

Office of Research

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Publication Highlights

DEPARTMENT OF EPIDEMIOLOGY

High Impact Journal Recognition: Diabetes Care (Impact Factor: 17.152)

HLA Genotype and Probiotics Modify the Association Between Timing of Solid Food Introduction and Islet Autoimmunity in the TEDDY Study

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Diabetes Care

OBJECTIVE:

To study the interaction among HLA genotype, early probiotic exposure, and timing of complementary foods in relation to risk of islet autoimmunity (IA).

RESEARCH DESIGN AND METHODS:

The Environmental Determinants of Diabetes in the Young (TEDDY) study prospectively follows 8,676 children with increased genetic risk of type 1 diabetes. We used a Cox proportional hazards regression model adjusting for potential confounders to study early feeding and the risk of IA in a sample of 7,770 children.

RESULTS:

Any solid food introduced early (<6 months) was associated with increased risk of IA if the child had the HLA DR3/4 genotype and no probiotic exposure during the 1st year of life. Rice introduced at 4–5.9 months compared with later in the U.S. was associated with an increased risk of IA.

CONCLUSIONS:

Timing of solid food introduction, including rice, may be associated with IA in children with the HLA DR3/4 genotype not exposed to probiotics. The microbiome composition under these exposure combinations requires further study.

DEPARTMENT OF BIOSTATISTICS & INFORMATICS

Joint Cranial Bone Labeling and Landmark Detection in Pediatric CT Images Using Context Encoding

Liu, Jiawei; Xing, Fuyong; Shaikh, Abbas; French, Brooke; Linguraru, Marius George; Porras, Antonio R.
IEEE Transactions on Medical Imaging

Image segmentation, labeling, and landmark detection are essential tasks for pediatric craniofacial evaluation. Although deep neural networks have been recently adopted to segment cranial bones and locate cranial landmarks from computed tomography (CT) or magnetic resonance (MR) images, they may be hard to train and provide suboptimal results in some applications. First, they seldom leverage global contextual information that can improve object detection performance. Second, most methods rely on multi-stage algorithm designs that are inefficient and prone to error accumulation. Third, existing methods often target simple segmentation tasks and have shown low reliability in more challenging scenarios such as multiple cranial bone labeling in highly variable pediatric datasets. In this paper, we present a novel end-to-end neural network architecture based on DenseNet that incorporates context regularization to jointly label cranial bone plates and detect cranial base landmarks from CT images. Specifically, we designed a context-encoding module that encodes global context information as landmark displacement vector maps and uses it to guide feature learning for both bone labeling and landmark identification. We evaluated our model on a highly diverse pediatric CT image dataset of 274 normative subjects and 239 patients with craniosynostosis (age 0.63 ± 0.54 years, range 0–2 years). Our experiments demonstrate improved performance compared to state-of-the-art approaches.

LIFECOURSE EPIDEMIOLOGY OF ADIPOSITY & DIABETES CENTER

Maternal Psychosocial Stress During Pregnancy and Offspring Neurobehavioral Outcomes During Early Childhood in The Healthy Start Study

Dhaliwal, Satvinder K.; Dabelea, Dana; Lee-Winn, Angela E.; Crume, Tessa; Wilkening, Greta; Perng, Wei
ANNALS of Epidemiology

We evaluate singular and combined effects of prenatal maternal depression and stress on early childhood neurobehavioral outcomes among 536 mother-child pairs. First, we used multivariable linear regression to investigate associations of women's Edinburgh Postnatal Depression Scale (EPDS) score and Perceived Stress Scale (PSS) score, separately, with offspring Child Behavior Checklist score. Next, to assess the combined effect of EPDS and PSS, we dichotomized each score at the fourth versus first to third quartiles and created a four-level variable comprising combinations of high and low depression and stress. Across all models, we accounted for household chaos, hubbub, and order scale (CHAOS) score, an indicator of the household environment associated with offspring behavioral outcomes. Each one-unit increment in maternal EPDS and PSS scores corresponded with 0.75 (95% CI: 0.53, 0.96) and 0.72 (95% CI: 0.48, 0.95) units higher offspring total problems T-score, respectively. Children of women with high EPDS and PSS had highest T-scores for total problems. All associations remained materially unchanged after adjustment for CHAOS score. Prenatal maternal depression and stress is associated with worse neurobehavioral outcomes among offspring, with the most unfavorable outcomes among children whose mothers had high scores for both EPDS and PSS.

The In Silico Identification of Novel Broad-Spectrum Antidotes For Poisoning by Organophosphate Anticholinesterases

Habiballah, Sohaib; Chambers, Janice; Meek, Edward; Reisfeld, Brad

Journal of Computer-Aided Molecular Design

Because of their potential to cause serious adverse health effects, significant efforts have been made to develop antidotes for organophosphate (OP) anti-cholinesterases, such as nerve agents. To be optimally effective, antidotes must not only reactivate inhibited target enzymes, but also have the ability to cross the blood brain barrier (BBB). Progress has been made toward brain-penetrating acetylcholinesterase reactivators through the development of a new group of substituted phenoxyalkyl pyridinium oximes. To help in the selection and prioritization of compounds for future synthesis and testing within this class of chemicals, and to identify candidate broad-spectrum molecules, an in silico framework was developed to systematically generate structures and screen them for reactivation efficacy and BBB penetration potential.

CENTER FOR GLOBAL HEALTH

Palivizumab Prophylaxis in Preterm Infants and Subsequent Wheezing/Asthma: 10-Year Follow-Up Study

Kato, Masahiko; Mochizuki, Hiroyuki; Kama, Yuichi; Kusuda, Satoshi; Okada, Kenji; Yoshihara, Shigemi; Furuya, Hiroyuki; Simoes, Eric A. F.

Pediatric Pulmonology

Respiratory syncytial virus (RSV) causes not only infantile recurrent wheezing but also the development of asthma. To investigate whether palivizumab, an anti-RSV monoclonal antibody, prophylaxis given to preterm infants during the first RSV season reduces the incidence of subsequent recurrent wheezing and/or development of asthma, at 10 years of age. We conducted an observational prospective multicenter (52 registered hospitals in Japan) case-control study in preterm infants with a gestational age between 33 and 35 weeks followed for 6 years. During the 2007-2008 RSV season, the decision to administer palivizumab was made based on standard medical practice (SCELIA study). Here, we followed these subjects until 10 years of age. Parents of study subjects reported the patients' physician's assessment of recurrent wheezing/asthma, using a report card and a novel mobile phone-based reporting system using the internet. The relationship between RSV infection and asthma development, as well as the relationship between other factors and asthma development, were investigated. Of 154 preterm infants enrolled, 113 received palivizumab during the first year of life. At 10 years, although both recurrent wheezing and development of asthma were not significantly different between the treated and untreated groups, maternal smoking with aeroallergen sensitization of the patients was significantly correlated with physician-diagnosed asthma. In contrast to the prior study results at 6 years, by 10 years palivizumab prophylaxis had no impact on recurrent wheezing or asthma, but there was a significant correlation between maternal passive smoking with aeroallergen sensitization and development of asthma by 10 years of age.

CANCER CENTER

Building Data Infrastructure for Disease-Focused Health Economics Research

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Medical Care

Data infrastructure for cancer research is centered on registries that are often augmented with payer or hospital discharge databases, but these linkages are limited. A recent alternative in some states is to augment registry data with All-Payer Claims Databases (APCDs). These linkages capture patient-centered economic outcomes, including those driven by insurance and influence health equity, and can serve as a prototype for health economics research. To describe and assess the utility of a linkage between the Colorado APCD and Colorado Central Cancer Registry (CCCR) data for 2012-2017. This cohort study of 91,883 insured patients evaluated the Colorado APCD-CCCR linkage on its suitability to assess demographics, area-level data, insurance, and out-of-pocket expenses 3 and 6 months after cancer diagnosis. The linkage had high validity, with over 90% of patients in the CCCR linked to the APCD, but gaps in APCD health plans limited available claims at diagnosis. We highlight the advantages of the CCCR-APCD, such as granular race and ethnicity classification, area-level data, the ability to capture supplemental plans, medical and pharmacy out-of-pocket expenses, and transitions in insurance plans. Linked data between registries and APCDs can be a cornerstone of a robust data infrastructure and spur innovations in health economics research on cost, quality, and outcomes. A larger infrastructure could comprise a network of state APCDs that maintain linkages for research and surveillance.

DEPARTMENT OF HEALTH SYSTEMS, MANAGEMENT & POLICY

Tissue Plasminogen Activator Challenge Thrombelastography is The Most Accurate Assay in Predicting the Need for Massive Transfusion in Hypotensive Trauma Patients

Jiang, Jessie G.; Moore, Hunter B.; Moore, Ernest E.; Pieracci, Fredric; Sauaia, Angela
American Journal of Surgery

Tissue plasminogen activator (tPA) added to thrombelastography (TEG) detects hyperfibrinolysis by measuring clot lysis at 30 min (tPA-challenge-TEG). We hypothesize that tPA-challenge-TEG is a better predictor of massive transfusion (MT) than existing strategies in trauma patients with hypotension. Trauma activation patients (TAP, 2014-2020) with 1) systolic blood pressure <90 mmHg (early) or 2) those who arrived normotensive but developed hypotension within 1H postinjury (delayed) were analyzed. MT was defined as >10 RBC U/6H postinjury or death within 6H after ≥1 RBC unit. Area under the receiver operating characteristics curves were used to compare predictive performance. Youden index determined optimal cutoffs. tPA-challenge-TEG was the best predictor of MT in the early hypotension subgroup (N = 212) with positive (PPV) and negative predictive values (NPV) of 75.0%, and 77.6%, respectively. tPA-challenge-TEG was a better predictor of MT than all but TASH (PPV = 65.0%, NPV = 93.3%) in the delayed hypotension group (N = 125). The tPA-challenge-TEG is the most accurate predictor of MT in trauma patients arriving hypotensive and offers early recognition of MT in patients with delayed hypotension.

CENTERS FOR AMERICAN INDIAN & ALASKA NATIVE HEALTH

Feasibility, Acceptability and Effectiveness of A Culturally Informed Intervention to Decrease Stress and Promote Well-Being in Reservation-Based Native American Head Start Teachers

Wilson, Deborah H.; German, Danielle; Ricker, Adrian; Gourneau, Hilary; Hanson, Ginger C.; Mayhew, Justin; Brockie, Teresa N.; Sarche, Michelle
BMC Public Health

While benefiting from strong cultural ties to family, land and culture Native Americans residing on reservations experience psychological distress at rates 2.5 times that of the general population. Treatment utilization for psychological health in reservation-based communities is low with access to culturally appropriate care lacking. Evidence suggests that for mental health treatment, Native Americans prefer culturally informed care that respects Native perspectives on health and well-being. To decrease stress and promote well-being in tribal Head Start teachers we adapted and implemented a culturally focused intervention within a community-based participatory research framework using mixed methods. Feasibility and acceptability of the adapted 5-session curriculum was tested in a single arm intervention study with a sample of 18 teachers on the Fort Peck Reservation. Participants completed surveys at baseline and upon completion of the intervention. Within session observations and two post-intervention focus groups (n = 8, n = 10) were conducted to elaborate and explain the quantitative results eliciting participant experience of intervention effectiveness and feasibility, acceptability and appropriateness. Implementation outcomes were assessed quantitatively using the Acceptability of Intervention, Intervention Appropriateness, and Feasibility of Intervention measures. Quantitatively, attendance rate overall was 93% with no dropouts. Pretest/posttest surveys were analyzed using t-tests and Hedges g to measure effect size. Contrary to our hypothesis, self-perceived stress showed a small positive effect size, indicating that participants were more stressed post intervention. However, depression decreased, with tribal identity and resilience showing positive effect sizes. Content analysis for the qualitative data collected within session observations and post intervention focus groups revealed how lifetime traumas were affecting participants, providing some explanation for the increase in stress. Teachers reported that the sessions helped their psychological health and well-being, supporting feasibility of future interventions. Acceptability scored highest with a mean (SD) of 4.25 (.84) out of 5, appropriateness 4.18 (.86) and feasibility 4.06 (.96) supporting intervention to be acceptable, appropriate, and feasible. Utilizing a culturally based intervention to buffer stress and support the well-being of reservation-based teachers showed promise in helping them recognize their cultural strengths, stress, and need for ongoing support. Implementation outcomes show that intervention scale-out is feasible.

DEPARTMENT OF COMMUNITY AND BEHAVIORAL HEALTH & THE ROCKY MOUNTAIN PREVENTION RESEARCH CENTER

A Qualitative Study Identifying a Rural Community's Barriers and Facilitators to Addressing Adverse Childhood Experiences in Families with Young Children

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Health & Social Care in the Community

Adverse childhood experiences (ACEs) are traumatic events experienced before the age of 18 and include experiences of abuse, neglect, and household dysfunction. Exposure to ACEs early in life is a risk factor for adverse physical and mental health outcomes in adulthood, which may lead to subsequent child abuse, neglect, and household dysfunction. This study examined a rural community's barriers and facilitators to addressing ACEs in families with young children from the perspective of organizations serving children and families. The Innovation Corps (I-Corps) methodology was used to develop an ecosystem map of 64 community stakeholders, including 12 government, 13 healthcare, 27 early childhood education (ECE), and 12 community-based organizations, involved in the community's system of care for families with young children. Representatives from the stakeholder organizations identified in the ecosystem map were then recruited via purposeful and snowball sampling, and semistructured interviews were conducted with 37 participants. Transcribed notes and direct quotes were analyzed using a constant comparison analysis approach, and five themes emerged from the analysis. Barriers to addressing ACEs included limited mental health resources in ECE settings for both children and teachers, stigma, and limited access to local healthcare, while facilitators included establishing trusted relationships between organizations and families and using strengths-based approaches with families. This study characterized facilitators and barriers to addressing ACEs in families with young children residing in a rural community and provides guidance to inform future community-level ACEs interventions and policies.