects of transitioning from PCV13 to PCV15 or PCV20 in infants under the current 1 + 1 vaccination schedule were simulated, as was the impact of reduced carriage protection against PCV13 serotypes due to attenuation of immunogenicity in higher valency vaccines. The modelling suggested that use of PCV15 might increase the overall burden of invasive pneumococcal disease (IPD), as the decrease in vaccine-type IPD would be outweighed by an increase in IPD due to non-PCV15 serotypes. In contrast, PCV20 was projected to substantially reduce the overall burden IPD due to higher invasiveness of the additional serotypes covered by PCV20.

**Comment:** The surface capsular polysaccharide of *Streptococcus pneumoniae* determines the serotype and provokes a type-specific protective immune response. Of the 102 pneumococcal serotypes that have been identified so far, the serotypes most frequently isolated from patients with invasive disease are included in the vaccines. PCVs are inactivated vaccines that consist of type-specific pneumococcal polysaccharides conjugated to a carrier protein or proteins which elicit a T cell-dependent memory response during the first two years of life. PCV15 contains the 13 serotypes included in PCV13 plus serotypes 22F and 33F. PCV20 contains the 15 serotypes included in PCV15 plus serotypes 8, 10A, 11A, 12F, and 15B. Both are licensed to prevent pneumonia and IPD in children aged 6 weeks to 17 years.

Reference: Lancet Public Health 2024;9(9):e654–63 Abstract

#### Ivermectin therapy for young children with scabies infection

Authors: Gwee A et al.

**Summary:** This multicentre phase 2 trial in Laos investigated the pharmacokinetics and efficacy of oral ivermectin in young children with scabies. 100 children with scabies (aged 2–4 years, weighing 10–14kg) received an initial oral dose of ivermectin 3mg followed by a second dose 14 days later. The primary outcome was mean plasma ivermectin exposure (AUC<sub>0-∞</sub>) after the first dose compared to a historical control of Indigenous Australian children aged 5–11 years who weighed ≥15kg and received a 200  $\mu$ g/kg dose. The mean observed ivermectin AUC<sub>0-∞</sub> was comparable to that seen in the historical control group (815 vs 953  $\mu$ g h/L; p=ns). Ninety children had complete resolution of scabies by day 14. Adverse effects were mild and were reported by seven children.

**Comment:** Scabies is a cutaneous infestation caused by the mite *Sarcoptes scabiei*. Topical permethrin and oral ivermectin are the most common first-line treatments. Given its high efficacy and safety, permethrin is the preferred therapy for children. Topical sulphur, which is considered safe in infants, is typically used for the treatment of infants under the age of 2 months because of lack of regulatory approval for permethrin in this age group. However, in a recent survey among 57 dermatologists (including 48 paediatric dermatologists) about scabies treatment for infants under the age of 2 months, 47 (83%) reported experience with use of permethrin, and 38 (67%) considered permethrin the preferred therapy for infants in this age group (Pediatr Dermatol. 2021;38(2):431).

Reference: Lancet Reg Health West Pac. 2024;49:101144
Abstract

# Safety and durability of mRNA-1273-induced SARS-CoV-2 immune responses in adolescents

Authors: Figueroa AL et al.

**Summary:** The TeenCOVE study investigated the safety and durability of mRNA-1273—induced SARS-CoV-2 immune responses in adolescents. In part 1 of the study, 3733 vaccine-naïve adolescents aged 12–17 years were randomised 2:1 to received two doses of mRNA-1273 100µg or placebo, 28 days apart. Robust neutralising antibody (nAb) levels were observed through 12 months regardless of whether participants had tested negative or positive for SARS-CoV-2 infection at baseline. Spike binding antibody responses were also observed against alpha, beta, delta, and gamma variants. The two-dose mRNA-1273 100-µg primary series was generally well tolerated; one case of chest pain that was considered to be probable acute myocarditis resolved within 8 days of symptom onset. No serious adverse events were reported, and there were no cases of multisystem inflammatory syndrome. In part 2 of the study, a single 50µg dose of mRNA-1273 in previously unvaccinated adolescents with evidence of prior SARS-CoV-2 infection induced robust nAb responses within 28 days.

**Comment:** Vaccines to prevent SARS-CoV-2 infection are considered the most promising approach for curbing the COVID-19 pandemic. This vaccine is authorised for use for those aged 6 months and above, with an adjustment in the recommended dosage in those aged 6 months to 4 years ( $2\times25\mu g$  IM doses 4–8 weeks apart), and those aged 5–11 years ( $1\times25\mu g$  IM dose). The dose for 12 years and older is a single IM dose of  $50\mu g$ . Children and adolescents aged 6 months to 17 years with comorbidities (e.g. severe obesity, moderate or severe immunosuppression) are considered medium priority groups and persons who have not been vaccinated should receive one dose. A further vaccination is not recommended for those that have been previously vaccinated.

Reference: EClinicalMedicine 2024;74:102720

**Abstract** 

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## A vaping cessation text message program for adolescent E-cigarette users

Authors: Graham AL et al.

Summary: This study evaluated the effectiveness of a text message programme for nicotine vaping cessation among adolescents. 1503 adolescents (mean age 16.4 years) were recruited via social media advertisements and were randomised 1:1 to the intervention group or an assessment-only group (controls). Participants were eligible if they reported past 30-day e-cigarette use, were interested in quitting within 30 days, and owned a mobile phone with an active text message plan. All of them received monthly text messages assessing their e-cigarette use. The assessment-only group received only study retention text messages, whereas the intervention group also received an interactive text message programme for vaping cessation that delivered cognitive and behavioural coping skills training and social support. The primary outcome was self-reported 30-day point-prevalence abstinence from vaping at 7 months. Point-prevalence abstinence rates were 37.8% in the intervention group and 28.0% in controls (relative risk 1.35, 95% CI 1.17-1.57; p<0.001).

**Comment:** It is very difficult to remain a "social smoker" because occasional use easily progresses to nicotine dependence. A minority of adolescents who smoke can quit without intervention. Because most adolescents cite adverse health effects as their primary motivation for quitting, paediatricians and other paediatric health care providers can play an important role in helping teens with smoking cessation. Behavioural support including text messaging should be offered to all adolescents who smoke. Occasional use smokers may be less receptive to an intervention but also may be more successful if they attempt cessation before they become more nicotine dependent.

Reference: JAMA 2024;332(9):713-21

<u>Abstract</u>

# Pandemic stringency measures and hospital admissions for eating disorders

Authors: Roumeliotis N et al.

**Summary:** This Canadian study investigated the impact of public health stringency measures during the COVID-19 pandemic on hospitalisations for eating disorders. Data were provided by the Canadian Institute for Health Information and the Institut National d'Excellence en Santé et Services Sociaux. Overall, 11,289 individuals were hospitalised for eating disorders across Canada during the study period (77% were females aged 12–17 years). A time-series analysis in females aged 12–17 years showed that a 10% increase in public health stringency during the pandemic was associated with a significant increase in hospitalisation rates in Quebec (adjusted rate ratio [ARR] 1.05, 95% CI 1.01–1.07), Ontario (ARR 1.05, 95% CI 1.03–1.07), the Prairies (ARR 1.08, 95% CI 1.03–1.13), and British Columbia (ARR 1.11, 95% CI 1.05–1.16). The excess hospitalisations were highest at the 1-year mark in all regions.

Comment: The pandemic significantly impacted young people with restrictive eating disorders as seen by increased hospitalisations and requests for outpatient care. A primary driver of the changes in eating disorder symptomatology may be lockdowns and quarantines due to boredom or minimal distraction from pathological thoughts, increased social isolation, increased social media and online use, gym and school closures, and changes in routines due to lockdowns and quarantines. During the pandemic there was an increase in the use of telemedicine as a treatment modality. When compared to no treatment, telemedicine was recognised as the best option during COVID-19 lockdowns; however some individuals expressed the preference for in-person treatment and planned to return to it once it became available (Schlissel et al. J Eat Disord. 2023;11:122).

Reference: JAMA Pediatr. 2024;178(9):879-87

<u>Abstract</u>

# Global prevalence of overweight and obesity in children and adolescents

Authors: Zhang X et al.

**Summary:** This systematic review and meta-analysis estimated the global prevalence of overweight and obesity in children and adolescents in 2000–2023. A search of MEDLINE, Web of Science, Embase, and Cochrane identified 2033 studies from 154 countries (involving 45,890,555 individuals aged <18 years) that were suitable for inclusion. Meta-analysis of the data showed that the pooled global prevalence of obesity in children and adolescents was 8.5%, and ranged from 0.4% in Vanuatu to 28.4% in Puerto Rico. The prevalence of obesity among children and adolescents was higher in high-income countries and those with Human Development Index scores ≥0.8. The prevalence of obesity was 1.5-fold higher in 2012–2023 than in 2000–2011. Children and adolescents with obesity were at increased risk for depression and hypertension. The pooled estimates of overweight and excess weight in children and adolescents were 14.8% and 22.2%, respectively.

**Comment:** Obesity arises from a complicated mix of genetics, biology, and environment, and leads to serious health problems. Children aged ≥2 years with a BMI ≥85<sup>th</sup> percentile warrant additional steps to monitor growth and potential obesity-related comorbidities and encourage healthy lifestyle behaviours. Prevention and treatment of obesity in children focuses on modifying behaviours that lead to excessive energy intake and insufficient energy expenditure. Guidance on cardiovascular health (rather than obesity *per se*) may assist with behaviour change. Counselling should be supportive rather than blaming, collaborative rather than prescriptive, and focus on long-term change rather than short-term, restrictive diets and exercise prescriptions, and involve the entire family rather than just the child alone.

Reference: JAMA Pediatr. 2024;178(8):800-13

Abstract



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#### Characteristics of children aged 5 and under presenting with ingestion: An analysis of cases from a tertiary child protection unit

Authors: Graus S & Tzioumi D

**Summary:** This retrospective Australian study investigated the proportion of children presenting to a tertiary children's hospital with ingestion (poisoning) who were subsequently referred for child protection assessment. A total of 203 children who presented to Sydney Children's Hospital with ingestion in 2016-2020 were included. The most common substances ingested were over-the-counter (45%) and prescription (41%) medications, and most (70%) of the children were discharged from the emergency department. Overall, 24 children (11.8%) were referred to the child protection unit. These children had a history of parental depression (64%) or other mental health conditions (41%), parent separation (77%) and family violence (64%).

**Comment:** Toxic exposures occur frequently in children throughout the world. Common patterns of paediatric poisoning consist of exploratory ingestions in children younger than 6 years of age and intentional ingestions and recreational drug use in older children and adolescents. The index of suspicion should be raised if the child is in the "at-risk" age group (1–4 years of age). Forced ingestion or intentional poisoning of children is a form of child abuse that overlaps with Munchausen syndrome by proxy (also known as medical child abuse). A variety of substances, including water, salt, pepper, and various drugs (prescription and illicit), may be used. The clinical presentation of occult ingestion can range from asymptomatic to critically ill.

Reference: J Paediatr Child Health 2024;60(9):397-401 **Abstract** 

#### Scurvy and vitamin C deficiency in an Australian tertiary children's hospital

Authors: van Heerden C et al.

**Summary:** This retrospective study investigated paediatric presentations of vitamin C deficiency (scurvy) at a tertiary paediatric hospital in Australia. 272 children aged ≤18 years who presented to The Royal Children's Hospital in Melbourne with low vitamin C levels (<23 µmol/L) were included. Of these, 13 (5%) had symptoms of vitamin C deficiency and a further 19 (7%) may have been symptomatic. Symptomatic children had significantly lower vitamin C levels than asymptomatic children, and disordered eating related to autism spectrum disorders was more common. Overall, 91% of children with vitamin C deficiency had comorbidities (neurodevelopmental disorders were the most common) and 65% had restricted eating.

**Comment:** Ascorbic acid (vitamin C) deficiency results in the clinical manifestations of scurvy. Infantile scurvy typically presents with irritability, pseudo-paralysis because of painful extremities, failure to thrive, and gingival haemorrhage. Scurvy should be considered in children presenting with musculoskeletal complaints, particularly in children with risk factors for non-traditional diets and formulas. The prominence of hair follicles on the thighs and buttocks and the eruption of coiled, fragmented hair with a characteristic corkscrew appearance are specific features. Petechiae found on the skin have a characteristic pale halo ring around a central erythematous core.

Reference: J Paediatr Child Health 2024;60(9):409-14

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