Abstract from Current Literatures

Childhood Cardiovascular Risk Factors and Adult Cardiovascular Events

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T, Magnussen CG, Viikari JS, Zhang N. Childhood cardiovascular risk factors and adult cardiovascular events. New England Journal of Medicine. 2022 May 19;386(20):1877-88.

Background: Childhood cardiovascular risk factors predict subclinical adult cardiovascular disease, but links to clinical events are unclear.

Methods: In a prospective cohort study involving participants in the International Childhood Cardiovascular Cohort (i3C) Consortium, we evaluated whether childhood risk factors (at the ages of 3 to 19 years) were associated with cardiovascular events in adulthood after a mean follow-up of 35 years. Body-mass index, systolic blood pressure, total cholesterol level, triglyceride level, and youth smoking were analyzed with the use of i3C-derived age- and sex-specific z scores and with a combined-risk z score that was calculated as the unweighted mean of the five risk z scores. An algebraically comparable adult combined-risk z score (before any cardiovascular event) was analyzed jointly with the childhood risk factors. Study outcomes were fatal cardiovascular events and fatal or nonfatal cardiovascular events, and analyses were performed after multiple imputation with the use of proportional-hazards regression.

Results: In the analysis of 319 fatal cardiovascular events that occurred among 38,589 participants (49.7% male and 15.0% Black; mean [±SD] age at childhood visits, 11.8±3.1 years), the hazard ratios for a fatal cardiovascular event in adulthood ranged from 1.30 (95% confidence interval [CI], 1.14 to 1.47) per unit increase in the z score for total cholesterol level to 1.61 (95% CI, 1.21 to 2.13) for youth smoking (yes vs. no). The hazard ratio for a fatal cardiovascular event with respect to the combined-risk z score was 2.71 (95% CI, 2.23 to 3.29) per unit increase. The hazard ratios and their 95% confidence intervals in the analyses of fatal cardiovascular events were similar to those in the analyses of 779 fatal or nonfatal cardiovascular events that occurred among 20,656 participants who could be evaluated for this outcome. In the analysis of 115 fatal cardiovascular events that occurred in a subgroup of 13,401 participants (31.0±5.6 years of age at the adult measurement) who had data on adult risk factors, the adjusted hazard ratio with respect to the childhood combined-risk z score was 3.54 (95% CI, 2.57 to 4.87) per unit increase, and the mutually adjusted hazard ratio with respect to the change in the combined-risk z score from childhood to adulthood was 2.88 (95% CI, 2.06 to 4.05) per unit increase. The results were similar in the analysis of 524 fatal or nonfatal cardiovascular events.

Conclusions: In this prospective cohort study, childhood risk factors and the change in the combined-risk z score between childhood and adulthood were associated with cardiovascular events in midlife. (Funded by the National Institutes of Health.)

Risk Factors for Severe COVID-19 in Children

Woodruff RC, Campbell AP, Taylor CA, Chai SJ, Kawasaki B, Meek J, Anderson EJ, Weigel A, Monroe ML, Reeg L, Bye E. Risk factors for severe COVID-19 in children. Pediatrics. 2022 Jan 1;149(1): e2021053418.

Objectives: Describe population-based rates and risk factors for pediatric severe coronavirus disease 2019 (COVID-19) (ie, ICU admission, invasive mechanical ventilation, or death).

Methods: During March 2020 to May 2021, the COVID-19–Associated Hospitalization Surveillance Network identified 3106 children hospitalized with laboratory-confirmed severe acute respiratory syndrome coronavirus 2 infection in 14 states. Among 2293 children primarily admitted for COVID-19, multivariable generalized estimating equations generated adjusted risk ratios (aRRs) and 95% confidence intervals (CIs) of the associations between demographic and medical characteristics abstracted from patient electronic medical records and severe COVID-19. We calculated age-adjusted cumulative population-based rates of severe COVID-19 among all children.

Results: Approximately 30% of hospitalized children had severe COVID-19; 0.5% died during

hospitalization. Among hospitalized children aged <2 years, chronic lung disease (aRR: 2.2; 95% CI: 1.1–4.3), neurologic disorders (aRR: 2.0; 95% CI: 1.5 2.6), cardiovascular disease (aRR: 1.7; 95% CI: 1.2 2.3), prematurity (aRR: 1.6; 95% CI: 1.1 2.2), and airway abnormality (aRR: 1.6; 95% CI: 1.1 2.2) were associated with severe COVID-19. Among hospitalized children aged 2 to 17 years, feeding tube dependence (aRR: 2.0; 95% CI: 1.5 2.5), diabetes mellitus (aRR: 1.9; 95% CI: 1.6 2.3) and obesity (aRR: 1.2; 95% CI: 1.0 1.4) were associated with severe COVID-19. Severe COVID-19 occurred among 12.0 per 100000 children overall and was highest among infants, Hispanic children, and non-Hispanic Black children.

Conclusions: Results identify children at potentially higher risk of severe COVID-19 who may benefit from prevention efforts, including vaccination. Rates establish a baseline for monitoring changes in pediatric illness severity after increased availability of COVID-19 vaccines and the emergence of new variants.

Subjects: Critical Care, Epidemiology, Infectious Diseases

IQ in Autism Spectrum Disorder: A Population-Based Birth Cohort Study

Katusic MZ, Myers SM, Weaver AL, Voigt RG. IQ in autism spectrum disorder: a population-based birth cohort study. Pediatrics. 2021 Dec 1;148(6).

Objectives: We aimed to describe the intellectual ability and ratio of boys to girls with average or higher IQ within autism spectrum disorder (ASD) cases identified in a population-based birth cohort. We hypothesized that research-identified individuals with ASD would be more likely to have average or higher IQ, compared to clinically diagnosed ASD. We also hypothesized the male to female ratio would decrease as the definition of ASD broadened.

Methods: ASD incident cases were identified from 31220 subjects in a population-based birth cohort. Research-defined autism spectrum disorder, inclusive criteria (ASD-R_I) was based on *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision*, autistic disorder (AD), Asperger Disorder, and pervasive developmental disorder not otherwise specified criteria. Research-defined autism spectrum disorder, narrow criteria (ASD-R_N) was a narrower definition based on *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* AD criteria. Clinical diagnoses of ASD were abstracted from medical and school records. Intellectual ability was based on the last IQ score or on documented diagnoses of intellectual disability if no scores available. Average or higher IQ was defined as IQ ≥86.

Results: A total of 59.1% of those with ASD-R_I (n = 890), 51.2% of those with ASD-R_N (n = 453), and 42.8% of those with clinically diagnosed autism spectrum disorder (n = 187) had average or higher IQ. Within the ASD-R_I and ASD-R_N groups, boys were more likely than girls to have an average or higher IQ (62.0% vs 51.3% [P = .004] and 54.1% vs. 42.5% [P = .03], respectively).

Conclusion: Our data suggest that nearly half of individuals with ASD have average or higher IQ. Boys with ASD are more likely to have average or higher IQ than girls. Patients with ASD and higher IQ remain at risk for not being identified.

Risk of SARS-CoV-2 reinfection in children: a prospective national surveillance study between January, 2020, and July, 2021, in England

Mensah AA, Campbell H, Stowe J, Seghezzo G, Simmons R, Lacy J, Bukasa A, O'Boyle S, Ramsay ME, Brown K, Ladhani SN. Risk of SARS-CoV-2 reinfections in children: a prospective national surveillance study between January, 2020, and July, 2021, in England. The Lancet Child & Adolescent Health. 2022 Jun 1;6(6):384-92.

Background: Reinfection after primary SARS-CoV-2 infection is uncommon in adults, but little is known about the risks, characteristics, severity, or outcomes of reinfection in children. We aimed to assess the risk of SARS-CoV-2 reinfection in children and compare this with the risk in adults, by analysis of national testing data for England.

Methods: In our prospective, national surveillance study to assess reinfection of SARS-CoV-2 in children in England, we used national SARS-CoV-2 testing data to estimate the risk of reinfection at least 90 days after primary infection from Jan 27, 2020, to July, 31, 2021, which encompassed the alpha (B.1.1.7) and delta (B.1.617.2) variant waves in England. Data from children up to age 16 years who met the criteria for reinfection were included. Disease severity was

assessed by linking reinfection cases to national hospital admission data, intensive care admission, and death registration datasets.

Findings: Reinfection rates closely followed community infection rates, with a small peak during the alpha wave and a larger peak during the delta wave. In children aged 16 years and younger, 688 418 primary infections and 2343 reinfections were identified. The overall reinfection rate was 66·88 per 100 000 population, which was higher in adults (72·53 per 100 000) than children (21·53 per 100 000). The reinfection rate after primary infection was 0·68% overall, 0·73% in adults compared with 0·18% in children age younger than 5 years, 0·24% in those aged 5–11 years, and 0·49% in those aged 12–16 years. Of the 109 children admitted to hospital with reinfection, 78 (72%) had comorbidities. Hospital admission rates were similar for the first (64 [2·7%] of 2343) and second episode (57 [2·4%] of 2343) and intensive care admissions were rare (seven children for the first episode and four for reinfections). There were 44 deaths within 28 days after primary infection (0·01%) and none after reinfection.

Interpretation: The risk of SARS-CoV-2 reinfection is strongly related to exposure due to community infection rates, especially during the delta variant wave. Children had a lower risk of reinfection than did adults, but reinfections were not associated with more severe disease or fatal outcomes.

Funding: UK Health Security Agency.

Global, regional, and national causes of under-5 mortality in 2000–19: an updated systematic analysis with implications for the Sustainable Development Goals

Perin J, Mulick A, Yeung D, Villavicencio F, Lopez G, Strong KL, Prieto-Merino D, Cousens S, Black RE, Liu L. Global, regional, and national causes of under-5 mortality in 2000–19: an updated systematic analysis with implications for the Sustainable Development Goals. The Lancet Child & Adolescent Health. 2022 Feb 1;6(2):106-15.

Background: Causes of mortality are a crucial input for health systems for identifying appropriate interventions for child survival. We present an updated series of cause-specific mortality for neonates and children younger than 5 years from 2000 to 2019.

Methods: We updated cause-specific mortality estimates for neonates and children aged 1–59 months, stratified by level (low, moderate, or high) of mortality. We made a substantial change in the statistical methods used for previous estimates, transitioning to a Bayesian framework that includes a structure to account for unreported causes in verbal autopsy studies. We also used systematic covariate selection in the multinomial framework, gave more weight to nationally representative verbal autopsy studies using a random effects model, and included mortality due to tuberculosis.

Findings: In 2019, there were 5·30 million deaths (95% uncertainty range 4·92–5·68) among children younger than 5 years, primarily due to preterm birth complications (17·7%, 16·1–19·5), lower respiratory infections (13·9%, 12·0–15·1), intrapartum-related events (11·6%, 10·6–12·5), and diarrhoea (9·1%, 7·9–9·9), with 49·2% (47·3–51·9) due to infectious causes. Vaccine-preventable deaths, such as for lower respiratory infections, meningitis, and measles, constituted 21·7% (20·4–25·6) of under-5 deaths, and many other causes, such as diarrhoea, were preventable with low-cost interventions. Under-5 mortality has declined substantially since 2000, primarily because of a decrease in mortality due to lower respiratory infections, diarrhoea, preterm birth complications, intrapartum-related events, malaria, and measles. There is considerable variation in the extent and trends in cause-specific mortality across regions and for different strata of all-cause under-5 mortality.

Interpretation: Progress is needed to improve child health and end preventable deaths among children younger than 5 years. Countries should strategize how to reduce mortality among this age group using interventions that are relevant to their specific causes of death.

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