

Department of Pediatrics Research Report



May 2016

Inside This Issue

| CHFS-Grant Program | | |
|-----------------------------------|-----|--|
| Image of Interest | | |
| Ketogenic Diet Clinic | | |
| Featured Researcher | | |
| Our Partners | | |
| Recent Publications/Presentations | | |
| Congratulations | | |
| Coming Events | | |
| Research Opportunities | | |
| Survey | P4 | |
| CHRTF | | |
| Contact Us | | |
| Abstracts | P5- | |
| View the online 回题就回 | | |
| version of the | | |
| Research Report! | | |



Children's Hospital Foundation of Saskatchewan Refines

Grant Program Lynn Redl-Huntington



Image of Interest

Kyra Kane, PT, PhD candidate in Health Sciences, is currently studying the effects of walking braces (ankle-foot orthoses) on gait mechanics and balance in children with cerebral palsy with supervisors Dr. Kristen Musselman and Dr. Joel Lanovaz. By individually optimizing the angle at which the child's ankle is supported in the brace, the study aims to improve evidence-based prescription guidelines for pediatric clinicians.

This piece is 9" x 12", embroidery thread, collage, acrylic paint, and bits of thread on canvas. Contact paper was used for the image transfers. Kyra's lab did a "paint your research project" activity last summer, and that inspired a series of these pieces.

Submitted by: Kyra Kane, PT, PhD Candidate

With overwhelming interest and increased demand, the Children's Hospital Foundation of Saskatchewan (CHFS) is updating its Grant Program to better support pediatric and maternal researchers.

With the Foundation becoming a dominant

funding source for pediatric and maternal research, the CHFS has created a formal external scientific advisory committee led by Dr. Gordon McKay, former Board Chair for the Saskatchewan Health Research Institute. Including representation from Pediatrics and Maternal Services as well as CHFS co-founder Dr. Alan Rosenberg, the new advisory committee is set to create new processes for reviewing and awarding research grants to the CHFS.

The CHFS disburses approximately \$1 million annually for current pediatric and maternal needs. Last year, research and education made up over 40% of approved grants with the remainder designated to equipment, technology and patient care. In addition, \$100,000 was designated again this year for a research chair position in the pediatric department for exceptional emerging researchers and research needs.



CHILDREN'S HOSPITAL FOUNDATION of Saskatchewan

"Supporting novel and high-impact pediatric and maternal health research is a high priority for the Foundation, as is enhancing new knowledge that will translate into refined pediatric and maternal healthcare," says pediatric intensivist Dr. Tanya Holt, Chair of the CHFS Grants Committee. "Re-evaluating the research application process is critical to ensure that these projects have maximum impact across Saskatchewan and the country."

Over the last several years, the CHFS has funded numerous innovative projects including work by Dr. Richard Huntsman on whether Cannabidiol may be a treatment option for children with Epileptic Encephalopathy; asthma research by Dr. Darryl Adamko that may lead to better testing for younger patients; promising work by Dr. Veronica McKinney, Dr. Tanya Holt, and Dr. Ivar Mendez on robotic technology to dramatically reduce the need for pediatric transport of seriously ill children from remote communities, and Dr. Marta Erlandson's CHAMPS-Children's Healthy Heart Camp in Saskatchewan, a first of its kind project in Canada.

"We are thrilled that Saskatchewan clinicians and academic researchers are interested in enhancing knowledge and practice in pediatric and maternal care and that they are looking to CHFS to support their *continued on P3...*

This issue of The Pediatric Research Report is sponsored by The Children's Health Research Trust Fund (P4 for more info.)

Ketogenic Diet Clinic

Dana Oleniuk, RD

was designed in 1924 by Dr. Russell Wilder at the Mayo Clinic. Despite being highly effective in treating epilepsy, its use decreased due to the surge of new anti-epileptic seizure medications in the 1940s. In the 1990s, its use began to increase again around the world. Its use became popularized after two children, Matthew of Matthew's Friends (UK) and Charlie of Charlie Foundation (USA)'s saw vast improvements on the Ketogenic Diet.

Matthew's and Charlie's parents had sought out an alternative treatment to medications when their children were seizing constantly, and seeing negative side effects of various anti-epileptic medications. Both children were eventually started on the Ketogenic Diet. Charlie was on the diet for 5 years, becoming seizure free, and Matthew was on it for 6 years, with a 90% reduction in seizures. Matthew and Charlie were then both successfully weaned off of the diet with no increase in seizures. Foundations in these countries continue to exist, with a new chapter of Matthew's Friends called Matthew's Friends Canada, which aims to raise awareness about the use of the Ketogenic Diet for epilepsy.

In many ways, the Ketogenic Diet is as much an art as it is a science. This high fat, adequate protein, and low carbohydrate diet has been used in Saskatchewan since 1992. Saskatchewan has had over 100 children on the diet, for varying lengths of time. Half of the children

The not-so-new, yet remarkable treatment called the Ketogenic Diet on the Ketogenic Diet will have reduction in seizures, while a small amount will become seizure free. In Saskatchewan, a 3-6 month trial is encouraged to allow diet fine tuning to try to reduce or eliminate seizures. Most children that find success with the Ketogenic Diet will stay on the diet for 2-3 years, and then be able to be weaned off and remain at the same level of seizure reduction or seizure freedom. This special diet changes the way energy is used in the body and produces ketone bodies from breaking down fat, which can lead to the reduction in the occurrence of epileptic seizures. Researchers believe that the chemical changes that occur lets the brain heal, which allows a child to remain with reduced or no seizures, even after the diet is later weaned.

> With increasing population and demand over recent years, Saskatoon Health Region has been able to expand from one pediatric dietitian to three part-time pediatric dietitians with the expertise to administer and supervise patients on the Ketogenic Diet. This medical therapy requires intensive education and care followed by regular and close monitoring. Special acknowledgement should be made to those individuals past and present who have continued to believe in the potential of the diet and advocated for the expansion of the program so that it is available to other families in need, such as Elaine Niebergall RD, Dr. Lowry, Dr. Huntsman, the rest of the Pediatric Neurology Team, our patients and their families.

> > continued on pg 4...

Featured Child Health Researcher

Dr. Hassan Vatanparast

Dr. Hassan Vatanparast joined the University of Saskatchewan in as a faculty member in 2010. He is currently Associate Professor with a joint appointment in the College of Pharmacy and Nutrition and School of Public Health. He is originally from Mashhad, Iran, where he completed his MD degree and entered to the public health sector as a physician and director of



a rural healthcare center. His interest in epidemiologic studies relating to child and maternal health encouraged him to complete his training in epidemiology and work as an epidemiologist. In his last position, he served as the director of Non-communicable Diseases Prevention and Control Department at the Provincial Health Center, Mashhad University of Medical Science, Khorasan Province, Iran. Realizing the epidemiologic transition from communicable diseases to nutrition and lifestyle-related non-communicable disease, he decided to expand his knowledge in the field of nutritional epidemiology by pursuing a PhD degree at the University of Saskatchewan.

In his PhD thesis project, Dr. Vatanparast worked on the Pediatric Bone Mineral Accrual Longitudinal Study (BMAS) to evaluate the trend in dietary intake from childhood to adulthood and its impact on bone health. He expanded his knowledge and experience in the field of Kinesiology by pursuing a two-year postdoctoral fellowship.

Dr. Vatanparast, along with his colleagues, is involved in several projects related to children's health and bone health in clinical and general populations. In clinical populations, Dr. Vatanparast and his team including Drs. J. Jones and W. El-Matary designed an international randomized controlled trial to evaluate the impact of high doses of vitamin D on disease activity in children suffering from Crohn's disease. Further, the study was converted to case series and retrospective cohort studies. They found that vitamin D has an impact on disease activity in Crohn's cases. In another study, currently, Dr. Vatanparast is working with Dr. Alan Rosenberg, Sarah Finch (PhD Candidate) and other co-investigators evaluating the impact of vitamin D on disease activity and biomarkers in Juvenile Idiopathic Arthritis (JIA). They are comparing the nutrition and indicator of JIA cases with a nationally representative sample of children in the same age group. Dr. Vatanparast has also been involved in an international

continued on pg 3...

Our Partners

Children's Hospital Foundation of Saskatchewan

The Children's Hospital Foundation of Saskatchewan (CHFS) continues to provide strong and increasing support for child health research in Saskatchewan through its research granting program. The CHFS has

provided funding to support trainee research and the Child Health Research Trainee Day presentations which are highlighted in this issue of the Research Report.



Clinical Investigator Program (CIP) for Residents

The CIP at the University of Saskatchewan is available to residents enrolled in a Royal College accredited residency program who have interest and potential for a career as a clinician investigator or clinician scientist. CIP offers two streams: A Graduate stream for participants enrolled in a graduate (M.Sc. or Ph.D.) program, and a Postdoctoral Stream for residents who already hold a Ph.D. and are interested in undertaking a structured research program. For further information about CIP, please contact Dr. Alan Rosenberg, alan.rosenberg@usask.ca.

CHFS-Research Grant Program

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ground-breaking and world-class work," says Brynn Boback-Lane, President and CEO of the CHFS. "No longer should Saskatchewan feel secondary to research done elsewhere in the country. We have intelligent and innovative people right here at home and we are proud to support their efforts."

The CHFS Grants Program supports funding within Children's Surgery, Children's Emergency, Oncology & Day Medicine, General Pediatrics/Outpatients, Pediatric Intensive Care & Step Down Unit, Maternal/Labour & Delivery, Developmental Rehabilitation/ Therapeutic Treatment, Programming/Special Initiatives, Neonatal Intensive Care Unit, Acute Care Pediatrics, and pediatric subspecialties such as endocrinology, hematology, and rheumatology.

ts funding within Children's The deadline for a Letter of Intent for Children's Hospital gy & Day Medicine, General Foundation of Saskatchewan research grants is September 30, 2016 with full approved research grant applications due by January 31, 2017. To learn more, please visit childrenshospitalsask.ca.

supplies, resources, and animals.

Lynn Redl-Huntington is the Director of Communications & Stewardship with the Children's Hospital Foundation of Saskatchewan

Researchers can obtain up to \$50,000 annually for up to three years

for a total of \$150,000 for research projects. Grants may be used to

cover materials, services, salaries of staff including research assistants

or technicians, equipment purchases or rentals as well as travel,

Dr. Hassan Vatanparast

study evaluating indicators and phenotypes of non-alcoholic fatty liver in obese children.

In the general population, evaluating nutrition and health status of Canadian children in a nationally representative sample has been one of Dr. Vatanparast's main interests. He and his colleagues have conducted several projects using national nutrition and health survey data, such as evaluating children's food groups and nutrients intakes, food security, and beverage consumption of Canadian children in association with obesity. He is also following his long-term interest in nutrition and bone health. The current Institute of Medicine Dietary Reference Intake (DRI) guidelines for calcium used the study by Dr. Vatanparast and his team as the main line of evidence to set DRI values for children and adolescents. He and his team are currently evaluating how the dietary intake and physical activity during childhood impact bone and cardiometabolic indicators in adulthood.

Improving nutrition and health status of children, particularly in at-risk populations, has been Dr. Vatanparast's passion. Newcomers to Canada, particularly refugee children, are at much higher nutrition and health risks compared to the general population. Before moving to Canada, Dr. Vatanparast established four primary healthcare clinics for refugees in Iran with the help of UNHCR and UNICEF providing healthcare services to mothers and children free of charge. Following that lifelong interest, he initiated the Healthy Immigrant Children program in Saskatchewan. Dr. Vatanparast and his colleagues conducted the first comprehensive study in Canada evaluating nutrition and health status of newcomer children. The results are alarming and require immediate attention by policy and service sectors. Along with his research, he and his team are working closely with settlement agencies by organizing workshops for children about healthy eating and physical activity. Dr. Vatanparast and his team along with school boards also designed and implemented a project titled Voices in Vision aimed to empower the confidence of newcomer children with the sense of cultural identity and expression of ideas about the new environment particularly from nutrition and health perspective.

Dr. Vatanparast is also involved in Healthy Start/Depart Santé intervention program (led by Dr. Anne Lies) aiming to improve physical activity and nutritional health of children aged 3-5 attending to childcare centres in Saskatchewan and New Brunswick. He is serving as a member of Steering and Evaluation Committees. He is also responsible for the evaluation of the nutrition component of the program through a randomized controlled trial. He and his colleagues from different disciplines with various expertise are currently working with other stakeholders including Provincial Public Health Nutritionist, childcare centers, and Saskatchewan Network for Health Services in French to develop provincial childcare nutritional guidelines. Dr. Vatanparast and the team are planning to initiate similar projects in developing countries where young children are at a high risk of accelerated nutrition transition and its consequences.

Dr. Vatanparast continues to collaborate with other researchers and stakeholders to explore how to improve healthier lifestyle for children, and design and implement proper interventions in that regard.

> Dr. Hassan Vatanparast is an Associate Professor with a joint appointment with the College of Pharmacy and Nutrition and the School of Public Health, University of Saskatchewan.

Recent Publications & Presentations from U of S Child Health Researchers

Bobbitt SA, Baugh LA, Andrew GH, Cook JL, Greene CR, JR Pei, Rasmussen CR. Caregiver needs and stress in caring for individuals with fetal alcohol spectrum disorder. Research in Developmental Disabilities 55 (2016) 100–113.
Bobbitt SA, Sonnenberg LK. Isolated gross motor delay with 'sitting on air' position in an otherwise healthy 17-month-old. Paediatr Child Health. 2016;21.
Bélanger M, Humbert L, Vatanparast H, Ward S, Muhajarine N, Chow AF, Engler-Stringer R, Donovan D, Carrier N, Leis A. A multilevel intervention to increase physical activity and improve healthy eating and physical literacy among young children (ages 3-5) attending early childcare centres: the Healthy Start-Départ Santé cluster randomised controlled trial study protocol. BMC Public Health. 2016;16:313.

• Engler-Stringer R, Muhajarine N, Ridalls T, Abonyi S, Vatanparast H, Whiting S, Walker R. The Good Food Junction: a Community-Based Food Store Intervention to Address Nutritional Health Inequities. JMIR Res Protoc. 2016;5:e52.

• Henry C, Whiting SJ, Finch SL, Zello GA, Vatanparast H. Impact of replacing regular chocolate milk with the reduced-sugar option on milk consumption in elementary schools in Saskatoon, Canada. Appl Physiol Nutr Metab. 2016;41:511-5.

- · Hurtubise JL, Howland JG. Effects of stress on behavioral flexibility in rodents. Neuroscience. 2016;16:30062-8.
- Li H, Bowen A, Szafron M, Moraros J, Muhajarine N. Maternal mental health: a shared care approach. Prim Health Care Res Dev. 2016;17:175-83.
- · Linde-Medina M, Boughner JC, Santana SE, Diogo R. Are more diverse parts of the mammalian skull more labile? Ecol Evol. 2016;6:2318-24.
- Montgomery JE, Wesolowski MJ, Wolkowski B, Chibbar R, Snead EC, Singh J, Pettitt M, Malhi PS, Barboza T, Adams G. Demonstration of synchrotron x-ray phase contrast imaging computed tomography of infiltrative transitional cell carcinoma of the prostatic urethra in a dog. J Med Imaging. 2016;3:015504.
- · Zahedi NO, Clarke AE, Ramsey-Goldman R, Yeung R, Hayward K, Oen K, Duffy CM, Rosenberg A, O'Neil KM, von Scheven E, Schanberg L, Labrecque J, Tse SM, Hasija R, Lee JL, Bernatsky S. Malignancy incidence in 5294 patients with juvenile arthritis. RMD Open. 2016;2:e000212.

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Ketogenic Diet Clinic

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Glenda is one mother who has a unique point of view as she has had one child previously on the Ketogenic Diet see positive results and be subsequently weaned and taken off the diet. She also has another child scheduled to be initiated on the diet this month. It is stories like Glenda's, which are so rewarding:

"Five years ago, our family desperately – but expectantly - turned to the Ketogenic Diet. Our infant son was suffering from severe epilepsy, and after two failed courses of drug therapy, we were losing not only time, but our son. Today we celebrate an active, mischievous, healthy, and thriving little boy who loves life. Our son was on the diet for 2.5 years and after being off of the diet for another 2.5 years, he remains seizure free, and on no medications. We believe that the Ketogenic Diet not only cured his epilepsy, but healed his brain. And now as we initiate the diet with our daughter, who has refractory epilepsy, we are both excited and hopeful, anticipating brighter and healthier days!"

Sask Kids Pediatric Epilepsy Program is thrilled to announce that it held its first official Ketogenic Diet Clinic on May 20, 2016 at Royal University Hospital. This interdisciplinary clinic (3 dietitians - Carolyn Olver, Dana Oleniuk, and Katelynn Johnson, along with neurologist Dr. Almubarak) allowed patients and their families to meet with a neurologist and dietitian with particular expertise in using the Ketogenic Diet for treatment of epileptic seizures. Physicians from across the province referred children from infancy to 18 years of age to the clinic, who had not responded to 2 or more anti-epileptic seizure medications or were having serious negative side effects from anti-seizure medication for consideration of this medical therapy.

The potential benefits of the Ketogenic Diet are numerous. There is the potential to cease, or at least reduce seizures and medications. There is the likelihood of fewer hospitalizations due to complications and consequences of on-going seizures. Above all, the diet offers hope of return to health and improved quality of life without the side effects of medications. Success on the Ketogenic Diet requires commitment and determination of the entire family. No one understands all the reasons why or how the diet works. But it can work for some children. For those that can fully commit to a 3-6 month trial to see if the diet will work for their child, may see benefit. Brains heal on the diet, quality of life can be restored (for child and family), and a child's potential can be realized; what could be more significant than that?

Dana Oleniuk is a Registered Dietician in the Pediatric Outpatient Department and the Ketogenic Diet Program, Royal University Hospital.



Research Project Opportunities

"Survey of Kawasaki Disease awareness among Saskatchewan physicians" Study format: Survey Contact: Dr. Alan Rosenberg, alan.rosenberg@usask.ca

"Relationship of ESR and CRP with inflammatory cytokine biomarkers" Study format: Database analysis Contact: Dr. Alan Rosenberg, alan.rosenberg@usask.ca

Congratulations!

Dr. Susan Bobbitt, Faculty, Division of Developmental Pediatrics, Department of Pediatrics, was involved, along with Drs. Debbi Andrews and William Mahoney, in the development of a new eCME course on School Children with Learning Disabilities. The course was designed to support primary care physicians in the development of skills for the initial assessment and management of children whose chief complaint is "trouble in school". Dr.



Bobbitt and her course were featured as one of the Canadian Pediatric Society's Top 15 of 2015!

For more information, visit http://www.cps.ca/uploads/ about/15in15-EN.PDF.



YOUR OPINION PLEASE!

We would appreciate your opinion about the Department of Pediatrics Research Report and suggestions for future editions.

Please complete a brief survey at: https://www.surveymonkey.com/s/NQVV6SB. Thank you!

The Children's Health Research Trust Fund (CHRTF) was established in 1983 to help raise funds to support child health research at the Children's University of Saskatchewan. As all donated funds Health Research are endowed, the CHRTF has continued to grow to become an important partner in helping advance

research in the Department of Pediatrics. For further information about the CHRTF: http://www.medicine.usask.ca/pediatrics/ research/CHRTF. To Donate to the CHRTF: http://give.usask.ca/ online/chrtf.php





Child Health Research Trainee Day March 24th, 2016 Presentation Abstracts

The Department of Pediatrics held the Child Health Research Trainee Day on March 24th, 2016. We had a total of 13 presenters, which consisted of residents, graduate students, post-doctoral fellows, and undergraduate students, from diverse fields such as Pediatrics, Kinesiology, Nutrition, Pharmacy, and Epidemiology, Each trainee presented their child health-related research, followed by questions and discussion from the audience of peers and faculty.

BARBOUR-TUCK E., ERLANDSON M.A., FOULDS H., MUHAJARINE N., BAXTER-JONES A.D.G.

Changes in fat mass distribution and weight status from adolescence to emerging adulthood: a 20 year longitudinal study.

Introduction: Fat accrual during growth is related to adult obesity and early onset of related diseases. Trunk fat deposition is associated with increased cardiovascular disease risk and development of metabolic syndrome, in both childhood and adulthood. The purpose of this study is to describe patterns of fat mass and weight status development from adolescence through to early adulthood and identify critical periods of fat accrual.

Methods: 126 participants (59 male) were measured serially from 1991 - 2011. Height measures were used to ascertain the age at peak height velocity (PHV) and measures were aligned by biological age (BA; years from PHV). Percentage total body fat (%TBF) was estimated from DXA scans. At PHV individuals were classified as normal weight (NW) or overweight/obese (OW/OB) status using established age and sex specific cut-offs for %TBF. Trunk fat (%TF) and lower limb fat (%LLF) and their ratio (T: LLF) were also derived. T-tests were used to analyze differences in %TBF, %TF and %LLF between sex, BA and weight status categories.

Results: Mean %TBF increased significantly from PHV to adulthood (p<0.05); %TBF surpassed the cut-off for NW at BA +4 years and BA +8 years (16 and 22 years) in females and males respectively (p<0.05). Females had greater %TBF, TF (g), LLF (g) at all ages compared to males, but less %TF and greater %LLF by BA +5 years (17 and 19 years in females males respectively) (p<0.05). The T: LLF ratio surpassed 1.0 at BA +17 (29 years) and +9 (23 years) in NW adolescent females and males respectively. For OW/OB adolescents 1.0 was surpassed at BA +3 (15 years) and BA + 6 (20 years) for females and males respectively. Differences in segmental variables for those who maintained NW and those who changed status arose at a BA +6 (20 years) in males and BA +12 (24 years) in females.

Conclusions: This study suggests that the prevalence of OW/OB increases and differences between weight classes at PHV disappear during late adolescence and emergent adulthood. Furthermore, during emerging adulthood fat deposit on the trunk becomes greater than the lower limbs, occurring earlier in those who were OW/OB adolescents.

KHAMIS M.H., AWAD H., ALLEN K., ADAMKO D.J., EL-ANEED A.

Improving the diagnosis of children's asthma through the investigation of the urinary metabolome using targeted mass spectrometry.

Background: Advances in perinatal-neonatal care have significantly reduced neonatal mortality; however, morbidities in survivors are still of concern. Recent morbidity trends and the lowest gestational age (GA) for morbidity-free survival (MFS) of extremely premature neonates born in Canada are unknown. Background: Asthma is the most diagnosed chronic childhood disease affecting over 13% of Canadian children. It causes frequent hospital visits and impaired quality of life. The guidelines for asthma treatment recommend the adjustment of the therapy based on the airway inflammation. However, this cannot be easily achieved in a typical outpatient clinic.

Metabolomics is the comprehensive identification and quantification of small molecules created by the cellular metabolism. Out of the "omics" family, metabolomics is characterized by its high dynamic flux, where changes in metabolite concentrations, in response to a stimulus, occur within seconds. Urine is an attractive option for metabolome biomarker discovery. It can be readily obtained in large quantities, non-invasively, with expected high participant compliance. It also poses low risk of infection to researchers.

Our group showed that 1H-NMR urine metabolomic analysis of asthmatic children contains a unique pattern of 50 differentially expressed metabolites compared with those without asthma. It is crucial to accurately quantify and validate these metabolites with respect to their sensitivity and specificity as

potential biomarkers using a more sensitive analytical platform such as mass spectrometry (MS). Therefore, the objective of this research is to develop liquid chromatography-tandem mass spectrometric (LC-MS/MS) methods to confirm the accuracy of the metabolites measured by 1H-NMR. A comprehensive list of differentially expressed endogenous urinary metabolites would serve as validated diagnostic or prognostic biomarkers for asthma.

Methods: The 50 targeted metabolites are classified into 3 groups based on their chemical structures. Groups 1 and 2 contain 37 metabolites and are quantified based on the differential isotope labeling (DIL) approach using C12/ C13 labeled dansyl chloride and dimethylaminophenacyl bromide derivatizing reagents, respectively.

Results: Two methods were successfully developed for the quantification of group 1 and 2 metabolites. Method 1 was validated as per the FDA guidelines with respect to accuracy, precision, stability, matrix effects, and dilution integrity. Patients' samples are now being analyzed for the contents of group 1 metabolites. Currently, method 2 is being validated before real samples can be analyzed.

Future work: complete validation of method 2, quantification of the metabolites in real urine samples, and finally, identification of the statistically significant diagnostic or prognostic biomarkers.

ABEYKOON H., MUHAJARINE N., ENGLER-STRINGER R.

Early health-related impact of a food store intervention.

Introduction: Nutrition environments influence what we eat and our health. This study investigates the early impact of a community-based food intervention, the Good Food Junction (GFJ), in a former food desert. The GFJ was a large scale, full service grocery store. The underlying hypothesis is that the GFJ improves healthy eating and health-related outcomes.

Objective: To investigate health-related impact of GFJ on its users over time and to see if this relationship is different for disadvantaged population groups (Aboriginals and seniors). Intersectionality theory suggests that disadvantaged social conditions would act synergistically on health. Guided by this theory, another objective is to investigate if multiple disadvantaged conditions (such as being Aboriginals or seniors, having low-income, and low education levels) act simultaneously and synergistically on health. Final objective, guided by the social ecological framework, is to understand how the primary association is modified by individuals' social ties and their sense of belonging to the community.

Methods: A longitudinal study was conducted by following up 156 GFJ users at 10-12, 16-18, and 22-24 months after opening the GFJ. They were inquired about their general health, household food security status, perceived neighbourhood social ties, and household demographics.

Results: Participants of the longitudinal study were between 21 and 91 years of age, and were predominantly female (75%) and self-identified as Aboriginals (41.7% to 53.59%). Annual household income was \$30,000 or less for more than half (54.5% to 60.8%) of the participants while more than one fifth were less than high school (19.1% to 28.8%) or university (20.9% to 27.8%) educated. Analysis is in progress and will use a generalized estimating equations approach to account for the correlated data.

Conclusion: Results of the study will be useful for advancing knowledge on food environment interventions.

RASUL S., MUHAJARINE N., BOWEN A.

Examining the factors that moderate and mediate the effects on the relationship between depression and anxiety and major pregnancy complications and birth outcomes.

Background: Pregnancy is one of the most exciting and significant events of a woman's life but due to some social and psychosocial factors many women experience depression, anxiety, and mental stress during and after their pregnancy. Many studies found that depression and anxiety during pregnancy are also associated with pregnancy complications and poor birth outcomes but there is relatively less evidence that indicate the specific roles of the risk factors, e.g. either as moderating or mediating effects on the relationship.

Purpose: The study aims to examine the relationship between depression and anxiety in pregnancy and pregnancy complications and poor birth outcomes. Hence, this study also seeks to understand how this primary relationship could be modified and mediated by other variables i.e. any abuse or use of drugs or alcohol.

Methods: Secondary data will be used from Feelings in Pregnancy and Motherhood (FIP) study. The study included a cohort of 649 high-risk women in Saskatoon. The participants were invited to take part in longitudinal follow up at 3 times: Time 1 - early pregnancy (17.4 ± 4.9 weeks), Time 2 = later pregnancy (30.6 ± 2.7 weeks) and time 3 = once after their babies were born (4.2 ± 2.1 weeks). Self reported data were collected through face to face interview. Edinburgh Postnatal Depression Scale (EPDS) was used to assess the depression and anxiety.

Results: Not available yet.

Conclusion: In light of this study, effective community intervention could help to improve physical and psychological wellbeing of both mother and baby, during and after pregnancy, and later in life.

RUNALLS S., TOMCZAK C., WRIGHT K., KAKADEKAR A., PHARIS S., POCKETT C., ERLANDSON M.

Body composition and physical activity levels of children with congenital heart defects.

Introduction: Previous studies have found children with congenital heart defects (CHD) to be markedly less physically active and have higher rates of obesity compared to typically developing peers. These risk factors are likely to predispose children with CHD to chronic conditions such as cardiovascular disease and osteoporosis later in life. Physical inactivity is an established risk factor for childhood obesity, as well as lower bone density and cardiovascular disease in adulthood. However, while it is established that children with CHD have markedly low levels of physical activity and exponentially higher rates of obesity, little is known of their musculoskeletal health. The purpose of this study was to investigate the body composition and physical activity behaviours of children with congenital heart defects.

Methods: Twenty nine children, 7-15 years of age, with congenital heart defects were age and sex matched to 24 typically developing controls. Lean mass, fat mass, and total body, lumbar spine, and hip bone mineral content (BMC) was measured by dual energy x-ray absorptiometry (DXA). Physical activity was assessed using accelerometry to determine minutes of moderate-to-vigorous physical activity per day (MVPA) and the Physical Activity Questionnaire for Children (PAQ-C) or Physical Activity Questionnaire for Adolescents (PAQ-A) to determine a physical activity (PA) summary score. Physical activity data was compared between the groups using independent sample t-tests and the DXA data by multivariate analysis of covariance (covariates: age, sex, height, and weight).

Result: There were no differences between children with CHD and controls in height or weight and DXA derived % total body fat or lean mass (p>0.05). There were also no differences the physical activity variables between the two groups (p>0.05). Children with CHD had significantly lower adjusted total body bone mineral content (7.5%) and total hip bone mineral content (15.1%) (p<0.05).

Conclusion: In contrast to previous studies we did not find any difference in physical activity levels or body fat between children with CHD and their typically developing peers. However, despite the lack of difference in physical activity levels, we found that children with CHD had compromised bone parameters at the total body and hip. This is important as lower bone mineral content in childhood increases the risk of fracture during growth as well later in life.

WILSON-GERWING T.D., ROSENBERG A.M.

Biomarkers of age-related inflammation and pain associated with collageninduced arthritis: towards novel targeted treatments.

Background/Purpose: Arthritis is among the most common chronic diseases in both children and adults. Inflammation and pain are features in both age groups but there are age-related disparities in clinical manifestations, disease courses, and treatment efficacy and safety. Collagen-Induced Arthritis (CIA) in rodents is a model of arthritis that has utility in assessing pathogenic processes associated with inflammation and pain. We have established the CIA model in both adult and juvenile animals. This study examined plasma levels of multiple cytokines and chemokines in adult and juvenile animals with CIA. The identification of age-related markers of pain and inflammation in CIA should both improve the understanding of age-specific inflammatory/pain processes and help design tailored treatment interventions.

Methods: Juvenile (5 wks old) and young adult (13 wks old) male Wistar rats were immunized with an emulsion of bovine type II collagen/incomplete Freund's adjuvant. Naïve juvenile and adult rats served as controls. Baseline measures included paw thickness, thermal and mechanical thresholds, and footprint analysis. Following arthritis onset, measures were repeated every 3 days. For each animal, the Maximum Daily Arthritis Index (MAI) score and daily weight were measured. Fourteen days after arthritis onset, animals were euthanized and blood and tissues collected. Plasma was assayed by enzyme immunoassay with a rat 27-plex cytokine/chemokine array.

Results: Juvenile CIA rats had significantly lower MAI compared to adults (p<0.0001). Adult CIA rats had significant increases in the thickness of the ankle (p=<0.0001), the paw distal to the tarsus (p=<0.0001) and the phalanges (p=<0.0001) while juvenile rats had significant increase only in paw thickness distal to the tarsus (p=<0.0001). Analysis of chemokine/cytokine profiles revealed that Juvenile CIA, but not Adult CIA rats had significant changes in levels of interleukin (IL)-10 (p=0.0245), IL-12 (p=0.0075), IL-5 (p=0.0021) and fracktalkine (p=0.0002). In addition, Adult CIA rats, but not Juvenile CIA rats had significant changes in levels of MIP-1a (p=0.0113), LIX (p<0.0001) and RANTES (p<0.0001). Both Adult and Juvenile CIA rats demonstrated significant changes in levels of G-CSF, Eotaxin IL-1a, Leptin, IL-13, IL-17a, MCP-1, GRO/KC, VEGF (all p<0.0001), MIP-2 (p=0.0003) and TNF- α (p=0.0002).

Conclusion: Adult rats have more severe CIA than juveniles. Our results indicate age-related differences in markers of inflammation and pain associated with CIA, as measured in plasma, identify potentially key targets for tailored treatment interventions. Future studies will: 1) correlate these systemic findings with sensory neuron markers and 2) determine whether these findings are applicable to the human population.

BJORKMAN K., KAWALILAK C., JOHNSTON J.D., KONTULAINEN S.

Boys have more favourable bone micro-architecture than girls prior to the pubertal growth spurt.

Objective: To assess sex-differences in bone size and micro-architecture at the distal radius (wrist) and tibia (ankle) in children and to characterize the relationship between bone properties and biological age.

Methods: We obtained distal radius and tibia scans from 60 boys and 70 girls (mean age: 9.6; SD: 1.4years) with high-resolution peripheral quantitative computed tomography. We assessed total, cortical and trabecular bone size (area) and micro-architecture (cortical thickness, trabecular thickness, and number). Biological age was calculated using validated equations estimating participant's age from peak-height velocity (PHV). We included participants with biological age of 0-3 years preceding PHV. Girls who had reached menarche were excluded. We used linear regression analysis to compare bone properties after adjusting for height, weight and biological age. We report significant (P<0.05) percent-differences between sexes and characterize the relationships between cortical thickness and biological age at both sites.

Results: At the distal radius, boys had greater: total area (10%), cortical area (32%), trabecular area (9%), trabecular thickness (7%), trabecular number (5%) and cortical thickness (28%). At the distal tibia boys and girls appeared to increase at similar rates with maturity, however, boys had greater: total area (8%), cortical area (23%), trabecular area (8%) and cortical thickness (20%). Rate of maturity-related increases in cortical thickness were observed at the distal tibia in both sexes but this relationship was apparent at the distal radius only in boys.

Discussion: Results suggest that boys develop favourable bone geometry and micro-architecture, particularly at the distal radius before puberty (and menarche in girls). These findings suggest that local factors (mechanical loading) as opposed to systemic factors (hormones) may mitigate sex-specific bone micro-architectural development prior to puberty. These results are important as they provide further insight into sex-specific differences between boys and girls prior to puberty. Findings will facilitate future studies incorporating specific exercises as a means to improve bone size and micro-architecture development, particularly in girls.Survey Module (HFSSM) and Behavioural Risk Factor Surveillance System (BRFSS) six-item fruit and vegetable module, and 24 hour recalls. Data will be collected at two time points, prior to participation in the program and at the end of participation, allowing this study to examine the success of the nutritional support voucher intervention. This research study provides an opportunity to investigate nutrition during pregnancy, an important time during the healthy development of a child. This investigation will add needed research to the body of Canadian literature.

MAGALIE C., TANYA H.

Pulmonary embolism in a child with ARDS secondary to foreign body aspiration.

Background: Acute respiratory distress syndrome (ARDS) is a relatively rare disorder in childhood and pulmonary embolism is even less common. Pulmonary micro and macrothrombosis have been well documented in adults with ARDS. To our knowledge, there has been no prior published case reports of pulmonary thromboembolism in the context of ARDS in the pediatric population.

Case presentation: An 18 months old boy was admitted to the pediatric intensive care unit following a rigid bronchoscopy for foreign body aspiration. He developed progressive acute respiratory distress syndrome (ARDS) within 72h of admission. He was treated with lung protective ventilation strategies, prone positioning, corticosteroids, and broad spectrum antibiotics. One week into his admission, after an initial improvement, his oxygenation and ventilation worsened again and he developed signs of dead space. He did not respond to a trial of inhaled nitric oxide, but showed improvement in his oxygenation following initiation of milrinone. He had a chest CT scan that revealed a perfusion defect of the right base suggesting a pulmonary embolism. Although he had a jugular venous catheter, there was no associated thrombus on ultrasound. An extensive work up was performed, and no coagulation disorder was identified. A heparin infusion was initiated and within 48h his oxygenation, ventilation, and dead space had normalized.

Discussion: Intravascular pulmonary thrombi in adults with ARDS have been attributed to excessive fibrin accumulation secondary to endothelial injury as well as local and systemic inflammatory mediated pro-coagulant and anti-fibrinolytic changes. Other potential factors include platelet aggregation, vasoconstriction, extrinsic vascular compression, and in later phases fibrocellular obliteration. Increased dead space, such as seen in this patient, has been demonstrated in patients with ARDS and may reflect pulmonary vascular obstruction. The increased dead space observed in this patient was an important component of his hypoxemia and was attributed to his pulmonary embolism. He likely benefited from milrinone because of its inotropic and vasodilator properties. His improvement following initiation of heparin was probably multifactorial and in part due to the continued benefits of milrinone as well as the natural evolution of ARDS.

Conclusion: With mortality rates as high as 10-20%, pediatric pulmonary embolism remains under diagnosed and likely under treated. We suggest that ARDS may be an important and unrecognized risk factor for pulmonary embolism in children. Pulmonary embolism should be considered in patients with acute cardiorespiratory deterioration or worsening hypoxemia as well as in patients with increased dead space.

REZAEI E., TROST B., HOGAN D., KUSALIK T., ROSENBERG A.M., FOR THE BBOP CONSORTIUM

Biologically-based approach to evaluate classification criteria for chronic childhood arthritis.

Background: Childhood arthritis is a heterogeneous group of diseases. Efforts have been made to establish acceptable classification criteria for the disease. This has resulted in periodic refinements that strive to more precisely reflect subset-specific pathophysiology, treatment responses, and treatment outcomes. The International League for Associations for Rheumatology (ILAR) defined juvenile idiopathic arthritis (JIA) and proposed seven subgroups mainly based on clinical information. ILAR classifications have limitations: clinical courses are not consistent, and they do not reliably guide treatment choices or predict treatment responses. Advanced data analysis methods provide reliable tools to extract precise knowledge from large sets of heterogeneous data. Unsupervised data mining is a robust method to interrogate diverse data with the goal of improving disease classification.

Objective: To generate a robust taxonomy for chronic childhood arthritis based on clinical and biomarker profiles.

Methods: 150 newly diagnosed, treatment naïve children, with JIA from 11 participating Canadian Pediatric Rheumatology Programs participated in the BBOP Study (Biologically Based Outcome Predictors in JIA). The data included clinical manifestations and biomarkers. Data were collected at enrollment and six- month after. Categorical Principal Component Analysis (CAT-PCA) was used for variable reduction and K-means method for clustering purpose with the partitioning around medoids (PAM) algorithm. A dissimilarity matrix was generated using DAISY, as the original variables were of mixed types (numerical, binary, and etc.). The results were compared with the ILAR subgroups.

Insensitivity to data perturbation was tested using Leave One-Out-Variable (LOOV) method and the median test. SPSS Statistics Professional version 23, R version 3.2.2, and Circos version 0.69 were used.

Results: From 191 variables 16 highly informative ones were identified to determine clusters, using variance accented for (VAF) \geq 70%. The clinical variables chosen were sex and the number of involved joints; other variables included plasma levels of inflammatory biomarkers. To optimize number of clusters, internal and external K-means clustering validation criteria were considered. Accordingly, k=5 was the ultimate choice. Therefore, five clusters were identified in each visit. Both visits consist of more homogeneous subgroups compare to ILAR subgroups. Clusters are more homogenous in visit 2 compared to visit 1. Patient clusters were insensitive to single variable removal using the LOOV and the median test.

Conclusion: The need to re-classify JIA led us to use data-driven, unsupervised, machine learning algorithms. Distinctive patterns recognized within the data provide insight into the underlying biology of JIA, enabling us to more precisely approach childhood arthritis based on the underlying biology.

LANE V., VATANPARAST H.

Newcomer children's experiences in Saskatchewan's healthcare system.

Newcomers are usually healthy when they arrive in Canada, but subsequently experience health declines shortly thereafter. Some research has found that newcomers access healthcare less than the Canadian population and experience many barriers to care. It is important to understand how healthcare access issues maybe impacting the health of newcomer children.

This study evaluates healthcare access issues among newcomers families with children aged three to thirteen years who have been in Canada less than five years. In-depth interviews were completed with 18 parents and 18 service providers to understand barriers and supports to healthcare access.

Overall, the greatest barrier to accessing healthcare services was health system navigation difficulties. Participants talked about difficulties with understanding how and where to access care that resulted in confusion and service delays. Language difficulties were the second most common barrier. Service providers described their difficulties with both making appointments with newcomers and having good communication to facilitate shared understanding of health issues. Closely linked to language difficulties are interpretation issues. Many participants talked about difficulties with accessing interpretations services and the appropriateness of some interpretation services. Health region staff have access to telephone interpretation services and staff volunteers when needed, but they do not always make consistent use of these services. Sometimes children learn English faster than their parents and are relied on as interpreters for healthcare appointments, which is not necessarily appropriate. When newcomers arrive they are covered by several federal and provincial healthcare benefit programs. Recent changes to interim federal health benefits have created confusion around eligibility so some healthcare providers have been reluctant to provide care. Newcomers frequently spoke about concerns with high drug costs that are covered by provincial health benefits programs, but they were not aware. Service providers perceived that gender and cultural concerns are a barrier. Cultural beliefs and attitudes of both healthcare providers and newcomer clients can influence the process and outcomes of healthcare delivery. With regards to children's behavioural management issues, differing cultural beliefs can result in disjointed treatment plans across different environments.

The study results indicate the need to evaluate how the health system can be adjusted to be more responsive to the healthcare needs of newcomer children and their families. Provincially we need to ensure that all newcomers are aware of provincial health benefit programs. Health regions may consider providing training to increase the cultural competency of staff and the use of available interpretation services.

NG H.Y., SLOMP S., LODHI A., DIETZ J., WILSON-GERWING T., HOLT T., ROSENBERG A.M.

High Mobility Box 1 Protein in Children with Systemic Inflammation.

Background: High Mobility Box 1 Protein (HMGB1) is a nuclear protein that stabilizes DNA and modulates gene expression. In the presence of sepsis and other systemic inflammatory conditions HMGB1 is released from the cell. Extracellularly HMGB1 mediates an array of cell signaling pathways including stimulating innate immunity and promoting downstream pro-inflammatory cytokines. Elevated levels of HMGB1 are found in sepsis and a variety of other systemic inflammatory conditions including, as examples, Kawasaki Disease, autoimmune vasculitides, inflammatory bowel disease, and necrotizing enterocolitis. Objectives: The objective of this project was to evaluate HMGB-1 as an early biomarker of sepsis and assess its utility in predicting disease course and outcome. For comparison we assessed HMGB-1 in children with two other systemic inflammatory conditions, Kawasaki Disease (KD) and systemic onset juvenile idiopathic arthritis (sJIA) and in non-inflammatory controls.

Methods: Children (age <18 years) with sepsis or Kawasaki Disease were prospectively enrolled on admission. Data from new onset, treatment naive sJIA participants were derived from the BBOP Study (Biologically-based

Outcome Predictors in JIA; www.bbop.ca). Blood was collected in P100 vacutainers (BD) and the plasma stored at -800C until assayed. HMGB1 was measured at 1:100 plasma dilution by enzyme immunoassay (Biomatrix).

| Diagnosis | N (%) | $\bar{\chi}$ HMGB1 (±SD) ng/ml |
|------------|------------|-----------------------------------|
| Sepsis | 20 (35.7%) | 46.86 (47.11) |
| sJIA | 23 (41.1%) | 42.57 (47.81) |
| KD | 7 (12.5%) | 107.67 (27.20) |
| Non-sepsis | 6 (10.7%) | 33.46 (278.76) |

Results: The study population comprised 56 participants (Table). HMGB1 levels were higher in KD than in non-KD participants (p<.001). HMGB1 were higher in KD compared to sepsis (p=.001), non-sepsis (p=.001) and sJIA (p<.001). There was no correlation of HMGB1 with age (r-.082) and no difference of HMGB1 between sexes.

Conclusions: The results of this study show that HMGB1 levels are significantly higher in children with KD than in other systemic inflammatory conditions. A larger cohort is required to determine if HMGB1 will predict disease course and outcomes. In particular, we will continue to enroll subjects to determine if HMGB1 at first presentation can predict non-response to IVIgG in KD, predict the likelihood of needing to re-treat with IVIgG, and if HMGB1 is predictive of coronary artery aneurysms/thrombosis. We aim to expand our study to other systemic inflammatory diseases to determine if HMGB1 could be a biomarker more generally valuable in predicting outcomes and guiding early therapy in systemic inflammation.

FINCH S., HOSSEINI Z., ROSENBERG A., VATANPARAST H.

Vitamin D status and anthropometric measurements in a Canadian population of children with Juvenile Idiopathic Arthritis in comparison with a nationally representative sample of healthy children.

Introduction: Children with Juvenile Idiopathic Arthritis (JIA) often experience nutrition related concerns. Nutritional impairment while not the sole cause, can contribute to reduced growth, osteoporosis, anaemia and suboptimal body composition in children with JIA. As new medications and treatments have become available it is important to monitor growth outcomes as they may have changed.

Methods: This research aimed to evaluate vitamin D status, and growth parameters in children and adolescents with JIA and compare with those of healthy children and adolescents in a nationally representative sample. Data from two studies was used: the Biologically Based Outcome Predictors (BBOP) in Juvenile Idiopathic Arthritis and the Canadian Health Measures Survey. BBOP is a prospective cohort study (December 2007- December 2012). One hundred and thirty-six patients aged (6-17 years old) with new onset JIA recruited from multiple centres across Canada were used for this analysis. The Canadian Health Measure Survey (CHMS) data from cycle 1and cycle 2 (2007-2011) provided the required information for healthy children. Sociodemographic, life style and clinical data were collected and blood samples were obtained. The CHMS data were weighted and bootstrapped to obtain population-level estimates. Patients were compared by sex, age group and JIA subtype.

Results: More females (n=101) than males (n=35) were diagnosed with JIA. Mean 25(OH)D status significantly higher for JIA patients (79 \pm 3 nmol/L vs 68 \pm 2 nmol/L) with 15% of children with JIA having 25(OH)D below 30 nmol/L compared with 23% of healthy children. There was a reduction in 25(OH)D

status in older age groups, and healthy females ages 9-13 had lower vitamin D status than females with JIA. The proportion of children who were underweight, normal weight, overweight and obese did not differ between JIA and healthy children. Healthy children who drank milk everyday had a higher vitamin D status than those who did not. Significantly fewer children with JIA reported drinking milk every day. Children with JIA had higher white blood cell, neutrophil counts and CRP levels than healthy children. They also had higher CPR concentrations as well.

Conclusion: Children with JIA (at disease onset) do not differ from healthy children in terms of growth characteristics. Vitamin D status appears to be adequate in the majority of children with JIA at disease onset however biochemical measures of inflammation are higher. How growth parameters change throughout the disease course in JIA cases in comparison with healthy children, warrants further research.

JEONG J., FOWLER S., ROSENBERG A.M.

Evaluating the correlation between elevated serum antibody assay levels and positive intestinal biopsies for diagnosing celiac disease in the pediatric population.

Introduction: Unlike other Canadian jurisdictions, the Saskatoon Health Region measures lgA antibodies to both tissue transglutaminase (tTG) and to deamidated gliadin peptide (DGP) during initial screening for celiac disease. Though lgA tTG titre levels compared to biopsy results have been studied in other centers, Saskatchewan is unique in that the lgA DGP titres are included as part of initial celiac screening. Therefore, we have the opportunity to use existing data to determine how lgA tTG and lgA DGP individually and in combination correlate with small bowel celiac histopathology.

Objectives: The purpose of this study is to:

1. Confirm that specific quantitative lgA tTG levels are predictive of celiac disease.

2. Determine a level of lgA DGP antibodies which correlates with positive intestinal biopsies and evaluate the utility of lgA anti-DGP antibodies in diagnosing celiac disease.

3. Determine if a specific titre of lgA tTG antibodies in combination with lgA DGP antibodies is more predictive of biopsy proven celiac disease than either biomarker alone.

Hypothesis: We expect that the lgA tTG levels will correlate more strongly with the intestinal biopsy results compared to the lgA DGP levels. Therefore we do not believe there is additional benefit in spending money performing the lgA DGP as part of the initial celiac disease screen.

Methods: This is a retrospective health record reviewofpediatric patients who meet the following criteria: 1. Age at first presentation younger than age 17 years; 2. Had lgA tTG and lgA DGP testing done at the immunodiagnostic laboratory, Saskatoon Health Region; 3. Had an intestinal biopsy for suspected celiac disease.

Data to be collected will include: 1. IgA tTG and IgA DGP levels; 2. Biopsy result- celiac disease or not celiac disease; celiac disease stage (Marsh score 0-4); 3. Age at biomarker testing and at biopsy; 4.Sex.

We will collect information on 245 subjects to achieve minimum sensitivity and specificity values of 85% and 90% respectively at a 95% confidence level with a 10-percentage point margin of error.

Significance: If IgA DGP titres correlate with positive intestinal biopsies then current guidelines for celiac disease screening should be altered to include IgA DGP as part of initial screening. However, if results show a decrease correlation between IgA DGP and positive intestinal biopsies compared to the already proven correlation between IgA tTG and positive intestinal biopsies, IgA DGP be eliminated from the initial celiac disease screening tests in the Saskatoon Health Region resulting in cost savings.

Thank you to our presenters, The Department of Pediatrics Research Office, SPRING (Saskatchewan Pediatric Research and Innovation Group) and The Children's Hospital Foundation of Saskatchewan.







