JOURNAL ABSTRACTS

Plant-Based Beverages in the Diets of Infants and Young Children

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ABSTRACT

Plant-based beverage intake in the US increased 61% from 2012 to 2017 owing to interest in vegetarian and vegan diets and plant-based options, environmental and ethical concerns, perceived health benefits, cow's milk allergy and intolerance, and taste preferences. In 2016, 5% of children aged 2 to 4 years enrolled in the Feeding Infants and Toddlers Study, one of the largest dietary intake studies in the US, consumed plant-based milk on the day of the survey, an increase from past years. However, little is known about patterns of plant-based beverage intake among children aged 12 to 24 months, for which a nutrient-dense diet is particularly important for optimal growth and development. A recent National Academies of Sciences, Engineering, and Medicine committee report summarized the recommendations from authoritative bodies in high-income countries on plant-based beverage intake for young children. Overall, most of the authoritative bodies recommended against the provision of plant-based beverages to young children, with some nuances in the guidance provided. Across the guideline documents reviewed, however, the National Academies committee identified a range of methodological approaches, which has implications for both the consistency and quality of guideline documents. In the future, it is important for organizations to collaborate on the planning and development of guidelines, including the process of conducting systematic evidence reviews, the report concluded.

Effect of Collaborative Care on Persistent Postconcussive Symptoms in Adolescents: A Randomized Clinical Trial

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ABSTRACT

Key Points: Question What is the effectiveness of collaborative care with cognitive behavioral therapy for treating adolescents with persistent postconcussive symptoms? **Findings:** In this randomized clinical trial of 200 adolescents, those who received collaborative care reported fewer postconcussive symptoms at 3 and 12 months and higher health-related quality of life at 12 months compared with a control group receiving usual care. **Meaning:** These findings suggest that collaborative care with cognitive behavioral therapy is a promising treatment to alleviate symptoms and improve functioning for adolescents with persistent postconcussive symptoms. **Abstract:** Importance Despite the high level of impairment for adolescents with persistent postconcussive symptoms, few studies have tested whether such problems can be remediated. **Objective:** To examine whether collaborative care treatment is associated with improvements in postconcussive, quality of life, anxiety, and depressive symptoms over 1 year, compared with usual care. **Design, Setting, and Participants:** The Collaborative Care Model for Treatment of Persistent Symptoms After Concussion Among Youth II Trial was a randomized clinical trial conducted from March 2017 to May 2020 with follow-up assessments at 3, 6, and 12 months. Participants were recruited from pediatric primary care, sports medicine, neurology, and rehabilitation clinics in western Washington. Adolescents aged 11 to 18 years with a diagnosed sports-related or recreational-related concussion within the past 9 months and with at least 3 symptoms persisting at least 1 month after injury were eligible. Data analysis was performed from June to September 2020. **Interventions:** The collaborative care intervention included cognitive behavioral therapy and care management, delivered mostly through telehealth, throughout the 6-month treatment period, with enhanced medication consultation when warranted. The comparator group was usual care provided in specialty clinics. **Main Outcomes and Measures:** Primary outcomes were adolescents' reports of postconcussive, quality of life, anxiety, and depressive symptoms. Secondary outcomes were parent-reported symptoms. **Results:** Of the 390 eligible adolescents, 201 (51.5%) agreed to participate, and 200 were enrolled (mean [SD] age, 14.7 [1.7] years; 124 girls [62.0%]), with 96% to 98% 3- to 12-month retention. Ninety-nine participants were randomized to usual care, and 101 were randomized to collaborative care. Adolescents who received collaborative care reported significant improvements in Health Behavior Inventory scores compared with usual care at 3 months (3.4 point decrease; 95% CI, -6.6 to -0.1 point decrease) and 12 months (4.1 point decrease; 95% CI, -7.7 to -0.4 point decrease). In addition, youth-reported Pediatric Quality of Life Inventory scores at 12 months improved by a mean of 4.7 points (95% CI, 0.05 to 9.3 points) in the intervention group compared with the control group. No differences emerged by group over time for adolescent depressive or anxiety symptoms or for parent-reported outcomes. **Conclusions and Relevance:** Although both groups improved over time, youth receiving the collaborative care intervention had fewer symptoms and better quality of life over 1 year. Intervention delivery through telehealth broadens the reach of this treatment.

Complementary and Alternative Medicine Used by Children in Military Pediatric Clinics

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ABSTRACT

The objective of this study was to evaluate the prevalence, types, perceived effects, and factors that influence the use of complementary and alternative medicine (CAM) by military children. A parent survey was administered in two military general pediatric clinics from June to September 2009. Parents completed surveys about their children including the following items: demographic information, a list of specific CAM therapies, family CAM use, and child health status. Caregivers completed 278 surveys. The overall use of CAM was 23%. The most common type of CAM used was herbal therapy (34%). The CAM therapies most commonly reported to be very helpful were special diets (67%), melatonin (57%), vitamins and minerals used at doses higher than the recommended daily allowance (50%), and massage therapy (50%). The majority of users reported no side-effects (96%). Among CAM users, 53% had discussed their CAM use with a physician and 47% had seen a CAM practitioner. Factors associated with CAM use in multiple regression analysis included chronic conditions ($p = 0.001$), parent/sibling use of CAM ($p < 0.001$), and parent age over 30 years ($p = 0.02$). Primary sources of CAM information were friends and family (68%) and doctors (44%). Common reasons for using CAM were to promote general health (70%), to relieve symptoms (56%), and to improve quality of life (48%). Eighty percent (80%) of all respondents indicated they would use CAM if recommended by a physician. In this military population with access to universal health care, CAM use is higher than the U.S. national average and nearly double that of the 2007 National Health Interview Survey study. Patients with chronic conditions, family members using CAM, and parental age over 30 years are more likely to use CAM. CAM is perceived as helpful with minimal to no side-effects. Pediatricians should inquire about CAM use and be prepared to provide guidance on this topic.

Association Between Epidural Analgesia During Labor and Risk of Autism Spectrum Disorders in Offspring

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ABSTRACT

Key Points: Question: Is there an association between maternal labor epidural analgesia given for vaginal delivery and risk of autism spectrum disorders in children? **Findings:** In this multiethnic population-based clinical birth cohort that included 147,895 children, autism spectrum disorders were diagnosed in 1.9% of the children delivered vaginally with epidural analgesia vs 1.3% of the children delivered vaginally without the exposure, a 37% relative increase in risk that was significant after adjusting for potential confounders. **Meaning:** This study suggests that exposure to epidural analgesia for vaginal delivery may be associated with increased risk of autism in children; further research is warranted to confirm the study findings and understand the potential mechanisms. **Importance:** Although the safety of labor epidural analgesia (LEA) for neonates has been well documented, the long-term health effects of LEA on offspring remain to be investigated. **Objective:** To assess the association between maternal LEA exposure and risk of autism spectrum disorders (ASDs) in offspring. **Design, Setting, and Participants:** Data for this retrospective longitudinal birth cohort study were derived from electronic medical records from a population-based clinical birth cohort. A total of 147 895 singleton children delivered vaginally between January 1, 2008, and December 31, 2015, in a single integrated health care system were included. Children were followed up from the age of 1 year until the first date of the following occurrences: clinical diagnosis of ASD, last date of health plan enrollment, death, or the study end date of December 31, 2018. **Exposures:** Use and duration of LEA. **Main Outcomes and Measures:** The main outcome was clinical diagnosis of ASD. Cox proportional hazards regression analysis was used to estimate the hazard ratio (HR) of ASD associated with LEA exposure. Results Among the cohort of 147 895 singleton children (74 425 boys [50.3%]; mean [SD] gestational age at delivery, 38.9 [1.5] weeks), 109 719 (74.2%) were exposed to maternal LEA. Fever during labor was observed in 13 055 mothers (11.9%) in the LEA group and 510 of 38 176 mothers (1.3%) in the non-LEA group. Autism spectrum disorders were diagnosed in 2039 children (1.9%) in the LEA group and 485 children (1.3%) in the non-LEA group. After adjusting for potential confounders, including birth year, medical center, maternal age at delivery, parity, race/ethnicity, educational level, household income, history of comorbidity, diabetes during pregnancy, smoking during pregnancy, preeclampsia or eclampsia, prepregnancy body mass index, gestational weight gain, gestational age at delivery, and birth weight, the HR associated with LEA vs non-LEA exposure was 1.37 (95% CI, 1.23-1.53). Relative to the unexposed group, the adjusted HR associated with LEA exposure of less than 4 hours was 1.33 (95% CI, 1.17-1.53), with LEA exposure of 4 to 8 hours was 1.35 (95% CI, 1.20-1.53), and with LEA exposure of more than 8 hours was 1.46 (95% CI, 1.27-1.69). Within the LEA group, there was a significant trend of ASD risk associated with increasing duration of LEA exposure after adjusting for covariates (HR for linear trend, 1.05 [95% CI, 1.01-1.09] per 4 hours). Adding fever to the model did not change the HR estimate associated with LEA exposure (adjusted HR for LEA vs non-LEA, 1.37 [95% CI, 1.22-1.53]). **Conclusions and Relevance:** This study suggests that maternal LEA may be associated with increased ASD risk in children. The risk appears to not be directly associated with epidural-related maternal fever.

Pediatric Osteopathic Manipulative Medicine: A Scoping Review

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ABSTRACT

Context: A common reproach precluding the use of osteopathic manipulative medicine (OMM) in pediatrics is a lack of evidence regarding its safety, feasibility, and effectiveness. **Objective:** We conducted a systematic, scoping review of pediatric osteopathic medicine to identify gaps in the literature and make recommendations for future research. **Data sources:** We searched 10 databases using 6 key words and medical subject heading terms for any primary articles reporting OMM use in children published from database inception until initiation of the study. **Study selection:** Articles were selected if they reported primary data on OMM conducted in the United States on patient(s) 0 to 18 years old. **Data extraction:** Baseline study characteristics were collected from each article and the Grading of Recommendations, Assessment, Development, and Evaluations system was used to critically appraise each study. **Results:** Database search yielded 315 unique articles with 30 studies fulfilling inclusion and exclusion criteria. Of these, 13 reported the data required to demonstrate statistically significant results, and no significant adverse events were reported. The majority of studies were graded as providing weak clinical evidence because of significant methodologic flaws and biases. **Limitations:** The review was limited to US-based studies and reports. Minimal discrepancies between reviewers were resolved via an objective third reviewer. **Conclusions:** There is little strong, scientific, evidence-based literature demonstrating the therapeutic benefit of OMM for pediatric care. No strong clinical recommendations can be made, but it can be medically tolerated given its low risk profile. High-quality, scientifically rigorous OMM research is required to evaluate safety, feasibility, and efficacy in pediatrics.

Association Between Disturbed Sleep and Depression in Children and Youths: A Systematic Review and Meta-analysis of Cohort Studies

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ABSTRACT

Key Points: Question Is disturbed sleep associated with depression in children and youths? **Findings:** In this meta-analysis of 16 studies including 27 073 patients, pooled estimates supported the role of disturbed sleep as a risk factor for depression in children and youths. Effect size estimates were small but statistically significant. **Meaning:** This study suggests that disturbed sleep is a component of the multifaceted risk profile of depression and should be included in prevention programs as early as childhood. **Importance:** Disturbed sleep represents a potentially modifiable risk factor for depression in children and youths that can be targeted in prevention programs. **Objective:** To evaluate the association between disturbed sleep and depression in children and youths using meta-analytic methods. **Data Sources:** Embase, MEDLINE, PsycINFO, Scopus, Web of Science, and ProQuest Dissertations & Theses Global were searched for articles published from 1980 to August 2019. **Study Selection:** Prospective cohort studies reporting estimates, adjusted for baseline depression, of the association between disturbed sleep and depression in 5- to 24-year-old participants from community and clinical-based samples with any comorbid diagnosis. Case series and reports, systematic reviews, meta-analyses, and treatment, theoretical, and position studies were excluded. A total of 8700 studies met the selection criteria. This study adhered to the guidelines of the Preferred Reporting Items for Systematic Reviews (PRISMA) and Meta-analyses and the Meta-analysis of Observational Studies in Epidemiology (MOOSE) statements. Data Extraction and Synthesis Study screening and data extraction were conducted by 2 authors at all stages. To pool effect estimates, a fixed-effect model was used if $I2<50\%$; otherwise, a random-effects model was used. The I2 statistic was used to assess heterogeneity. The risk of bias was assessed using the Research Triangle Institute Item Bank tool. Metaregression analyses were used to explore the heterogeneity associated with type of ascertainment, type of and assessment tool for disturbed sleep and depression, follow-up duration, disturbed sleep at follow-up, and age at baseline. **Main Outcome and Measures:** Disturbed sleep included sleep disturbances or insomnia. Depression included depressive disorders or dimensional constructs of depression. Covariates included age, sex, and sociodemographic variables. **Results:** A total of 22 studies (including 28 895 patients) were included in the study, of which 16 (including 27 073 patients) were included in the meta-analysis. The pooled ß coefficient of the association between disturbed sleep and depression was 0.11 (95% CI, 0.06-0.15; $P<.001$; $n=14\,067$; $I2=50.8\%$), and the pooled odds ratio of depression in those with vs without disturbed sleep was 1.50 (95% CI, 1.13-2.00; $P=.005$; $n=13\,006$; $I2=87.7\%$). Metaregression and sensitivity analyses showed no evidence that pooled estimates differed across any covariate. Substantial publication bias was found. **Conclusions and Relevance:** This meta-analysis found a small but statistically significant effect size indicating an association between sleep disruption and depressive symptoms in children and youths. The high prevalence of disturbed sleep implies a large cohort of vulnerable children and youths who could develop depression. Disrupted sleep should be included in multifaceted prevention programs starting in childhood.

Quantitative imaging of tongue kinematics during infant feeding and adult swallowing reveals highly conserved patterns

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ABSTRACT

Tongue motility is an essential physiological component of human feeding from infancy through adulthood. At present, it is a challenge to distinguish among the many pathologies of swallowing due to the absence of quantitative tools. We objectively quantified tongue kinematics from ultrasound imaging during infant and adult feeding. The functional advantage of this method is presented in several subjects with swallowing difficulties. We demonstrated for the first time the differences in tongue kinematics during breast- and bottle-feeding, showing the arrhythmic sucking pattern during bottle-feeding as compared with breastfeeding in the same infant with torticollis. The method clearly displayed the improvement of tongue motility after frenotomy in infants with either tongue-tie or restrictive labial frenulum. The analysis also revealed the absence of posterior tongue peristalsis required for safe swallowing in an infant with dysphagia. We also analyzed for the first time the tongue kinematics in an adult during water bolus swallowing demonstrating tongue peristaltic-like movements in both anterior and posterior segments. First, the anterior segment undulates to close off the oral cavity and the posterior segment held the bolus, and then, the posterior tongue propelled the bolus to the pharynx. The present methodology of quantitative imaging revealed highly conserved patterns of tongue kinematics that can differentiate between swallowing pathologies and evaluate treatment interventions. The method is novel and objective and has the potential to advance knowledge about the normal swallowing and management of feeding disorders.

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Association of the Timing of School Closings and Behavioral Changes With the Evolution of the Coronavirus Disease 2019 Pandemic in the US

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ABSTRACT

Key Points: Question: What are the independent associations of voluntary behavioral change and legal restrictions, such as state-mandated school closings, with the subsequent spread of the coronavirus disease 2019 (COVID-19) pandemic in the US? **Findings:** In this cross-sectional study of US COVID-19 data, voluntary behavioral changes, such as reductions in time spent at work, had an association with COVID-19 incidence and mortality that was 3 times stronger than that of school closures. **Meaning:** These findings suggest that less harmful ways of preventing severe acute respiratory syndrome coronavirus 2 transmission are available than mandatory school closures. **Importance:** The consequences of school closures for children's health are profound, but existing evidence on their effectiveness in limiting severe acute respiratory syndrome coronavirus 2 transmission is unsettled. **Objective:** To determine the independent associations of voluntary behavioral change, school closures, and bans on large gatherings with the incidence and mortality due to coronavirus disease 2019 (COVID-19). **Design, Setting, and Participants:** This population-based, interrupted-time-series analysis of lagged independent variables used publicly available observational data from US states during a 60-day period from March 8 to May 18, 2020. The behavioral measures were collected from anonymized cell phone or internet data for individuals in the US and compared with a baseline of January 3 to February 6, 2020. Estimates were also controlled for several state-level characteristics. **Exposures:** Days since school closure, days since a ban on gatherings of 10 or more people, and days since residents voluntarily conducted a 15% or more decline in time spent at work via Google Mobility data. **Main Outcomes and Measures:** The natural log of 7-day mean COVID-19 incidence and mortality. **Results:** During the study period, the rate of restaurant dining declined from 1 year earlier by a mean (SD) of 98.3% (5.2%) during the study period. Time at work declined by a mean (SD) of 40.0% (7.9%); time at home increased by a mean (SD) of 15.4% (3.7%). In fully adjusted models, a delay of 1 day in implementing mandatory school closures was associated with a 3.5% reduction (incidence rate ratio [IRR], 0.965; 95% CI, 0.946-0.984) in incidence, whereas each day of delay in behavioral change was associated with a 9.3% reduction (IRR, 0.907; 95% CI, 0.890-0.925) in incidence. For mortality, each day of delay in school closures was associated with a subsequent 3.8% reduction (IRR, 0.962; 95% CI, 0.926-0.998), and each day of delay in behavioral change was associated with a 9.8% reduction (IRR, 0.902; 95% CI, 0.869-0.936). Simulations suggest that a 2-week delay in school closures alone would have been associated with an additional 23 000 (95% CI, 2000-62 000) deaths, whereas a 2-week delay in voluntary behavioral change with school closures remaining the same would have been associated with an additional 140 000 (95% CI, 65 000-294 000) deaths. **Conclusions and Relevance:** In light of the harm to children of closing schools, these findings suggest that policy makers should consider better leveraging the public's willingness to protect itself through voluntary behavioral change.

Harnessing the Web: How Chiropractic Education Survives and Thrives During the COVID-19 Pandemic: Chiropractic Educators Research Forum (CERF), December 5, 2020

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ABSTRACT

This conference was convened by the Chiropractic Educators Research Forum (CERF) on December 5, 2020. This meeting provided a forum for the presentation of scholarly works in chiropractic education theory and practice. This conference specifically focused on research related to chiropractic education during the COVID-19 pandemic. During the December 2020 CERF meeting, presenters and panelists took an in depth look at how programs worked to meet program objectives, graduation requirements, accreditation, and other activities during the COVID-19 pandemic.
Keywords: Chiropractic, Education, Congress [Publication Type], COVID-19 [Supplementary Concept]

Family-Centered Prevention Effects on the Association Between Racial Discrimination and Mental Health in Black Adolescents: Secondary Analysis of 2 Randomized Clinical Trials

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ABSTRACT

Key Points: Question Is participation in a family-centered prevention program, designed to enhance caregiving practices, associated with protection of Black adolescents from the effects of racial discrimination on their mental health? **Findings:** This secondary analyses of data from 2 randomized clinical trials found that participation in a family-centered prevention program was associated with protection of Black adolescents from the effects of racial discrimination on conduct problems (in both trials) and on depression/anxiety symptoms (in 1 trial). These associations were partially explained by intervention-induced changes in protective parenting. **Meaning:** These findings suggest that family-centered prevention programs reduce the effects of racial discrimination on subsequent increases in mental health problems among Black adolescents. **Importance:** Some Black adolescents who frequently experience racial discrimination develop mental health problems. Protective caregiving may buffer adolescents from the negative mental health outcomes associated with experiencing racial discrimination. **Objective:** To examine if participation in programs that enhance protective caregiving will attenuate the positive association between Black adolescents' encounters with discrimination and subsequent increases in mental health problems. **Design, Setting, and Participants:** This secondary analysis used data from 2 randomized clinical trials testing family-centered prevention programs: the Strong African American Families—Teen (SAAF—T) program and the Adults in the Making (AIM) program. The programs were implemented in community locations convenient for participants in 12 rural Georgia counties. For the SAAF—T trial, Black adolescents and their primary caregivers were recruited from 2007 to 2008. In the AIM trial Black adolescents and their primary caregivers were recruited from 2006 to 2007. Data for this study were analyzed from June to August 2020. **Exposures:** Adolescents provided data at baseline on the frequency of their encounters with racial discrimination. Treatment group participants in each trial took part in a family-centered prevention program designed to prevent substance use and mental health problems. SAAF—T is a 5-session, 10-hour psychosocial intervention for families with a Black adolescent aged 14 to 16 years. AIM is a 6-session, 12-hour psychosocial intervention for families with a Black youth who is a high school senior. **Main Outcomes and Measures:** The primary outcomes were mental health problems, including conduct problems and depression or anxiety symptoms. **Results:** The SAAF—T study included 502 Black adolescents (mean [SD] age, 16.0 [0.6] years; 281 [56.0%] girls), including 252 randomized to the intervention and 250 randomized to the control, and the AIM trial included 367 Black adolescents (mean [SD] age, 17.7 [0.8] years; 217 [59.1%] girls and women), including 187 randomized to the intervention and 180 randomized to the control. Adolescents assigned to the SAAF—T intervention group who frequently experienced discrimination at baseline evinced fewer subsequent increases in conduct problems (incident risk ratio, 0.530 [95% CI, 0.340 to 0.783]). Adolescents assigned to the AIM intervention group who frequently experienced discrimination at baseline evinced fewer subsequent increases in conduct problems (mean difference, -0.361 [95% CI, -0.577 to -0.144]) and fewer subsequent increases in depression or anxiety symptoms (mean difference, -0.220 [95% CI -0.402 to -0.038]). Moderated mediation analyses suggested that enhanced protective caregiving was partially responsible for all observed interaction effects (indirect effect: SAAF-T conduct problems, -0.063 [95% CI, -0.127 to -0.001]; AIM conduct problems, -0.048 [95% CI, -0.095 to -0.001]; AIM depression or anxious symptoms, -0.036 [95% CI, -0.074 to 0]). **Conclusions and Relevance:** This secondary analysis of 2 randomized clinical trials found that participation in family-centered preventive interventions attenuated the association between frequent exposure to discriminatory behaviors and subsequent mental health problems. Notably, all but 1 of the treatment and moderated-mediation findings were reproduced across the SAAF—T and AIM trials.

Trial Registrations: ClinicalTrials.gov Identifiers: SAAF—T, NCT04501471; AIM, NCT04510116

Shedding light on excessive crying in babies

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ABSTRACT

Background: Excessive and inconsolable crying behavior in otherwise healthy infants (a condition called infant colic (IC)) is very distressing to parents, may lead to maternal depression, and in extreme cases, may result in shaken baby syndrome. Despite the high prevalence of this condition (20% of healthy infants), the underlying neural mechanisms of IC are still unknown. **Methods:** By employing the latest magnetic resonance imaging (MRI) techniques in newborns, we prospectively investigated whether newborns' early brain responses to a sensory stimulus (smell) is associated with a subsequent crying behavior. **Results:** In our sample population of 21 healthy breastfed newborns, those who developed IC at 6 weeks exhibited brain activation and functional connectivity in primary and secondary olfactory brain areas that were distinct from those in babies that did not develop IC. Different activation in brain regions known to be involved in sensory integration was also observed in colicky babies. These responses measured shortly after birth were highly correlated with the mean crying time at 6 weeks of age. **Conclusions:** Our results offer novel insights into IC pathophysiology by demonstrating that, shortly after birth, the central nervous system of babies developing IC has already greater reactivity to sensory stimuli than that of their noncolicky peers. **Impact:** Shortly after birth, the central nervous system of colicky infants has a greater sensitivity to olfactory stimuli than that of their noncolicky peers. This early sensitivity explains as much as 48% of their subsequent crying behavior at 6 weeks of life. Brain activation patterns to olfactory stimuli in colicky infants include not only primary olfactory areas but also brain regions involved in pain processing, emotional valence attribution, and self-regulation.This study links earlier findings in fields as diverse as gastroenterology and behavioral psychology and has the potential of helping healthcare professionals to define strategies to advise families.

Preterm Birth and the Development of Visual Attention During the First 2 Years of Life: A Systematic Review and Meta-analysis

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ABSTRACT

Key Points: Question: Is preterm birth associated with visual attention impairments in early life, and if so, in which attention functions? Findings: This systematic review and meta-analysis of 53 studies including 2047 preterm-born and 1951 full-term—born neonates and infants found that preterm birth was significantly associated with impairments in visual attention functioning. Despite a short-term advantage in visual-following in preterm infants, deficits cascaded from basic orienting responses to focused attention during the first 2 years of life. **Meaning:** The findings suggest that preterm birth is associated with challenges in the development of visual attention beginning in the early stages of life. **Importance:** Preterm birth is associated with an increased risk for long-lasting attention deficits. Early-life markers of attention abnormalities have not been established to date but could provide insights into the pathogenesis of attention abnormalities and could help identify susceptible individuals. **Objective:** To examine whether preterm birth is associated with visual attention impairments in early life, and if so, in which attention functions and at which developmental period during the first 2 years of life. **Data Sources:** PubMed and PsycINFO were searched on November 17, 2019, to identify studies involving visual attention outcomes in infants born preterm vs full term. **Study Selection:** Peer-reviewed studies from the past 50 years met the eligibility criteria if they directly assessed visual attention outcomes until the age of 2 years in generally healthy infants born preterm or full term. The selection process was conducted by 2 independent reviewers. **Data Extraction and Synthesis:** The Meta-analysis of Observational Studies in Epidemiology (MOOSE) reporting guideline was followed. Random-effects models were used to determine standardized mean differences. The risk of bias was assessed both within and between studies. **Main Outcomes and Measures:** Five nascent indices of visual attention were analyzed, including very basic functions–namely, the abilities to follow and fixate on visual targets–and more complex functions, such as visual processing (ie, habituation), recognition memory (ie, novelty preference), and the ability to effortfully focus attention for learning. **Results:** A total of 53 studies were included, with 69 effect sizes and assessing a total of 3998 infants (2047 born preterm and 1951 born full term; of the 3376 for whom sex was reported, 1693 [50.1%] were girls). Preterm birth was associated with impairments in various attention indices, including visual-following in infancy (Cohen d, -0.77; 95% CI, -1.23 to -0.31), latency to fixate (Cohen d, -0.18; 95% CI, -0.33 to -0.02), novelty preference (Cohen d, -0.20; 95% CI, -0.32 to -0.08), and focused attention (Cohen d, -0.28; 95% CI, -0.45 to -0.11). In the neonatal period, preterm birth was associated with superior visual-following (Cohen d, 0.22; 95% CI, 0.03 to 0.40), possibly owing to the additional extrauterine exposure to sensory stimulation. However, this early association waned rapidly in infancy (Cohen d, —0.77; 95% CI, —1.23 to —0.31). **Conclusions and Relevance:** The findings suggest that preterm birth is associated with impingements to visual attention development in early life, as manifested in basic and then complex forms of attention. Advancements in neonatal care may underlie improvements found in the current era and accentuate several early protective factors.

Association of Race/Ethnicity and Social Disadvantage With Autism Prevalence in 7 Million School Children in England

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ABSTRACT

Importance: The global prevalence of autism spectrum disorder (ASD) has been reported to be between 1% and 2% of the population, with little research in Black, Asian, and other racial/ethnic minority groups. Accurate estimates of ASD prevalence are vital to planning diagnostic, educational, health, and social care services and may detect possible access barriers to diagnostic pathways and services and inequalities based on social determinants of health. **Objective:** To evaluate whether socioeconomic disadvantage is associated with ASD prevalence and the likelihood of accessing ASD services in racial/ethnic minority and disadvantaged groups in England. **Design, Setting, and Participants:** This case-control prevalence cohort study used the Spring School Census 2017 from the Pupil Level Annual Schools Census of the National Pupil Database, which is a total population sample that includes all English children, adolescents, and young adults aged 2 to 21 years in state-funded education. Data were collected on January 17, 2017, and analyzed from August 2, 2018, to January 28, 2020. **Exposures:** Age and sex were treated as a priori confounders while assessing correlates of ASD status according to (1) race/ethnicity, (2) social disadvantage, (3) first language spoken, (4) Education, Health and Care Plan or ASD Special Educational Needs and Disability support status, and (5) mediation analysis to assess how social disadvantage and language might affect ASD status. **Main Outcomes and Measures:** Sex- and age-standardized ASD prevalence by race/ethnicity and 326 English local authority districts in pupils aged 5 to 19 years. **Results:** The final population sample consisted of 7 047 238 pupils (50.99% male; mean [SD] age, 10.18 [3.47] years) and included 119 821 pupils with ASD, of whom 21 660 also had learning difficulties (18.08%). The standardized prevalence of ASD was 1.76% (95% CI, 1.75%-1.77%), with male pupils showing a prevalence of 2.81% (95% CI, 2.79%-2.83%) and female pupils a prevalence of 0.65% (95% CI, 0.64%-0.66%), for a male-to-female ratio (MFR) of 4.32:1. Standardized prevalence was highest in Black pupils (2.11% [95% CI, 2.06%-2.16%]; MFR, 4.68:1) and lowest in Roma/Irish Travelers (0.85% [95% CI, 0.67%-1.03%]; MFR, 2.84:1). Pupils with ASD were more likely to face social disadvantage (adjusted prevalence ratio, 1.61; 95% CI, 1.59-1.63) and to speak English as an additional language (adjusted prevalence ratio, 0.64; 95% CI, 0.63-0.65). The effect of race/ethnicity on ASD status was mediated mostly through social disadvantage, with Black pupils having the largest effect (standardized mediation coefficient, 0.018; $P < .001$) and 12.41% of indirect effects through this way. **Conclusions and Relevance:** These findings suggest that significant differences in ASD prevalence exist across racial/ethnic groups and geographic areas and local authority districts, indicating possible differential phenotypic prevalence or differences in detection or referral for racial/ethnic minority groups.

Relationship Between Neonatal Vitamin D at Birth and Risk of Autism Spectrum Disorders: the NBSIB Study

Wu, D.M., Wen, X., Han, X.R., Wang, S., Wang, Y.J., Shen, M., Fan, S.H., Zhuang, J., Li, M.Q., Hu, B., Sun, C.H., Bao, Y.X., Yan, J., Lu, J. and Zheng, Y.L.
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ABSTRACT

Previous studies suggested that lower vitamin D might be a risk factor for autism spectrum disorders (ASDs). The aim of this study was to estimate the prevalence of ASDs in 3-year-old Chinese children and to examine the association between neonatal vitamin D status and risk of ASDs. We conducted a study of live births who had taken part in expanded newborn screening (NBS), with outpatient follow-up when the children 3-year old. The children were confirmed for ASDs in outpatient by the Autism Diagnostic Interview-Revised and Diagnostic and Statistical Manual of Mental Disorders (DSM)-5 criteria. Intellectual disability (ID) status was defined by the intelligence quotient (IQ < 80) for all the participants. The study design included a 1:4 case to control design. The concentration of 25-hydroxyvitamin D3 [25(OH)D3] in children with ASD and controls were assessed from neonatal dried blood samples. A total of 310 children were diagnosed as having ASDs; thus, the prevalence was 1.11% (95% CI, 0.99% to 1.23%). The concentration of 25(OH)D3 in 310 ASD and 1240 controls were assessed. The median 25(OH)D3 level was significantly lower in children with ASD as compared to controls ($p < 0.0001$). Compared with the fourth quartiles, the relative risk (RR) of ASDs was significantly increased for neonates in each of the three lower quartiles of the distribution of 25(OH)D3, and increased risk of ASDs by 260% (RR for lowest quartile: 3.6; 95% CI, 1.8 to 7.2; $p < 0.001$), 150% (RR for second quartile: 2.5; 95% CI, 1.4 to 3.5; $p = 0.024$), and 90% (RR for third quartile: 1.9; 95% CI, 1.1 to 3.3; $p = 0.08$), respectively. Furthermore, the nonlinear nature of the ID-risk relationship was more prominent when the data were assessed in deciles. This model predicted the lowest relative risk of ID in the 72rd percentile (corresponding to 48.1 nmol/L of 25(OH)D3). Neonatal vitamin D status was significantly associated with the risk of ASDs and intellectual disability. The nature of those relationships was nonlinear. © 2017 American Society for Bone and Mineral Research.

Maternal vitamin D status and infant outcomes in rural Vietnam: a prospective cohort study

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ABSTRACT

Objective: Vitamin D deficiency affects 1 billion people globally. It has an important role in bone homeostasis, brain development and modulation of the immune system and yet the impact of antenatal vitamin D deficiency on infant outcomes is poorly understood. We assessed the association of 25- hydroxyvitamin D levels (25-OHD) in late pregnancy and early infant growth and developmental outcomes in rural Vietnam. **Design and methods:** A prospective cohort study of 960 women who had previously participated in a double-blind cluster randomized controlled trial of antenatal micronutrient supplementation in rural Vietnam was undertaken. Maternal 25-OHD concentration was measured at 32 weeks gestation, and infants were followed until 6 months of age. Main outcome measures were cognitive, motor, socio-emotional and language scores using the Bayley Scales of Infant Development, 3rd edition, and infant length-for-age z scores at 6 months of age. **Results:** 60% (582/960) of women had 25-OHD levels <75 nmol/L at 32 weeks gestation. Infants born to women with 25-OHD deficiency (<37.5 nmol/L) had reduced developmental language scores compared to those born to women who were vitamin D replete (≥75 nmol/L) (Mean Difference (MD) -3.48, 95% Confidence Interval (CI) -5.67 to -1.28). For every 25 nmol increase in 25-OHD concentration in late pregnancy, infant length-for-age z scores at 6 months of age decreased by 0.08 (95% CI -0.15 to -0.02). **Conclusions:** Low maternal 25- hydroxyvitamin D levels during late pregnancy are of concern in rural Vietnam, and are associated with reduced language developmental outcomes at 6 months of age. Our findings strengthen the evidence for giving vitamin D supplementation during pregnancy.

https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0099005

Association Between Proton Pump Inhibitor Use and Risk of Asthma in Children

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ABSTRACT

Key Points: Question: Is proton pump inhibitor (PPI) use associated with risk of asthma in children? **Findings:** This propensity score–matched cohort study included 80 870 pairs of children who were and were not new users of PPIs. The incidence rate of asthma was 21.8 per 1000 person-years among those who initiated PPI use and 14.0 per 1000 person-years among those who did not; the hazard ratio increased by 57%. **Meaning:** These findings suggest that asthma is one of several potential adverse events that should be considered when prescribing PPIs to children. **Importance:** The use of proton pump inhibitors (PPIs) in children has increased substantially in recent years, concurrently with emerging concerns that these drugs may increase the risk of asthma. Whether PPI use in the broad pediatric population is associated with increased risk of asthma is not known. **Objective:** To investigate the association between PPI use and risk of asthma in children. **Design, Setting, and Participants:** This nationwide cohort study collected registry data in Sweden from January 1, 2007, to December 31, 2016. Children and adolescents 17 years or younger were matched by age and propensity score into 80 870 pairs of those who initiated PPI use and those who did not. Data were analyzed from February 1 to September 1, 2020. **Exposures:** Initiation of PPI use. **Main Outcomes and Measures:** The primary analysis examined the risk of incident asthma with a median follow-up to 3.0 (interquartile range, 2.1-3.0) years. Cox proportional hazards regression was used to estimate hazard ratios (HRs). **Results:** Among the 80 870 pairs (63.0% girls; mean [SD] age, 12.9 [4.8] years), those who initiated PPI use had a higher incidence rate of asthma (21.8 events per 1000 person-years) compared with noninitiators (14.0 events per 1000 person-years), with an HR of 1.57 (95% CI, 1.49-1.64). The risk of asthma was significantly increased across all age groups and was highest for infants and toddlers with an HR of 1.83 (95% CI, 1.65-2.03) in the group younger than 6 months and 1.91 (95% CI, 1.65-2.22) in the group 6 months to younger than 2 years ($P < .001$ for interaction). The HRs for individual PPIs were 1.64 (95% CI, 1.50-1.79) for esomeprazole, 1.49 (95% CI, 1.25-1.78) for lansoprazole, 1.43 (95% CI, 1.35-1.51) for omeprazole, and 2.33 (95% CI, 1.30-4.18) for pantoprazole. In analyses of the timing of asthma onset after PPI initiation, the HRs were 1.62 (95% CI, 1.42-1.85) for 0 to 90 days, 1.73 (95% CI, 1.52-1.98) for 91 to 180 days, and 1.53 (95% CI, 1.45-1.62) for 181 days to end of follow-up. The association was consistent through all sensitivity analyses, including high-dimensional propensity score matching (HR, 1.48; 95% CI, 1.41-1.55). **Conclusions and Relevance:** In this cohort study, initiation of PPI use compared with nonuse was associated with an increased risk of asthma in children. Proton pump inhibitors should be prescribed to children only when clearly indicated, weighing the potential benefit against potential harm.

Association of Child and Family Attributes With Outcomes in Children With Autism

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ABSTRACT

Key Points: Question: How prevalent is "doing well" in 5 developmental domains (communication, socialization, activities of daily living, internalizing, externalizing) as assessed by proficiency and growth in children with autism spectrum disorder in midchildhood, and what attributes of children and families are associated with it? **Findings:** In this cohort study including 272 children, between 20% and 49% of children with autism spectrum disorder were proficient within the 5 developmental domains, while 13% to 34% of children demonstrated growth. Doing well was associated with preschool scores on that specific outcome domain, as well as early language skills, household income, and family functioning. **Meaning:** These findings demonstrate the potential usefulness of taking a strengths-based approach to outcome assessments, while the importance of family income and functioning remind us that disabilities do not exist apart from a social context. **Importance:** The prevalence and attributes of positive outcomes (or doing well) among children with autism spectrum disorder (ASD) in midchildhood are not well known. **Objective:** To estimate the prevalence of doing well according to metrics of proficiency and growth and to investigate the extent to which significant associations exist between child- and family-level variables and doing well. **Design, Setting, and Participants:** This longitudinal cohort study included children with ASD from regional clinics across Canada. Participants were sampled 3 times between ages 2 and 4.9 years (T1) and twice in follow-up into middle childhood (T2). Data were analyzed March 2018 through January 2020. **Exposures:** Language and IQ assessments at first sample; household income, parent coping, and family functioning. **Main Outcomes and Measures:** Key outcome domains of developmental health included measures of socialization, communication, independent living skills, and measures of internalizing and externalizing behaviors. Thresholds for doing well in these domains by either proficiency or growth were established. The extent to which language, IQ, household income, parent coping, and family functioning were associated with assessed outcomes was determined by logistic regression. The association between outcomes and concurrent Autism Diagnostic Observation Schedule (ADOS) classification scores was also estimated. **Results:** In a total cohort of 272 children (234 [86.0%] boys; mean [SD] age, 10.76 [0.26] years), approximately 78.8% (95% CI, 73.2%-84.4%) of the sample were estimated to be doing well by either metric on at least 1 domain, and 23.6% (95% CI, 17.7%-29.4%) were doing well in 4 or 5 domains. It was possible to be doing well by either proficiency or growth and still meet ADOS criteria for ASD. For the growth metric, between 61.5% (95% CI, 40.7%-79.1%) and 79.6% (95% CI, 66.0%-88.9%) of participants had ADOS scores of 4 or greater; for the proficiency metric, between 63.8% (95% CI, 48.4%-76.9%) and 75.8% (95% CI, 63.0%-85.4%) had scores of 4 or greater. Doing well by either metric for all domains was associated with T1 scores on that outcome domain (eg, T1 daily living skills associated with doing well at T2 daily living by the proficiency metric as measured by the Vineland Adaptive Behavior Scales—Second Edition daily living skills scale [202 participants]: ß = 0.07; OR, 1.07; 95% CI, 1.03-1.11; P < .001). Doing well in socialization by the growth metric was also associated with better T1 language skills scores (202 participants) (ß= 0.04; OR, 1.04; 95% CI, 1.00-1.07, P = .04). Doing well in externalizing by the growth metric was also associated with higher household income at T1 (178 participants) (ß= 0.10; OR, 1.10; 95% CI, 1.06-1.15; P < .001). Better family functioning at T1 was associated with doing well on both socialization and externalizing by proficiency metric and on internalizing by growth metric (socialization by proficiency [202 participants]: ß= -1.01; OR, 0.36; 95% CI, 0.14-0.93; P = .04; externalizing by proficiency [178 participants]: ß = 1.00; OR, 0.37; 95% CI, 0.16-0.82; P = .02; internalizing by growth [178 participants]: ß= -1.03; OR, 0.36; 95% CI, 0.16-0.79; P = .01). **Conclusions and Relevance:** This cohort study found that a substantial proportion of children with ASD were doing well by middle childhood in at least 1 key domain of developmental health, and that doing well was possible even in the context of continuing to meet criteria for ASD. These results support a strengths-based approach to treatment planning that should include robust support for families to increase the potential likelihood of doing well later in life.

Antenatal Vitamin D Status Is Not Associated with Standard Neurodevelopmental Assessments at Age 5 Years in a Well-Characterized Prospective Maternal-Infant Cohort

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ABSTRACT

Objective: We aimed to explore associations between maternal and neonatal vitamin D status with childhood neurodevelopmental outcomes. **Methods:** Comprehensive clinical, demographic, and lifestyle data were collected prospectively in 734 maternal-infant dyads from the Cork BASELINE Birth Cohort Study. Serum 25-hydroxyvitamin D [25(OH)D] concentrations were quantified at 15 weeks of gestation and in umbilical cord sera at birth via a CDC-accredited liquid chromatography-tandem mass spectrometry method. Children were assessed at age 5 y through the use of the Kaufman Brief Intelligence Test (2nd Edition, KBIT-2) and the Child Behaviour Checklist (CBCL). Linear regression was used to explore associations between 25(OH)D and neurodevelopmental outcomes. **Results:** 25(OH)D concentrations were <30 nmol/L in 15% of maternal and 45% of umbilical cord sera and <50 nmol/L in 42% of mothers and 80% of cords. At age 5 y, the mean ± SD KBIT-2 intelligence quotient (IQ) composite score was 104.6 ± 8.6; scores were 107.2 ± 10.0 in verbal and 99.8 ± 8.8 in nonverbal tasks. Developmental delay (scores <85) was seen in <3% of children across all domains. The mean ± SD CBCL total problem score was 21.3 ± 17.5; scores in the abnormal/clinical range for internal, external, and total problem scales were present in 12%, 4%, and 6% of participants, respectively. KBIT-2 and CBCL subscale scores at 5 y were not different between children exposed to low antenatal vitamin D status, either at 30 or 50 nmol/L 25(OH)D thresholds. Neither maternal nor cord 25(OH)D (per 10 nmol/L) were associated with KBIT-2 IQ composite scores [adjusted ß (95% CI): maternal -0.01 (-0.03, 0.02); cord 0.01 (-0.03, 0.04] or CBCL total problem scores [maternal 0.01 (-0.04, 0.05); cord 0.01 (-0.07, 0.09)]. **Conclusion:** In this well-characterized prospective maternal-infant cohort, we found no evidence that antenatal 25(OH)D concentrations are associated with neurodevelopmental outcomes at 5 y.

The BASELINE Study was registered at www.clinicaltrials.gov as NCT01498965; the SCOPE Study was registered at http://www.anzctr.org.au as ACTRN12607000551493.

Maternal Plasma 25-Hydroxyvitamin D during Gestation Is Positively Associated with Neurocognitive Development in Offspring at Age 4—6 Years

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ABSTRACT

Background: Vitamin D is critical to embryonic neuronal differentiation and other developmental processes that may affect future neurocognitive function. However, observational studies have found inconsistent associations between gestational vitamin D and neurocognitive outcomes. **Objectives:** We examined the association of gestational 25-hydroxyvitamin D [25(OH)D] with children's IQ at 4—6 y, and explored whether associations differed by race. **Methods:** This study used data from the CANDLE (Conditions Affecting Neurocognitive Development and Learning in Early Childhood) cohort. Between 2006 and 2011, CANDLE recruited 1503 women in their second trimester of healthy singleton pregnancies. Inclusion criteria for this analysis were gestation of ≥34 wk and availability of 25(OH)D and IQ data. Associations between second-trimester 25(OH)D plasma concentration and Stanford-Binet IQ scores in offspring at 4—6 y were examined using multivariable linear regression; interaction terms were used to explore possible effect modification by race. **Results:** Mean ± SD 25(OH)D concentration among 1019 eligible dyads was 21.6 ± 8.4 ng/mL, measured at a mean ± SD gestational age of 23.0 ± 3.0 wk. Vitamin D deficiency [25(OH)D < 20 ng/mL] was observed in 45.6%. Maternal 25(OH)D differed by race with a mean ± SD of 19.8 ± 7.2 ng/mL in Blacks sand 25.9 ± 9.3 ng/mL in Whites ($P < 0.001$). In adjusted models a 10-ng/mL increase in 25(OH)D was associated with a 1.17-point higher Full Scale IQ (95% CI: 0.27, 2.06 points), a 1.17-point higher Verbal IQ (95% CI: 0.19, 2.15 points), and a 1.03-point higher Nonverbal IQ (95% CI: 0.10, 1.95 points). We observed no evidence of effect modification by race. **Conclusions:** Second-trimester maternal 25(OH)D was positively associated with IQ at 4—6 y, suggesting that gestational vitamin D status may be an important predictor of neurocognitive development. These findings may help inform prenatal nutrition recommendations and may be especially relevant for Black and other dark-skinned women at high risk of vitamin D deficiency.

Keywords: vitamin D, 25-hydroxyvitamin D, neurodevelopment, IQ, prenatal nutrition
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Association Between Maternal Caffeine Consumption and Metabolism and Neonatal Anthropometry: A Secondary Analysis of the NICHD Fetal Growth Studies—Singletons

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ABSTRACT

Key Points: Question: Is maternal caffeine intake associated with neonatal anthropometry? **Findings:** In this cohort study of 2055 women from 12 clinical sites, measures of caffeine consumption (plasma caffeine and paraxanthine and self-reported consumption) were associated with neonatal size at birth. Increasing caffeine measures were significantly associated with lower birth weight, shorter length, and smaller head, arm, and thigh circumference. **Meaning:** In this study, caffeine consumption during pregnancy, even in amounts less than the recommended 200 mg per day, was associated with smaller neonatal anthropometric measurements. **Importance:** Higher caffeine consumption during pregnancy has been associated with lower birth weight. However, associations of caffeine consumption, based on both plasma concentrations of caffeine and its metabolites, and self-reported caffeinated beverage intake, with multiple measures of neonatal anthropometry, have yet to be examined. **Objective:** To evaluate the association between maternal caffeine intake and neonatal anthropometry, testing effect modification by fast or slow caffeine metabolism genotype. **Design, Setting, and Participants:** A longitudinal cohort study, the National Institute of Child Health and Human Development Fetal Growth Studies—Singletons, enrolled 2055 nonsmoking women at low risk for fetal growth abnormalities with complete information on caffeine consumption from 12 US clinical sites between 2009 and 2013. Secondary analysis was completed in 2020. **Exposures:** Caffeine was evaluated by both plasma concentrations of caffeine and paraxanthine and self-reported caffeinated beverage consumption measured/reported at 10-13 weeks gestation. Caffeine metabolism defined as fast or slow using genotype information from the single nucleotide variant rs762551 (CYP1A2*1F). **Main Outcomes and Measures:** Neonatal anthropometric measures, including birth weight, length, and head, abdominal, arm, and thigh circumferences, skin fold and fat mass measures. The ß coefficients represent the change in neonatal anthropometric measure per SD change in exposure. **Results:** A total of 2055 participants had a mean (SD) age of 28.3 (5.5) years, mean (SD) body mass index of 23.6 (3.0), and 580 (28.2%) were Hispanic, 562 (27.4%) were White, 518 (25.2%) were Black, and 395 (19.2%) were Asian/Pacific Islander. Delivery occurred at a mean (SD) of 39.2 (1.7) gestational weeks. Compared with the first quartile of plasma caffeine level (≤28 ng/mL), neonates of women in the fourth quartile (>659 ng/mL) had lower birth weight (ß = -84.3 g; 95% CI, -145.9 to -22.6 g; P = .04 for trend), length (ß = -0.44 cm; 95% CI, -0.78 to -0.12 cm; P = .04 for trend), and head (ß= -0.28 cm; 95% CI, -0.47 to -0.09 cm; P < .001 for trend), arm (ß = -0.25 cm; 95% CI, -0.41 to -0.09 cm: P = .02 for trend), and thigh (ß = -0.29 cm; 95% CI, -0.58 to -0.04 cm; P = .07 for trend) circumference. Similar reductions were observed for paraxanthine quartiles, and for continuous measures of caffeine and paraxanthine concentrations. Compared with women who reported drinking no caffeinated beverages, women who consumed approximately 50 mg per day (~1/2 cup of coffee) had neonates with lower birth weight (ß = -66 g; 95% CI, -121 to -10 g), smaller arm (ß = -0.17 cm; 95% CI, -0.31 to -0.02 cm) and thigh (ß = -0.32 cm; 95% CI, -0.55 to -0.09 cm) circumference, and smaller anterior flank skin fold (ß = -0.24 mm; 95% CI, -0.47 to -0.01 mm). Results did not differ by fast or slow caffeine metabolism genotype. **Conclusions and Relevance:** In this cohort study, small reductions in neonatal anthropometric measurements with increasing caffeine consumption were observed. Findings suggest that caffeine consumption during pregnancy, even at levels much lower than the recommended 200 mg per day of caffeine, are associated with decreased fetal growth.

The global summit on the efficacy and effectiveness of spinal manipulative therapy for the prevention and treatment of non-musculoskeletal disorders: a systematic review of the literature

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Chiropractic & Manual Therapies (2021) 29:8

ABSTRACT

Background: A small proportion of chiropractors, osteopaths, and other manual medicine providers use spinal manipulative therapy (SMT) to manage non-musculoskeletal disorders. However, the efficacy and effectiveness of these interventions to prevent or treat non-musculoskeletal disorders remain controversial. Objectives: We convened a Global Summit of international scientists to conduct a systematic review of the literature to determine the efficacy and effectiveness of SMT for the primary, secondary and tertiary prevention of non-musculoskeletal disorders. Global summit: The Global Summit took place on September 14—15, 2019 in Toronto, Canada. It was attended by 50 researchers from 8 countries and 28 observers from 18 chiropractic organizations. At the summit, participants critically appraised the literature and synthesized the evidence. **Systematic review of the literature:** We searched MEDLINE, Embase, the Cochrane Central Register of Controlled Trials, the Cumulative Index to Nursing and Allied Health, and the Index to Chiropractic Literature from inception to May 15, 2019 using subject headings specific to each database and free text words relevant to manipulation/ manual therapy, effectiveness, prevention, treatment, and non-musculoskeletal disorders. Eligible for review were randomized controlled trials published in English. The methodological quality of eligible studies was assessed independently by reviewers using the Scottish Intercollegiate Guidelines Network (SIGN) criteria for randomized controlled trials. We synthesized the evidence from articles with high or acceptable methodological quality according to the Synthesis without Meta-Analysis (SWiM) Guideline. The final risk of bias and evidence tables were reviewed by researchers who attended the Global Summit and 75% (38/50) had to approve the content to reach consensus. Results: We retrieved 4997 citations, removed 1123 duplicates and screened 3874 citations. Of those, the eligibility of 32 articles was evaluated at the Global Summit and 16 articles were included in our systematic review. Our synthesis included six randomized controlled trials with acceptable or high methodological quality (reported in seven articles). These trials investigated the efficacy or effectiveness of SMT for the management of infantile colic, childhood asthma, hypertension, primary dysmenorrhea, and migraine. None of the trials evaluated the effectiveness of SMT in preventing the occurrence of non-musculoskeletal disorders. Consensus was reached on the content of all risk of bias and evidence tables. All randomized controlled trials with high or acceptable quality found that SMT was not superior to sham interventions for the treatment of these non-musculoskeletal disorders. Six of 50 participants (12%) in the Global Summit did not approve the final report. Conclusion: Our systematic review included six randomized clinical trials (534 participants) of acceptable or high quality investigating the efficacy or effectiveness of SMT for the treatment of non-musculoskeletal disorders. We found no evidence of an effect of SMT for the management of non-musculoskeletal disorders including infantile colic, childhood asthma, hypertension, primary dysmenorrhea, and migraine. This finding challenges the validity of the theory that treating spinal dysfunctions with SMT has a physiological effect on organs and their function. Governments, payers, regulators, educators, and clinicians should consider this evidence when developing policies about the use and reimbursement of SMT for non-musculoskeletal disorders. Keywords: Spinal manipulation, Mobilization, Effectiveness, Efficacy, Systematic review, Non-musculoskeletal, Chiropractic

https://chiromt.biomedcentral.com/track/pdf/10.1186/s12998-021-00362-9.pdf

Distance Management of Spinal Disorders in the COVID-19 pandemic and beyond: Evidence-based Patient and Clinician Guides from the Global Spine Care Initiative

Haldeman S, Nordin M, Tavares P, Mullerpatan R, Kopansky-Giles D, Setlhare V, Chou R, Hurwitz E, Treanor C, Hartvigsen J, Schneider M, Gay R, Moss J, Haldeman J, Gryfe D, Wilke A, Brown R, Outerbridge G, Eberspaecher S, Carroll L, Engelbrecht R, Graham K, Cashion N, Ince S, Moon E

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ABSTRACT

Background: The COVID-19 pandemic has greatly limited patients' access to care for spine-related symptoms and disorders. However, physical distancing between clinicians and patients with spine-related symptoms is not solely limited to restrictions imposed by pandemic-related lockdowns. In most low- and middle-income countries, as well as many underserved marginalized communities in high-income countries, there is little to no access to clinicians trained in evidence-based care for people experiencing spinal pain. **Objective:** The aim of this study is to describe the development and present the components of evidence-based patient and clinician guides for the management of spinal disorders where in-person care is not available. **Methods:** Ultimately, two sets of guides were developed (one for patients and one for clinicians) by extracting information from the published Global Spine Care Initiative (GSCI) papers. An international, interprofessional team of 29 participants from 10 countries on 4 continents participated. The team included practitioners in family medicine, neurology, physiatry, rheumatology, psychology, chiropractic, physical therapy, and yoga, as well as epidemiologists, research methodologists, and laypeople. The participants were invited to review, edit, and comment on the guides in an open iterative consensus process. **Results:** The Patient Guide is a simple 2-step process. The first step describes the nature of the symptoms or concerns. The second step provides information that a patient can use when considering self-care, determining whether to contact a clinician, or considering seeking emergency care. The Clinician Guide is a 5-step process: (1) Obtain and document patient demographics, location of primary clinical symptoms, and psychosocial information. (2) Review the symptoms noted in the patient guide. (3) Determine the GSCI classification of the patient's spine-related complaints. (4) Ask additional questions to determine the GSCI subclassification of the symptom pattern. (5) Consider appropriate treatment interventions. **Conclusions:** The Patient and Clinician Guides are designed to be sufficiently clear to be useful to all patients and clinicians, irrespective of their location, education, professional qualifications, and experience. However, they are comprehensive enough to provide guidance on the management of all spine-related symptoms or disorders, including triage for serious and specific diseases. They are consistent with widely accepted evidence-based clinical practice guidelines. They also allow for adequate documentation and medical record keeping. These guides should be of value during periods of government-mandated physical or social distancing due to infectious diseases, such as during the COVID-19 pandemic. They should also be of value in underserved communities in high-, middle-, and low-income countries where there is a dearth of accessible trained spine care clinicians. These guides have the potential to reduce the overutilization of unnecessary and expensive interventions while empowering patients to self-manage uncomplicated spinal pain with the assistance of their clinician, either through direct in-person consultation or via telehealth communication.
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Extrapolating Beyond the Data in a Systematic Review of Spinal Manipulation for Nonmusculoskeletal Disorders: A Fall From the Summit

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ABSTRACT

Objective: The purpose of this article is to discuss a literature review–a recent systematic review of nonmusculoskeletal disorders–that demonstrates the potential for faulty conclusions and misguided policy implications, and to offer an alternate interpretation of the data using present models and criteria. **Methods:** We participated in a chiropractic meeting (Global Summit) that aimed to perform a systematic review of the literature on the efficacy and effectiveness of mobilization or spinal manipulative therapy (SMT) for the primary, secondary, and tertiary prevention and treatment of nonmusculoskeletal disorders. After considering an early draft of the resulting manuscript, we identified points of concern and therefore declined authorship. The present article was developed to describe those concerns about the review and its conclusions. **Results:** Three main concerns were identified: the inherent limitations of a systematic review of 6 articles on the topic of SMT for nonmusculoskeletal disorders, the lack of biological plausibility of collapsing 5 different disorders into a single category, and considerations for best practices when using evidence in policy-making. We propose that the following conclusion is more consistent with a review of the 6 articles. The small cadre of high- or moderate-quality randomized controlled trials reviewed in this study found either no or equivocal effects from SMT as a stand-alone treatment for infantile colic, childhood asthma, hypertension, primary dysmenorrhea, or migraine, and found no or low-quality evidence available to support other nonmusculoskeletal conditions. Therefore, further research is needed to determine if SMT may have an effect in these and other nonmusculoskeletal conditions. Until the results of such research are available, the benefits of SMT for specific or general nonmusculoskeletal disorders should not be promoted as having strong supportive evidence. Further, a lack of evidence cannot be interpreted as counterevidence, nor used as evidence of falsification or verification. **Conclusion:** Based on the available evidence, some statements generated from the Summit were extrapolated beyond the data, have the potential to misrepresent the literature, and should be used with caution. Given that none of the trials included in the literature review were definitively negative, the current evidence suggests that more research on nonmusculoskeletal conditions is warranted before any definitive conclusions can be made. Governments, insurers, payers, regulators, educators, and clinicians should avoid using systematic reviews in decisions where the research is insufficient to determine the clinical appropriateness of specific care.
Key Indexing Terms: Humans; Manipulation, Spinal; Publications; Policy Making; Public Health.

EDITORIAL: Gratitude for chiropractic's canaries in the coal-mine

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Asia Pacific Chiropractic Journal · Editorial
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ABSTRACT

Our previous editorial (Ebrall, 2021) expressed concern with a report by Côté et al (2021). We were the first to call out this paper for what we saw it to be, an unashamed use of purported scientific method to set a self-serving political agenda. It is always nervous to make such a big call, especially against persons holding hallowed status in our profession, but today we see they have feet of clay and the *Journal* has been vindicated by not just one, but many canaries calling out their concerns. Thankfully our profession's canaries are highly reputable scientists, writers, and educators who represent the best of our contemporary thought.

In a nutshell, Cô té et al undertook inquiry with questionable methods and with a good dose of spin, turned into into a 'global summit' meant to inform decision makers. Their conclusions were unfavourable to our profession, but of course, were also unfounded as many others now show. The lead was taken by the newly appointed Chair of the WFC Research Committee, Christine Goertz, and her paper Goetz et al (2021). It drew three conclusions, none of them favourable:

- some statements generated from the Summit were extrapolated beyond the data, have the potential to misrepresent the literature;
- the current evidence suggests that more research on nonmusculoskeletal conditions is warranted before any definitive conclusions can be made; and, critically
- Governments, insurers, payers, regulators, educators, and clinicians should avoid using systematic reviews in decisions where the research is insufficient to determine the clinical appropriateness of specific care

Readers should be under no misunderstanding that Goertz et al write with authority. In my Editorial of September 2020 (Ebrall, 2020) I stated 'We are strongly of the view that our profession must move towards research with integrity and we are confident that Goertz will lead the WFC in this direction.' In her role as Chair of the WFC Research Committee Goertz and her colleagues have made a clear statement that the chiropractic research committee will no longer play politics and will instead exercise their considerable skills in producing quality research outputs that will advance the profession in the clinical sense.

The *Journal's* Editorial Board has concluded that Goetz et al are correct in their expressed concerns that Cô té et al (2021):

'Privileged certain forms of evidence over others' and that this 'may ultimately be a political act, not a scientific one'; and
Made 'strong policy implications based on weak scientific evidence' which we agree is indeed 'a cause for concern'.

However we question their view that is 'disconcerting' for policy-makers, to whom Côté et al directed their conclusion, to be excluded from discussion regarding findings that they are recommended to follow. Our concern is that policy-makers are expected to make policy based on the best-available evidence. They are not researchers but may well benefit from expert research guidance of the nature Goetz and both the WFC and ICA are able to offer. We see it is erroneous to bring policymakers to the table while evidence is being formulated; this is a specialised, high-skill process far beyond consensus arguments and other confrontational styles of Western decision-making.

Let the policy-makers be informed of the evidence and what it says, perhaps by commissioned reports from appropriate panels of clinical experts and researchers, and don't confuse policy making with evidence generation. Evidence interpretation and application? Yes. Evidence generation? No. Understanding and meaning? Well, this editorial proposes we leave that to our philosophers.